KDIGO Clinical Practice Guideline on Diabetes Management in CKD

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Missing from photo: Clint Hurst, Kamlesh Khunti, Hiddo Lambers-Heerspink, Wasu Olowu, Sophia Zoungas

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Scope of the Clinical Practice Guideline

In

- Types 1 and 2 diabetes
- All stages of CKD
  - Kidney transplant recipients
  - Dialysis
- Interventions addressed with rigorous data (RCTs)
  - Lifestyle
  - Pharmacotherapy
  - Systems

Out

- Interventions covered elsewhere
  - Blood pressure
  - Lipids
- Prevention & screening
- Topics with insufficient data
  - Diagnosis
  - Emerging & pipeline therapies

Challenges to the Guideline

- What to do when evidence is lacking?
  - Balance providing guidance with rigor

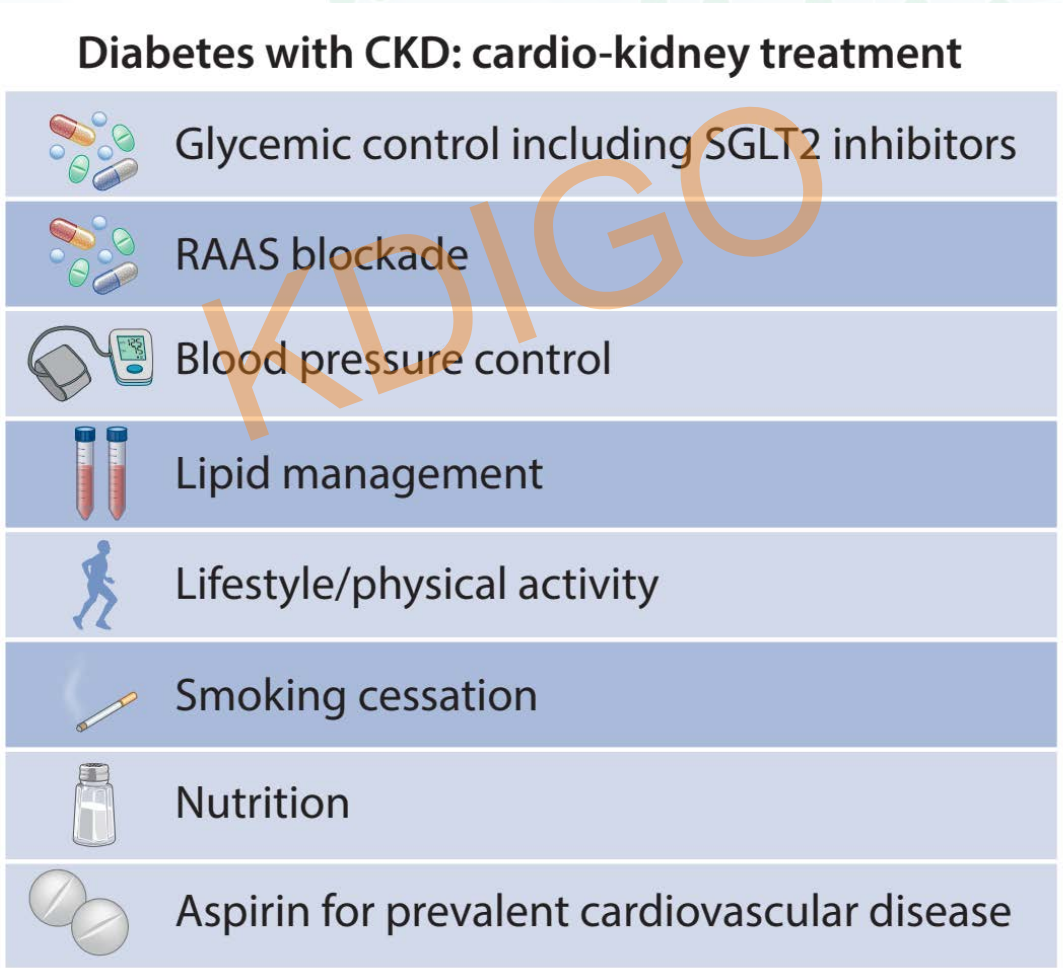
- How to address clinically relevant groups of patients?
  - Type 1 and Type 2 diabetes
  - CKD stages
  - ESKD
  - Transplant recipients

Diabetes & CKD Guideline Contents

- Chapter 1. Comprehensive Care in Patients with Diabetes and CKD
  - Comprehensive management
  - RAAS blockade
  - Smoking
- Chapter 2. Glycemic Monitoring and Targets in Patients with Diabetes and CKD
- Chapter 3. Lifestyle Interventions in Patients with Diabetes and CKD
- Chapter 4. Antihyperglycemic Therapies in Patients with Diabetes and CKD
- Chapter 5. Approaches to Management of Patients with Diabetes and CKD

