# راهکارهای کنترل دیابت در بیمار با بیماری مزمن کلیه

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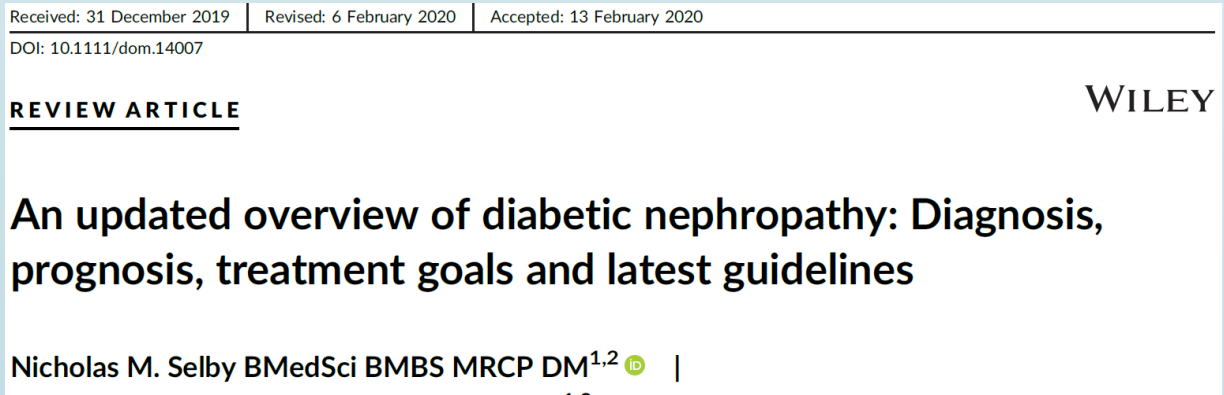
# INTRODUCTION

- Diabetic nephropathy (DN) is a clinical syndrome characterized by persistent albuminuria and a progressive decline in renal function, and the term infers the presence of a typical pattern of glomerular disease.
- DN is reported to occur in 20% to 50% of those living with diabetes and is the single commonest cause of end-stage kidney disease



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REVIEW ARTICLE

WILEY

**An updated overview of diabetic nephropathy: Diagnosis, prognosis, treatment goals and latest guidelines**

Nicholas M. Selby BMedSci BMBS MRCP DM[1,2] |

# ALBUMINURIA CATEGORIES IN CKD

| Category | AER (mg/24 h) | ACR (approximate equivalent) (mg/mmol) | ACR (approximate equivalent) (mg/g) | Terms |
|---|---|---|---|---|
| A1 | <30 | <3 | <30 | Normal to mildly increased |
| A2 | 30–300 | 3–30 | 30–300 | Moderately increased[a] |
| A3 | >300 | >30 | >300 | Severely increased[b] |

ACR, albumin-creatinine ratio; AER, albumin excretion rate; CKD, chronic kidney disease.

[a]Relative to young-adult level.

[b]Including nephrotic syndrome (AER usually >2200 mg/24 h [ACR >2200 mg/g; >220 mg/mmol]).

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# Clinical features of DN

- The hallmark of established DN is persistent albuminuria (category A3, severely increased), with co-existing retinopathy and no evidence of alternative kidney disease
- As well as indicating increased cardiovascular risk in both T1DM and T2DM,20,21 the traditional paradigm is that the onset of moderately increased albuminuria (A2), previously termed microalbuminuria, predicts the onset of established DN.

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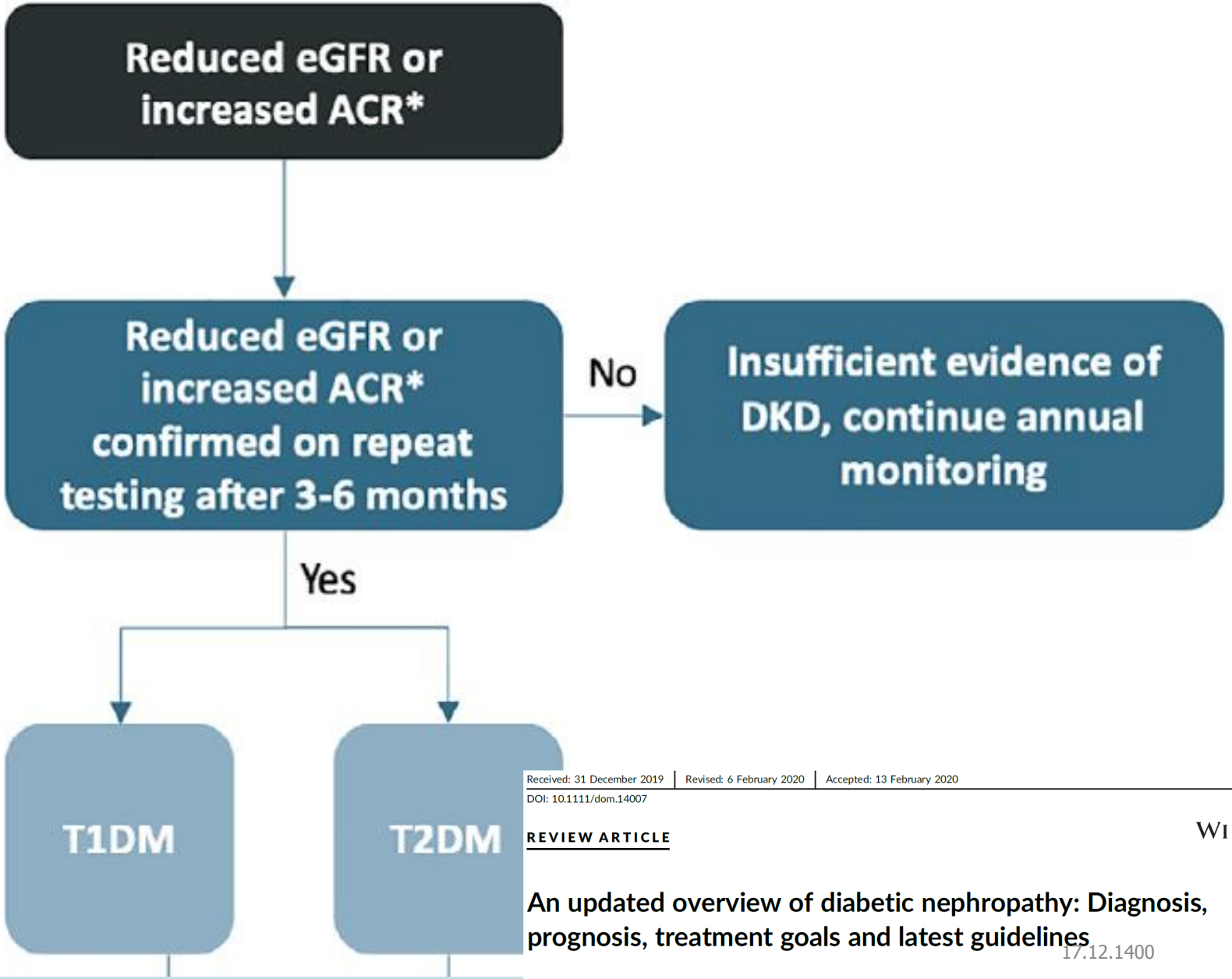
# Non-albuminuric DKD

- It is increasingly recognized that reductions in eGFR can occur in the setting of normal urinary albumin excretion in both T1DM and T2DM.
- In general, non-proteinuric CKD often points towards etiologies that are ischemic in nature or in which tubulo-interstitial pathologies predominate.
- However, non-proteinuric DN has also been described in association with the typical histopathological changes of diabetic glomerulopathy

1. Screening

2. Confirmation of abnormal results

3. Assessment of likelihood of DKD

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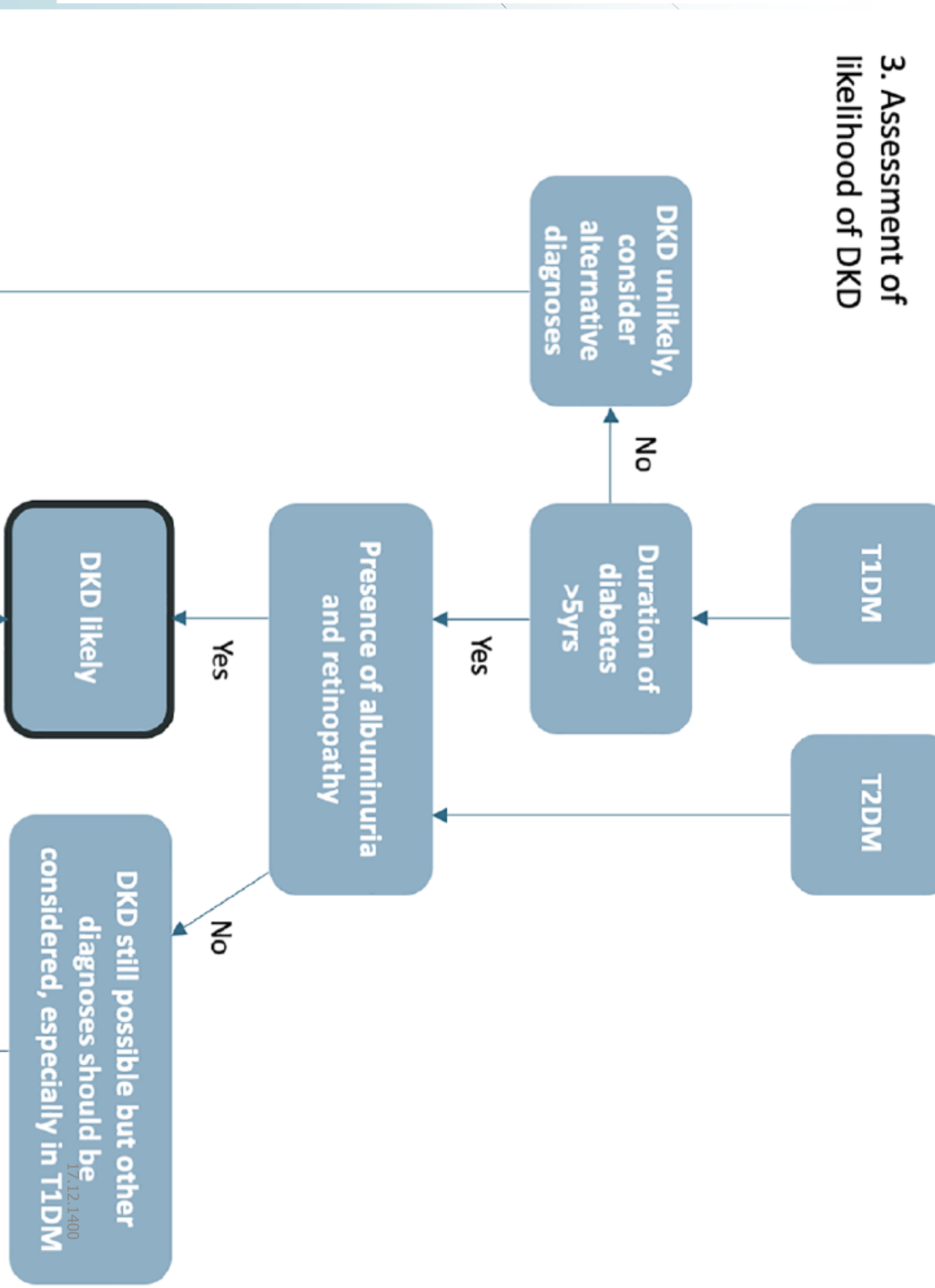

