ACE CLINICAL GUIDANCE

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Chronic kidney disease

Early detection

Objective	Scope	Target audience
To enhance timely detection of chronic kidney disease (CKD)	Identification of patients at increased risk of CKD, as well as diagnosis and staging of CKD	This clinical guidance is relevant to all healthcare professionals caring for patients at risk of CKD, especially those in primary care

Chronic kidney disease (CKD) is defined as abnormalities of kidney function or structure persisting for at least three months, with implications for health.[1] In 2017, the estimated global prevalence of CKD was 9.1%.[2] In Singapore, the prevalence of CKD among residents aged 18 to 74 years was 8.8% in 2019–2020,[3] and CKD has remained in the top ten causes of death from 2009 to 2019 with CKD-related deaths rising by 76% within that decade.[4]

Timely CKD detection and management play a major part in slowing down or preventing progression to kidney failure or other complications. Early detection is particularly significant given that patients are asymptomatic in the early stages of CKD. Primary healthcare professionals play an essential role in identifying patients at increased risk of CKD to detect it early.

Statement of Intent

This ACE Clinical Guidance (ACG) provides concise, evidence-based recommendations and serves as a common starting point nationally for clinical decision-making. It is underpinned by a wide array of considerations contextualised to Singapore, based on best available evidence at the time of development. The ACG is not exhaustive of the subject matter and does not replace clinical judgement. The recommendations in the ACG are not mandatory, and the responsibility for making decisions appropriate to the circumstances of the individual patient remains at all times with the healthcare professional.

ACE agency for care effectiveness

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Identification of patients at increased risk of CKD

Recommendation 1

Identify patients at increased risk of CKD by assessing their risk factors and determine the need to evaluate for CKD.

Identifying patients at increased risk who will benefit from evaluation for CKD enables timely detection and management of CKD.[1] This involves assessing the patient's overall risk of CKD, as well as other aspects of the patient's health status (for example, their age and frailty) to determine the extent to which they can benefit from evaluation for CKD.

Key risk factors associated with the overall risk of CKD are listed in Table 1.

Table 1. Risk factors for CKD*

Cardiometabolic risk factors	Renal risk factors	Other risk factors
Cardiovascular disease	Family history of CKD or ESKD	Age (especially ≥65 years)
Diabetes mellitus†	Hereditary kidney disease	Hyperuricaemia or gout
Hypertension†	History of AKI	Nephrotoxic medications (including frequent or chronic NSAID use)
Obesity (BMI ≥27.5 kg/m²)	Recurrent kidney stones	
Metabolic syndrome	Multi-system diseases that impact the kidneys (such as SLE)	Smoking

AKI, acute kidney injury; BMI, body mass index; CKD, chronic kidney disease; ESKD, end-stage kidney disease; NSAID, non-steroidal anti-inflammatory drug; SLE, systemic lupus erythematosus

* This table presents more commonly known risk factors for CKD; it is not an exhaustive list. Bolding denotes risk factors that are particularly important for CKD.

† Including presentations associated with pregnancy.

Cardiovascular disease, diabetes, hypertension, and obesity are particularly important risk factors for CKD (in bold in Table 1). The cardiometabolic risk inherent in these risk factors, that is, high blood glucose, high blood pressure, and high BMI—along with related risk factors such as hyperlipidaemia and smoking—are modifiable and can be managed to reduce the patient's risk of CKD and associated significant comorbidities or complications, including cardiovascular mortality.

While recognising risk factors is integral to assessing the patient's overall risk of CKD, this does not mean that all patients with CKD risk factors would require evaluation for CKD. For example, evaluation for CKD may be prudent for a healthy 40-year-old patient with a strong family history of CKD despite their young age, but may not be warranted for a healthy 40-year-old patient who is a social smoker.

Recommendation 2 starting on page 3 and Recommendation 3 starting on page 5 provide more details on evaluation for CKD.

CKD diagnosis

Recommendation 2

Diagnose CKD if any of the following is present for at least three months:
- **GFR <60 mL/min/1.73m²**
- **UACR ≥3 mg/mmol (≥30 mg/g)**
- **Other marker of kidney damage**

Evaluation for CKD involves investigating for abnormalities of kidney function or structure in relation to the diagnostic criteria for CKD as shown above.

