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Association of British Clinical Diabetologists and UK Kidney Association joint clinical practice guidelines for the pharmacological management of hyperglycaemia in adults with type 2 diabetes and CKD

Janaka Karalliedde, King's College London
Kieran McCafferty Queen Mary University London and Barts Health NHS Trust , London
Peter Winocour, East and North Herts NHS Trust, Hertfordshire
Tahseen A Chowdhury, Royal London Hospital, London
Naresh Kanumilli Northenden Group Practice, Manchester,
Parijat De, City Hospital, Birmingham
Andrew H Frankel, Imperial College Healthcare NHS Trust, London
Ciara Doherty Guy's and St Thomas' Hospital London
Nicola Milne, Brooklands and Northenden Primary Care Network Manchester
Rosa M Montero, St George's Hospital, London
Eirini Loudaki King's College Hospital London
Debasish Banerjee, St George's University Hospitals NHS Foundation Trust & City St George's University of London
Ritwika Mallik University College London NHS Trust London
Adnan Sharif, University Hospitals Birmingham, Birmingham
Sagen Zac-Varghese East and North Herts NHS Trust Hertfordshire
Srikanth Bellary Aston University, UK
Gabrielle Goldet Imperial College Healthcare NHS Trust, London
Ketan Dhatariya Norfolk and Norwich University Hospitals NHS Foundation Trust and Norwich Medical School, University of East Anglia
Stephen C Bain, Swansea University, Swansea
Indranil Dasgupta, Heartlands Hospital, Birmingham and Warwick Medical School, University of Warwick, Coventry

Abstract

A growing and significant number of people with diabetes develop chronic kidney disease (CKD) and diabetes related CKD is a leading cause of end-stage kidney disease (ESKD). People with diabetes and CKD have high morbidity and mortality, predominantly related to cardiovascular disease (CVD).

Hyperglycaemia and hypertension are modifiable risk factors to prevent onset and progression of CKD and related CVD. Recent clinical trials of people with type 2 diabetes and CKD have demonstrated reduction in composite kidney endpoint events (significant decline in kidney function, need for kidney replacement therapy and kidney related death) and cardiovascular risk with sodium glucose co-transporter-2 (SGLT-2) inhibitors, non-steroidal mineralocorticoid receptor antagonists (nsMRAs) and glucagon-like peptide 1 (GLP-1) receptor agonists.

The Association of British Clinical Diabetologists and UK Kidney Association Diabetic Kidney Disease Clinical Speciality Group have previously undertaken a narrative review and critical appraisal of the available evidence to inform clinical practice guidelines for the pharmacological management of hyperglycaemia in adults with type 2 diabetes and CKD. This 2025 abbreviated updated guidance from a multidisciplinary group of healthcare professionals from primary and secondary care settings summarises the key recommendations and recent evidence that has implications for clinical practice for health care professionals who treat people with type 2 diabetes and CKD

Background

International clinical guidelines advocate a multifactorial approach to the management of CKD secondary to type 2 diabetes (T2DM)(1, 2). A fundamental and foundational component of this approach is lifestyle interventions, such as a healthy diet and physical exercise to achieve weight loss, and smoking cessation. In parallel, pharmacological treatment and management of glucose, blood pressure, and lipids is recommended. For many decades, renin-angiotensin system inhibition (RASi) was the only proven effective treatment for slowing the progression of CKD and the effect of this class of agents was independent of their antihypertensive properties.(3, 4).(5, 6).

Of note these trials were not powered sufficiently to draw conclusions from their cardiovascular endpoints. Although RASi demonstrated a significant reduction in kidney endpoints, a significant residual risk of kidney disease progression (5-7) was observed with more than 30% of participants progressing to the primary kidney endpoint (8, 9)

Sodium-glucose cotransporter-2 (SGLT2) inhibitors were originally licensed as glucose-lowering agents in T2DM. However, in cardiovascular outcomes trials that were designed primarily to establish the CVD safety of this class, a reduction in kidney events explored as secondary outcomes was observed (10).

Subsequently clinical trials with dedicated primary kidney endpoints demonstrated significant reductions in kidney disease events and associated cardiovascular disease burden including heart failure (11). Following on from the emergence of SGLT2 inhibition for CKD, non-steroidal mineralocorticoid receptor antagonists (nsMRAs) and glucagon-like peptide 1 (GLP-1) receptor agonists have also recently demonstrated kidney and cardiovascular benefits effects in people with T2DM and CKD (11, 12).

This article summarises the key recommendations for clinical care practice from a group of multi-disciplinary primary (community) and secondary care based health care professions involved in the care of people with T2DM and CKD. For definitions of the evidence grades, please see supplement material figure 1. These recommendations are based on a narrative review of the Cochrane Library, PubMed/MEDLINE, Google Scholar and Embase carried out initially between October 2013 and December 2020 and further review carried out from December 2020 and February 2025 for the current update, using the following keywords: type 2 diabetes, chronic kidney disease, diabetic nephropathy, hyperglycaemia, hypertension, SGLT-2 inhibitors, non-steroidal mineralocorticoid antagonists pioglitazone, DPP-4 inhibitors, GLP-1 analogues and anti-diabetic medications, kidney failure, end stage kidney disease.

Glycaemic targets for the prevention and management of chronic kidney disease in people with diabetes

The management of diabetes is predicated on the basis of reducing hyperglycaemia to improve osmotic symptoms, with supportive evidence that this will prevent the onset, and slow down progression of kidney and vascular complications over time (1).

The precise level of glycaemic control that delivers optimal benefit remains contentious because, inevitably, the individualised approach to care and the evidence base from different cohorts do not allow clear extrapolation. The glycaemic management of people with type 1 diabetes and type 2 diabetes and the respective kidney benefits require separate consideration, which in part reflects the different evidence base and lifetime risks of complications with the greater risk for

hypoglycaemia that arises when several concurrent therapies are used alongside insulin as kidney function deteriorates(1).

The risks of hypoglycaemia are greater in people with diabetes and CKD especially if people are on insulin treatment, sulfonylurea or glinides (1). Individualised pragmatic glycaemic goals that balance the benefits and risks of intensive glucose lowering in people with diabetes and CKD and patient education on hypoglycaemia avoidance and self-management are needed. In addition, the risk–benefit equation of tighter glycaemic control for kidney and vascular complications alters as CKD progresses.

There has also been an important shift in emphasis in recent international guidance for people with T2DM with a specific emphasis on selection of medications where independent of their glucose lowering effects those with evidence base for cardio-kidney protection should be prioritised (1, 13).

HbA1c targets for people who have type 2 diabetes and CKD.

Individualised HbA1c targets should be applied in the management of people with CKD. We therefore recommend that individualised HbA1c targets should be applied in the management of people with T2DM and CKD, using the levels suggested in Table 1. These target ranges are based on opinion of the writing committee as there is limited high grade evidence in people with CKD.

At present, it would be prudent to consider a HbA1c target of 58 mmol/mol (7.5%) for most people with CKD if their glucose lowering therapies include insulin and a target of up to 68 mmol/mol (8.4%) in frail people with more advanced CKD (stage 4 and above). In people with more advanced CKD particularly with eGFR <30 ml/min/1.73m^2, HbA1c has more limitations and we would advise monitoring of

capillary blood glucose or continuous glucose monitoring (CGM) to aid clinical decision and treatment choice (14, 15).

