Executive summary of the 2020 KDIGO Diabetes Management in CKD Guideline: evidence-based advances in monitoring and treatment

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The Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease represents the first KDIGO guideline on this subject. The guideline comes at a time when advances in diabetes technology and therapeutics offer new options to manage the large population of patients with diabetes and chronic kidney disease (CKD) at high risk of poor health outcomes. An enlarging base of high-quality evidence from randomized clinical trials is available to evaluate important new treatments offering organ protection, such as sodium-glucose cotransporter-2 inhibitors and glucagon-like peptide-1 receptor agonists. The goal of the new guideline is to provide evidence-based recommendations to optimize the clinical care of people with diabetes and CKD by integrating new options with existing management strategies. In addition, the guideline contains practice points to facilitate implementation when insufficient data are available to make well-justified recommendations or when additional guidance may be useful for clinical application. The guideline covers comprehensive care of patients with diabetes and CKD, glycemic monitoring and targets, lifestyle interventions, antihyperglycemic therapies, and self-management and health systems approaches to management of patients with diabetes and CKD.

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This is the first Kidney Disease: Improving Global Outcomes (KDIGO) Guideline for Diabetes Management in Chronic Kidney Disease. The guideline comes at a pivotal time, with substantial growth in the public health burden of diabetes and chronic kidney disease (CKD), and with recent development of new therapies applicable to this population.[1,2]

The goal of the new guideline is to provide evidence-based recommendations and practice points to optimize the clinical

Chapter 1: Comprehensive care in patients with diabetes and CKD	
• **Practice Point 1.1.1**	Patients with diabetes and CKD should be treated with a comprehensive strategy to reduce risks of kidney disease progression and cardiovascular disease (Figure 2).
• **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*).
• **Recommendation 1.3.1**	We recommend advising patients with diabetes and CKD who use tobacco to quit using tobacco products (*1D*).
Chapter 2: Glycemic monitoring and targets in patients with diabetes and CKD	
• **Recommendation 2.1.1**	We recommend using hemoglobin A1c (HbA1c) to monitor glycemic control in patients with diabetes and CKD (*1C*).
• **Recommendation 2.2.1**	We recommend an individualized HbA1c target ranging from <6.5% to <8.0% in patients with diabetes and CKD not treated with dialysis (Figure 3) (*1C*).
Chapter 3: Lifestyle interventions in patients with diabetes and CKD	
• **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)/day for those with diabetes and CKD not treated with dialysis (*2C*).
• **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*).
• **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*).
Chapter 4: Antihyperglycemic therapies in patients with type 2 diabetes (T2D) and CKD	
• **Practice Point 4.1**	Glycemic management for patients with T2D and CKD should include lifestyle therapy, first-line treatment with metformin and a sodium–glucose cotransporter-2 inhibitor (SGLT2i), and additional drug therapy as needed for glycemic control (Figures 4, 5, and 6).
• **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*).
• **Recommendation 4.2.1**	We recommend treating patients with T2D, CKD, and an eGFR ≥30 ml/min per 1.73 m^2 with an SGLT2i (*1A*).
• **Recommendation 4.3.1**	In patients with T2D and CKD who have not achieved individualized glycemic targets despite use of metformin and SGLT2i, or who are unable to use those medications, we recommend a long-acting glucagon-like peptide-1 receptor agonist (GLP-1 RA) (*1B*).
Chapter 5: Approaches to management of patients with diabetes and CKD	
• **Recommendation 5.1.1**	We recommend that a structured self-management educational program be implemented for care of people with diabetes and CKD (Figure 7) (*1C*).
• **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*).

Figure 1 | Recommendations and select practice points from the Kidney Disease: Improving Global Outcomes 2020 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease (CKD). eGFR, estimated glomerular filtration rate; SGLT2, sodium–glucose cotransporter-2; T2D, type 2 diabetes.

care of people with diabetes and CKD by integrating new therapies with existing management approaches. The guideline was written by an international Work Group that included 2 patients and was diverse in clinical expertise, supported by a dedicated Evidence Review Team and professional KDIGO staff. The Work Group aimed to generate a useful resource for clinicians and patients that addressed relevant questions with actionable recommendations, took on controversial topics when there was sufficient evidence to do so, and communicated evidence and recommendations clearly. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework was used to evaluate the quality of evidence and strength of recommendations.[3] A broad audience was targeted, including all types of clinicians caring for people with diabetes and CKD.

