Best-Practice Perspectives on Improving Early Detection and Management of Chronic Kidney Disease Associated With Type 2 Diabetes in Primary Care

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Chronic kidney disease (CKD) is a progressive disease that can lead to kidney failure and increases the risk of cardiovascular disease (CVD), cardiovascular mortality, and all-cause mortality (1,2). Diabetes is a major risk factor for developing CKD (3) and CVD independent of CKD (4). Approximately 37 million people in the United States have CKD, and most (90%) are unaware they have the condition, so their CKD remains undiagnosed in primary care (3). Although treatment guidelines recommend screening at least annually for CKD in people with type 2 diabetes (5–7), uptake of screening for CKD in adults with diabetes remains low in routine clinical care (8). In the United States, prescription rates of guideline-recommended medications that have been shown to prevent CKD progression in people with CKD associated with type 2 diabetes also remain low (9,10).

Most patients with risk factors for CKD are managed in primary care (11); therefore, primary care providers (PCPs) play an important role in the early detection of CKD. Targeted screening and early initiation of guideline-recommended treatments by PCPs is important to slow CKD progression and the development of comorbidities such as CVD. This fact underscores the need to support and facilitate awareness among PCPs to improve current screening, diagnosis, and treatment of CKD in primary care, especially if clinical evidence suggests that patients may benefit from an alternative approach.

In this review, we give our perspectives and views on three important issues: *1*) how adoption of screening across primary care could be improved, *2*) why medications for CKD associated with type 2 diabetes are under-prescribed in primary care and how this could be improved, and *3*) the possibility that a lack of awareness by nonspecialist PCPs of the clinical trial data supporting guideline recommendations for the treatment of CKD and type 2 diabetes is a barrier in primary care. To address the third issue, we have developed plain-language visual representations summarizing how these clinical data relate to the guideline recommendations, which are available in the Supplementary Material, along with a plain-language summary of this article.

Current Approach to Screening for CKD in Patients With Type 2 Diabetes

Early identification of CKD (i.e., when CKD is at stage 1–3a) (7), followed by risk stratification and treatment, reduces the risk of CKD progression and adverse outcomes (12).

Early screening for CKD in patients with type 2 diabetes is crucial because, often, CKD has no symptoms in its earlier stages (1); therefore, detection relies on routine assessment of kidney function. Clinical practice guidelines recommend screening for CKD in all people with type 2 diabetes using a dual assessment of urinary albumin (using a spot urinary albumin-to-creatinine ratio [UACR]) and estimated glomerular filtration rate (eGFR) at diabetes diagnosis and at least annually thereafter, regardless of treatment (6,7). Based on the 2022 Kidney Disease: Improving Global Outcomes (KDIGO) guidelines, CKD is diagnosed when there is evidence of persistently elevated urine albumin excretion (UACR $\geq$30 mg/g) and/or persistently reduced eGFR ($<$60 mL/min/1.73 m^2) for more than 3 months (7). UACR is a measure of the amount of albumin present in urine relative to the amount of creatinine in urine and is a marker of kidney damage. eGFR is a measure of the rate at which blood is filtered through the kidneys and is a marker of kidney function.

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When used together, these measurements can improve CKD diagnosis accuracy and risk estimation (13).

Despite the benefits of early diagnosis, screening in patients with risk factors for CKD is occurring at suboptimal levels (14), which delays early diagnosis and intervention. Research shows that uptake of CKD screening remains inconsistent, and adherence to CKD screening guidelines is selective in the United States (14–16). For example, a 2021 retrospective claims database study found that only 37.2% of patients with newly diagnosed type 2 diabetes were tested for CKD within the first year of diabetes diagnosis (14). Although rates of eGFR testing were high (>80%), rates of UACR-based testing were much lower, at <50% (14). Another study analyzed electronic health record (EHR) data from 24 health care organizations in the United States and found that, although eGFR testing was uniformly high (89.5%) in patients with type 2 diabetes, rates of UACR testing were suboptimal (52.9%) and variable across organizations (15).

A consequence of low screening uptake is delayed diagnosis until CKD reaches an advanced stage (stage 3b or higher), when the disease is more difficult to treat and manage. We believe that eGFR or UACR testing in isolation is not sensitive or specific enough to reliably detect and stage CKD. Therefore, both eGFR and UACR testing should be performed simultaneously in people with type 2 diabetes to improve early detection of CKD, and these measurements should be plotted using the KDIGO heat map to determine CKD stage and progression risk (Figure 1) (7).

The reasons for low adoption of screening in primary care are unclear, but multiple factors may be involved. These include fear of frightening patients by delivering a CKD diagnosis, lower priority of CKD as a clinical issue (e.g., if the patient has other comorbidities considered of higher priority), high work load, limited time (including limited time available for patient appointments), therapeutic inertia (i.e., failure to initiate or

