Clinical Practice Guideline and Pathways for the Evaluation and Management of Adults with Type 2 Diabetes Mellitus and Chronic Kidney Disease in the Family and Community Practice

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Executive Summary

Background

Diabetes mellitus (DM) is a significant and growing global health concern. Worldwide, 537 million adults have diabetes and 206 million of them are from the Western Pacific Region[1]. Local prevalence continues to remain high at 7.5%, with 4,303,899 adult Filipinos suffering from diabetes in 2021. DM significantly contributes to the growing burden of chronic kidney disease (CKD) worldwide with about 50% of end-stage renal disease (ESRD) being due to diabetic nephropathy alone. Likewise, 60% of Filipinos on maintenance dialysis have ESRD due to DM and hypertension. The primary care setting is the initial point of contact between healthcare providers and patients with type 2 diabetes, hence, the development of clinical practice guidelines that will provide guidance in caring for patients with stable complications of diabetes. The guideline is the first of 3 that are being developed by the Philippine Academy of Family Physicians for the diagnosis and management of adult patients with type 2 diabetes and stable microvascular complications - nephropathy, retinopathy and neuropathy.

Objective

This guideline aims to provide evidence-based recommendations on the diagnosis and management of adults with type 2 diabetes mellitus (T2DM) and early stage CKD and is divided into 5 main sections - Clinical Assessment, Diagnostic Tests, Pharmacologic Treatment, Non-pharmacologic Treatment and Patient Outcomes.

Methods

The method of guideline development followed the ADAPTE process. The Technical Working Group identified 19 key questions after consultation with colleagues and patients. Recommendations were adopted from high-quality clinical practice guidelines whenever applicable for most of the key clinical questions. On the other hand, the De Novo method of evidence review was used to answer key clinical questions for which recommendations from reviewed guidelines were not available. A modified GRADEPro was used in assessing the quality of evidence - high, moderate, low or very low. Following external review by a nephrologist, the draft recommendations were sent to the members of the consensus panel. Voting on whether to include or not by the consensus panel was facilitated to determine the strength of each recommendation - strong, moderate or weak.

Recommendations

After reviewing 3 high-quality clinical practice guidelines and the current evidence, the technical working group was able to develop 40 recommendations for the 19 key clinical questions.

Summary of Recommendations

Table 1. Summary of recommendations for the diagnosis and management of adult type 2 diabetic patients with nephropathy

No.	Recommendations	Strength of Recommendations	Quality of Evidence
Clinical Assessment: History and Physical Examination			
KQ1. Among adults with type 2 Diabetes Mellitus (T2DM), what components of the history taking and physical examination should be focused on when screening for chronic kidney disease (CKD)?			
1.1	Perform a thorough history taking, focusing on obtaining the following information: a. Personal Medical and Family History: i. Demographic profile (age, sex, race/ ethnicity) ii. Signs and symptoms of CKD (fatigue, shortness of breath, decreased appetite, leg swelling, muscle cramps, heartburn, itching, sexual dysfunction, poor sleep, pain, drowsiness, bone/joint pain, poor mobility, frothy urine) iii. Risk factors for developing CKD iv. Exposure to nephrotoxic agents (broad spectrum antibiotics, NSAIDs, Chemotherapy) v. Smoking history (pack/years) vi. Nutritional assessment b. Social and environmental history c. Last menstrual period and lactation status, if applicable	Strong	Very Low
1.2	Perform a thorough physical examination to assess for the following: a. High blood pressure b. Fluid retention (edema, ascites, rales) c. Anemia (Pallor) d. Weight loss and muscle wasting e. Changes in skin color	Strong	Very Low
1.3	Assess for nutrition and protein energy status by obtaining anthropometric measurements, body composition, and performing hand grip tests.	Strong	Very Low
KQ2: Among adults with T2DM with CKD, what components of the history taking and physical exam should be focused on to recognize other comorbidities / complications?			
2	Patients with CKD should be evaluated for the possible complications such as malnutrition, anemia, bone and mineral disorder, acid-base and electrolyte imbalance, risks for infection, peripheral artery disease and ASCVD	Strong	Very Low to Moderate
KQ3: What components of the psychosocial history should be elicited to guide management of adults with T2DM and CKD?			
3.1	Assess for the psychosocial factors related to CKD such as baseline knowledge on CKD, family and community resources, coping mechanisms, and patient preference.	Strong	Very Low
3.2	Utilize appropriate family assessment tools in patients with T2DM and DKD to guide in formulating a management plan. This can be done over several patient visits.	Strong	Very Low

Diagnostic Tests			
KQ4: Among adults with T2DM, what tests are recommended in the diagnosis and evaluation of CKD?			
4.1	Request for urine albumin AND estimated glomerular filtration rate (eGFR) among adults with type 2 diabetes during the first visit and annually thereafter, to diagnose and evaluate for CKD	Strong	Moderate
4.2	Offer imaging studies based on individualized need for patient management, and if available.	Strong	Moderate
KQ5: Among adults with T2DM and CKD, what tests should be used to monitor treatment response?			
5	Request for urine albumin AND estimated glomerular filtration rate (eGFR) to monitor for progression of CKD.	Strong	Moderate
KQ6: Among adults with T2DM and CKD, what tests should be used to monitor comorbidities and complications?			
6	Offer the following laboratory tests to assess for comorbidities and complications of CKD in adults with type 2 diabetes and CKD: A. Total cholesterol, LDL, HDL and triglycerides to guide with management and establish possible underlying causes of chronic kidney disease. B. Hemoglobin level to assess for anemia C. eGFR and serum electrolytes regularly, in patients concurrently on potentially nephrotoxic agents D. Serum calcium, phosphate, PTH, and alkaline phosphatase activity in patients with GFR <60 ml/min/1.73m2 (G3a or lower) to establish a possibility of bone and mineral disorder. E. Diagnostic work up for underlying cardiac disease in those with related signs and symptoms, that follows recommendations from locally accepted guidelines. F. Repeat serum creatinine and potassium 2 4 weeks after initiation or increase in dose of RASi (ACEi or ARBs), MRA, nsMRA, and diuretics G. Vit B level for those on Metformin for 4 years or longer, if available	Strong Strong Strong Strong Strong Strong	Low Moderate Moderate Moderate Moderate Very Low Moderate

