# INTRODUCING THE KDIGO CKD 2024


ROBERT KALYESUBULA MD, FISN, PHD, FRCP

ADOPTED FROM KDIGO GUIDELINE BY

ADEERA LEVIN, MD, FRCPC

PAUL E. STEVENS, MB, FRCP


MAKERERE UNIVERSITY

wellcome connecting science

# Talk Outline

- Introduction
  - Chapter 1. Evaluation of CKD
  - Chapter 2. Risk assessment in people with CKD
  - Chapter 3. Delaying CKD progression and managing its complications
  - Chapter 4. Medication management and drug stewardship in CKD
  - Chapter 5. Optimal models of care
  - Chapter 6. Research recommendations

# GUIDELINE GOALS

- Assist healthcare providers caring for people with CKD, both adults and children
- Generate a useful resource for clinicians and patients by providing
  - Actionable recommendations based on formal evidence review
  - Practice points that serve to direct clinical care or activities for which an evidence review was not conducted
  - Useful infographics
  - Areas for future research
- Stay true to evidence
- Highlight international considerations to enable directed implementation and advocacy activities where resources are insufficient

# Evaluation – CKD Definition

CKD is defined as abnormalities of kidney structure or function, present for >3 months, with implications for health. The definition includes many different markers of kidney damage, not just decreased GFR and ACR and the cause of CKD should be actively sought (Figure). CKD is classified according to **C**ause, **G**FR, and **A**CR to establish severity and guide the type and timing of interventions.

# Detection and Evaluation of CKD

## 1.1.1 Detection of CKD

### Practice Point 1.1.1.1: Test people at risk for and with chronic kidney disease (CKD) using both urine albumin measurement and assessment of glomerular filtration rate (GFR).

**Table 4 | Use of GFR and albuminuria**

| | Current level | | |
|---|---|---|---|
| **Clinical decisions** | **GFR** | **Albuminuria** | **Change in the level of GFR** |
| Diagnosis and staging | • Detection of CKD<br>• Evaluation for kidney donation | • Detection of CKD | • Detection of AKI and AKD<br>• Detection of CKD progression |
| Treatment | • Referral to nephrologists<br>• Patient and family education about CKD and benefit of lifestyle changes<br>• Monitor progression of GFR decline<br>• Referral for kidney transplantation<br>• Placement of dialysis access<br>• Dosage and monitoring for medications cleared by the kidney<br>• Determine safety of diagnostic tests or procedures<br>• Eligibility for clinical trials | • Referral to nephrologists<br>• Patient and family education about CKD and benefit of lifestyle changes<br>• Monitor progression of GFR decline<br>• Eligibility for clinical trials | • Treatment of AKI<br>• Monitoring drug toxicity<br>• Re-evaluate CKD treatment strategies |
| Risk assessment | • Risk of CKD complications<br>• Risk for CKD progression<br>• Risk of CVD<br>• Risk for medication errors<br>• Risk for perioperative complications<br>• Risk for mortality<br>• Fertility and risk of complications of pregnancy | • Risk for CKD progression<br>• Risk for CVD<br>• Risk for mortality<br>• Fertility and risk of complications of pregnancy | • Risk for kidney failure<br>• Risk for CVD, HF, and mortality<br>• Risk for adverse pregnancy outcome |

# Detection and Evaluation of CKD

## 1.1.2 Methods for staging of CKD

**Recommendation 1.1.2.1: In adults at risk for CKD, we recommend using creatinine-based estimated glomerular filtration rate (eGFRcr). If cystatin C is available, the GFR stage should be estimated from the combination of creatinine and cystatin C (creatinine and cystatin C–based estimated glomerular filtration rate [eGFRcr-cys]) (1B).**

# Evaluation – Distinguish Between AKD and CKD

It is important to distinguish between AKD and CKD and to establish chronicity.