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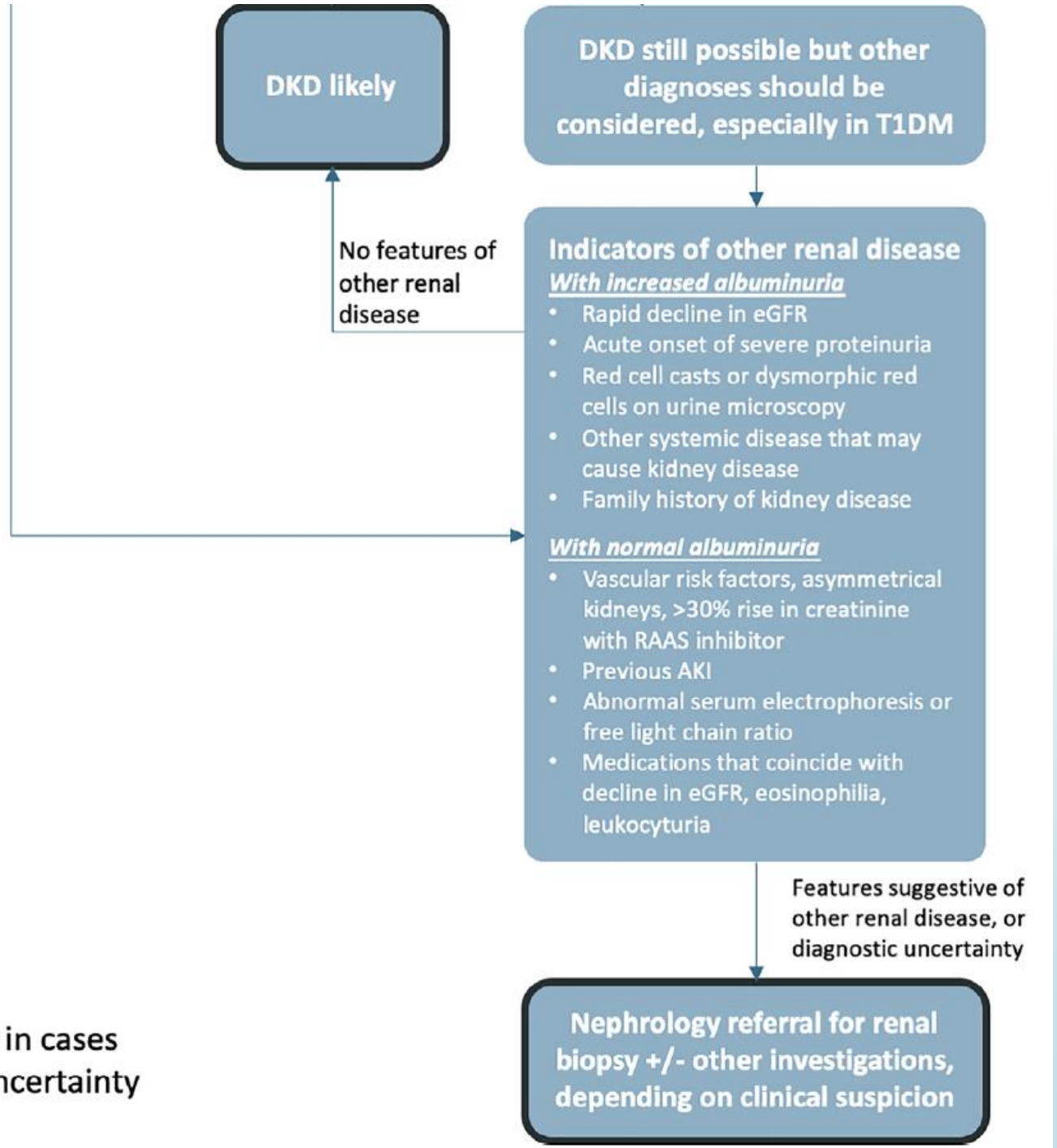
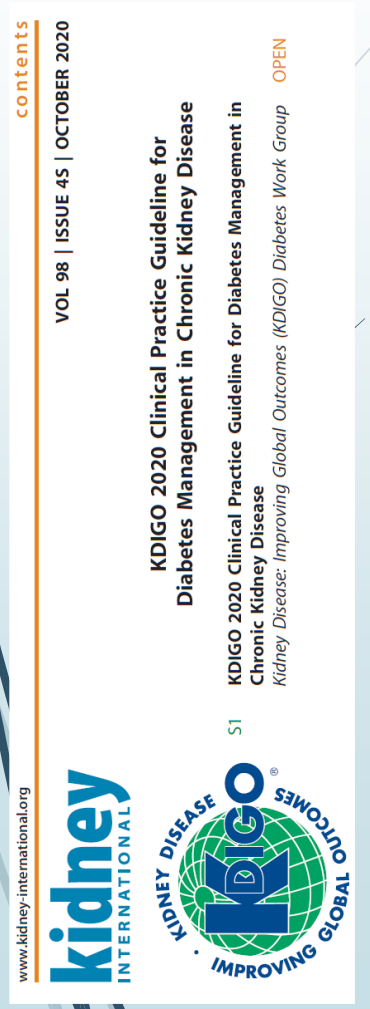
4. Renal biopsy in cases of diagnostic uncertainty

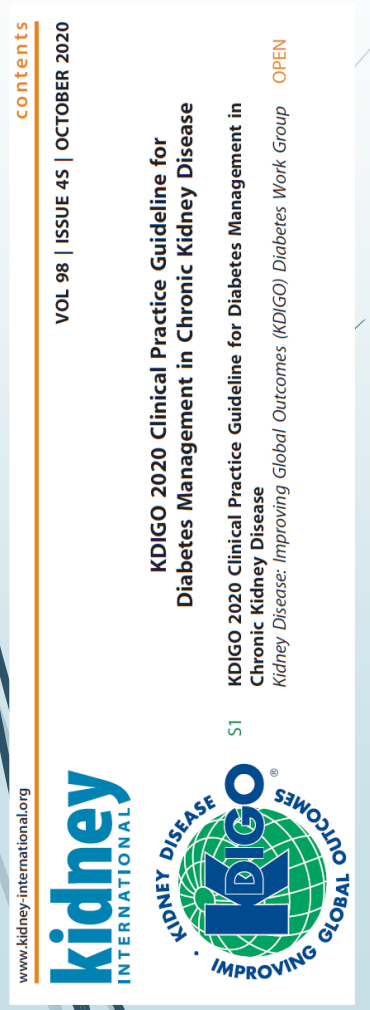


# Comprehensive diabetes and CKD management




- Optimal management of CKD in diabetes is a complex, multidisciplinary, cross-functional team effort.
- Since multi-morbidity is common among people with diabetes and CKD, care usually involves many other specialties, including but not limited to ophthalmology, neurology, orthopedic surgery, and cardiology.

# Comprehensive diabetes and CKD management




- With the patient at the center, the team includes medical doctors, nurses, dietitians, educators, lab technicians, podiatrists, family members, and potentially many others depending on local organization and structure.

