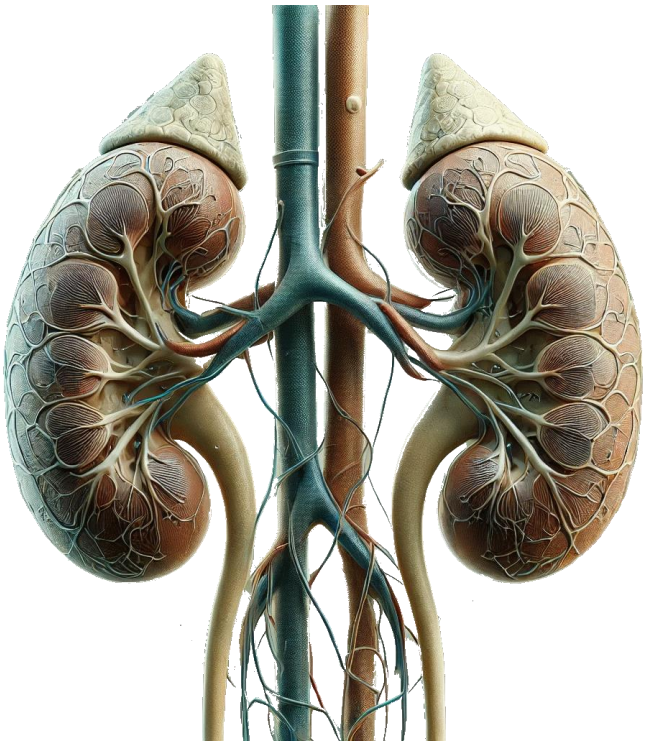
Yaroslav Mykhalko

CHRONIC KIDNEY DISEASE MANAGEMENT IN PRIMARY CARE

(Based on KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease)



Uzhhorod 2025

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Educational manual

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The educational manual highlights key aspects of managing patients with chronic kidney disease – from timely diagnosis and assessment of risk factors to the implementation of scientifically based treatments aimed at slowing the progression of the disease and achieving better clinical outcomes.

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CONTENTS

ABBREVIATIONS

ACEi	angiotensin-converting enzyme inhibitor(s)
ACR	albumin-to-creatinine ratio
ADPKD	utosomal dominant polycystic kidney disease
AER	albumin excretion rate
AIDS	acquired immune deficiency syndrome
AKD	acute kidney disease
AKI	acute kidney injury
ARB	angiotensin II receptor blocker
ASCVD	atherosclerotic cardiovascular disease
BMI	body mass index
BP	blood pressure
BSA	body surface area
CKD	chronic kidney disease
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
CKD-PC	Chronic Kidney Disease Prognosis Consortium
CT	computed tomography
CVD	cardiovascular disease
DALY	disability-adjusted life-year
eGFR	estimated glomerular filtration rate
eGFRcr	creatinine-based estimated glomerular filtration rate
eGFRcr-cys	creatinine and cystatin C-based estimated glomerular filtration rate
eGFRcys	cystatin C-based estimated glomerular filtration rate
GBD	Global Burden of Disease
GFR	glomerular filtration rate
GLP-1 RA	glucagon-like peptide-1 receptor agonist(s)
HIV	human immunodeficiency virus
HRQoL	health-related quality of life
IgAN	immunoglobulin A nephropathy
KDIGO	Kidney Disease: Improving Global Outcomes

KFRE	Kidney Failure Risk Equation
KRT	kidney replacement therapy
LDL	low-density lipoprotein
MDRD	Modification of Diet in Renal Disease
mGFR	measured glomerular filtration rate
MRA	mineralocorticoid receptor antagonist(s)
NOAC	non-vitamin K antagonist oral anticoagulant
NSAIDs	nonsteroidal anti-inflammatory drugs
OTC	over-the-counter
PCR	protein-to-creatinine ratio
PCSK-9	proprotein convertase subtilisin/kexin type-9
POCT	point-of-care testing
QoL	quality of life
RAAS	renin-angiotensin-aldosterone system
RASi	renin-angiotensin system inhibitor
RBC	red blood cell
SBP	systolic blood pressure
SCr	serum creatinine
SGLT2i	sodium-glucose cotransporter-2 inhibitor(s)
T2D	type 2 diabetes

INTRODUCTION

Chronic Kidney Disease (CKD) is a significant and growing public health challenge globally, with considerable implications for morbidity, mortality, and healthcare resources. Data from the Global Burden of Disease (GBD) study highlights CKD as one of the most impactful chronic diseases worldwide. According to recent analyses, CKD affects more than 850 million people–far exceeding the prevalence of conditions such as diabetes, cancer, and HIV/AIDS combined. This staggering burden underscores the need for early intervention and effective management, particularly in primary care settings where early-stage CKD patients are typically first diagnosed.

CKD is marked by both high mortality rates and substantial disability, measured in disability-adjusted life-years (DALYs), which reflect both years of life lost and years lived with disability. In 2019, CKD was responsible for over 41 million DALYs and caused approximately 1.43 million deaths globally. The disease burden is most acute in regions with lower socioeconomic conditions, where healthcare resources and access to specialist care may be limited. This demographic disparity emphasizes the need for primary care physicians to adopt proactive and standardized approaches in CKD management to mitigate disease progression and reduce associated cardiovascular risks.

The 2024 KDIGO Clinical Practice Guideline for the Evaluation and Management of CKD reflects the latest advancements in research, diagnostics, and treatment, providing an evidence-based framework to guide clinical decision-making. These updated guidelines emphasize early detection, precise risk stratification, and individualized therapeutic approaches to slow CKD progression, manage complications, and improve patient outcomes.

This educational manual is specifically tailored for primary care physicians, recognizing their pivotal role in the early identification and longitudinal management of CKD. By bridging the recommendations of the KDIGO 2024 guidelines with practical considerations in primary care settings, this resource aims to empower clinicians with the tools and knowledge necessary to deliver optimal care. Key topics include the implementation of lifestyle interventions, pharmacological management, monitoring strategies, and timely referral criteria.

This document outlines recommendations for equipping primary care physicians with evidence-based strategies to optimize the screening, diagnosis, classification, management and monitoring of patients with CKD, aligning clinical practice with the latest global data on disease prevalence, progression and associated risk factors.

WHAT IS CHRONIC KIDNEY DISEASE

CKD is defined as abnormalities of kidney structure or function, present for a minimum of 3 months, with implications for health.

This definition underlines that CKD is a long-term condition. These abnormalities can be detected through various tests, such as changes in urine composition, reduced glomerular filtration rate (GFR), or imaging findings that indicate damage to the kidneys. CKD can also involve structural changes like scarring or thinning of kidney tissue, which are often due to underlying conditions such as diabetes or hypertension.

The definition of CKD highlights that for a diagnosis to be made, these kidney issues must be present for a minimum of three months, and they are not simply temporary or reversible. This prolonged duration is important because it distinguishes CKD from acute kidney problems that may resolve.

Additionally, the term "implications for health" refers to the potential long-term effects of CKD, including complications such as cardiovascular disease, electrolyte imbalances, and eventual kidney failure. If left untreated or poorly managed, CKD can progressively worsen, leading to a decline in kidney function and requiring interventions such as dialysis or a kidney transplant. Thus, recognizing and managing CKD early is crucial to prevent these severe health consequences.

Diagnostic criteria for CKD

The diagnostic criteria for CKD involve two main components: markers of kidney damage and a decreased GFR. For CKD to be

diagnosed, one of these criteria must be present for at least three months.

1. Markers of Kidney Damage (One or More)

These markers indicate that the kidneys are not functioning normally or have been damaged in some way. Each of the following markers reflects a different aspect of kidney health:

- Albuminuria (albumin-to-creatinine ratio (ACR) ≥ 30 mg/g [≥3 mg/mmol]). Normally, the kidneys filter out waste while retaining important proteins like albumin. When the kidneys are damaged, they may allow albumin to leak into the urine. An ACR of 30 mg/g or higher indicates kidney damage and is an early marker of kidney disease.
- Urine Sediment Abnormalities. This refers to the presence of abnormal substances in the urine when examined under a microscope, such as casts, cells, or crystals, which can indicate kidney injury. For instance, the presence of red blood cells may suggest glomerular damage, while white blood cells can point to inflammation.
- Persistent Hematuria. When blood is consistently found in the urine over a period of time, it can indicate damage to the kidneys. Persistent hematuria can be a sign of glomerular disease, analgesic nephropathy, or tumors, among other conditions.
- Electrolyte and Other Abnormalities Due to Tubular Disorders. The kidneys play a key role in maintaining a proper balance of electrolytes (like sodium, potassium, calcium) and other substances. When kidney tubules are damaged, they may fail to properly reabsorb or excrete these substances. The examples of these disorders include hypokalemia (Gitelman syndrome, Bartter syndrome), hyperkalemia (Type IV renal tubular acidosis), hypophosphatemia (Fanconi syndrome), hypomagnesemia (Gitelman syndrome), hyponatremia, Type I (distal) or Type II (proximal) renal tubular acidosis, renal glycosuria, aminoaciduria (Fanconi syndrome).

- Abnormalities Detected by Histology. Histological abnormalities refer to changes observed in kidney tissue when examined under a microscope (glomerulosclerosis, mesangial expansion, basement membrane thickening, crescent formation, tubular atrophy, tubular dilatation, amyloid deposits).
- Structural Abnormalities Detected by Imaging. Kidney imaging studies, such as ultrasound, CT scans, or MRI, may reveal structural problems like kidney cysts, kidney shrinkage, or obstructions that suggest kidney damage. Structural abnormalities can indicate conditions like polycystic kidney disease, tumors, or hydronephrosis.
- History of Kidney Transplantation. A history of kidney transplantation is considered a marker of kidney damage because it implies that the patient had advanced kidney disease requiring a transplant. While the transplanted kidney may function well, the underlying condition that caused the original kidney failure is an indicator of past damage.

2. Decreased GFR (GFR <60 ml/min per 1.73 m²)

The GFR is a measure of how well the kidneys are filtering waste from the blood. A GFR of less than 60 ml/min per 1.73 m² indicates that kidney function is significantly reduced.

These criteria reflect both functional and structural abnormalities in the kidneys, which can lead to worsening kidney function and increased risk for other health problems.

While symptoms such as edema, arterial hypertension, oliguria , and fatigue may commonly occur in CKD patients, they are not sufficient for diagnosis on their own. These symptoms may vary widely among patients, and some individuals with CKD might not exhibit any of these signs at all. Conversely, these symptoms can also occur in various other conditions unrelated to CKD, which means they cannot be used independently to confirm a CKD diagnosis.

Thus, while these symptoms may prompt to investigate potential kidney issues, they are not considered as diagnostic

criteria. Only when kidney damage markers or a reduced GFR are confirmed over the required timeframe can CKD be definitively diagnosed. This approach ensures an accurate diagnosis, guiding appropriate management and treatment for patients truly affected by CKD.

The chronicity matters

Once the presence of kidney structure or function abnormalities persists for over three months, confirming this chronicity is essential for diagnosing CKD and guiding treatment decisions. Here are some practical steps to establish chronicity:

- review of past measurements/estimations of GFR;
- review of past measurements of albuminuria or proteinuria and urine microscopic examinations;
- imaging findings such as reduced kidney size and reduction in cortical thickness;
- kidney pathological findings such as fibrosis and atrophy;
- medical history, especially conditions known to cause or contribute to CKD;
- repeat measurements within and beyond the 3-month point.

It's important not to assume chronicity based on a single abnormal estimated GFR (eGFR) or ACR result, as a single measurement may reflect a recent acute kidney injury (AKI) or acute kidney disease (AKD) rather than CKD. AKI and AKD can cause temporary changes in kidney function and protein levels in urine, which may mimic chronic disease if measured only once. To distinguish chronic from acute conditions, it is necessary to confirm that these abnormalities persist over a minimum period of three months through repeated testing.

When CKD is suspected based on decreased GFR or elevated ACR at the initial presentation, it may be appropriate to start treatment immediately if other clinical indicators strongly suggest

chronic disease. Indicators such as a known history of diabetes, hypertension, imaging findings like reduced kidney size, or previous laboratory records showing persistent abnormalities can reinforce the likelihood of CKD rather than an acute condition. In these cases, early intervention can help slow disease progression and manage associated risks, even while further testing confirms chronicity.

Questions for Self-Assessment

1. What is the minimum duration for kidney abnormalities to be classified as CKD?
2. Why is it important to distinguish CKD from acute kidney problems?
3. What are some potential long-term health consequences of untreated CKD?
4. Why is early recognition and management of CKD critical?
5. What are the two main components of CKD diagnostic criteria?
6. Define albuminuria and explain its significance in diagnosing CKD.
7. How do histological abnormalities help in diagnosing CKD? Provide examples.
8. What GFR level is considered diagnostic for CKD?
9. What does persistent hematuria indicate, and why is it significant in CKD?
10. How can electrolyte imbalances signal kidney tubular disorders? Provide examples of such imbalances.
11. What structural abnormalities can imaging reveal in CKD patients?
12. Why are symptoms like edema and fatigue not sufficient to diagnose CKD?

13. How do diagnostic criteria ensure the accurate identification of CKD?
14. What practical steps can confirm the chronicity of kidney damage?
15. Why is it crucial not to base CKD diagnosis on a single abnormal GFR or ACR result?
16. How can medical history and imaging findings support the diagnosis of chronic CKD over acute conditions?
17. Why might treatment for CKD begin before chronicity is confirmed?
18. How can conditions like diabetes and hypertension contribute to the likelihood of CKD?

SCREENING FOR CKD

While there is still no universal consensus on the approach to CKD screening, it is widely supported for individuals at higher risk, such as those with diabetes and hypertension, the two most prevalent causes of CKD. Systematic reviews have demonstrated that screening for CKD in these high-risk populations is not only cost-effective but also critical in improving health outcomes, particularly when combined with evidence-based treatments like sodium-glucose cotransporter-2 inhibitors (SGLT2i). These treatments have shown to help slow the progression of CKD, especially in those with diabetes and hypertension, which further supports the case for early detection and management.

Early identification of CKD is particularly important, even for individuals who are asymptomatic, as kidney damage often progresses silently until the later stages. With appropriate risk stratification and targeted treatments, it is possible to significantly delay or even prevent the progression of kidney disease. This is especially valuable in primary care settings, where most of the population receives their routine healthcare. By implementing CKD screening in these settings, healthcare providers can more effectively identify patients at risk and initiate early interventions. The main risk factors for the CKD include:

- hypertension, diabetes, cardiovascular disease (including heart failure, Prior AKI/AKD;
- geographical areas with high prevalence of CKD (areas with endemic CKDu, areas with high prevalence of APOL1 genetic variants, environmental exposures);
- genitourinary disorders (structural urinary tract disease, recurrent kidney calculi);
- multisystem diseases/chronic inflammatory conditions (systemic lupus erythematosus, vasculitis, HIV);

- iatrogenic (drug-induced nephrotoxicity and radiation nephritis);
- family history or known genetic variant associated with CKD (kidney failure, regardless of identified cause, kidney disease recognized to be associated with genetic abnormality (e;g;, PKD, APOL1-mediated kidney disease, and Alport syndrome));
- gestational conditions (preterm birth, small for gestational age infant, pre-eclampsia/eclampsia);
- occupational exposures that promote CKD risk (cadmium, lead, and mercury exposure, polycyclic hydrocarbons, pesticides).

Key populations that should be screened for CKD include:

- People with diabetes, especially those with type 2 diabetes (who should begin screening at the time of diagnosis), and type 1 diabetes (where screening should start five years after diagnosis). CKD is often already detectable in individuals with diabetes at the time of diagnosis, making early screening critical for optimal management.
- People with hypertension or cardiovascular disease (CVD), as these conditions significantly increase the likelihood of developing CKD. Hypertension, in particular, is both a cause and a consequence of kidney disease, making early screening and management even more crucial.
- Individuals with a family history of CKD, as well as those with specific genetic risk factors that may predispose them to kidney disease. Screening is also important for people who have been exposed to environmental toxins, nephrotoxic medications, or have a history of excessive analgesic or herbal medication use, depending on regional risk factors.

In regions with limited healthcare resources, it is especially important to prioritize high-risk populations for screening to ensure that early detection and treatment programs are cost-effective and practical. By focusing on those most likely to benefit

from early intervention, healthcare systems can better allocate resources and improve long-term health outcomes for those at greatest risk of CKD.

Screening algorithm for CKD is shown on fig. 1.

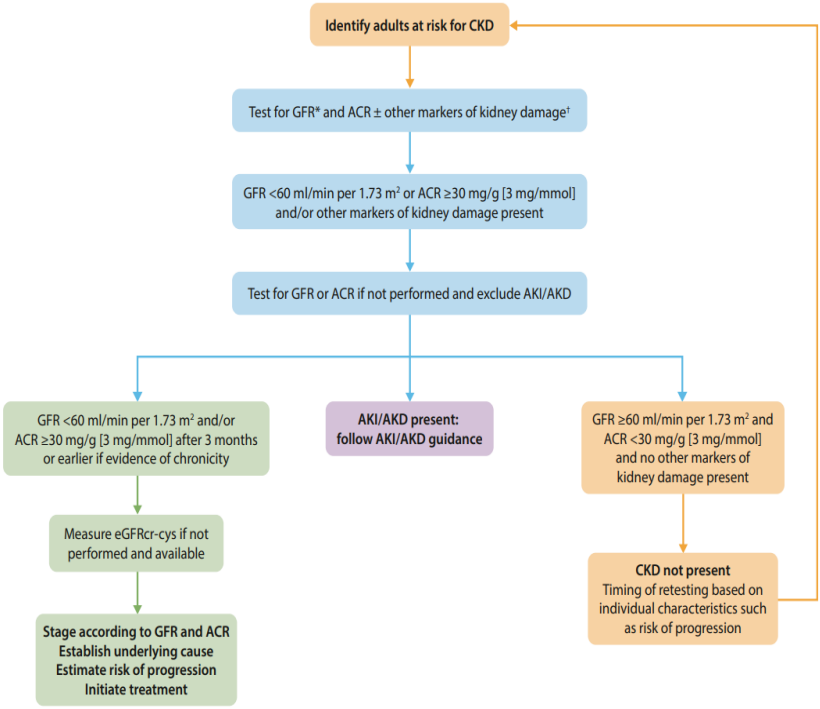

Figure 1. Screening algorithm for diagnosis of CKD in adults.