# Detection and Evaluation of CKD

## 1.1.4 Evaluation of cause

## Practice Point 1.1.4.2: Use tests to establish a cause based on resources available (Table 6).

**Table 6 | 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.<br>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<br>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 |
| Laboratory tests: serologic, urine tests | Chemistry including acid base and electrolytes, serologic tests such as anti-PLA2R, ANCA, anti-GBM antibodies<br>Serum-free light chains, serum, and urine protein electrophoresis/immunofixation<br>Urinalysis and urine sediment examination | Refer to *KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases*[22]<br>Increasing recognition of the role of light chains in kidney disease even in the absence of multiple myeloma (monoclonal gammopathy of renal significance [MGRS])[98]<br>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.<br>Recognition that genetic causes are more common and may present without classic family history[99,100] |

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.

# Detection and Evaluation of CKD

## Actionable genes in kidney disease

# Detection and Evaluation of CKD

## Proposed organization for implementing genetics in nephrology

# Evaluation of GFR

**Table 7 | Description of initial and supportive tests for the evaluation of GFR**

| GFR assessment method | Specific tests | Guidance for use and implementation |
|---|---|---|
| Estimated GFR | Creatinine (eGFRcr) | Most used method to assess GFR. In most cases, initial test for the evaluation of GFR.<br>Standardized assay required to decrease between-center analytical variation |
| | Cystatin C (eGFRcr-cys, eGFRcys) | Used in selected circumstances as listed in Table 8<br>Standardized assay required to decrease between-center analytical variation |
| mGFR | Gold standard. Urinary or plasma clearance of exogenous markers (e.g., iohexol, iothalamate, $^{51}$Cr-EDTA, and $^{99m}$Tc-DTPA) | Used in selected circumstances as listed in Table 8<br>Standard protocols for clearance methods and for the standardized assay |
| Timed urine clearance | Creatinine | Highly prone to errors and recommended only when no other options for supportive tests for GFR evaluation; performance under supervised conditions may decrease error |
| Nuclear medicine imaging | Imaging of the kidneys after injection of tracer cleared by the kidneys (e.g.,$^{99m}$Tc-DTPA scintigraphy) | Highly prone to errors; not recommended |

# Evaluation of GFR

## 1.2.3 Guidance to clinical laboratories

## Practice Point 1.2.3.1: Implement the laboratory standards of care outlined in Table 11 to ensure accuracy and reliability when assessing GFR using creatinine and cystatin C.

**Table 11 | Implementation standards to ensure accuracy and reliability of GFR assessments using creatinine and cystatin C**

- Report eGFR in addition to the serum concentrations of filtration markers using validated equations.
- Report eGFR rounded to the nearest whole number and relative to a body surface area (BSA) of 1.73 $m^2$ in adults using the units ml/min per 1.73 $m^2$.
- Reported eGFR levels <60 ml/min per 1.73 $m^2$ should be flagged as being low.
- When reporting levels of filtration markers, report:
  - (i) SCr concentration rounded to the nearest whole number when expressed as standard international units (μmol/l) and rounded to the nearest 100th of a whole number when expressed as conventional units (mg/dl);
  - (ii) serum cystatin C concentration rounded to the nearest 100th of a whole number when expressed as conventional units (mg/l).
- Measure filtration markers using a specific, precise (coefficient of variation [CV] <2.3% for creatinine and <2.0% for cystatin C) assay with calibration traceable to the international standard reference materials and desirable bias (<3.7% for creatinine and <3.2% for cystatin C) compared with reference methodology (or appropriate international standard reference method group target in external quality assessment [EQA] for cystatin C).
- Use an enzymatic method to assay creatinine, where possible.
- Separate serum/plasma from red blood cells by centrifugation within 12 hours of venipuncture.
- When cystatin C is measured, measure creatinine on the same sample to enable calculation of eGFRcr-cys.

eGFR, estimated glomerular filtration rate; eGFRcr-cys, estimated glomerular filtration rate based on creatinine and cystatin C; GFR, glomerular filtration rate; SCr, serum creatinine.

# Evaluation of GFR

1.2.4 Selection of GFR estimating equations

Practice Point 1.2.4.1: Use the same equation within geographical regions (as defined locally [e.g., continent, country, region] and as large as possible). Within such regions, equations may differ for adults and children.

Practice Point 1.2.4.2: Use of race in the computation of eGFR should be avoided.

