KDIGO DIABETES IN CKD:

QUICK REFERENCE GUIDE

This guide presents the recommendation statements from the KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease

Chapter 1

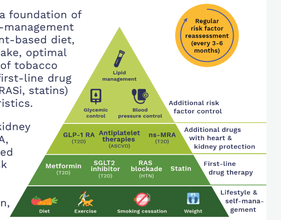
COMPREHENSIVE CARE IN PATIENTS WITH DIABETES AND CKD

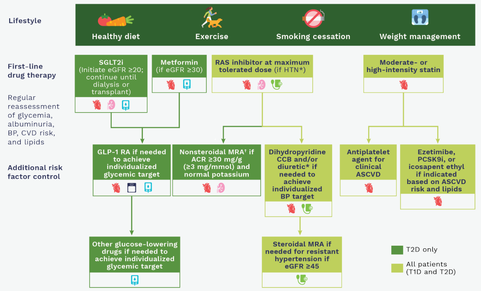
KEY CONCEPTS

→ Patients with diabetes and CKD are at high risk of CKD progression and cardiovascular disease that requires a comprehensive strategy from a multidisciplinary team of health care professionals.

→ This approach should include a foundation of lifestyle modification and self-management (maintenance of a healthy plant-based diet, proper protein and sodium intake, optimal weight and exercise; absence of tobacco use), upon which are layered first-line drug therapies (metformin, SGLT2i, RASi, statins) according to clinical characteristics.

→ Additional drugs with proven kidney and heart protection (GLP-1 RA, ns-MRA, antiplatelets) as guided by assessments of residual risk are administered with further interventions to control risk factors (glycemia, hypertension, dyslipidemia) if applicable.





Chapter 1

COMPREHENSIVE CARE IN PATIENTS WITH DIABETES AND CKD - RAS BLOCKADE

KEY CONCEPTS

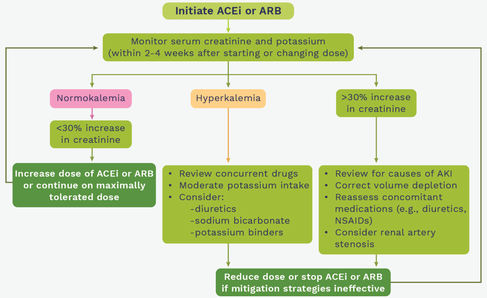
→ ACEi/ARB should be initiated in patients with diabetes, hypertension and albuminuria and titrated to the maximum tolerated dose.

→ Monitor for changes in BP, serum creatinine and serum potassium within 2-4 weeks of ACEi/ARB initiation or dose escalation since RAS blockade can induce a transient decrease in the eGFR or a transient increase in serum creatinine and/or potassium.

→ Patients should be maintained on ACEi or ARB unless serum creatinine rises by more than 30% within 4 weeks of initiation or dose escalation. Episodes of hyperkalemia can often be effectively managed with various strategies below before decreasing the dose or discontinuing RASi therapy.

→ Combined use of ACEi and ARB should be avoided. Similarly, the use of a direct renin inhibitor with an ACEi or ARB should be avoided.

→ Given the adverse fetal effects of ACEi/ARB, women who are considering pregnancy or who are pregnant should discontinue the use of these therapies.



WHAT THE GUIDELINE SAYS:

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).

Chapter 1

COMPREHENSIVE CARE IN PATIENTS WITH DIABETES AND CKD - SGLT2i

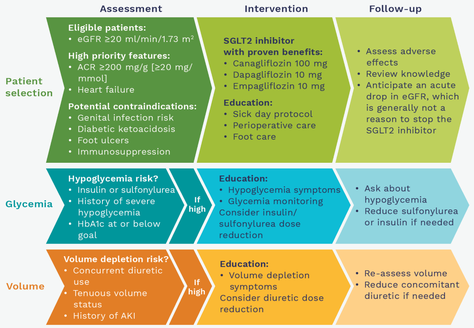
KEY CONCEPTS

→ SGLT2i should be initiated in patients with T2D, CKD and eGFR ≥20 ml/min/1.73 m². Currently SGLT2i with approved indications for kidney and heart protection include canagliflozin, dapagliflozin, and empagliflozin.

→ Once an SGLT2i is initiated, it is reasonable to continue an SGLT2i even if the eGFR falls below 20 ml/min per 1.73 m², unless it is not tolerated or kidney replacement therapy is initiated. The use of SGLT2i in dialysis and transplant patients is currently unsupported.

→ A modest drop in eGFR (≤30%) after SGLT2i administration should not prompt discontinuation of therapy. If decrease is >30%, assess risk for hypovolemia and consider decreasing diuretic dose. SGLT2i may be temporarily withheld during surgery or critical illness.