Pharmacologic Management			
KQ7: Among adults with T2DM and CKD, what medications are effective in achieving glycemic targets and preventing or delaying progression of CKD?			
7	Offer the following to achieve glycemic targets and prevent or delay the progression of nephropathy: a. Sodium glucose cotransporter 2 inhibitors (SGLT2i) with primary evidence of reducing CKD progression b. Metformin for patients with T2D, CKD with an eGFR ≥30 ml/min per 1.73 m2 c. Do not give Metformin for patients with eGFR <30 mL/min/1.73 m2	Strong	Moderate
KQ8: Among adults with T2DM and CKD who have not achieved individualized glycemic targets despite the use of metformin and SGLT2i, what additional medication/s are effective in achieving glycemic targets and preventing or delaying the progression of CKD?			
8	Offer Long acting GLP 1 RA with proven CKD benefit 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.	Strong	High
KQ9. Among adults with T2DM and CKD, what additional medications are effective in reducing cardiovascular risk and delay progression of CKD?			
9	Offer an ACE inhibitor or angiotensin receptor blocker for treatment of hypertension to reduce cardiovascular risk and delay progression of CKD	Strong	High
KQ10: Among adults with T2DM, CKD, and heart failure or established atherosclerotic cardiovascular disease, what medications are recommended for cardiovascular and kidney risk reduction?			
10.1	Initiate a sodium glucose cotransporter 2 inhibitor with proven benefit in patients with type 2 diabetes and established heart failure to reduce the risk of worsening heart failure and cardiovascular death**.** Offer combined therapy with a sodium glucose co transporter 2 inhibitor (SGLT2i) and a glucagon like peptide 1 receptor agonist (GLP1 RA) with demonstrated cardiovascular benefit in patients with type 2 diabetes and CKD and heart failure, established atherosclerotic cardiovascular disease or multiple risk factors for atherosclerotic cardiovascular disease.	Strong	High
10.2	Offer non steroidal Mineralocorticoid Receptor Antagonists (eg. Finerenone) to adults with type 2 diabetes and CKD with concomitant heart failure who are at increased risk for cardiovascular events or chronic kidney disease progression and unable to use an SGLT2 inhibitor.	Strong	High
KQ11: Among adults with T2DM with CKD, what additional medication/s are recommended for the primary prevention of atherosclerotic cardiovascular diseases?			
11	Initiate statin therapy, in addition to lifestyle therapy among patients with T2DM and CKD, to achieve target levels. Titration and target reduction are individualized based on clinical profile and risk stratification.	Strong	Moderate
KQ12. Among adults with T2DM and CKD, what additional medications are effective in delaying progression of CKD?			
12.1	Offer Ketoanalogue supplementation with low protein diet to patients with higher eGFR (≥30ml/min/1.73m2) to delay progression of CKD	Strong	Moderate
12.2	Evidence on the role of probiotics in delaying the progression of CKD is insufficient to recommend its use	Moderate	Moderate

12.3	Offer bicarbonate supplementation to patients with CKD stages 4 5 with low serum bicarbonate levels (<22 mmol/L)	Strong	Low
KQ13. Among adults with T2DM and CKD, what medications are effective in the management of anemia?			
13.1	Initiate oral iron therapy in patients with chronic kidney disease (CKD), including those with type 2 diabetes mellitus, who are not on dialysis, if on initial evaluation hemoglobin (Hb) levels are found to be <13 g/dL in males or <12 g/dL in females, if with serum ferritin <100 ng/mL and transferrin saturation (TSAT) <40%, or Serum ferritin between 100–300 ng/mL and TSAT <25%	Strong	High
13.2	Initiate epoetin in patients with persistent anemia after iron deficiency has been corrected or ruled out. Correct all reversible causes of anemia—such as iron deficiency and underlying inflammation—before starting treatment with erythropoiesis stimulating agents (ESAs).	Strong	Moderate
Non-Pharmacologic Management			
KQ14: Among adults with T2DM and CKD, what are the recommended non-pharmacologic patient-centered interventions to improve patient outcomes?			
14.1	Provide diabetes self management education and support	Strong	Moderate
14.2	Discuss initial medical nutrition therapy with focus on appropriate protein and salt intake and/or referral to nutritionist dietician for individualized medical nutrition therapy (MNT)	Strong	Low
14.3	Discuss weight management and physical activity based on general recommendations among patients with diabetes mellitus	Strong	Low
14.4	Screen for tobacco and vape use and discuss, assess, and identify barriers on smoking cessation among T2DM patients with nephropathy using tobacco products	Strong	Low
14.5	Offer teleconsultation for monitoring control, adherence to management, and lifestyle modification	Strong	Very Low
KQ15: Among adults with T2DM and CKD, what are the recommended non-pharmacologic family-focused interventions to improve patient outcomes?			
15.1	Provide family directed health education on diabetes and CKD (address family misperceptions and lifestyle)	Strong	Very Low
15.2	Involve a family member or a caregiver on DM2 nephropathy management and education	Strong	Very Low
KQ16: Among adults with T2DM and CKD, what are the recommended non-pharmacologic community-oriented interventions to improve patient outcomes?			
16.1	Navigate patients through existing community resources as one strategy in addressing barriers to care.	Strong	Very Low

16.2	Encourage patients to participate in existing community lifestyle programs such as DM club and other related support groups.	Strong	Very Low
16.3	Encourage patients to participate in existing credible online/virtual support groups and communities.	Strong	Very Low
Patient Outcomes			
KQ17: What are the desired clinical and non-clinical outcomes following treatment among adults with T2DM and CKD?			
17.1	Aware of the importance of adherence to treatment regimen	Strong	Low
17.2	Received individual or group based self management education to improve blood pressure and glycemic control, self efficacy and patient satisfaction.	Strong	Low
17.3	Albuminuria reduced by >30% or to levels < 300mg/m to delay progression of diabetic kidney disease and decrease cardiovascular risk.	Strong	Moderate
17.4	Achieved glycemic control based on individualized target for HbA1c level among adult diabetic type II patients with CKD or the equivalent plasma glucose to delay progression of kidney disease .	Strong	High
17.5	Achieved blood pressure control with a target BP of < 130/80 mmHg to reduce risk for cardiovascular disease.	Strong	High
17.6	LDL level reduced to <70mg/dl to reduce cardiovascular risk.	Strong	High
KQ18: How should treatment goals be monitored in the care of adults with T2DM and CKD?			
18.1	Changes in blood pressure, serum creatinine and serum potassium are monitored within 2 4 weeks of initiation or increase in the dose of an ACE inhibitor or ARB.	Strong	Very Low
18.2	Follow up visits among adult patients with type 2 diabetes nephropathy are advised after 6 months to 1 year, based on the staging of chronic kidney disease to guide therapy and for monitoring . (Very Low)	Strong	Very Low
KQ19. What are the indications for referral to Nephrology specialist care among adults with T2DM and CKD?			
19	Referred for Nephrology specialist care if with CKD G4, G5, A3, or G3bA2.	Strong	High

Dissemination and Implementation

The final recommendations for clinical practice will be disseminated through publication in the PAFP journal, The Filipino Family Physician and hrough a series of lectures beginning at the PAFP Annual Convention and via round-table discussions in the different PAFP chapters. To encourage implementation, the clinical practice guidelines will also be incorporated in both hospital and the community practice, through the hospital-based and practice-based training programs in the different institutions and in program or chapter-led quality assurance activities.

Background

Diabetes mellitus (DM) is a significant and growing global health concern. Worldwide, 537 million adults have diabetes and 206 million of them are from the Western Pacific Region[1]. The Philippines has recorded 4,303,899 adults with diabetes in 2021. Its prevalence rate continues to remain high at 7.5%. DM is significantly contributing to the growing burden of chronic kidney disease worldwide with about 50% of end-stage renal disease (ESRD) being caused by diabetic nephropathy alone. Likewise, 60% of Filipinos on maintenance dialysis have ESRD due to DM and hypertension. One Filipino develops CKD every hour or 120 Filipinos per million population per year. Hence, CKD is a major contributor as to why kidney diseases are the 7th leading cause of death in the Philippines.

The Asia Pacific Society of Nephrology and Association of British Clinical Diabetologists (ABCD) use the term diabetic nephropathy (DN) to describe damage to the glomerulus among people with DM which manifests as proteinuria, hypertension and renal edema. DKD is the umbrella term to include both DN and CKD from DN. A presumptive kidney disease caused by DM is labelled as diabetic kidney disease (DKD) wherein DKD is a clinical diagnosis in the absence of a kidney biopsy[3,4]. On the other hand, the term DKD is avoided by KDIGO to avoid the connotation that, in all cases, CKD is caused by diabetes. People with both CKD and diabetes can be attributed to the latter diagnostically, unless there is evidence to suggest other causes[4].

