ABCD–UKKA concise recommendations for management of CKD in type 2 diabetes

This 2024 overview of the management of chronic kidney disease (CKD) in type 2 diabetes from the Association of British Clinical Diabetologists and UK Kidney Association (ABCD–UKKA), published in *Diabetic Medicine*, collates and summarises the latest evidence and uses it to provide pragmatic recommendations for practising clinicians. This overview provides a four-tiered approach, highlights the importance of holistic, individualised, multiple risk factor intervention to improve cardiorenal outcomes, and raises awareness of the inadequacies and inequities in the management of diabetic CKD in the UK. The recommendations are broadly aligned with those from other global organisations, including the Kidney Disease Improving Global Outcomes and American Diabetes Association (KDIGO–ADA) consensus statement.

Pam Brown
GP in Swansea

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In the UK, diabetes is the commonest cause of chronic kidney disease (CKD), accounting for half of all people with CKD and one third of those with end-stage renal disease. Of the 5 million people in the UK with diabetes, 40% will develop CKD at some stage, and people with both diabetes and CKD are at higher risk of developing cardiovascular disease (CVD) and mortality, even compared to those with diabetes or CKD alone.

In the present review published in *Diabetic Medicine*, Dasgupta and colleagues summarise the Association of British Clinical Diabetologists and UK Kidney Association (ABCD–UKKA) guidelines on glycaemia, blood pressure (BP) and lipid management in people with CKD and type 2 diabetes, along with their consensus statement on the use of finerenone in progressive CKD, combining these four guidelines (see *Box 1*) into a pragmatic, four-tier, implementable guideline for clinicians.

The four tiers are summarised in *Figure 1*.

Tier 1

Simultaneous multiple risk factor interventions are recommended to slow the progression of CKD and reduce CVD, since individualised glycaemic and BP optimisation with lifestyle and drug therapy can help prevent CKD progression and reduce cardiovascular risk.

Lifestyle advice

- Salt reduction to <90 mmol sodium daily (<5 g salt or <2 g sodium).
- Alcohol <14 units/week.
- Maintain optimal weight (BMI 20–25 kg/m^2).
- Smoking cessation.
- Physical activity at least 30 minutes daily on 5 days per week.

Glucose lowering

- Metformin built up to 1 g twice daily. Reduce to 500 mg twice daily if eGFR is <45 mL/min/1.73 m^2 and stopped if <30 (specialist, individualised advice may be appropriate if eGFR is 25–30).
- SGLT2 inhibitors for glucose lowering and, in addition to ACE inhibitors/ARBs, to slow progression of CKD in people with or without type 2 diabetes.
- The renal and cardiovascular benefits of SGLT2 inhibitors are independent of glucose-lowering effects and persist at eGFR <45 mL/min/1.73 m^2, while minimal glucose lowering occurs below this eGFR. SGLT2 inhibitors can be used down to eGFR >20. Add additional glucose-lowering drugs if needed.
- GLP-1 receptor agonists lower HbA_{1c} and reduce cardiovascular risk and albuminuria; one cardiorenal outcomes study demonstrates slowing of CKD progression with semaglutide

Box 1. Full ABCD/UKKA guidelines reviewed. Click links to access.

- Management of hyperglycaemia
- Management of hypertension and RAS blockade
- Management of lipids
- Finerenone in the management of diabetic kidney disease