The scope of the new guideline includes patients with type 1 diabetes (T1D), type 2 diabetes (T2D), and all severities of CKD, including patients treated with dialysis or

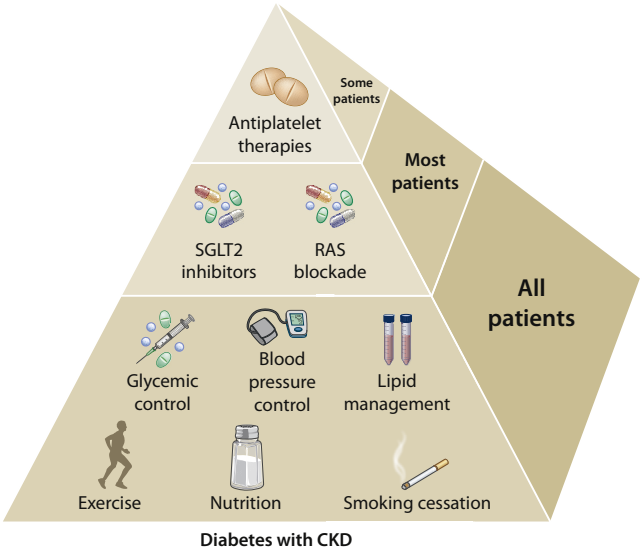

Figure 2 | Kidney–heart risk factor management. Glycemic control is based on insulin for type 1 diabetes and a combination of metformin and sodium–glucose cotransporter-2 (SGLT2) inhibitors for type 2 diabetes, when estimated glomerular filtration rate is ≥30 ml/min per 1.73 m^2. SGLT2 inhibitors are recommended for patients with type 2 diabetes and chronic kidney disease. Renin–angiotensin system (RAS) inhibition is recommended for patients with albuminuria and hypertension. Aspirin should generally be used lifelong for secondary prevention among those with established cardiovascular disease and may be considered for primary prevention among high-risk individuals, with dual antiplatelet therapy used in patients after acute coronary syndrome or percutaneous coronary intervention.

kidney transplantation. Where appropriate, differences in recommendations according to diabetes type or CKD severity are highlighted. The guideline focuses on interventions addressed with rigorous data (especially randomized clinical trials), including lifestyle, pharmacotherapy, and systems interventions. Topics with insufficient evidence evaluating clinical outcomes were not addressed. Readers are referred to related KDIGO guidelines for recommendations on treatment of blood pressure and lipids, and to guidelines from primary care and diabetes organizations for recommendations on prevention and screening of CKD in diabetes.

The new guideline is organized into 5 chapters (Figure 1). Here in this summary, we outline by chapter the 12 evidence-based recommendations, including the general rationale for these recommendations, along with selected practice points. Practice points are opinion-based statements that lack sufficient evidence for a formal recommendation but were considered important by the Work Group to guide clinical care. Readers are referred to the full guideline for a comprehensive description of benefits and harms, level of evidence, factors affecting implementation, additional practice points, and recommendations for future research (https://www.kidney-international.org/issue/S0085-2538(20)X0010-X). In addition, the primary data and meta-analyses used to generate this guideline are available on the MAGICapp platform (https://kdigo.org/guidelines/diabetes-ckd/).

Chapter 1: Comprehensive care in patients with diabetes and CKD

Patients with diabetes and CKD have multisystem disease that requires treatment from a multidisciplinary team of health care professionals. These patients are at high risk of CKD progression and cardiovascular disease (CVD).[4,5] Comprehensive management includes a foundation of lifestyle intervention and risk factor management, with additional pharmacotherapy in selected patients (Figure 2).[6]

Patients with T1D or T2D, hypertension, and albuminuria (persistent albumin-creatinine ratio ≥30 mg/g [3 mg/mmol]) should be treated with a renin–angiotensin system inhibitor (RASi). Multiple clinical trials in these populations demonstrate that RASi reduces risk of CKD progression in a manner that may be independent of blood pressure control.[7] RASi should be titrated to the maximum antihypertensive dose, as done in pivotal clinical trials, or the highest tolerated dose. Serum potassium and creatinine should be monitored. Measures to control potassium should be considered when serum potassium is elevated to continue RASi when possible.

Patients with diabetes, hypertension, and normal albumin excretion are at lower risk of CKD progression. In this population, existing evidence does not demonstrate clear clinical benefits of RASi for CKD progression, and other agents are also appropriate for blood pressure management. There are few data evaluating clinical benefits and risks of RASi with diabetes and albuminuria who do not have hypertension.

