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CLINICAL GUIDELINE

Diabetes Management in Chronic Kidney Disease: Synopsis of the KDIGO 2022 Clinical Practice Guideline Update

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Description: The KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease is an update of the 2020 guideline from Kidney Disease: Improving Global Outcomes (KDIGO).

Methods: The KDIGO Work Group updated the guideline, which included reviewing and grading new evidence that was identified and summarized. As in the previous guideline, the Work Group used the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach to appraise evidence and rate the strength of recommendations and expert judgment to develop consensus practice points. New evidence led to updating of recommendations in the chapters Comprehensive Care in Patients With Diabetes and CKD (Chapter 1) and Glucose-Lowering Therapies in Patients With T2D and CKD (Chapter 4). New evidence did not change recommendations in the chapters Glycemic Monitoring and Targets in Patients With Diabetes and CKD (Chapter 2), Lifestyle Interventions in Patients With Diabetes and CKD (Chapter 3), and Approaches to Management of Patients With Diabetes and CKD (Chapter 5).

Recommendations: The updated guideline includes 13 recommendations and 52 practice points for clinicians caring for patients with diabetes and chronic kidney disease (CKD). A focus on preserving kidney function and maintaining well-being is recommended using a layered approach to care, starting with a foundation of lifestyle interventions, self-management, and first-line pharmacotherapy (such as sodium–glucose cotransporter-2 inhibitors) demonstrated to improve clinical outcomes. To this are added additional drugs with heart and kidney protection, such as glucagon-like peptide-1 receptor agonists and nonsteroidal mineralocorticoid receptor antagonists, and interventions to control risk factors for CKD progression and cardiovascular events, such as blood pressure, glycemia, and lipids.

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In light of the emergence of new high-quality evidence, the KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease (1) update follows only 2 years after the original 2020 guideline (2). The overall scope and systematic literature search for the update were unchanged from the original guideline and addressed both type 1 diabetes (T1D) and type 2 diabetes (T2D), all stages of chronic kidney disease (CKD), and patients who had a kidney transplant or those treated with hemodialysis or peritoneal dialysis (2). High-quality evidence on patient care, specifically from randomized controlled trials, was evaluated. This led to revision of recommendations on what constitutes comprehensive care, use of sodium–glucose cotransporter-2 (SGLT2) inhibitors, and use of glucagon-like peptide-1 receptor agonists (GLP-1 RAs), as well as the introduction of a new section on use of mineralocorticoid receptor antagonists (MRAs).

Methods

Full methods for the guideline development process are described in the KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease (1). The guideline follows international standards for guideline development (3, 4) and has been reported in accordance with the AGREE II (Appraisal of Guidelines for Research and Evaluation II) reporting checklist (5).

The original Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Guideline Work Group (WG) was reconvened for this update. The WG comprised nephrologists, endocrinologists, cardiologists, primary care physicians, registered dietitians, and patients. Conflicts of interest were fully disclosed and published alongside the guideline.

Cochrane Kidney and Transplant, the Evidence Review Team (ERT), conducted the literature searches for each topic covered in the 2020 guideline in December 2021, limiting the searches to randomized controlled trials only, and updated these searches in February 2022 at the time of the public review. The evidence synthesis and meta-analysis methods undertaken for the KDIGO 2020 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease were followed for the 2022 guideline update (2). Newly identified evidence was presented to the WG, who reviewed the ERT summaries to determine if a full quantitative reassessment and reconsideration of recommendations was justified. For these topics, the ERT updated the evidence synthesis (both narrative and quantitative) and reassessed the grading for the quality of the evidence base using GRADE (Grading of

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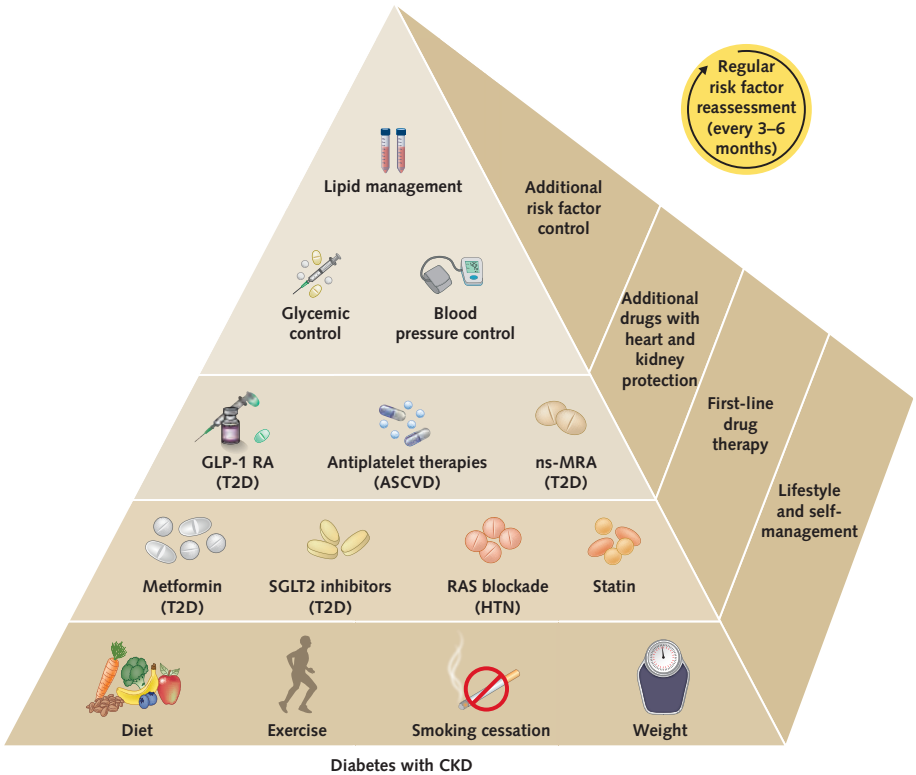
Figure 1. Kidney–heart risk factor management.