Comprehensive Care in Patients with Diabetes and CKD

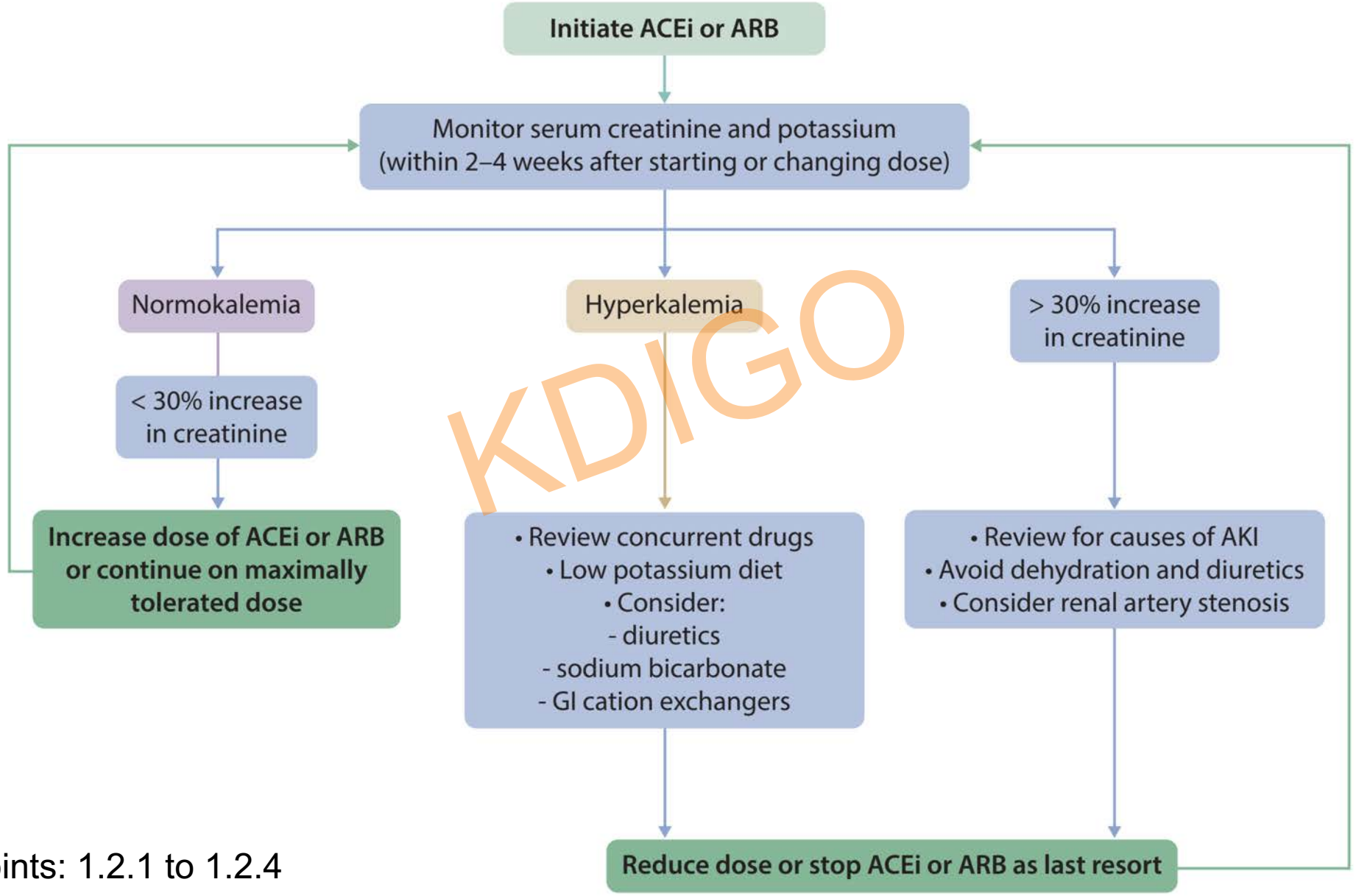
Practice Point 1.1.1. Patients with diabetes and CKD should be treated with a comprehensive strategy to reduce risks of kidney disease progression and cardiovascular disease.



Comprehensive Care in Patients with Diabetes and CKD

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 should be titrated to the highest approved dose that is well tolerated *(1B)*.

Comprehensive Care in Patients with Diabetes and CKD

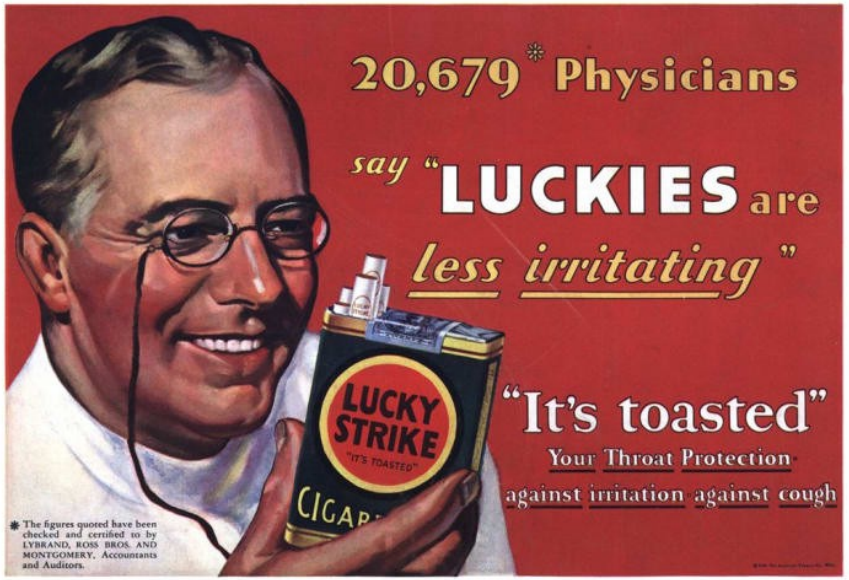


Practice Points: 1.2.1 to 1.2.4

Comprehensive Care in Patients with Diabetes and CKD

- **Recommendation 1.3.1. We recommend advising patients with diabetes and CKD who use tobacco to quit using tobacco products *(1D)*.**

- Practice Point 1.3.1. Physicians should counsel patients with diabetes and CKD to reduce second-hand smoke exposure.