Global burden of DKD and ESRD has a major impact on healthcare costs and resources; making screening, early detection and preventive treatment important strategies to mitigate this worldwide pandemic. However, optimal management of CKD in the background of DM is complex, requiring cross-functional and multidisciplinary effort[4]. Bridging diabetes and nephrology management in primary care is unique as it requires optimal control of hyperglycemia while controlling cardiovascular risk factors such as hypertension, dyslipidemia, obesity, diet, smoking, and physical activity[5]. KDIGO also affirms the critical role of structured and individualized patient education and shared decision making in the management. Lastly, the most effective way to mitigate CKD in DM is the prevention of DM in the general population[5].

Objectives

This guideline aims to provide evidence-based recommendations on the diagnosis and management of adult type 2 diabetic patients with early stage nephropathy. These recommendations will guide practitioners when evaluating adults with type 2 Diabetes Mellitus (T2DM) with chronic kidney disease (CKD) on the initial and subsequent visits by providing patient history and physical exam findings that must be elicited and focused on. The guideline also provides recommendations on the nonpharmacologic, including recommendations on family-focused and community oriented interventions among adults with T2DM on initial and subsequent visits and pharmacologic aspects of the management and important patient outcomes that must be achieved for each clinic visit.

Scope and Purpose

This guideline includes recommendations on initial evaluation using history taking and physical examination, screening and diagnosis, pharmacologic and non-pharmacologic management and patient outcomes and monitoring of chronic kidney disease in adults with T2DM in the primary care setting. This clinical pathway may serve as a guide for the early identification and early intervention of CKD to delay progression, reduce mortality, and manage comorbidities. Recommendations on diagnostic and therapeutic management apply only to T2DM with chronic kidney disease stage 1 to 3a. Patients with CKD stage 3b, 4 and 5 must be referred for subspecialty care.

This guideline is intended for use by family physicians, primary care physicians, and generalists who provide care to adults with T2DM and non-dialytic chronic kidney disease, Stage I-IIIa.

Method of Development

Clinical Practice Guideline Development

This clinical pathway was developed by the Philippine Academy of the Family Physicians (PAFP) and is intended to be utilized by its members in their family and community practice. The ADAPTE process was utilized in the development of the clinical pathway. The process followed these steps:

1. Formation of the technical working group and the consensus panel
2. Determination of the clinical questions for review
3. Searching for clinical practice guidelines
4. Appraising the validity of clinical practice guidelines using the AGREE II checklist
5. Decision making on the adaptation of recommendations
6. Drafting the recommendations
7. External review of the guideline

Technical Working Group and Consensus Panel

The Technical Working Group is composed of Family and Community Medicine specialists who have background in research and are active clinical practitioners. Most have already been engaged previously in clinical pathways development initiated by PAFP. All the members underwent orientation and training in guideline development, in utilizing tools such as the AGREE II checklist and GRADEPro and in the formulation of guideline recommendations. The members were divided into groups of 2, each of which was tasked to review existing evidence and draft the recommendations for the assigned clinical question.

The Consensus Panel is composed of Family and Community Medicine practitioners in the rural and urban setting, representing clinicians in private practice, government institutions and the community. A representative from the patient population is also included in the Consensus Panel.

Technical Working Group
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Formulating the Scope and Review Questions

The Technical Working Group adopted the existing template in determining the scope and the clinical questions, routinely utilized by the PAFP. This template incorporates the patient-centered, family-focused and community-oriented approach to patient care in family practice and divides the clinical guideline into 5 sections namely clinical assessment, laboratory and other diagnostic tests, pharmacologic and non-pharmacologic treatment and patient outcomes. Consultation with other family medicine practitioners and patients was done in identifying important outcomes that the TWG focused on while developing the guideline.

The scope of the guideline was defined by the care setting where family practitioners most often encounter the patient population of interest. This guideline is intended to be used in the care of adult type diabetic patients with nephropathy in the primary care setting. Twenty-one (21) key clinical questions based on the aforementioned 5 sections, were identified and formulated using the PICO framework.

Clinical Assessment
KQ1. Among adults with T2DM, what components of the history taking and physical examination should be focused on when screening for CKD? *KQ2: Among adults with T2DM, what components of the history taking and physical exam should be focused on to recognize other comorbidities / complications?* *KQ3: What components of the psychosocial history should be elicited to guide management of adults with T2DM and CKD?*
Diagnostic Tests
KQ4: Among adults with T2DM, what tests are recommended in the diagnosis and evaluation of CKD? *KQ5: Among adults with T2DM and CKD, what tests should be used to monitor treatment response?* *KQ6: Among adults with T2DM and CKD, what tests should be used to monitor comorbidities and complications?*
Pharmacologic Treatment
KQ7: Among adults with T2DM and CKD, what medications are effective in achieving glycemic targets and preventing or delaying progression of CKD? *KQ8: Among adults with T2DM and CKD who have not achieved individualized glycemic targets despite the use of metformin and SGLT2i, what additional medication/s are effective in achieving glycemic targets and preventing or delaying the progression of CKD?* *KQ9. Among adults with T2DM and CKD, what additional medications are effective in reducing cardiovascular risk and delay progression of CKD?* *KQ10: Among adults with T2DM, CKD, and heart failure or established atherosclerotic cardiovascular disease, what medications are recommended for cardiovascular and kidney risk reduction?* *KQ11: Among adults with T2DM with CKD, what kind of statin is indicated for primary prevention and secondary prevention of atherosclerotic cardiovascular diseases?* *KQ12. Among adults with T2DM and CKD, what additional medications are effective in delaying progression of CKD?* *KQ13. Among adults with T2DM and CKD, what medications are effective in the management of anemia?*

Non pharmacologic Treatment
KQ14: Among adults with T2DM and CKD, what are the recommended non-pharmacologic patient-centered interventions to improve patient outcomes? *KQ15: Among adults with T2DM and CKD, what are the recommended non-pharmacologic family-focused interventions to improve patient outcomes?* *KQ16: Among adults with T2DM and CKD, what are the recommended non-pharmacologic community-oriented interventions to improve patient outcomes?*
Patient Outcomes
KQ17: What are the desired clinical and non-clinical outcomes following treatment among adults with T2DM and CKD? *KQ18: How should treatment goals be monitored in the care of adults with T2DM and CKD?* *KQ19. What are the indications for referral to Nephrology specialist care among adults with T2DM and CKD?*

Searching, Selecting and Appraising the Evidence

The members of the Technical Working Group first searched for existing clinical practice guidelines on the diagnosis and management of type 2 diabetic patients with nephropathy. Two clinical practice guidelines from reputable organizations - American Diabetes Association and KDIGO were included in the initial list. Further search for other clinical practice guidelines was conducted, utilizing the terms "guidelines", "clinical practice guidelines","diabetes", "type 2 diabetes" and "nephropathy" "chronic kidney disease", "diabetic kidney disease". Eight clinical practice guidelines were initially identified, each of which was independently appraised by 2 members of the TWG using the AGREE II checklist. Only the guidelines with a score of at least 70 were then reviewed. These guidelines include the 2023 American Diabetes Association Standards of Care in the management of diabetes (2023 ADA), the 2022 Kidney Diseases: Improving Global Outcomes Clinical practice Guideline for Diabetes Management in Chronic Kidney Disease (2022 KDIGO) and the 2021 Association of British Clinical Diabetologists Clinical Practice Guidelines for the Management of Hyperglycaemina in Adults with Diabetic Kidney Disease (2021 ABCD). If these guidelines do not include recommendations for particular key questions, the de novo method is utilized to gather evidence and formulate new recommendations. Benefit, harm and cost were taken into account in drafting the recommendations and were emphasized in the consensus panel discussions. recommendations were updated with the release of the 2024 American Diabetes Association Standards of Care in Diabetes and the 2024 KDIGO Clinical practice Guideline for Diabetes Management in Chronic Kidney Disease.