Patients with diabetes and chronic kidney disease should be treated with a comprehensive approach to improve kidney and cardiovascular outcomes. This approach should include a foundation of lifestyle modification and self-management for all patients, on which are layered first-line drug therapies according to clinical characteristics (*in parentheses*), additional drugs with proven kidney and heart protection as guided by assessments of residual risk, and additional interventions as needed to further control risk factors. Glycemic control is based on insulin for type 1 diabetes and a combination of metformin and SGLT2 inhibitors for T2D. Metformin may be given when the estimated glomerular filtration rate (eGFR) is ≥30 mL/min/1.73 m^2; SGLT2 inhibitor therapy should be initiated when eGFR is ≥20 mL/min/1.73 m^2 and continued as tolerated until dialysis or transplantation is initiated. RAS inhibition is recommended for patients with albuminuria and HTN. GLP-1 RAs are the preferred glucose-lowering drugs for patients with T2D–especially if the patient is overweight or obese, if SGLT2 inhibitors with or without metformin are insufficient to meet glycemic targets, or if the patient cannot use SGLT2 inhibitors or metformin. An ns-MRA can be added to first-line therapy for patients with T2D and high residual risks for kidney disease progression and cardiovascular events, as evidenced by persistent albuminuria (>30 mg/g creatinine). Aspirin generally should be used lifelong for secondary prevention among those with established cardiovascular disease and may be considered for primary prevention among patients with high risk for ASCVD. ASCVD = atherosclerotic cardiovascular disease; GLP-1 RA = glucagon-like peptide-1 receptor agonist; HTN = hypertension; ns-MRA = nonsteroidal mineralocorticoid receptor antagonist; RAS = renin-angiotensin system; SGLT2 = sodium–glucose cotransporter-2; T2D = type 2 diabetes. (Reproduced from Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group [1]; used under CC BY-NC-ND 4.0.).

Recommendations Assessment, Development and Evaluation) methods (6).

The WG met virtually to discuss and finalize the guideline statements through consensus. As before, the WG developed recommendations using the GRADE Evidence to Decision framework and considered the balance of benefits and harms, quality of evidence, values and preferences, resource use and costs, and considerations for implementation for each recommendation statement (7). In addition to the 13 graded recommendations, 52 ungraded practice points were developed to provide clinicians with expert input or guidance for implementation (**Appendix Table**, available at Annals.org).

Comprehensive Care

The updated 2022 guideline advocates a comprehensive, holistic approach to patient care, including control of multiple risk factors and a collaborative partnership among patients with CKD, health care providers, and health systems to implement evidence-based recommendations that have demonstrated improved clinical outcomes (**Figure 1**) (1, 8–11). Lifestyle interventions are an important key feature of the recommendations, and the updated recommendations now include therapies that have been shown to improve cardiovascular and kidney outcomes in patients with diabetes and CKD. Specifically, SGLT2 inhibitors are the preferred first-line pharmacologic therapy for patients with T2D and CKD, regardless of glycemic control, with other glucose-lowering therapies added to the SGLT2 inhibitors to maintain individualized glycemic targets (**Figure 2**).

SGLT2 Inhibitors

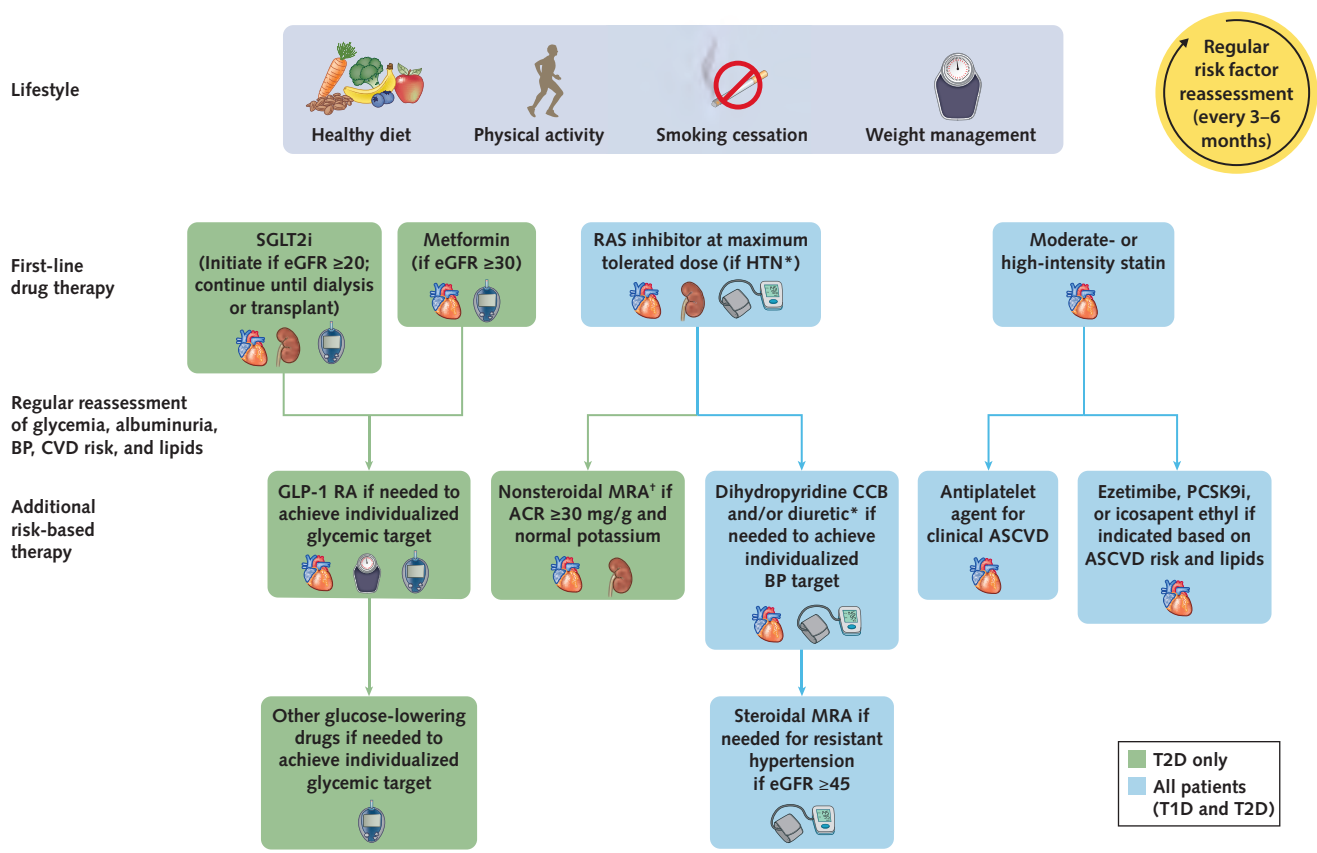
The KDIGO 2020 guideline recommended SGLT2 inhibitors for patients with kidney disease and an estimated