There are few data evaluating smoking cessation in patients with diabetes and CKD. Nonetheless, the potential harm of smoking is compelling, and all patients should be counseled to avoid tobacco products. Aspirin should generally be used lifelong for secondary prevention among those with established CVD and may be considered for primary prevention among high-risk individuals, with dual antiplatelet therapy used in patients after acute coronary syndrome or percutaneous coronary intervention.

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

Hemoglobin A1c is the fundamental tool used for glycemic monitoring of patients with diabetes. This practice is supported by clinical trials demonstrating that targeting lower versus higher hemoglobin A1c values improves some clinically relevant outcomes, particularly microvascular damage.[8,9] However, hemoglobin A1c is known to be inaccurate and imprecise in kidney failure.[10] In particular, shortened red blood cell lifespan leads to a bias toward low hemoglobin A1c among patients treated with dialysis and erythropoietin-stimulating agents.

Published studies suggest that the accuracy and precision of hemoglobin A1c, compared with direct measurements of blood glucose, do not vary by estimated glomerular filtration rate (eGFR) down to an eGFR of 30 ml/min per 1.73 m^2.[11] Therefore, the Work Group recommended using hemoglobin A1c to monitor glycemic control in patients with diabetes and CKD, consistent with general diabetes care. At lower

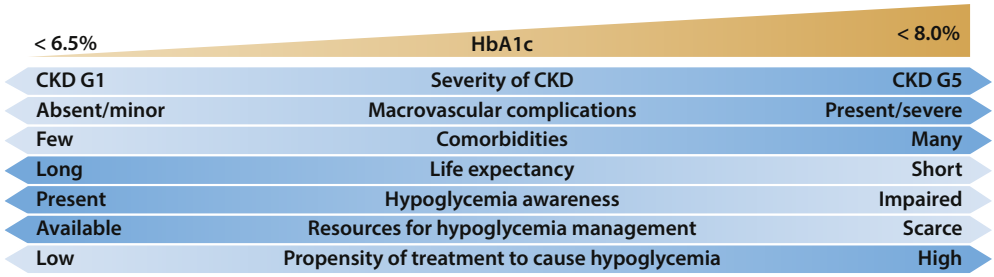

Figure 3 | Factors guiding decisions on individual glycated hemoglobin (HbA1c) targets. CKD, chronic kidney disease; G1, estimated glomerular filtration rate (eGFR) >90 ml/min per 1.73 m^2; G5, eGFR <15 ml/min per 1.73 m^2.

levels of eGFR and particularly with kidney failure, inaccuracy and imprecision of hemoglobin A1c may be increased. Hemoglobin A1c values should be interpreted with these limitations in mind.

Continuous glucose monitoring (CGM) is a new technology that directly measures blood glucose and is not biased by CKD. CGM may be useful to index hemoglobin A1c values for patients in whom hemoglobin A1c is not concordant with directly measured blood glucose levels or clinical symptoms.[11,12] In addition, CGM and self-monitoring of blood glucose can be used for short-term titration of treatments, prevention of hypoglycemia, and improvement of overall glycemic control.[13] Monitoring of blood glucose is particularly relevant when the treatment includes antihyperglycemic therapies associated with risk of hypoglycemia, such as insulin or sulfonylureas.

The guideline recommends that glycemic targets be individualized, consistent with recommendations from leading diabetes organizations worldwide.[14] For hemoglobin A1c, appropriate individualized targets may vary from as low as <6.5% to as high as <8%, depending on patient factors (Figure 3). Risk factors for hypoglycemia figure prominently in this scheme. Importantly, an enlarging menu of medications not associated with hypoglycemia is available for treatment of T2D, potentially allowing more aggressive glycemic targets for appropriate patients. In addition, CGM or self-monitoring of blood glucose may facilitate more aggressive targets while mitigating risk of hypoglycemia. For some patients, metrics derived from CGM (such as time in range, 70–180 mg/dl [3.9–10.0 mmol/l]) may serve as appropriate treatment targets, in addition to or instead of hemoglobin A1c.[15]

Chapter 3: Lifestyle interventions in patients with diabetes and CKD

Patients with diabetes and CKD often receive a surfeit of advice to promote or restrict intake of certain foods or nutrients. This input may conflict with patients' cultural or personal values and preferences, and it may lead to substantial confusion or exasperation. Adding to this, recommendations for intake in diabetes may contrast those for CKD. In this context, the Work Group felt it important that the overriding message of dietary advice be that patients should consume a balanced, healthy diet that is 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.