Formulating the Recommendations

In formulating the recommendations for this guideline, important outcomes that were considered included delay in the progression of kidney disease, reduction in risk of cardiovascular diseases and quality of life. Using the ADAPTE method, most of the recommendations were adapted from high-quality clinical practice guidelines after reviewing and appraising the evidence. For the other key questions, data were extracted from relevant articles, evidence was summarized and new recommendations were formulated.

Search Terms for the De Novo Method

Key Question	Search Terms	Databases
KQ1	diabetes AND ("Kidney disease" or "Nephropathy") AND screen*	PubMed, Cochrane, Google Scholar
KQ2	diabetes AND ("Kidney disease" or "Nephropathy") AND complications	PubMed, Cochrane, Google Scholar
KQ15/KQ16	diabetes AND ("Kidney disease" or "Nephropathy") AND fam* OR commun*	PubMed, Cochrane, Google Scholar
KQ15	diabetes AND ("Kidney disease" or "Nephropathy") AND fam*	PubMed, Cochrane, Google Scholar
KQ16	diabetes AND ("Kidney disease" or "Nephropathy") AND commun*	PubMed, Cochrane, Google Scholar
KQ18	hyperkalemia AND creatinine AND "ACE inhibitor" AND CKD AND diabetes	PubMed

Grading of the Recommendations

Quality of Evidence

Modified GradePro was used in assessing the quality of evidence which may be ranked as High, Moderate, Low or Very Low. For decisions on intervention, evidence from RCTs and meta-analysis of RCTs was initially graded as high quality while evidence from observational studies and meta-analysis of observational studies was initially graded as low quality. For decisions on diagnostic tests, evidence from cross-sectional, cohort studies and meta-analysis of such studies was initially graded as high quality while evidence from case-control studies and meta-analysis of case control studies was initially graded as low quality. For decisions on clinical assessment, evidence from observational studies was initially graded as high quality. The quality of the evidence was downgraded if there was significant risk of bias, inconsistency, indirectness, imprecision and publication bias while grade was upgraded when there was large effect dose, dose response gradient, and if methods of addressing confounders were used.

Strength of Recommendation

Consensus Panel

The draft recommendations along with the evidence were sent to the Consensus Panel for initial assessment 1 week before the panel voting. An Evidence-to-Decision (EtD) questionnaire based on the EtD Framework6 was also provided for the panel members to fill out and use as criteria in assessing whether a recommendation will be adopted or not.

EtD criteria:

1. *Is the problem a priority?*
2. *Do the desirable effects (benefit) outweigh the undesirable effects (harm)?*
3. *What is the overall certainty of the evidence of effects?*
4. *Are the resources and costs needed to implement the recommendation available and affordable?*
5. *Is the recommendation feasible in our practice?*
6. *Does the recommendation address equity, fairness and respect for patient rights?*
7. *Will the recommendation be acceptable to all key stakeholders?*
8. *Should this recommendation be included in the guideline?*

Based on the panel vote, the recommendation was graded as Strong, if all the panel members or 100% voted for the adoption, Moderate, if at least 80 – 99% of the panel voted for the adoption or Weak, if 60 - 79% voted for the adoption of the recommendation.

External Review and Updating

This clinical practice guideline was sent to a Nephrologist for review and feedback. Revisions, if necessary, were made based on the comments. The technical working group intends to revisit the recommendation and review new evidence for updating every 3 years.

Recommendations and Evidence of Summaries

Clinical Assessment: History and Physical Examination

KQ1. Among adults with T2DM, what components of the history taking and physical examination should be focused on when screening for CKD?

Recommendation 1.1: Perform a thorough history-taking, focusing on obtaining the following information: (Strong SOR, Very Low QOE)

a. Personal Medical and Family History:
    i. Demographic profile (age, sex, race/ ethnicity)
    ii. Signs and symptoms of CKD (fatigue, shortness of breath, decreased appetite, leg swelling, muscle cramps, heartburn, itching, sexual dysfunction, poor sleep, pain, drowsiness, bone/joint pain, poor mobility)
    iii. Risk factors for developing CKD
    iv. Exposure to nephrotoxic agents (broad spectrum antibiotics, NSAIDs, Chemotherapy)
    v. Smoking history (pack/years)
    vi. Nutritional assessment
b. Social and environmental history
c. The last menstrual period and lactation status, for women —- *should be obtained during history-taking since some medications are contraindicated during pregnancy and breastfeeding*.

The diagnosis of CKD is made through a thorough history taking and physical examination[7,8]. Uremic symptoms are commonly recognized late, leading to inadequate treatment and poor quality of life. Fatigue is the most prevalent symptom in patients with CKD not on RRT, while sexual dysfunction is reported to be the most severe.[2] Other symptoms are shown in table 1. Family history, medications, social and environmental factors, symptoms and signs of systemic diseases, and duration of existing diseases should also be elicited during the patient encounter. Selected diagnostic tests may be done depending on the clinical context and resource availability. Details on specific social and environmental history elicit were not detailed in the KDIGO guidelines; however, resource availability relating to the patient's ability to afford diagnostic tests was mentioned. There is a need to tailor-fit diagnostic tests requested based on the more probable cause of CKD. Smoking history needs to be determined, since lifestyle factors such as smoking may contribute to worsening of CKD. Current smokers should be advised to quit, and may be referred to smoking cessation programs. Last menstrual period and lactation status is necessary, since some recommended medications for CKD have not been extensively studied in women.

CKD may not be secondary to primary kidney disease but may be primarily due to diabetes mellitus, vascular disease, and hypertension. In a patient with CKD and DM, the cause of the CKD is usually attributed to the DM unless it is proven otherwise; thus, screening for other

conditions that may cause or aggravate CKD becomes integral to assessing patients with CKD[8].

Table 2 enumerates additional factors that should be elicited in history taking and physical examination. These factors can possibly increase the likelihood of the diagnosis of CKD. According to data from the ADA and the KDIGO, priority conditions for CKD screening include hypertension, diabetes and CVD. Patients with type 2 diabetes mellitus should be screened for CKD at diagnosis, while patients with type 1 diabetes mellitus should be screened 5 years after diagnosis. Patients with recent or multiple episodes of AKI and those who are "partially diagnosed" with CKD (either by GFR or albuminuria, but not fully staged). Other candidates for screening include patient groups in table 2.[8] Evidence show that screening may be cost-effective, and hence the population screening is recommended over selective screening.