glomerular filtration rate (eGFR) of at least 30 mL/min/1.73 m^2 (1). The updated guideline now recommends initiation of SGLT2 inhibitor therapy in those with an eGFR of at least 20 mL/min/1.73 m^2 (**Appendix Figure**, available at Annals.org).

Since the original guideline was published, 7 large trials examining the cardiovascular and kidney effects of various SGLT2 inhibitors have reported results (12–18). These results warranted a lowering of the eGFR threshold for use of SGLT2 inhibitors. Furthermore, given the strong evidence in diverse patient populations with CKD, including those without diabetes, this topic was moved from Chapter 4 (Glucose-Lowering Therapies in Patients With T2D and CKD) to Chapter 1 (Comprehensive Care in Patients With Diabetes and CKD). This change acknowledges the evidence that benefit of SGLT2 inhibitors is independent of glycemic control and the recommendation to use SGLT2 inhibitors for organ protection (heart and kidney) in patients with CKD.

Of the 7 new trials, 4 trials (2 including patients with heart failure with reduced ejection fraction [17, 18] and 2 enrolling patients with heart failure with preserved ejection fraction [12, 14]) demonstrated benefits for cardiovascular events and kidney disease progression as a prespecified secondary end point. In the CKD population, the DAPA-CKD (Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease) trial (16) and SCORED (Effect of Sotagliflozin on Cardiovascular and Renal Events in Patients with Type 2 Diabetes and Moderate Renal Impairment Who Are at Cardiovascular Risk) trial (13) enrolled patients with CKD and eGFR as low as 25 mL/min/1.73 m^2. The DAPA-CKD trial, which included patients with and without diabetes, reported kidney and cardiovascular benefits for

Figure 2. Holistic approach for improving outcomes in patients with diabetes and CKD.



Icons indicate the following benefits: BP cuff = BP lowering; glucometer = glucose lowering; heart = heart protection; kidney = kidney protection; and scale = weight management. ACR = albumin-creatinine ratio; ASCVD = atherosclerotic cardiovascular disease; BP = blood pressure; CCB = calcium-channel blocker; CVD = cardiovascular disease; eGFR = estimated glomerular filtration rate; GLP-1 RA = glucagon-like peptide-1 receptor agonist; HTN = hypertension; MRA = mineralocorticoid receptor antagonist; PCSK9i = proprotein convertase subtilisin/kexin type 9 inhibitor; RAS = renin-angiotensin system; SGLT2i = sodium-glucose cotransporter-2 inhibitor; T1D = type 1 diabetes; T2D = type 2 diabetes. (Reproduced from Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group [1]; used under CC BY-NC-ND 4.0.)

* Angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker should be first-line therapy for HTN when albuminuria is present; otherwise, dihydropyridine CCB or diuretic can also be considered. All 3 classes are often needed to attain BP targets.

† Finerenone is currently the only nonsteroidal MRA with proven clinical kidney and cardiovascular benefits.

both subsets of patients. In addition, the EMPA-KIDNEY (Study of Heart and Kidney Protection With Empagliflozin) trial (19) was stopped early because of clear efficacy; namely, empagliflozin therapy led to a lower risk for progression of kidney disease or death from cardiovascular causes than placebo in a population with CKD and eGFR as low as 20 mL/min/1.73 m^2, with and without albuminuria, and with and without diabetes.

The newer trials showed cardiovascular and kidney benefits across all categories of eGFR, and altogether trials have demonstrated similar benefits across categories of albuminuria (including normal albumin excretion) (12–19). EMPA-KIDNEY, as well as the heart failure trials EMPEROR-Reduced (Empagliflozin Outcome Trial in Patients With Chronic Heart Failure With Reduced Ejection Fraction) (18) and EMPEROR-Preserved (Empagliflozin Outcome Trial in Patients With Chronic Heart Failure With Preserved Ejection Fraction) (12), included participants with eGFR as low as 20 mL/min/1.73 m^2. Sodium–glucose cotransporter-2 inhibitors are likely to have reduced glucose-lowering efficacy at lower eGFR, and the cardiovascular and kidney benefits reported in these trials were proportionately greater than the reductions in hemoglobin A_{1c}, suggesting that the kidney and cardiovascular benefits are not primarily attributable to the glucose-lowering effects of SGLT2 inhibitors. Therefore, the updated guideline recommends the use of SGLT2 inhibitors among all patients with T2D and CKD (based on albuminuria or low eGFR without albuminuria) with an eGFR of at least 20 mL/min/1.73 m^2 (Grade 1A).