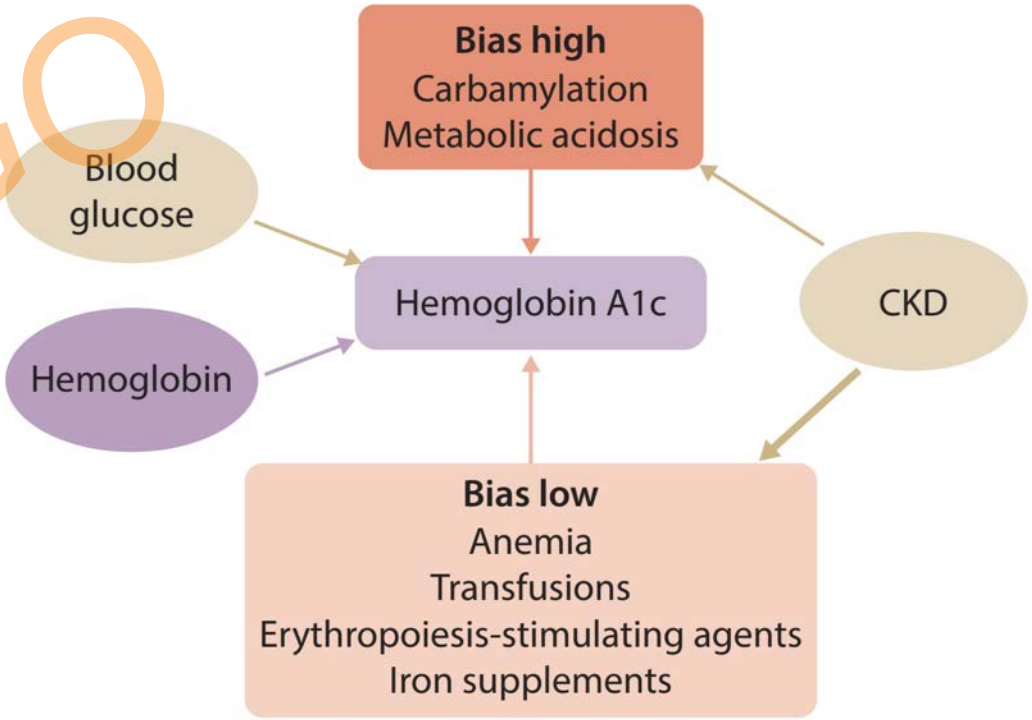


Glycemic Monitoring and Targets in Patients with Diabetes and CKD

Recommendation 2.1.1. We recommend hemoglobin A1c (HbA1c) to monitor glycemic control in patients with diabetes and CKD *(1C)*.

Practice Point 2.1.1. Monitoring by HbA1c twice per year is reasonable. HbA1c may be measured as often as four times per year if the glycemic target is not met or after change in anti-hyperglycemic therapy.

Practice Point 2.1.2. Accuracy and precision of HbA1c measurement declines with advanced CKD, particularly among patients treated by dialysis (low reliability of HbA1c).



Glycemic Monitoring and Targets in Patients with Diabetes and CKD

Practice Point 2.1.3. A continuous glucose management indicator (CGMI) can be used to index glycemia for individuals in whom HbA1c is not concordant with directly measured blood glucose levels or clinical symptoms.

Practice Point 2.1.4. SMBG or CGM may help to prevent hypoglycemia and improve glycemic control when anti-hyperglycemic therapies associated with risk of hypoglycemia are used.

Practice Point 2.1.5. For patients with CKD and Type 2 diabetes who choose not to do daily glycemic monitoring by SMBG or CGM, anti-hyperglycemic agents that pose a lower risk of hypoglycemia are preferred.

Practice Point 2.1.6. CGM devices are rapidly evolving with multiple functionalities (e.g. CGMI, real-time and flash glycemia monitoring). Newer CGM devices may offer advantages for certain patients, depending on their values, goals, and preferences.

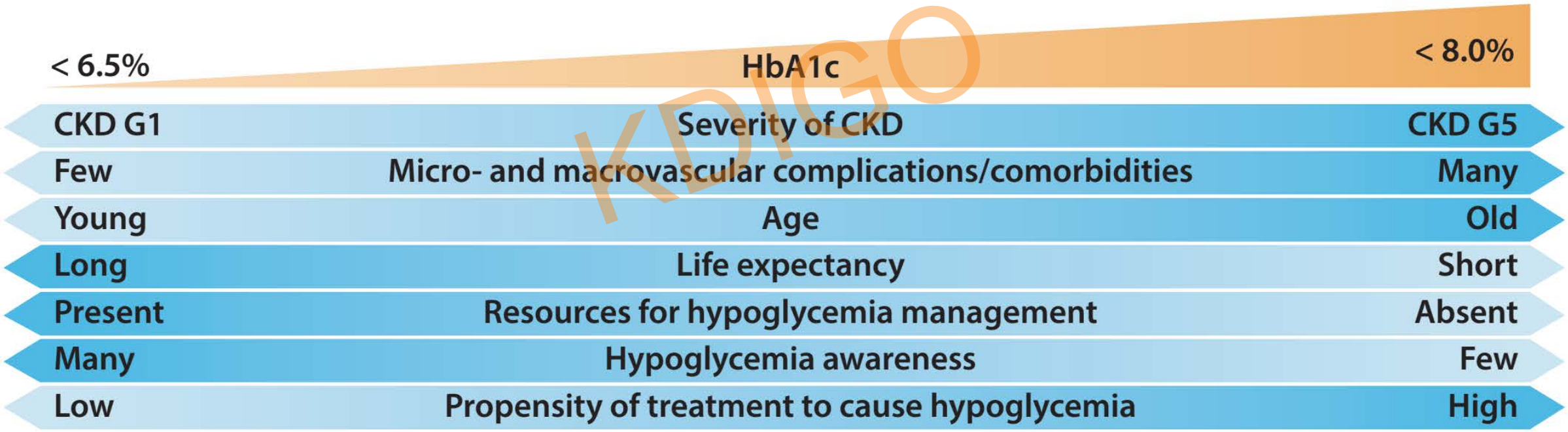
Glycemic Monitoring and Targets in Patients with Diabetes and CKD

Frequency of HbA1c and CGMI in CKD

Population	Measure	Frequency of HbA1c	Reliability	CGMI
CKD G1–G3b	Yes	• Twice per year • Up to four times per year if not achieving target or change in therapy	High	Occasionally useful
CKD G4–G5 including treatment by dialysis or kidney transplant	Yes	• Twice per year • Up to four times per year if not achieving target or change in therapy	Low	Commonly useful

Glycemic Monitoring and Targets in Patients with Diabetes and CKD

Recommendation 2.2.1. We recommend an individualized HbA1c target ranging from <6.5% to <8.0% in patients with diabetes and non-dialysis dependent CKD *(1C)*.