Recommendation 1.2: Perform a thorough physical examination to assess for the following: *(Strong SOR, Very Low QOE)*

a. High blood pressure
b. Fluid retention (edema, ascites, rales)
c. Anemia (Pallor)
d. Weight loss and muscle wasting
e. Changes in skin color

The 2024 KDIGO guidelines emphasize the need for early detection and treatment of hypertension and CVD, along with diabetes - which are common risk factors for CKD. Hence, clinicians are recommended to assess blood pressure of patients in every visit and look for home BP

Table 1. Symptoms, prevalence and severity in patients with CKD[8]

Symptom	Prevalence	Severity Score
Fatigue	**70%**	22.8
Poor Mobility	56%	19
Bone/joint pain	55%	no data
Drowsiness	53%	22.5
Pain	53%	22.5
Poor sleep	49%	23.8
Sexual dysfunction	48%	**56.4**
Itching	46%	25
Heartburn	46%	no data
Muscle cramps	46%	no data
Leg swelling	45%	no data
Decreased appetite	42%	19.8
Shortness of breath	42%	15

Table 2. Factors that increase the likelihood and rate of CKD diagnosis[8]

Domains	Examples
Common risk factors	Hypertension Diabetes Cardiovascular disease (including heart failure) Prior AKI/AKD
People who live in geographical areas with high prevalence of CKD	Areas endemic with CKD of undetermined origin Areas with high prevalence of *APOL1* genetic variants Environmental exposures
Genitourinary disorders	Structural urinary tract disease Recurrent kidney calculi
Multisystem diseases/ Chronic inflammatory conditions	Systemic Lupus Erythematosus Vasculitis HIV
Iatrogenic	Drug induced nephrotoxicity Radiation nephritis
Family history or known genetic variants associated with CKD	Kidney failure, regardless of identified cause Kidney disease recognized to be associated with genetic abnormality (e.g., PKD, APOL1 mediated kidney disease, and Alport syndrome)
Gestational conditions	Preterm birth Small gestational size Pre eclampsia/ eclampsia
Occupational exposures	Cadmium, lead and mercury exposure Polycyclic hydrocarbons Pesticides

monitoring. Increased plasma volume and decreased plasma oncotic pressure in renal diseases can cause edema among patients with chronic kidney disease[9]. This often presents with bilateral or generalized swelling. Aside from peripheral edema, clinicians must also evaluate for other manifestations of fluid retention such as rales and ascites. Likewise, patients with chronic kidney disease should also be evaluated for anemia. Anemia in CKD often presents as hypoproliferative and normocytic[10]. Mild anemia can be asymptomatic with typical clinical features appearing depending on the severity.

Table 3. Signs and symptoms of anemia (adapted from Turner, et al, 2025)[10]

Symptoms on History Taking	Signs on Physical Examination
Weakness	Skin may be cool to touch
Tiredness	Tachypnea
Lethargy	Tachycardia
Restless legs	Hypotension
Shortness of breath	Pallor/Pale Conjunctiva
Chest pain	Systolic murmur
Reduced exercise tolerance	Koilonychia
Pica	

Recommendation 1.3: Perform Indicators to suggest nutrition and protein- energy status such as anthropometric measurements, body composition, and hand grip tests (*Strong SOR, Very Low to Low QOE*)

a. Weight: Use clinical judgment for measuring weight changes (eg, actual measured weight; history of weight changes; serial weight measurements; adjustments for the suspected impact of edema, ascites, and polycystic organs) due to the absence of standard reference norms
b. BMI (weight in kilograms/ height in meter squared): It is reasonable to obtain BMI for adults with CKD 1-3 who are clinically stable, to monitor for changes in body weight/ BMI and body composition at least every 6 months.
c. Waist circumference (WC): abdominal adiposity among Asians can be determined by WC of more than 90 cm in men and 80 cm in women.
d. Skinfold thickness measurements can be used to assess body fat for CKD patients in the absence of edema.
e. Hand grip test can be a surrogate measure for muscle strength and protein-nutrition status.

Nutritional status is assessed since poor nutritional intake and obesity are prevalent among patients with CKD. Using a food record/ diary to assess dietary intake of protein and calories is reliable and can provide accurate information as long as the patients are instructed well to record their food intake for at least 7 days. The possibility of underreporting remains a limitation and was seen in 72.5% of CKD patients not requiring dialysis and 52.5% of patients receiving peritoneal dialysis. Some patients may find the measurement of portion sizes cumbersome, limiting the accuracy of the reported data. One tool that can identify patients who would benefit from nutritional intervention is the 7-point Subjective Global Assessment (SGA) tool, combining clinical history, physical examination, and structured clinical parameters. However, this tool is mainly used among patients with CKD stage 5D. Other information to elicit are medication use, knowledge, beliefs, attitudes, access to food, depression, and cognitive function[11].

Measuring body composition is another way of determining a patient's nutritional status[12]. Indirect methods include anthropometric measurements such as height, weight, skinfolds, circumferences; bioelectrical impedance measurements, creatine kinetics, and near-infrared interactance. The gold standard for body composition is Dual-Energy X-Ray Absorptiometry (DXA) but is considered tedious due to labor and machine requirements and the possibility of inaccurate results due to CKD factors such as hydration status. The feasibility in performing these tests were raised during the consensus panel discussion. It was recommended that these tests be offered depending on availability and shared decision making.

Body Mass Index

BMI measurement is recommended at least every 6 months in patients with CKD 1-3[11]. It is simple to perform, quick, and does not require extraordinary equipment or effort. However, BMI is limited by the following - it is not an ideal marker of obesity since it cannot differentiate between adiposity and muscularity; and accuracy depends on regular height and weight monitoring. Evidence is also unclear on CKD mortality among patients who are overweight or obese. Nevertheless, BMI can still be of clinical use because there is an increased risk of CKD progression among individuals who are overweight[13]. BMI also has associations between comorbidities that increase CKD progression such as cardiovascular and other metabolic diseases. Lastly, mortality risk is increased among patients who were underweight but is not associated with being overweight or obese in patients with CKD[14,15].

Waist Circumference

Abdominal adiposity among Asians can be identified through a waist circumference (WC) of more than 90 cm in men and 80 in women[7]. It is associated with metabolic complications that can affect CKD progression. The odds of CKD was also positively associated with increased WC[16]. Among patients on maintenance hemodialysis, the odds of protein-energy wasting and inflammation increase as waist circumference increases[17].

Hand Grip Strength

Hand grip strength (HGS) can be used as a measure of muscle function and indirect measure of nutritional status among patients

with CKD. It was found to be correlated with protein-energy status and functional status hence, was recommended as a surrogate measure among patients with CKD[18-21]. nutritional status and levels of inflammatory markers. All-cause mortality and muscle strength have an inverse relationship wherein mortality rates were high among those with low grip strength[19-21].

KQ2: Among adults with T2DM, what components of the history taking and physical exam should be focused on to recognize other comorbidities / complications?