GLP-1 RAs

The recommended second-line drug class for glucose lowering in T2D and CKD continues to be GLP-1 RAs (**Figure 2**). One new trial (AMPLITUDE-O [Effect of Efpeglenatide on Cardiovascular Outcomes] [20]) was added to the evidence for cardiovascular benefits of GLP-1 RAs and bolstered the hypothesis that GLP-1 RAs may also improve kidney outcomes. Cardiovascular benefits of GLP-1 RAs have been reported across strata of eGFR and are the major rationale for recommending this class as the preferred glucose-lowering drug for patients with T2D and CKD who are not attaining glycemic goals despite use of SGLT2 inhibitors and metformin (or who cannot use SGLT2 inhibitors or metformin). Because weight loss may also be important for some patients with CKD, including those who want to lose weight before kidney transplantation, a new practice point highlighting the potential advantages of weight loss with GLP-1 RAs was added to the updated guideline (**Table**) (1).

Nonsteroidal MRAs

A new section on the use of MRAs has been included in the updated guideline (1); MRAs reduce residual proteinuria in those receiving renin–angiotensin system (RAS) inhibitors. Several small clinical trials have shown the antiproteinuric effects of steroidal MRAs without development of hyperkalemia; however, the beneficial effects of steroidal MRAs on kidney disease progression had not been established.

Two large, phase 3, clinical trials (FIDELIO-DKD [Finerenone in Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease] [21] and FIGARO-DKD [Finerenone in Reducing Cardiovascular Mortality and Morbidity in Diabetic Kidney Disease] [22]) evaluated the kidney and cardiovascular benefits of finerenone, a novel nonsteroidal MRA (ns-MRA), in those with T2D and CKD. Both FIDELIO-DKD and FIGARO-DKD included participants with T2D who were receiving the maximum tolerated dose of a RAS inhibitor and had residual albuminuria (albumin–creatinine ratio ≥30 mg/g) and a serum potassium level less than 4.8 mmol/L at screening. The mean eGFR of the study population was 57.6 mL/min/1.73 m^2, and two thirds of the population had an albumin–creatinine ratio above 300 mg/g. In the FIDELIO-DKD trial, finerenone significantly reduced the primary composite kidney outcome (kidney failure, sustained ≥40% decrease in eGFR, or death from kidney causes) by 18% (hazard ratio [HR], 0.82 [95% CI, 0.73 to 0.93]) and the secondary composite cardiovascular outcome (death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for heart failure) by 14% (HR, 0.86 [CI, 0.75 to 0.99]) (21). In the FIGARO-DKD trial, finerenone reduced the primary composite cardiovascular outcome by 13% (HR, 0.87 [CI, 0.76 to 0.98]) (22).

In the prespecified pooled analyses of the 2 trials (FIDELITY [Finerenone in Chronic Kidney Disease and Type 2 Diabetes: Combined FIDELIO-DKD and FIGARO-DKD Trial Programme Analysis] [23]), a 14% lower risk for the cardiovascular composite outcome was shown in those treated with finerenone compared with placebo (HR, 0.86 [CI, 0.78 to 0.95]) (23). Finerenone also reduced the risk for the kidney composite outcome (kidney failure, ≥57% decrease in eGFR, or death from kidney causes; HR, 0.77 [CI, 0.67 to 0.88]) and the risk for kidney failure (initiation of maintenance dialysis or kidney transplantation; HR, 0.80 [CI, 0.64 to 0.99]). The main safety concern was hyperkalemia, which was more common with finerenone than placebo (14% vs. 6.9%). However, the cumulative incidence of permanent discontinuation of study drug treatment due to hyperkalemia was low overall—1.7% and 0.6% among finerenone and placebo recipients, respectively—with no deaths due to hyperkalemia reported in a study population with normal serum potassium levels at study entry (23).

On the basis of the high-quality evidence from the FIGARO-DKD and FIDELIO-DKD trials, the use of an ns-MRA with proven kidney or cardiovascular benefit is now recommended for patients with T2D, eGFR of at least 25 mL/min/1.73 m^2, normal serum potassium concentration, and albuminuria (albumin–creatinine ratio ≥30 mg/g) despite receiving the maximum tolerated dose of a RAS inhibitor (Grade 2A; new recommendation in the 2022 guideline update). The recommendation is level 2—weak or "we suggest"—for the following reasons: availability of efficacy and safety data (especially hyperkalemia) for only 1 drug in the class, underrepresentation of patients with moderate albuminuria, lack of data about the additive effects of SGLT2 inhibitors and MRAs, and lack of real-world data showing the safety of ns-MRAs.

DISCUSSION

The updated KDIGO 2022 guideline advocates a layered approach to care, starting with a foundation of lifestyle interventions and first-line pharmacotherapy demonstrated to improve clinical outcomes (1). To this, other therapies are added to reduce risk for adverse outcomes and to control risk factors for CKD progression and cardiovascular events, such as blood pressure, glycemia, and lipids. Although other guidelines have suggested viewing multifactorial therapy as "pillars" of care (24–26), the KDIGO layered approach includes the preference for starting new treatments one at a time and then reassessing response and residual risk to further refine therapy. To maximize the tolerability of combination treatments, the guideline recommends the serial introduction of medications that improve intrarenal hemodynamics (such as RAS inhibitors, SGLT2 inhibitors, MRAs, diuretics, and other antihypertensive medications). Ongoing monitoring is critical to ensuring that each patient ultimately receives the optimal therapeutic regimen.

With new therapies that can reduce progression of CKD and diminish the burden of cardiovascular disease, including heart failure, health care providers should focus on preserving kidney function and maintaining well-being rather than replacing kidney function (27). The beneficial effects of SGLT2 inhibitors, ns-MRAs, and GLP-1 RAs on CKD and cardiovascular disease provide an opportunity to achieve these goals and save millions of lives, but these therapies will only benefit patients with diabetes and CKD if implemented widely. Successful implementation will necessarily involve collective efforts from all stakeholders, including patients with diabetes and CKD as well as health systems, payers, regulators, and life science industries (28). It will also require concerted action for early detection of CKD, education of health care providers in multidisciplinary interventions, and empowerment of patients with diabetes and CKD to ensure engagement and self-care (29). Of note, implementation will require community outreach efforts to make care accessible and equitable, with patient preferences and priorities shaping strategies.