Questions for Self-Assessment

1. Why is early identification of CKD critical, even in asymptomatic individuals?

2. How does CKD screening improve health outcomes for individuals with diabetes and hypertension?
3. Who are considered high-risk populations for CKD screening?
4. Why is screening for CKD especially important in people with diabetes, and how does the timing of screening differ between type 1 and type 2 diabetes?
5. What role does a family history of CKD play in determining the need for screening?
6. List the main risk factors for CKD and explain how each contributes to the disease.
7. How do occupational and environmental exposures increase the risk of CKD? Provide examples.
8. What genetic conditions are associated with an increased risk of CKD?
9. Why are primary care settings well-suited for CKD screening?
10. How can risk stratification in primary care help prevent the progression of kidney disease?
11. Why is it particularly important to prioritize high-risk populations for CKD screening in regions with limited healthcare resources?
12. How can targeted screening improve the cost-effectiveness of healthcare systems in these regions?
13. What are some evidence-based treatments for CKD that have shown to slow disease progression in high-risk patients?
14. How do sodium-glucose cotransporter-2 inhibitors (SGLT2i) benefit individuals with CKD, particularly those with diabetes and hypertension?

CKD CLASSIFICATION

CKD is classified based on Cause, GFR category (G1–G5), and Albuminuria category (A1–A3), abbreviated as CGA.

The classification system for CKD is based on two key dimensions: GFR and the degree of albuminuria. GFR reflects the kidneys' ability to filter waste and excess fluid from the blood, while albuminuria refers to the presence of the protein albumin in the urine, which is a marker of kidney damage. Together, these two measures help determine the stage of CKD and provide insight into the degree of kidney impairment and the risk for further complications.

However, this dual dimension of GFR and albuminuria is often overlooked or misunderstood by healthcare providers, including both clinicians and students. The emphasis is sometimes placed solely on GFR when assessing kidney function, with less attention given to the degree of albuminuria. Yet, albuminuria is a crucial marker that can indicate early kidney damage, even when GFR is still relatively preserved. The presence of albumin in the urine, especially at higher levels, suggests that the kidneys are leaking proteins, which can lead to further renal injury and cardiovascular problems if not managed properly.

Understanding that both GFR and albuminuria contribute to the overall assessment of kidney health is essential for accurate diagnosis, monitoring, and treatment planning. For instance, a patient with mild to moderate decreases in GFR but high levels of albuminuria may be at higher risk for progression to end-stage kidney disease (ESKD) than someone with a similar GFR but normal levels of albumin in the urine.

Failure to recognize the importance of both GFR and albuminuria in CKD classification can lead to underestimation of kidney damage and an incomplete treatment approach. Clinicians should be trained to consider both aspects together, ensuring a

comprehensive understanding of the patient's kidney function and risk. This approach will help guide more personalized and effective management strategies for individuals with CKD.

CKD is classified into 5 categories based on GFR (Tab. 1).

The normal range for GFR in healthy adults typically falls between 90 ml/min per 1.73 m² and 120 ml/min per 1.73 m², though this can vary slightly based on factors such as age, sex, and body size. GFR is a critical indicator of kidney function, as it reflects how efficiently the kidneys are filtering waste and excess fluids from the blood. A GFR in this range suggests that the kidneys are working properly.

Table 1

GFR categories in CKD

GFR Category	GFR (ml/min per 1.73 m²)	Terms
G1	≥90	Normal or high
G2	60–89	Mildly decreased
G3a	45–59	Mildly to moderately decreased
G3b	30–44	Moderately to severely decreased
G4	15–29	Severely decreased
G5	<15	Kidney failure

However, when the GFR exceeds 120 ml/min per 1.73 m², it may indicate a state of hyperfiltration. This can occur under certain conditions, such as early-stage diabetes, obesity, high-protein diets, or during periods of increased kidney blood flow. While hyperfiltration may not cause immediate harm to the kidneys, it is often a sign that the kidneys are under increased stress.

In conditions like diabetes, hyperfiltration can initially be a compensatory response to the increased blood sugar levels. The kidneys filter more blood to try to remove excess glucose, leading

to an elevated GFR. In the early stages, this may not cause any obvious symptoms, but over time, the constant strain on the kidneys can lead to structural damage and functional decline. This damage may eventually progress to diabetic nephropathy, a common cause of CKD.

Hyperfiltration is also seen in other conditions, such as hypertension or glomerulonephritis, where the kidneys may be trying to compensate for underlying damage. In obesity, the increased metabolic demands and higher blood volume can put additional strain on the kidneys, leading to hyperfiltration.

Even though GFR greater than 120 ml/min per 1.73 m^2 can occur temporarily or in some healthy individuals it's important to monitor the GFR over time. Persistent hyperfiltration may be an early warning sign that the kidneys are at risk for developing CKD, as ongoing stress on the kidneys can lead to fibrosis and impaired kidney function.

In some cases hyperfiltration may be caused by physiological conditions such as:

- **Pregnancy**. During pregnancy, there is an increase in blood volume and cardiac output to support the growing fetus. This can lead to increased renal blood flow and, subsequently, an elevated GFR. This physiological response helps to efficiently eliminate waste products and maintain fluid and electrolyte balance for both the mother and the developing fetus.
- **Exercise**. Physical activity, especially intense or prolonged exercise, increases cardiac output and blood flow throughout the body, including the kidneys. In athletes or individuals engaged in vigorous physical activity, GFR can temporarily increase. This increase in renal blood flow and GFR generally returns to baseline after the activity ends.
- **High-Protein Diets.** Consuming a diet high in protein can lead to physiological hyperfiltration. High protein intake increases the demand for filtration, especially for nitrogen waste products like urea and creatinine. This causes an increase in GFR as the kidneys work to excrete these

metabolites. While this is a normal response, chronic excessive protein intake may lead to kidney damage over time, particularly if other risk factors like hypertension or pre-existing kidney conditions are present.

- **Insulin** increases renal blood flow by stimulating NO generation in the renal vasculature.
- **Growth hormone**. Growth hormone has a direct impact on kidney function by increasing renal blood flow and GFR, which is especially important during periods of rapid growth, such as in adolescence.

As already mentioned, determining the level of albuminuria is an important component not only for establishing a diagnosis of CKD (one of the markers of kidney damage), but also for classification. Thus, CKD is classified into 3 categories based on albuminuria (Tab. 2).

Table 2

Albuminuria Categories in CKD

Category	**AER (mg/d)**	**ACR**		**Terms**
		mg/mmol	mg/g	
A1	<30	<3	<30	Normal to mildly increased
A2	30–300	3–30	30–300	Moderately increased
A3	>300	>30	>300	Severely increased
AER, albumin excretion rate; ACR, albumin-to-creatinine ratio				

Questions for Self-Assessment

1. What does the CGA acronym stand for in CKD classification?
2. Why is it important to consider both GFR and albuminuria when assessing CKD?
3. What GFR range is considered normal or high in CKD classification?
4. At what GFR level is kidney failure classified, and how is it categorized?
5. Define hyperfiltration and describe its potential implications for kidney health.
6. What are some physiological conditions that may cause temporary hyperfiltration?
7. How does hyperfiltration in early-stage diabetes contribute to kidney stress?
8. Why is persistent hyperfiltration considered a risk factor for CKD?
9. How is albuminuria categorized in CKD classification?
10. What are the AER and ACR ranges for each albuminuria category?
11. Why is albuminuria considered a critical marker of kidney damage?
12. How can a patient with mild GFR reduction but severe albuminuria differ in risk compared to one with normal albuminuria levels?
13. What are the potential consequences of failing to account for albuminuria in CKD classification?
14. How does CKD classification guide diagnosis, monitoring, and treatment planning?
15. What are some ways clinicians can improve their understanding of the role of both GFR and albuminuria in CKD assessment?
16. How does pregnancy influence GFR, and why is this change important?

17. Explain how high-protein diets can affect GFR and the potential long-term risks.
18. What role does insulin play in increasing renal blood flow?

DETECTION AND EVALUATION OF CKD

The early detection of CKD is essential for effective management and preventing progression to more severe stages. Evaluating CKD involves assessing both kidney function and potential signs of kidney damage, primarily through urine albumin measurement and estimated GFR (eGFR). These tests enable timely diagnosis and intervention, particularly in people at high risk for CKD.

For individuals at risk for CKD, conduct both urine albumin measurement and GFR assessment. Urine albumin measurement provides insight into kidney damage, while GFR reflects kidney function. Together, these tests offer a comprehensive view of kidney health, enhancing diagnostic accuracy and helping identify CKD at earlier stages.

If elevated urinary ACR, hematuria, or low eGFR is detected incidentally, confirm the findings by repeating the tests. Single abnormal results may occur due to temporary factors like dehydration or infection, so repeat testing helps avoid misdiagnosis and ensures that persistent abnormalities indicating CKD are not overlooked.

In adults at risk for CKD use creatinine-based estimated GFR (eGFRcr). If cystatin C is available, the GFR category should be estimated from the combination of creatinine and cystatin C (creatinine and cystatin C–based estimated GFR [eGFRcr-cys]).

Estimating GFR is crucial for identifying and monitoring CKD. Creatinine-based eGFR (eGFRcr) is the standard initial test, as serum creatinine (SCr) is a commonly available, cost-effective biomarker. Creatinine-based eGFR provides a reliable estimate in most cases, helping identify individuals who might be at risk for or are developing CKD.

However, the accuracy of creatinine-based GFR estimation can be affected by factors such as muscle mass, age, gender, and certain medical conditions. Using a combined creatinine and cystatin C-based eGFR (eGFRcr-cys) can improve the accuracy of the GFR estimate, especially in cases where precision is critical for clinical decision-making. Cystatin C, unlike creatinine, is less influenced by muscle mass and other demographic factors, making it a valuable supplementary marker.

The combined eGFRcr-cys is particularly beneficial when evaluating patients who have borderline GFR values, unexplained changes in kidney function, or conditions that may interfere with creatinine metabolism. This approach ensures a more comprehensive evaluation, enabling clinicians to make more accurate diagnoses and treatment decisions, especially in early or uncertain cases of CKD.

Evaluation of cause in CKD

Identifying the underlying cause of CKD is important for tailoring appropriate treatment, managing disease progression, and addressing any potentially modifiable risk factors. CKD can result from a variety of causes, including genetic predispositions, environmental exposures, lifestyle factors, and specific health conditions. A thorough evaluation helps to clarify these factors and guide comprehensive management strategies.

Establish the cause of CKD by conducting a detailed assessment that includes:

- clinical context. Consider the overall health profile and risk factors specific to the patient.
- personal and family history. Review history of kidney disease, hypertension, diabetes, or other relevant conditions that may increase CKD risk.

- social and environmental factors. Assess lifestyle, occupational exposures, and environmental conditions that may impact kidney health.
- medications. Evaluate current and past medications for any nephrotoxic effects, especially long-term use of medications known to impact renal function.
- physical examination. Identify any physical signs that may suggest specific causes, such as signs of systemic disease.
- laboratory measures. Urinalysis and urine sediment, urine , serologic tests.
- imaging. Use ultrasound or other imaging methods to assess kidney size, structure, and other abnormalities.
- genetic and pathologic diagnosis. Consider genetic testing if there is a family history of kidney disease or if hereditary kidney conditions are suspected. Kidney biopsy may also help clarify the cause if findings suggest pathology consistent with a specific diagnosis.

Use tests to establish a cause based on resources available (Tab. 3).

Kidney biopsy is an acceptable, safe, diagnostic test to evaluate cause and guide treatment decisions when clinically appropriate. It is a valuable diagnostic tool for identifying the specific cause of CKD, particularly when the underlying condition is unclear or when results from imaging, lab tests, and clinical history are inconclusive. Kidney biopsies can reveal underlying pathological features that are not detectable by non-invasive tests, enabling a more targeted and accurate diagnosis.

When to consider a biopsy:

- the cause of CKD cannot be reliably determined through other diagnostic means and when knowledge of the pathology will impact management decisions;
- suspected glomerular disease;
- unexplained rapid kidney function decline;
- nephrotic syndrome;
- suspicion of autoimmune kidney diseases.

Table 3

Guidance for the selection of additional tests for evaluation of cause

Test Category	Examples	Comment or Key References
Imaging	Ultrasound, intravenous urography, CT kidneys, ureters bladder, nuclear medicine studies, MRI	Assess kidney structure (i.e., kidney shape, size, symmetry, and evidence of obstruction) for cystic disease and reflux disease. Evolving role of additional technologies (e.g., 3D ultrasound)
Kidney Biopsy	Ultrasound-guided percutaneous	Usually examined by light microscopy, immunofluorescence, and electron microscopy, and, in some situations, may include molecular diagnostics. Used for exact diagnosis, planning treatment, assessing activity and chronicity of disease, and likelihood of treatment response; may also be used to assess genetic disease

Test Category	Examples	Comment or Key References
Laboratory Tests: Serologic, Urine Tests	Chemistry including acid-base and electrolytes, serologic tests such as anti-PLA2R, ANCA, anti-GBM antibodies Serum-free light chains, serum, and urine protein electrophoresis/immunofixation Urinalysis and urine sediment examination	Refer to *KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases*. Increasing recognition of the role of light chains in kidney disease even in the absence of multiple myeloma (monoclonal gammopathy of renal significance [MGRS]). Presence of persistent hematuria or albuminuria is critical in determining differential diagnosis
Genetic Testing	APOL1, COL4A3, COL4A4, COL4A5, NPHS1, UMOD, HNF1B, PKD1, PKD2	Evolving as a tool for diagnosis, increased utilization is expected. Recognition that genetic causes are more common and may present without classic family history.

ANCA, antineutrophil cytoplasmic antibody; APOL1, apolipoprotein 1; COL4A, type IV collagen alpha chain; CT, computed tomography; GBM, glomerular basement membrane; HNF1B, hepatocyte nuclear factor 1B; MRI, magnetic resonance imaging; NPHS1, congenital nephrotic syndrome; PKD1, polycystic kidney disease-1; PKD2, polycystic kidney disease-2; PLA2R, M-type phospholipase A2 receptor; UMOD, uromodulin.

Modern kidney biopsy techniques are considered safe and are usually performed under imaging guidance (ultrasound or CT) to minimize risks. Common complications, such as minor bleeding, are typically manageable, and serious risks are low when done by experienced practitioners.

GFR and kidney function

The GFR is a crucial marker in assessing kidney function. However, it is important to note that the kidneys have several other vital functions beyond just filtration, including reabsorption and secretion, acid-base balance, blood pressure, and red blood cell production.

Use the term "GFR" specifically when referring to the kidney function of glomerular filtration. This term is used to quantify the rate at which the kidneys filter blood, typically measured in milliliters per minute (ml/min).

When referring to the broader spectrum of activities performed by the kidneys, use the more general term "kidney function(s)". This includes not only glomerular filtration but also the kidneys' role in:

- electrolyte balance. Maintaining appropriate levels of sodium, potassium, calcium, and other electrolytes.
- acid-base regulation. Ensuring the body's pH remains within a narrow, healthy range.
- blood pressure control. Regulating fluid balance and renin-angiotensin-aldosterone system (RAAS) function to influence blood pressure.
- erythropoiesis. Producing erythropoietin, which stimulates the production of red blood cells in the bone marrow.

Using SCr and an estimating equation for the initial assessment of GFR is a standard method used in most clinical settings to estimate kidney function based on SCr levels (Tab. 4). It is an efficient, cost-effective way to estimate GFR, particularly for

screening and routine monitoring of kidney health. But understanding when to use more precise measurements is essential in complex cases.

Table 4

Indications for use of cystatin C

Domain	Specific Clinical Condition	Cause of Decreased Accuracy	Comments on GFR Evaluation
Body Habitus and Changes in Muscle Mass	Eating disorders	Non-GFR determinants of SCr	eGFRcys may be appropriate if no comorbid illness other than reduction in muscle mass.
	Extreme sport/ exercise/ bodybuilder	Non-GFR determinants of SCr	eGFRcys may be appropriate if an increase in muscle mass is the only abnormality.
	Above-knee amputation	Non-GFR determinants of SCr	eGFRcys may be appropriate in those without comorbid conditions; suggest eGFRcr-cys if comorbid illness exists.
	Spinal cord injury with paraplegia/ paraparesis or quadriplegia/quadriparesis	Non-GFR determinants of SCr	eGFRcys may be appropriate in those without comorbid illness; suggest eGFRcr-cys if comorbid illness exists.