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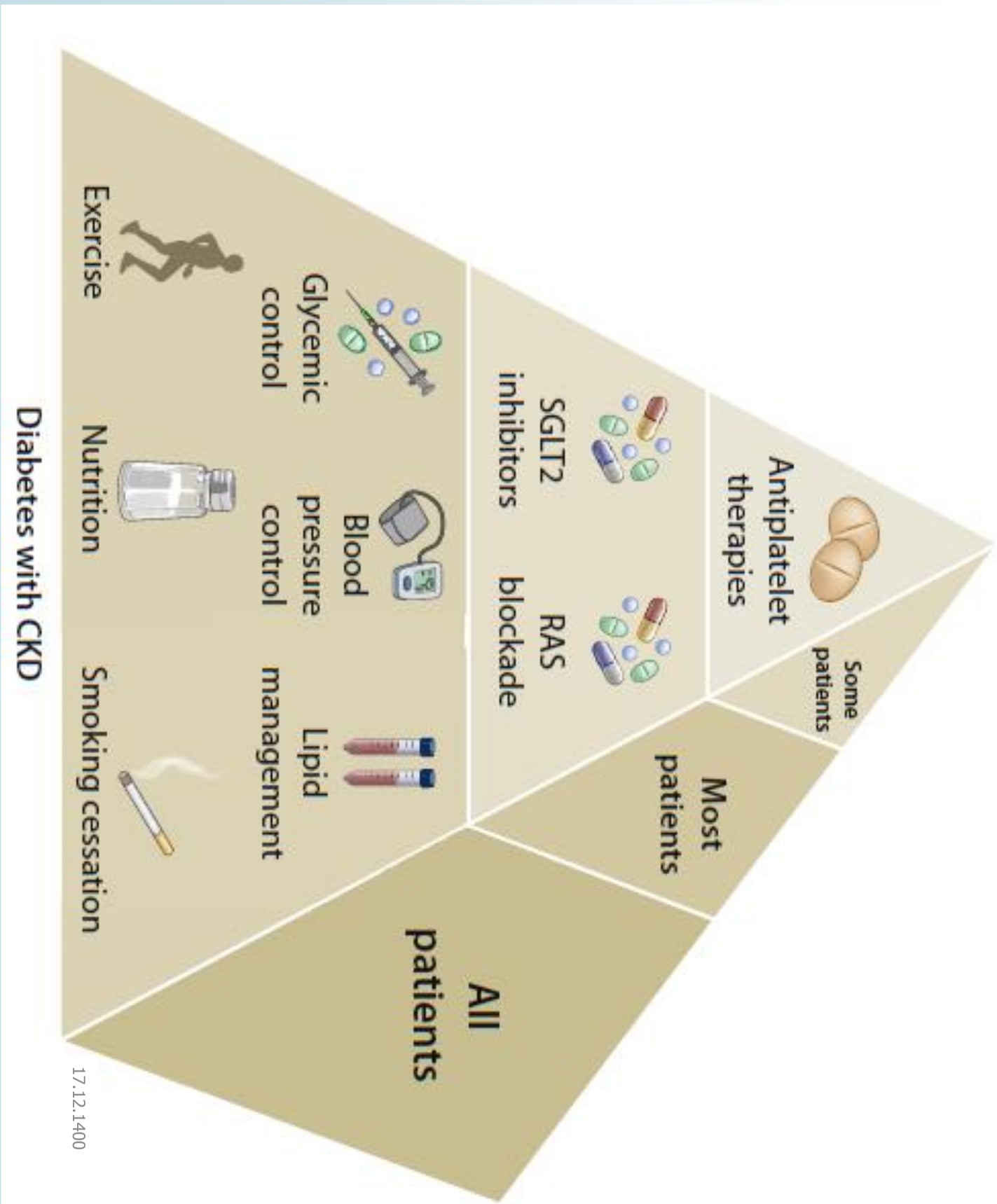
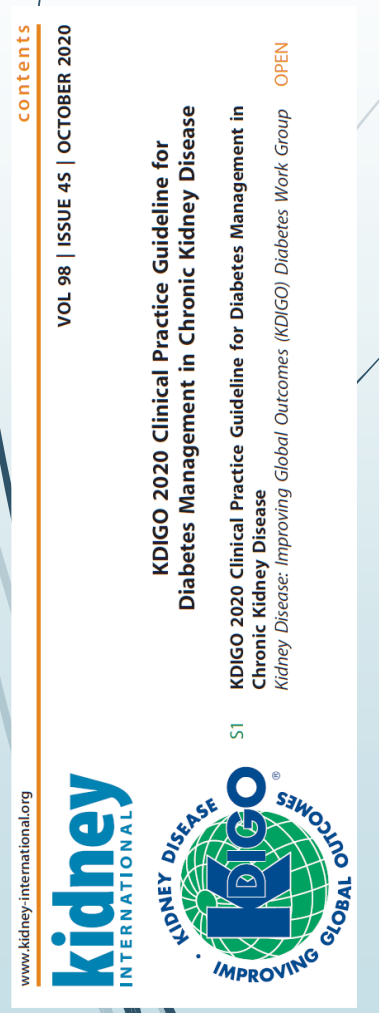
**Practice Point 1.1.1: Patients with diabetes and chronic kidney disease (CKD) should be treated with a comprehensive strategy to reduce risks of kidney disease progression and cardiovascular disease (Figure 2).**

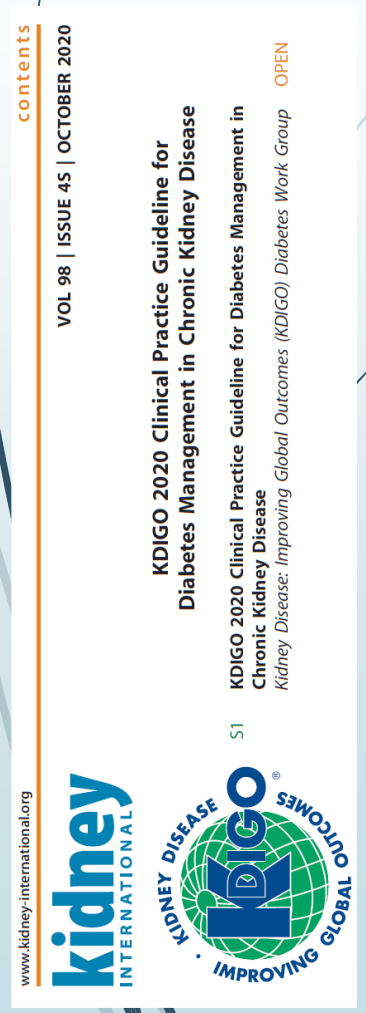


# 1.2 Renin-angiotensin system (RAS) blockade




***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).***

*This recommendation places a high value on the potential benefits of RAS blockade with ACEi or ARBs for slowing the progression of CKD in patients with diabetes, while it places a relatively lower value on the side effects of these drugs and the need to monitor kidney function and serum potassium.*




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 (Figure 4).

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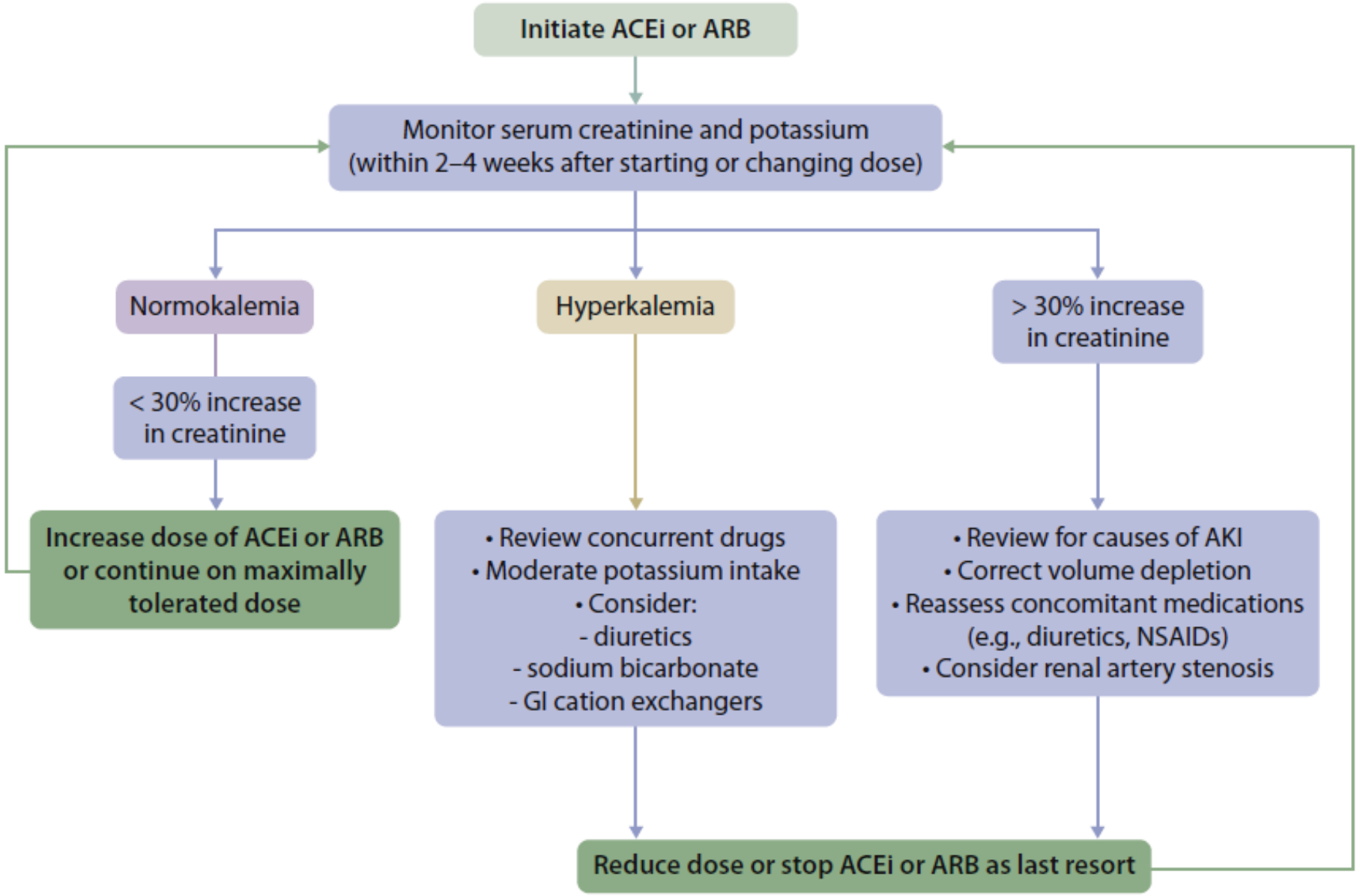


**Figure 4| Monitoring of serum creatinine and potassium during ACEi or ARB treatment—dose adjustment and monitoring of side effects.** ACEi, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; ARB, angiotensin II receptor blocker; GI, gastrointestinal; NSAID

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Practice Point 1.2.8: Mineralocorticoid receptor antagonists are effective for the management of refractory hypertension but may cause hyperkalemia or a reversible decline in glomerular filtration, particularly among patients with a low eGFR.

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

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# 2.1 Glycemic monitoring

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

| Population | HbA1c | | | GMI |
|---|---|---|---|---|
| | Measure | Frequency | Reliability | |
| CKD G1–G3b | Yes | • Twice per year<br>• Up to 4 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<br>• Up to 4 times per year if not achieving target or change in therapy | Low | Likely useful |

**Figure 6 | Frequency of HbA1c measurement and use of GMI in CKD.** CKD, chronic kidney disease; G1–G3b, estimated glomerular filtration rate ≥30 ml/min per 1.73 $m^2$; G4–G5, eGFR <30 ml/min per 1.73 $m^2$; GMI, glucose management indicator; HbA1c, glycated hemoglobin.