Evaluating kidney function–GFR

Glomerular filtration rate (GFR) is generally accepted as the best overall index of kidney function.[1] As measuring 'true' GFR is cumbersome and difficult to perform accurately, serum creatinine-based estimating equations are commonly used to obtain the estimated GFR (eGFR). GFR is a more sensitive marker for CKD than serum creatinine alone.[1,5,6] GFR <60 mL/min/1.73m² is internationally accepted as the threshold for CKD, and is associated with increased risk of adverse renal outcomes (including higher risk of CKD progression, dialysis, CKD-related death, and AKI), cardiovascular and all-cause mortality.[7-10]

eGFR equations: MDRD and CKD-EPI

The Modification of Diet in Renal Disease (MDRD) and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations both estimate GFR based on serum creatinine, age, gender, and are adjusted for body surface area. CKD-EPI is more accurate, particularly at higher GFR, enabling reporting of numeric values for GFR up to 90 mL/min/1.73m² (relevant for more detailed staging of CKD—see Recommendation 3 starting on page 5).

Acute kidney injury

Acute kidney injury (AKI) is defined as any of the following:[11,12]
- Increase in serum creatinine of ≥0.3 mg/dL (≥26.5 µmol/L) within 48 hours
- Increase in serum creatinine ≥1.5 times of baseline, which is known or presumed to have occurred within the prior 7 days
- Urine volume <0.5 mL/kg/h for 6 hours

While evaluating patients for CKD, be cognisant of the possibility of AKI. If AKI is suspected, repeat a serum creatinine test as soon as practicable (other tests may also be required). Patients with eGFR <60 mL/min/1.73m², particularly when AKI is suspected, should have a repeat serum creatinine as soon as practicable to rule out AKI.

Evaluating kidney damage–UACR or other markers of kidney damage

Albuminuria is a common marker of kidney damage, as albumin is the main protein found in urine in many presentations of kidney diseases, including CKD resulting from diabetes or hypertension. Urine albumin:creatinine ratio (UACR) is the recommended measure of albuminuria instead of urine protein:creatinine ratio (UPCR) because UACR is better than UPCR for detecting early progressive kidney damage.[1,13-15] UACR ≥3 mg/mmol (≥30 mg/g) is internationally accepted as the threshold for CKD, and is associated with increased risk of adverse renal outcomes (including higher risk of CKD progression, dialysis, CKD-related death, and AKI), cardiovascular and all-cause mortality.[7-10]

Albuminuria threshold

For ease of clinical application and in line with international consensus, this clinical guidance adopts a common albuminuria threshold of UACR ≥3 mg/mmol (≥30 mg/g) for both males and females,[1] while acknowledging that gender-specific thresholds may still be used in some practice settings in Singapore. Patients should be appropriately tested and followed up whether common or gender-specific thresholds are used.

Other markers of kidney damage may be used for diagnostic purposes in addition to, or instead of, albuminuria. Examples include urine sediment abnormalities (such as casts) and imaging abnormalities (such as hydronephrosis on ultrasound). A history of kidney transplantation is also considered a marker of kidney damage and immediately qualifies as CKD (regardless of GFR or UACR levels).

Table 2. Key information for ordering and interpreting eGFR and UACR

	eGFR	UACR
When to repeat the test	Repeat 3 months after the initial test to confirm if patient has CKD (may also be repeated sooner if clinically indicated).	Repeat 3 months after the initial test to confirm if patient has CKD (may also be repeated sooner if clinically indicated).
Factors that could influence the test results (without necessarily affecting kidney function)	Factors that could increase serum creatinine (hence decrease eGFR) include:[1,16] • High muscle mass • High-protein diet • Medications that increase serum creatinine without necessarily affecting kidney function (for example, trimethoprim) Factors that could decrease serum creatinine (hence increase eGFR) include:[1,16] • Low muscle mass (for example, patients with sarcopaenia, paraplegia, amputation, or muscular dystrophy) • Malnutrition, inflammation, or deconditioning (for example, patients with cancer or severe cardiovascular disease, hospitalised patients) • Low-protein diet	Factors that could increase albuminuria (hence increase UACR) include:[1,17] • Menstruation • Urinary tract infection • Heavy exercise within last 24 hours • Congestive heart failure Factors that could decrease urine creatinine (hence increase UACR):[1] • Female gender • Older age • Low muscle mass (for example, patients with sarcopaenia, paraplegia, amputation, or muscular dystrophy)
Practical considerations	Advise patient to abstain from high-protein food such as meat for 12 hours prior to the test.[18] Patients with eGFR <60 mL/min/1.73m^2 should have a repeat serum creatinine as soon as practicable to rule out AKI, particularly when AKI is suspected.	A 24-hour collection is not necessary. An early morning spot urine sample is preferred as it correlates well with 24-hour protein excretion, and has relatively low intra-individual variability. A UACR ≥3 mg/mmol (≥30 mg/g) based on a random urine sample should be repeated on an early morning urine sample.