Domain	Specific Clinical Condition	Cause of Decreased Accuracy	Comments on GFR Evaluation
	Class III obesity (BMI >40 or >35 kg/m²)	Non-GFR determinants of SCr and SCys	eGFRcr-cys demonstrated to be most accurate.
Lifestyle	Smoking	Non-GFR determinants of SCys	Minimal data; suggest eGFRcr if no changes to non-GFR determinants of SCr or comorbid illness.
Diet	Low-protein diet Keto diets, Vegetarian, High-protein diets, and creatine supplements	Non-GFR determinants of SCr	Minimal data; suggest eGFRcr if no changes to non-GFR determinants of SCr or comorbid illness.
Illness Other Than CKD	Malnutrition	Chronic illness impacting SCr and SCys	eGFRcr-cys may be less accurate due to malnutrition/inflammation; suggest mGFR for treatment decisions.
	Cancer	Chronic illness impacting SCr and SCys	eGFRcr-cys is generally accurate but may be less so in frail or high cell-turnover cancers;

Domain	Specific Clinical Condition	Cause of Decreased Accuracy	Comments on GFR Evaluation
			suggest mGFR.
Illness Other Than CKD	Heart failure	Chronic illness impacting SCr and SCys	eGFRcys less biased but with low accuracy; suggest eGFRcr-cys or eGFRcys routinely, mGFR for treatment.
	Cirrhosis	Chronic illness impacting SCr and SCys	eGFRcys less biased with low accuracy; suggest eGFRcr-cys or eGFRcys routinely, mGFR for treatment decisions.
	Catabolic consuming diseases (e.g., tuberculosis, AIDS)	Chronic illness impacting SCr and SCys	Limited data; eGFRcr-cys may be inaccurate; use eGFRcr-cys for routine, mGFR for treatment.
	Muscle wasting diseases	Chronic illness impacting SCr and SCys	Limited data; large bias in eGFRcr/eGFRcys; suggest eGFRcr-cys for routine, mGFR for treatment decisions.

Domain	Specific Clinical Condition	Cause of Decreased Accuracy	Comments on GFR Evaluation
Medication Effects	Steroids (anabolic/hormone)	Non-GFR determinants of SCr; effect on SCys unknown	Physiological effect on SCys unknown; suggest eGFRcr-cys.
	Decreased tubular secretion	Non-GFR determinants of SCr	eGFRcys may be appropriate if medication only affects creatinine; suggest mGFR for treatment.
	Broad-spectrum antibiotics (decreased extrarenal elimination)	Non-GFR determinants of SCr	eGFRcys may be appropriate if medication only affects creatinine; suggest mGFR for treatment.

eGFRcr-cys (creatinine-cystatin C-based equation) should be used in clinical situations where eGFRcr (creatinine-based) is less accurate, and GFR significantly impacts clinical decisions. The combined use of creatinine and cystatin C offers better accuracy, especially in certain patient populations such as those with low muscle mass, obesity, or extremes of age, where SCr alone may be misleading. This method should be preferred when precise GFR measurement is required for decision-making (e.g., medication dosing).

For more accurate assessment of GFR, especially when treatment decisions rely on precise GFR measurements, it is recommended to MEASURE GFR using plasma or urinary

clearance of an exogenous filtration marker (e.g., inulin, iohexol). This is particularly useful when clinical decisions depend on exact GFR values, such as in cases of kidney transplantation, dialysis initiation, or when other methods are insufficient for accurate assessment.

It is important to be aware of the variability and factors that can affect SCr and cystatin C measurements, such as age, gender, diet, and certain medications. These factors can introduce errors in estimating kidney function, so clinical judgment should always accompany eGFR values in treatment decisions.

Interpretation of SCr level requires consideration of dietary intake. SCr levels can be influenced by factors such as high-protein diets or dehydration, so interpreting SCr results requires considering the individual's diet and hydration status. This ensures more accurate interpretation of kidney function and avoids misdiagnosis or inappropriate treatment.

The assessment of kidney function through GFR is a dynamic process that requires an understanding of potential errors and limitations in various estimating equations. In clinical practice, estimating GFR over time or in specific patient populations requires careful attention to the accuracy and relevance of the methods used.

Cystatin C is a more stable marker of kidney function than creatinine and is less influenced by factors like muscle mass, diet, and age. When comparing eGFR based on creatinine (eGFRcr) to eGFR based on cystatin C (eGFRcys), significant differences may emerge, either overestimating or underestimating kidney function depending on the patient's characteristics. These differences can offer valuable insights into the underlying kidney function or pathology. For example, a patient with low muscle mass may have a higher eGFRcr than eGFRcys, which could indicate a lower level of kidney function than initially estimated.

It is recommended to use a validated GFR estimating equation to derive GFR from serum filtration markers (eGFR) rather than relying on the serum filtration markers alone.

Estimating GFR using validated equations (such as the MDRD or CKD-EPI formulas) allows for more accurate and reliable assessments of kidney function compared to using individual serum filtration markers like creatinine or cystatin C alone. These equations take into account variables like age, sex, and sometimes race (though this is becoming less common), which improves the precision of GFR estimates in different populations.

To ensure consistency and accuracy, healthcare providers should use region-specific validated GFR estimating equations. These equations are often derived from population data that reflect the local demographic characteristics (such as ethnicity, diet, and healthcare access), so using the correct regional equation enhances the precision of the estimated GFR.

The inclusion of race in GFR estimating equations has been a subject of significant debate, as it may perpetuate racial disparities in healthcare. Recent updates to GFR equations, such as the CKD-EPI equation, have removed race as a factor, in recognition of the fact that race is a social construct and does not biologically dictate kidney function. Avoiding race-based adjustments in eGFR calculations is now recommended to reduce biases and ensure more equitable healthcare outcomes across different populations.

Recommendations and practice points on the evaluation of albuminuria

Use the following measurements for initial testing of albuminuria (in descending order of preference). In all cases, a first void in the morning midstream sample is preferred in adults:

- urine ACR, or
- reagent strip urinalysis for albumin and ACR with automated reading.
- If measuring urine protein:
- urine protein-to-creatinine ratio (PCR),

- reagent strip urinalysis for total protein with automated reading, or
- reagent strip urinalysis for total protein with manual reading.

The ACR is considered the gold standard for detecting albuminuria, especially when measured using a first-morning void. This approach is preferred because it accounts for variations in urine concentration. For protein measurement, the PCR is also useful, but ACR is generally prioritized in albuminuria assessment.

Use more accurate methods when albuminuria is detected using less accurate methods. Confirm reagent strip positive albuminuria and/or proteinuria by quantitative laboratory measurement and express as a ratio to urine creatinine wherever possible (i.e., quantify the ACR or PCR if initial semiquantitative tests are positive).

If an initial test (such as reagent strip urinalysis) on a random untimed urine suggests albuminuria, it is crucial to confirm the result with a more accurate, quantitative method by re-measuring ACR or PCR using a first-morning void for consistency. This confirmation step helps avoid false positives and ensures that albuminuria is accurately diagnosed.

Understand factors that may affect interpretation of measurements of urine albumin and urine creatinine and order confirmatory tests as indicated.

Several factors can influence the accuracy of urine ACR measurements, including hydration status, exercise, diet, and the presence of infections or other conditions (Tab. 5). It is important to consider these factors when interpreting results and to order additional confirmatory tests.

Table 5

Factors causing biological variation in urine albumin or urine protein

Factor	Falsely Elevated ACR or PCR	False Decrease in ACR or PCR
Variability in urine albumin or protein		
Hematuria, Menstruation, Exercise	Increases albumin and protein in the urine	
Infection	Symptomatic urinary infection can cause production of protein from the organism	
Nonalbumin proteins		Other proteins may be missed by albumin reagent strips
Variability in urinary creatinine concentration		
Biological sex	Females have lower urinary creatinine excretion, therefore higher ACR and PCR	Males have higher urinary creatinine excretion, therefore lower ACR and PCR
Weight	Low urinary creatinine excretion with low weight can cause high ACR or PCR relative to timed excretion	High urinary creatinine excretion with high weight can cause low ACR or PCR relative to timed excretion
Changes in creatinine excretion	Lower urinary creatinine excretion with AKI or low-protein intake	High urinary creatinine excretion with high-protein intake or exercise

Point-of-care testing (POCT) for CKD

POCT is suggested as an option for creatinine and urine albumin measurements in situations where laboratory access is either not available or where immediate testing results could enhance patient care and clinical decision-making. POCT is particularly useful in resource-limited settings or for situations requiring rapid results for timely treatment.

To ensure the reliability and accuracy of POCT, it is crucial to adhere to quality standards across all phases: specimen collection, testing, and result interpretation. POCT devices must meet stringent quality control standards, and regular external quality assessments should be conducted to ensure consistency. This is essential to minimize the risk of inaccurate results that could lead to incorrect clinical decisions.

When POCT devices are employed to measure creatinine, it is important to calculate the estimated GFR (eGFR) using a formula that aligns with local or regional standards. This ensures the GFR estimate is accurate and consistent with local practices, which may vary depending on the population and available resources.

POCT devices that test for albuminuria should ideally also measure creatinine in order to calculate the ACR, which is essential for diagnosing and monitoring kidney disease. These devices must demonstrate high sensitivity, producing positive results for at least 85% of individuals with significant albuminuria (defined as ACR ≥30 mg/g or ≥3 mg/mmol). This ensures the device's effectiveness in detecting clinically relevant albuminuria, which is crucial for early CKD detection.

Questions for Self-Assessment

1. Why is early detection of CKD crucial for patient outcomes?
2. What two key tests are primarily used to detect CKD, and what do they measure?

3. How does eGFR help in the detection of CKD, and which factors might affect its accuracy?
4. Why is it important to confirm elevated urinary ACR, hematuria, or low eGFR with repeated testing?
5. What is the difference between creatinine-based eGFR and cystatin C-based eGFR?
6. Under what circumstances should creatinine-cystatin C-based eGFR (eGFRcr-cys) be preferred over creatinine-based eGFR?
7. How can eGFRcr-cys improve the accuracy of kidney function estimation?
8. List the different components of the clinical assessment to determine the cause of CKD.
9. How does a patient's personal and family history influence CKD risk assessment?
10. Why are medications and social/environmental factors important to consider when evaluating CKD?
11. Under what circumstances is a kidney biopsy recommended, and what information can it provide?
12. What is the significance of GFR in kidney function assessment, and how does it relate to other kidney functions?
13. What are the other vital functions of the kidneys besides glomerular filtration?
14. How do factors such as diet, hydration, and muscle mass influence SCr and GFR estimates?
15. Why is it necessary to measure GFR using plasma or urinary clearance of exogenous filtration markers in some cases?
16. How does using a validated GFR estimating equation improve the accuracy of kidney function assessments?
17. What are the potential issues associated with using race-based adjustments in GFR equations, and how have recent updates addressed these?
18. What is the preferred method for initial albuminuria testing, and why is a first-morning void sample recommended?
19. Explain the significance of using ACR over PCR for albuminuria detection.

20. What steps should be taken if initial tests suggest albuminuria or proteinuria using less accurate methods?
21. What factors can affect the accuracy of urine albumin and creatinine measurements?
22. Why is it important to confirm abnormal urine albumin findings with quantitative methods?
23. What are the advantages of point-of-care testing for creatinine and urine albumin measurements?
24. How can POCT contribute to timely decision-making in CKD management?
25. What are the key quality control measures for POCT devices, and why are they essential for accurate results?
26. Why is it important for POCT devices to measure both creatinine and albumin to calculate ACR?

MONITORING FOR PROGRESSION OF CKD BASED ON GFR AND ACR CATEGORIES

Regular monitoring of kidney function is essential in CKD to track disease progression. Annual assessment of albuminuria and GFR helps healthcare providers identify early signs of worsening kidney function. Albuminuria is a marker of kidney damage, and GFR provides a measure of kidney function. Annual monitoring enables timely interventions to slow the progression of CKD, adjust treatments, and improve long-term outcomes.

Some individuals are at higher risk of CKD progression due to factors such as diabetes, hypertension, or a family history of kidney disease. For these patients, more frequent testing is important to closely monitor kidney function. By assessing albuminuria and GFR more frequently, clinicians can detect any early signs of deterioration and adjust treatment plans more promptly. Regular monitoring in high-risk individuals enables timely interventions (e.g., optimizing blood pressure control, using renoprotective medications) to prevent or slow further kidney damage.

A significant change in eGFR, specifically a decline of more than 20%, is considered beyond normal variation and should prompt further investigation. GFR typically fluctuates within a small range over time, but a >20% drop indicates potential worsening of kidney function. This can be due to various causes such as acute kidney injury (AKI), progression of CKD, or the onset of other health conditions. It’s important for healthcare providers to evaluate the cause of the eGFR change, and adjust the management plan accordingly, such as optimizing medications or addressing underlying conditions that could be contributing to kidney decline.

Hemodynamically active therapies, such as angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARBs), and certain diuretics, can have significant effects on kidney function. While these therapies are often prescribed to protect kidney function, they can sometimes lead to a temporary drop in GFR, particularly in the initial stages of treatment. However, a reduction in GFR of more than 30% after starting such therapies is considered abnormal and exceeds typical variability. This significant decline warrants evaluation to ensure that the therapy is not causing harm, and to assess whether dosage adjustments or a change in treatment approach is necessary.

For albuminuria monitoring of people with CKD, a doubling of the ACR on a subsequent test exceeds laboratory variability and warrants evaluation. The ACR is a key marker for kidney damage, particularly albuminuria, which is a hallmark of CKD. An increase in ACR suggests worsening kidney damage. If the ACR doubles from a previous test, this is considered a significant change that exceeds the expected variability in lab results. Such a change should trigger further investigation to identify the underlying cause of the worsening albuminuria. It may indicate progression of CKD, uncontrolled blood pressure, or other factors like infection, dehydration, or worsening diabetes. Early identification of increased albuminuria allows for timely interventions to potentially prevent further kidney damage.

Risk prediction in people with CKD

For individuals with CKD stages G3–G5, using validated risk prediction models is recommended to estimate the likelihood of kidney failure (end-stage renal disease, ESRD). These models use factors such as eGFR, ACR, comorbid conditions (e.g., diabetes, hypertension), and other clinical data to calculate the risk of kidney failure over a defined period. By using validated risk equations, healthcare providers can identify patients at higher risk

of progression to kidney failure and take proactive measures to delay or prevent it, such as early referral to nephrology, intensified management, or timely planning for kidney replacement therapy (KRT).

Externally validated risk equations for predicting kidney failure in the general (CKD G3–G5) population:

- Kidney Failure Risk Equation – KFRE (https://www.kidneyfailurerisk.com/, https://www.ckdpc.org/risk-models.html),
- Kaiser Permanente Northwest (KPNW) Prediction Model
- 6-variable risk score (Z6 score).

For people with CKD who have a 5-year kidney failure risk of 3% to 5%, nephrology referral should be considered, especially when the eGFR or albuminuria suggests moderate to high-risk progression. The 3% to 5% risk threshold allows clinicians to identify individuals who may benefit from specialized care, even if their kidney function (eGFR) or albuminuria is not at a very severe stage. This is particularly important for ensuring that high-risk individuals receive appropriate monitoring, tailored interventions, and potentially disease-modifying treatments early in their course of CKD.

A 2-year risk of kidney failure greater than 10% is a critical threshold that should guide the initiation of more intensive multidisciplinary care for CKD patients. This risk level indicates that the individual is at significant risk of progressing to kidney failure within a short time frame, which warrants more focused care and frequent monitoring. Multidisciplinary teams, including nephrologists, dietitians, educators, and social workers, should be involved to help manage the complexities of CKD and to begin planning for potential KRT. Factors such as the patient's overall health, comorbidities, and preferences should be integrated into the decision-making process.

For individuals with CKD at high risk (greater than 40%) of progressing to kidney failure within two years, it is essential to begin preparing for KRT. This preparation includes educating the patient about different treatment options (e.g., dialysis modalities,

kidney transplantation), as well as addressing logistics such as vascular access planning for dialysis or referral for kidney transplant evaluation. This high-risk threshold should prompt early discussions on the potential need for KRT, with emphasis on informed decision-making, patient preferences, and addressing any psychosocial factors that could influence treatment choice.

Risk prediction models for kidney failure are typically validated in individuals with more advanced stages of CKD (G3–G5) and may not be as accurate or applicable for those with earlier stages of CKD (G1–G2). This is because the progression of CKD in these early stages is often slower, and the factors influencing the development of kidney failure may differ. As a result, risk equations used for G3–G5 may not reflect the progression dynamics of people in the G1–G2 stages, and alternative methods may be required for early-stage CKD risk assessment. This distinction is crucial for making accurate clinical decisions for individuals with different stages of kidney disease.

People with certain kidney diseases, such as immunoglobulin A nephropathy (IgAN) or autosomal dominant polycystic kidney disease (ADPKD), may have different risk profiles for progression to kidney failure compared to the general CKD population. These conditions often have specific pathophysiological features that influence their progression. Therefore, disease-specific, externally validated prediction equations should be used in these populations to more accurately estimate the risk of kidney failure. These equations account for the unique characteristics of each disease, leading to better-informed management and more individualized care plans. For these patients the Mayo Clinic Classification tool and the Predicting Renal Outcome in Polycystic Kidney Disease (PROPKD) score (https://adpkdsim.org/expert/prognostic-tools/propkd-score) and MEST histological score.