Dietary prescriptions should be individualized, incorporating values, preferences, and resources, and restricting certain foods or nutrients when appropriate (e.g., for treatment of hyperkalemia, when present). Decisions should be based on shared decision-making; include accredited nutrition providers, registered dietitians and diabetes educators, community health workers, peer counselors, or other health workers, who should be engaged in the multidisciplinary nutritional care of the patients; and consider cultural differences, food intolerances, variations in food resources, cooking skills, comorbidities, and cost when recommending dietary options to the patients and their family.

The guideline recommends that daily dietary protein intake be maintained at approximately 0.8 g per kg body weight, the World Health Organization recommendation for the general population.[16] Published trials do not provide compelling evidence that restricting dietary protein intake to lower levels improves kidney or other clinical outcomes. For patients treated with dialysis, particularly peritoneal dialysis, an increase in daily dietary protein intake to 1.0–1.2 g per kg body weight is advised to offset catabolism and negative nitrogen balance.

CKD often leads to sodium retention, which increases blood pressure, and risks of CKD progression and cardiovascular events. There is some evidence, largely from populations broader than diabetes and CKD, that the reduction of dietary sodium reduces these adverse outcomes. Therefore, the Work Group suggested that sodium intake be limited to <2 g/d (or <5 g sodium chloride), consistent with the KDIGO guideline on blood pressure management and international guidelines on the prevention and treatment of CVD.[17]

Patients with diabetes and CKD have lower levels of physical activity along with reduced overall fitness levels as compared with the general population,[18] but very few clinical trials have examined the impact of different exercise programs and implementation of routine physical activity in this population. In the general population and in those with diabetes, improvement in physical activity levels offers

			Primary outcome		Kidney outcomes		
Drug	**Trial**	**Kidney-related eligibility criteria**	**Primary outcome**	**Effect on primary outcome**	**Effect on albuminuria or albuminuria-containing composite outcome**	**Effect on GFR loss[a]**	**Adverse effects**
SGLT2 inhibitors							
Empagliflozin	EMPA-REG OUTCOME	eGFR ≥30 ml/min per 1.73 m²	MACE	↓	↓↓	↓↓	Genital mycotic infections, DKA
Canagliflozin	CANVAS trials	eGFR ≥30 ml/min per 1.73 m²	MACE	↓	↓↓	↓↓	Genital mycotic infections, DKA, amputation
	CREDENCE	ACR >300 mg/g [30 mg/mmol] and eGFR 30–90 ml/min per 1.73 m²	Progression of CKD[b]	↓↓	↓↓	↓↓	Genital mycotic infections, DKA
Dapagliflozin	DECLARE-TIMI 58	CrCl ≥60 ml/min	Dual primary outcomes: MACE and the composite of hospitalization for heart failure or CV death[c]	↔/↓	↓	↓↓	Genital mycotic infections, DKA
GLP-1 receptor agonists							
Lixisenatide	ELIXA	eGFR ≥30 ml/min per 1.73 m²	MACE	↔	↓	↔	None notable
Liraglutide	LEADER	eGFR ≥15 ml/min per 1.73 m²	MACE	↓	↓	↔	GI
Semaglutide[d]	SUSTAIN-6	Patients treated with dialysis excluded	MACE	↓	↓↓	NA	GI
	PIONEER 6	eGFR ≥30 ml/min per 1.73 m²	MACE	↔	NA	NA	GI
Exenatide	EXSCEL	eGFR ≥30 ml/min per 1.73 m²	MACE	↔	↔	↔	None notable
Albiglutide	HARMONY	eGFR ≥30 ml/min per 1.73 m²	MACE	↓	↔	NA	Injection site reactions
Dulaglutide	REWIND	eGFR ≥15 ml/min per 1.73 m²	MACE	↓	↓	↓	GI
DPP-4 inhibitors							
Saxagliptin	SAVOR-TIMI 53	eGFR ≥15 ml/min per 1.73 m²	MACE	↔	↓	↔	HF; any hypoglycemic event (minor and major) also more common
Alogliptin	EXAMINE	Patients treated with dialysis excluded	MACE	↔	NA	NA	None notable
Sitagliptin	TECOS	eGFR ≥30 ml/min per 1.73 m²	MACE	↔	NA	NA	None notable
Linagliptin	CARMELINA	eGFR ≥15 ml/min per 1.73 m²	Progression of CKD[b]	↔	↓	↔	None notable

