

Diabetes: CKD

1. Background information



- Type 2 diabetes (T2D) represents the main cause of chronic kidney disease (CKD) and end-stage renal disease,¹ accounting for almost 50% of all patients starting renal replacement therapy worldwide.²
- At least half of those with T2D will develop CKD.³
- CKD is associated with increased risk of morbidity and premature mortality in people with diabetes.³

CKD describes abnormal kidney function or structure present for over 3 months. Either of the following must be present:⁴

- ✓ Markers of kidney damage*, or
- ✓ Estimated glomerular filtration rate (eGFR) <60 ml/min/1.73m².

*Albuminuria (albumin:creatinine ratio [ACR] >3 mg/mmol); urine sediment abnormalities; electrolyte and other abnormalities due to tubular disorders; abnormalities detected by histology; structural abnormalities detected by imaging; history of kidney transplantation.

2. Process



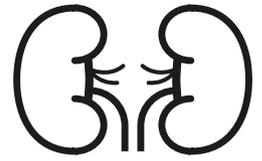
- Screen annually to detect CKD.**^{5,6}
 - Serum creatinine to calculate eGFR (kidney function).
 - Urine albumin/creatinine ratio (kidney damage).

- Refer to Table I for frequency of monitoring CKD according to classification stage.**

Table I: Recommended frequency of monitoring.⁶

The numbers in this table indicate recommended frequency of monitoring per year		ACR categories (mg/mmol), description and range		
		A1 <3 Normal to mildly increased	A2 3–30 Moderately increased	A3 >30 Severely increased
GFR categories (ml/min/1.73m ²), description and range	G1 ≥90 Normal or high	≤1	1	≥1
	G2 60–89 Mild reduction related to normal range for a young adult	≤1	1	≥1
	G3a 45–59 Mild-moderate reduction	1	1	2
	G3b 30–44 Moderate-severe reduction	≤2	2	≥2
	G4 15–29 Severe reduction	2	2	3
	G5 <15 Kidney failure	4	≥4	≥4

Adapted from NICE CG182, 2014



3. For initial detection



Screen for CKD using two simple tests:⁶

Spot urine for ACR.

Serum creatinine for eGFR.

ACR is the method of preference to detect elevated protein. The recommended method to evaluate albuminuria is to measure urinary ACR in a spot urine sample.⁶

Table II: Using ACR in the diagnosis of renal disease.

ACR	False positives	ACR procedure
<ul style="list-style-type: none"> Albuminuria is the earliest manifestation of renal disease in people with diabetes.⁷ It is a predictor of nephropathy (and CKD progression) AND an independent risk factor for cardiovascular disease.⁷ Proteinuria is the hallmark of diabetic nephropathy but can be absent in CKD where glomerular disease is not the dominant pathology.⁸ Do not use reagent strips to identify proteinuria as they are not sensitive for detecting low levels of proteinuria and are only semi quantitative.⁶ For detection use ACR in preference to protein creatinine ratio (it is more sensitive at lower levels).⁶ 	<ul style="list-style-type: none"> If first urine sample of the day is not available, use a random sample (but be aware that this is associated with an increased risk of false positive results).⁹ False positives are also more likely with increasing age and low muscle mass. Dipstick to exclude for signs of infection or haematuria (follow local pathways). 	<ul style="list-style-type: none"> If ACR >70 mg/mmol – diagnose severe albuminuria (no need to repeat).⁶ ACR 3–70 mg/mmol confirm with subsequent early morning sample.⁶ If 2nd ACR 3–70 mg/mmol – diagnose microalbuminuria and code.¹⁰ If 2nd ACR <3 mg/mmol repeat 3rd ACR to confirm persistent albuminuria.^{10*}

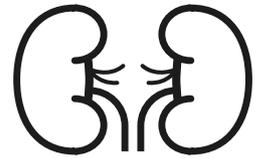
*For classification see Table I

eGFR is a key indicator of renal function. Normal eGFR is usually >90 ml/min/1.73m².⁶

Table III: Using eGFR in diagnosis of renal disease.⁶

eGFR	Cause of false low	Cause of false high
<ul style="list-style-type: none"> To diagnose CKD Stages 3 to 5 requires two eGFR readings <60 ml/min/1.73m² more than three months apart (with no readings of ≥60 ml/min/1.73m² in between). eGFR values of ≥60 ml/min/1.73m² become less accurate as true GFR increases. With a new finding of reduced eGFR, repeat the eGFR within 2 weeks to exclude causes of acute deterioration of eGFR (e.g. acute kidney injury or starting renin–angiotensin system antagonist therapy). If acute kidney injury (AKI) suspected, follow NICE NG148.¹¹ If AKI not suspected but eGFR remains <60 ml/min/1.73m², repeat eGFR after at least 90 days to confirm diagnosis. Deterioration in eGFR in those with short duration of diabetes in the absence of retinopathy should raise suspicions of non-diabetic kidney disease and referral for renal biopsy may be appropriate.¹² 	<ul style="list-style-type: none"> Increased muscle mass (e.g. body builders). High protein intake/meat 12 hours before. Delay in processing sample (>12 hours). Dehydration. 	<ul style="list-style-type: none"> Reduced muscle mass (e.g. muscle wasting, amputations).