Prediction of cardiovascular risk in people with CKD

People with CKD are at a significantly increased risk for cardiovascular diseases (CVD), including heart failure, coronary artery disease, and stroke. Traditional cardiovascular risk models, which typically focus on factors like blood pressure, cholesterol levels, and smoking, may not be fully accurate for people with CKD because kidney function (eGFR) and albuminuria are strong independent risk factors for cardiovascular events. Therefore, it is recommended to use externally validated cardiovascular risk prediction models that have been specifically developed for CKD populations or that integrate eGFR and albuminuria into the risk assessment. These models take into account the unique risk profile of CKD patients and provide more precise predictions to guide preventive therapies such as statin use, blood pressure control, and other cardiovascular interventions aimed at reducing risk.

Some examples of externally validated models for cardiovascular risk prediction include:

- pooled cohort equations [PCE]/Systematic COronary Risk Evaluation [SCORE] - Predicted 10 year risk of atherosclerotic CVD (https://ckdpcrisk.org/ckdpatchpce/);
- QRISK3 - calculates a person's risk of developing a heart attack or stroke over the next 10 years. It is only valid if the patient does not already have a diagnosis of coronary heart disease (including angina or heart attack) or stroke/transient ischaemic attack (https://www.qrisk.org/);
- Predicting Risk of CVD EVENTs (PREVENT) equations - used for primary prevention patients (those without atherosclerotic cardiovascular disease or heart failure) only (https://professional.heart.org/en/guidelines-and-statements/prevent-calculator).

For mortality risk prediction to guide discussions about goals of care, use externally validated models that predict all-cause mortality specifically developed in the CKD population. CKD is a

major predictor of increased all-cause mortality, and people with advanced CKD or end-stage renal disease (ESRD) often face a higher risk of death from both cardiovascular and non-cardiovascular causes. In clinical practice, understanding a patient's mortality risk is essential for making informed decisions about their care, particularly when discussing goals of care, treatment intensity, and end-of-life decisions. It is recommended to use externally validated models that specifically predict all-cause mortality in the CKD population to help guide these discussions. These models integrate factors like kidney function (eGFR), albuminuria, comorbidities (e.g., diabetes, hypertension, heart disease), and other clinical indicators to estimate a patient's likelihood of mortality over a defined period.

Some examples of externally validated mortality risk prediction models include:

- CKD Prognosis Consortium (CKD-PC) model. For multiple outcomes in CKD G4-G5 predict the risk of death, nonfatal CVD event, or kidney failure in adults at 2 and 4 years (https://ckdpcrisk.org/lowgfrevents/)
- Predicted 10 year risk of Cardiovascular Mortality (https://ckdpcrisk.org/ckdpatchscore/).

Questions for Self-Assessment

1. Why is it important to monitor albuminuria and GFR annually in individuals with CKD?
2. How does albuminuria serve as a marker for kidney damage, and why is it essential to track it regularly in CKD patients?
3. What are the key factors that increase the risk of CKD progression, and how do they influence monitoring frequency?
4. How should healthcare providers interpret a significant change in eGFR, specifically a decline of more than 20%, and what steps should be taken following this change?

5. How do hemodynamically active therapies, such as ACE inhibitors or ARBs, affect kidney function, and when should adjustments be made if GFR declines significantly?
6. What does a doubling of the ACR on a subsequent test indicate, and why is it important to investigate further?
7. How can risk prediction models help in assessing the likelihood of kidney failure in individuals with CKD stages G3–G5?
8. What should be done for individuals with CKD and a 5-year kidney failure risk of 3% to 5%?
9. Why is a 2-year risk of kidney failure greater than 10% considered a critical threshold for initiating more intensive care?
10. What factors should be considered when preparing individuals with CKD at high risk (greater than 40%) of kidney failure for kidney replacement therapy (KRT)?
11. Why are risk prediction models for kidney failure less accurate in individuals with early stages of CKD (G1–G2)?
12. How do conditions like immunoglobulin A nephropathy (IgAN) or autosomal dominant polycystic kidney disease (ADPKD) affect risk prediction for kidney failure, and what models are recommended for these patients?
13. Why is it essential to consider both kidney function (eGFR) and albuminuria when assessing cardiovascular risk in individuals with CKD?
14. What are some validated models for cardiovascular risk prediction in CKD, and why are they preferred over traditional models?
15. How do mortality risk prediction models help guide discussions about treatment goals and end-of-life care for individuals with advanced CKD or ESRD?
16. What factors should be considered when using mortality risk prediction models for CKD patients, and how do they impact clinical decision-making?

DELAYING CKD PROGRESSION AND MANAGING ITS COMPLICATION

CKD requires a multifaceted approach to slow its progression and manage the various health complications associated with it. A comprehensive treatment strategy in CKD involves a combination of lifestyle modifications, medication, monitoring, and managing risk factors, as well as addressing complications that may arise as kidney function declines. Each component plays a role in improving outcomes for people with CKD, preserving kidney function, and preventing complications such as cardiovascular disease, anemia, bone disease, and electrolyte imbalances.

Physical activity

Encourage moderate-intensity physical activity for people with CKD, aiming for a cumulative duration of at least 150 minutes per week, adjusted as needed to match their cardiovascular and physical tolerance.

Regular physical activity has been shown to improve cardiovascular health, muscle strength, and overall quality of life, especially in people with CKD, who often experience fatigue and muscle weakness. Engaging in 150 minutes per week of moderate-intensity exercise, such as brisk walking, cycling, or swimming, is beneficial for maintaining a healthy heart, reducing BP (BP), managing weight, and lowering inflammation - all critical for people with CKD, as they are at higher risk for cardiovascular complications.

Physical activity can also support mental health, helping to alleviate symptoms of depression and anxiety, which are common in people with CKD.

However, it's important to tailor the activity level to the individual's physical ability and cardiovascular health. For some individuals, especially those in later stages of CKD, a lower duration or intensity may be more suitable. Healthcare providers should assess each person's tolerance and capabilities to recommend a safe, effective exercise plan that aligns with their overall health status and CKD progression.

Encouraging regular, moderate exercise is a proactive way to enhance the well-being of individuals with CKD and improve their overall health outcomes.

When recommending physical activity for individuals with CKD, healthcare providers must take a holistic approach that considers various factors, including age, ethnic background, comorbidities, and resource access. Age can influence the intensity and type of exercise that is safe and beneficial, with older adults often requiring lower-impact or gentler activities. For example, joint pain and decreased muscle mass may limit an elderly person's ability to engage in high-intensity activities, necessitating modifications such as walking or swimming. Ethnic background may also play a role in physical activity recommendations, as cultural differences can affect exercise preferences and accessibility. Providers should consider culturally appropriate activities that patients feel comfortable with and enjoy, which may improve adherence to exercise recommendations.

In addition, comorbidities, such as diabetes, heart disease, or musculoskeletal disorders, may require adjustments to physical activity programs. For example, someone with diabetes may need more careful monitoring of blood glucose levels during exercise, while a person with heart disease may need to avoid strenuous exertion. Finally, access to resources - including gyms, parks, or exercise classes - should also be considered when advising physical activity. For those with limited access, home-based

exercises or low-cost community programs may be more feasible options, and providers should support patients by helping them explore these alternatives.

People with CKD should be advised to avoid sedentary behavior. Sedentary behavior is detrimental to the health of individuals with CKD. Prolonged sitting or inactivity is associated with an increased risk of cardiovascular disease, muscle wasting, and poorer kidney outcomes. For individuals with CKD, sedentary behavior can also worsen insulin resistance, elevate BP, and contribute to the progression of kidney disease. Physical activity helps improve circulation, supports heart health, and can maintain muscle mass, all of which are important for people with kidney disease. Healthcare providers should actively encourage patients to avoid long periods of sitting, even if they are unable to engage in formal exercise. Simple strategies, such as standing or walking every 30 minutes, can reduce the harmful effects of prolonged sedentary time. Providers can also recommend low-impact activities like stretching or light walking throughout the day to keep the body active.

For people at higher risk of falls, healthcare providers should provide advice on the intensity of physical activity (low, moderate, or vigorous) and the type of exercises (aerobic vs. resistance, or both). For individuals with CKD who are at higher risk of falls, it is critical to tailor physical activity recommendations to minimize the risk of injury. Older adults or those with balance issues, joint instability, or neurological conditions may be more susceptible to falls during exercise. Healthcare providers should advise on the intensity of physical activity, recommending low or moderate-intensity activities for those at higher fall risk rather than vigorous-intensity exercises. Exercises that improve balance and coordination, such as tai chi, yoga, or specific strength training, should be prioritized.

Additionally, aerobic exercises like walking or cycling can improve cardiovascular health and endurance, while resistance exercises help strengthen muscles and bones, which can also aid in fall prevention. A combination of both types of exercise may be

recommended, but care should be taken to focus on balance and muscle strength training. If necessary, referrals to physical or occupational therapy can be made to design a tailored exercise plan that considers the patient's fall risk while still promoting overall health.

Physicians should consider advising/encouraging people with obesity and CKD to lose weight. BMI relates to levels of adiposity on a population scale (though imperfectly), and a BMI of over 25 kg/m^2 in adults (i.e., overweight or obese) is associated with an increased risk of multiple chronic diseases including development of CKD. Such adiposity-CKD associations appear to be causal. Obesity is a major risk factor for both the development and progression of CKD. In individuals with CKD, excess weight can worsen hypertension, insulin resistance, and inflammation, all of which contribute to kidney damage. Physicians should consider advising individuals with obesity and CKD to work toward achieving a healthy weight as part of a comprehensive management plan. Weight loss can improve kidney function by reducing the burden on the kidneys, lowering BP, and improving glycemic control in patients with diabetes.

However, weight loss recommendations should be approached carefully, as rapid or extreme weight loss can be harmful to people with kidney disease. It is essential to advise patients to aim for gradual weight loss through dietary modifications and increased physical activity, while ensuring that they continue to meet their nutritional needs. Referral to a renal dietitian can help patients adopt a kidney-friendly diet that supports weight loss without exacerbating kidney issues. Exercise, including both aerobic and resistance training, can further aid weight loss while enhancing overall health. Physicians should also monitor kidney function regularly to ensure that the weight loss process is not adversely affecting the patient's renal health.

Diet recommendations

Advise people with CKD to adopt healthy and diverse diets with a higher consumption of plant-based foods compared to animal-based foods and a lower consumption of ultraprocessed foods. For individuals with CKD, a healthy and diverse diet is essential to managing the disease and reducing the risk of complications. Plant-based foods, including fruits, vegetables, whole grains, legumes, nuts, and seeds, should be emphasized in the diet. These foods are generally lower in saturated fat and cholesterol and are rich in fiber, antioxidants, and beneficial nutrients, all of which support overall health. A plant-based diet has also been shown to have a protective effect on kidney function, reducing the risk of further progression of CKD, and it can improve cardiovascular health, which is crucial for CKD patients who are at higher risk for heart disease. A plant-based diet is rich in antiinflammatory 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 Approaches to Stop Hypertension (DASH) and Mediterranean diet can be recommended. By definition, vegan and vegetarian diets are plant-based.

Animal-based foods tend to be higher in saturated fat and protein, which, when consumed in excess, can exacerbate kidney function decline. Moreover, animal proteins can increase the kidney's workload and may lead to increased kidney filtration and the accumulation of waste products that could worsen renal function. While some animal-based proteins are necessary in the diet, the focus should be on reducing the quantity of animal-based foods and encouraging more plant-based sources of protein.

Additionally, ultraprocessed foods–such as packaged snacks, sugary beverages, and ready-to-eat meals–should be minimized or avoided. These foods are often high in unhealthy fats, sodium, added sugars, and artificial additives, which can contribute to

weight gain, increased BP, and poorer kidney function. Ultraprocessed foods such as 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.

Overall, adopting a plant-centered diet that minimizes processed and animal-based foods can have significant benefits for CKD management, including better control of BP, improved glycemic control, and potentially slowed progression of kidney disease.

Use renal dietitians or accredited nutrition providers to educate people with CKD about dietary adaptations regarding sodium, phosphorus, potassium, and protein intake, tailored to their individual needs, and severity of CKD and other comorbid conditions.

Dietary management is a key component in slowing the progression of CKD and managing its associated complications. Renal dietitians or accredited nutrition providers are essential for providing specialized guidance to people with CKD regarding sodium, phosphorus, potassium, and protein intake. These nutrients must be carefully managed, as imbalances can significantly impact kidney function and overall health:

- **Sodium**. Excess sodium intake can lead to high BP, fluid retention, and worsening kidney function. People with CKD should be encouraged to limit their sodium intake, which can be done by reducing the consumption of salt and processed foods. Sodium should be carefully monitored and tailored based on the severity of CKD and the individual's BP control needs.
- **Phosphorus**. In CKD, the kidneys' ability to excrete excess phosphorus is diminished, leading to elevated levels in the blood, which can cause bone mineral disorders and vascular calcification. Limiting high-phosphorus foods (such as dairy, nuts, and processed meats) and using phosphate binders (as prescribed) may be necessary. A renal dietitian can provide

specific recommendations to help manage phosphorus levels based on the patient's stage of CKD.

- **Potassium**. Potassium levels can become dangerously high in CKD because the kidneys are less able to remove excess potassium from the blood. Elevated potassium levels can lead to cardiac arrhythmias. Renal dietitians can help individuals with CKD manage their potassium intake by advising on appropriate food choices. Foods such as bananas, tomatoes, potatoes, and leafy greens may need to be limited or carefully portioned, depending on the severity of the kidney dysfunction.
- **Protein**. Protein intake is an important consideration in CKD, as excessive protein consumption can increase the kidneys' workload, potentially accelerating kidney function decline. However, protein is also essential for maintaining muscle mass and overall health. A renal dietitian can help balance protein intake, often recommending a moderate protein diet, with adjustments based on the patient's stage of CKD, comorbid conditions (such as diabetes), and whether the patient is undergoing dialysis. In some cases, a low-protein diet may be recommended to protect kidney function.

Protein intake

In general, the protein intake should be 0.8 g/kg body weight/d in adults with CKD G3–G5. High protein intake (>1.3 g/kg body weight/d) should be avoided in adults with CKD at risk of progression.

In adults with CKD, excessive protein intake–especially greater than 1.3 grams per kilogram of body weight per day–can increase the kidneys' workload, potentially accelerating the decline in kidney function. Higher protein intake can lead to increased GFR and hyperfiltration, which over time can contribute to kidney damage and worsen the progression of CKD. Therefore, it is important for healthcare providers to monitor and limit protein intake in individuals with CKD, particularly those at risk of

progression to more severe stages of kidney disease or kidney failure.

The goal is to tailor protein intake based on the patient's stage of CKD, balancing the need for adequate nutrition while avoiding excess protein that can strain the kidneys. For most individuals with CKD, a moderate protein intake is often recommended to support muscle mass and prevent malnutrition without overloading the kidneys.

Average protein content of foods in grams:

- meat, poultry, fish, seafood: 28 g (1 oz) = 6-8 g protein;
- 1 egg = 6-8 g protein;
- dairy, milk, yogurt: 250 ml (8 oz) = 8-10 g protein;
- cheese: 28 g (1 oz) = 6-8 g protein;
- legumes, dried beans, nuts, seeds: 100 g (0.5 cup) cooked = 7-10 g protein;
- whole grains, cereals: 100 g (0.5 cup) cooked = 3-6 g protein;
- starchy vegetables, breads: 2-4 g protein.

In adults with CKD who are willing and able, and who are at risk of kidney failure, consider prescribing, under close supervision, a very low–protein diet (0.3–0.4 g/kg body weight/d) supplemented with essential amino acids or ketoacid analogs (up to 0.6 g/kg body weight/d).

For individuals with CKD who are at high risk of progression to kidney failure, implementing a very low-protein diet (0.3–0.4 grams of protein per kilogram of body weight per day) may be considered as part of a strategy to slow disease progression. This approach is intended to reduce the kidneys' workload by limiting protein intake, which in turn can help reduce glomerular hyperfiltration and decrease the buildup of nitrogenous waste products in the body.

However, very low-protein diets can be nutritionally challenging, and it is crucial to supplement this diet with essential amino acids or ketoacid analogs (up to 0.6 grams per kilogram of body weight per day) to prevent malnutrition and maintain overall health. These supplements provide the necessary building blocks

for protein synthesis, ensuring that the patient receives sufficient nutrition despite the low intake of dietary protein.

Such a diet should be prescribed under close supervision, particularly with regular monitoring of nutritional status, electrolyte balance, and kidney function, to ensure that the patient does not experience adverse effects such as malnutrition, muscle wasting, or electrolyte imbalances. This strategy should only be pursued for patients who are willing and able to adhere to such a restrictive diet, as it requires significant lifestyle adjustments and commitment.

Do not prescribe low- or very low–protein diets in metabolically unstable people with CKD. In patients with metabolic instability, such as those with acute kidney injury (AKI), severe malnutrition, electrolyte disturbances, sarcopenia, cachexia or other critical conditions, prescribing a low- or very low-protein diet is not recommended. In these cases, the risk of further compromising the patient's nutritional status outweighs the potential benefits of reducing protein intake. These individuals may already be at risk for muscle wasting, fluid imbalances, and metabolic derangements that could be exacerbated by a restrictive diet.

The focus in metabolically unstable patients should be on stabilizing their condition, correcting any metabolic abnormalities, and addressing underlying issues. Once metabolic stability is achieved and the patient's overall health improves, dietary modifications, including the consideration of protein restrictions, can be reassessed.

In such cases, adequate caloric intake and balanced nutrition should take precedence over protein restriction. The use of nutritional support and individualized dietary guidance from renal dietitians or nutrition specialists can ensure that the patient maintains sufficient energy and protein intake, promoting recovery and avoiding further complications related to malnutrition.