Figure 4 | Overview of select large, placebo-controlled clinical outcome trials assessing the benefits and harms of sodium–glucose cotransporter-2 (SGLT2) inhibitors, glucagon-like peptide-1 (GLP-1) receptor agonists, and dipeptidyl peptidase-4 (DPP-4) inhibitors. ACR, albumin-creatinine ratio; CKD, chronic kidney disease; CrCl, creatinine clearance; CV, cardiovascular; DKA, diabetic ketoacidosis; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; GFR, glomerular filtration rate; GI, gastrointestinal symptoms (e.g., nausea and vomiting); HF, hospitalization for heart failure; MACE, major adverse cardiovascular events including myocardial infarction, stroke, and cardiovascular death (3-point MACE), with or without the addition of hospitalization for unstable angina (4-point MACE); NA, data not published. ↔, no significant difference; ↓, significant reduction in risk, with hazard ratio (HR) estimate >0.7 and 95% confidence interval (CI) not overlapping 1. ↓↓, significant reduction in risk, with HR estimate ≤0.7 and 95% CI not overlapping 1. [a]Variable composite outcomes that include loss of eGFR, ESKD, and related outcomes. [b]Progression of CKD defined in CREDENCE as doubling of serum creatinine, ESKD, or death from kidney or cardiovascular causes and in CARMELINA as 40% decline in eGFR, ESKD, or renal death. [c]DECLARE-TIMI 58 dual primary outcomes: (i) MACE and (ii) the composite of hospitalization for heart failure or CV death. [d]SUSTAIN-6: injectable semaglutide; PIONEER 6: oral semaglutide.

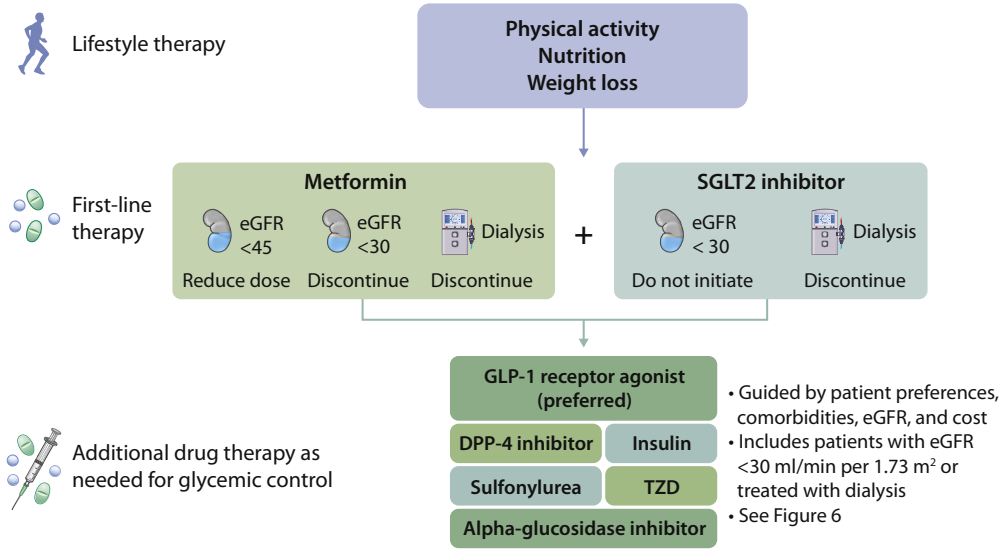

Figure 5 | Treatment algorithm for selecting antihyperglycemic drugs for patients with type 2 diabetes and chronic kidney disease. Kidney icon indicates estimated glomerular filtration rate (eGFR; ml/min per 1.73 m^2); dialysis machine icon indicates dialysis. DPP-4, dipeptidyl peptidase-4; GLP-1, glucagon-like peptide-1; SGLT2, sodium–glucose cotransporter-2; TZD, thiazolidinedione.

cardiometabolic, kidney, and cognitive benefits.[19] Thus, moderate-intensity physical activity for a cumulative duration of at least 150 minutes per week is recommended and sedentary behavior should be avoided. It is often necessary to individualize the advice for implementation to be successful. For obese patients, weight loss may help improve glycemic control, blood pressure, other metabolic parameters, and clinical outcomes. However, evidence review did not yield convincing data demonstrating clinical benefits of weight loss interventions among people with diabetes and CKD, and interventions targeting caloric intake may cause harm by promoting malnutrition, particularly in advanced CKD. Therefore, weight loss interventions were highlighted as an area for which additional research is needed, and recommendations for clinical care were not made.