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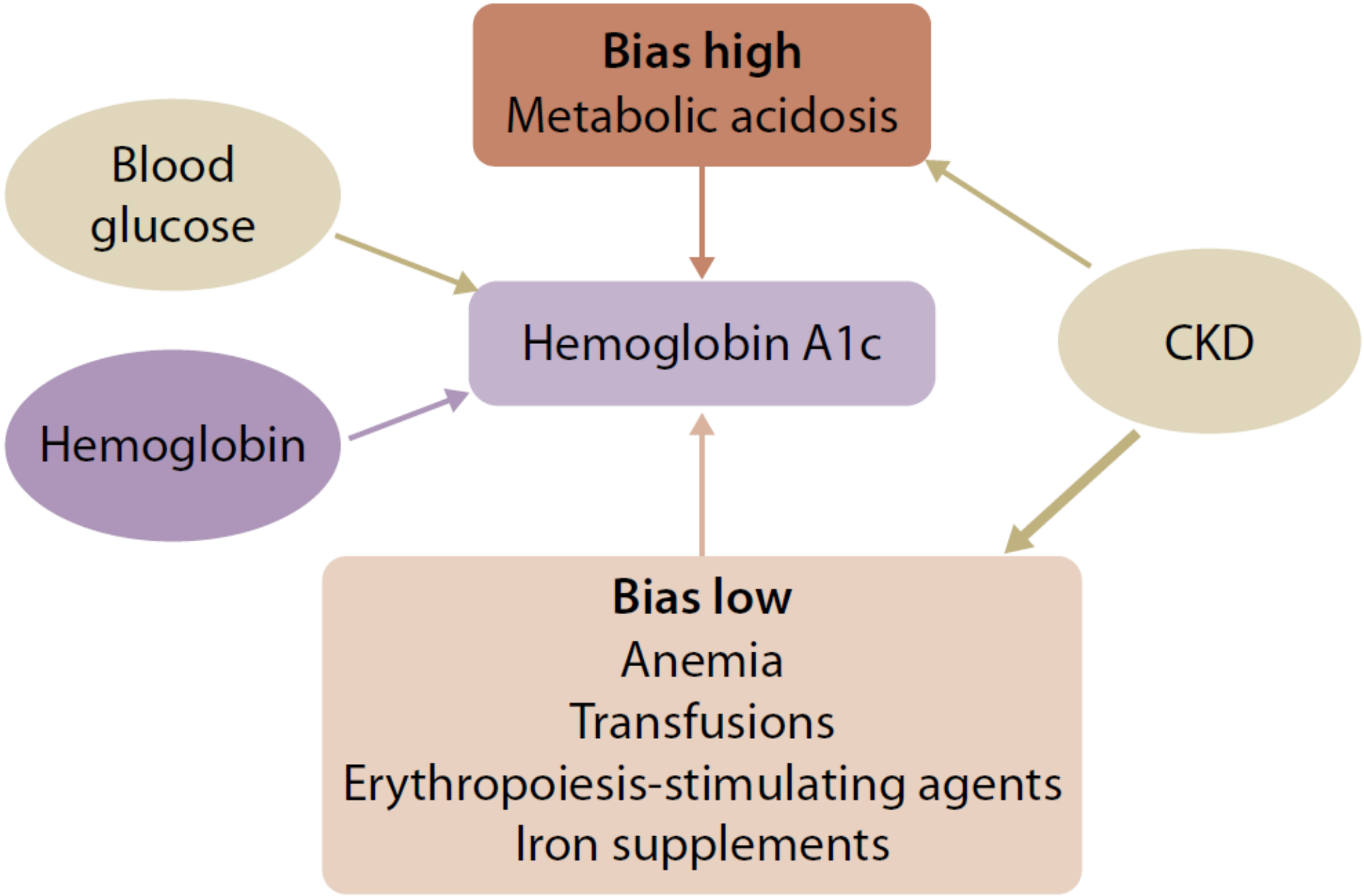


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**Figure 5 | Effects of CKD-related factors on HbA1c.** CKD, chronic kidney disease; HbA1c, glycated hemoglobin.

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**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 HbA1c is not concordant with directly measured blood glucose levels or clinical symptoms.**

CGM and self-monitoring of blood glucose (SMBG) yield direct measurements of interstitial and blood glucose, respectively, that are not known to be biased by CKD or its treatments, including dialysis or kidney transplant (Figure 7[126]). Therefore, if it is a clinical concern that HbA1c may be yielding biased estimates of long-term glycemia

## Self-monitoring of blood glucose (SMBG)

Self-sampling of blood via fingerstick for capillary glucose measurement using glucometers

Since sampling is performed intermittently, episodes of hypoglycemia or hyperglycemia are often harder to detect

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## Continuous glucose monitoring (CGM)

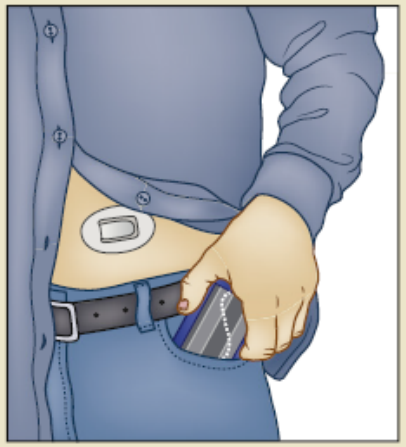
Minimally invasive subcutaneous sensors which sample interstitial glucose at regular intervals (e.g., every 5–15 min)

There are three categories of CGMs:

### (a) Retrospective CGM

Glucose levels are not visible while the device is worn. Instead, a report is generated for evaluation after the CGM is removed

### (b) Real-time CGM (rtCGM)



Refers to sensors transmitting and/or displaying the data automatically throughout the day, so that the patient can review glucose levels and adjust treatment as needed

### (c) Intermittently scanned CGM

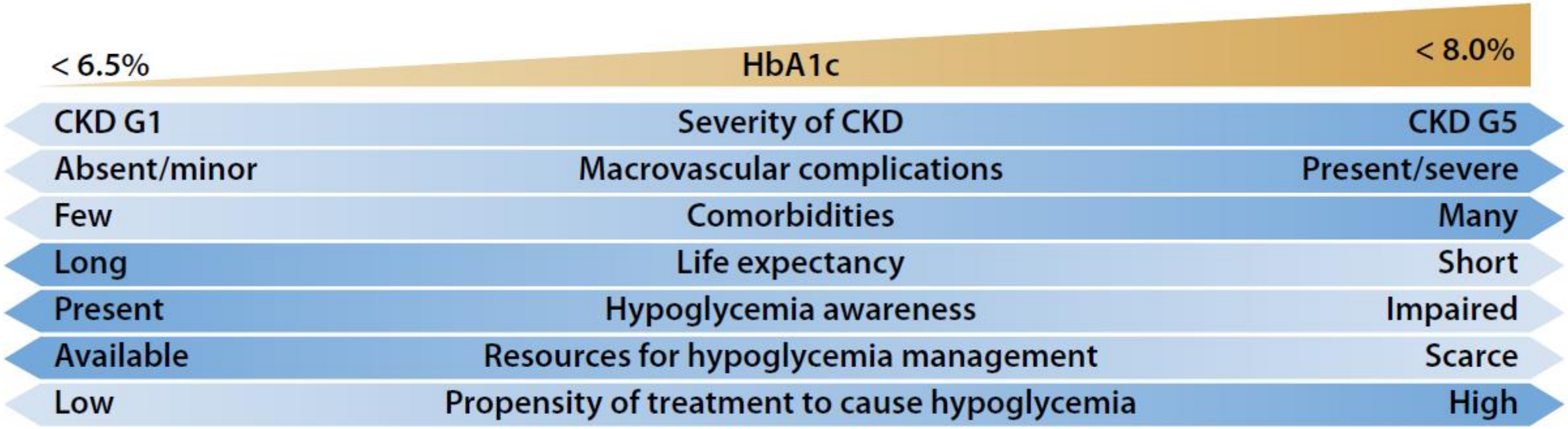

Also known as 'flash' CGM or FGM for short. Glucose levels can be seen while the device is worn when they are queried

## Glucose management indicator (GMI)

Provides a measure of average blood glucose levels calculated from CGM readings, expressed in units of A1C (%), that can be used to gauge whether clinical A1C levels are falsely high or low

# 2.2 Glycemic targets

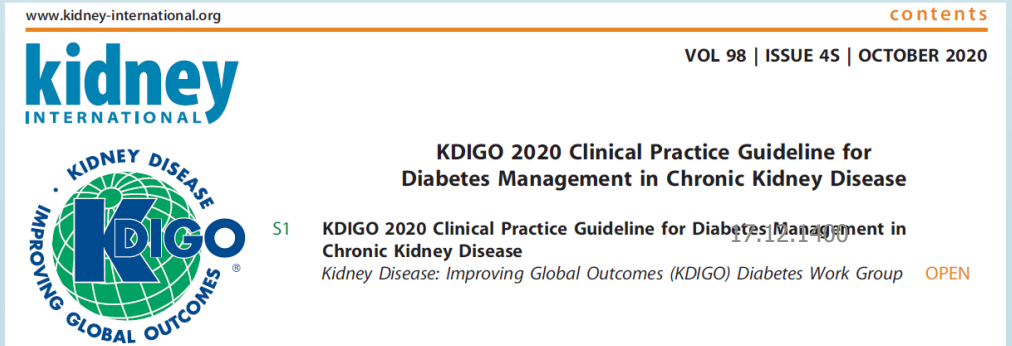
***Recommendation 2.2.1: We recommend an individualized HbA1c target ranging from <6.5% to <8.0% in patients with diabetes and CKD not treated with dialysis (Figure 9) (1C).***



# 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)/d for those with diabetes and CKD not treated with dialysis (2C).***