In older adults with CKD, nutritional management should consider potential challenges stemming from simultaneous and

potentially conflicting risks of CKD progression and malnutrition/protein-energy wasting. In older adults, protein targets should be set after careful individual assessment to identify the most urgent clinical challenge.

Geriatric guidelines recommend protein intakes of 1.0–1.2 g/kg body weight/d to prevent age-related malnutrition and prevent sarcopenia. Such protein intakes may be appropriate in some people with stable or slowly progressing CKD, whose clinical picture is dominated by old age and related challenges to their nutritional and functional status. On the other hand, protein restriction may be appropriate in older adults whose primary clinical challenge is CKD with significant progression, provided they are metabolically stable. The course of action should consider patient preferences and when necessary, involve family members and caregivers.

Sodium Intake in CKD

In individuals with CKD, sodium intake plays a crucial role in managing fluid balance, BP, and overall kidney function. Excessive sodium intake can contribute to fluid retention, worsening hypertension, and accelerating the decline in kidney function. Therefore, it is generally recommended to restrict sodium intake to less than 2 grams per day (or <90 mmol of sodium per day, or <5 grams of sodium chloride per day) for people with CKD.

Reducing sodium intake can help lower BP, decrease edema, and reduce the burden on the kidneys. This can be especially important for individuals with hypertension, a major risk factor for CKD progression. Sodium restriction has also been shown to be beneficial in preventing or managing cardiovascular complications, which are common in individuals with CKD.

However, the amount of sodium restriction should be individualized based on the severity of CKD, the presence of comorbidities (such as heart failure or diabetes), and other clinical factors like hydration status and electrolyte levels.

Dietary sodium restriction is usually not appropriate for patients with sodium-wasting nephropathy. Sodium-wasting nephropathy is a condition in which the kidneys are unable to properly reabsorb sodium, leading to excessive sodium loss in the urine. This can result in hyponatremia, dehydration, and impaired fluid balance. In these cases, restricting sodium intake further could exacerbate the condition by increasing the risk of sodium depletion and electrolyte imbalances, which can be harmful. Patients with sodium-wasting nephropathy may need to increase their sodium intake to prevent these complications and maintain proper fluid and electrolyte balance.

Therefore, it is essential for healthcare providers to assess the underlying cause of CKD and tailor sodium recommendations based on the specific kidney pathology. For patients with sodium-wasting nephropathy, monitoring and adjusting sodium intake should be done under careful supervision to prevent adverse outcomes.

Questions for Self-Assessment

1. Why is a multifaceted approach essential in the management of CKD progression, and what are the main components of this strategy?
2. What is the recommended amount of moderate-intensity physical activity for people with CKD, and what are the benefits of engaging in such physical activity?
3. How can physical activity help manage cardiovascular health, muscle strength, and overall well-being in CKD patients?
4. How should physical activity recommendations be tailored for individuals with CKD?
5. How do factors such as age, ethnic background, comorbidities, and resource access influence the physical activity plan for CKD patients?
6. Why is it important for people with CKD to avoid sedentary behavior?

7. What simple strategies can healthcare providers recommend to patients with CKD to reduce the harmful effects of sedentary behavior?
8. How should physical activity recommendations be adjusted for CKD patients who are at higher risk of falls?
9. What are the benefits of aerobic and resistance exercises for CKD patients?
10. How should healthcare providers manage exercise programs for individuals with CKD and obesity?
11. Why is weight loss an important goal for CKD patients with obesity?
12. What precautions should be taken when advising CKD patients to lose weight, and why is gradual weight loss preferred over rapid weight loss?
13. How can a renal dietitian assist CKD patients in achieving weight loss while maintaining kidney health, and why is this approach important?
14. What role does exercise, both aerobic and resistance, play in supporting weight loss for CKD patients, and how does it benefit kidney function?
15. Why is it essential to regularly monitor kidney function during the weight loss process for CKD patients, and what potential risks should be avoided?
16. Why is a plant-based diet recommended for people with CKD, and what benefits does it offer in managing the disease?
17. How can a plant-based diet help reduce proteinuria, decrease metabolic acidosis, and improve cardiovascular health in CKD patients?
18. What are the risks associated with excessive consumption of animal-based foods for individuals with CKD?
19. Why should ultraprocessed foods be minimized or avoided for individuals with CKD?
20. What are the key nutrients that need to be managed carefully in the diet of people with CKD, and why is it important to

tailor dietary recommendations based on CKD severity and comorbid conditions?

21. How can renal dietitians assist CKD patients in managing sodium, phosphorus, potassium, and protein intake?
22. What is the recommended sodium intake for people with CKD, and how does excessive sodium intake impact kidney function and overall health?
23. How can high phosphorus levels in CKD patients affect bone mineral health and vascular calcification, and what dietary modifications can help control phosphorus levels?
24. Why is potassium management critical for individuals with CKD, and which foods should be limited to avoid elevated potassium levels?
25. How should protein intake be managed in individuals with CKD, particularly those at risk of progression to kidney failure?
26. What is the recommended protein intake for adults with CKD stages G3–G5, and what risks are associated with high protein intake?
27. What is a very low-protein diet, and when might it be considered for individuals with CKD?
28. Why is a very low-protein diet not recommended for patients who are metabolically unstable or have conditions like acute kidney injury (AKI)?
29. How should protein intake be managed in older adults with CKD, and what challenges should be considered when setting protein targets for this population?
30. What are the risks of restricting sodium intake too much in patients with sodium-wasting nephropathy, and how should sodium recommendations be adjusted for these individuals?

PHARMACOLOGICAL TREATMENT

Blood pressure management

For adults with CKD and high BP, controlling systolic BP (SBP) is crucial to slow disease progression and reduce the risk of cardiovascular events. Recent guidelines suggest that adults with CKD and high BP should aim for a target SBP of <120 mm Hg, provided this target is well tolerated by the patient. Achieving this target can help reduce the strain on the kidneys, slow the progression of kidney damage, and lower the risk of cardiovascular complications, such as heart attack and stroke.

This target of <120 mm Hg is especially important in patients with albuminuria, as managing BP at this level has been shown to decrease proteinuria and improve long-term kidney outcomes. BP control should be done using standardized office BP measurements, which are essential for accurate assessment and monitoring of treatment efficacy.

However, the ability to achieve and tolerate a target of <120 mm Hg may vary based on individual health status, other comorbidities, and age. Healthcare providers should tailor BP management to the specific needs and conditions of the patient, ensuring that any interventions do not cause harm or undue side effects.

While a target SBP of <120 mm Hg is recommended for most adults with CKD and high BP, it may not be appropriate for all patients. In individuals with frailty, high risk of falls and fractures, very limited life expectancy, or symptomatic postural hypotension, a less intensive BP-lowering therapy should be considered.

For frail individuals, who often have decreased reserves to tolerate medications or changes in BP, aggressive BP lowering may cause adverse effects such as dizziness, falls, or kidney injury. Postural hypotension is a particular concern for these patients, as it can increase the risk of falls, fractures, and associated complications. In such cases, slightly higher BP targets may be more appropriate to avoid these risks.

Similarly, for patients with limited life expectancy, the benefits of achieving a very low BP may be minimal, and aggressive BP management may lead to unnecessary discomfort or complications without significantly improving outcomes. For these patients, a more individualized approach to BP management should be adopted, considering both the potential benefits and harms of intensive BP lowering.

Healthcare providers should carefully assess the patient's overall health status, comorbidities, and goals of care when making decisions about BP treatment intensity.

Renin-Angiotensin-System Inhibitors (RASi)

The renin-angiotensin system (RAS) plays a central role in regulating BP, fluid balance, and kidney function. In CKD , the use of RASi, including angiotensin-converting enzyme inhibitors (ACEi) and angiotensin II receptor blockers (ARB), has been shown to reduce albuminuria, slow the progression of kidney damage, and improve cardiovascular outcomes.

For individuals with CKD (G1–G4) and severely increased albuminuria (A3), regardless of whether they have diabetes or not, RASi (ACE inhibitors or ARBs) are recommended as a first-line treatment. These medications help to reduce albuminuria and have been shown to slow down the progression of kidney damage. The recommendation is particularly strong, reflecting robust evidence supporting their effectiveness in severely increased albuminuria in CKD patients, even if they do not have diabetes.

For patients with CKD (G1–G4) and moderately increased albuminuria (A2), the use of RASi is suggested, though the evidence supporting this approach is less robust than for those

with severely increased albuminuria. This recommendation applies to patients without diabetes, but it still emphasizes the need for ACEi or ARB therapy in order to reduce albuminuria and slow CKD progression. The recommendation is based on the understanding that moderately increased albuminuria can still indicate significant kidney damage that warrants intervention, but the strength of evidence for this treatment is somewhat weaker compared to the severe albuminuria group.

For individuals with CKD (G1–G4) and moderately-to-severely increased albuminuria (A2 and A3), combined with diabetes, the recommendation to start RAS inhibitors (either ACEi or ARB) is strong. For patients with diabetes and albuminuria treatment with an ACEi or ARB may be considered even in case of normal BP. Diabetes is a well-known risk factor for kidney disease, and when coupled with increased albuminuria, it greatly raises the risk of further kidney deterioration. By starting RAS inhibitors, these patients can benefit from a reduction in proteinuria, which can significantly reduce the risk of progressive kidney failure. The evidence for this treatment approach is considered high, given the proven benefits of RASi in both diabetic and non-diabetic CKD patients with albuminuria.

Despite the efficacy of individual RAS inhibitors in managing CKD and albuminuria, it is strongly recommended that patients with CKD should avoid combining ACEi, ARB, and direct renin inhibitors (DRI). This combination therapy significantly increases the risk of hyperkalemia, acute kidney injury, and hypotension, particularly in patients with CKD. The potential harms of combination therapy outweigh the benefits, as studies have shown that this approach does not provide superior protection against CKD progression compared to using a single agent (ACEi or ARB) and significantly increases the risk of serious adverse effects. Therefore, this combination should be avoided in all CKD patients, regardless of diabetes status.

RASi (ACEi or ARB) should be administered using the highest approved dose that is tolerated to achieve the benefits described because the proven benefits were achieved in trials using these

doses. These benefits include slowing CKD progression, reducing proteinuria, and improving cardiovascular outcomes. When starting or adjusting doses of ACEi or ARB, healthcare providers should aim for the highest dose that the patient can tolerate, in order to maximize the potential benefits. It is important to monitor patients closely for any adverse effects, especially when increasing doses.

Changes in BP, serum creatinine, and serum potassium should be checked within 2–4 weeks of initiation or increase in the dose of a RASi, depending on the current GFR and serum potassium. After initiation of RASi therapy, patients typically experience an increase in serum creatinine and a corresponding decrease in GFR. However, in most patients, these values return to baseline values within 2–4 weeks. This period is critical to assess how the body is responding to the medication and to ensure there are no significant adverse effects, such as hypotension, acute kidney injury, or hyperkalemia. The timing and frequency of these checks may vary based on the patient's current GFR and serum potassium levels.

Hyperkalemia is a common side effect of RAS inhibitors. However, in many cases, hyperkalemia can be managed with interventions to lower potassium levels, such as dietary modifications, use of potassium-binding agents, or adjustments in other medications. Decreasing the dose or stopping the RASi is usually not necessary unless potassium levels cannot be controlled, as the benefits of RAS inhibitors outweigh the risks when managed appropriately.

ACEi or ARB therapy should generally be continued unless there is a significant rise in serum creatinine (more than 30% within 4 weeks) after starting or increasing the dose. A rise in serum creatinine beyond this threshold could indicate worsening kidney function and further investigation or dose adjustments may be required. Close monitoring during the first few weeks is essential to detect any adverse effects early.

In certain situations, it may be necessary to reduce the dose or discontinue ACEi or ARB therapy. This is particularly true if the

patient experiences symptomatic hypotension, uncontrolled hyperkalemia, or develops uremic symptoms while managing kidney failure. In patients with kidney failure (eGFR <15 ml/min per 1.73 m^2), the risks of continuing these medications might outweigh the benefits, and adjustments should be made to prevent further complications.

Consider starting people with CKD with normal to mildly increased albuminuria (A1) on RASi (ACEi or ARB) for specific indications (e.g., to treat hypertension or heart failure with low ejection fraction). While RAS inhibitors are typically used for patients with moderate to severe albuminuria, they may also be beneficial in patients with CKD and normal to mildly increased albuminuria (A1) for specific indications, such as hypertension or heart failure with low ejection fraction (LVEF). In these cases, ACEi or ARB therapy can help manage BP and cardiac function, even if the level of albuminuria is not significantly elevated. The decision to start these medications should be individualized based on the patient's comorbidities and overall health.

Although temporarily stopping RASi may be a valid treatment strategy for emergent hyperkalemia, it's advised to ensure the reinitiation of treatments once the adverse event is resolved, so that people are not deprived of a needed medication.

ACEi or ARB therapy should generally be continued in patients with CKD, even if their eGFR falls below 30 ml/min per 1.73 m^2. Studies have shown that these medications can still provide benefits in advanced stages of CKD by reducing albuminuria, slowing kidney function decline, and improving cardiovascular health. However, careful monitoring is essential, as patients in this stage may be more vulnerable to adverse effects such as hyperkalemia and hypotension.

Glycemic control

Glycemic monitoring and targets.

Monitoring long-term glycemic control by HbA1c twice per year is reasonable for patients with diabetes. HbA1c may be measured as often as 4 times per year if the glycemic target is not met or after a change in glucose-lowering therapy.

Accuracy and precision of HbA1c measurement declines with advanced CKD (G4–G5), particularly among patients treated by dialysis, in whom HbA1c measurements have low reliability.

A glucose management indicator (GMI) derived from continuous glucose monitoring (CGM) data can be used to index glycemia for individuals in whom HbA1c is not concordant with directly measured blood glucose levels or clinical symptoms.

Daily glycemic monitoring with CGM or self-monitoring of blood glucose (SMBG) may help prevent hypoglycemia and improve glycemic control when glucose-lowering therapies associated with risk of hypoglycemia are used.

For patients with T2D and CKD who choose not to do daily glycemic monitoring by CGM or SMBG, glucose-lowering agents that pose a lower risk of hypoglycemia are preferred and should be administered in doses that are appropriate for the level of eGFR.

CGM devices are rapidly evolving with multiple functionalities (e.g., real-time and intermittently scanned CGM). Newer CGM devices may offer advantages for certain patients, depending on their values, goals, and preferences.

It is important to individualize HbA1c target ranging from <6.5% to <8.0% in patients with diabetes and CKD not treated with dialysis.

Safe achievement of lower HbA1c targets (e.g., <6.5% or <7.0%) may be facilitated by CGM or SMBG and by selection of glucose-lowering agents that are not associated with hypoglycemia.

CGM metrics, such as time in range and time in hypoglycemia, may be considered as alternatives to HbA1c for defining glycemic targets in some patients.

Glucose-lowering therapies

Glycemic management for patients with T2D and CKD should include lifestyle therapy, first-line treatment with both metformin and a sodium-glucose cotransporter-2 inhibitor (SGLT2i), and additional drug therapy as needed for glycemic control.

Most patients with T2D, CKD, and eGFR ≥30 ml/min per 1.73 m2 would benefit from treatment with both metformin and an SGLT2i.

Patient preferences, comorbidities, eGFR, and cost should guide selection of additional drugs to manage glycemia, when needed, with glucagon-like peptide-1 receptor agonist (GLP-1 RA) generally preferred.

Metformin.

Patients with T2D, CKD, and eGFR ≥30 ml/min/1.73 m² should be treated with Metformin. Metformin is the first-line medication for managing T2D in patients with CKD who have an eGFR of 30 ml/min/1.73 m² or higher. It effectively lowers blood glucose levels, improves insulin sensitivity, and has cardiovascular benefits, making it suitable for individuals with diabetes and CKD. Using metformin in this population helps to reduce the progression of diabetes-related complications while minimizing the risk of adverse effects such as lactic acidosis, which is rare when appropriately monitored.

Kidney transplant recipients with T2D and an eGFR ≥30 ml/min/1.73 m² or higher should also be treated with metformin following the same guidance as non-transplant patients. Metformin is safe and beneficial for these individuals, provided their kidney function is stable and meets the eGFR threshold. Regular monitoring ensures safety, given the complexities associated with transplant patients, including immunosuppressive therapy and risk of graft dysfunction.

Patients receiving metformin should undergo regular eGFR monitoring to ensure ongoing safety and effectiveness of the treatment. When eGFR falls below 60 ml/min/1.73 m², there is an increased risk of drug accumulation and potential lactic acidosis, necessitating closer observation. Thus, eGFR monitoring frequency should be increased.

When a patient's eGFR drops below 45 ml/min/1.73 m², the dose of metformin should be reduced to lower the risk of drug accumulation and potential adverse effects, such as lactic acidosis. For patients with an eGFR between 45 and 59 ml/min/1.73 m², individualized dose adjustments may also be necessary based on their tolerance, overall health, and other risk factors. In these patients dose reduction may be considered in the presence of conditions that predispose patients to hypoperfusion and hypoxemia.

The maximum dose should be halved when the eGFR declines to 30–45 ml/min per 1.73 m². This ensures that patients continue to benefit from metformin while minimizing risks. Providers should be cautious and consider reducing the dose or discontinuing metformin if kidney function declines further.

Treatment should be discontinued when the eGFR declines to <30 ml/min per 1.73 m², or when the patient is initiated on dialysis, whichever is earlier.