Chapter 4: Antihyperglycemic therapies in patients with type 2 diabetes and CKD

New antihyperglycemic drugs have been developed and approved for clinical use, including sodium–glucose cotransporter-2 inhibitors (SGLT2i), glucagon-like peptide-1 receptor agonists (GLP-1 RA), and dipeptidyl peptidase-4 inhibitors (DPP4i).[2] Many drugs within these new classes have been tested in large clinical trials of people with T2D that evaluated clinically important cardiovascular and kidney outcomes (Figure 4). These trials provide substantial evidence to inform treatment. Guided by a rigorous systematic review of published studies, the Work Group synthesized these data to recommend preferred courses of therapy for patients with T2D and CKD. Data evaluating new drugs and comparing treatments are sparse for patients with T1D and CKD, for whom therapy focuses on insulin. Therefore, antihyperglycemic management in T1D was deferred to existing diabetes guidelines.

The guideline recommends that glycemic management for patients with T2D and CKD should include lifestyle therapy, first-line treatment with metformin and an SGLT2i, and additional drug therapy as needed for glycemic control (Figure 5). The Work Group concluded that most patients with diabetes, CKD, and eGFR ≥30 ml/min per 1.73 m^2 would benefit from treatment with both metformin, an inexpensive and generally well-tolerated medication that effectively lowers blood glucose, and an SGLT2i, which has been demonstrated to offer substantial benefits in reducing risks of CKD and CVD. When these drugs are not available or not tolerated, or when they are insufficient to attain individualized glycemic goals, additional drugs should be selected based on patient preferences, comorbidities, eGFR, and cost (Figure 6). In general, GLP-1 RA are preferred additional agents because of their demonstrated beneficial effects to reduce cardiovascular events, particularly among people with prevalent atherosclerotic CVD, and also their potential to prevent onset of severely increased albuminuria (formerly known as macroalbuminuria) and possibly slow decline in eGFR.

Metformin has been shown to be effective in reducing hemoglobin A1c in patients with T2D, with low risks for hypoglycemia in both the general population and patients with CKD. In addition, metformin helps to prevent weight gain, achieve weight reduction in obese patients, and reduce cardiovascular events as shown in the United Kingdom Prospective Diabetes Study (UKPDS).[20,21] Metformin is excreted by the kidneys, and accumulation with reduced kidney function may increase risk of lactic acidosis, which is low in absolute terms.[22] Therefore, eGFR should be monitored for

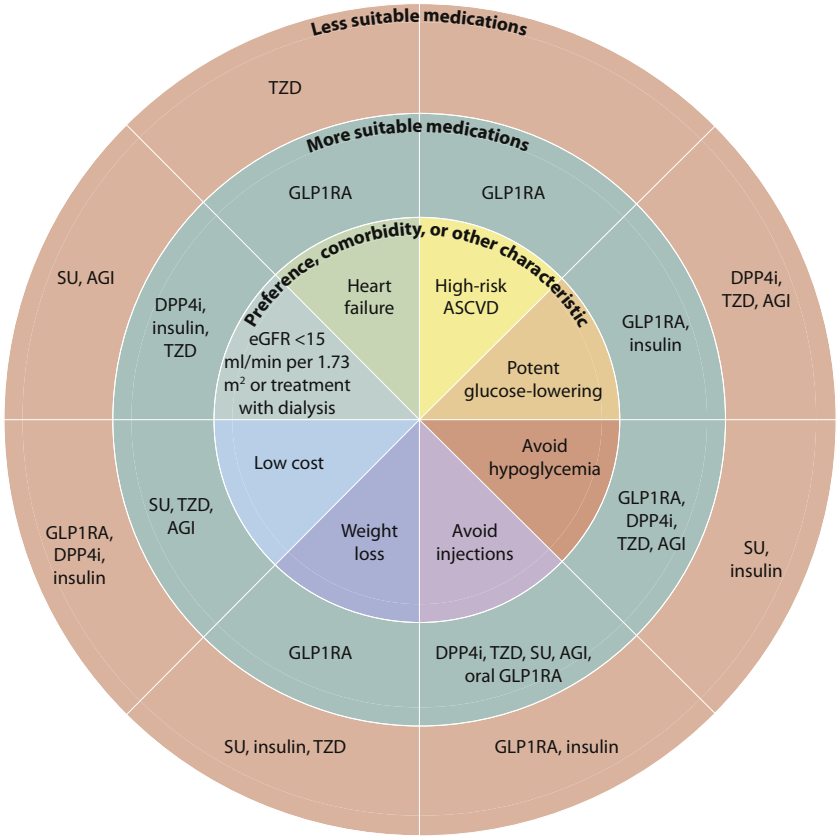

Figure 6 | Patient factors influencing the selection of glucose-lowering drugs other than sodium–glucose cotransporter-2 inhibitors and metformin in type 2 diabetes and chronic kidney disease. AGI, alpha-glucosidase inhibitor; ASCVD, atherosclerotic cardiovascular disease; DPP4i, dipeptidyl peptidase-4 inhibitor; eGFR, estimated glomerular filtration rate; GLP1RA, glucagon-like peptide-1 receptor agonist; SU, sulfonylurea; TZD, thiazolidinedione.