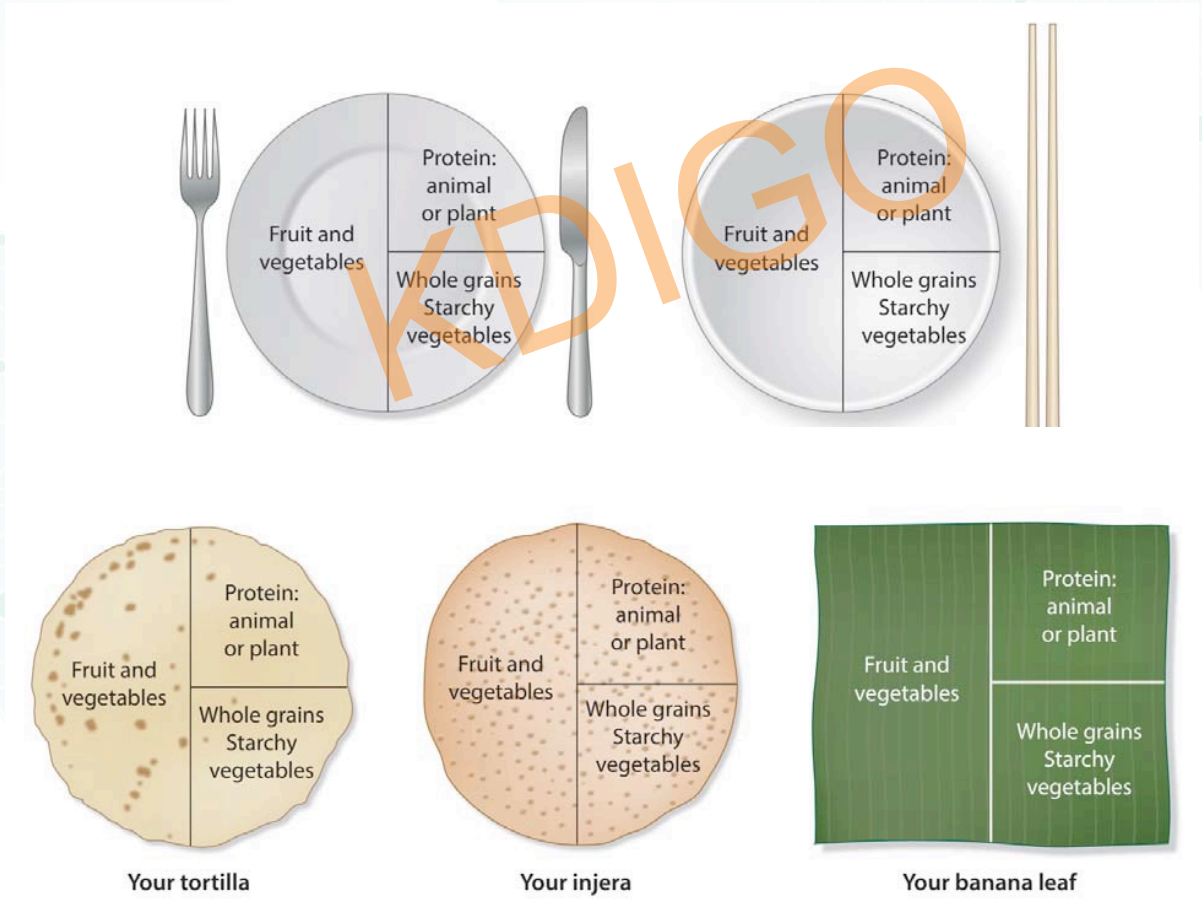
Glycemic Monitoring and Targets in Patients with Diabetes and CKD

Practice Point 2.2.1. Safe achievement of lower HbA1c targets (e.g., <6.5% or <7.0%) may be facilitated by SMBG or CGM and by selection of anti-hyperglycemic 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 HbA1c for defining glycemic targets in some patients.

Lifestyle Interventions in Patients with Diabetes and CKD

Practice Point 3.1.1. Patients with diabetes and CKD should consume a 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.



Lifestyle Interventions in Patients with Diabetes and CKD

Recommendation 3.1.1. We suggest maintaining protein intake of 0.8 g of protein/kg (weight)/day for those with diabetes and non-dialysis CKD (*2C*).

Practice Point 3.1.2. Patients treated with hemodialysis, and particularly peritoneal dialysis, should consume between 1.0 and 1.2 g of protein/kg (weight)/day.

Animal proteins

Meat, poultry, fish, seafood, eggs:
28 g (1 oz) = 6 8 g protein
1 egg = 6–8 g protein

Dairy, milk, yoghurt, cheese:
250 cc (8 oz) = 8–10 g protein
28 g (1 oz) cheese = 6–8 g protein