Metformin interferes with intestinal vitamin B12 absorption and long-term use of this drug (over four years) is associated with a higher risk of vitamin B12 deficiency. This deficiency can lead to symptoms such as fatigue, neuropathy, and anemia, which may be particularly concerning in patients with CKD who are already at risk for similar complications. Regular monitoring of vitamin B12 levels helps to detect and address deficiencies early, ensuring optimal patient health and preventing complications that may mimic or exacerbate diabetic neuropathy. Supplementation should be provided as needed.

Sodium-glucose cotransporter-2 inhibitors (SGLT2i).

It is recommended to treat patients with T2D, CKD, and an eGFR ≥20 ml/ min per 1.73 m2 with an SGLT2i. These drugs have shown considerable benefits in managing CKD, including reducing the progression of kidney dysfunction, improving cardiovascular outcomes, and providing protective effects against both kidney failure and heart failure. However, there are specific considerations for their use, particularly in individuals with severe kidney dysfunction or during certain medical situations.

Once an SGLT2i is initiated, it is reasonable to continue an SGLT2i even if the eGFR falls below 20 ml/min per 1.73 m², unless it is not tolerated or kidney replacement therapy (KRT) is initiated. Research has shown that these medications can continue to provide benefits even when the eGFR falls below 20 ml/min per 1.73 m², a stage often associated with more severe CKD. Therefore, once an SGLT2i is started and well-tolerated, it is generally recommended to continue the medication unless the patient experiences adverse effects or begins KRT (e.g., dialysis or a kidney transplant). Continuing SGLT2i therapy at lower levels of kidney function is important to maintain its protective effects and prevent further kidney deterioration.

SGLT2 inhibitors work by promoting the excretion of glucose through the urine. During times of prolonged fasting, surgery, or critical medical illness, there is an increased risk of ketosis. SGLT2i use can increase the risk of diabetic ketoacidosis (DKA) or euglycemic ketoacidosis, particularly during periods when the body is under stress or when glucose intake is severely restricted (e.g., during fasting or surgery). Therefore, it is reasonable to withhold the use of SGLT2i during these situations until the patient's condition stabilizes. This precaution helps mitigate the risk of adverse metabolic disturbances, including ketoacidosis, which can be life-threatening if not managed promptly.

In general, it is recommended to treat adults with CKD with an SGLT2i for the following:

- eGFR ≥20 ml/min per 1.73 m² with urine ACR ≥200 mg/g (≥20 mg/mmol), or

- heart failure, irrespective of the level of albuminuria.

SGLT2 inhibitors (e.g., dapagliflozin, empagliflozin) are highly recommended for adults with CKD who meet specific criteria. One of the main indications for starting SGLT2i treatment is having an eGFR of ≥20 ml/min per 1.73 m² combined with significant albuminuria (urine ACR ≥200 mg/g or ≥20 mg/mmol). Furthermore it is considered safe to even initiate an SGLT2i when the eGFR falls below 20 ml/min per 1.73 m2 and continue their use until the time KRT is initiated. This is because SGLT2 inhibitors have been shown to reduce kidney disease progression and improve outcomes for individuals with significant proteinuria.

Additionally, heart failure is another key indication for SGLT2i treatment, irrespective of the level of albuminuria. This reflects the broad efficacy of SGLT2 inhibitors in heart failure management, where they have demonstrated benefits in heart failure Therefore, adults with CKD and heart failure are encouraged to start SGLT2i therapy as part of comprehensive treatment, independent of the degree of albuminuria.

When initiating SGLT2 inhibitors, a reversible decrease in eGFR is commonly observed. This initial reduction is typically transient and does not reflect worsening kidney function in the long term. Therefore, this initial decrease in eGFR is generally not an indication to stop the therapy.

Importantly, SGLT2i use does not require changing the routine monitoring frequency for CKD. Standard monitoring of eGFR and albuminuria should continue as per usual clinical practice. CKD progression and therapeutic decisions should be guided by ongoing assessment of kidney function, with close attention to changes in albuminuria, rather than focusing solely on the transient eGFR decrease at the start of treatment. This ensures that patients benefit from SGLT2 inhibitors without unnecessary interruptions in therapy.

In addition to patients with higher levels of albuminuria (ACR ≥200 mg/g or ≥20 mg/mmol) and those with heart failure, SGLT2 inhibitors (SGLT2i) are also recommended for adults with CKD who have an eGFR between 20 and 45 ml/min per 1.73 m² and

urine ACR <200 mg/g (<20 mg/mmol). The benefits of SGLT2 inhibitors in this group of patients include reducing the risk of CKD progression, improving cardiovascular outcomes, and potentially reducing mortality. These medications help slow the progression of kidney disease by inhibiting the reabsorption of glucose in the kidneys, which also has the added benefit of reducing blood sugar levels, as well as lowering BP.

Mineralocorticoid receptor antagonists (MRA).

Using a nonsteroidal MRA (finerenone) with proven kidney or cardiovascular benefits for adults with T2D, an eGFR >25 ml/min per 1.73 m^2, normal serum potassium concentration, and albuminuria (>30 mg/g or >3 mg/mmol) is suggested, despite being on the maximum tolerated dose of a renin-angiotensin system inhibitor (RASi).

Nonsteroidal MRAs are most appropriate for adults with T2D who are at high risk of CKD progression and cardiovascular events, as shown by persistent albuminuria despite other standard-of-care therapies. This population is at significant risk for kidney deterioration and heart-related issues, and adding a nonsteroidal MRA can help mitigate these risks.

A nonsteroidal MRA may be used in conjunction with RASi and SGLT2i to treat T2D and CKD in adults, providing a more comprehensive approach to managing both diabetes-related kidney disease and associated cardiovascular risks.

To reduce the risk of hyperkalemia, it's essential to select patients with consistently normal serum potassium levels and regularly monitor serum potassium levels after initiating nonsteroidal MRA therapy. Since MRAs can increase potassium levels, careful monitoring helps prevent dangerous elevations in potassium, which can lead to cardiac arrhythmias and other complications.

When choosing a nonsteroidal MRA, priority should be given to agents with documented benefits for both kidney protection and cardiovascular health. These medications are specifically designed to target the mineralocorticoid receptor, which plays a key role in

regulating BP, sodium balance, and fluid retention, all of which are crucial in patients with both CKD and T2D.

While steroidal MRAs (spironolactone, eplerenone) can be used for conditions such as heart failure, hyperaldosteronism, or refractory hypertension, they can lead to hyperkalemia or a temporary decline in GFR , particularly in patients with a low GFR. As a result, steroidal MRAs should be used with caution, especially in individuals with significant renal impairment.

Glucagon-like peptide-1 receptor agonists (GLP-1 RA).

In adults with T2D and CKD who have not achieved their individualized glycemic targets despite the use of metformin and SGLT2 inhibitors, or in those who are unable to use these medications, a long-acting GLP-1 receptor agonist (GLP-1 RA) are recommended.

When selecting a GLP-1 RA, the priority should be to choose agents with documented cardiovascular benefits. Many GLP-1 RA, particularly those with long-acting formulations, have been shown to reduce the risk of major cardiovascular events such as heart attack, stroke, and cardiovascular death in patients with T2D and CKD. This makes them an ideal choice for individuals who are at high risk for both diabetes complications and cardiovascular disease. Long-acting GLP-1 RAs are prioritized ahead of insulin in people with T2D and CKD. GLP-1 RAs with proven cardiovascular benefit that do not require dose adjustment in CKD include liraglutide, semaglutide (injectable), and dulaglutide.

Metabolic acidosis

Metabolic acidosis, characterized by a decrease in serum bicarbonate, is a common complication in CKD. It can lead to several adverse effects, such as bone mineral loss, muscle wasting, worsening kidney function, and an increased risk of cardiovascular disease.

In people with CKD, consider using pharmacological treatment with or without dietary interventions to prevent the development of metabolic acidosis, particularly when serum bicarbonate levels fall below 18 mmol/l in adults. Early intervention with appropriate medications, such as sodium bicarbonate or potassium citrate, and adjustments to dietary intake can help correct the imbalance and improve patient outcomes. Potassium-based formulations can cause hyperkalemia in CKD, although they can be used if hypokalemia is present. Hence, close monitoring of potassium is warranted.

Monitor the treatment for metabolic acidosis carefully to ensure that it does not result in serum bicarbonate concentrations exceeding the upper limit of normal. Excessive alkalinization could have detrimental effects on BP control, serum potassium levels, and fluid status. Close monitoring is essential to adjust the dosage of bicarbonate supplements or other alkalizing agents to avoid overcorrection. For instance, a significant increase in bicarbonate may lead to alkalosis, which can cause adverse effects like hypokalemia, muscle cramps, and altered cardiac rhythm, as well as impact BP regulation. Balancing the bicarbonate levels is critical in CKD management to prevent both acidosis and alkalosis, optimizing kidney and cardiovascular health.

Dietary modifications that limit the consumption of acid-rich foods and/or increase the intake of alkaline-rich foods reduce the net endogenous acid production and can serve as an additional strategy to control metabolic acidosis in people with CKD.

Hyperkalemia

Hyperkalemia is uncommon when the eGFR is >60 ml/min per 1.73 m^2 and increases with lower GFR.

It is crucial to be aware of the variability in potassium laboratory measurements. Various factors can influence potassium

levels in the blood, and these should be considered when interpreting test results. These factors include:

- **Diurnal variation**. Potassium levels can fluctuate throughout the day, typically being higher in the morning and lower in the evening.
- **Seasonal variation**. Potassium levels may change with seasons, potentially due to diet, hydration status, and other environmental factors.
- **Sample type**. Differences between plasma and serum samples (with serum values being typically higher) can affect potassium measurement accuracy.
- **Medications**. Certain drugs, such as potassium-sparing diuretics, ACE inhibitors, Heparin, ARBs, and nonsteroidal anti-inflammatory drugs (NSAIDs), can increase potassium levels. Conversely, diuretics like furosemide can lower potassium.

When managing nonemergent hyperkalemia, it is essential to consider the local availability or formulary restrictions of pharmacologic agents that can help manage elevated potassium levels. Potassium exchange agents, such as sodium polystyrene sulfonate, sodium zirconium cyclosilicate and patiromer, are commonly used to lower potassium but may not always be readily available or accessible depending on the healthcare system or region. Alternative options for hyperkalemia management should be considered in such situations, keeping in mind the cost, efficacy, and tolerability of the available treatments.

Once moderate or severe hyperkalemia has been identified in an adult, timing for rechecking potassium levels is critical. Regular monitoring should occur to evaluate the effectiveness of interventions and ensure that potassium levels are returning to a safe range. The timing of follow-up potassium checks will depend on the initial potassium level, the treatment initiated, and the clinical context, but it should generally be done within 2–4 hours after emergency treatments or after adjusting medications. For non-emergent hyperkalemia, follow-up measurements may be

scheduled within 24 hours to assess the ongoing impact of dietary and pharmacologic treatments.

For people with CKD G3–G5 and emergent hyperkalemia, an individualized approach should be implemented. This approach should incorporate both dietary and pharmacologic interventions, taking into account the patient's comorbidities, quality of life (QoL), and specific treatment goals. Renal dietitians or accredited nutrition providers should be involved in assessment and education to provide personalized recommendations on potassium management. This is particularly important for those with severe CKD, where both dietary restriction of potassium and medications may be necessary to prevent life-threatening levels of potassium.

For people with CKD G3–G5 who have a history of hyperkalemia, or for those at risk during certain stages of the disease, dietary interventions should aim to limit the intake of foods rich in bioavailable potassium (highly processed foods, meats, dairy products, juices, and salt substitutes made with potassium chloride) which can exacerbate hyperkalemia. Prevention strategies should be implemented during times when the risk of hyperkalemia is higher (e.g., during acute illness or after adjustments in medications). A focus on whole, unprocessed foods, which generally have lower potassium content, and ensuring appropriate potassium monitoring can help manage levels and prevent complications.

Hyperuricemia

Acid-lowering interventions should be offered for individuals with CKD who present with symptomatic hyperuricemia. Elevated uric acid levels can lead to gout and contribute to CKD progression, especially when symptomatic. Managing hyperuricemia in these patients can help prevent further kidney damage and alleviate symptoms associated with gout, such as joint pain and inflammation.

Consider initiating uric acid-lowering therapy after the first episode of gout, particularly when there is no avoidable precipitant (e.g., dehydration or excessive alcohol intake) or when the serum uric acid concentration exceeds 9 mg/dL (535 μmol/L). The risk of developing chronic gout and kidney damage increases with prolonged hyperuricemia, so early intervention is beneficial to reduce the burden of disease.

For people with CKD and symptomatic hyperuricemia, xanthine oxidase inhibitors (e.g., allopurinol or febuxostat) should be preferred over uricosuric agents. Uricosuric agents (probenecid) increase the excretion of uric acid by the kidneys, but they may not be as effective in people with compromised renal function and may pose risks, such as increasing the risk of kidney stones. Xanthine oxidase inhibitors, on the other hand, work by reducing the production of uric acid, making them a safer and more effective choice in individuals with CKD. In one double-blind randomized trial (CARES) it was shown that the overall mortality and cardiovascular mortality were higher in the febuxostat group than in the allopurinol group.

For the symptomatic treatment of acute gout in patients with CKD, low-dose colchicine or intra-articular/oral glucocorticoids are preferred over NSAIDs. Nonsteroidal anti-inflammatory drugs (NSAIDs) can exacerbate kidney dysfunction, especially in those with existing CKD, and should be avoided when possible. Colchicine and glucocorticoids offer effective relief from acute gout attacks while minimizing the risk of further kidney damage. For colchicine, the US Food and Drug Administration (FDA)-approved dosing (1.2 mg immediately followed by 0.6 mg an hour later, with ongoing anti-inflammatory therapy until the flare resolves). Dose adjustment should be considered for CKD G5. Short courses of glucocorticoids titrated to symptoms response (e.g., 30 mg prednisolone orally for 3–5 days) could be used as an alternative.

In addition to pharmacological treatments, nonpharmacological interventions can help prevent gout and reduce uric acid levels. This includes:

- Limiting alcohol intake. Alcohol, particularly beer, can increase uric acid levels.
- Reducing intake of meats. Reducing consumption of purine-rich foods (such as organ meats, red meat, and seafood) can help decrease uric acid production.
- Avoiding high-fructose corn syrup. High-fructose corn syrup, often found in processed foods and sugary beverages, can increase uric acid levels and exacerbate gout.

These dietary changes, when combined with medical treatments, can play a significant role in managing and preventing gout in people with CKD.

Avoid using uric acid-lowering agents in asymptomatic hyperuricemia for CKD progression. While elevated uric acid levels are associated with CKD progression, there is insufficient evidence to support the routine use of uric acid-lowering therapy in individuals who are asymptomatic (i.e., no signs of gout or related symptoms). Therefore, treatment should focus on symptomatic patients or those with a history of gout, rather than those without symptoms.

Lipid management

For adults aged 50 years or older with CKD and an eGFR <60 ml/min/1.73 m² (G3a-G5), but who are not on chronic dialysis or kidney transplantation, it is recommended to start treatment with a statin or a statin/ezetimibe combination. This population is at high risk for cardiovascular disease (CVD), and lipid-lowering treatment can significantly reduce the risk of heart attacks, strokes, and cardiovascular mortality.

For adults aged 50 or older with CKD and an eGFR ≥60 ml/min/1.73 m² (G1-G2), treatment with a statin is recommended. Even in the absence of severe kidney impairment, statin therapy is beneficial in reducing cardiovascular events in patients with CKD,

as they are still at increased risk for heart disease, stroke, and vascular complications.

For adults aged 18–49 years with CKD but not on dialysis or transplantation, statin therapy is suggested in the presence of one or more of the following risk factors:

- known coronary artery disease (history of myocardial infarction or coronary revascularization),
- diabetes mellitus,
- prior ischemic stroke, or
- estimated 10-year incidence of coronary death or nonfatal myocardial infarction >10%.

These individuals are at a higher cardiovascular risk and may benefit from early initiation of statin therapy to prevent future heart attacks and strokes.

Estimate the 10-year cardiovascular risk using a validated risk tool. CKD patch for the Systematic Coronary Risk Evaluation (SCORE) tool and the American Heart Association PREVENT, equations are the only ones validated. This helps guide statin therapy decisions, especially in patients aged 18-49 years with CKD.

When choosing statin-based regimens, aim to maximize the reduction in low-density lipoprotein (LDL) cholesterol. This strategy is intended to achieve the largest treatment benefit in reducing the risk of cardiovascular events and preventing disease progression in CKD patients. Higher LDL reduction is associated with a decreased risk of both heart disease and kidney function decline.

For adults aged 18-49 years with CKD, statin therapy may still be appropriate even with a lower risk (i.e., an estimated 10-year risk of <10% for coronary death or nonfatal myocardial infarction). The decision to initiate statins in this group should consider individual risk factors, including other comorbidities such as diabetes, hypertension, or previous cardiovascular events.

For people with CKD who meet the indications for proprotein convertase subtilisin/kexin type 9 (PCSK-9) inhibitors (e.g., those who cannot tolerate statins or require additional lipid-lowering),

these medications should be considered. PCSK-9 inhibitors can significantly lower LDL cholesterol and are used in high-risk individuals, particularly when statins alone do not achieve desired lipid targets. Current examples of recommendations for the use of PCSK-9 inhibitors from the cardiology community (and licensed indications) include as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or for people with clinical atherosclerotic cardiovascular disease (ASCVD) who require additional lowering of LDL cholesterol.