It remains unclear with no evidence to date whether it is appropriate and or safe to have a lower glycaemic HbA1c target of 52 mmol/mol (6.9%) for reduction in CKD onset or progression with novel agents such as GLP-1 RA, dual GLP-1 RA and Glucose-dependent insulinotropic polypeptide (GIP) agonist or SGLT-2 inhibitors which have lower burden of hypoglycaemia. From the current evidence, there is no basis to seek HbA1c values of lower than 52 mmol/mol (6.9%) in older people with T2DM and CKD with medication.

Kidney function measurements in determining medication dosages in diabetes

We recommend that eGFR is utilised, preferably using the more accurate serum creatinine based Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, without adjustment for race/ethnicity, when determining if certain therapies can be used to adjust medication dosages in diabetes (16, 17). It is important to recognise that eGFR equations have several limitations (18), and hence an individualised pragmatic approach needs to be taken when deciding to initiate or cease medications solely on the basis of kidney function due to these limitations. In the clinical scenarios where creatinine based eGFR equations may be less reliable (e.g. extremes of body weight) we would recommend using cystatin based eGFR equations as a more accurate eGFR will better guide/determine treatments adjustment /changes in dosing.

Glucose-lowering therapies for people who have type 2 diabetes and CKD:

The selection of individual classes of drug, tailored to the comorbidities that are frequently seen alongside CKD, will also influence therapy selection (Figure 1 and Table 2). In addition, judicious combinations of different classes of drugs would need consideration. Although these guidelines focus on individual classes of glucose-lowering drugs, combinations of different classes are frequently prescribed to people with CKD. There is a relative dearth of studies providing high-quality evidence that specifically evaluate different drug combinations in people with T2DM and CKD and this is clearly an area for both further research and clinical audit.

Recommendations

1 Individualised HbA1c targets should be applied in the management of people with CKD, using the levels suggested in Table 1. (Grade 1B).

2 Additional comorbidities, that are frequently seen alongside CKD, and risk of hypoglycaemia should also influence therapy selection and HbA1c targets. In people who progress to advanced stages of CKD (eGFR <45 ml/min) or those with rapid progression of CKD more frequent monitoring of HbA1c and kidney function may be required. (Table 1 and 2 and Figure 1) (Grade 1B).

3 Combinations of different classes of drugs are often needed to manage glycaemia in CKD; judicious combinations of different classes should be considered based on their benefits and harms (Grade 2D).

Insulin therapy in people with CKD

Recommendations

1 There is no firm evidence that insulin therapy reduces the risk of progressive kidney disease. Therefore, the aim of insulin therapy should be to improve glycaemic control and improve quality of life, with a low risk of hypoglycaemia (Grade 1C).

2 Insulin requirements are likely to rise in the early stages of CKD due to increased insulin resistance (Grade 1C).

3 As eGFR declines, insulin requirements are likely to diminish through reduced kidney insulin clearance. In people with CKD stage 3b and below who are on insulin, and whose HbA1c is 58 mmol/mol (7.5%) or below, reduction of insulin dose should be considered (Grade 1C).

4 People with CKD who are treated with insulin should undertake regular glucose monitoring (Grade 1C).

5 In people who are less able to manage with the requirements of a basal bolus regime, once daily regimes with longer-acting insulins should be considered (Grade 1D).

6 If people experience hypoglycaemia on neutral protamine Hagedorn (NPH) insulin or premixed insulins, conversion to analogue insulins may be of benefit (Grade 1C).

Metformin

The dose of metformin should be decreased to 500mg twice a day if eGFR is less than 45 mL/minute/1.73m^2 and omitted if eGFR is less than 30 mL/minute/1.73m^2. However as stated previously limitations of eGFR measurements need to be

appreciated especially in those at extremes of body weight. Treatment should be paused in people at risk of tissue hypoxia or sudden deterioration in kidney function, for example, dehydration, severe infection, shock, sepsis, acute heart failure, respiratory failure or hepatic impairment, or those who have recently had a myocardial infarction (19).

For most people, the benefits of metformin greatly outweigh the very small lactic acidosis risk. There may be subgroups of people who are at higher risk of lactic acidosis (not just due to impaired kidney function), however, the practical advice for clinicians and people contained in Table 3 and Figure 1 is relevant and in general supports the ongoing use of metformin for people with stable CKD stage 3.

Recommendations

1 Metformin can be used down to an eGFR of 30 mL/min/1.73m^2. The dosage should be reduced to 500mg twice a day when the eGFR falls below 45 mL/min/1.73m^2 (Grade 1B).

3 Metformin should be paused during periods of acute illness, particularly when a person has acute kidney injury (AKI). Everyone who is treated with metformin should be given sick day guidance, which should be reiterated at every medication review (Grade 1B).

4 In people with eGFR <60 ml/min1.73m^2 metformin should be withheld 24 hours prior to and up to 48 hours after any procedure that requires the use of radiographic contrast media (Grade 1B).

SGLT-2 inhibitors

This section summarises recent outcome trials where kidney outcomes were assessed as primary endpoint in people with T2DM and CKD with SGLT-2 inhibitors. Three clinical trials (summarised in brief below) have consistently shown that SGLT-2 inhibition on top of standard of care (RASi) significantly reduces the risk of progression of CKD and associated CVD in people with T2DM and CKD.

Canagliflozin and Kidney Events in Diabetes with Established Nephropathy Clinical Evaluation (CREDENCE) was the first study of an SGLT-2 inhibitor to have kidney outcomes in its primary composite endpoint (20). People with T2DM and albuminuric CKD were randomised to receive canagliflozin 100 mg once daily or placebo. All participants had an eGFR of 30 to <90 mL/min/1.73m^2, albuminuria [urine albumin: creatinine ratio (ACR) >33.9–565 mg/mmol (>300 to 5,000 mg/g)] and received RAS blockade. Sixty per cent of recruits had an eGFR of 30–60 mL/min/1.73m^2. The primary endpoint was a composite of ESKD (dialysis, transplantation, or sustained eGFR of <15 mL/min/1.73m^2), a doubling of the serum creatinine or death from kidney or cardiovascular causes.

The relative risk of the primary endpoint was significantly lower in the canagliflozin group with event rates of 43.2 versus 61.2 per 1,000 patient-years (HR 0.70; 95% CI 0.59–0.82; p=0.00001). The relative risk of the kidney -specific composite of ESKD, doubling of the creatinine level, or death from kidney causes was lower by 34% (HR 0.66; 95% CI 0.53–0.81; p<0.001) and end-stage kidney disease was lower by 32% (HR 0.68; 95% CI 0.54–0.86; p=0.002).(20) Of note, in this high-risk population there were no significant increases in rates of lower limb amputation or fracture.

The canagliflozin group also had a lower risk of cardiovascular death, myocardial infarction, or stroke (HR 0.80; 95% CI, 0.67 to 0.95; P=0.01) and hospitalization for heart failure (HR 0.61; 95% CI, 0.47 to 0.80; P<0.001).

The Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease (DAPA-CKD) trial assessed the effect of dapagliflozin on kidney and cardiovascular events in people with CKD (both with and without T2DM).(21). In this study 4,094 participants with an eGFR between 25–75 mL/min/1.73m^2 and urine ACR of 22.6–565 mg/mmol (200–5,000 mg/g) were randomised to receive dapagliflozin 10mg once daily or placebo. The primary outcome was a composite of sustained decline in eGFR of at least 50%, ESKD, or death from kidney or cardiovascular causes. Over a median of 2.4 years, the primary outcome event occurred in 197 of 2,152 participants (9.2%) in the dapagliflozin group and 312 of 2,152 participants (14.5%) in the placebo group (HR 0.61; 95% CI 0.51 to 0.72; p<0.001). The hazard ratio for the kidney composite of a sustained decline in eGFR of at least 50%, ESKD, or death from kidney causes was 0.56 (95% CI 0.45 to 0.68; p<0.001). The effects observed were similar in people with T2DM to those without (21). Similarly, the hazard ratio for the composite of death from cardiovascular causes or hospitalization for heart failure was HR 0.71 (95% CI, 0.55 to 0.92; P=0.009).

The EMPA-KIDNEY (The Study of Heart and Kidney Protection With Empagliflozin) trial included 6609 people with CKD with an eGFR 20-45 mL/min/1.73m^2 (irrespective of the presence of albuminuria) or 45-90 mL/min/1.73m^2 with raised urine ACR of >200 mg/g (22.6 mmol/mol) who were randomised to receive empagliflozin 10mg once daily or placebo (22). The primary outcome was a composite of progression of kidney disease (defined as end-stage kidney disease, a sustained decrease in eGFR to <10 mL/min/1.73m^2 ,a sustained

decrease in eGFR of ≥40% from baseline, or death from renal causes) or death from cardiovascular causes. During a median of 2.0 years of follow-up, progression of kidney disease or death from cardiovascular causes occurred in 432 of 3304 patients (13.1%) in the empagliflozin group and in 558 of 3305 patients (16.9%) in the placebo group (HR, 0.72; 95% confidence interval [CI], 0.64 to 0.82; P<0.001)(22). All cause hospitalisation was significantly lower for the empagliflozin group than in the placebo group (HR ratio, 0.86; 95% CI, 0.78 to 0.95; P=0.003).

The recent post trial follow up reported that in 4891 (74%) people enrolled where the use of open-label SGLT-2 inhibitors was similar in the two groups (43% in the empagliflozin group and 40% in the placebo group during the post-trial period, the hazard ratio for a primary-outcome event was 0.87 (95% CI, 0.76 to 0.99) which confirms there is a continued cardio-renal benefit of empagliflozin for up to 12 months post discontinuation but importantly highlights the need for the therapy be persisted with to maintain the observed 'on treatment' greater risk reduction and related benefit (23). A collaborative meta-analysis that integrated the kidney outcomes from large placebo-controlled trials of SGLT2 inhibitors from the SGLT2 inhibitor Meta-Analysis Cardio-Renal Trialists' Consortium (SMART-C) concluded that in addition to the established cardiovascular benefits of SGLT2 inhibitors, clinical evidence support their use for modifying risk of CKD progression and AKI, in patients with T2DM at high cardiovascular risk, and in patients with CKD or heart failure irrespective of diabetes status, primary kidney disease or baseline kidney function (24).

Practical aspects of using SGLT-2 inhibitors in people with T2DM and CKD

The observed kidney and cardiovascular benefits of SGLT-2 inhibitors are independent of the HbA1c lowering effects of these agents in people with T2DM.

In people with diabetes and eGFR<45 ml/min/1.73 m^2, treatment with SGLT-2 inhibitors do not lower HbA1c significantly(1). A SGLT-2 inhibitor can be initiated for kidney protection above an eGFR >20 ml/min/1.73m2, however, if further glucose lowering is required adding another class of medications to optimise diabetes control is recommended (1).

If dapagliflozin, canagliflozin or empagliflozin is started for CKD, the medication can be continued until dialysis initiation or renal transplantation (Figure 1). Regardless of urine ACR we also recommend the initiation of dapagliflozin or empagliflozin for people with T2DM and CKD where eGFR>20mL/min/1.73m^2.

Diabetic ketoacidosis (DKA) secondary to SGLT-2 inhibitor is rare in T2DM with reported incidence between 1 in 1000 to 1 in 10,000 people (1, 24).

SGLT-2 inhibitor induced DKA can present with normoglycaemia or moderately raised glucose levels. It is important for clinicians to be aware of this so that diagnosis is not missed. Fournier's gangrene (necrotising fasciitis of the genitalia or perineum) is a rare but potentially life-threatening condition that is associated with several predisposing risk factors such poorly controlled diabetes, chronic alcoholism, renal failure, liver cirrhosis, and obesity (25-27). Fournier's gangrene affects predominantly men and may present as severe pain or tenderness, erythema, and swelling in the genital or perineal area, with fever or malaise(25). Post-marketing cases of Fournier's gangrene have been reported to be associated with the use of SGLT2 inhibitors (26, 27). For example in the UK data from 2012 to 2018 reported by the medicines health regulatory agency (MHRA) noted 6 events of Fournier's gangrene (4 in men and 2 in

women) in association with SGLT2 inhibitors(28). This corresponds to a UK estimated exposure to SGLT2 inhibitors of 548,565 patient-years of treatment. People taking SGLT2 inhibitors should be advised to seek urgent medical attention if they experience severe pain, tenderness, erythema, or swelling in the genital or perineal area accompanied by fever or malaise. If Fournier's gangrene is suspected**,** SGLT2 inhibitor treatment should be stopped and treatment started urgently (including antibiotics and surgical debridement) as appropriate.

Recommendations

1. We recommend the consideration of starting SGLT-2 inhibitors in **all** individuals with type 2 diabetes and CKD with an eGFR ≥20 ml/min/1.73 m2, (Grade 1A).

2. Where individuals are already receiving treatment with insulin or sulfonylureas, a reduction in dose of these drugs should be considered in people T2DM and CKD with eGFR >45 ml/min/1.73 m2 and HbA1c that is not very high (e.g. <64 mmol/mol (8%) so as to reduce the risk of hypoglycaemia (Grade 1A).

3. The initiation of SGLT-2 inhibitors in people who have active foot disease (ulceration, infection, sepsis and ischaemia) should be avoided and these agents should be paused in people who develop active infected and/or vascular foot complications while on treatment. SGLT-2 inhibitors should only be reinstated after foot problems have fully resolved and following discussion with the multidisciplinary foot team (expert opinion, no high-grade evidence)

4. SGLT-2 inhibitors should be withdrawn in all people who develop DKA. However, if a definitive cause for DKA is identified (e.g. low-calorie diet, post-

operative catabolic state, inappropriate cessation of insulin) reinstatement of SGLT-2 inhibitor may be considered depending on careful assessment of the individualised risks and benefits by a diabetes specialist. (expert opinion, no high-grade evidence)

5. We do not recommend routine assessment of kidney function (creatinine and/or eGFR) within 6–8 weeks of SGLT-2 initiation since there is likely to be a transient and physiological deterioration and this is not a reason to withdraw the drug. (expert opinion, no high-grade evidence)

6. We recommend that sick day guidance applies, during which SGLT-2 inhibitors should be temporarily paused in scenarios for example when people are unable to maintain any oral fluid or food intake for >24 hours or in settings of acute medical emergencies requiring urgent hospitalisation or prior to major surgery (expert opinion, no high-grade evidence). It is however essential that once the acute event has resolved and the person has recovered that the SGLT-2 inhibitor is promptly restarted.