**Special considerations**

*Pediatric considerations*

Practice Point 1.2.4.3: Estimate GFR in children using validated equations that have been developed or validated in comparable populations.

# Evaluation of Albuminuria

## 1.3.1 Guidance for physicians and other healthcare providers

Practice Point 1.3.1.1: 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 and children.

(i) urine ACR, or
(ii) reagent strip urinalysis for albumin and ACR with automated reading.

If measuring urine protein, use the following measurements:

(i) urine protein-to-creatinine ratio (PCR),
(ii) reagent strip urinalysis for total protein with automated reading, or
(iii) reagent strip urinalysis for total protein with manual reading.

# Point-of-care Testing

**Recommendation 1.4.1: We suggest that point-of-care testing (POCT) may be used for creatinine and urine albumin measurement where access to a laboratory is limited or providing a test at the point-of-care facilitates the clinical pathway (2C).**

Practice Point 1.4.1: Whenever a POCT device is used for creatinine and urine albumin testing, ensure that the same preanalytical, analytical, and postanalytical quality criteria relating to the specimen collection and performance of the device, including external quality assessment, and the interpretation of the result is used.

# Evaluation –CKD Care Across the Life Span

CKD impacts people across the lifespan and as a chronic condition, care is influenced by changes in life circumstances. Use a personalized approach to diagnosis, risk assessment, and management that considers age, sex, and gender. At the extremes of age - the very young and the very old - diagnostic procedures, treatment aims, treatment modalities, and decision-making differ due to differences in prognosis, treatment options, and prioritization.

# Evaluation – Diagnosis of CKD in Older Adults

Epidemiological population data support retaining the threshold GFR of 60 ml/min/1.73 m2 for diagnosis of CKD in older adults, even in the absence of significant albuminuria, with consistently elevated and increasing relative risk of adverse outcomes below this threshold.

# Evaluation – Improving Accuracy of GFR Assessment

Estimating GFR from a combination of creatinine and cystatin C (eGFRcr-cys) improves accuracy and strengthens risk relationships. GFR should be measured where more accurate ascertainment of GFR will impact treatment decisions.

# Evaluation – Accuracy and Reliability

Understand the variability of GFR and urinary albumin and the value and limitations of the methodology of assessment when determining whether a change is a true change. Implement the requisite laboratory standards of care to ensure accuracy and reliability.

# Evaluation – Use a Validated GFR Estimating Equation

Use a validated GFR estimating equation to derive GFR from serum filtration markers (eGFR) and use the same equation within geographical regions recognizing that these equations may differ for adults and children.

# Evaluation – Point-of-Care Tests

Point-of-care tests (POCT) for creatinine (blood and saliva) and urine albumin measurement are available, and if adequately quality-assured, are accurate enough to facilitate the clinical pathway where access to a laboratory is limited.

# Overview on Monitoring for Progression of CKD Based upon GFR and ACR Categories

# Evaluation – Timing Assessment and Reevaluation

Timing of follow up and reassessment using validated risk prediction tools and clinical evaluation, together with education, may inform better selection of targets of care to support people and families living with CKD. This approach is part of longitudinal care.

# Evaluation – Use Validated Risk Assessment Tools

Use validated risk assessment tools to aid in decision-making and timing of multidisciplinary care. Choose the appropriate tool for the event of interest: kidney failure treatment, cardiac events, or mortality.

# Risk Prediction in People with CKD

Practice Point 2.2.1: A 5-year kidney failure risk of 3%–5% can be used to determine need for nephrology referral in addition to criteria based on eGFR or urine ACR, and other clinical considerations.

Practice Point 2.2.2: A 2-year kidney failure risk of >10% can be used to determine the timing of multidisciplinary care in addition to eGFR-based criteria and other clinical considerations.

# Management of People with or at Risk of CKD

# CKD TREATMENT AND RISK MODIFICATION

Practice Point 3.1.1: Treat people with CKD with a comprehensive treatment strategy to reduce risks of progression of CKD and its associated complications.