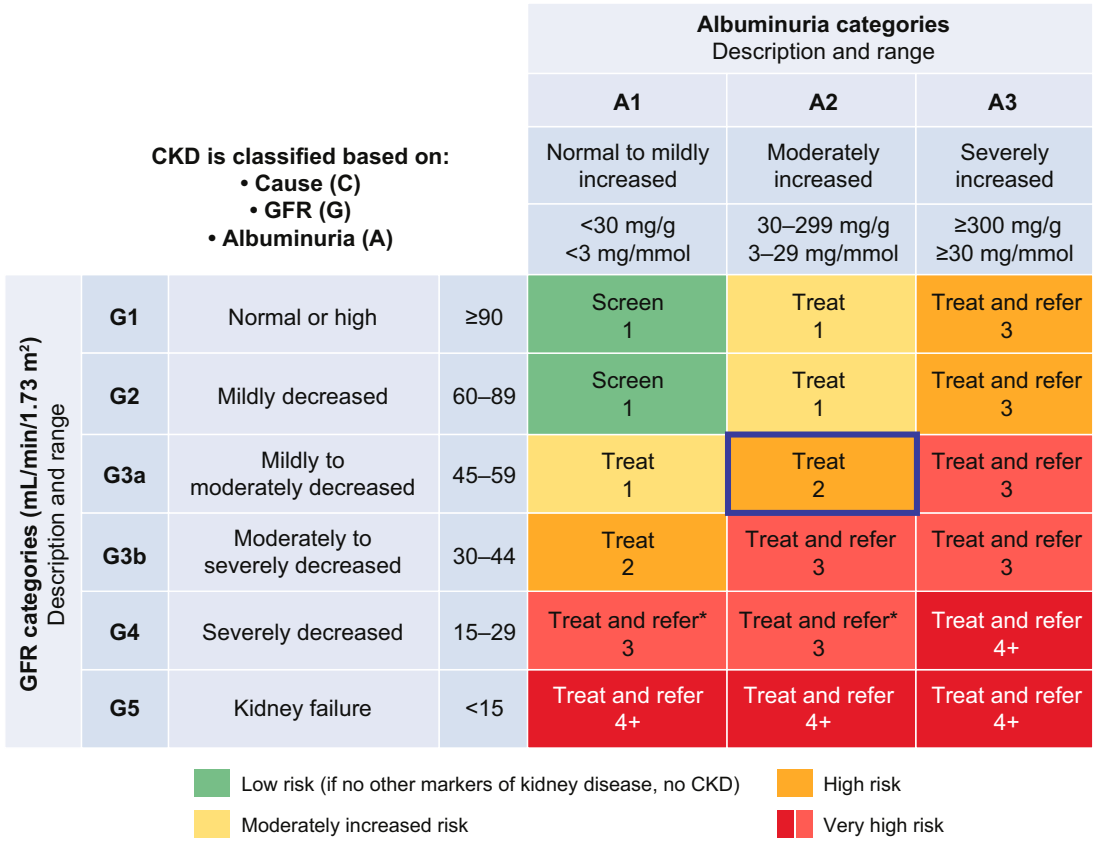

FIGURE 1 ADA-KDIGO 2022 consensus report heat map and plotted UACR and eGFR results to determine CKD stage and progression risk for a sample patient. The heat map represents risk for CKD progression using glomerular filtration rate (GFR) and UACR measurement categories. Numbers in each box indicate the recommended monitoring frequency per year. The box outlined in blue represents a results plot for a sample patient with a UACR of 200 mg/g and an eGFR of 50 mL/min/1.73 m^2. Based on the heat map, the patient has stage 3a CKD (if confirmed with repeat testing) and is at high risk of CKD progression, additional morbidity, and mortality. This patient should receive appropriate treatment for prevention of CKD progression and should be monitored twice per year. Adapted from ref. 5.

intensify therapy in a timely manner based on evidence-based clinical guidelines) (17,18), the perception by some clinicians that kidney decline is expected with age, and the belief by some that nothing can be done about kidney disease if a patient is at high risk (11). Furthermore, low adoption of screening may be attributed to health system–related barriers such as a lack of incentives or reimbursement for interventions such as CKD screening and prevention (11,19). We also believe that factors such as rigid practice protocols and procedures may prevent uptake of CKD screening (e.g., if protocols are too inflexible to consider individualized screening based on a patient's risk factors and medical history or if they limit the use or ordering of certain tests to screen for CKD).

Authors' Perspectives: Improving CKD Screening Uptake and Efficiency of CKD Diagnosis and Staging in Primary Care

Include CKD Screening as Part of Routine Clinic Visits

As noted previously, improving uptake of CKD screening is crucial for early detection and better management of CKD in people with type 2 diabetes. Indeed, simplifying the CKD screening process and making it less time-consuming for patients and PCPs may improve uptake.

With this in mind, we think ordering a panel of tests, rather than individual tests, could improve screening uptake and efficiency in primary care. The basic metabolic panel (BMP) and comprehensive metabolic panel (CMP) are tests that measure substances in the blood. A CMP includes tests for albumin, creatinine, blood urea nitrogen, glucose, potassium, and sodium, among other substances (20). People with type 2 diabetes may visit their doctor's office for routine diabetes care that includes an A1C test every 3–4 months (21). Having a diabetes/renal panel that offers the option of also ordering a BMP/CMP and UACR test along with the A1C should reduce the amount of administrative work and time needed to perform these tests and, consequently, may improve CKD screening uptake in clinical practices.

For patients who already have a CKD diagnosis, the CMP is often used during clinic visits to assess kidney function via creatinine and eGFR, as well as urinalysis (22,23). However, a UACR should be performed as well as a BMP/CMP test because above-normal levels of urine albumin indicate kidney damage and are a marker of cardiovascular disease risk. Indeed, the American Diabetes Association's (ADA's) *Standards of Care in Diabetes—2024* recommends that patients with established CKD have their UACR and eGFR monitored one to four times per year depending on their CKD stage (6). We suggest that UACR should be used with the BMP/CMP blood test, based on patients' needs.

To support CKD diagnosis, staging, and treatment planning, we recommend including the KDIGO heat map (Figure 1) with every set of eGFR and UACR laboratory test results, if results are positive. To support PCPs further, plotting patients' eGFR and UACR results onto the KDIGO heat map (as a supplement to the standard test result outputs) may help to streamline the diagnosis process and assist with determining CKD progression risk. This approach is similar to that used in cardiovascular risk scoring in clinical practice (e.g., the Framingham risk score and Framingham tables) (24). Furthermore, the KDIGO heat map can also be used as a patient education tool.

Other potential methods to improve screening uptake in primary care, specifically to address the current low levels of UACR testing, include implementing standing orders for nonphysician PCPs (e.g., nurses, medical assistants, and pharmacists) (25,26) to collect in-office urine specimens with the goal of simplifying the testing process. This task could also happen during routine office visits. EHR-based reminders (visible to clinic staff) for urine albumin screening in patients who are at high risk of developing CKD may also help in this effort (27). A study including 21 primary care practices across 13 U.S. states found that the practices implementing strategies to improve CKD identification (including standing order and EHR reminders) resulted in a >20% increase in urine albumin testing for annual screening in patients with diabetes and annual monitoring in patients with CKD, compared with practices that did not implement CKD identification strategies (27).