The cost of new therapies is clearly a barrier to implementation (30). However, avoiding or delaying costly kidney replacement therapy with the use of these agents may make it cost-effective to implement new therapies (31–33) while we await more data to support broader access. Creating a convincing case for the use of CKD therapies as part of a health system strategy for value-based care, along with lowering the cost of new therapies, is essential to translating theoretical cost-effectiveness analyses into reality. This guideline suggests that policymakers and institutional decision makers implement team-based, integrated care focused on risk evaluation and patient empowerment to provide comprehensive care for patients with diabetes and CKD (28).

Multiple professional societies issue recommendations for care of patients with diabetes, CKD, or both (34), and the existence of multiple guidelines can create the appearance of inconsistency. To address this concern, concurrent with delivery of the 2022 guideline, KDIGO partnered with the American Diabetes Association to issue a consensus report on the diagnosis and management of diabetes and CKD (35). This report provides aligned, evidence-based recommendations from these 2 professional societies and emphasizes high-priority interventions (35). In addition, the consensus report addresses aspects of CKD prevention, screening, and diagnosis, which are important clinical topics not explicitly covered in the KDIGO guideline. Implementation of evidence-based treatments is now critical to improving the outcomes of patients living with diabetes and CKD.

Table. Key Changes in the KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease*

SGLT2 inhibitors

The GFR threshold for the use of SGLT2 inhibitors has been lowered to ≥20 mL/min/1.73 m^2. This affects Recommendation 1.3.1 and Practice Point 1.3.6 in the updated guideline.

Recommendation 1.3.1: We recommend treating patients with type 2 diabetes (T2D), CKD, and an eGFR ≥20 ml/min per 1.73 m^2 with an SGLT2i (1A).

Practice Point 1.3.6: Once an SGLT2i is initiated, it is reasonable to continue an SGLT2i even if the eGFR falls below 20 ml/min per 1.73 m^2, unless it is not tolerated or kidney replacement therapy is initiated.

A new practice point was added that states:

Practice Point 1.3.1: The recommendation for SGLT2i is for kidney and cardiovascular protection and SGLT2i have been shown to have safety and benefit in CKD patients, even for those without T2D. Thus, if patients are already being treated with other glucose-lowering agents, an SGLT2i can be added to the current treatment regimen.

Nonsteroidal MRAs

A new section related to the use of nonsteroidal MRAs was added to the guideline. This section includes the following statements:

Recommendation 1.4.1: We suggest a nonsteroidal mineralocorticoid receptor antagonist with proven kidney or cardiovascular benefit for patients with T2D, an eGFR ≥25 ml/min per 1.73 m^2, normal serum potassium concentration, and albuminuria (≥30 mg/g [≥3 mg/mmol]) despite maximum tolerated dose of RAS inhibitor (RASi) (2A).

Practice Point 1.4.1: Nonsteroidal MRA are most appropriate for patients with T2D who are at high risk of CKD progression and cardiovascular events, as demonstrated by persistent albuminuria despite other standard-of-care therapies.

Practice Point 1.4.2: A nonsteroidal MRA can be added to a RASi and an SGLT2i for treatment of T2D and CKD.

Practice Point 1.4.3: To mitigate risk of hyperkalemia, select patients with consistently normal serum potassium concentration and monitor serum potassium regularly after initiation of a nonsteroidal MRA.

Practice Point 1.4.4: The choice of a nonsteroidal MRA should prioritize agents with documented kidney or cardiovascular benefits.

Practice Point 1.4.5: A steroidal MRA should be used for treatment of heart failure, hyperaldosteronism, or refractory hypertension, but may cause hyperkalemia or a reversible decline in glomerular filtration, particularly among patients with a low GFR.

GLP-1 RAs

A new practice point was added that states:

Practice Point 4.2.5. GLP-1 RA may be preferentially used in patients with obesity, T2D, and CKD to promote intentional weight loss.

* Recommendations and practice points are quoted from reference 1. CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; GFR = glomerular filtration rate; GLP-1 RA = glucagon-like peptide-1 receptor agonist; KDIGO = Kidney Disease: Improving Global Outcomes; MRA = mineralocorticoid receptor antagonist; RASi = renin–angiotensin system inhibitor; SGLT2 = sodium–glucose cotransporter-2; SGLT2i = SGLT2 inhibitor(s); T2D = type 2 diabetes.