Recommendations 2.1: Patients with CKD should be evaluated for the possible complications such as malnutrition, anemia, bone and mineral disorder, acid-base and electrolyte imbalance, risks for infection, peripheral artery disease, ASCVD. (*Strong SOR, Very Low QOE*)

Anemia

Anemia is defined as hemoglobin concentration lower than the established cut-off by the World Health Organization, as shown in Table 5[22]. These cut-offs are consistently used in studies of anemia with CKD. It is common in patients with CKD and is associated with poor outcomes. A diagnosis of anemia due to CKD should be considered a diagnosis of exclusion, and thus, evaluation for other possible causes of anemia should be undertaken. The most commonly encountered reversible cause of worsening of anemia not related to CKD is iron deficiency anemia[8]. Common symptoms of anemia in CKD include low energy, fatigue, and decreased physical function, which can cause negative perceived quality of life with associated psychosocial outcomes. In addition, anemia may also present with headaches, dizziness, difficulty breathing, irregular bowel movements, broken/ brittle nails, changes in menstrual pattern, sexual dysfunction and edema. However, clinical symptoms are non-

Table 4. Possible complications of CKD

Complication	Screening tests/Evaluation
Malnutrition	Nutrition screening
Anemia	History: Low energy, fatigue, decreased physical function, headaches, dizziness, difficulty breathing, irregular bowel movements, broken/brittle nails, changes in menstrual pattern, sexual dysfunction, edema Physical Examination (PE): Pallor
Bone and Mineral Disorder	History and PE: advancing age, menopausal status in women, previous osteoporotic fracture, long term glucocorticoid therapy, low body weight (less than 58 kg or 127lbs), parental history of hip fracture, cigarette smoking, excess alcohol consumption, and use of anticonvulsants or benzodiazepines, sedentary lifestyle, poor health or frailty, and low calcium intake, recurrent falls, poor balance and weak quadriceps muscle strength, impaired eyesight, and environmental factors such as slippery floors, poor lighting FRAX or OSTA Score for osteoporosis in the absence of Bone DEXA scan
Acid base and electrolyte imbalance	Signs and symptoms of acidosis such as gastrointestinal losses, medications, and chronic conditions such as diabetes mellitus, hyperventilation
Risks for infection	advanced age, high burden of coexisting illnesses such as diabetes, hypoalbuminemia, immunosuppressive therapy, nephrotic syndrome, uremia, anemia, and malnutrition, and high prevalence of functional disabilities.
Peripheral Artery Disease	exertional leg symptoms (claudication or other walking impairment), ischemic rest pain, and non healing wounds, and vascular examination through inspection of the legs and feet, palpation of lower extremity pulses, and auscultation for femoral bruits Signs and symptoms of atypical leg pain
ASCVD	Patients with established CKD and Diabetes Mellitus type 2 should be considered at high risk or very high risk for developing ASCVD. Patients with very high risk features include the following: a. Documented ASCVD b. T2DM with established ASCVD and/or severe target organ damage i. eGFR < 45 mL/min/1.73m^2 irrespective of albuminuria ii. eGFR 45 59 mL/min/1.73m2 with kg microalbuminuria UACR 30 300mg/g iii. Proteinuria, UACR > 300mg/g iv. Presence of microvascular disease ≥ 3 sites

specific and that diagnostic work-up in patients presenting with fatigue, lack of energy and concentration, or dyspnea should also include non-anemic causes[23]. Pallor can be appreciated during physical examination of the following sites: conjunctivae (sensitivity: 19% - 97%, specificity: 65% - 100%), nailbed (sensitivity: 41% - 65%, specificity: 58% - 93%), and palms (sensitivity: 33% - 91%, specificity: 54% - 93%)24. If at least 2 sites were examined, the collective sensitivity is 26% - 96%, while the specificity is 13-99%.

Table 5. Hemoglobin thresholds in anemia

Age or Gender Group	Hemoglobin Threshold, g/dL (g/L)
Non pregnant females > 15 yo	12.0 (120)
Pregnant females > 15 yo	11.0 (110)
Men > 15 yo	13.0 (130)

Adapted from the World Health Organization. Worldwide prevalence of anaemia 1993-2005: WHO global database on anaemia

Bone and Mineral Disorders

Abnormalities in serum calcium, phosphate, PTH and Vitamin D derivatives progress as kidney function declines. This places patients at increased risk of fractures compared with the general population, with incident hip fractures associated with significant morbidity and mortality. Since these abnormalities appear relatively late in the course of CKD, it is recommended to evaluate these parameters earlier to decrease the burden of illness and improve quality of life[8]. The diagnosis of CKD with Mineral and Bone Disorders (CKD-MBD) is based on demonstrating biochemical abnormalities, bone abnormalities, and vascular calcification. This is difficult to do at the initial consult; however, CKD-MBD may be suspected in patients at high risk for osteoporosis.

Osteoporosis is defined as spinal or hip bone mineral density (BMD) from dual-energy x-ray absorptiometry (DEXA) assessment that is more than or equal to 2.5 standard deviations below the reference mean for young adult females or a T-score of less than or equal to - 2.5[25]. Risk factors identified for osteoporosis include the following: advancing age, menopausal status in women, previous osteoporotic fracture, long-term glucocorticoid therapy, low body weight (less than 58 kg or 127lbs), parental history of hip fracture, cigarette smoking, excess alcohol consumption, and use of anticonvulsants or benzodiazepines. In addition, other risk factors that need to be elicited include sedentary lifestyle, poor health or frailty, and low calcium intake. Other risk factors independent of BMD for fractures include recurrent falls, poor balance and weak quadriceps muscle strength, impaired eyesight and environmental factors such as slippery floors and poor lighting.

The US Preventive Services Task Force (USPSTF) recommends osteoporosis screening in women 65 years and older and post-menopausal women younger than 65 years old who are at increased risk for osteoporosis as determined by a formal clinical risk assessment tool, such as the FRAX. A local study was done to translate and validate the FRAX Tool into Filipino[26]. Modifications were made to account for cultural differences during the translation. The Filipino version of FRAX was acceptable and reliable; however, the study was limited by convenience sampling of patients in a tertiary hospital, and that some of the questionnaires were interviewer-assisted since some patients were unable to read and/or write[26].

According to the 2011 consensus statements on osteoporosis diagnosis, prevention and management in the Philippines, there is moderate quality of evidence in using the Osteoporosis Screening Tool for Asians (OSTA) score to identify an individual's risk for osteoporosis in areas where central DEXA scans are unavailable[27]. The OSTA score relies on age and body weight and has been used to identify people necessitating BMD measurements. The OSTA score can be calculated as 0.2 x (Weight in kg - Age in years). Scores from -20 to -4 are considered at HIGH risk for osteoporosis, -4 to -1 are at MODERATE risk for osteoporosis, while those between -1 to 20 are considered LOW risk for osteoporosis. The validation of OSTA score among Filipinos are as follows: Males - Sensitivity 90%, Specificity 66%, AUC 0.8475; Females - Sensitivity 97%, Specificity 59%, AUC 0.8506[28]. Several studies concluded that results of OSTA are comparable to other indices in identifying patients at risk for osteoporosis and to FRAX and PIO[29,30]. The feasibility in performing these tests were raised during the consensus panel discussion. It was recommended that these tests be offered depending on availability and shared decision making.

Metabolic Acidosis

Metabolic acidosis is common in CKD and can lead to bone demineralization, muscle mass loss, further worsening of renal function and risk of death[8]. Clinical evaluation is directed to elicit potential causes of acid-base disorders such as gastrointestinal losses, medications and chronic conditions such as diabetes mellitus, while physical examination may reveal hyperventilation as a compensatory respiratory alkalosis.