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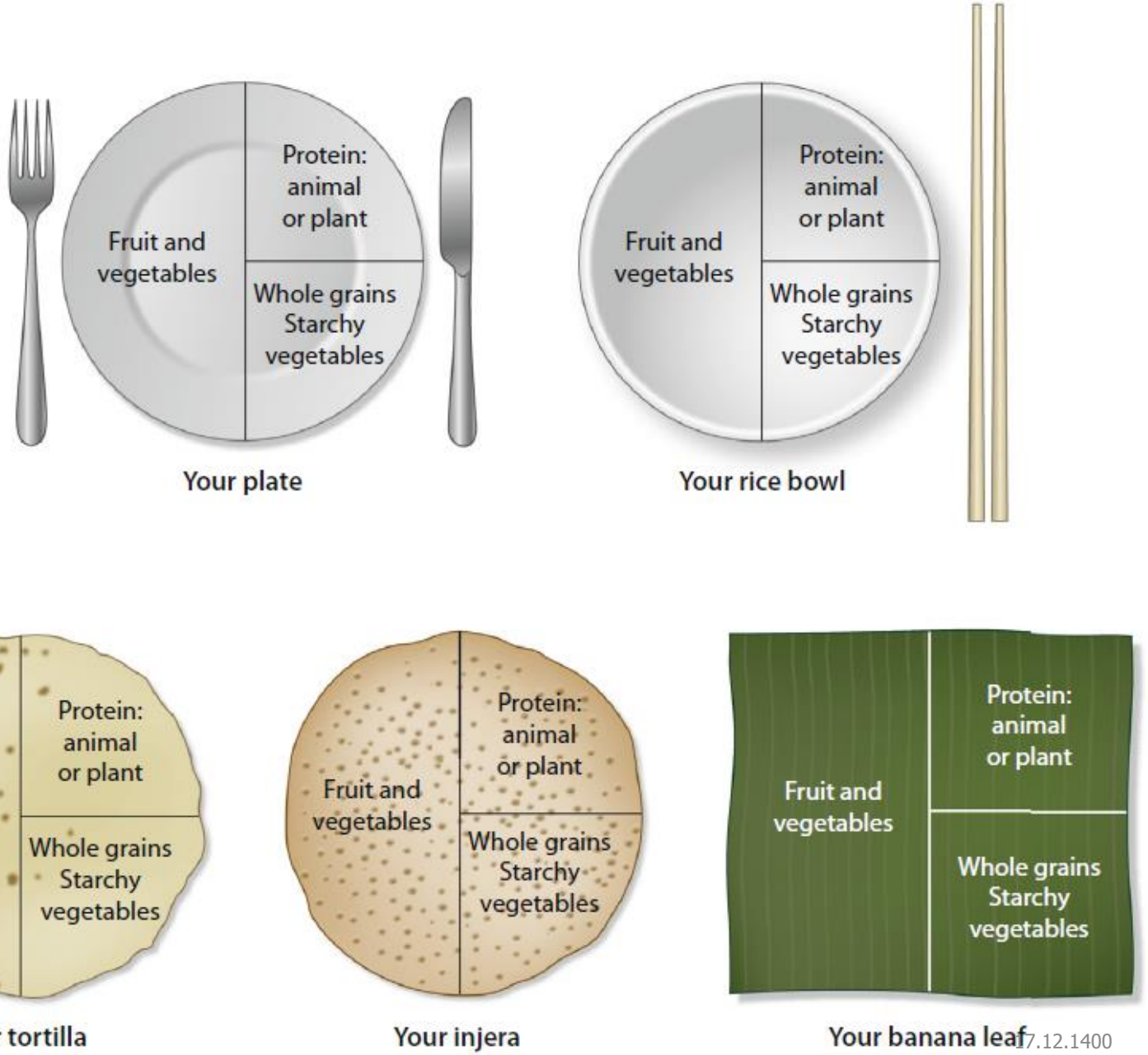


**Figure 10 | What does a healthy kidney diet look like?**

## Animal proteins

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

**Dairy, milk, yogurt, cheese:**
250 ml (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

**Figure 12 | Average protein content of foods in grams.**

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***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).***

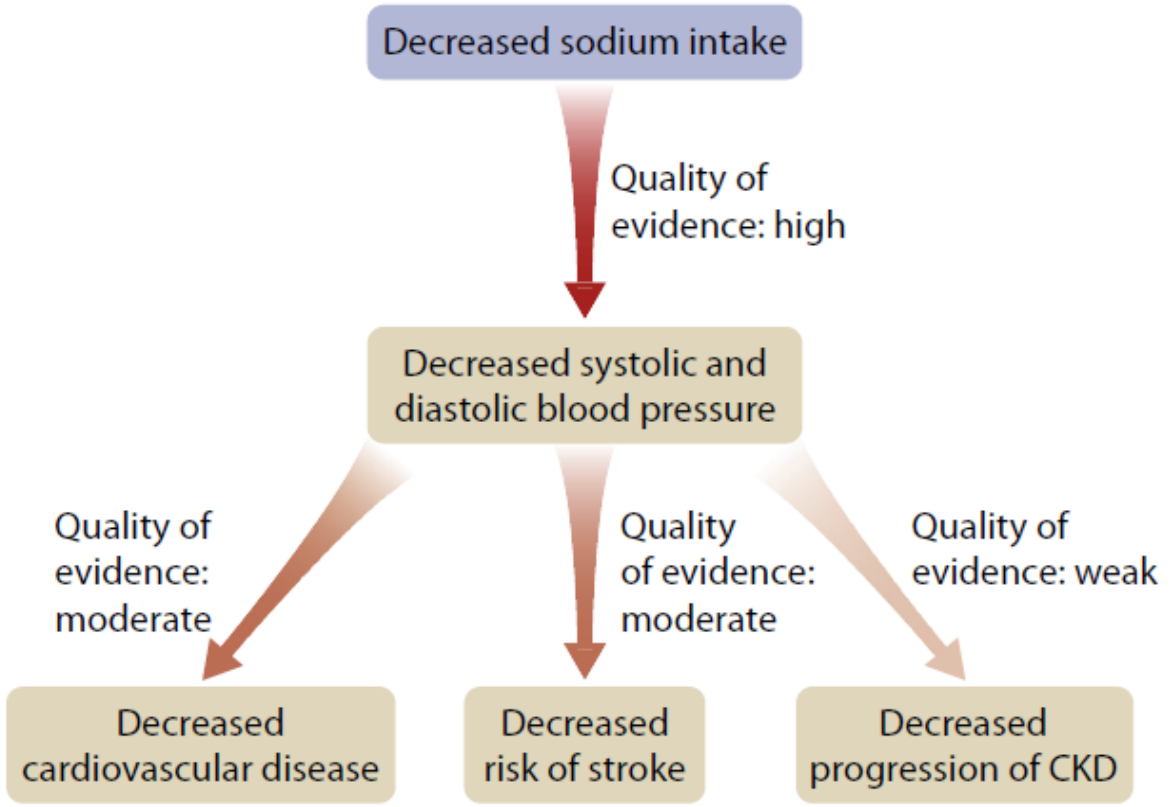


**Figure 13 | Effects of decreased sodium intake on various outcomes and accompanying quality of evidence.**[201] CKD, chronic kidney disease.


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**Figure 14 | Ten ways to cut out salt.**

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# 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).***

| Intensity of physical activity | METs | Examples |
|---|---|---|
| Sedentary | <1.5 | Sitting, watching television, reclining |
| Light | 1.6–2.9 | Slow walking, household work such as cooking, cleaning |
| Moderate | 3.0–5.9 | Brisk walking, biking, yoga, swimming |
| Vigorous | >6 | Running, biking, swimming, lifting heavy weights |

**Figure 15 | Examples of various levels of physical activity and their associated METs.** A metabolic equivalent (MET) is a unit useful for describing the energy expenditure of a specific activity. A MET is the ratio of the rate of energy expended during an activity to the rate of energy expended at rest. Reproduced with permission from Beddhu S, Wei G, Marcus RL, et al. Light-intensity physical activities and mortality in the United States general population and CKD subpopulation. *Clin J Am Soc Nephrol.* 2015;10:1145–1153.[208] Copyright © American Society of Nephrology.

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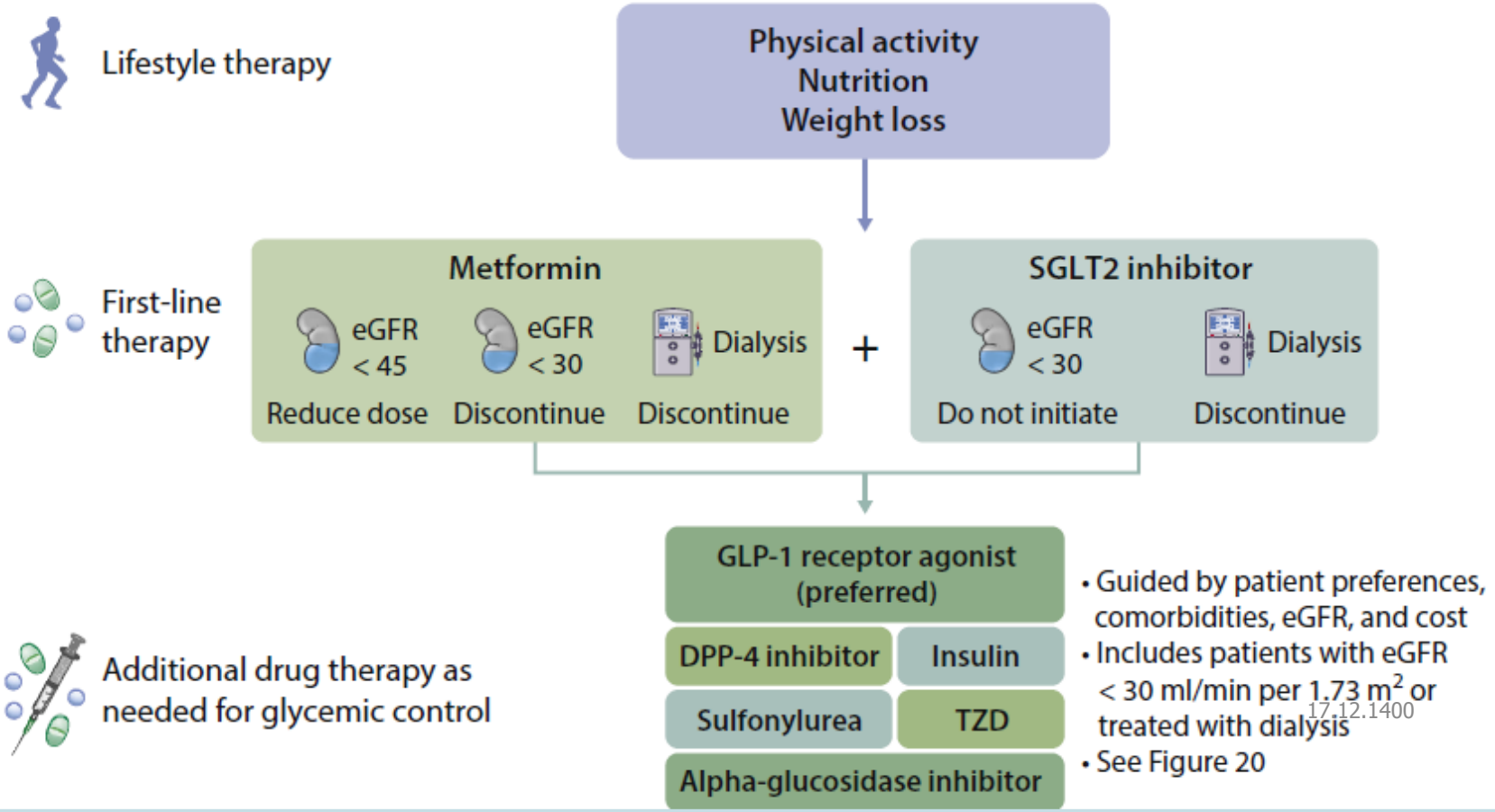
# Chapter 4: Antihyperglycemic therapies in patients with type 2 diabetes (T2D) and CKD