Theoretical Models for Improving Screening and Diagnosis of CKD in Patients With Type 2 Diabetes

As they become available, new tests or methods that aim to improve the accuracy of predicting CKD progression risk may be useful in identifying risk in early-stage CKD (e.g., implementation of a triple-marker screen for CKD that consists of cystatin C, creatinine, and albuminuria vs. the current double marker, which is creatinine and albumin). Cystatin C is a biomarker for renal function and may be a useful addition to creatinine to more accurately assess eGFR (6). This approach, which is part of the C^3 (Cascade of Care) initiative, aims to enhance early CKD detection and risk stratification (28),

although it is not currently widely used in primary care settings. Another example is the AFINION ACR (albumin, creatinine, and albumin/creatinine ratio) test, which is a rapid point-of-care test for microalbuminuria using a urine sample and can be used for early identification of kidney disease in patients with diabetes and/or hypertension (29). Finally, the KidneyIntelX.dkd laboratory test developed by Renalytix can predict the risk of rapid progressive decline in kidney function in patients with stages 1–3b CKD (30). This test uses prognostic kidney disease biomarker results from a patient's blood sample and combines these with clinical features data from the patient's medical record (e.g., eGFR, UACR, systolic blood pressure, and serum calcium) to produce a risk score. Such tests could be used as an add-on to the KDIGO heat map to support risk assessment. The U.S. Food and Drug Administration (FDA) recently approved marketing authorization for the KidneyIntelX.dkd prognostic test for use in adult patients with type 2 diabetes and early-stage CKD (31).

Another theoretical model is the e-phenotype for CKD, which is a digital phenotype (based on a consensus definition of CKD in the EHR) that combines the clinical data in EHRs (e.g., screening dates, test results, and other clinical data) with an automated machine learning algorithm to predict the risk of CKD progression in individual patients (32).

Figure 2 provides our overview of the various approaches and strategies noted in this section that could increase the uptake of CKD screening and improve the speed of diagnosis and staging of CKD in primary care.

Current Approach to Drug Management of CKD Associated With Type 2 Diabetes

Both the ADA and KDIGO guidelines recommend a comprehensive and multifaceted approach to early CKD management that includes lifestyle modifications with pharmacologic interventions (Figure 3) (5). Recommended changes for people with type 2 diabetes include maintaining a healthy weight; eating a healthy, well-balanced diet that is low in sodium; regularly exercising; and ceasing smoking, if applicable (6,7). In addition to these lifestyle modifications, increasing water consumption may have a beneficial effect on kidney function; however, the overall effects of increasing water consumption are unclear (33–35).

The ideal approach for supporting patients who have CKD and type 2 diabetes is through the integrated efforts of a multidisciplinary team (5), although primary care is usually the first point of contact for most patients with early-stage CKD (36). Therefore, a comprehensive and holistic treatment approach in primary care is needed (5). Because CKD cannot be cured, the aim of treatment is to slow CKD progression and reduce the risk of complications (37).

Table 1 presents the ADA's 2024 Standards of Care recommendations for reducing CKD progression and/or

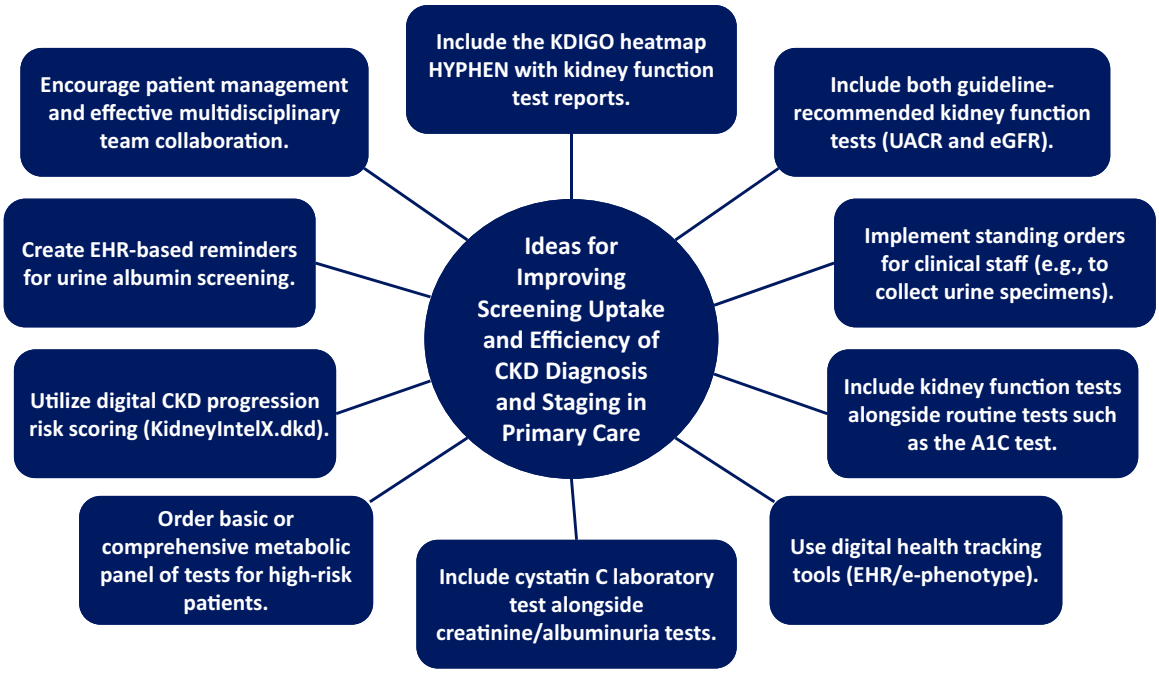

FIGURE 2 Ideas for improving uptake of screening and efficiency of CKD diagnosis and staging in primary care.