Along with lipid-modifying therapy, consider recommending a plant-based "Mediterranean-style" diet for people with CKD. This diet emphasizes fruits, vegetables, whole grains, nuts, seeds, legumes, and healthy fats, and has been shown to reduce cardiovascular risk. It is an appropriate adjunct to pharmacologic therapy for heart disease prevention in CKD patients.

Antiplatelet therapy in CKD

For people with CKD and established ischemic cardiovascular disease (e.g., myocardial infarction, coronary revascularization), oral low-dose aspirin is recommended for secondary prevention of recurrent ischemic cardiovascular events. Aspirin helps reduce the risk of further heart attacks and stroke in individuals who have already experienced a cardiovascular event.

If a patient with CKD is intolerant to aspirin, consider using other antiplatelet therapies, such as $P2Y_{12}$ inhibitors (e.g., clopidogrel). These medications can serve as an alternative for preventing further cardiovascular events in individuals who cannot tolerate aspirin due to side effects such as gastrointestinal bleeding or intolerance.

CKD and atrial fibrillation

Follow established strategies for the diagnosis and management of atrial fibrillation:

- **Step 1. Diagnosis -** In people with CKD, use opportunistic pulse-based screening (e.g., taking at when measuring BP), followed by a 12-lead ECG if an irregularly irregular pulse is identified. If reported symptoms suggest atrial fibrillation, but a 12-lead ECG is nondiagnostic, request Holter ECG testing.
- **Step 2. Prophylaxis against stroke and systemic thromboembolism -** Oral anticoagulation (with necessary dose adjustment, depending on eGFR and stage of CKD) should be considered for preventing stroke in people with CKD with atrial fibrillation (they are likely to have an increased CHA2DS2-VASc risk factor for stroke and are at high risk even with a score of 0-1). A bleeding risk score (e.g., HAS-BLED score) should be considered to identify modifiable risk factors which can be managed (e.g., alcohol advice, use of a proton pump inhibitor).
- **Step 3. Rate/rhythm control -** Consider reversible causes of atrial fibrillation. Use medical therapy (e.g., beta blockade) to control ventricular rate to less than about 90 bpm at rest to decrease symptoms and related complications. For people with persistent symptoms despite adequate rate control, consider rhythm control with cardioversion, antiarrhythmic therapy and/or catheter ablation.

In people with CKD G1–G4 (eGFR ≥15 ml/min/1.73 m²), it is recommended to use non-vitamin K antagonist oral anticoagulants (NOACs) rather than traditional vitamin K antagonists (e.g., warfarin) for thromboprophylaxis in atrial fibrillation. NOACs, such as apixaban, dabigatran, rivaroxaban, and edoxaban, offer several advantages over warfarin, including:

- Lower risk of major bleeding,
- Fewer dietary restrictions (no need for routine vitamin K monitoring),
- No need for frequent INR testing, and

- More predictable pharmacokinetics.

NOACs are increasingly preferred in patients with atrial fibrillation, as they have been shown to be effective and safer than warfarin in preventing stroke and thromboembolic events in individuals with CKD.

The dose of NOACs should be adjusted according to the patient's kidney function (eGFR). For patients with CKD G4–G5 (eGFR <30 ml/min/1.73 m^2), extra caution is required. Renal function can significantly affect the metabolism and clearance of NOACs, and impaired kidney function can increase the risk of drug accumulation, leading to bleeding complications. Thus, it is important to:

- monitor renal function regularly, especially in those with advanced CKD,
- adjust the NOAC dose accordingly to ensure both safety and effectiveness, and
- consider alternative therapies if kidney function declines significantly (e.g., dialysis patients).

Different NOACs have varying requirements for dose adjustment based on renal function, so it is essential to refer to the specific product guidelines for each drug.

When discontinuing NOACs prior to an elective procedure, the timing of discontinuation must take into account:

- the bleeding risk of the procedure,
- the specific NOAC prescribed, and
- the patient's kidney function (eGFR).

For elective surgeries or procedures, it is crucial to balance the risk of thromboembolism (e.g., stroke in atrial fibrillation) with the risk of bleeding. The timing of NOAC discontinuation will depend on the half-life of the drug and the patient's renal function:

- In patients with lower eGFR, the drug may stay in the system longer, increasing bleeding risk.
- For high-bleeding-risk procedures, NOACs may need to be discontinued several days in advance, while for lower-risk procedures, the discontinuation window can be shorter.

Questions for Self-Assessment

1. What is the recommended target systolic blood pressure (SBP) for adults with CKD and high BP, and what is the rationale for this target?
2. How does albuminuria influence blood pressure management in CKD patients?
3. In what scenarios might a less intensive BP-lowering therapy be considered for CKD patients?
4. What are the potential risks of aggressive BP lowering in frail individuals or those with postural hypotension?
5. Why is BP control essential for patients with CKD in terms of cardiovascular outcomes?
6. What is the role of standardized office BP measurements in assessing treatment efficacy?
7. For patients with frailty or limited life expectancy, how should BP management differ?
8. Which RAS inhibitors are recommended for individuals with CKD (G1–G4) and severely increased albuminuria (A3)?
9. Why should patients with CKD avoid combining ACE inhibitors (ACEi), ARBs, and direct renin inhibitors (DRIs)?
10. What monitoring is essential after starting or increasing the dose of a RAS inhibitor (ACEi or ARB)?
11. What are the potential side effects of RAS inhibitors, and how can they be managed?
12. Why should ACEi or ARB therapy be continued in patients with CKD, even with reduced eGFR below 30 ml/min per 1.73 m^2?
13. In which situations might ACEi or ARB therapy need to be reduced or discontinued in CKD patients?
14. How can hyperkalemia be managed in patients on RAS inhibitors?
15. What is the recommended frequency for monitoring long-term glycemic control (HbA1c) in patients with diabetes and CKD?

16. How does the accuracy of HbA1c measurement change in patients with advanced CKD (G4–G5), especially those on dialysis?
17. What are the advantages of using continuous glucose monitoring (CGM) in managing glycemia for CKD patients?
18. Why might daily glycemic monitoring by CGM or SMBG be necessary for some patients with T2D and CKD?
19. What is the ideal HbA1c target for patients with diabetes and CKD not on dialysis?
20. How can CGM metrics like time in range and time in hypoglycemia be used to guide glycemic control in certain patients?
21. What is the role of metformin in managing type 2 diabetes (T2D) in patients with CKD, and when should the dose be adjusted?
22. Why is metformin not recommended for patients with CKD when their eGFR falls below 30 ml/min/1.73 m^2?
23. What are the potential side effects of long-term metformin use in CKD patients, and how can they be managed?
24. What is the role of sodium-glucose cotransporter-2 inhibitors (SGLT2i) in managing CKD with T2D?
25. What are the risks associated with using SGLT2 inhibitors during periods of fasting, surgery, or critical illness?
26. How does the initial decrease in eGFR after starting SGLT2 inhibitors affect treatment decisions?
27. Why is it important to continue monitoring eGFR and albuminuria in CKD patients taking SGLT2 inhibitors?
28. In patients with CKD and heart failure, how do SGLT2 inhibitors improve outcomes, and when should these medications be considered?
29. What is the primary indication for using nonsteroidal mineralocorticoid receptor antagonists (MRAs) in patients with Type 2 Diabetes (T2D) and chronic kidney disease (CKD)?
30. Which factors should be considered before starting a nonsteroidal MRA in patients with T2D and CKD?

31. What are the potential risks associated with using steroidal MRAs in patients with renal impairment?
32. How do nonsteroidal MRAs contribute to managing CKD and cardiovascular risks in T2D patients?
33. In which patient populations are long-acting GLP-1 receptor agonists recommended for managing T2D and CKD?
34. What cardiovascular benefits do long-acting GLP-1 receptor agonists offer for T2D patients with CKD?
35. Which GLP-1 receptor agonists are considered suitable for patients with CKD, and why?
36. What is metabolic acidosis, and why is it a concern in CKD?
37. What treatment options are available for correcting metabolic acidosis in people with CKD?
38. What precautions should be taken to avoid overcorrecting metabolic acidosis and causing alkalosis?
39. How does the eGFR influence the risk of hyperkalemia in CKD patients?
40. Which factors should be considered when interpreting potassium levels in CKD patients?
41. What are the monitoring strategies and treatments for managing hyperkalemia in patients with CKD?
42. When should uric acid-lowering therapy be initiated in CKD patients with hyperuricemia?
43. Why is xanthine oxidase inhibitor therapy preferred over uricosuric agents for CKD patients with hyperuricemia?
44. What dietary modifications can help reduce uric acid levels in patients with CKD?
45. At what age and eGFR levels should statin therapy be initiated in CKD patients to reduce cardiovascular risks?
46. Which risk factors should be considered when initiating statin therapy for CKD patients aged 18–49 years?
47. How do PCSK-9 inhibitors fit into lipid management for high-risk CKD patients who cannot tolerate statins?
48. What is the role of low-dose aspirin in preventing ischemic cardiovascular events in CKD patients?

49. Which alternatives to aspirin are considered for patients with CKD who are intolerant to aspirin?
50. How should atrial fibrillation be diagnosed and managed in CKD patients?
51. Why are non-vitamin K antagonist oral anticoagulants (NOACs) preferred over vitamin K antagonists in CKD patients with AF?
52. What considerations should be taken into account when adjusting NOAC doses in patients with advanced CKD?
53. What are the key factors to consider when discontinuing NOACs before an elective procedure in CKD patients?

MEDICATION MANAGEMENT AND DRUG STEWARDSHIP IN CKD

Medication choices and monitoring for safety

People with CKD are often more vulnerable to the nephrotoxic effects of certain medications. This heightened sensitivity can lead to acute kidney injury (AKI) or exacerbate the progression of existing kidney disease. Therefore, when prescribing medications with known nephrotoxic potential (like NSAIDs, nephrotoxic antivirals, and bisphosphonates), healthcare providers must always weigh the benefits against the potential harms. While some medications may be necessary for treating other conditions, alternative treatments with less risk to kidney function should be considered. The goal is to minimize harm while ensuring the effectiveness of treatment.

For people with CKD who are prescribed medications with narrow therapeutic windows or those known to be potentially nephrotoxic, it is essential to monitor eGFR, electrolytes, and therapeutic medication levels (when applicable). This includes routine follow-up in both outpatient and hospital settings to detect any early signs of renal impairment or adverse reactions. Regular monitoring ensures that medications are not contributing to further kidney damage and allows for prompt adjustments to the dosage or switching to alternative treatments when necessary. Close attention should be paid to medications like ACEi, ARBs, lithium, methotrexate, NSAIDs, diuretics, and antibiotics, which are commonly implicated in kidney-related adverse effects.

People with CKD should be cautious with over-the-counter (OTC) medications, as well as dietary supplements and herbal remedies, many of which can adversely affect kidney function. These products may contain ingredients that are nephrotoxic or interfere with prescribed treatments, leading to drug interactions or worsening of kidney disease. Therefore, healthcare providers should review the full range of substances the patient is using, including OTC drugs, vitamins, herbal supplements, and dietary remedies, to ensure that they do not pose a risk to kidney health. Educating patients about the potential harms of unregulated substances can help reduce preventable kidney damage.

For women with CKD who are of childbearing potential, it is crucial to review the teratogenicity of any prescribed medications. Pregnancy may pose a risk of CKD progression for people with established CKD. On the other hand many drugs can have harmful effects on both pregnancy and fetal development. In addition to reviewing the safety of medications, healthcare providers should offer regular reproductive counseling that aligns with the patient's values and preferences. This may include guidance on contraception options, as well as discussions about the timing of pregnancy, the potential risks to kidney function during pregnancy, and the need for close monitoring of CKD during gestation. Early planning and counseling can help ensure safer outcomes for both the patient and the unborn child.

Dose adjustments by level of GFR

When prescribing medications that are primarily eliminated through the kidneys (or their active metabolites are excreted by the kidneys), it is essential to take the GFR into account. Kidney function, as indicated by GFR, directly influences the body's ability to clear certain drugs. If the kidneys are not functioning optimally, medications may accumulate in the bloodstream, leading to toxicity or adverse effects. Therefore, adjusting the

dose or selecting alternative medications based on a patient's GFR is crucial in managing medications cleared by the kidneys effectively.

For most people and clinical scenarios, the use of validated eGFR equations, which typically rely on serum creatinine (SCr), is sufficient for drug dosing. These equations are widely used in practice because they provide a reliable estimate of kidney function, which in turn informs dosing decisions for medications that are renal-dependent. For the vast majority of patients, eGFR based on serum creatinine is adequate for determining drug dosing adjustments, ensuring safety and efficacy.

In situations where greater precision is required – such as for drugs with a narrow therapeutic range, where the risk of toxicity is high, or in clinical cases where eGFR estimates may be unreliable – it may be necessary to use equations that combine both creatinine and cystatin C or to directly measure GFR. These more sophisticated methods provide a more accurate representation of kidney function, enabling safer and more precise dosing decisions. This is particularly important for patients receiving high-risk medications or those with conditions where standard eGFR equations may not provide accurate results (e.g., severe malnutrition, obesity, or extremes in age).

In patients with extremes of body weight, the use of eGFR values that are non-indexed for body surface area (BSA) may be more appropriate. This approach can be crucial for individuals with either obesity or low body weight, as their BSA may significantly differ from the standard population. This adjustment ensures more accurate drug dosing, particularly for medications with a narrow therapeutic window or those that require a minimum concentration to be effective. By considering BSA, clinicians can optimize drug therapy while reducing the risk of toxicity or insufficient efficacy.

Nonindexed eGFR can be obtained by multiplying the indexed eGFR results by the person’s BSA and dividing by 1.73 m^2, or by using an appropriate online calculator.

When the GFR or the volume of distribution (Vd) is not in a steady state – for example, during periods of acute illness or dehydration – drug dosing should be carefully adapted. In such situations, the body's ability to clear medications can be altered, leading to fluctuations in drug levels and potentially harmful effects. Adjustments should be made based on the patient's current kidney function and clinical status, and clinicians should monitor for signs of under- or over-dosing, especially for drugs with a narrow therapeutic index.

People with CKD often take multiple medications due to the presence of comorbid conditions and complex disease management needs. This increases the risk of drug interactions, adverse effects, and non-adherence. Therefore, it is essential to perform a thorough medication review periodically and whenever there is a transition of care (e.g., hospital admission or discharge). This review should assess whether the medications are still indicated, whether they are being taken as prescribed, and whether any interactions or side effects could be complicating the management of CKD or other health conditions. Regular reviews help ensure that the medication regimen is optimized and safe.

When medications are temporarily discontinued during acute illness or a medical procedure, it is important to have a clear plan for when to restart those medications. This includes communicating the plan to both the affected person and the healthcare providers involved. Documentation of this plan should be included in the medical record to prevent confusion or delays in resuming treatment. Failure to restart essential medications after an acute event (such as surgery or hospitalization) can lead to unintended harm, such as exacerbation of kidney disease or the underlying condition.

In the 48–72 hours prior to elective surgery or during the acute management of adverse effects, certain medications (e.g., metformin, ACE inhibitors, ARBs, SGLT2 inhibitors) may need to be temporarily discontinued to prevent complications. This is especially important in cases where medications might interfere with kidney function, BP regulation, or fluid balance. However, it

is crucial to note that failure to restart these medications after surgery or the acute event could lead to detrimental effects, such as worsened kidney function, uncontrolled BP, or increased risk of cardiovascular events. A well-coordinated plan should ensure that these medications are appropriately resumed after the event.

Strategies to promote drug stewardship in CKD management

Effective drug stewardship is essential in optimizing medication use and minimizing risks, particularly for individuals with CKD. People with CKD often take multiple medications to manage various aspects of their condition and comorbidities, which can increase the risk of adverse effects, drug interactions, and non-adherence. To improve patient outcomes and ensure safe medication use, several strategies can be employed.

Education plays a crucial role in promoting drug stewardship. It is important to educate patients with CKD on both the benefits and risks of the medications they are prescribed. Patients need to understand the potential adverse effects that can arise from their medications, especially given their kidney condition, as CKD can alter drug metabolism and excretion.

When patients are well-informed, they are more likely to identify and report any adverse events promptly, which can be managed early to prevent further complications. Education should cover:

- How medications work and their intended benefits.
- Possible side effects and symptoms to watch for.
- The importance of adherence to prescribed regimens and timely follow-up for monitoring.
- How to report adverse reactions or new symptoms, and the importance of ongoing communication with healthcare providers.

This knowledge empowers patients to actively participate in their own healthcare, potentially preventing harmful outcomes associated with improper medication use.

Promoting effective drug stewardship for people with CKD involves collaborative relationships among healthcare providers, including doctors, nurses, pharmacists, and other specialists. By working together, healthcare teams can ensure that the medications prescribed are appropriate, safe, and well-tolerated, considering the complexities of managing CKD.

Pharmacists, in particular, play a critical role in:

- Reviewing medications for potential interactions or contraindications.
- Ensuring that dosing adjustments are made based on kidney function.
- Monitoring for side effects, especially those related to renal function, electrolyte imbalances, and drug toxicity.
- Offering patient education on medication adherence and proper use.

Healthcare teams should also utilize tools and resources – such as clinical guidelines, medication databases, and medication therapy management systems–to support comprehensive medication reviews. This collaborative approach can improve medication safety, reduce polypharmacy risks, and optimize therapy for people with CKD.