Practice Point 4.2: Most patients with T2D, CKD, and an eGFR ≥30 ml/min per 1.73 $m^2$ would benefit from treatment with both metformin and an SGLT2i.

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 (Figure 18).



| | | | 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 19 | Overview of select large, placebo-controlled clinical outcome trials assessing the benefits and harms of SGLT2 inhibitors, GLP-1 receptor agonists, and DPP-4 inhibitors.** ACR, albumin-creatinine ratio; CKD, chronic kidney disease; CrCl, creatinine clearance; CV, cardiovascular; DKA, diabetic ketoacidosis; DPP-4, dipeptidyl peptidase-4; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; GFR, glomerular filtration rate; GI, gastrointestinal symptoms (e.g., nausea and vomiting); GLP-1, glucagon-like peptide-1; 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; SGLT2, sodium–glucose cotransporter-2. ↔, 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.

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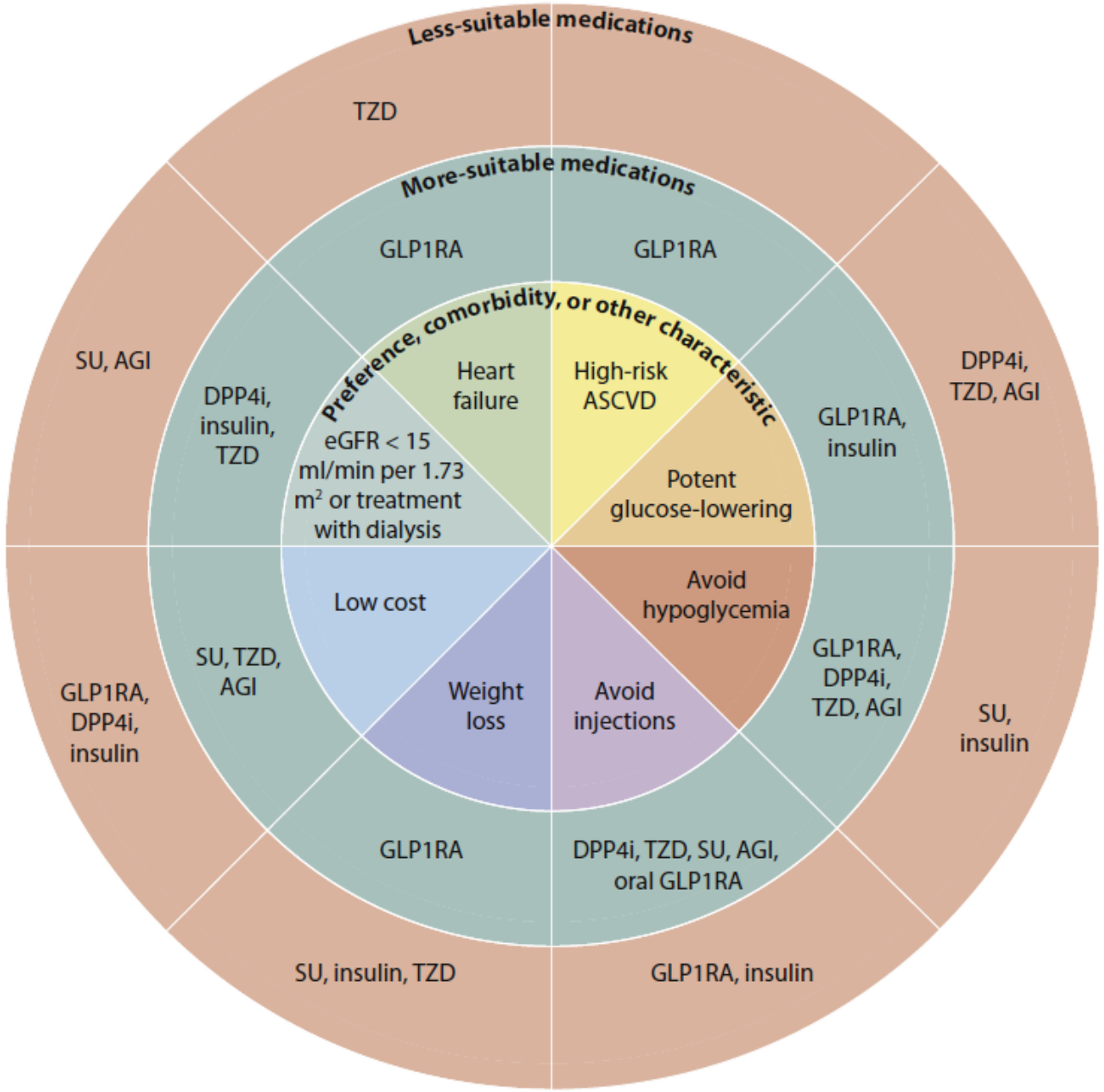


**Figure 20 | Patient factors influencing the selection of glucose-lowering drugs other than SGLT2i and metformin in T2D and CKD.** AGI, alpha-glucosidase inhibitor; ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; DPP4i, dipeptidyl peptidase-4 inhibitor; eGFR, estimated glomerular filtration rate; GLP1RA, glucagon-like peptide-1 receptor agonist; SGLT2i, sodium–glucose cotransporter-2 inhibitor; SU, sulfonylurea; T2D, type 2 diabetes; TZD, thiazolidinedione.

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## 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).***

*This recommendation places a high value on the efficacy of metformin in lowering HbA1c level, its widespread availability and low cost, its good safety profile, and its potential benefits in weight gain prevention and cardiovascular protection. The recommendation places a low value on the lack of evidence that metformin has any renoprotective effects or mortality benefits in the CKD population.*

| Formulation | Dosage forms | Starting dose | Maximum dose |
|---|---|---|---|
| Metformin, immediate release | Tablet, oral: 500 mg, 850 mg, 1000 mg | 500 mg once or twice daily<br>OR<br>850 mg once daily | Usual maintenance dose: 1 g twice daily<br>OR<br>850 mg twice daily<br>Maximum: 2.55 g/d |
| Metformin, extended release | Tablet, oral: 500 mg, 750 mg, 1000 mg | 500 mg once daily<br>OR<br>1 g once daily | 2 g/d |

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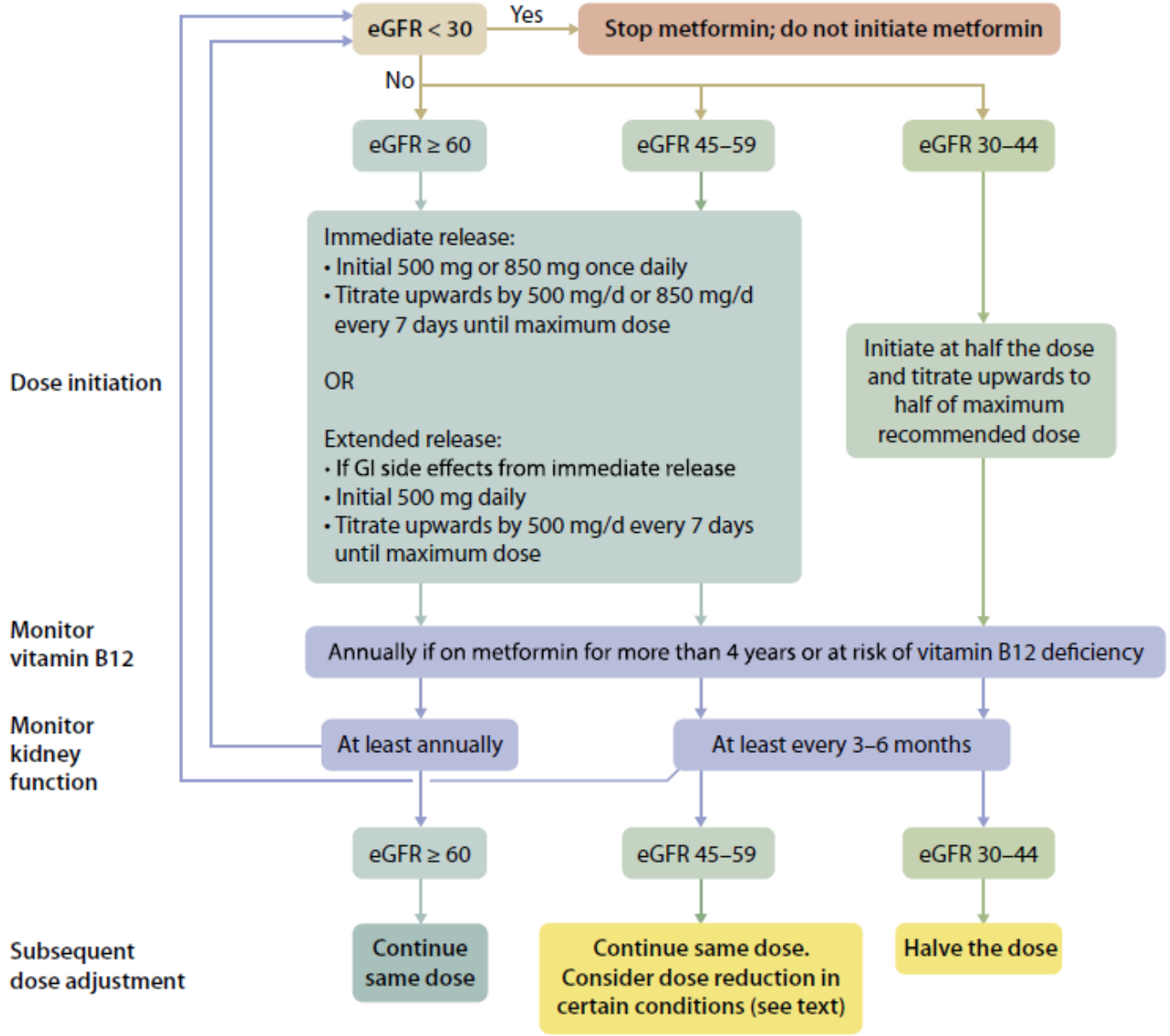