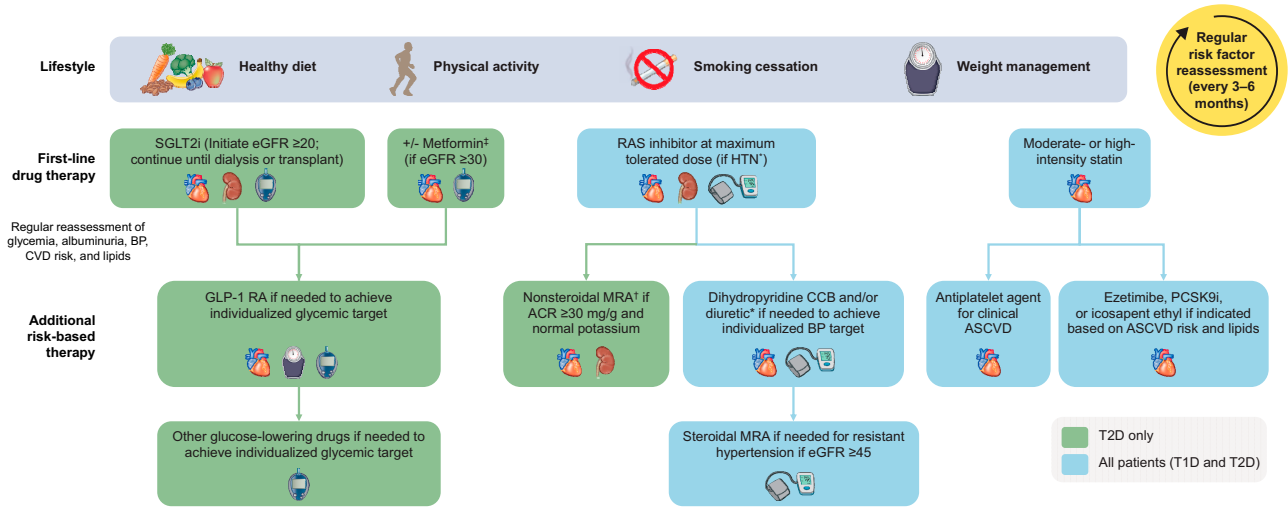

FIGURE 3 ADA/KDIGO 2022 treatment algorithm for patients with CKD associated with type 2 diabetes. *ACEi or ARB should be first-line therapy for HTN when albuminuria is present; otherwise, dihydropyridine CCB or diuretic can also be considered. All three classes are often needed to attain BP targets. †Finerenone is currently the only nonsteroidal MRA with proven clinical kidney and cardiovascular benefits. ‡If eGFR is 30–44 mL/min/1.73 m^2, initiate metformin at half the recommended dose (for immediate or extended-release formulations) and titrate upward to half of maximum recommended dose, if tolerated. If eGFR is <30 mL/min/1.73 m^2, stop metformin or do not initiate metformin. Monitor kidney function (at least every 3–6 months) with eGFR <60 mL/min/1.73 m^2. Initiate monitoring for possible vitamin B12 deficiency when people are treated with metformin for >4 years. Icons presented indicate the following benefits: BP cuff, blood pressure lowering; glucose meter, glucose lowering; heart, heart protection; kidney, kidney protection; scale, weight management. ACEi, ACE inhibitor; ACR, albumin-to-creatinine ratio; ASCVD, atherosclerotic cardiovascular disease; BP, blood pressure; CCB, calcium channel blocker; HTN, hypertension; PCSK9i, PCSK9 inhibitor; RA, receptor agonist; SGLT2i, sodium–glucose cotransporter 2 inhibitor; T1D, type 1 diabetes; T2D, type 2 diabetes. Adapted from ref. 5.

cardiovascular events in patients with CKD and type 2 diabetes, as well as an overview of the studies behind these recommendations and applicable FDA drug label information (38–46). Despite these evidence-based recommendations, patients with type 2 diabetes and CKD are not being prescribed (or are not being prescribed early enough) guideline-recommended treatments for CKD (10).

For patients already receiving medications for CKD and type 2 diabetes, prescribing errors, such as prescribing contraindicated medications or incorrect/nonoptimized dosing, are common in patients who have impaired kidney function (47,48) and at all stages of CKD (49). For example, nonsteroidal anti-inflammatory drugs (NSAIDs) are linked to increased risk of acute kidney injury (AKI) and worsening kidney function (50,51) and so should be avoided or used with caution in patients with CKD, and especially those with advanced CKD. NSAIDs also should not be taken in combination with certain drug classes such as diuretics and renin-angiotensin system (RAS) inhibitors because of the increased risk of AKI (52). Avoiding use of contrast agents (which are often used in tests such as MRI, computed tomography, and angiography) in people with CKD (>30 mL/min/1.73 m^2) may also be warranted because of their association with AKI (53), although the risk for people with reduced kidney function may be overstated (54). Additionally, medications that are excreted by the kidneys may need dosage adjustment based on patients' level of kidney function (55) or whether they are on dialysis. Thus, when prescribing medications for patients with CKD, PCPs must consider each patient's full medication history (including current status) and review this information with each patient at each visit. PCPs should also refer to FDA-approved drug labeling information to check that medications are suitable for use in a given patient and to make sure the medication is dosed correctly according to the patient's kidney function (56).