Glucagon-like peptide-1 receptor agonists (GLP-1 RA) and dual GLP-1 RA and GIP agonists

Systematic reviews and meta-analyses suggest a clear beneficial class effect of GLP-1 receptor agonists (GLP-1 RA) on the risk of cardiovascular disease (CVD) and albuminuria reduction (29, 30). Currently there is one primary kidney endpoint study reported with this class of agent in 3533 participants with T2DM and CKD where the Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes trial (FLOW) (12) was evaluated. In this study, participants with T2DM with eGFR

50 to 75 ml/min/1.73 m^2 and a urinary ACR between 33.9 mg/mmol (>300 mg/g) and 565 mg/mmol (<5000 mg/g) or an eGFR of 25 to <50 ml/min/1.73 m^2 and ACR between 11.3 mg/mmol and 565 mg/mmol) (100-5000 mg/g) were randomised to receive subcutaneous semaglutide at a dose of 1.0 mg weekly or placebo. The primary outcome was major kidney disease events, a composite of the onset of kidney failure (dialysis, transplantation, or an eGFR of <15 ml/min/1.73 m^2, at least a 50% reduction in the eGFR from baseline, or death from kidney-related or cardiovascular causes).

This trial demonstrated both renal benefits and CVD mortality benefits with a 24% relative risk reduction of the risk of a primary outcome of major kidney disease events in the semaglutide group than in the placebo group (331 vs. 410 first events; hazard ratio, 0.76; 95% confidence interval [CI], 0.66 to 0.88; P = 0.0003). The risk of major cardiovascular events was 18% lower (hazard ratio, 0.82; 95% CI, 0.68 to 0.98; P=0.029), and the risk of death from any cause 20% lower (hazard ratio, 0.80; 95% CI, 0.67 to 0.95, P=0.01) in the semaglutide group as compared to placebo (12).

The dose of injectable semaglutide was up-titrated from starting dose of 0.25 mg per week to 1mg weekly over 8 weeks (0.25 to 0.50 mg over weeks and 0.5 to 1.0 mg over further 4 weeks). Similar benefits for the composite of the kidney-specific components of the primary outcome (hazard ratio, 0.79; 95% CI, 0.66 to 0.94) and for death from cardiovascular causes (hazard ratio, 0.71; 95% CI, 0.56 to 0.89) were observed. These results were observed as compared to standard of care (placebo group) which was RAS blockade and of note ~15.6% of the cohort were on SGLT-2 inhibition at baseline and no major heterogeneity of treatment effect observed in those on this combination. This evidence for the beneficial impact of GLP-1 RA on kidney outcomes has been observed in several studies where reduction in albuminuria and

prevention of eGFR fall were reported when analyses as secondary or exploratory outcomes (1, 30-32). Further primary kidney endpoint trials with other agents in this class of medications in people with CKD are ongoing and include promising data from dual GLP-1 RA and GIP agonist Tirzepatide (33). Please see Figure 1 for detailed information on frequently used GLP-1 RA and GLP-1 RA/GIP dosing considerations in CKD

Recommendations

1 We recommend the consideration of injectable once weekly semaglutide (1mg s/c weekly) in people with T2DM and albuminuric CKD who have eGFR >25 ml/min/1.73 m2, irrespective of glycaemic control. (Grade 1B).

2 Other agents within the class of GLP-1 RA or GLP-1 RA /GIP dual agonists can be used for the improvement of glycaemic control with a low risk of both hypoglycaemia and beneficial effects of weight loss in obese people with T2DM and CKD (Grade 1A).

3 There is evidence of protection from cardiovascular disease with some GLP-1RAs in people who have T2DM and a high risk of cardiovascular disease (Grade 1A).

4 People with CKD who are treated with GLP-1RAs or GLP-1 RA /GIP dual agonists need to only perform regular self-monitoring of blood glucose when they are also being treated with drugs that can cause hypoglycaemia (sulfonylureas and insulins) (Grade 1A).

5 We recommend caution for the use of GLP-1 RA or GLP-1 RA /GIP dual agonists in people with CKD with advanced active diabetic retinopathy (proliferative diabetic retinopathy) and elevated HbA1c (>86 mmol/mol or 10%) and if

treatment is started avoidance of rapid reduction in HbA1c and liaising with ophthalmology teams to ensure retinal surveillance is in place (expert opinion no high grade evidence)

Dipeptidyl peptidase-4 inhibitors

Dipeptidyl peptidase-4 inhibitors (DPP-4 inhibitors) bind selectively to DPP-4 and prevent the rapid hydrolysis GLP-1. They have a modest glucose-lowering effect, compared with other oral hypoglycaemic agents. DPP-4 inhibitors are known to have a very low risk of hypoglycaemia and are generally associated with a favourable safety and tolerability profile in people with type 2 diabetes and mild-to-severe kidney impairment (see Figure 1) (34).

Recommendations

1 We recommend that people with CKD of all stages are suitable for treatment with DPP-4 inhibitors (Grade 1B).

2 We recommend that doses of DPP-4 inhibitors are appropriately reduced in accordance with the degree of kidney impairment (including maintenance haemodialysis) except linagliptin (Grade 1B).

3 People with CKD can be safely prescribed DPP-4 inhibitors without the risk of hypoglycaemia or weight gain at all stages of kidney disease (Grade 1B).

4 There are no current data to suggest that DPP-4 inhibitors (except saxagliptin) are associated with an excess risk of hospitalisation for heart failure (Grade 1A).

Sulfonylureas

There is very little comparative randomised controlled trial evidence of the use of Sulfonylureas (SUs) in CKD. People with type 2 diabetes and CKD who are on

SU treatment are at increased risk of hypoglycaemia. We therefore advise regular capillary blood glucose (CBG) monitoring for people with CKD on SU treatment. All SU should be avoided where possible in advanced CKD (stage 4 and 5). Please see table 2,3 and Figure 1 for more detailed information and practical clinical considerations when using SUs in CKD.

Pioglitazone

Pioglitazone is one of the few oral glucose-lowering drugs that is licensed for use in people with eGFR of <30 mL/min/1.73m^2. Pioglitazone should be avoided if there is evidence of heart failure or macular oedema or osteoporosis. As these co-morbidities may be frequent in people with CKD people should be carefully and regularly monitored for fluid retention or other adverse effects. For more detailed information on the use of pioglitazone in CKD and related recommendations please see table 2,3 and Figure 1 and this recent review (35)

Non-steroidal mineralocorticoid receptor antagonists (nsMRAs)

Our main focus in this article was on pharmacological management of hyperglycaemia in people with T2DM and CKD. However the emerging role of Finerenone a nsMRA is important to acknowledge as this class of medications have emerged as an additional pillar for the management of T2DM and CKD (36). A recent review highlights the clinical utility and consideration of starting nsMRA (37). Steroidal mineralocorticoid receptor antagonists like spironolactone and eplerenone lower blood pressure, reduce albuminuria proteinuria, delay progression of CKD and reduce mortality in heart failure (37, 38). However, their use is often limited by their tendency to cause hyperkalaemia an effect which pronounced in people with T2DM

and CKD. Finerenone is a non-steroidal mineralocorticoid receptor antagonists with greater mineralocorticoid receptor affinity and selectivity(37). These characteristics of finerenone are associated with less hyperkalaemia and minimal gynaecomastia compared with the steroidal agents (37). Based on the strong evidence of cardio-renal protection offered by the addition of finerenone to RAS inhibition observed in recent randomised controlled trials we suggest in people with T2DM and CKD who have persistent albuminuria (ACR >30 mg/mmol) despite the use of maximum tolerated doses of RASi and SGLT2i, to consider addition of finerenone (37, 39). Finerenone can be used if eGFR is more than or equal to 25 mL/min/1.73m2 and serum potassium is normal (<5 mmol/L). It is important to monitor serum potassium level after commencing treatment and the dose of finerenone will need to be adjusted according to potassium levels. Further detailed guidance on the practical use of finerenone in people with T2DM and CKD is available in this recent recommendation (37)

Cost effectiveness of newer treatments

CKD has a significant financial burden for many countries worldwide. The mean annual costs of CKD increases substantially with CKD stage with a recent global study of 31 countries reporting annual costs for CKD stage 3A of US$ 3,070 which rises significantly in stage 5 CKD [haemodialysis $ 57,334 ; peritoneal dialysis $49,490 with transplantation costs of – $75,326 (incident); $16,672 (ongoing)](40) The authors noted that these costs for CKD are much higher compared to other diseases such as myocardial infarction ($18,294 per year) and heart failure ($8463 per year) (40).