Imaging studies in CKD management

Imaging studies are critical for diagnosing and managing CKD, but they also present potential risks, particularly when radiocontrast agents are used. People with CKD are at an increased risk for contrast-associated AKI, and other complications from imaging procedures, especially those involving contrast media. The use of imaging in this population should therefore be approached with caution, ensuring that the

benefits outweigh the risks. The following practice points provide guidance for appropriate imaging study use in individuals with CKD.

When considering imaging studies, healthcare providers should evaluate the clinical indication in line with general population guidelines. However, for individuals with CKD, the risks and benefits should be carefully weighed on an individual basis. CKD may modify the safety of certain imaging techniques, especially those requiring contrast agents. For example, procedures like CT scans, angiograms, or MRIs that involve radiocontrast may pose a higher risk of kidney damage in people with reduced kidney function.

Thus, imaging should only be pursued when the clinical benefit of the study outweighs the potential harm from exposure to contrast agents, particularly when the patient's eGFR is lower, indicating a more compromised kidney function. In all cases, alternative imaging options that do not use contrast agents (e.g., ultrasound or non-contrast MRI) should be considered where appropriate.

People with CKD are particularly vulnerable to AKI when undergoing procedures that involve intra-arterial contrast agents, such as cardiac procedures (e.g., coronary angiography). To mitigate the risk, it is essential to assess each patient's risk for AKI prior to administering contrast media.

Validated tools, such as Mehran Contrast-Induced Nephropathy (CIN) Risk Score, can help clinicians evaluate the likelihood of AKI in people with CKD.

Once the risks are assessed, steps can be taken to optimize kidney protection, such as using the smallest possible contrast volume, hydrating the patient appropriately, and ensuring close monitoring of kidney function post-procedure.

For individuals with CKD (specifically those with GFR <60 ml/min per 1.73 m^2, which corresponds to CKD stages G3a–G5), intravenous contrast media can still be used safely during elective investigations, but it should be managed according to consensus guidelines from radiology societies. These guidelines provide

recommendations on minimizing the risks of CIN. In cases where an alternative imaging modality without contrast can be used, it should be considered, especially in patients with more advanced CKD.

For patients with severe CKD (eGFR <30 ml/min per 1.73 m^2), the use of gadolinium-containing contrast agents should be approached with caution. Gadolinium-based contrast agents are used in MRI scans and can pose risks for nephrogenic systemic fibrosis (NSF) in patients with severely impaired kidney function.

To minimize this risk, individuals requiring gadolinium contrast should be offered American College of Radiology (ACR) group II or III agents (gadobenate dimeglumine, gadobutrol, gadoteridol, gadoterate meglumine, and gadoxetate disodium), which are classified as having a lower risk of nephrogenic systemic fibrosis. These agents have been found to be safer for people with advanced CKD, as they are less likely to deposit in tissues and cause harm.

Questions for Self-Assessment

1. What are the main concerns when prescribing medications to individuals with CKD?
2. Which medications are commonly associated with kidney-related adverse effects and require careful monitoring?
3. Why is it important to consider over-the-counter medications, herbal remedies, and dietary supplements in CKD management?
4. What steps should healthcare providers take to educate CKD patients about the risks of unregulated substances and how they may affect kidney health?
5. For women with CKD of childbearing potential, what considerations should be taken into account when prescribing medications?
6. How does GFR impact the body's ability to eliminate medications, and why is it important for dosing decisions?

7. In which situations might a more precise measure of GFR, such as combining creatinine and cystatin C or direct GFR measurement, be necessary?
8. What is the role of body surface area (BSA) in medication dosing for people with CKD, and when should it be considered?
9. What should be done when GFR or the volume of distribution is not in a steady state, such as during acute illness or dehydration?
10. Why is it important to conduct a thorough medication review for CKD patients, and when should this review take place?
11. What role does patient education play in optimizing medication use and minimizing risks in CKD management?
12. What are some key aspects of patient education to improve medication adherence and early detection of adverse effects?
13. How can healthcare teams collaborate to ensure safe and effective medication management in CKD patients?
14. What specific role do pharmacists play in CKD medication management?
15. What is the risk of contrast-induced nephropathy (CIN) in individuals with CKD, and how can these risks be minimized?
16. Why should healthcare providers consider alternative imaging methods without contrast agents for CKD patients?
17. What validated tools are available to assess the risk of acute kidney injury (AKI) from contrast exposure in CKD patients?
18. How should gadolinium-based contrast agents be used cautiously in patients with severe CKD, and what agents are considered safer for these individuals?
19. What steps should be taken to protect kidney function during imaging procedures that involve contrast media in CKD patients?
20. How can drug stewardship principles be incorporated into routine care for individuals with CKD to ensure long-term health outcomes?

21. What strategies would you use to create a comprehensive medication management plan for a CKD patient with multiple comorbidities?

OPTIMAL MODELS OF PATIENT'S CARE

The patient should be referred to a nephrologist if:

- Cause of CKD is uncertain.
- Hereditary kidney disease.
- Recurrent extensive nephrolithiasis.
- A >3%–5% 5-year risk of requiring KRT measured using a validated risk equation.
- eGFR <30 ml/min per 1.73 m^2.
- A sustained fall in GFR of >20% or >30% in those people initiating hemodynamically active therapies.
- Consistent finding of significant albuminuria (ACR ≥300 mg/g [≥30 mg/mmol] or AER ≥300 mg/24 hours, approximately equivalent to PCR ≥500 mg/g [≥50 mg/mmol] or protein excretion rate (PER) ≥500 mg/24 h) in combination with hematuria.
- ≥2-fold increase in albuminuria in people with significant albuminuria undergoing monitoring.
- A consistent finding of ACR >700 mg/g [>70 mg/mmol].
- Urinary red cell casts, RBC >20 per high power field sustained and not readily explained.
- CKD and hypertension refractory to treatment ≥4 antihypertensive agents.
- Persistent abnormalities of serum potassium.
- Acidosis.
- Anemia.
- Bone disease.
- Malnutrition.

Symptom identification, assessment, and management

People with progressive CKD often experience a range of distressing symptoms that can impact their quality of life (QoL) and daily functioning. These symptoms may worsen as kidney function declines, making it essential for healthcare providers to proactively identify and manage them. The following practice points provide guidance on the systematic assessment and effective management of symptoms in individuals with CKD to promote better health outcomes and improve overall well-being.

People with progressive CKD are at risk of developing uremic symptoms – manifestations of toxin buildup in the blood due to reduced kidney function. Key uremic symptoms include reduced appetite, nausea, fatigue, and lethargy. To monitor these symptoms effectively, healthcare providers are encouraged to ask about uremic symptoms at each consultation, particularly in those with advanced CKD.

Using a standardized and validated tool for assessing uremic symptoms can help track changes over time and identify patterns that may indicate worsening kidney function. Regular assessment ensures that symptoms are promptly recognized and managed, thereby reducing discomfort and maintaining better quality of life.

Management of common symptoms in CKD

For people living with CKD, managing symptoms like fatigue, nausea, and poor appetite is crucial to improve their health-related quality of life (HRQoL).

As CKD progresses, malnutrition becomes a greater concern due to factors like poor appetite, involuntary weight loss, and increased frailty. Malnutrition can lead to adverse outcomes,

including a higher risk of infections, weakness, and poorer prognosis in CKD.

People with CKD stages G4–G5, those over the age of 65 or individuals displaying signs of malnutrition, such as involuntary weight loss, frailty, or poor appetite, should be screened for malnutrition twice a year using a validated assessment tool. This regular screening helps detect early signs of nutritional deficiencies and supports timely interventions to prevent further decline in health.

For people who show signs of malnutrition, medical nutrition therapy (MNT) can be highly beneficial. MNT should ideally be provided by renal dietitians or accredited nutrition providers who have expertise in managing dietary needs in CKD. This specialized nutritional support focuses on individualized dietary plans to improve caloric intake, balance nutrients, and address the unique metabolic needs of those with CKD.

By addressing nutritional deficiencies, MNT helps stabilize health, prevent weight loss, and enhance overall quality of life for those with CKD.

Team-based integrated care

As CKD progresses, the complexity of care increases, making a team-based, integrated care model essential for supporting patients through the various stages of the disease. A multidisciplinary approach addresses the medical, nutritional, psychological, and social aspects of care, empowering individuals to manage their health actively and make informed decisions. Thus, a patient-centered care team, educational programs, and telehealth technologies are very important in providing comprehensive, individualized care to people with CKD.

People with CKD benefit from a multidisciplinary care team that provides coordinated, patient-centered support across various aspects of CKD management. This team should ideally include:

nephrologist endocrinologist, cardiologist, transplant surgeon, psychologist, nurse, pharmacist, renal dietitian or accredited nutrition provider, social worker.

The specific components for CKD models of care include:

- Navigation system that leads to appropriate and timely referral. This relies on a good healthcare system.
- An education program that includes both general CKD and KRT education, including conservative management, where appropriate.
- Surveillance protocols for laboratory and clinic visits, attention to cardiovascular comorbidities, and CKDassociated comorbidities such as anemia, a vaccination program.
- Management that includes self-care management particularly lifestyle modification including diet, exercise, and smoking cessation, as well as medications and psychosocial support for issues such as social bereavement, depression, and anxiety.
- Three-way communication between people with CKD, their multidisciplinary specialist care team, and their primary care providers

This integrated approach ensures comprehensive, person-centered care that considers each patient's unique needs, values, and preferences.

Educational programs for people with CKD are crucial in promoting informed and activated patients who can actively participate in their care decisions. Involving care partners (such as family members, friends, or caregivers) can enhance understanding, support decision-making, and ensure continuity of care outside clinical settings. Education should address 3 main issues:

- standardized educational topics and resources,
- strategy to provide education effectively, and
- patient-centered concept.

These programs empower patients and their care partners to feel more confident and knowledgeable about CKD, which can improve health outcomes and quality of life.

Telehealth offers a flexible, accessible way to deliver education and support for people with CKD. Utilizing web-based platforms, mobile applications, virtual consultations, and wearable devices can make CKD care more convenient, especially for those with mobility or transportation challenges. Telehealth allows:

- Remote monitoring of symptoms and vital signs, helping clinicians detect issues early.
- Virtual visits to maintain regular follow-up and support without requiring in-person appointments.
- Education modules and apps that help patients learn about CKD at their own pace.
- Wearable devices to track health metrics (e.g., BP, activity levels) that can be shared with the care team for ongoing assessment.

This technology-driven approach facilitates timely interventions, consistent patient engagement, and improved self-management, which are especially beneficial for people with CKD living in remote or underserved areas.

Care for young adults with CKD transitioning to adult providers

When young individuals with CKD transition from pediatric to adult care, there are unique challenges and risks associated with this process. These challenges are partly due to the physiological and psychological maturation stages that are still ongoing in individuals under 25 years of age. Adult care providers must be aware of these factors and take steps to ensure that young people with CKD receive appropriate, tailored care during this critical transition period.

Young adults, particularly those under the age of 25 are at a high risk for adverse outcomes, not only due to the progression of CKD but also because of incomplete brain and emotional development. The transition from pediatric to adult care can be

particularly challenging during this period of growth, making it essential for providers to be sensitive to both their medical and psychosocial needs. Special attention should be given to the support systems in place for these individuals, including family and caregivers.

To ease the transition from pediatric to adult care, young people with CKD should be encouraged to visit the adult care clinic informally before their first formal appointment. These informal visits allow the patient to familiarize themselves with the clinic environment, meet potential care team members, and address any concerns in a low-pressure setting. This step can help reduce anxiety about the transition, increase comfort with the new healthcare environment, and foster a sense of continuity in care.

Young individuals with CKD may require more frequent assessments compared to older adults with the same stage of CKD. These assessments are crucial to monitor both the progression of the disease and the psychological impact of the transition. Frequent monitoring helps ensure early identification of issues that may arise due to physiological, emotional, or social factors.

With the young person's consent, caregivers or significant others should be involved in the care process, particularly during the first 1-3 years after the transition. Their involvement provides essential emotional and practical support to the young person, as they adjust to adult care and take on more responsibility for their health management.

Guidance on timing dialysis initiation for people with CKD

The initiation of dialysis should be based on a holistic evaluation of multiple factors rather than a single metric like GFR alone. Providers should assess the severity of symptoms associated with advanced kidney disease, such as fatigue, nausea,

or decreased appetite, alongside clinical signs, quality of life considerations, and patient preferences. Laboratory abnormalities, including electrolyte imbalances and fluid overload, should also be reviewed. This approach allows healthcare providers to tailor the timing of dialysis initiation to the individual's needs, focusing on optimizing symptom control and maintaining quality of life as long as possible without unnecessarily early intervention.

Initiate dialysis if the presence of one or more of the following situations is evident:

- Symptoms or signs attributable to kidney failure (e.g., neurological signs and symptoms attributable to uremia, pericarditis, anorexia, medically resistant acid-based or electrolyte abnormalities, intractable pruritus, serositis, and acid-base or electrolyte abnormalities).
- Inability to control volume status or BP.
- Progressive deterioration in nutritional status refractory to dietary intervention, or cognitive impairment.

In individuals with advanced CKD, planning for KRT – which includes preemptive kidney transplantation and/or dialysis access – is essential to optimize outcomes and minimize complications associated with an urgent need for dialysis.

When an individual's GFR declines to below 15–20 ml/min per 1.73 m^2 or their risk of needing KRT exceeds 40% over the next two years, healthcare providers should begin planning for KRT options. This includes evaluating candidacy for a preemptive kidney transplant, which, if feasible, offers many benefits, including better long-term kidney function and lower mortality compared to starting with dialysis. In parallel, planning for dialysis access (such as the creation of an arteriovenous fistula or placement of a peritoneal dialysis catheter) ensures that the individual is ready to start dialysis without delay if transplantation is not immediately available or if dialysis becomes necessary.

Questions for Self-Assessment

1. What are the key criteria for referring a patient with CKD to a nephrologist?
2. Why is it important to refer a patient with an eGFR <30 ml/min per 1.73 m^2 to a nephrologist?
3. How does a sustained fall in GFR of >20% or >30% impact the decision to refer a patient to a nephrologist?
4. What are the common uremic symptoms in CKD, and why is it crucial to monitor them in patients with advanced CKD?
5. How can healthcare providers effectively assess and track uremic symptoms in CKD patients?
6. How does malnutrition contribute to poor outcomes in CKD, and what steps should be taken to manage malnutrition?
7. What is the role of medical nutrition therapy (MNT) in the management of malnutrition in CKD?
8. Which patients with CKD should be screened for malnutrition, and how often should this screening occur?
9. Why is it essential to address fatigue, nausea, and poor appetite in CKD patients?
10. How can education programs improve patient engagement and health outcomes in CKD care?
11. In what ways can telehealth technologies enhance CKD management, particularly in remote or underserved areas?
12. What are the challenges young adults with CKD face when transitioning from pediatric to adult care, and how can healthcare providers support this transition?
13. Why is it important for caregivers or significant others to be involved in the care process during the first few years of transitioning to adult care?
14. How does frequent monitoring during the transition period help identify issues related to CKD progression or emotional well-being?
15. What are the clinical signs and symptoms that indicate the need for dialysis initiation in advanced CKD patients?

16. How should the timing of dialysis initiation be determined in patients with advanced CKD?
17. Why is it essential to plan for kidney replacement therapy (KRT) options, including preemptive kidney transplantation, when the patient's GFR declines below 15-20 ml/min per 1.73 m^2?
18. What are the benefits of a multidisciplinary care team in managing patients with CKD, and how can team collaboration optimize patient outcomes?
19. What are the key functions of a renal dietitian in the management of CKD?
20. How can a well-coordinated communication system between CKD patients, their care team, and primary care providers improve management and outcomes?
21. How does the education program for CKD patients contribute to improved health outcomes?
22. How should care providers integrate the use of standardized educational topics and patient-centered strategies into CKD care?

EPILOGUE

Chronic Kidney Disease (CKD) remains a formidable challenge, one that continues to test the limits of medical knowledge, healthcare systems, and the resolve of patients and their families. Yet, with every challenge comes an opportunity—a chance to innovate, to care, and to transform lives. This book has sought to illuminate those opportunities by providing a comprehensive, evidence-based guide to the detection, evaluation, and management of CKD.

As we close this journey through the complexities of CKD, it is essential to reflect on the dual responsibility that healthcare professionals carry: advancing the science and delivering compassionate care. The insights shared within these pages are not merely theoretical constructs; they are tools designed to enable clinicians to act decisively, to intervene early, and to make meaningful differences in the lives of their patients.

Through the integration of lifestyle interventions, pharmacological therapies, and team-based care models, clinicians can now better address CKD's multifaceted nature. The emphasis on early detection, precise risk stratification, and individualized care plans provides a roadmap for slowing disease progression, reducing complications, and improving quality of life.

Yet, the journey does not end here. CKD is a dynamic and evolving field, with new research, technologies, and strategies emerging regularly. Healthcare professionals must remain committed to lifelong learning, adapting their approaches as new evidence becomes available. By doing so, we honor not only the progress achieved thus far but also the potential to make even greater strides in the future.

This book is dedicated to those on the frontlines of CKD care: the physicians, nurses, dietitians, and allied healthcare professionals who work tirelessly to improve outcomes for their

patients. It is also a tribute to the patients and families who face the challenges of CKD with resilience and courage. Together, through collaboration and commitment, we can turn the tide against CKD and create a future of hope and healing.

Let this book serve as both a resource and a source of inspiration, reminding us that every small step in the fight against CKD brings us closer to a healthier, more equitable world. The responsibility is great, but so is the potential for meaningful change.

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Electronic educational publication

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Educational manual