Including a clinical pharmacist in the primary care team via a collaborative drug therapy management agreement allows pharmacists to perform services that can support physicians with medication optimization (57). For example, an author of this article who is also a clinical pharmacist is a member of the primary care team at the center where she works. Her role includes supporting a physician on the team by performing routine testing (including eGFR and UACR testing, plotting results on the KDIGO heat map), thus ensuring that patients receive the right medications at the right dose, as well as alternating patient appointments with the physician, depending on the status of the patient. Such services can help to reduce drug-related problems in patients

TABLE 1 Overview of the ADA's 2024 *Standards of Care* Treatment Recommendations and FDA-Approved Drug Indications for CKD Associated With Type 2 Diabetes

Drug Name	Basis of the Guideline Recommendation (Evidence of Kidney and/or Cardiovascular Benefit)		FDA-Approved Drug Label Information Specific to CKD and/or Patients With CKD and CVD	Relevant ADA 2024 Standards of Care Recommendation(s)	Authors' Observations
	Phase 3 Clinical Trial	Clinical Trial Key Inclusion Criteria			
ADA 2024 Recommendation 11.5a: For people with type 2 diabetes and diabetic kidney disease (DKD), use of a sodium–glucose cotransporter 2 (SGLT2) inhibitor is recommended to reduce CKD progression and cardiovascular events in patients with an eGFR ≥20 mL/min/1.73 m^2 and urinary albumin ≥200 mg/g creatinine.					
Canagliflozin	CREDENCE (38)	• eGFR 30 to <90 mL/min/1.73 m^2 and UACR >300–5,000 mg/g • Participants had type 2 diabetes and CKD and were taking a stable dose of an ACE inhibitor or ARB	"Use [canagliflozin] to reduce risk of ESKD, doubling of serum creatinine, CV death, and hospitalization for HF in adults with T2D and diabetic nephropathy with albuminuria."* Other relevant information: • Insufficient data to support initiation if eGFR <30 mL/min/1.73 m^2 and UACR >300 mg/day or if eGFR <45 mL/min/1.73 m^2 and UACR ≤300 mg/day • If patient is already on therapy and eGFR <30 mL/min/1.73 m^2 and UACR >300 mg/day, treatment can continue (even if not needed for glycemic control) • Do not use in patients on dialysis	11.5a	• FDA approved for CKD in 2020 (39) • 2020 indication based on primary/secondary outcome measures of CREDENCE study and not based on inclusion criteria, subanalysis, or further studies after CREDENCE completed • 2024 ADA recommendation based on CREDENCE study, but also on any subanalyses and inclusion criteria further supporting kidney and CV efficacy
ADA 2024 Recommendation 11.5b: For people with type 2 diabetes and DKD, use of an SGLT2 inhibitor is recommended to reduce CKD progression and cardiovascular events in patients with an eGFR ≥20 mL/min/1.73 m^2 and urinary albumin ranging from normal to 200 mg/g creatinine **ADA 2024 Recommendation 11.5c:** For cardiovascular risk reduction in people with type 2 diabetes and CKD, consider use of an SGLT2 inhibitor (if eGFR is ≥20 mL/min/1.73 m^2), a GLP-1 receptor agonist, or a nonsteroidal MRA (if eGFR is ≥25 mL/min/1.73 m^2).					
Dapagliflozin	DAPA-CKD (40)	• Participants had CKD, and 68% had type 2 diabetes • Most were taking a stable dose of an ACE inhibitor or ARB • eGFR 25–75 mL/min/1.73 m^2 and UACR 200–5,000 mg/g	"Use [dapagliflozin] to reduce the risk of sustained eGFR decline, ESKD, cardiovascular death, and hospitalization for HF in adults with CKD at risk of progression."* Other relevant information: • Use for glycemic control if eGFR ≥45 mL/min/1.73 m^2 • Use if eGFR 25 to <45 mL/min/1.73 m^2 for kidney/cardiovascular benefit. • With eGFR <25 mL/min/1.73 m^2, initiation is not recommended but continue existing treatment to reduce risk of eGFR decline, ESKD, cardiovascular death, and HF • Do not use in patient on dialysis	11.5a, 11.5b, and 11.5c	• FDA approved for CKD in 2021 (41) • 2021 indication based on primary/secondary outcome measures of DAPA-CKD study and not based on inclusion criteria, subanalysis, or further studies after DAPA-CKD completed • No requirement for albuminuria for initiation • ADA 2024 recommendation based on DAPA-CKD study, but also on any subanalyses and inclusion criteria further supporting kidney and cardiovascular efficacy (DECLARE-TIMI 58 supports efficacy with no albuminuria; subanalysis from DAPA-CKD supports eGFR ≥20 mL/min/1.73 m^2)

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TABLE 1 Overview of the ADA's 2024 *Standards of Care* Treatment Recommendations and FDA-Approved Drug Indications for CKD Associated With Type 2 Diabetes (Continued)