In this context there have been several systematic reviews as well as detailed cost effectiveness studies that have demonstrated the benefits of newer therapies for CKD

(41-45). National Institute for Health and Care Excellence (NICE) UK evidence review and related cost effectiveness analyses demonstrated that SGLT-2 inhibitors were cost effective in UK health setting for people with T2DM and CKD and these findings in part informed changes in national T2DM guidelines where early adoption and consideration for this class of agent for cardio-renal protection independent of baseline HbA1c was proposed.(46, 47).

However as far as we are aware there are to date no high quality cost effectiveness analyses/studies that specifically looking at dual or triple combination of newer treatments on top of background RAS inhibition with ACE inhibitor or angiotensin receptor blocker. This lack of studies reflects the limited evidence and data available at present from randomised controlled trials or large registries that have specifically looked at benefits of multiple combination treatment in CKD.

Factors that influence cost-effectiveness and access include medication acquisition costs, cost of CKD and related co-morbidity management (as people with longer survival will experience greater lifetime costs for CKD and associated co-morbidities such as cardiovascular disease).

Newer treatments for CKD offer significant promise and are generally cost effective but can be expensive with substantial budget/financial impact given the potentially large treatment population. However cost-effectiveness will improve over time with increasing numbers of agents moving to generic compounds which well lower medication costs, as well as competition which can further reduce costs.

The identification of a large number of individuals with or at risk for CKD who may be suitable for newer medications can overwhelming to health care systems (private, out of pocket, insurance bases or public/state funded or hybrid models of care) and related economics. Therefore cost-effectiveness needs to be routinely incorporated

into clinical guidelines to help guide optimal decisions as clear concise information on value-for-money and related improvement in health equity will help guide and inform health care delivery

Conclusion

People with T2DM and CKD have increased risk of morbidity and mortality. Hyperglycaemia is a modifiable risk factor for cardiovascular complications and progression of CKD. Individualised HbA1c targets should be applied in the management of people with CKD, using the levels suggested in this guidance.

Delaying ESKD and reducing CVD risk are essential to improve outcomes in this high-risk population. There is now conclusive evidence and consensus that SGLT-2 inhibitors significantly reduce progression of CKD and onset of ESKD in people with T2DM and CKD on top of standard care which is RASi. More recently there is evidence for the use nsMRA and GLP-1 RA which can also delay progression of CKD which has resulted in a concept of pillars of cardio-renal pharmacotherapy for CKD and thereby the potential for addressing residual cardio-renal risk with a multi-pronged approach with medications that act on distinct pathways to confer organ protection. (9, 48). Despite advances in the field a major barrier is the lack of implementation and inequality of access/ delivery of guideline based interventions and treatments for people with T2DM and CKD (49). In view of this, we propose a tiered approach with addressing key foundational goals first to address cardio-renal disease in T2DM and CKD (39). Indeed as most people with T2DM will succumb to premature CVD before reaching ESKD it is essential that a cardio-renal focus is emphasised from the outset.

Figure 2 highlights the tiered approach we propose to address burden of CKD progression as well as high CVD risk in people with T2DM and CKD. We

acknowledge that there is currently limited randomised control trial data on the role of combination therapy or triple therapy with GLP-1 RA, SGLT-2 inhibitors or nsMRA on reducing progression of kidney disease. The available data to date from secondary or sub-analyses of trials, simulation type analyses from recent studies and real world data suggest potential complementary and additive effects and in our opinion combination treatment GLP-1 RA and SGLT-2 inhibitors should be considered early in the management of CKD in people with diabetes (50). Such a combination approach may aid cardio-renal risk reduction by targeting residual risk and improve glycaemic control with low risk of hypoglycaemia in people with T2DM CKD. In people with residual albuminuria despite combination treatment with GLP-1 RA and SGLT-2 inhibitors adding in a nsMRA in people at high risk of progression to kidney failure or with known heart failure.

The mainstay of the management of CKD in type-2 diabetes are RASi, SGLT-2 inhibition, GLP-1 RA, nsMRA and lipid lowering therapy in conjunction with lifestyle modification to reduce the progression of CKD and CVD risk. The management of people with T2DM and CKD require an individualised approach where combination therapy of these key pillars of care will need to be utilised to address and mitigate residual risk of cardio-renal disease.

Disclosures

• SB reports receiving personal fees from Abbott, AstraZeneca, Boehringer Ingelheim, Eli Lilly, Merck Sharp & Dohme, Novo Nordisk, and Sanofi Aventis and being a shareholder in Glycosmedia. • DB reports receiving speaker fees from Vifor Pharma; honoraria for advisory board from Bayer, Medice; and research grant from AstraZeneca. • ID reports receiving research grants from Medtronic and Sanofi-Genzyme, receiving honoraria for attending advisory board and speaker meetings from GlaxoSmithKline, AstraZeneca, and Sanofi-Genzyme, and being the national

lead for 3 GSK trials. • PD reports receiving honoraria for advisory work and/or lecture fees from AstraZeneca, Boehringer Ingelheim, Eli Lilly, Merck Sharp & Dohme, Napp Pharmaceuticals, Novo Nordisk, and Sanofi. • JK reports receiving research grants from AstraZeneca and Sanofi and receiving speaker fees and attending advisory boards from Boehringer Ingelheim, AstraZeneca, Sanofi, and Napp. • KM reports receiving speaker fees and attending advisory board from Vifor, AstraZeneca, Bayer, Boehringer Ingelheim, Pharmacomsos, Napp, Vifor Fresenius and receiving a grant from AstraZeneca. • PW reports receiving honoraria for delivering educational meetings and/or attending advisory boards for Abbott, AstraZeneca, Bayer, Boehringer Ingelheim, Eli Lilly, Merck Sharp & Dohme, Napp, Sanofi, Novo, and Vifor Pharmaceuticals. NM reports receiving honoraria for delivering educational meetings and/or attending advisory boards and conferences for Abbott, AstraZeneca, Bayer, Boehringer Ingelheim, Eli Lilly, Menarini, Novo Nordisk and Roche.

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All the other authors declared no competing interests.