Cardiovascular Disease

Existing studies have shown a strong and independent association between CVD (e.g., acute coronary syndrome, stroke, heart failure, sudden cardiac death) and CKD. There is a 43% increased risk for CVD events in those within CKD 3A (eGFR 45-59 mL/min/1.73m^2), and a 343% increased risk in patients in CKD 5 (eGFR < 15 mL/min/1.73m^2)[8]. In a retrospective study among 218 patients with biopsy-proven chronic kidney disease secondary to type 2 diabetes mellitus, the median 10-year ASCVD risk score was 14.1%, with ASCVD risk scores of 10.9%, 12.3%, 16.5% and 14.8%, for CKD stage 1, 2, 3 and 4, respectively (p-value of 0.268). Patients with higher ASCVD risk were noted to have lower eGFR, higher systolic blood pressure and more severe renal interstitial inflammation. On multivariate logistic analysis, high ASCVD risk (> 14.1%) is an independent risk factor for renal dysfunction (OR 3.997, 95% CI 1.385 - 11.530, p = 0.010) but not for end-stage renal disease. Patients with CKD stage 1 secondary to type 2 diabetes mellitus had comparable ASCVD risk scores to patients in

the later stages[31]. The presence of higher ASCVD risk indicates severe renal insufficiency but does not necessarily indicate a prognosis for renal outcomes. In a systematic review, other risk factors including left ventricular hypertrophy HR 1.78, CI 1.354 - 2.351, p<0.001; serum albumin HR 0.624, CI 0.519 - 0.749, p<0,001; hemoglobin HR 0.901, CI 0.856 - 0.948, p<0.001; phosphate HR 1.198, CI 1.084 - 1.325, p<0.001; and, urate HR 1.068, CI 1.021 - 1.117, p<0.004) have been shown to have a significant effect on combined CV events (e.g., acute coronary syndrome, congestive heart failure and ischemic stroke) and thus, need to be also assessed. The 2021 European Society of Cardiology guideline recommends that systematic global CVD risk assessment should be done in any patient with major cardiovascular risk factor (e.g., family history of premature CVD, FH, CVD risk factors such as smoking, arterial hypertension, DM, raised lipid level, obesity, or comorbidities increasing CVD risk) (*Recommendation Class I, Level C*). CKD are only classified as either high risk or very high risk for developing CVD. (*Recommendation I, Class A*). Patients at very high risk for ASCVD include adults with T2DM and severe target damage: with eGFRA eGFR < 45 mL/min/1.73m^2 irrespective of albuminuria, eGFR 45-59 mL/min/1.73m^2 with microalbuminuria UACR 30-300mg/g, Proteinuria, UACR > 300mg/g and presence of microvascular disease ≥ 3 sites. It should be noted though that the guideline used Europeans as its population.

Peripheral Arterial Disease

The KDIGO recommends that adults with CKD be regularly examined for signs of peripheral arterial disease (PAD) with consideration for usual approaches to therapy and that adults with CKD and diabetes mellitus should be offered regular podiatric assessment[8]. Similarly, the 2016 AHA/ACC guidelines recommended patients with increased risk for PAD to undergo a comprehensive assessment to check for exertional leg symptoms (claudication or other walking impairment), ischemic rest pain and non-healing wounds, and vascular examination through inspection of the legs and feet, palpation of lower extremity pulses, and auscultation for femoral bruits[32]. Patients with features suggestive of PAD should undergo resting ankle-brachial index (ABI) with or without segmental pressures and waveforms, and results should be reported as abnormal (ABI ≤ 0.90), borderline (ABI 0.91 - 0.99), or non-compressible (ABI > 1.40). Measurement of ABI is reasonable In patients without features of but are at increased risk for developing PAD. In 2020, the Asia-Pacific Peripheral Artery Disease Consensus Statement Technical Working Group included additional physical examination findings - extremity atrophy, hair loss and brittle nails, albeit with poor sensitivity for PAD[33]. Atypical symptoms that may contribute to the diagnosis of PAD are shown in Table 6 (AHA, 2015). Leg pain on exertion and rest, which begins at rest must be distinguished from the rest pain of critical limb ischemia[34].

Risk for Infections

Patients with CKD are at risk for bacterial infections (e.g., urinary tract infection, pneumonia, sepsis) due to alterations in primary host defense8. Risk factors for infection in people with CKD include advanced age, high burden of coexisting illnesses such as diabetes, hypoalbuminemia, immunosuppressive therapy, nephrotic syndrome, uremia, anemia and malnutrition, and high prevalence of functional disabilities. Vaccination status should be assessed since there is evidence that vaccination is underutilized as an infection prevention strategy in CKD and ESRD patients. Current studies have been limited by small study sizes with variability in subject follow-up and ascertainment of vaccine effectivity. Vaccination with influenza vaccine and pneumococcal vaccine is recommended. Hepatitis B vaccination is recommended for patients likely to require renal replacement therapy.

Table 6. Atypical leg pain in peripheral arterial disease[34]

	Leg Pain/ Carry On	Leg Pain on Exertion and Rest
Leg symptom features	Exertional leg pain that does not stop the patient from continuing to work	Exertional leg pain that sometimes begins at rest among PAD patients without critical limb ischemia
Prevalence among people with PAD	~ 10%	~ 20%
Clinical characteristics when compared with people with intermittent claudication	Fewer depressive symptoms Higher ABI values	Higher prevalence: DM, Spinal Stenosis Reduced peripheral sensation Greater number of comorbidities
Functional impairment when compared with people with intermittent claudication	Data are mixed with some evidence for less functional impairment, and some showing no difference compared with PAD patients with claudication	Greater functional impairment Faster functional decline

Adapted from McDermott, Mary McGrae. "Lower extremity manifestations of peripheral artery disease: the pathophysiologic and functional implications of leg ischemia." Circulation research vol. 116,9 (2015): 1540-50. doi:10.1161/CIRCRESAHA.114.303517

KQ3: What components of the psychosocial history should be elicited to guide management of adults with T2DM and CKD?

Recommendation 3.1: Assess for the psychosocial factors related to CKD such as baseline knowledge on CKD, family and community resources, coping mechanisms, and patient preference. (Strong SOR, Very Low QOE)

T2DM patients with CKD should be assessed for psychosocial factors related to DKD. This may include the following in order to properly assess their condition and guide in formulating a management plan:

a. Baseline knowledge on CKD and disease progression, including misperceptions, thoughts and feelings associated with the disease
b. Familial and extrafamilial resources, including sources of financial support
c. Existing coping mechanisms
d. How the patient wishes to be managed, including restrictions

Recommendation 3.2: Utilize appropriate family assessment tools in patients with T2DM and DKD to guide in formulating a management plan. These tools can be done over several patient visits. (Strong SOR, Very Low QOE):

a. Genogram
b. Family map
c. Family APGAR
d. SCREEM/SCREEM-RES
e. Family lifeline
f. Ecomap

In an observational study among 6972 patients with Type 2 Diabetes Mellitus without microalbuminuria from the Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial (ONTARGET, 2015) that have diabetes mellitus without microalbuminuria, lifestyle and social factors were found to be associated with the progression of diabetes-related chronic kidney disease and lifestyle/ social factors. High social network score, high physical activity and moderate alcohol intake were associated with less decrease in glomerular filtration rate, and less increase in albuminuria[35].