AKI, acute kidney injury; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; UACR, urine albumin:creatinine ratio

Incidental dipstick findings[19]

During routine health screening, such as annual medical examinations, a urine dipstick test may detect proteinuria or haematuria. False-positive and false-negative results are not unusual in dipstick urinalysis. Any findings of concern, for example persistent proteinuria or haematuria, should prompt further investigations to rule out serious aetiologies.

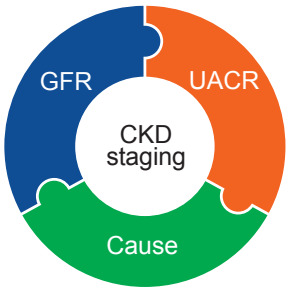
CKD staging

Recommendation 3

Determine the stage of CKD based on GFR, UACR, and the cause(s) of CKD.

Once CKD is diagnosed, the stage of CKD needs to be determined to inform prognosis and management. CKD staging is based on cause and severity, with the latter reflected by GFR and UACR. This is a shift away from previous approach where CKD staging only focused on GFR.[1] GFR and UACR are categorised quantitatively, while cause is described qualitatively. All three form essential components of CKD staging.

Figure 1. Components of CKD staging



GFR continues to be used in CKD staging as the overall marker of the severity of reduced kidney function.

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

‡ Range based on Kidney Disease: Improving Global Outcomes (KDIGO) 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease.[1]

UACR (measuring albuminuria) is included as another component of CKD staging not only because it is a marker of kidney damage severity, but also because it is associated with the progression of kidney disease.

Category	Description	UACR range§	
		(mg/mmol)	(mg/g)
A1	Normal to mildly increased	<3	<30
A2	Moderately increased	3-30	30-300
A3	Severely increased	>30	>300

§ Range based on Kidney Disease: Improving Global Outcomes (KDIGO) 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease.[1]

The **cause** of disease is included as part of CKD staging as it is fundamentally important in prognostication and choice of cause-specific treatments. The cause of CKD should be established by considering findings from the patient's history and physical examination. For many patients, the risk factor(s) prompting evaluation for CKD in the first place (such as diabetes, hypertension, or family history of CKD) may offer a plausible cause of CKD. Clinical judgement needs to be exercised regarding whether this provides a sufficient explanation, or whether further investigations are warranted to determine the cause (or in some cases, additional causes), for example:[1]

- Complete urinalysis (including urine microscopy) to detect haematuria, pyuria, or casts
- Ultrasound to examine kidney structure
- Serum and urine electrolytes to investigate for renal tubular disorders

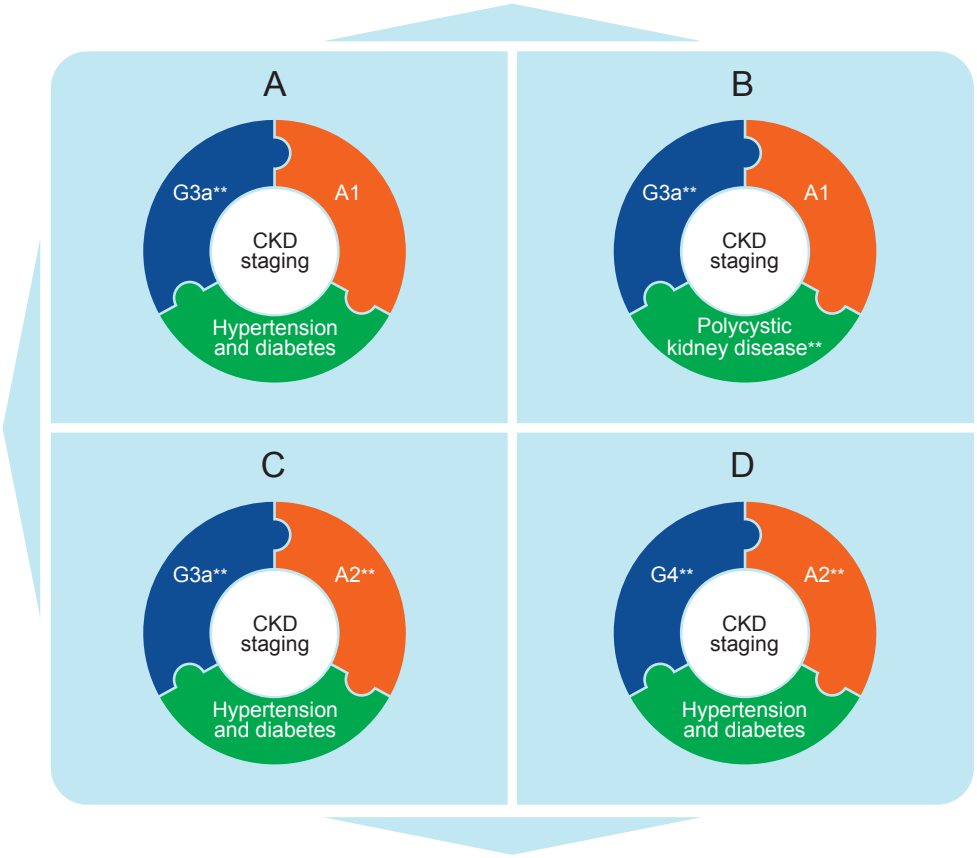
Unlike GFR and UACR which can be quantified and categorised numerically in CKD staging, cause is described qualitatively. Collectively, the quantitative (GFR and UACR) and qualitative (cause) components of CKD staging provide essential information to determine the patient's prognosis and most appropriate management. The importance of each component of CKD staging is illustrated through some clinical scenarios in Figure 2 below.