Supplementary Material

Figure 1. Evidence grades for the recommendations

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Figure 1 Glucose-lowering therapies – current licensing indications based on eGFR and cardio-kidney protection

Note that **Sick day guidance** applies to metformin, all SGLT-2 inhibitors and GLP-1 agonists
*Monitor for fluid retention, contraindicated in heart failure, macular oedema ,**CrCl – creatinine clearance and Cystatin C may be used as an estimate of glomerular filtration rate to help clinical decision making (CrCl calculated using Cockcroft–Gault equation)
†Dapagliflozin and Empagliflozin can be initiated and continued for treatment of heart failure without reference to kidney function but no current evidence for initiation if eGFR <20, ‡Canagliflozin can be initiated for kidney protection down to an eGFR of 30 ml/min/1.73 m2 and be continued thereafter until the onset of dialysis or transplantation. Dapagliflozin** and Empagliflozin can be initiated for kidney protection down to an eGFR of 15 ml/min/1.73 m2 and be continued thereafter until the onset of dialysis or transplantation

Figure 2 A tiered approach to managing people with type 2 diabetes and CKD An overview of the joint Association of British Clinical Diabetologists and UK Kidney Association (ABCD-UKKA) guidelines.
With permission from Diabet Med. 2024; 00:e15450. doi:10.1111/dme.15450.
*Indvidualised approach to intensive risk factor controal and monitoring which can be based on factors such as life time cardiovascular and renal risk, life expectancy, frailty and resocurces

Table 1. Proposed Glycaemic targets in people with type 2 diabetes and CKD

Glycaemic target range	**CKD stage and albuminuria**	**Age**
48–58 mmol/mol (6.5–7.5%)* Aim for <52 mmol/mol (6.9%)	CKD stages 1–2	People who are aged <40 **Diet controlled at any age
52–58 mmol/mol (6.9–7.5%)	CKD stages 3–4 May be appropriate with a GLP-1 and/ or SGLT-2 inhibitor-based treatment regime without insulin	Any age
58–68 mmol/mol (7.5–8.5 %)	CKD stages 3–4 and those with CKD stage 5 who are on dialysis. Especially in people with albuminuria who are on an insulin-based regime∇	Any age

*Confirmatory blood glucose or continuous glucose monitoring (CGM) if concern of hypoglycaemia and/or anaemia as HbA1c will be less reliable in advanced CKD stage 4/5

∇Recognition of cardio-kidney benefits with SGLT-2 inhibitors and GLP-1 analogue therapy

**Over 20% of people with CKD (especially older people aged >75) solely dietary controlled can have HbA1c 42–48 mmol/mol (6–6.5%) without hypoglycaemia

These recommendations are based on opinion of the writing group as these is limited high grade evidence in CKD

Table 2. Relative and absolute contraindications to the selection of blood glucose-lowering therapies in people with T2DM and CKD

Condition	Drug	Note
Retinopathy	Pioglitazone	Absolute contraindication in diabetic maculopathy
	Semaglutide	Relative contraindication in people with marked hyperglycaemia (HbA1c >91 mmol/mol (10.5%) who have diabetic retinopathy requiring active ophthalmology treatment or follow-up: caution is advised
Bone health	Pioglitazone	Absolute contraindication in people who have had previous osteoporotic fractures; or relative contraindication in those with post-menopausal osteoporosis with neuropathy
	Canagliflozin	Relative contraindication in people with established osteoporotic fractures.
Foot health	SGLT-2 inhibitors	Absolute contraindication if a person has active diabetic foot disease with vascular complications or sepsis.
Heart failure	Pioglitazone	Absolute contraindication in people with established treated heart failure and where at-risk people have a raised natriuretic peptides or symptoms suggestive of heart failure
	Saxagliptin	Absolute contraindication in people with treated established heart failure
Pancreatic health	GLP-1 analogues and GLP-1 RA /GIP dual agonists	Absolute contraindication of GLP-1 analogues where an individual has previously documented pancreatitis; relative contraindication in people who are at risk of pancreatitis with raised triglycerides, those on steroid therapy, those using other drugs that are associated with pancreatitis or those with documented alcoholism
Bladder health	SGLT-2 inhibitors	Relative contraindication of all medications in this class in people who have documented neuropathic bladder and recurrent urinary infections
	Pioglitazone	Bladder cancer – contraindication to continuation or starting pioglitazone
Biliary tract health	GLP-1 analogues and GLP-1 GIP receptor agonists	Relative contraindication if a person has active gall bladder disease

Table 3. Action to be taken for selected medications when treating people with type 2 diabetes and CKD

Metformin	
eGFR level	**Action to be taken**
For all	• Practitioners have to weigh up the glycaemic and cardiovascular benefits against the rare risk of associated lactic acidosis.
>60 ml/min/1.73 m2	• No kidney contraindication to metformin. • Some of these people are at increased risk due to other risk factors (see advice for increased vigilance groups in the bottom row of this table).
45–60 ml/min/1.73 m2	• Continue use in people who were established on metformin, but review the dose in light of glycaemic control needs (maximum dose 2000mg/day). • For new individuals who have no major active comorbidities, metformin commencement can be considered if age-related life expectancy is normal and vascular/diabetes risks are present. • Increase monitoring of kidney function (to every 3–6 months).
30–45 ml/min/1.73 m2	• Continue or commence with caution and explain the risks and benefits to the person. • Use lowest dose that achieves glycaemic control (suggest a 50% dose up to 1,000 mg/day). • Closely monitor kidney function (every 3 months).
<30 ml/min/1.73 m2	• At this level of kidney function, we cannot give firm recommendations about the ongoing use of metformin. • Some specialists may choose to use metformin in selected people where they see that the benefits outweigh the risks. • Pharmacokinetic work would suggest that if metformin is used, a dose of 500–1,000 mg/day would result in 95% of people having peak metformin concentrations of <5 mg/L.
Dialysis	• No current role
AKI (or at risk of AKI)	Review and consider (temporarily) stopping* metformin in those who: • have acute changes in kidney function (a fall in eGFR of >10 ml/min/1.73 m2 over a period of days or weeks) • are at risk of AKI such as: o acute volume depletion and dehydration eg gastrointestinal upset, stomas, change in diuretic dose o during operative procedures with a high risk of hypotension or volume depletion o in the presence of hypotension or shock, eg severe infection o intravascular administration of iodinated contrast drugs (stop metformin on the day of and 2 days after X-ray related intravenous contrast use) o co-administration with nephrotoxic drugs, eg non-steroidal anti-inflammatory drugs (NSAIDs) o those with acute illness who are also on drugs that are known precipitants of AKI in association with any angiotensin-converting

	enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) (such as non-steroidal anti-inflammatory drugs (NSAIDs)), especially combined with diuretics • those with previous episodes of AKI. *Duration of stopping metformin should be based on the likely period of risk. In general, it should be resumed at a low dose after discharge.
Recovery from AKI	• Once urine flow has returned to normal and GFR is >30 ml/min/1.73 m2, resume metformin at a low dose (eg 500–1,000 mg/day). • Monitor glucose control in outpatients and primary care before considering the further need for increasing doses.
Increased vigilance	Increased vigilance is needed for the following groups of people who are likely to be at a higher risk of lactic acidosis even with normal kidney function: • those with decompensated cardiac or respiratory failure • those with acute conditions that may cause tissue hypoxia, eg recent myocardial infarction (MI) or shock • those with hepatic insufficiency, acute alcohol intoxication or alcoholism.