PRACTICAL APPROACH TO INITIATING SGLT2i IN PATIENTS WITH T2D AND CKD



WHAT THE GUIDELINE SAYS:

Recommendation 1.3.1: We recommend treating patients with type 2 diabetes (T2D), CKD, and an eGFR ≥20 ml/min per 1.73 m² with an SGLT2i (1A).

Chapter 1

COMPREHENSIVE CARE IN PATIENTS WITH DIABETES AND CKD - MRA

KEY CONCEPTS

→ A nonsteroidal mineralocorticoid receptor antagonist (ns-MRA), finerenone, has demonstrated kidney and cardiovascular benefits for patients with T2D, CKD and eGFR ≥25 ml/min/1.73 m². Its use is suggested in those with normal serum potassium concentration and presence of albuminuria (≥30 mg/g [≥3 mg/mmol]) despite maximum tolerated dose of RASi.

→ An ns-MRA can be added to a RASi and an SGLT2i for treatment of T2D and CKD.

→ Initiate finerenone at 10 mg for patients with eGFR <60 ml/min/1.73 m² or 20 mg for patients with eGFR ≥60 ml/min/1.73 m² and serum potassium ≤4.8 mmol/l. Monitor potassium at 1 month and every 4 months thereafter. Continue with current dose if serum potassium is 4.9-5.5 mmol/L. If serum potassium is >5.5 mmol/l, hold finerenone and adjust diet or medications. Resume finerenone only when serum potassium is ≤5.0 mmol/l.

→ Steroidal MRA can be used in patients with CKD and diabetes who also have heart failure, hyperaldosteronism, or refractory hypertension. However, steroidal MRA and ns-MRA should not be combined. If a patient has indications for both but not treated with either, the most clinically pressing indication should drive the MRA selection.

K^+ ≤4.8 mmol/l

- Initiate finerenone
  - 10 mg daily if eGFR 25-59 ml/min per 1.73 m²
  - 20 mg daily if eGFR ≥ 60 ml/min per 1.73 m²
- Monitor K^+ at 1 month after initiation and then every 4 mos.
- Increase dose to 20 mg daily, if on 10 mg daily
- Restart 10 mg daily if previously held for hyperkalemia and K^+ now ≤5.0 mmol/l

K^+ 4.9-5.5 mmol/l

- Continue finerenone 10 mg or 20 mg
- Monitor K^+ every 4 months

K^+ >5.5 mmol/l

- Hold finerenone
- Consider adjustments to diet or concomitant medications to mitigate hyperkalemia
- Recheck K^+
- Consider reinitiation if/when K^+ ≤5.0 mmol/l

WHAT THE GUIDELINE SAYS:

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/1.73 m², normal serum potassium concentration, and albuminuria (≥30 mg/g [≥3 mg/mmol]) despite maximum tolerated dose of RAS inhibitor (RASi) (2A).

Chapter 2

GLYCEMIC MONITORING AND TARGETS IN PATIENTS WITH DIABETES AND CKD

KEY CONCEPTS

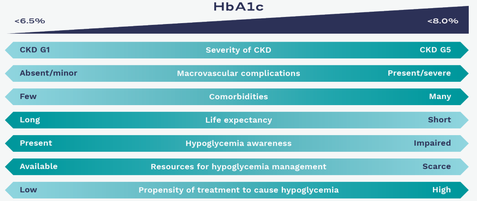
→ HbA1c, glycated hemoglobin, is recommended to monitor glycemic control in patients with diabetes and CKD. Monitoring twice per year is reasonable and can be as often as 4 times per year if glycemic target is not met or there is a change in glucose-lowering therapy.

→ Precision and accuracy of HbA1c measurement declines with advanced CKD (G4-G5) since inflammatory states and metabolic acidosis can bias towards higher HbA1c while conditions such as anemia and transfusions that affect red blood cell survival or turnover can bias toward lower HbA1c.

→ For individuals in whom HbA1c measurements are not concordant with directly measured blood glucose or clinical symptoms, continuous glucose monitoring (CGM) can be used to index glycemia.

→ Self-monitoring of blood glucose (SMBG) or the use of CGM can help monitor for episodes of hypoglycemia. For patients who wish to do neither, glucose-lowering therapies that pose lower hypoglycemic risks are preferred.

→ HbA1c target ranging from <6.5% to <8.0% is appropriate for patients with diabetes and CKD (not on dialysis) and should be individualized based on patient preferences, severity of CKD, presence of macrovascular complications or comorbidities, life expectancy, hypoglycemia burden, choice of glucose-lowering agents, and availability of resources or support system.



WHAT THE GUIDELINE SAYS:

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 (1C).