Drug Name	Basis of the Guideline Recommendation (Evidence of Kidney and/or Cardiovascular Benefit)		FDA-Approved Drug Label Information Specific to CKD and/or Patients With CKD and CVD	Relevant ADA 2024 Standards of Care Recommendation(s)	Authors' Observations
	Phase 3 Clinical Trial	Clinical Trial Key Inclusion Criteria			
Empagliflozin	EMPA-KIDNEY (42)	• Participants had CKD, and 44% had type 2 diabetes • 85% were taking an ACE inhibitor or ARB at a clinically appropriate dose • eGFR ≥20 but <45 mL/min/1.73 m^2 or eGFR ≥45 but <90 mL/min/1.73 m^2 and UACR ≥200 mg/g	"Use [empagliflozin] to reduce the risk of sustained decline in eGFR, ESKD, cardiovascular death, and hospitalization in adults with CKD at risk for progression."	11.5a, 11.5b, and 11.5c	• FDA approved for CKD in 2023 (43) • ADA (2024) recommendations based on results from EMPA-KIDNEY and EMPA-REG OUTCOME (efficacy with no albuminuria); and EMPEROR-Reduced subanalysis (supports eGFR ≥20 mL/min/1.73 m^2)
ADA 2024 Recommendation 11.5d: As people with CKD and albuminuria are at increased risk for cardiovascular events and CKD progression, a nonsteroidal MRA that has been shown to be effective in clinical trials is recommended to reduce cardiovascular events and CKD progression (if eGFR is ≥25 mL/min/1.73 m^2). Potassium levels should be monitored.					
Finerenone	FIGARO-DKD (46)	• Participants had CKD and type 2 diabetes and were taking an ACE inhibitor or ARB at the maximum tolerated dose • eGFR of 25–90 mL/min/1.73 m^2 and UACR 30 to <300 mg/g or eGFR ≥60 mL/min/1.73 m^2 and UACR 300–5,000 mg/g	"Use (finerenone) to reduce the risk of sustained eGFR decline, ESKD, cardiovascular death, nonfatal myocardial infarction, and hospitalization for heart failure in adult patients with CKD associated with T2D." Other relevant information: • Recommended starting dose: ○ Use 20 mg once daily if eGFR ≥60 mL/min/1.73 m^2 ○ Use 10 mg once daily if eGFR ≥25 and <60 mL/min/1.73 m^2 ○ Target daily dose of 20 mg ○ Do not use if eGFR <25 mL/min/1.73 m^2 ○ Do not use if serum potassium >5 mEq/L	11.5c and 11.5d	• FDA approved for CKD in type 2 diabetes in 2021 (45) • 2021 indication based on primary/secondary outcome measures of FIDELIO-DKD and updated in 2022 to include FIGARO-DKD. Indication statement not based on inclusion criteria, subanalysis, or further studies (such as FIDELITY analysis) after FIDELIO-DKD/FIGARO-DKD studies completed • No requirement for albuminuria for initiation • ADA (2024) recommendations based on results from FIDELIO-DKD/FIGARO-DKD and also considered results from FIDELITY analysis
	FIDELIO-DKD (44)	• Participants had CKD and type 2 diabetes and were taking an ACE inhibitor or ARB at the maximum tolerated dose • eGFR 25 to <60 mL/min/1.73 m^2 and UACR 30 to <300 mg/g or eGFR 25 to <75 mL/min/1.73 m^2 and UACR 300–5,000 mg/g			

*As an adjunct to diet and exercise. CREDENCE, Computed TomogRaphic Evaluation of Atherosclerotic Determinants of Myocardial IsChEmia trial; CV, cardiovascular; DAPA-CKD, Dapagliflozin And Prevention of Adverse Outcomes in CKD trial; DECLARE-TIMI 58, Dapagliflozin Effect on Cardiovascular Events–Thrombolysis in Myocardial Infarction 58 trial; EMPA-KIDNEY, Study of Heart and Kidney Protection With Empagliflozin; EMPA-REG OUTCOME, BI 10773 (Empagliflozin) Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients; EMPEROR-Reduced, Empagliflozin Outcome Trial in Patients with Chronic Heart Failure and a Reduced Ejection Fraction; ESKD, end-stage kidney disease; FIDELITY, Combined FIDELIO-DKD and FIGARO-DKD Trial Program Analysis; HF, heart failure.

with CKD (58), and we believe that including a pharmacist for monitoring and drug therapy management enables physicians to spend more time on diagnostics and managing more complex patients.

Early Versus Late Prescribing and Prescribing Hesitancy

As stated previously, despite compelling evidence from multiple clinical trials, as well as clinical practice recommendations, prescription rates of medications that have known effects with regard to preventing CKD progression remain at suboptimal levels. For example, between 2017 and 2020, only 54.8% of adults with CKD and diabetes in the United States were taking an ACE inhibitor or an angiotensin receptor blocker (ARB) (59). Another study using data from a U.S. integrated health system that included 7,199 people with diabetes and CKD found that 80.3% of patients were not prescribed a sodium–glucose cotransporter 2 (SGLT2) inhibitor, and 42.0% were not prescribed an RAS inhibitor despite studies indicating that these patients could benefit from these medications (10). Additionally, in 2021, a cross-sectional study using data from the Mass General Brigham CKD registry found that SGLT2 inhibitors were prescribed to just 6% of 22,653 patients with type 2 diabetes and stage 3–5 CKD, despite the fact that these patients could have benefited (60). Another analysis based on National Health and Nutrition Examination Survey (NHANES) data from 2017 to 2020 found that the prevalence of SGLT2 inhibitor use was 5.8% in adults with type 2 diabetes and an eGFR ≥30 mL/min/1.73 m^2 (61).

Currently, there is a lack of published data on finerenone prescribing habits because this drug received FDA approval in 2021 and has only recently (in 2022) been included in treatment guidelines for patients with type 2 diabetes and CKD. Much of the published data on finerenone are based on the phase 3 clinical trials (FIDELIO-DKD [Efficacy and Safety of Finerenone in Subjects With Type 2 Diabetes Mellitus and Diabetic Kidney Disease] and FIGARO-DKD [Efficacy and Safety of Finerenone in Subjects With Type 2 Diabetes Mellitus and the Clinical Diagnosis of Diabetic Kidney Disease]); results from the FINE-REAL trial (completion expected in 2028) will look at finerenone prescribing practices in routine (real-world) medical settings (NCT05348733) (62).

We believe such drug prescribing hesitancy is happening in both primary and secondary care settings; nephrologists are not prescribing SGLT2 inhibitors or finerenone, and physician PCPs are still hesitant as well; this situation persists despite both of these drug classes having shown both kidney- and cardiovascular-protective effects in patients with type 2 diabetes and CKD (38,40,42,44,46). Nephrologists, as secondary care providers, specialize in treating advanced CKD and are not positioned to provide preventive care. Therefore, as the main care providers working with patients who have early-stage CKD, PCPs play a crucial role in CKD diagnosis and treatment to delay CKD progression.

Prescribing medications that help prevent kidney disease progression after CKD has already progressed to an advanced stage may reduce the treatment benefit because of the extent of established kidney function decline and cardiovascular damage. Looking at this another way, PCPs would not wait until after their at-risk patients have experienced a cardiovascular event before prescribing a statin (63); similarly, PCPs should not wait until after their patients reach advanced-stage CKD before initiating progression-preventive treatment. Of course, this is an irrelevant point for patients who present with advanced-stage CKD.