**Figure 22 | Suggested approach in dosing metformin based on the level of kidney function.** eGFR, estimated glomerular filtration rate (in ml/min per 1.73 $m^2$); GI, gastrointestinal.

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***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).***

| | EMPA-REG[244] | CANVAS[241] | DECLARE-TIMI 58[243] | CREDENCE[242] |
|---|---|---|---|---|
| **Drug** | Empagliflozin 10 mg, 25 mg once daily | Canagliflozin 100 mg, 300 mg once daily | Dapagliflozin 10 mg once daily | Canagliflozin 100 mg once daily |
| **Total of participants** | 7020 | 10,142 | 17,160 | 4401 |
| **N (%) with CVD** | 7020 (100%) | 6656 (66%) | 6974 (41%) | 2220 (50%) |
| **eGFR criteria for enrollment** | ≥30 ml/min per 1.73 $m^2$ | ≥30 ml/min per 1.73 $m^2$ | CrCl ≥60 ml/min, 45% had eGFR 60–90 | 30–90 ml/min per 1.73 $m^2$, ACR 300–5000 mg/g |
| **Mean eGFR at enrollment (ml/min per 1.73 $m^2$)** | 74 | 76 | 85 | 56 |
| **N (%) with eGFR <60** | 1819 (26%) | 2039 (20%) | 1265 (7.4%) | 2592 (59%) |
| **ACR** | No criteria. ACR <30 mg/g (3 mg/mmol) in 60%; 30–300 mg/g (3–30 mg/mmol) in 30%; >300 mg/g (30 mg/mmol) in 10% | No criteria. Median ACR 12.3 mg/g (1.23 mg/mmol) | No criteria | Criteria: ACR >300–5000 mg/g (30–500 mg/mmol); median ACR 927 mg/g (92.7 mg/mmol) |
| **Follow-up (median, yr)** | 3.1 | 2.4 | 4.2 | 2.6 |
| **Primary outcome(s)** | MACE | MACE | (1) MACE; (2) Composite CV death or hospitalization for HF | Composite kidney |
| **CV outcome results** | MACE: HR: 0.86; 95% CI: 0.74–0.99; hospitalization for HF: HR: 0.65; 95% CI: 0.50–0.85 | MACE: HR: 0.86; 95% CI: 0.75–0.97; hospitalization for HF: HR: 0.67; 95% CI: 0.52–0.87 | MACE: HF: 0.93; 95% CI: 0.84–1.03; CV death or hospitalization for HF: HR: 0.83; 95% CI: 0.73–0.95 | CV death, MI, stroke: HR: 0.80; 95% CI: 0.67–0.95; hospitalization for HF: HR: 0.61; 95% CI: 0.47–0.80 |
| **Kidney outcome** | Incident or worsening nephropathy (progression to severely increased albuminuria, doubling of SCr, initiation of KRT, or renal death) and incident albuminuria | Composite doubling in SCr, ESKD, or death from renal causes | Composite of ≥40% decrease in eGFR to <60 ml/min per 1.73 $m^2$, ESKD, CV, or renal death | Composite of ESKD outcomes, doubling SCr, or death from renal or CV causes |
| **Kidney outcome results** | Incident/worsening nephropathy: 12.7% vs. 18.8% in canagliflozin vs. placebo [HR: 0.61; 95% CI: 0.53–0.70]. Incident albuminuria: NS | Composite kidney: 1.5 vs. 2.8 1000 patient-years in the canagliflozin vs. placebo [HR: 0.53; 95% CI: 0.33–0.84[271]] | Composite kidney: HR: 0.76; 95% CI: 0.67–0.87 | Primary kidney: HR: 0.70; 95% CI: 0.59–0.82 |

**Figure 23| Cardiovascular and kidney outcome trials for SGLT2 inhibitors.** ACR, albumin-creatinine ratio; CI, confidence interval; CrCl, creatinine clearance; CV, cardiovascular; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; GFR, glomerular filtration rate; HF, heart failure; HR, hazard ratio; KRT, kidney replacement therapy; MACE, major adverse cardiovascular events; MI, myocardial infarction; NS, not significant; SCr, serum creatinine; SGLT2, sodium–glucose cotransporter-2; T2D, type 2 diabetes.

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Practice Point 4.2.1: An SGLT2i can be added to other antihyperglycemic medications for patients whose glycemic targets are not currently met or who are meeting glycemic targets but can safely attain a lower target (Figure 24).

Practice Point 4.2.2: 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 addition of an SGLT2i.

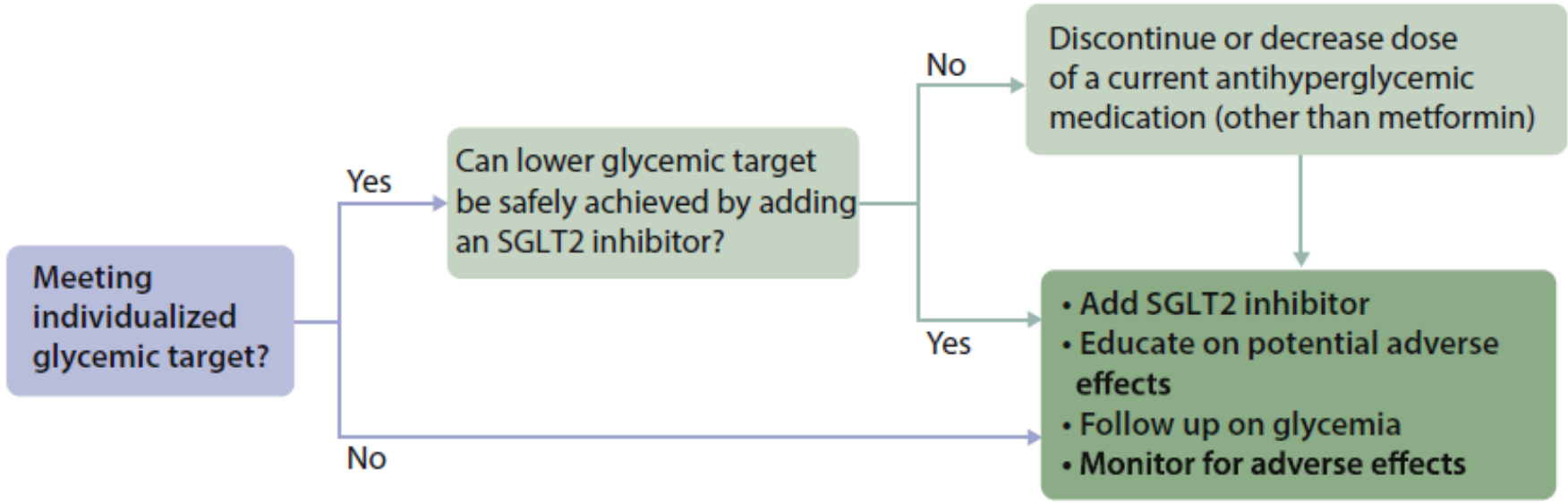


**Figure 24| Algorithm for initiation of SGLT2 inhibitor therapy for patients with T2D, CKD, and eGFR ≥30 ml/min per 1.73 $m^2$, who are already being treated with antihyperglycemic medications.** CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; SGLT2, sodium–glucose cotransporter-2; T2D, type 2 diabetes.

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

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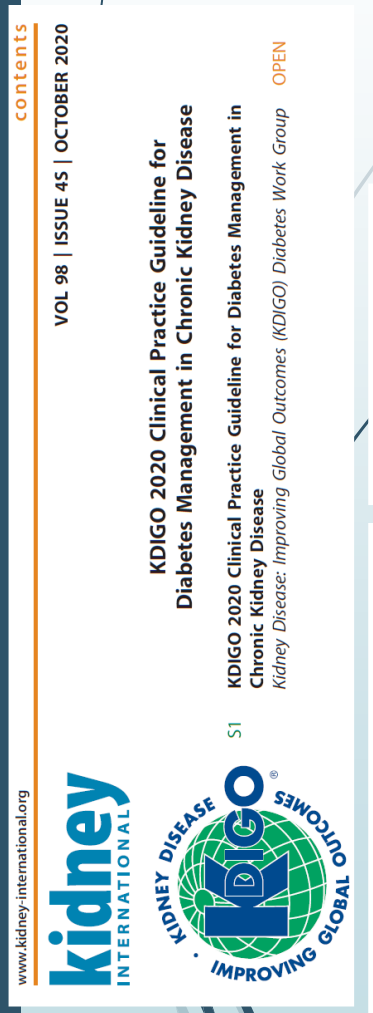
**Practice Point 4.2.4: It is reasonable to withhold SGLT2i during times of prolonged fasting, surgery, or critical medical illness (when patients may be at greater risk for ketosis).**

For patients with T2D, there is a small but increased risk of euglycemic diabetic ketoacidosis with SGLT2i (see the Harms