# Management – Comprehensive Treatment Strategy

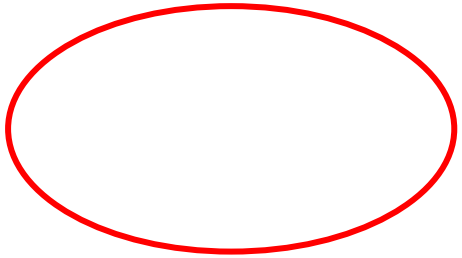
Treat people with CKD with a comprehensive treatment strategy to reduce risks of progression of CKD and its associated complications encompassing education, lifestyle, exercise, smoking cessation, diet, and medications, where indicated.

# Management – Healthy and Diverse Diet

Adopting a healthy and diverse diet with a higher consumption of plant-based foods compared to animal-based foods and a lower consumption of ultra-processed foods has the potential to benefit complications related to progressive CKD such as acidosis, hyperkalemia, and hyperphosphatemia with less risk of protein energy-wasting.

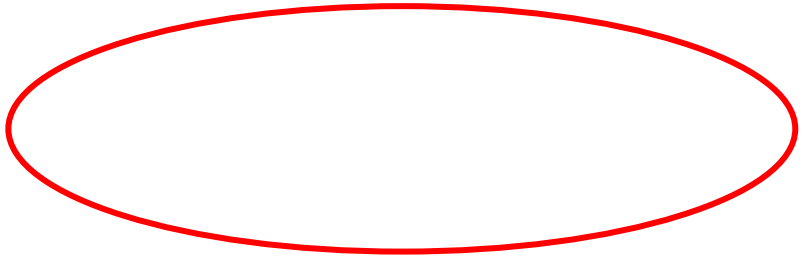
# Management – Individualize BP Control

Individualize BP-lowering therapy and treatment targets in people with frailty, high risk of falls, very limited life expectancy, or symptomatic postural hypotension.



# MANAGEMENT – RASI AND SGLT2I

Treatments that delay progression of CKD with a strong evidence base include RASi and SGLT2i. In people with CKD and heart failure, SGLT2i confer benefits irrespective of albuminuria.



# Management – Acute Changes in eGFR

Initial dips in eGFR are expected following initiation of hemodynamically active therapies, including both RASI and SGLT2i. GFR reductions of ≥30% from baseline exceed the expected variability and warrant evaluation.

# Management – Cardiovascular Disease and Imaging

Estimate 10-year cardiovascular risk using a validated risk tool that incorporates CKD to guide treatment for prevention of cardiovascular disease. CKD is not a contraindication to an invasive strategy for people with acute or unstable heart disease. Imaging studies are not necessarily contraindicated in people with CKD and the risks and benefits should be determined on an individual basis. Strategies to mitigate risks from imaging studies using contrast media are easily implemented.

# Management – Perform Thorough Medication Review

Perform thorough medication review periodically and at transitions of care to assess adherence, continued indication, and potential drug interactions because people with CKD often have complex medication regimens and are seen by multiple specialists. Review and limit the use of over-the-counter medicines, dietary, or herbal remedies that may be harmful for people with CKD. For most people and clinical settings, validated eGFR equations using SCr are appropriate for drug-dosing. Remember, a validated measured GFR is most accurate.

# Management – Discontinuation and Restart of Medications

If medications are discontinued during an acute illness, communicate a clear plan of when to restart the discontinued medications to the affected person and healthcare providers, and ensure documentation in the medical record. Failure to restart these medications may lead to unintentional harm.

# Management – Symptom Control in CKD

The identification and assessment of symptoms in people with progressive CKD is important for highlighting changes in clinical management, redirecting treatment toward patient-centered management, and may lead to discussion about appropriate supportive care options. Effective communication and shared decision-making should be key principles between healthcare providers and the people they treat, allowing them to work in partnership to identify symptom burden, possible treatment strategies and person-centered solutions.

# Management – Advanced Care Planning

Plans addressing future health care states should be jointly agreed with people with CKD and their families/carers and known to all. Advanced care planning for those choosing supportive care is particularly important.

# TEAM-BASED INTEGRATED CARE


THANK YOU