Early initiation of treatment may also have benefits beyond delaying CKD progression; for example, it may help to reduce the risk of complications more common with advanced disease (64) and may have cost-saving benefits (65) because advanced CKD is more expensive to treat than early-stage CKD (66). It is also important to remind ourselves that a high-cholesterol and/or high-salt diet and uncontrolled hyperglycemia are risk factors for developing CKD in type 2 diabetes, so statins, antihyperglycemic drugs, and dietary adjustments, as well as lifestyle modifications, are important treatment approaches (Figure 3).

Barriers to Prescribing

There are several barriers to implementing guideline-recommended cardiorenal therapies for patients with CKD associated with type 2 diabetes. One such barrier is therapeutic inertia, as defined earlier in this article. Therapeutic inertia may prevent or delay initiation of SGLT2 inhibitors, glucagon-like peptide 1 (GLP-1) receptor agonists, and/or newer drug classes such as the nonsteroidal mineralocorticoid receptor antagonist (MRA) finerenone in CKD, despite evidence supporting their use (67). Instead, PCPs may prescribe treatments they are more familiar with rather than alternatives because they feel assured of the former's efficacy and safety (67).

Therapeutic inertia may be more pronounced in primary care. In one study, intensification of glucose-lowering medications was greater and A1C was lower in patients seen by specialists compared with those treated by PCPs

(68). Specialists may be less affected by therapeutic inertia because they are able to focus more closely on fewer clinical issues and may be more familiar than physician PCPs with prescribing and intensifying certain medications (68). Therapeutic inertia is also commonly seen in the management of proteinuria in patients with type 2 diabetes (in 40.3% of these cases in primary care) (69).

Other barriers to implementing certain evidence-based treatments in CKD are lack of CKD awareness and knowledge among patients and providers, lack of patient engagement, polypharmacy associated with multimorbidity, practice setting constraints (e.g., limited access to specialists and high workload), fragmented CKD care (e.g., between health care professionals or between health care settings), social determinants of health (i.e., lack of access to care and medicines because of race/ethnicity and other social factors), and cost (70,71). Additionally, we believe time constraints are a significant barrier; physician PCPs may not have enough time to provide guideline-recommended care for patients with chronic, multimorbid disease (71,72).

One way to reduce the time demands on physician PCPs is to adopt team-based care, including nonphysician team members, in the practice. For example, a simulation study applied preventive and chronic disease care guidelines to a hypothetical panel of 2,500 patients who were representative of the U.S. adult population based on 2017–2018 NHANES data. Researchers estimated that physician PCPs would require 26.7 hours/day to provide guideline-recommended primary care (clearly unattainable!), but this time demand was reduced to 9.3 hours/day with team-based care (72).

Including professionals from other disciplines on the health care team (e.g., nurse practitioners, physician associates, clinical pharmacists, and diabetes care and education specialists) to collaborate with physicians can help to overcome some of these barriers. For example, clinical pharmacists can help patients enroll in medication assistance programs (73); navigate the prior authorization process for medications, if required (74); and help patients understand their health insurance plans and out-of-pocket medication costs (75,76). Lack of access to a clinical pharmacist can be a barrier in some practices, but with most states now allowing collaborative practice agreements (77) and, with them, the ability to bill for services, accessibility should improve.

Additionally, it is important for PCPs to identify which professionals are present within their clinical setting and available to join the team. Empowering other clinic staff members to assist PCPs (e.g., with navigating insurance formularies) may also be beneficial to alleviate the administrative workload.

PCPs' beliefs may also be a significant barrier to treatment initiation in CKD and may contribute to therapeutic inertia. For example, a belief that there is nothing to be done about kidney disease if a patient is at high risk (71) or a belief that certain treatments may cause side effects such as hyperkalemia that cannot be managed may result in PCPs not prescribing guideline-recommended therapies or discontinuing them prematurely.

We believe clinicians who are resistant to initiating certain medications for type 2 diabetes or CKD should recognize their own barriers to prescribing and work to overcome them because, if clinical practice guidelines recommend their use based on robust evidence and outcome data, their patients could benefit (assuming appropriate consideration of patient preferences and comorbidities). For example, an author of this article who is also a physician PCP and diabetologist describes her own hesitation to prescribe a medication to a patient who has CKD and residual proteinuria (despite current treatments) because of the time it takes to implement this therapy and assumed patient resistance to it. The PCP author's specific barriers to prescribing were *1*) the additional time needed for initiation and optimization of a new drug (as well as navigating cost and health insurance issues) and *2*) the effort needed to explain the rationale to a patient she felt would not want to take the treatment. The PCP author did prescribe the medication with success, and the patient did not show the anticipated resistance to the treatment.

Authors' Perspectives: Responding to Prescribing Barriers in Primary Care

In the previous section, we noted many of the barriers to guideline-recommended prescribing in primary care and the potentially detrimental significance of these barriers to patient care. In this section, we give our perspectives as front-line clinicians in the diagnosis and management of CKD (specifically, a clinical pharmacist, a physician PCP, and an endocrinologist) on three important elements that we believe contribute to therapeutic inertia in primary care and how these could be addressed. These issues include *1*) lack of awareness of clinical trial data (and thus lack of confidence in the drug), *2*) later prescribing when earlier prescribing may benefit a patient (i.e., linear vs. pillar treatment approaches), and *3*) fear of drug side effects.

Improving accessibility of the clinical trial data supporting guideline recommendations

In our view, lack of knowledge of the design, results, and interpretation of the clinical trials supporting clinical practice recommendations is an important barrier to initiating evidence-based drug treatments in CKD associated with type 2 diabetes and contributes to nonadherence to such recommendations.