Figure 2. Clinical scenarios illustrating the importance of GFR, UACR, and cause in CKD staging

Despite having the same GFR and UACR categories, patients in scenarios A and B may have different prognosis and would be managed differently because of the different causes of their CKD.

Despite having the same GFR category and CKD cause, patient in scenario C has more severe albuminuria than patient in scenario A (as reflected by the higher UACR category), hence patient in scenario C is expected to:

- Have a poorer prognosis (i.e. progress to kidney failure more quickly without appropriate management)
- Have a more stringent blood pressure target



Despite having the same UACR category and CKD cause, patient in scenario D has poorer kidney function than patient in scenario C (as reflected by the higher GFR category), which would lead to different prognosis and selection of medications for managing CKD or comorbidities.

CKD, chronic kidney disease; GFR, glomerular filtration rate; UACR, urine albumin:creatinine ratio

** Findings present for at least three months which meet CKD diagnostic criteria (see Recommendation 2 on page 3).

Management, patient education, and follow-up for patients with CKD

Recommendation 4

For patients diagnosed with CKD, discuss the diagnosis and management options with the patient.

Once CKD is diagnosed and staged, appropriate management is critical to slow down or prevent progression of CKD to kidney failure or other complications. Management of CKD (including pharmacotherapy) will be the focus of a separate clinical guidance.

Patient education and involvement are widely accepted as integral parts of chronic disease management. Increased patient knowledge about CKD can improve health outcomes.[20] Conversely, a patient's lack of knowledge, passive attitude towards self-management, and insufficient patient-healthcare professional communication can be barriers to optimal CKD management.[21] Therefore, it is important for healthcare professionals to engage patients with CKD in a discussion about their diagnosis and management options. Points to include when discussing CKD with patients should be tailored to the patient's individual circumstances:

- Explaining what CKD is, including current stage of CKD, health implications and likely prognosis.
- Reassuring the patient that proper management can slow down the progression of CKD.
- Explaining the possible cause(s) and risk factor(s) contributing to the patient's CKD, and how these can be further assessed.
- Discussing the management options with the patient, including emphasising the importance of managing modifiable cause(s) and risk factor(s), and optimising management of related comorbidities.
- Explaining how medications can help the patient manage some of the cause(s) and risk factor(s), and the importance of adhering to the medications prescribed.
- Explaining how the patient can actively participate in their own care (for example, attend regular follow-up visits and maintain a healthy lifestyle, including a balanced diet, physical activity, and smoking cessation).

Follow-up for patients at increased risk of but do not have CKD

Recommendation 5

For patients who do not have CKD but are at increased risk, monitor for CKD regularly.

Patients who are at increased risk but do not have CKD should still be followed up regularly. While all patients at increased risk of CKD should be followed up at least annually, closer monitoring may be indicated in some cases, for example when risk factors are poorly controlled.

Referral

Recommendation 6

Referral to a specialist could be made at any point.

Specialist referral could be considered at any point, and is usually indicated for patients who have CKD with:

- GFR <30 mL/min/1.73m^2 (GFR categories G4 and G5)[1,18,22,23]
- Persistent significant albuminuria [UACR category A3 (UACR >30 mg/mmol (>300 mg/g))][1,18,22]
- Hypertension refractory to optimised antihypertensive treatment[1,18,22,23]
- Sustained decline in GFR of >5 mL/min/1.73m^2 per year[23]
- Persistent microscopic haematuria or an episode of gross haematuria
- Known or suspected rare or genetic causes of CKD[18,23]
- Known or suspected renal artery stenosis[1,18,23]

The choice of specialist depends on the reason for referral.

References

Scan the QR code for the reference list to this clinical guidance

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