patients treated with metformin; metformin dose should be reduced when the eGFR is less than 45 ml/min per 1.73 m^2 (and for some patients with eGFR 45–59 ml/min per 1.73 m^2 who are at high risk of acute kidney injury); and metformin should be discontinued for patients with eGFR less than 30 ml/min per 1.73 m^2 or kidney failure (Figure 5). Metformin may cause vitamin B12 deficiency, and thusly B12 monitoring is advised for patients with long-term use (>4 years).[23]

SGLT2i were evaluated in patients with T2D in 3 cardiovascular outcomes trials (EMPA-REG OUTCOME, CANVAS trials, and DECLARE-TIMI 58) and 1 dedicated kidney outcomes study conducted specifically in a CKD population (CREDENCE).[24–27] These trials showed consistently large beneficial effects for reduction of cardiovascular events (meta-analysis hazard ratio [HR]: 0.89; 95% confidence interval [CI]: 0.82–0.96 for major adverse cardiovascular events) and CKD progression (meta-analysis HR: 0.64; 95% CI: 0.57–0.72). At the time of this publication, results from a second RCT of SGLT2i among patients exclusively with CKD were presented at the 2020 European Society of Cardiology meeting. DAPA-CKD demonstrated a substantial risk reduction in the primary endpoint (sustained ≥50% reduction in eGFR, kidney failure, or renal or cardiovascular death) compared to placebo (HR: 0.61; 95% CI: 0.51–0.72). Results were similar by diabetes status, and baseline levels of eGFR and albuminuria, which is consistent with published SGLT2i trials among patients with diabetes. In addition, the cardiovascular benefits of an SGLT2i were confirmed in 2 trials of patients with heart failure and reduced ejection fraction (DAPA-HF and EMPEROR-Reduced).[28,29] Adverse events included genital mycotic infections, diabetic ketoacidosis, and in 1 study, a concern for lower limb amputation. Rates of severe hypoglycemia were not increased, except in some subsets of participants treated with insulin or a sulfonylurea. Benefits were observed across all categories of eGFR (as low as 30–44 ml/min per 1.73 m^2) and albuminuria (including normal albumin excretion), despite reduced glucose-lowering potency at lower eGFR. Benefits were out of proportion to reduction in hemoglobin A1c and did not appear to depend on glucose-lowering. On the basis of these data, the Work Group felt that most patients with T2D, CKD, and eGFR ≥30 ml/min per 1.73 m^2 would choose treatment with an SGLT2i, regardless of levels of albuminuria or eGFR, or level of glycemic control. Choice of SGLT2i should prioritize agents with documented kidney or cardiovascular benefits.

The Work Group used available data to provide a number of practice points guiding implementation of SGLT2i, including integration with concomitant medications and monitoring. The Work Group advised that an SGLT2i can be simply added to other antihyperglycemic medications for

Figure 7 | Key objectives of effective diabetes self-management education programs. Reproduced from *The Lancet Diabetes & Endocrinology*, Volume 6, Chatterjee S, Davies MJ, Heller S, et al. Diabetes structured self-management education programmes: a narrative review and current innovations, 130–142, Copyright © 2018, with permission from Elsevier.[29]

patients whose glycemic targets are not currently met and for patients who are meeting glycemic targets but can safely attain a lower target (e.g., patients with hemoglobin A1c at goal treated with metformin alone or other drugs with low risk of hypoglycemia). For patients in whom additional glucose-lowering may increase risk for hypoglycemia (e.g., those treated with insulin or sulfonylureas and currently meeting glycemic targets), it may be necessary to stop or reduce the dose of an antihyperglycemic drug other than metformin to facilitate the addition of an SGLT2i. All patients should be educated on potential adverse effects, and follow-up should assess glycemia and adverse effects. SGLT2i cause modest volume contraction, blood pressure reduction, and weight loss. For patients at risk for hypovolemia (e.g., due to concomitant diuretic use), providers should consider decreasing dose of a diuretic, advise patients about symptoms of volume depletion and low blood pressure, and follow up volume status after drug initiation.