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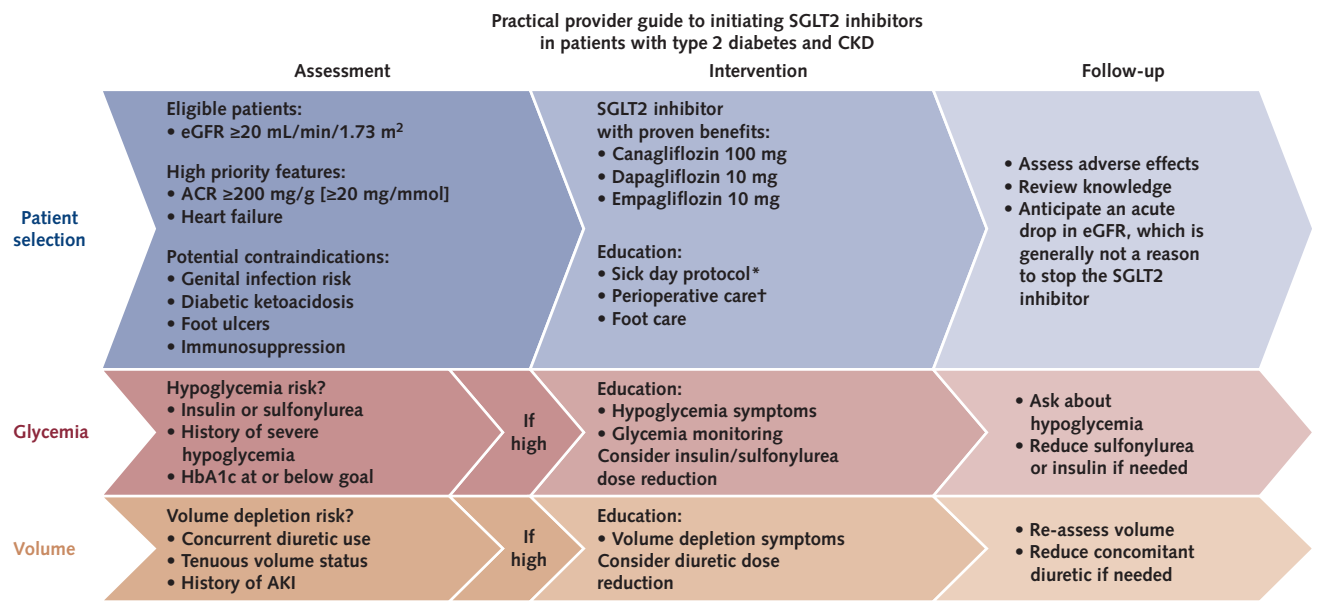
Appendix Figure. Practical approach to initiating SGLT2 inhibitors in patients with type 2 diabetes and CKD.



ACR = albumin–creatinine ratio; AKI = acute kidney injury; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; HbA1c = glycated hemoglobin; SGLT2 = sodium–glucose cotransporter-2. (Reproduced from Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group [1]; used under CC BY-NC-ND 4.0.)
* Sick day protocol (for illness or excessive exercise or alcohol intake): Temporarily withhold SGLT2 inhibitors; keep drinking and eating (if possible); check blood glucose and blood ketone levels more often; and seek medical help early, especially if patient has nausea and vomiting.
† Periprocedural/perioperative care: Inform patients about risk for diabetic ketoacidosis, especially in patients with long disease duration during acute illnesses due to relative insulin insufficiency and increased stress hormones; withhold SGLT2 inhibitors the day of day-stay procedures and limit fasting to minimum required; withhold SGLT2 inhibitors at least 2 d in advance and on the day of a procedure requiring ≥1 d in the hospital and/or bowel preparation (which may require increasing doses of other glucose-lowering drugs during that time); measure both blood glucose and blood ketone levels on hospital admission (proceed with procedure if the patient is clinically well and ketone concentration is ≤1.0 mmol/L); and restart SGLT2 inhibitor therapy after procedure only when patient is eating and drinking normally.

Appendix Table. Selected Recommendations and Practice Points From the KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease*

Chapter 1. Comprehensive care in patients with diabetes and CKD

1.1. Comprehensive diabetes and CKD management

Practice Point 1.1.1: Patients with diabetes and chronic kidney disease (CKD) should be treated with a comprehensive strategy to reduce risks of kidney disease progression and cardiovascular disease.

1.2. Renin–angiotensin system (RAS) blockade

*Recommendation 1.2.1: We recommend that treatment with an angiotensin-converting enzyme inhibitor (ACEi) or an angiotensin II receptor blocker (ARB) be initiated in patients with diabetes, hypertension, and albuminuria, and that these medications be titrated to the highest approved dose that is tolerated (*1B*).*

Practice Point 1.2.1: For patients with diabetes, albuminuria, and normal blood pressure, treatment with an ACEi or ARB may be considered.

Practice Point 1.2.2: Monitor for changes in blood pressure, serum creatinine, and serum potassium within 2–4 weeks of initiation or increase in the dose of an ACEi or ARB.

Practice Point 1.2.3: Continue ACEi or ARB therapy unless serum creatinine rises by more than 30% within 4 weeks following initiation of treatment or an increase in dose.

Practice Point 1.2.4: Advise contraception in women who are receiving ACEi or ARB therapy and discontinue these agents in women who are considering pregnancy or who become pregnant.

Practice Point 1.2.5: Hyperkalemia associated with the use of an ACEi or ARB can often be managed by measures to reduce serum potassium levels rather than decreasing the dose or stopping the ACEi or ARB immediately.

Practice Point 1.2.6: Reduce the dose or discontinue ACEi or ARB therapy in the setting of either symptomatic hypotension or uncontrolled hyperkalemia despite the medical treatment outlined in Practice Point 1.2.5, or to reduce uremic symptoms while treating kidney failure (estimated glomerular filtration rate [eGFR] <15 ml/min per 1.73 m^2).

Practice Point 1.2.7: Use only one agent at a time to block the RAS. The combination of an ACEi with an ARB, or the combination of an ACEi or ARB with a direct renin inhibitor, is potentially harmful.

1.3. Sodium–glucose cotransporter-2 inhibitors (SGLT2i)

*Recommendation 1.3.1: We recommend treating patients with type 2 diabetes (T2D), CKD, and an eGFR ≥20 ml/min per 1.73 m^2 with an SGLT2i (*1A*).*

Practice Point 1.3.1: The recommendation for SGLT2i is for kidney and cardiovascular protection and SGLT2i have been shown to have safety and bene fit in CKD patients, even for those without T2D. Thus, if patients are already being treated with other glucose-lowering agents, an SGLT2i can be added to the current treatment regimen.

Practice Point 1.3.2: The choice of an SGLT2i should prioritize agents with documented kidney or cardiovascular benefits and take eGFR into account.

Practice Point 1.3.3: It is reasonable to withhold SGLT2i during times of prolonged fasting, surgery, or critical medical illness (when patients may be at greater risk for ketosis).