GLP-1 receptor agonists (GLP-1 RA): exenatide (Byetta™ and Bydureon™), liraglutide, lixisenatide, dulaglutide, semaglutide, dual GLP-1 RA and GIP agonist tirzepatide	
eGFR level	**Action to be taken**
For all	• Older people: No dose adjustment is required based on age. Therapeutic experience in people ≥75 years of age is limited • Paediatric population: The safety and efficacy in children aged up to 18 years have not yet been established. No data are available. • Should not be used in people with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. • No experience in those with congestive heart failure NYHA class IV and, therefore, not recommended in these people. • If pancreatitis is suspected, drug should be discontinued; if confirmed, then should not be restarted. Caution should be exercised in people with a history of pancreatitis.
>60 ml/min/1.73 m2	• No kidney contraindication to initiation or continuation. • Semaglutide injectable may be commenced for glucose lowering and kidney protection.
45–60 ml/min/1.73 m2	• No kidney contraindication to initiation or continuation. • Semaglutide injectable may be commenced for glucose lowering and kidney protection.
30–45 ml/min/1.73 m2	• Byetta™ and lixisenatide to be used 'with caution' in people with creatinine clearance 30-50 mL/min, Bydureon™ should be stopped. • Liraglutide, dulaglutide, tirzepatide and semaglutide have no kidney contraindication to initiation or continuation at standard doses.

	• Semaglutide injectable may be commenced for glucose lowering and kidney protection.
<30 ml/min/1.73 m2	• Liraglutide, dulaglutide, semaglutide and tirzepatide have no kidney contraindication to initiation or continuation at standard doses. • Semaglutide injectable may be commenced for kidney protection. • Bydureon ™ should be stopped
Dialysis	• No current role
AKI (or at risk of AKI)	Review and consider (temporarily) stopping* in people who: • have acute changes in kidney function (a fall in eGFR of >10 ml/min/1.73 m2 over a period of days or weeks) • are at risk of AKI such as: o acute volume depletion and dehydration eg gastrointestinal upset, stomas, change in diuretic dose o operative procedures with a high risk of hypotension or volume depletion o in the presence of hypotension or shock, eg severe infection • have had previous episodes of AKI. *Duration of stopping GLP-1 RA, GLP-1 RA/GIP dual agonist should be based on the likely period of risk. Essential to restart medications promptly once person is stable clinically and potential risks resolving

DPP-4 inhibitors: vildagliptin, saxagliptin, sitagliptin, linagliptin, alogliptin	
eGFR level	**Action to be taken**
For all	• Older people (≥65 years): In general, no dose adjustment is recommended based on age. • Paediatric population: The safety and efficacy of DPP-4 inhibitors in children aged 0 to <18 years have not yet been established. No data are available. • Vildagliptin should not be used in hepatic impairment. No dose adjustments are needed for mild to moderate hepatic impairment with linagliptin, alogliptin, sitagliptin or saxagliptin. Caution needs to be exercised with sitagliptin use in those with severe hepatic impairment.. Alogliptin and saxagliptin are not recommended in severe hepatic impairment. Only linagliptin is licensed for use in severe hepatic impairment. • Acute pancreatitis: DPP-4 inhibitors are associated with risk of developing acute pancreatitis. Caution should be exercised in those with history of pancreatitis. If pancreatitis is confirmed, DPP4 inhibitors should not be restarted. • Heart failure: DPP-4 inhibitors do not increase risk of major CV events or risk of hospitalisation for heart failure except saxagliptin, which is contraindicated in heart failure.
>60 ml/min/1.73 m2	• No kidney contraindication to initiation or continuation.
45–60 ml/min/1.73 m2	• eGFR <50 ml/min/1.73 m2, reduce dose of , vildagliptin to 50 mg once daily and alogliptin to 12.5 mg daily • No dose reduction needed for linagliptin, sitagliptin or saxagliptin.
30–45 ml/min/1.73 m2	• Reduce dose of sitagliptin to 50 mg daily, vildagliptin to 50 mg once daily, alogliptin to 12.5 mg daily and saxagliptin to 2.5 mg daily. • No dose reduction needed for linagliptin. • Vildagliptin has limited data and should be used with caution.
<30 ml/min/1.73 m2	• Reduce dose of sitagliptin to 25 mg daily, alogliptin to 6.25 mg daily and saxagliptin to 2.5 mg daily. • No dose reduction needed for linagliptin. • Vildagliptin has limited data and should be used with caution.
Dialysis	• Reduce dose of sitagliptin to 25 mg daily, and alogliptin to 6.25 mg daily. • No dose reduction needed for linagliptin. • Saxagliptin is not recommended. • Vildagliptin has limited data and should be used with caution.

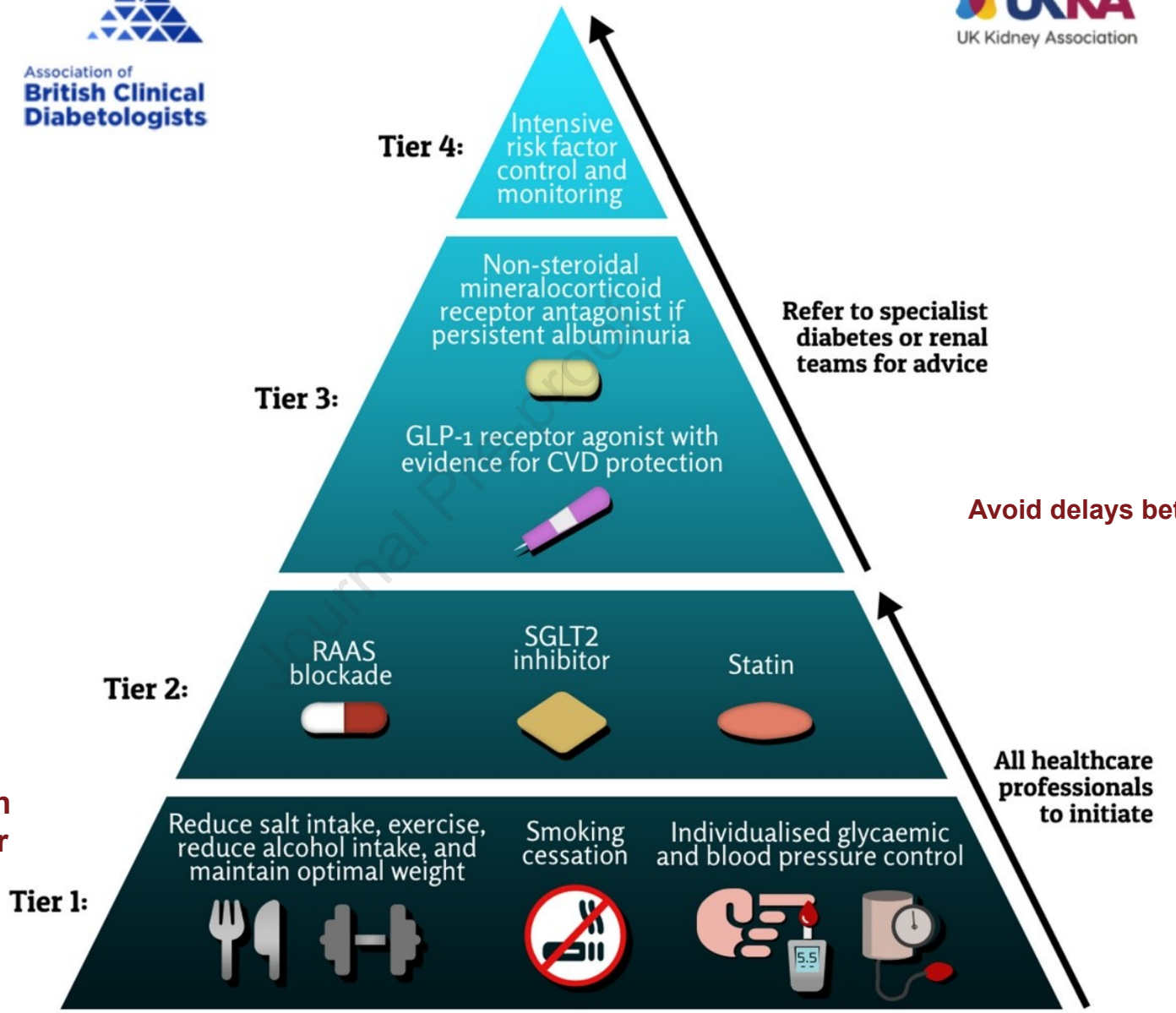
SGLT-2 inhibitors: canagliflozin, dapagliflozin, empagliflozin, ertugliflozin	
eGFR level	**Action to be taken**
For all	• Older people (≥65 years): In general, no dose adjustment is recommended based on age. However the increased risk of volume depletion in frail older people should be considered • Paediatric population: The safety and efficacy of dapagliflozin in children aged up to 18 years have not yet been established. No data are available. • Active foot disease (either ulceration with sepsis or ischaemia) avoid initiation and withdraw if this occurs. • Diabetic ketoacidosis: permanently discontinue if people develop DKA related to treatment.
>60 ml/min/1.73 m2	• No kidney contraindication to initiation or continuation. • Canagliflozin 100 mg daily may be commenced for glucose lowering and kidney protection. Dose can be increased to 300mg for additional glucose lowering • Dapagliflozin 10 mg daily may be commenced/continued for glucose lowering, heart failure and kidney protection. • Empagliflozin 10mg daily may be commenced/continued for glucose lowering heart failure and kidney protection. Dose can be increased to 25mg for additional glucose lowering
45–60 ml/min/1.73 m2	• Canagliflozin 100 mg daily may be commenced/continued for glucose lowering and kidney protection. • Dapagliflozin 10 mg daily may be commenced/continued for glucose lowering, heart failure and kidney protection. • Empagliflozin 10mg daily may be commenced/continued for glucose lowering, heart failure and kidney protection • For other drugs in this class (such as Ertugliflozin), current UK licence recommends against initiation (see recommendations). Continuation of medication should be at the lower dose for canagliflozin and empagliflozin.
30–45 ml/min/1.73 m2	• Canagliflozin 100 mg daily may be commenced/continued for kidney protection. • Dapagliflozin 10 mg daily may be commenced/continued for kidney protection and heart failure. • Empagliflozin 10mg daily may be commenced/continued for kidney protection and heart failure • For glucose lowering, current licence recommends against initiation or continuation.