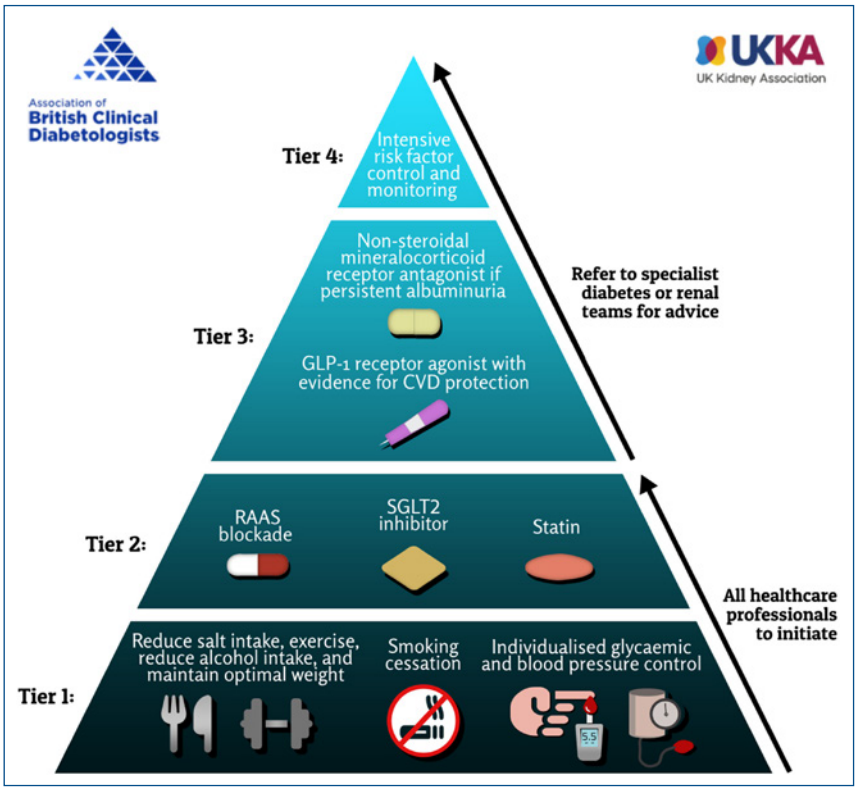

Figure 1. Four-tier approach to managing chronic kidney disease.
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in addition to ACE inhibitors/ARBs (see previous *Diabetes Distilled*).

- ➤ Those taking SGLT2 inhibitors in the FLOW study gained the same benefit from semaglutide; therefore, the authors recommend considering the combination of GLP-1 receptor agonists and SGLT2 inhibitors early in people with CKD and type 2 diabetes.

Hypertension

- Accurate measurement and monitoring of BP, as in British and Irish Hypertension Society guidance, is important. Treatment thresholds depend on age, type of diabetes, presence of CKD and albuminuria.
- BP has the greatest impact on progression of CKD in people with type 2 diabetes:
  - ➤ If ACR 3–30 mg/mmol, CKD stage 1–3 or CKD stage 4–5 with ACR >30 mg/mmol: **target BP ≤130/80 mmHg**.
  - ➤ If CKD stage 4–5 without albuminuria or on dialysis: **target BP ≤140/90 mmHg**.
- First-line treatment: ACE inhibitor, or ARB if not tolerated, then follow NICE NG136 treatment algorithm for second-line and subsequent treatments (CCB or diuretic, then add the other).
- In advanced CKD and treatment-resistant hypertension (uncontrolled on three or more agents, including a diuretic, at maximum tolerated dose), adding a thiazide diuretic may reduce BP.

Tier 2

Tier 2 interventions can be started alongside those in tier 1, both in primary care.

Renin–angiotensin system blockade (ACE inhibitors/ARBs)

- In addition to BP lowering, these drugs reduce risk of CKD progression by 16–20% but have no effect on CVD risk.
  - ➤ Titrate up to maximum licensed and tolerated dose, with checks of potassium and renal function.
  - ➤ Check electrolytes and eGFR 1–2 weeks after initiation and each dose titration. An eGFR reduction is expected:
    - – If >25% eGFR reduction: stop, repeat test and consider other causes (e.g. hypovolaemia, NSAIDs).
    - – If ≤25% reduction: continue and repeat bloods after 1–2 weeks.
    - – If potassium increases but is less than 6 mmol/L: can continue treatment. Give advice to reduce high-potassium foods and avoid salt substitutes (see *Box 2*). Repeat tests after 1–2 weeks.
- Do not use both an ACE inhibitor and an ARB.
- Pause ACEi/ARB treatment (and metformin and SGLT2 inhibitors) during acute illness. Discuss sick day rules.

Box 2. Reducing risk of hyperkalaemia.

Check if people are using salt substitutes (e.g. LoSalt), which are high in potassium.

High-potassium fruits:
Avocado, guava, kiwi, banana, melon, pomegranate, orange and orange juice, dried fruits including prunes and raisins.

High-potassium vegetables:
Potato, sweet potato, tomato, mushroom, Brussels sprout, courgette and squash, broccoli, tomato or vegetable juice.

SGLT2 inhibitors

- Result in a further 30% reduction in progression of CKD even in those on optimal ACEi/ARB therapy.
- Reduce CVD and mortality, and result in 3 mmHg additional BP lowering.
- Use in all with CKD and type 2 diabetes if eGFR is >15 mL/min/1.73 m^2.
- Discuss sick day rules.

Lipid lowering

ABCD–UKKA lipid guidelines in people with CKD and type 2 diabetes provide full details of the recommendations.

- Each 1 mmol/L reduction in LDL cholesterol reduces CVD events by 21%:
  - ➤ Benefit reduces as eGFR decreases.
  - ➤ No benefit in those with end-stage renal disease on dialysis.
  - ➤ LDL reduction benefits return following renal transplant.
- People with CKD and type 2 diabetes should receive optimal doses of statin for primary prevention.
  - ➤ If intolerant of full-dose statin, give ezetimibe ± a lower statin dose.
- Pragmatic treatment targets in those with CKD and type 2 diabetes:
  - ➤ Total cholesterol ≤4.0 mmol/L.
  - ➤ Non-HDL cholesterol ≤2.5 mmol/L.
  - ➤ LDL cholesterol ≤1.8 mmol/L.
- Start with atorvastatin 20 mg and titrate or change to higher potency statin (rosuvastatin).
- Seek specialist advice if eGFR is <30 mL/min/1.73 m^2 or if there is a need to use a fibrate in people with CKD.
- If statin intolerance: ezetimibe alone or in combination with bempedoic acid.
- At any stage, add icosapent ethyl 2 g twice daily if triglycerides >1.7 mmol/L and LDL cholesterol 1.04–2.6 mmol/L on statin **and** with established CVD.
- See full guideline for newer agent use – evidence of effect down to CKD stage 3b.