Practice Point 1.3.4: If a patient is at risk for hypovolemia, consider decreasing thiazide or loop diuretic dosages before commencement of SGLT2i treatment, advise patients about symptoms of volume depletion and low blood pressure, and follow up on volume status after drug initiation.

Practice Point 1.3.5: A reversible decrease in the eGFR with commencement of SGLT2i treatment may occur and is generally not an indication to discontinue therapy.

Practice Point 1.3.6: Once an SGLT2i is initiated, it is reasonable to continue an SGLT2i even if the eGFR falls below 20 ml/min per 1.73 m^2, unless it is not tolerated or kidney replacement therapy is initiated.

Practice Point 1.3.7: SGLT2i have not been adequately studied in kidney transplant recipients, who may benefit from SGLT2i treatment, but are immuno-suppressed and potentially at increased risk for infections; therefore, the recommendation to use SGLT2i does not apply to kidney transplant recipients (see Recommendation 1.3.1).

1.4. Mineralocorticoid receptor antagonists (MRA)

*Recommendation 1.4.1: We suggest a nonsteroidal mineralocorticoid receptor antagonist with proven kidney or cardiovascular benefit for patients with T2D, an eGFR ≥25 ml/min per 1.73 m^2, normal serum potassium concentration, and albuminuria (≥30 mg/g [≥3 mg/mmol]) despite maximum tolerated dose of RAS inhibitor (RASi) (*2A*).*

Practice Point 1.4.1: Nonsteroidal MRA are most appropriate for patients with T2D who are at high risk of CKD progression and cardiovascular events, as demonstrated by persistent albuminuria despite other standard-of-care therapies.

Practice Point 1.4.2: A nonsteroidal MRA can be added to a RASi and an SGLT2i for treatment of T2D and CKD.

Practice Point 1.4.3: To mitigate risk of hyperkalemia, select patients with consistently normal serum potassium concentration and monitor serum potassium regularly after initiation of a nonsteroidal MRA.

Practice Point 1.4.4: The choice of a nonsteroidal MRA should prioritize agents with documented kidney or cardiovascular benefits.

Practice Point 1.4.5: A steroidal MRA should be used for treatment of heart failure, hyperaldosteronism, or refractory hypertension, but may cause hyperkalemia or a reversible decline in glomerular filtration, particularly among patients with a low GFR.

1.5. Smoking cessation

*Recommendation 1.5.1: We recommend advising patients with diabetes and CKD who use tobacco to quit using tobacco products (*1D*).*

Practice Point 1.5.1: Physicians should counsel patients with diabetes and CKD to reduce secondhand smoke exposure.

Chapter 2. Glycemic monitoring and targets in patients with diabetes and CKD

2.1. Glycemic monitoring

*Recommendation 2.1.1: We recommend using hemoglobin A1c (HbA_{1c}) to monitor glycemic control in patients with diabetes and CKD (*1C*).*

Practice Point 2.1.1: Monitoring long-term glycemic control by HbA_{1c} twice per year is reasonable for patients with diabetes. HbA_{1c} may be measured as often as 4 times per year if the glycemic target is not met or after a change in glucose-lowering therapy.

Practice Point 2.1.2: Accuracy and precision of HbA_{1c} measurement declines with advanced CKD (G4–G5), particularly among patients treated by dialysis, in whom HbA_{1c} measurements have low reliability.

Practice Point 2.1.3: A glucose management indicator (GMI) derived from continuous glucose monitoring (CGM) data can be used to index glycemia for individuals in whom HbA_{1c} is not concordant with directly measured blood glucose levels or clinical symptoms.

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Practice Point 2.1.4: Daily glycemic monitoring with CGM or self-monitoring of blood glucose (SMBG) may help prevent hypoglycemia and improve glycemic control when glucose-lowering therapies associated with risk of hypoglycemia are used.
Practice Point 2.1.5: For patients with T2D and CKD who choose not to do daily glycemic monitoring by CGM or SMBG, glucose-lowering agents that pose a lower risk of hypoglycemia are preferred and should be administered in doses that are appropriate for the level of eGFR.
Practice Point 2.1.6: CGM devices are rapidly evolving with multiple functionalities (e.g., real-time and intermittently scanned CGM). Newer CGM devices may offer advantages for certain patients, depending on their values, goals, and preferences.

2.2. Glycemic targets

*Recommendation 2.2.1: We recommend an individualized HbA_{1c} target ranging from <6.5% to <8.0% in patients with diabetes and CKD not treated with dialysis (*1C*).*
Practice Point 2.2.1: Safe achievement of lower HbA_{1c} targets (e.g., <6.5% or <7.0%) may be facilitated by CGM or SMBG and by selection of glucose-lowering agents that are not associated with hypoglycemia.
Practice Point 2.2.2: CGM metrics, such as time in range and time in hypoglycemia, may be considered as alternatives to HbA_{1c} for defining glycemic targets in some patients.

Chapter 3. Lifestyle interventions in patients with diabetes and CKD

3.1. Nutrition intake

Practice Point 3.1.1: Patients with diabetes and CKD should consume an individualized diet high in vegetables, fruits, whole grains, fiber, legumes, plant-based proteins, unsaturated fats, and nuts; and lower in processed meats, refined carbohydrates, and sweetened beverages.
*Recommendation 3.1.1: We suggest maintaining a protein intake of 0.8 g protein/kg (weight)/d for those with diabetes and CKD not treated with dialysis (*2C*).*
Practice Point 3.1.2: Patients treated with hemodialysis, and particularly peritoneal dialysis, should consume between 1.0 and 1.2 g protein/kg (weight)/d.
*Recommendation 3.1.2: We suggest that sodium intake be <2 g of sodium per day (or <90 mmol of sodium per day, or <5 g of sodium chloride per day) in patients with diabetes and CKD (*2C*).*
Practice Point 3.1.3: Shared decision-making should be a cornerstone of patient-centered nutrition management in patients with diabetes and CKD.
Practice Point 3.1.4: Accredited nutrition providers, registered dietitians and diabetes educators, community health workers, peer counselors, or other health workers should be engaged in the multidisciplinary nutrition care of patients with diabetes and CKD.
Practice Point 3.1.5: Healthcare providers should consider cultural differences, food intolerances, variations in food resources, cooking skills, comorbidities, and cost when recommending dietary options to patients and their families.