Plant proteins

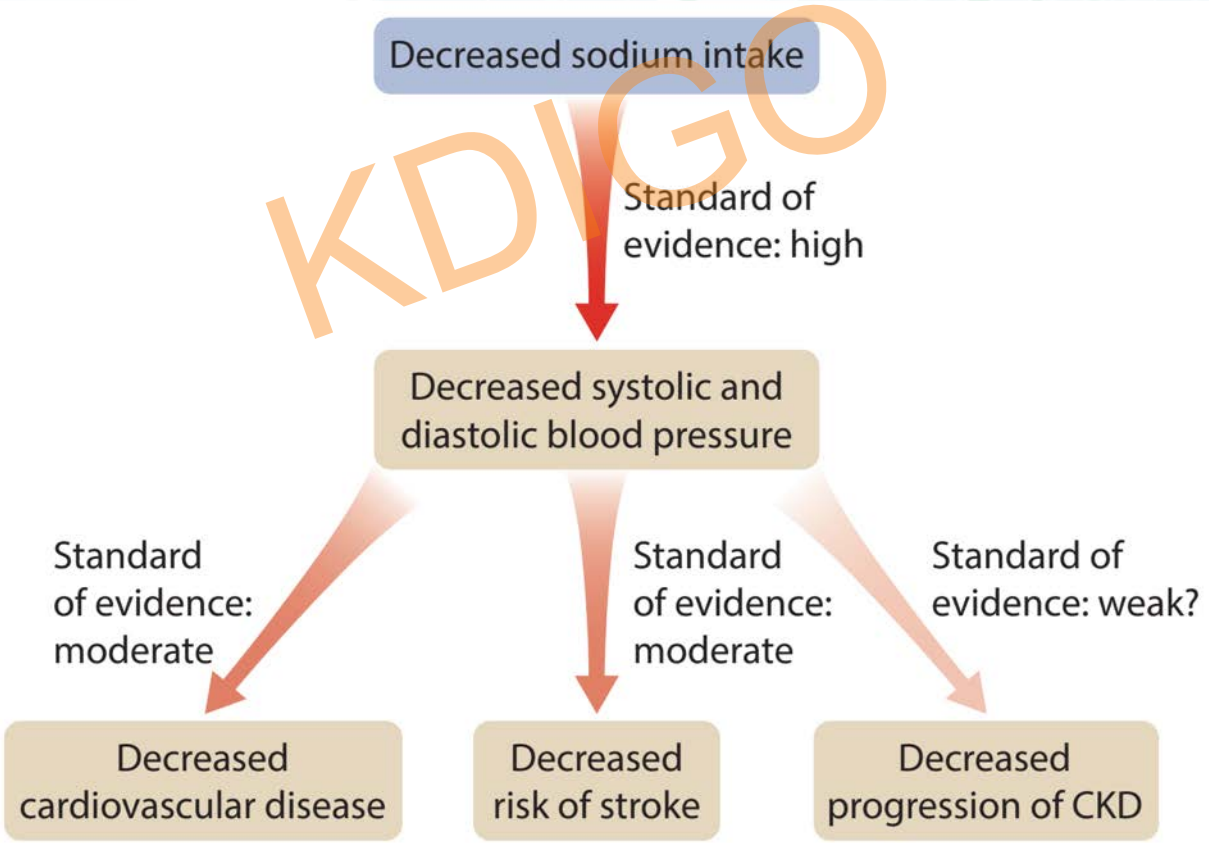
Legumes, dried beans, nuts, seeds:
100 g (0.5 cup) cooked = 7 10 g protein

Whole grains, cereals:
100 g (0.5 cup) cooked = 3–6 g protein

Starchy vegetables, breads:
2–4 g protein

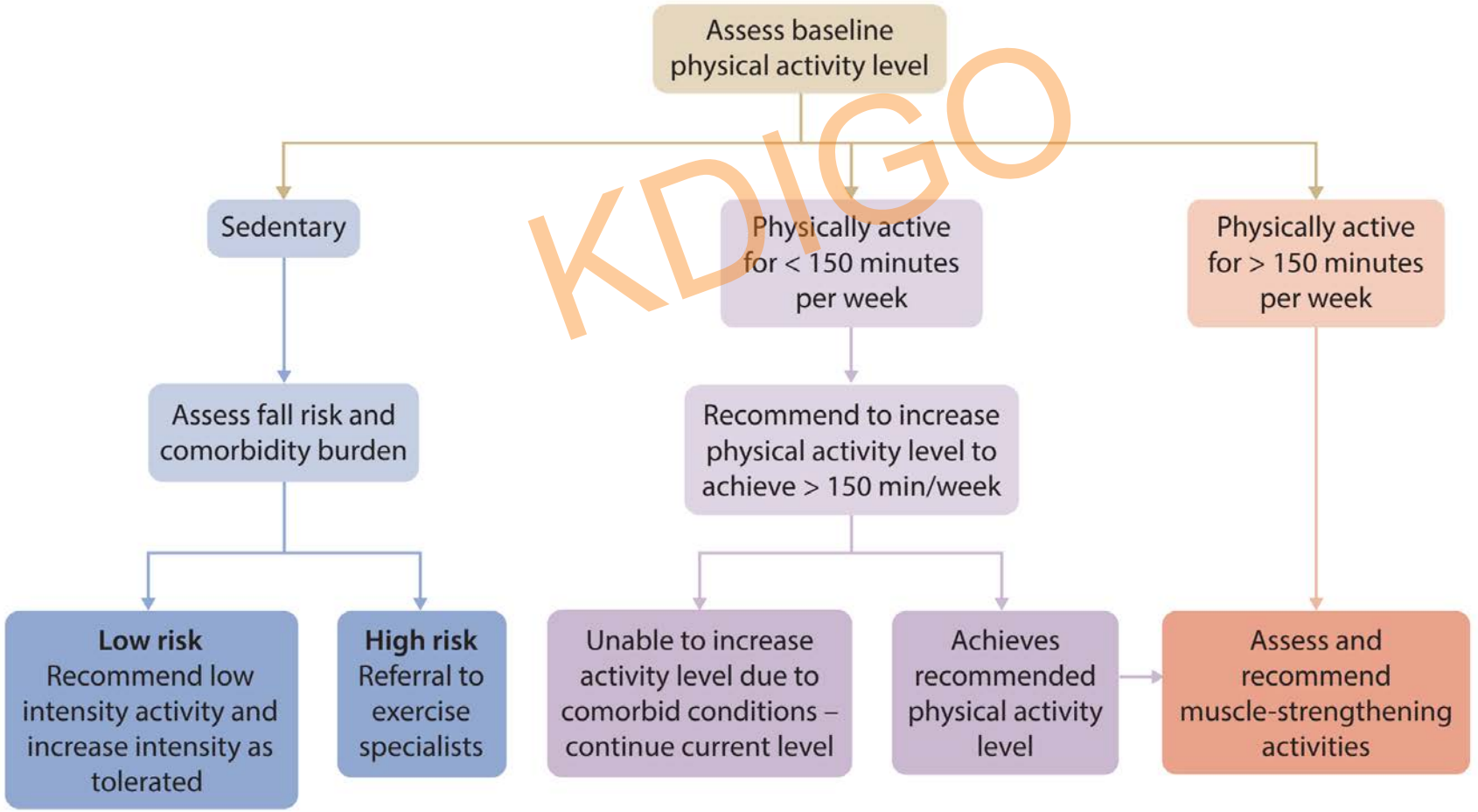
Lifestyle Interventions in Patients with Diabetes and CKD

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)*.



Lifestyle Interventions in Patients with Diabetes and CKD

Recommendation 3.2.1. We recommend that patients with diabetes and CKD should 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)*.