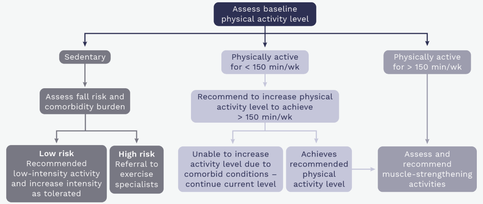
Chapter 3

LIFESTYLE INTERVENTIONS IN PATIENTS WITH DIABETES AND CKD

KEY CONCEPTS

- Patients with diabetes and CKD should adopt a diet high in vegetables, fruits, whole grains, etc. and avoid a diet consisting of processed meats, refined carbohydrates and sweetened beverages.
- It is suggested that patients with diabetes and CKD not on dialysis maintain a protein intake of 0.8 g/kg (weight)/day while those on dialysis can consume between 1.0-1.2 g/kg (weight)/day.
- It is suggested that patients with diabetes and CKD consume <2 g (<90 mmol) sodium/day, which is equivalent to 5 g of salt (NaCl)/day.
- Patients with diabetes and CKD are advised to perform moderate-intensity physical activity for a duration of at least 150 minutes per week. Exercise intensity should be tailored for those who are frail or are at risk for falls.
- Sedentary behavior should be avoided and patients with obesity, diabetes and CKD with eGFR ≥30 ml/min/1.73 m² are encouraged to lose weight.
- Patients with diabetes and CKD should avoid consumption of tobacco products.

SUGGESTED APPROACH TO ADDRESS PHYSICAL INACTIVITY AND SEDENTARY BEHAVIOR



WHAT THE GUIDELINE SAYS:

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

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).

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).

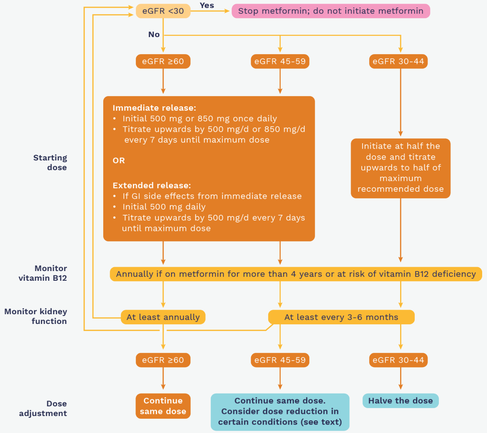
Chapter 4

GLUCOSE-LOWERING THERAPIES IN PATIENTS WITH T2D AND CKD

KEY CONCEPTS

- The treatment algorithm for selecting glucose-lowering therapies for patients with T2D and CKD includes lifestyle therapy, first-line therapy, and additional drug therapy as needed for glycemic control.

- Metformin should be initiated in patients with T2D, CKD and eGFR ≥30 ml/min/1.73 m². Most patients would also benefit from concomitant use of SGLT2i . Increase monitoring when eGFR <60 ml/min/1.73 m² and consider adjusting dose as needed. When eGFR declines to 30-44 ml/min/1.73 m², maximum dose should be halved. Metformin should be discontinued when eGFR <30 ml/min/1.73 m². Vitamin B12 deficiency should be monitored in those on metformin for more than 4 years.



Chapter 4

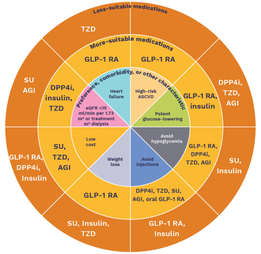
GLUCOSE-LOWERING THERAPIES IN PATIENTS WITH T2D AND CKD

KEY CONCEPTS

- A long-acting GLP-1 RA is recommended for patients with T2D and CKD who have not achieved glycemic targets despite the use of metformin and SGLT2i. The choice of GLP-1 RA should be guided by agents with documented cardiovascular benefits (i.e., liraglutide, semaglutide [injectable] and dulaglutide). Listing of available GLP-1 RA is provided below.
- GLP-1 RA should not be combined with DPP-4 (dipeptidyl peptidase-4) inhibitors.
- GLP-1 RA has shown to promote intentional weight loss and may be useful in patients with obesity, T2D and CKD.

GLP-1 RA	Dose	CKD dose adjustment
Dulaglutide	0.75 and 1.5 mg Once weekly	No adjustment / Use if eGFR >15
Exenatide	10 µg Twice daily	Use if CrCl >30
Exenatide Extended release	2 mg Once weekly	Use if eGFR >45
Liraglutide	1.2 and 1.8 mg Once daily	No adjustment; Limited data for severe CKD
Lixisenatide	10 µg and 20 µg Once daily	No adjustment; Not recommended if eGFR <15; Limited data for severe CKD
Semaglutide Injectable	0.5 mg and 1 mg Once weekly	No adjustment; Limited data for severe CKD
Semaglutide Oral	3 mg, 7 mg, and 14 mg Once daily	No adjustment; Limited data for severe CKD

- If patients still do not meet glycemic targets after lifestyle therapy, metformin and SGLT2i, GLP-1 RA are generally preferred. Other classes of medications can be considered based on patient factors and preferences below:



WHAT THE GUIDELINE SAYS:

Recommendation 4.1.1: We recommend treating patients with T2D, CKD, and an eGFR ≥30 ml/min per 1.73 m² with metformin (1B).