3.2. Physical activity

*Recommendation 3.2.1: We recommend that patients with diabetes and CKD be advised to undertake moderate-intensity physical activity for a cumulative duration of at least 150 minutes per week, or to a level compatible with their cardiovascular and physical tolerance (*1D*).*
Practice Point 3.2.1: Recommendations for physical activity should consider age, ethnic background, presence of other comorbidities, and access to resources.
Practice Point 3.2.2: Patients should be advised to avoid sedentary behavior.
Practice Point 3.2.3: For patients at higher risk of falls, healthcare providers should provide advice on the intensity of physical activity (low, moderate, or vigorous) and the type of exercises (aerobic vs. resistance, or both).
Practice Point 3.2.4: Physicians should consider advising/encouraging patients with obesity, diabetes, and CKD to lose weight, particularly patients with eGFR ≥30 ml/min per 1.73 m^2.

Chapter 4. Glucose-lowering therapies in patients with T2D and CKD

Practice Point 4.1: Glycemic management for patients with T2D and CKD should include lifestyle therapy, first-line treatment with both metformin and a sodium-glucose cotransporter-2 inhibitor (SGLT2i), and additional drug therapy as needed for glycemic control.
Practice Point 4.2: Most patients with T2D, CKD, and eGFR ≥30 ml/min per 1.73 m^2 would benefit from treatment with both metformin and an SGLT2i.
Practice Point 4.3: Patient preferences, comorbidities, eGFR, and cost should guide selection of additional drugs to manage glycemia, when needed, with glucagon-like peptide-1 receptor agonist (GLP-1 RA) generally preferred.

4.1. Metformin

*Recommendation 4.1.1: We recommend treating patients with T2D, CKD, and an eGFR ≥30 ml/min per 1.73 m^2 with metformin (*1B*).*
Practice Point 4.1.1: Treat kidney transplant recipients with T2D and an eGFR ≥30 ml/min per 1.73 m^2 with metformin according to recommendations for patients with T2D and CKD.
Practice Point 4.1.2: Monitor eGFR in patients treated with metformin. Increase the frequency of monitoring when the eGFR is <60 ml/min per 1.73 m^2.
Practice Point 4.1.3: Adjust the dose of metformin when the eGFR is <45 ml/min per 1.73 m^2, and for some patients when the eGFR is 45–59 ml/min per 1.73 m^2.
Practice Point 4.1.4: Monitor patients for vitamin B12 deficiency when they are treated with metformin for more than 4 years.

4.2. Glucagon-like peptide-1 receptor agonists (GLP-1 RA)

*Recommendation 4.2.1: In patients with T2D and CKD who have not achieved individualized glycemic targets despite use of metformin and SGLT2i treatment, or who are unable to use those medications, we recommend a long-acting GLP-1 RA (*1B*).*
Practice Point 4.2.1: The choice of GLP-1 RA should prioritize agents with documented cardiovascular benefits.
Practice Point 4.2.2: To minimize gastrointestinal side effects, start with a low dose of GLP-1 RA, and titrate up slowly.
Practice Point 4.2.3: GLP-1 RA should not be used in combination with dipeptidyl peptidase-4 (DPP-4) inhibitors.
Practice Point 4.2.4: The risk of hypoglycemia is generally low with GLP-1 RA when used alone, but risk is increased when GLP-1 RA is used concomitantly with other medications such as sulfonylureas or insulin. The doses of sulfonylurea and/or insulin may need to be reduced.
Practice Point 4.2.5: GLP-1 RA may be preferentially used in patients with obesity, T2D, and CKD to promote intentional weight loss.

Chapter 5. Approaches to management of patients with diabetes and CKD

5.1. Self-management education programs

*Recommendation 5.1.1: We recommend that a structured self-management educational program be implemented for care of people with diabetes and CKD (*1C*).*
Practice Point 5.1.1: Healthcare systems should consider implementing a structured self-management program for patients with diabetes and CKD, taking into consideration local context, cultures, and availability of resources.

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Appendix Table–Continued

5.2. Team-based integrated care

Recommendation 5.2.1: We suggest that policymakers and institutional decision-makers implement team-based, integrated care focused on risk evaluation and patient empowerment to provide comprehensive care in patients with diabetes and CKD (2B).

Practice Point 5.2.1: Team-based integrated care, supported by decision-makers, should be delivered by physicians and nonphysician personnel (e.g., trained nurses and dieticians, pharmacists, healthcare assistants, community workers, and peer supporters) preferably with knowledge of CKD.

* Recommendations and practice points are quoted from reference 1.

ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor blocker; CGM = continuous glucose monitoring; CKD = chronic kidney disease; DPP-4 = dipeptidyl peptidase-4; eGFR = estimated glomerular filtration rate; GFR = glomerular filtration rate; G = grade; GLP-1 RA = glucagon-like peptide-1 receptor agonist; GMI = glucose management indicator; HbA_{1c} = hemoglobin A_{1c}; KDIGO = Kidney Disease: Improving Global Outcomes; MRA = mineralocorticoid receptor antagonist; RAS = renin–angiotensin system; RASi = RAS inhibitor; SGLT2i = sodium–glucose cotransporter-2 inhibitor(s); SMBG = self-monitoring of blood glucose; T2D = type 2 diabetes.