Anti-hyperglycemic Therapies in Patients with Diabetes and CKD

Lifestyle therapy

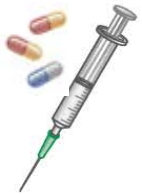
Physical activity
Nutrition
Weight loss

Base drug therapy

Metformin
- eGFR ≥ 30 mL/min/1.73m^2: dose per eGFR
- eGFR < 30 mL/min/1.73m^2: discontinue
- Dialysis: discontinue

and

SGLT-2 inhibitor
- eGFR ≥ 30 mL/min/1.73m^2
- eGFR < 30 mL/min/1.73m^2: do not intitate
- Dialysis: discontinue



Additional drug therapy as needed for glycemic control, guided by patient preferences, comorbidities, eGFR, and cost

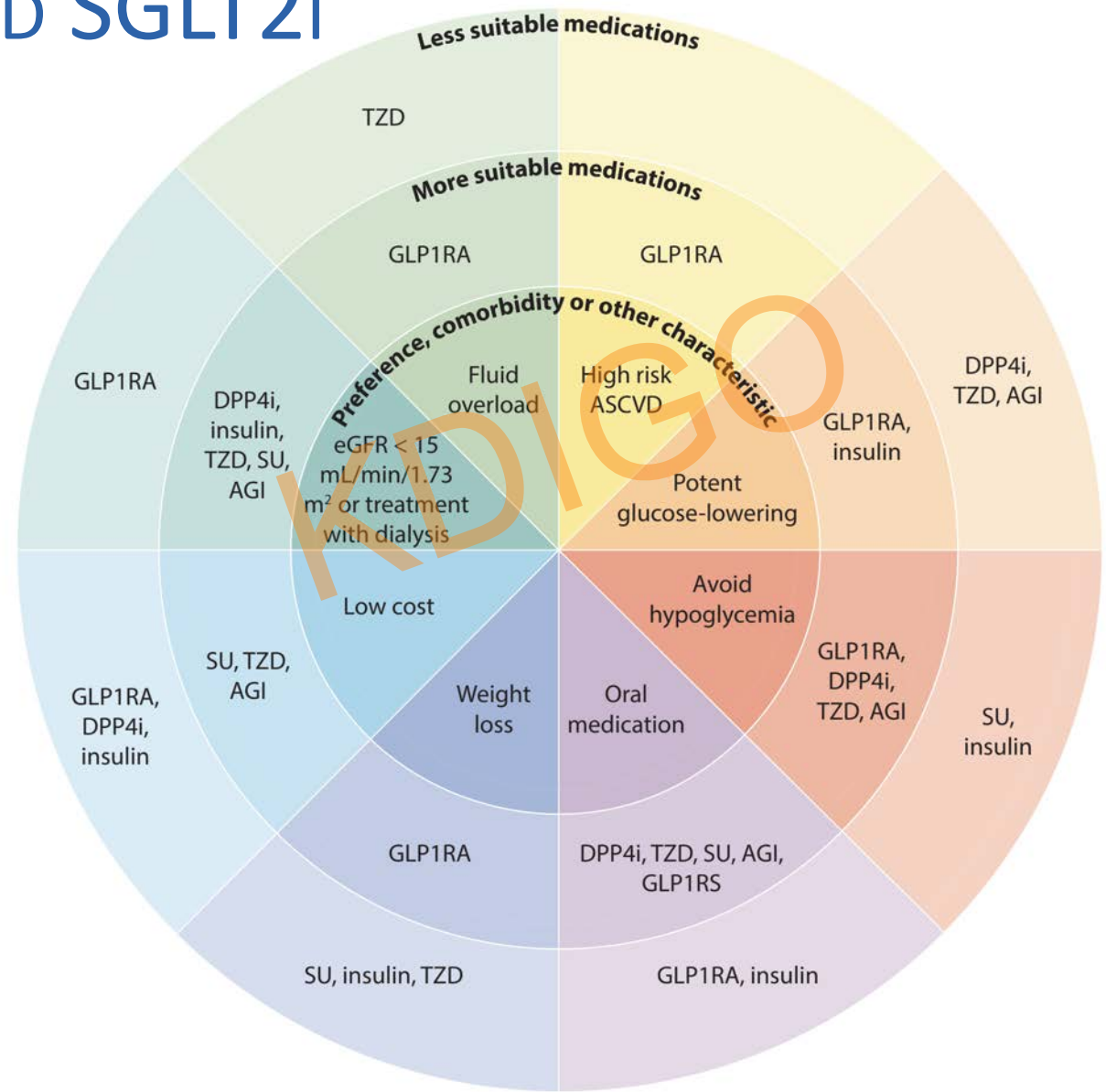
GLP-1R agonist (preferred)

DPP-4 inhibitor | **Insulins**

Sulfonylurea | **TZD**

Alpha-glucosidase inhibitors

Consideration for glucose-lowering medication after Metformin and SGLT2i



Anti-hyperglycemic Therapies in Patients with Diabetes and CKD

Recommendation 4.1.1. In patients with Type 2 diabetes, CKD, and eGFR ≥30 ml/min/1.73 m^2, we recommend that metformin be used as the first-line treatment for hyperglycemia *(1B)*.