Because of time constraints, physician PCPs may have limited opportunities for self-education and training around specialist topics such as CKD management. Indeed, physician PCPs have reported having limited knowledge of CKD (71) but a desire to learn more about the condition (36). As a result, physician PCPs may have limited understanding about CKD and the evidence-based drug treatment options that may slow its progression and provide cardiovascular benefit.

We believe this knowledge gap could be addressed by ensuring that PCPs are aware of the evidence supporting the recommendations for a particular drug or drug combination in CKD and type 2 diabetes. To assist in this task, we have developed several visual representations that link the key clinical trial data to the associated clinical practice recommendation (Supplementary Figure S1). These plain-language visual representations are aimed at time-limited PCPs and are in an accessible and digestible format. Because this is a visual representation and so not intended to be a comprehensive guide, we have focused on the ADA's 2024 Standards of Care recommended treatment options for patients who have type 2 diabetes, persistent albuminuria, and reduced kidney function.

Using an early combination therapy (pillar) approach

Using a theoretical pillar treatment approach (i.e., prescribing medications of different classes in combination at the same time and at an early disease stage), as opposed to a linear treatment approach (i.e., a stepwise progression through which medications are prescribed one at a time) could reduce the time delay in treatment initiation and ultimately reduce the risk of CKD progression.

The theoretical pillar approach for cardiorenal benefit in people with CKD and type 2 diabetes consists of the three pillars of treatment (an RAS inhibitor [ACE inhibitor or ARB], an SGLT2 inhibitor, and a nonsteroidal MRA [finerenone]) plus an emerging fourth pillar (a GLP-1 receptor agonist), with all treatment pillars built on a foundation of lifestyle modification (78). GLP-1 receptor agonist therapy is an emerging pillar in this treatment approach because of the potential cardiorenal benefits of agents in this drug class in patients with CKD and type 2 diabetes (79,80). Although they are not currently a standard of care for CKD, because of the positive cardiorenal data of specific GLP-1 receptor agonists, the ADA's 2024 Standards of Care recommends considering their use for additional cardiovascular risk reduction in patients with type 2 diabetes and CKD if eGFR is ≥25 mL/min/1.73 m^2 (6). However, the additive benefit of these treatment pillars is a matter of opinion; further research is needed to ascertain the value of combination therapies.

Overcoming the fear of side effects

Physician PCPs' fear of possible side effects from drug treatments may be a barrier to prescribing or continuing certain medications in primary care. This factor is particularly true for newer medications that have less supporting real-world evidence and are not as well known. We believe it is important to initiate a drug treatment if a patient may benefit from it and to then monitor and manage side effects by adjusting or readjusting doses as needed or by adding a treatment that counteracts the side effect.

For example, hyperkalemia (high blood potassium levels) can occur because of reduced kidney function, but also as a side effect of drugs targeted at reducing kidney disease progression or hypertension in patients with CKD and type 2 diabetes (45,81,82). Hyperkalemia can be managed through increased monitoring and the use of a loop or thiazide diuretic or potassium binder; this approach is preferred versus discontinuing the CKD protective or antihypertensive drug. The STABILIZE-CKD trial is currently underway and will explore the effects of the selective potassium binder sodium zirconium cyclosilicate for hyperkalemia management as an adjunct to ACE inhibitor or ARB therapy to determine whether the drug will allow people to stay on an RAS inhibitor for longer and thereby slow CKD progression (83). Sodium zirconium cyclosilicate is a newer and potentially more appropriate potassium binder for managing hyperkalemia in CKD because it has been shown to have a favorable safety profile (84).

We also believe that fear of drug side effects, although valid, can be managed easily and should not lead to withholding a proven drug therapy known to prevent end-stage kidney disease and cardiovascular death. We are of the opinion that, even without symptoms, CKD must be aggressively managed starting early in its course.

Conclusion

Early detection and early treatment of CKD in patients with type 2 diabetes has major health, quality-of-life, and cost benefits, and this is an important message for clinicians who work in primary care. Unfortunately, uptake of CKD screening in people with type 2 diabetes and early initiation of renoprotective and cardioprotective drugs such as SGLT2 inhibitors and the nonsteroidal MRA finerenone remain suboptimal. Incorporating CKD screening using a renal profile as part of a person's routine clinic visits could increase screening uptake in primary care and consequently facilitate diagnosis of CKD earlier, when it is easier to manage.

We believe that an important barrier to prescribing, and particularly early prescribing, in primary care is a lack of awareness about the clinical trial data supporting guidelines for CKD treatment, which could be addressed by provision of plain-language visuals showing how the clinical trial data link to the specific guideline recommendations. Other barriers are fear of side effects and inflexibility in prescribing approach, whereby clinicians wait until a patient's kidney function has worsened before prescribing another class of kidney-protective drug (i.e., follow a linear approach) versus initiating combination therapy from the outset (i.e., follow the theoretical pillar approach).

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J.D.G. is on the speakers' bureau for Abbott Diabetes, Bayer, Boehringer Ingelheim, Eli Lilly, Novo Nordisk, and Xeris. R.B. serves on advisory panels for AstraZeneca, Novo Nordisk, and Sanofi; has received research support for Amarin, Amgen, AstraZeneca, Boehringer Ingelheim, Ironwood, Janssen, Novo Nordisk, and Sanofi; and is on speakers' bureaus for Amarin, Amgen, Boehringer Ingelheim, Kowa, Eli Lilly, Novo Nordisk, and Sanofi. E.M. has received consulting fees from Abbott Diabetes, AstraZeneca, Boehringer Ingelheim, Eli Lilly, Merck, Novo Nordisk, and Sanofi and has been a speaker for Abbott Diabetes, Boehringer Ingelheim, Eli Lilly, and Novo Nordisk. No other potential conflicts of interest relevant to this article were reported.

AUTHOR CONTRIBUTIONS

All of the authors contributed to writing and reviewing the manuscript and approved the final manuscript for submission. J.D.G. is the guarantor of this work and, as such, had full access to all the data reported and takes responsibility for the integrity of the data and accuracy of the content.

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