CKD is classified according to eGFR (G1–G5) and ACR (A1–A3), see Table I.



4. Monitoring

Monitor CKD progression.⁶

Follow the recommended frequency of testing as shown in Table I.

- Accelerated progression of CKD is a sustained decrease in eGFR of $\geq 25\%$ and change in eGFR category within 12 months OR sustained decrease in eGFR of 15 ml/min/1.73m² per year: Renal referral should be considered.

Check haemoglobin (Hb).

- If not already measured, check the haemoglobin level in people with a GFR of less than 45 ml/min/1.73 m² to identify anaemia. Determine the subsequent frequency of testing by the measured value and the clinical circumstances.⁶
- Offer pneumococcal vaccination in those with CKD and reinforcing vaccination every 5 years in those with nephrotic syndrome, CKD at stages 4 and 5 and those on kidney dialysis or with kidney transplantation.¹³

Optimise CV risk reduction.

Blood pressure

- In people with CKD and diabetes aim to keep the systolic blood pressure below 130 mmHg (target range 120–129 mmHg) and the diastolic blood pressure below 80 mmHg.⁶

Lipids

- Offer statins as per NICE CG181 (section 1.3.27).^{6,14}

Address lifestyle factors⁶

Ask about lifestyle and where appropriate offer advice to include:

- Healthy eating that includes a diet rich in a variety of vegetables and fruits and whole grains, healthy natural fats (olive oil, nuts, fish) and dairy (milk, yogurt, cheese). A variety of protein including seafood, lean meat, poultry, eggs, legumes, soy, seeds and nuts. Limit sugar-sweetened foods and drinks, refined carbohydrates and processed foods.
- Avoiding high protein (>1.3 g/kg per day if at risk of CKD progression).¹⁵
- Supporting individuals who are overweight to lose weight.

- Smoking cessation advice for smokers.
- Providing information about local initiatives that support and promote healthy lifestyle.

Optimise HbA_{1c} and reduce the risk of further complications.

- The presence of specific comorbidities such as CKD mandate an individualised approach to the choice of glucose-lowering agents. The medication selected through shared decision making between the patient and healthcare professional should be based on individual preferences and goals.¹⁶
- Most SGLT2 inhibitors should not be initiated in patients if eGFR <60 mL/min/1.73m²; for dosing details, see relevant SmPCs.

Review dose of current medications in the light of declining eGFR.

Acute kidney injury

- Acute kidney injury (AKI) is a term covering a spectrum of injury to the kidneys, which can result from several causes. It is a clinical syndrome rather than a biochemical diagnosis.¹¹

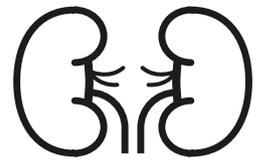
Minimise risk of AKI:

Consider AKI if:¹¹

- Rise in serum creatinine of 26 $\mu\text{mol/l}$ or greater within 48 hours.
- $\geq 50\%$ rise in serum creatinine over past 7 days.
- A fall in urine output to less than 0.5 ml/kg/hour for more than 6 hours in adults.

Give sick day advice^{17,18,19}

- During intercurrent illness especially where dehydrated, advise to withhold SGLT2 inhibitors, metformin, GLP-1 receptor agonists, some SUs, ACEi/ARBs, diuretics and NSAIDs medicines until recovered.
- Keep well hydrated but if unable to eat or drink, or where there is persistent vomiting or diarrhoea; contact GP or specialist nurse for advice.



Indication for referral to specialist:⁶

- eGFR <30 ml/min/1.73m² (G4 or G5).
- Sustained decrease in eGFR of ≥25%, and a change in eGFR category or sustained decrease in eGFR of ≥15 ml/min/1.73m² within 12 months.
- Hypertension poorly controlled and on at least four agents.
- Suspected renal artery stenosis.
- ACR 70 mg/mmol or more, unless known to be caused by diabetes and already appropriately treated.
- ACR 30 mg/mmol or more (ACR category A3), together with haematuria.
- Known or suspected rare or genetic cases of CKD.

5. Checklist for improving your practice



- Are all your T2D patients receiving ACR and eGFR testing at least once a year?
- Do you regularly review your T2D patients to ensure they are being offered diet/lifestyle counselling and are on optimised appropriate medications?

6. Useful resources



- **Diabetes UK: Information prescription on diabetes and kidney disease.**
<http://bit.ly/2NZ60Ja>
- **NHS information.**
<https://www.thinkkidneys.nhs.uk/>
- **TREND-UK Prescribing guidance in patients with renal impairment.**
http://diabetestimes.co.uk/wp-content/uploads/2017/07/HCP_Renal_TREND.pdf

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