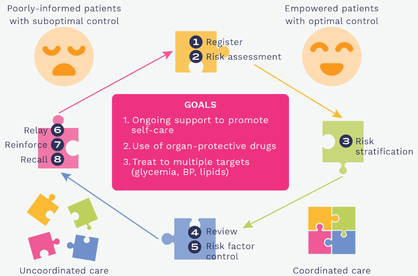
Recommendation 4.2.1: In patients with T2D and CKD who have not achieved individualized glycemic targets despite use of metformin and SGLT2i treatment, or who are unable to use those medications, we recommend a long-acting GLP-1 RA (1B).

Chapter 5

APPROACHES TO MANAGEMENT OF PATIENTS WITH DIABETES AND CKD

KEY CONCEPTS

- A structured self-management education program is recommended for the care of people with diabetes and CKD, with considerations paid to local context, cultures, and availability of resources.
- Key objectives of effective diabetes self-management education programs include:
  - Improve diabetes-related knowledge, beliefs, and skills
  - Improve self-management and self-motivation
  - Encourage adoption and maintenance of healthy lifestyles
  - Improve vascular risk factors
  - Increase engagement with medication, glucose monitoring, and complication screening programs
  - Reduce risk to prevent (or better manage) diabetes-related complications
  - Improve emotional and mental well-being, treatment satisfaction, and quality of life
- Self-management education programs should be operated within a framework of team-based integrated care promoted by policy-makers and institutional decision-makers that focuses on risk evaluation and patient empowerment as part of patients' comprehensive care.
- Effective team-based integrated care should be supported and delivered by physicians and other allied health professionals such as trained nurses, dieticians, pharmacists, healthcare assistants, community workers and peer supporters.



WHAT THE GUIDELINE SAYS:

Recommendation 5.1.1: We recommend that a structured self-management educational program be implemented for care of people with diabetes and CKD (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).

2022 DIABETES IN CKD GUIDELINE HIGHLIGHTS

- ✓ **Comprehensive care:** Patients with diabetes and CKD have multisystem disease that requires treatment including a foundation of lifestyle intervention (healthy diet, exercise, weight management, no smoking) and drug therapy that improves kidney and cardiovascular outcomes (glucose, lipids, blood pressure).
- ✓ **Nutrition intake:** 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. Sodium (<2 g/day) and protein intake (0.8 g/kg/day) in accordance with recommendations for the general population should be followed.
- ✓ **SGLT2i:** should be initiated for patients with T2D and CKD when eGFR is ≥20 ml/min/1.73 m² and can be continued after initiation at lower levels of eGFR. SGLT2i markedly reduce risks of CKD progression, heart failure, and atherosclerotic cardiovascular diseases, even when blood glucose is already controlled.
- ✓ **Metformin:** Metformin should be used for patients with T2D and CKD when eGFR is ≥30 ml/min/1.73 m². For such patients, metformin is a safe, effective, and inexpensive drug to control blood glucose and reduce diabetes complications.
- ✓ **Glycemic monitoring and targets:** HbA1c should be measured regularly. Reliability decreases with advanced CKD, particularly for patients treated with dialysis, and results should be interpreted with caution. CGM or SMBG may also be useful, especially for treatment associated with risk of hypoglycemia. Targets for glycemic control should be individualized, ranging from <6.5% to <8.0%.
- ✓ **GLP-1 RA:** 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.
- ✓ **RAS blockade:** Patients with T1D or T2D, hypertension, and albuminuria (persistent ACR ≥30 mg/g [≥3 mg/mmol] should be treated with a RAS inhibitor (ACEi or ARB), titrated to the maximum approved or highest tolerated dose. Serum potassium and creatinine should be monitored.
- ✓ **Nonsteroidal mineralocorticoid receptor antagonists (ns-MRA):** ns-MRA reduce risks of CKD progression and cardiovascular events for people with T2D and residual albuminuria. They are suggested for patients with T2D, urine ACR ≥30 mg/g [≥3 mg/mmol] and normal serum potassium on other standard-of-care therapies. Serum potassium and creatinine should be monitored.
- ✓ **Approaches to management:** A team-based and integrated approach to manage these patients should focus on regular assessment, control of multiple risk factors, and structured education in self-management to protect kidney function and reduce risk of complications.

For more information, please consult:

KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. Kidney Int. 2022; 102(5S):S1–S127.

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