On average, SGLT2i cause a modest initial reduction in eGFR that is hemodynamic in nature and reversible. Long-term benefits with regard to GFR preservation are observed despite this initial decline, and a reversible decrease in eGFR with commencement of SGLT2i is generally not an indication to discontinue therapy. In the CREDENCE trial, canagliflozin was continued among participants whose eGFR fell below 30 ml/min per 1.73 m^2 during the study.[25] Based on the CREDENCE protocol, it is reasonable to continue an SGLT2i even if the eGFR falls below 30 ml/min per 1.73 m^2, unless not tolerated or kidney replacement therapy is initiated.

Kidney transplant patients may benefit substantially from SGLT2i but may also be at higher risk of infectious complications. As a result, SGLT2i were not recommended for kidney transplant patients until additional studies are completed.

Another new drug class is the long-acting GLP-1 RA (mostly injectables), which stimulate the incretin hormone pathway.[30] They have been shown to substantially improve blood glucose and hemoglobin A1c control, confer weight loss, and reduce blood pressure. More importantly, several GLP-1 RA agents have been shown to reduce major adverse cardiovascular events in patients with T2D and high cardiovascular risk (meta-analysis HR: 0.85; 95% CI: 0.76–0.95). In addition, these same GLP-1 RA agents have been shown to have favorable kidney benefits with substantial reduction in albuminuria and possibly preservation of eGFR (meta-analysis HR: 0.85; 95% CI: 0.73–1.00). In patients with T2D and CKD who have not achieved individualized glycemic targets despite use of metformin and SGLT2i, or who are unable to use those medications, a long-acting GLP-1 RA is recommended as part of the treatment. The cardiovascular outcome trials included patients with eGFR greater than 15 ml/min per 1.73 m^2, whereas data with GLP-1 RA in more advanced CKD are limited.

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

Informed decision-making requires that patients are empowered for self-management through education programs. These include face-to-face, group-based, or digital self-management programs. Diabetes self-management education programs are guided by learning and behavior change theories and are tailored to a person's needs, accounting for cultural, cognitive, and geographical factors. The overall objectives of self-management programs are to empower and enable individuals to develop self-management knowledge and skills, with the aim of reducing the risk of long-term microvascular and macrovascular complications, severe hypoglycemia, and diabetic ketoacidosis; to optimize individuals well-being and improve quality of life; and to achieve treatment satisfaction (Figure 7).[31] Potential benefits are improvements in clinical parameters (glycated hemoglobin, fasting glucose, body weight, blood pressure) and psychosocial outcomes (diabetes self-knowledge, self-efficacy, self-management skills, patient satisfaction). Ideal programs are tailored to individual preferences and learning styles and are continuously re-evaluated.

Patients with diabetes and CKD have multiple comorbidities, high risks of developing hypoglycemia and adverse drug reactions, multiple lifestyle demands, and psychosocial factors that influence behaviors and clinical outcomes. These clinical needs call for a concerted approach to care delivery to stratify risk, triage care, empower patients, and support decision-

making in a timely manner. Given the large number of patients with diabetes and CKD, the comparatively few health care providers, and the silent nature of risk factors and complications, it is recommended to leverage the complementary knowledge, skills, and experience of physician and nonphysician personnel. A team-based and integrated approach to manage these patients should focus on regular assessment, control of multiple risk factors, and self-management to protect kidney function and reduce risk of complications.

Comparison with other guidelines

This new KDIGO guideline shares many commonalities with guidelines from diabetes organizations as well as those from nephrology, cardiology, nutrition, and related disciplines. Principles fundamental to all include focus on comprehensive care, individualization of treatment plans, and emphasis of evidence-based therapies. In that context, this guideline reflects the steady but rapid evolution of available data on which to base recommendations, as reviewed using rigorous methodology by the Evidence Review Team. Compared with the consensus report on management of hyperglycemia in T2D from the American Diabetes Association/European Association for the Study of Diabetes (ADA/EASD), which was recently updated, similarities include recommendations for comprehensive lifestyle therapy, inclusion of metformin in first-line therapy, additional inclusion of SGLT2i for organ protection when CKD is present (even if not required for glycemic control), and self-management education.[32,33] Many other similarities exist, such as recommendations for RAS blockade for patients with hypertension and albuminuria, adaptation of treatments according to CKD severity, health systems organization of care, and others.

Conclusion

The new KDIGO guideline on diabetes management in CKD offers approaches for evidence-based care of people with diabetes and CKD, supplemented with practice points to inform clinical management and implementation. Evidence will continue to expand, and changes will be needed in the future. In the short term, additional evidence will be incorporated via the MAGICapp platform. It is the hope of the Work Group that clear guidance for the large, high-risk group of patients with diabetes and CKD contained in this guideline can facilitate implementation of better treatments, close the large gap between evidence and current practice, and improve outcomes in this population.

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