20-30 ml/min/1.73 m2	• Canagliflozin 100 mg daily may be continued for kidney protection until dialysis or kidney transplantation. • Empagliflozin 10mg daily may be commenced/continued for heart failure • Dapagliflozin 10 mg daily may be commenced/continued for heart failure. • Empagliflozin 10mg daily may be commenced/continued for kidney protection until dialysis or kidney transplantation. • Dapagliflozin 10mg daily may be commenced/continued for kidney protection until dialysis or kidney transplantation.
Dialysis	• No current role
AKI (or at risk of AKI)	Review and consider (temporarily) pausing * in people who: • have acute major changes in kidney function (a fall in eGFR of >10 ml/min/1.73 m2 over a period of days or weeks) * • are at risk of AKI such as: o acute volume depletion and dehydration eg gastrointestinal upset, stomas, change in diuretic dose o operative procedures with a high risk of hypotension or volume depletion o in the presence of hypotension or shock, eg severe infection • have had previous episodes of AKI. *Duration of pausing topping SGLT-2 inhibitor should be based on the likely period of risk. Essential to restart medications promptly once person is stable clinically and potential risks resolving

		Kidney impairment – CKD stage and eGFR (ml/min/1.73 m2)					
Drug	**Class of drug**	**1** **eGFR ≥90**	**2** **eGFR 60–89**	**3a** **eGFR 45–59**	**3b** **eGFR 30–44**	**4** **eGFR 15–29**	**5** **eGFR <15**
Metformin**	Biguanide				Reduce dose to 500 mg twice daily	eGFR may underestimate in obesity, potential role for 500 mg daily**	
Gliclazide, Glimeperide, Glipizide, Glyburide	Sulfonylurea	Monitor glucose	Monitor glucose	Monitor glucose	Dose reduction advised Monitor CBG	Off licence – high risk of hypoglycaemia; monitor glucose	
Dapagliflozin†	SGLT-2 inhibitor			May initiate at 10mg od and /or continue for diabetes, kidney protection and treatment of heart failure	May initiate at 10mg od and /or continue for kidney protection and treatment of heart failure	May initiate at 10mg od and /or continue for kidney protection or treatment of heart failure Limited experience for treatment of heart failure and kidney protection	Can be continued at 10mg od until kidney replacement therapy started. Do not initiate.
Canagliflozin‡	SGLT-2 inhibitor			May initiate at 100 mg od and/or continue for diabetes and kidney protection	May initiate at 100 mg od and/or continue for kidney protection	Continue at 100 mg od for kidney protection until kidney replacement therapy	
Empagliflozin †	SGLT-2 inhibitor			May initiate at 10mg od for treatment of diabetes, kidney protection and heart failure	May initiate at 10mg od for kidney protection and treatment of heart failure	May initiate at 10mg od in eGFR >20ml/min for kidney protection or treatment of heart failure. Limited experience for treatment of heart failure.	Can be continued at 10mg od until kidney replacement therapy started. Do not initiate.
Ertugliflozin	SGLT-2 inhibitor			Do not initiate	Do not initiate	Do not initiate	Do not initiate
Dulaglutide	GLP-1 agonist						
Semaglutide (injectable)	GLP-1 agonist			May initiate at 0.25mg weekly and up-titrate to 1mg weekly /or continue for kidney protection	May initiate at 0.25mg weekly and up-titrate to 1mg weekly /or continue for kidney protection	May initiate at 0.25mg weekly and up-titrate to 1mg weekly /or continue for kidney protection if eGFR >20 / or continue for kidney protection	Not recommended in ESKD
Tirzepatide	GLP-1 /GIP agonist						Caution in ESKD due to limited experience
Semaglutide (oral)	GLP-1 agonist						Not recommended in ESKD
Liraglutide	GLP-1 agonist						Not recommended in ESKD
Sitagliptin	DPP-4 inhibitor				Reduce dose to 50 mg	Reduce dose to 25 mg	Reduce dose to 25 mg
Saxagliptin	DPP-4 inhibitor				Reduce dose to 2.5 mg	Reduce dose to 2.5 mg	Not recommended in ESKD requiring haemodialysis
Linagliptin	DPP-4 inhibitor						
Pioglitazone*	Thiazolinedione						Not recommended in ESKD
Insulin		Monitor glucose	Monitor glucose	Monitor glucose	Dose reduction may be needed. Monitor glucose	Dose reduction should be needed. Monitor glucose	Dose reduction should be needed Monitor glucose

Association of British Clinical Diabetologists

UKKA UK Kidney Association



Avoid delays between Tiers

Tier 1 and Tier 2 can be initiated together