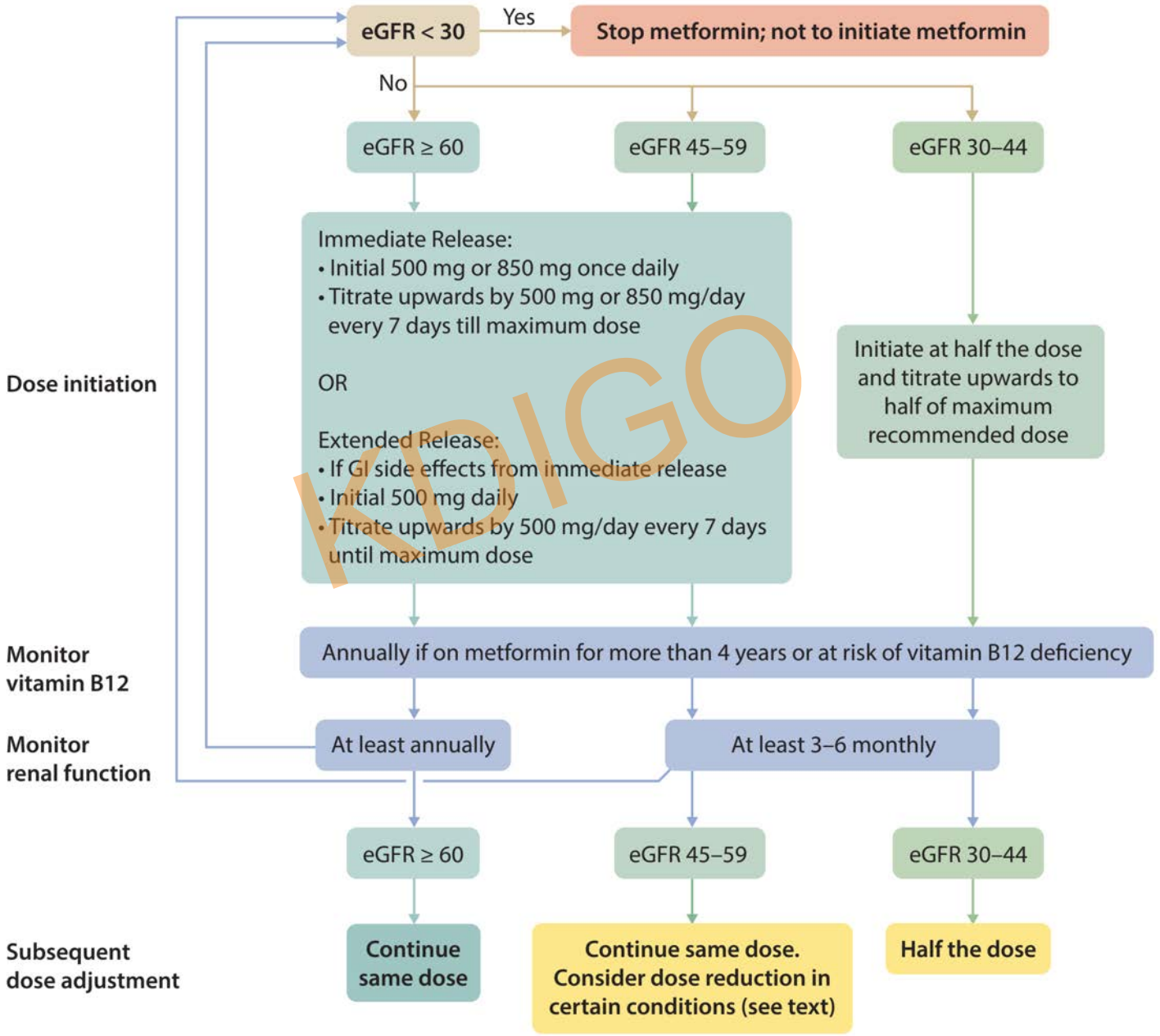
Practice Point 4.1.1. Treat kidney transplant recipients with T2DM and eGFR ≥30 ml/min/1.73 m^2 with metformin according to recommendations for patients with Type 2 diabetes and CKD.

Practice Point 4.1.2. Monitor eGFR in patients treated with metformin. Increase the frequency of monitoring when eGFR is <60 ml/min/1.73 m^2.

Practice Point 4.1.3. Adjust the dose of metformin when eGFR is less than 60 ml/min/1.73 m^2.

Practice Point 4.1.4. Monitor patients for vitamin B12 deficiency when they are treated with metformin for more than four years.

Anti-hyperglycemic Therapies in Patients with Diabetes and CKD



Anti-hyperglycemic Therapies in Patients with Diabetes and CKD

Recommendation 4.2.1. In patients with Type 2 diabetes, CKD, and eGFR ≥30 ml/min/1.73 m^2, we recommend including an SGLT-2 inhibitor (SGLT2i) in the antihyperglycemic treatment regimen *(1A)*.

Practice Point 4.2.1. A SGLT2i can be added to other antihyperglycemic medications for patients whose glycemic targets are not currently met and for patients who are meeting glycemic targets but can safely attain a lower target. (Figure 14)

Practice Point 4.2.2. For patients in which 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 addition of an SGLT2i.

Practice Point 4.2.3. Choice of SGLT2i should prioritize agents with documented kidney or cardiovascular benefits and take eGFR into account.

Effect of SGLT2 inhibitors on cardiovascular, renal and safety outcomes in patients with type 2 diabetes mellitus and chronic kidney disease: a systematic review and meta-analysis

Toyama & Neuen et al.

Diabetes, Obesity and Metabolism doi: 10.1111/dom.13648

@brendonneuen

27 included studies

Up to 7,363 participants

eGFR <60mL/min/1.73m^2

Overall effect estimate

P-heterogeneity for differences between individual agents

CV death, nonfatal MI, nonfatal stroke	Hospitalization for heart failure	eGFR slope	Renal composite outcome
RR 0.81 (95% CI 0.70-0.94)	**RR 0.61** (95% CI 0.48-0.78)	**1.35mL/min/1.73m^2/year** (95% CI 0.78-1.93)	**RR 0.71** (95% CI 0.53-0.95)
0.41	0.68	0.11	0.93

Conclusion: SGLT2 inhibitors reduce the risk of cardio-renal outcomes in patients with T2DM and CKD, without clear evidence of additional safety concerns beyond those already known for the class