Tier 3

Despite optimised glycaemic and BP optimisation and use of ACEi/ARBs and SGLT2 inhibitors, residual risk persists – 10% of people still reached end-stage renal disease and 7% still had a CVD event in treatment groups in the clinical trials.

- Mineralocorticoid antagonists (eplerenone and spironolactone) improve BP, decrease proteinuria and slow CKD progression, but high risk of hyperkalaemia in people with CKD and type 2 diabetes.
- Finerenone is a non-steroidal mineralocorticoid antagonist with less impact on potassium levels:
  - ➤ Strong evidence of cardiorenal protection in FIDELIO-CKD and FIGARO-CKD studies (see previous *Diabetes Distilled*).
  - ➤ Consider finerenone if persistent albuminuria >30 mg/mmol despite maximum tolerated doses of ACEi/ARB and on SGLT2 inhibitor, or if SGLT2 inhibitor not tolerated.
  - ➤ Use if eGFR is ≥25 mL/min/1.73 m^2 and potassium is <5 mmol/L.
- GLP-1 receptor agonists provide additional CVD reduction even in those on SGLT2 inhibitors; therefore, use both early in CKD and type 2 diabetes.

Tier 4

Most people with type 2 diabetes and CKD will die of CVD before reaching end-stage renal disease.

- Use Kidney Failure Risk Equation (KFRE) and QRISK3 calculators to assess risks of end-stage renal disease and CVD events.
- CKD Patch, developed by Johns Hopkins University based on the SCORE US CVD calculator, provides more accurate CVD and mortality risk estimates for those with CKD. The calculator allows change of units to input ACR and total cholesterol in UK values.
- If QRISK3 high and KFRE low, tighten BP and lipid control.
- If younger person with high risk of CKD progression and CVD, tighten BP, maximise ACEi/ARB, add a GLP-1 RA and monitor bloods regularly.

Involve people in their management and help them understand their risks and what they can do about them. Encourage home BP monitoring to improve medication adherence and motivation.

Pregnancy precautions

With younger onset of both type 2 diabetes and CKD, we need to remember the importance of counselling women of childbearing potential about the increased risk of pregnancy complications and the importance of stopping

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Diabetes & Primary Care **26**: 159–62

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potentially teratogenic drugs, such as statins, ACEi/ARBs and newer glucose-lowering agents, prior to conception.

Implications for practice

This paper reminds us of the significant inequalities and inequity in the delivery of care for CKD in people with type 2 diabetes. The guidance provides clarity on what we can do to reduce risk of CKD progression and cardiovascular events in primary care as soon as we identify the development of CKD in our patients with type 2 diabetes.

Although we are all aware of the increased cardiovascular risk associated with type 2 diabetes, many clinicians remain less aware of how this risk further increases with development of albuminuria or when eGFR falls below 60 mL/min/1.73 m^2 – that is, when CKD is diagnosed. Although we cannot code CKD until one or both of these have persisted for 90 days, there is no reason to delay optimising blood pressure and lipids, and supporting people to make lifestyle changes, immediately.

ACR measurement is an important part of these recommendations as it influences BP targets, initiation of ACEi/ARBs, prescribing of SGLT2 inhibitors and, more recently, initiation of GLP-1 RAs and finerenone. We can help all people with diabetes, hypertension or CKD understand the need for their ACR test by promoting it as part of the two-part "Kidney Health Check", as publicised by Professor Andrew Frankel. Giving people white-top urine pots at each appointment and initially asking for a random sample if first-pass urine is too challenging, overcomes some of the inertia.

In primary care, auditing our care of people with CKD and type 2 diabetes is very straightforward, and in England it is incentivised by Quality and Outcomes Framework (QOF) payments. Sadly, levels of ACR and eGFR monitoring have declined in parts of the UK where QOF has been removed, delaying the identification of CKD and early intervention.

Let's make those Kidney Health Checks a priority and use this paper to re-energise our efforts to optimise BP, lipids and glycaemia, and to use the evidence-based lifestyle and drug recommendations consistently to reduce the risk of CVD and CKD progression going forward. Our early efforts can significantly reduce later ill-health and poor quality of life. ■

Dasgupta I, Zac-Varghese S, Chaudhry K et al (2024) Current management of chronic kidney disease in type-2 diabetes – A tiered approach: An overview of the joint Association of British Clinical Diabetologists and UK Kidney association (ABCD–UKKA) guidelines. *Diabet Med* 17 Oct [Epub ahead of print]: e15450. https://doi.org/10.1111/dme.15450