**Practice Point 4.2.5: 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 4.2.6: A reversible decrease in the eGFR with commencement of SGLT2i treatment 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 the eGFR falls below 30 ml/min per 1.73 $m^2$, unless it is not tolerated or kidney replacement therapy is initiated.**

**Practice Point 4.2.8: SGLT2i have not been adequately studied in kidney transplant recipients, who may benefit from SGLT2i treatment, but are immunosuppressed and potentially at increased risk for infections; therefore, the recommendation to use SGLT2i does not apply to kidney transplant recipients (see Recommendation 4.2.1).**

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***Recommendation 4.3.1: 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).***

| GLP-1 RA | Dose | CKD adjustment |
|---|---|---|
| Dulaglutide | 0.75 mg and 1.5 mg once weekly | No dosage adjustment<br>Use with eGFR >15 ml/min per 1.73 $m^2$ |
| 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 | 0.6 mg, 1.2 mg, and 1.8 mg once daily | No dosage adjustment<br>Limited data for severe CKD |
| Lixisenatide | 10 µg and 20 µg once daily | No dosage adjustment<br>Limited data for severe CKD |
| Semaglutide (injection) | 0.5 mg and 1 mg once weekly | No dosage adjustment<br>Limited data for severe CKD |
| Semaglutide (oral) | 3 mg, 7 mg, or 14 mg daily | No dosage adjustment<br>Limited data for severe CKD |

**Figure 27 | Dosing for available GLP-1 RA and dose modification for CKD.** CKD, chronic kidney disease; CrCl, creatinine clearance; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide-1 receptor agonist.

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

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***Recommendation 5.1.1: We recommend that a structured self-management educational program be implemented for care of people with diabetes and CKD (Figure 28) (1C).***

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 and mental well-being, treatment satisfaction, and quality of life

**Figure 28 | 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.[332]

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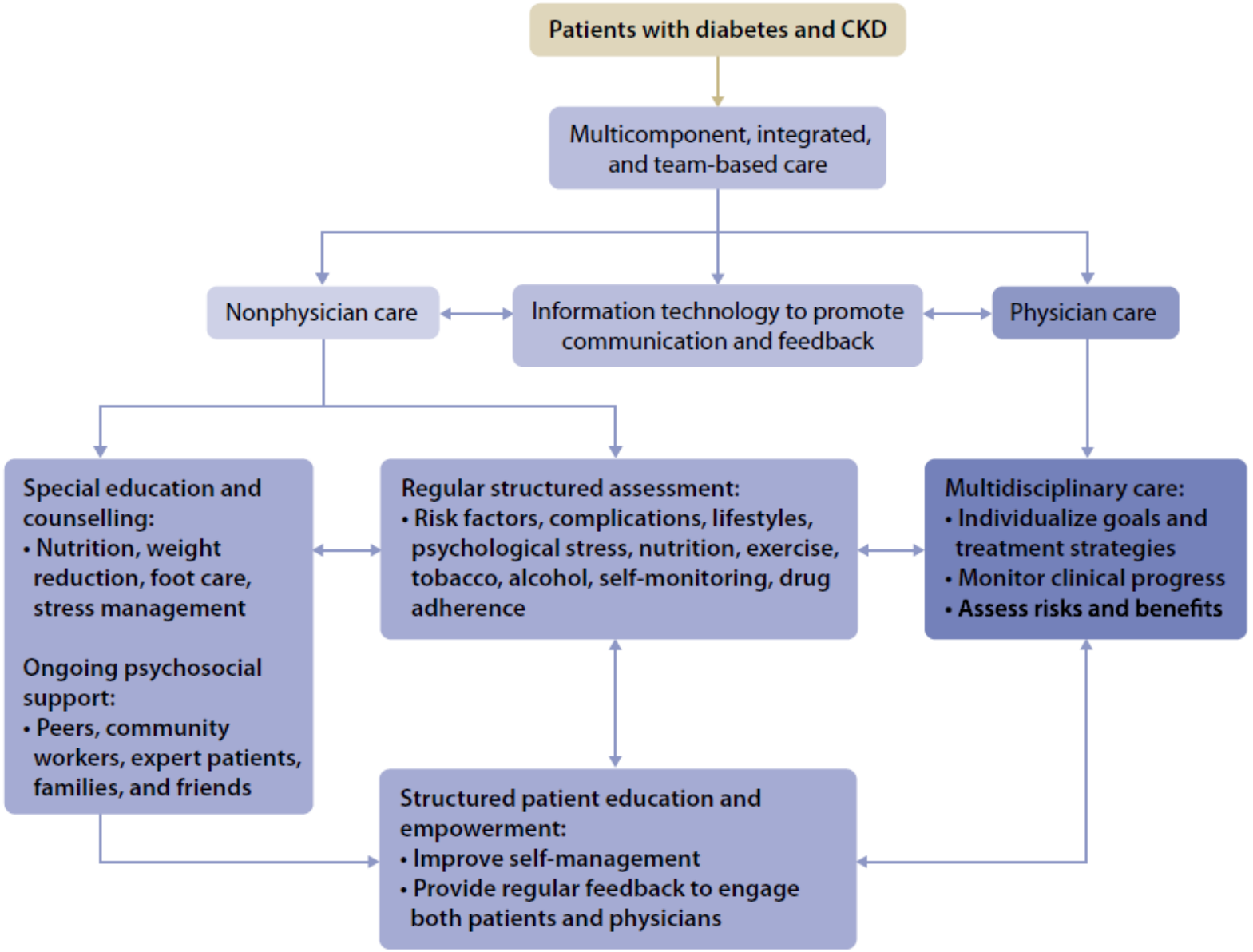


**Figure 31 | Integrated care approach to improve outcomes, self-management, and patient–provider communication in patients with diabetes and CKD.**[301,349–351] A schematic diagram showing the use of physician and nonphysician personnel to provide regular assessments, assisted by information technology, to facilitate individualized management and patient self-management with ongoing support in order to detect, monitor, and treat risk factors and complications early to reduce hospitalizations, multiple morbidities, and premature death. CKD, chronic kidney disease.

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# 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).***

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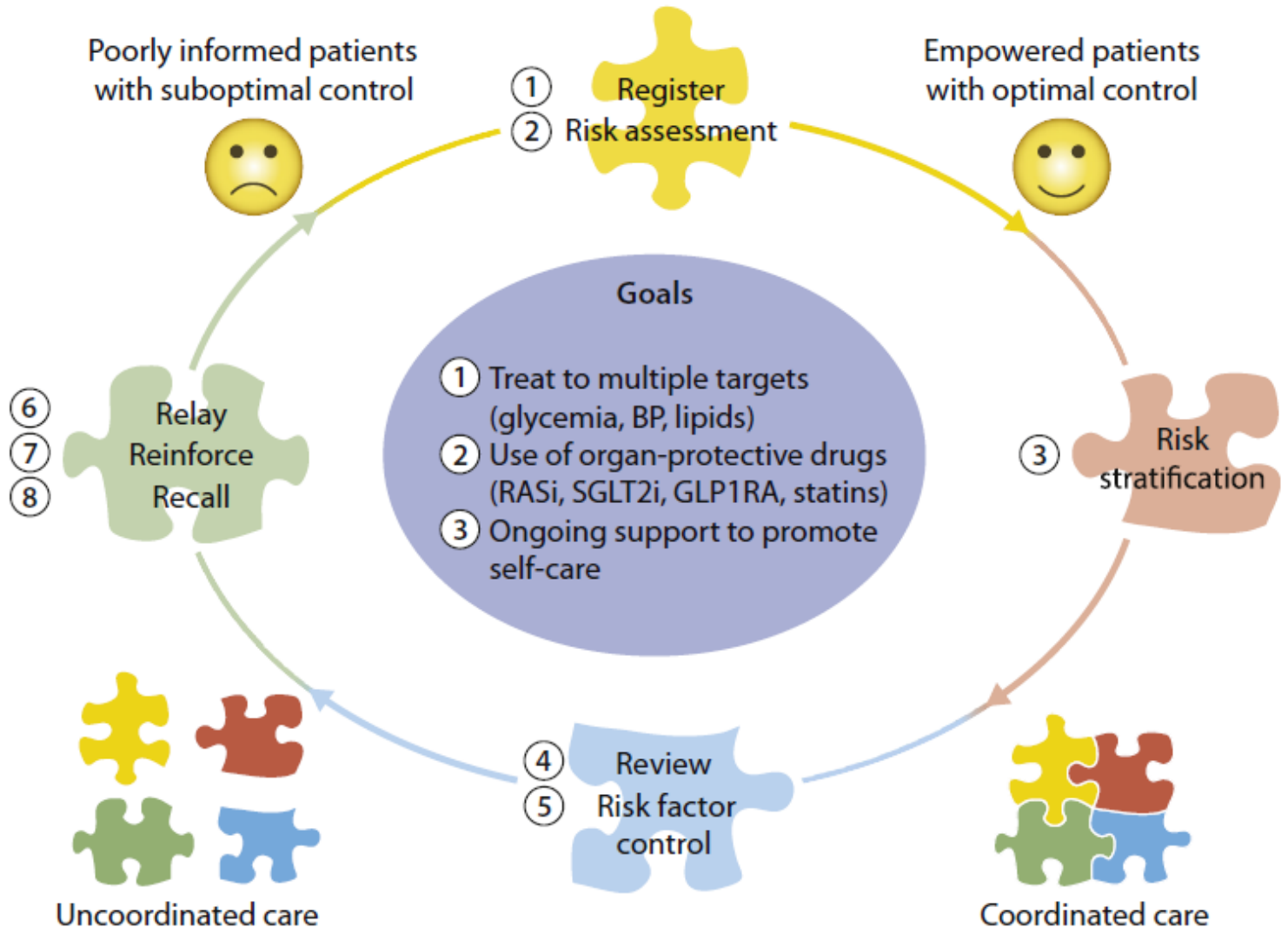


**Figure 33 | Team-based integrated care delivered by physicians and nonphysician personnel supported by decision-makers.** BP, blood pressure; GLP1RA, glucagon-like peptide-1 receptor agonist; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium–glucose cotransporter-2 inhibitor.