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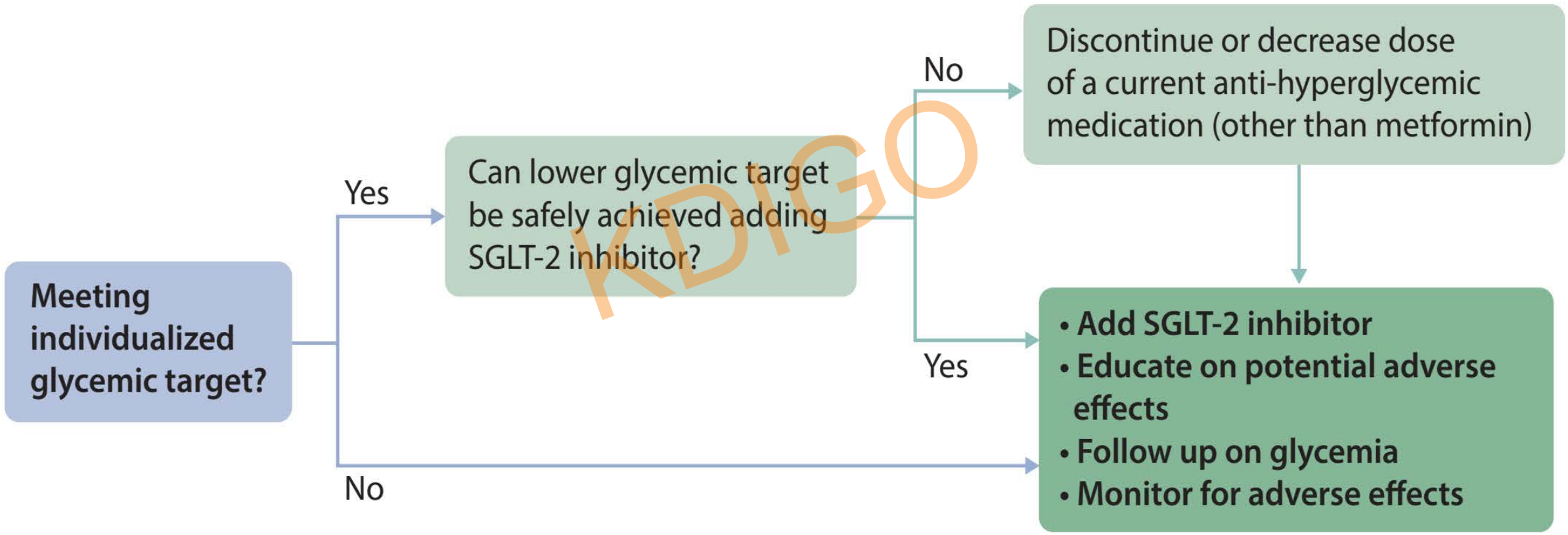
Anti-hyperglycemic Therapies in Patients with Diabetes and CKD



Anti-hyperglycemic Therapies in Patients with Diabetes and CKD

- Practice Point 4.2.4. It is reasonable to withhold SGLT2i during times of prolonged fasting or critical medical illness (at risk for ketosis).
- Practice Point 4.2.5. If a patient is at risk for hypovolemia, consider decreasing thiazide or loop diuretic dosages before commencement of SGLT2i; advise patients about symptoms of dehydration, low bp, and follow up volume status after drug initiation.
- Practice Point 4.2.6. A reversible decrease in eGFR with commencement of SGLT2i may occur and is generally not an indication to discontinue therapy.
- Practice Point 4.2.7. Once an SGLT2i is initiated, it is reasonable to continue an SGLT2i even if eGFR falls below 30 ml/min/1.73 m2, unless reversible changes in eGFR are precipitating uremic symptoms or other complications of CKD.
- Practice Point 4.2.8. SGLT2i have not been adequately studied in kidney transplant recipients; therefore, the recommendation to use SGLT2i does not apply to kidney transplant recipients.

Anti-hyperglycemic Therapies in Patients with Diabetes and CKD

- **Recommendation 4.3.1. In patients with Type 2 diabetes and CKD who have not achieved individualized glycemic targets despite use of metformin / SGLT2i, or who are unable to use those medications, we recommend a long acting glucagon-like peptide-1 receptor agonist (GLP-1 RA) *(1B)*.**
- Practice Point 4.3.1. Prefer those GLP-1 RA with documented CV benefits.
- Practice Point 4.3.2. To minimize GI side effects, start with a low dose of GLP-1 RA, and titrate up slowly.
- Practice Point 4.3.3. Do NOT combine GLP-1 RA with DPP-4 inhibitors.
- Practice Point 4.3.4. The risk of hypoglycemia is generally low with GLP-1 RA when used alone, but risk is increased when used concomitantly with other medications e.g. SU / insulin. The doses of SU and/or insulin may need to be reduced.

Anti-hyperglycemic Therapies in Patients with Diabetes and CKD

Table 11. Dosing for available GLP-1 RA agents and dose modification for CKD

GLP-1 receptor agonist	Dose	CKD adjustment
Dulaglutide	0.75 mg and 1.5 mg once weekly	No dosage adjustment Use with eGFR > 15 mL/min/1.73m^2
Exenatide	10 µg twice daily	Use with CrCl > 30 mL/min
Exenatide Extended-Release	2 mg once weekly	Use with CrCl > 30 mL/min
Liraglutide	1.2 mg and 1.8 mg once daily	No dosage adjustment Limited data for severe CKD
Semaglutide (injection)	0.5 mg and 1 mg once weekly	No dosage adjustment Limited data for severe CKD
Semaglutide (oral)	3 mg, 7 mg, or 14 mg daily	No dosage adjustment Limited data for severe CKD

Approaches to Management of Patients with Diabetes and CKD

Recommendation 5.1.1. We recommend 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 program providing education on self-management for patients with diabetes and CKD taking into consideration local context, cultures, and availability of resources.

Key objectives are to:

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 wellbeing, treatment satisfaction and quality of life

Approaches to Management of Patients with Diabetes and CKD

Recommendation 5.2.1. We suggest that policy-makers and institutional decision-makers should 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 non-physician personnel (e.g., nurses, healthcare assistants, community workers, peer supporters).

Overall Summary

- KDIGO guideline on Diabetes and CKD published October 2020
- Provide recommendations and practice points on:
  - Comprehensive Care
  - Glycemic Monitoring and Targets
  - Lifestyle Interventions
  - Antihyperglycemic Therapies
  - Approaches to Management of Patients
- Patient-centered decision-making and support; and consistent efforts at improving diet and exercise remain the foundation of all glycemic management
- Control of risk factors including RAAS blockade remains part of standard of care
- Glycemia is monitored with HbA1c and blood glucose
- Glycemic targets should be individualized with focus on increased risk for hypoglycemia with declining renal function
- Initial use of metformin, followed by SGLT2i is recommended
- Health care organizations should support a coordinated effort.

THANK YOU