A thematic synthesis of 7 studies (2022) on the psychosocial needs of CKD patients without renal replacement therapy (RRT) (n 130) identified 5 themes: (1) *addressing patient's CKD-related educational needs*, (2) *supporting the patient's relationships*, (3) *honoring the patient's need for control*, (4) *adjusting to change, and* (5) *recognizing fear of disease and treatment*[36]. Of the 7 studies that were included, 5 studies had participants without RRT (N= 62), 1 study had participants with AKI stage 3D (N = 47), and 1 study had participants across the stages of CKD. Informing patients about their condition was noted to improve their quality of life, decrease disease-related stress and enhance their self-management skills. Poor knowledge was attributed to insufficient information shared, and lack of shared information from the health team. The patients were not given sufficient time to ask questions and discuss concerns about the information shared to them causing frustration. It was recommended to give reading materials and video guides as an adjunct to clinical-led education rather than it being primarily the source of information. The study also highlighted the need to mobilize intrafamilial and extrafamilial support systems. The patient's peers or other patients with progressed CKD also influences the decision to undergo RRT. The experiences of the patient's peers help shape their expectations as the disease progresses. In addition, peers also serve as a coping mechanism offering emotional and psychosocial support, and hope. The patient's family and friends serve as decision and treatment partners offering support. In other cases, patients may feel guilt as they see themselves as a burden to their families. The study noted that the patients valued respecting their autonomy in making treatment related decisions, which aided in promoting self-efficacy and adherence to treatment. Some patients noted that they felt helpless and that their choice in the treatment did not matter to the attending healthcare team. The impact of the diagnosis of CKD to patients varies depending on the stage of the disease. Some patients would receive the diagnosis as a traumatic experience and undergo a grieving process. Denial of the illness and its progression prompts patients to use pathologic coping mechanisms to adjust to the illness, delaying medical management. Some patients also believed that RRT would affect their lives and their mental health. There was anxiety in the inevitability of the progression of CKD. The health condition affected their *financial security, social life, career and ability to have children*. On the other hand, acceptance of the disease promoted improved quality of life and increased hope[36].

During the consensus panel discussion, concerns regarding feasibility and acceptability to all key stakeholders were raised since the use of family assessment tools may not be applicable in all care settings especially those with high volume of patients. It was recommended that these tools be administered over several visits.

Diagnostic Tests

KQ4: Among adults with T2DM, what tests are recommended in the diagnosis and evaluation of CKD?

Recommendation 4.1: Request for urine albumin AND estimated glomerular filtration rate (eGFR) using serum creatinine among adults with type 2 diabetes during the first visit and annually thereafter. (Strong SOR, Moderate QOE)

Nephropathy may be diagnosed if there is either decrease in eGFR or if there is presence of kidney damage, such as seen with an assessment of albuminuria, all of which may be causing predicaments to health. Presence of nephropathy for more than 3 months (>90 days) indicates a chronic kidney condition. Evaluation of nephropathy may be by classification based on cause, GFR category and albuminuria category[37].

eGFR is widely accepted as the most useful overall index of kidney function and is estimated using serum creatinine and a GFR estimating equation. The preferred computation to be used is the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation[37,38]. Formula for estimation of GFR is seen in the next page; an online

calculator for CKD-EPI is available at nkdep.nih.gov[7]. THE 2009 CKD-EPI creatinine equation includes creatinine, age, race and sex[39]. The 2021 CKD-EPI equation[40] was refitted without race and is considered to underestimate the eGFR for black patients while overestimating it for non-blacks. Thus, the 2009 CKD-EPI creatinine equation is more accurate for the non-black race population.[38]

Testing for eGFR during the first visit aids as well with clinicians' decision on choosing glycemic lowering agents: such as use of sodium–glucose cotransporter-2 inhibitors (SGLT2i) for patients with eGFR ≥20 ml/min per 1.73 m^2; or mineralocorticoid receptor antagonists (MRA) for those with eGFR ≥25 ml/min per 1.73 m^2; or metformin for those with eGFR >30 ml/min per 1.73 m^2. A GFR of <60 ml/min/1.73m^2 (Stage G3a or less) is considered as abnormal and if persistent up to 3 months allows diagnosis of a chronic kidney disease[37,38]. Table 11 shows staging of CKD by GFR.

Cystatin C may be requested for adults with estimated GFR of 45-59 ml/min/1.73m^2 (G3a) to compute for eGFRcys/eGFRcreat-cys, with which CKD is confirmed if results are <60 ml/min/1.73m^2. For patients who are on metformin and are obese, malnourished, cancer patients, with heart failure, with liver cirrhosis, smoking or on steroids, use cystatin C in estimating GFR[7].

Albuminuria may be measured through a random spot urine collection of urinary albumin-to-creatinine ratio (uACR). Relationship of high levels of proteinuria and signs and symptoms of nephrotic syndrome is well known. Spot collections are less expensive but susceptible to false-negative and false positive, but 24hr urine collection are more burdensome and add little to no prediction to accuracy[7]. However, the first morning void in the midstream is recommended[37].

A measurement of urine albumin of ≥ 30 mg/g (moderately increased uACR) may indicate CKD and is a strong predictor of renal impairment progression. If uACR is unavailable, the use of urine Protein-to-Creatinine ratio (PCR) or reagent strip urinalysis (Urine Micral Test) may still be used for assessment of albuminuria especially in remote areas where diagnostic centers are difficult to find[37,7] However, one must note that the use of reagent strips is less accurate than laboratory measurements due to factors that may affect the strip such as concentrated urine, alkalinize urine, or presence of ammonium and other colored compounds[37].

Table 7. Formula for GFR

CKD-EPI 2009[39]

$$GFR = 141 \times \min(Scr/\kappa, 1)^{\alpha} \times \max(Scr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018 \text{ [if female]} \_ 1.159 \text{ [if black]}$$

Note: Scr = serum creatinine; κ = 0.9 for male, 0.7 for female; α = -0.411 for males, -0.329 for females; min = minimum of Scr/κ or max = maximum of Scr/κ or 1.

Source: Levy, et al. (2009). A new equation to estimate glomerular filtration rate. Ann Intern Med. 2009 May 5;150(9):604-12. doi 10.7326/0003-4819-150-9-200905050-00006

CKD-EPI 2021[40]

$$GFR = 142 \times \min(Scr/\kappa, 1)^{\alpha} \times \max(Scr/\kappa, 1)^{-1.209} \times 0.9938^{Age} \times 1.012 \text{ [if female]}$$

Note: Scr = serum creatinine; κ = 0.9 for male, 0.7 for female; α = -0.302 for males, -0.241 for females; min = minimum of Scr/κ or max = maximum of Scr/κ or 1.

Source: Inker LA, et al. New creatinine- and cystatin c–based equations to estimate GFR without race. doi:10.1056/NEJMoa2102953

Table 8. Staging of CKD by GFR

G1	≥ 90 ml/min/1.73m^2	Normal or High
G2	60-89 ml/min/1.73m^2	Mildly decreased
G3a	45-59 ml/min/1.73m^2	Mildly to moderately decreased
G3b	30-44 ml/min/1.73m^2	Moderately to severely decreased
G4	15-29 ml/min/1.73m^2	Severely decreased
G5	<15 ml/min/1.73m^2	Kidney Failure

Source: KDIGO, 2012

Table 9. Staging by albuminuria using uACR: (KDIGO 2012)

A1	<30mg/g OR <3mg/mmol	Normal to mildly increased
A2	30-300mg/g OR 3-30mg/mmol	Moderately increased
A3	>300mg/g OR >30mg/mmol	Severely increased

Recommendation 4.2: Offer imaging studies based on individualized need for patient management, and if available (Strong SOR, Moderate QOE)

Establishing a cause for kidney damage may be done based on clinical assessment and additional tests are not recommended for routine use. Additional diagnostic tests may include imaging studies (such as kidney ultrasound), kidney biopsy, and other laboratory tests to check for urine sediment abnormalities (urinalysis with renal tubular cells, red blood cell casts, white blood cell casts, coarse granular casts, wide casts, and large numbers of dysmorphic RBC), and electrolyte imbalances. When indicated based on clinical assessment, kidney ultrasound may be used to assess kidney shape, symmetry, and evidence of obstruction. Presence of nephrolithiasis warrants referral to a specialist service. Testing for electrolyte imbalances during the first visit may be done if clinically warranted[37].

KQ5: Among adults with T2DM and CKD, what tests should be used to monitor treatment response?

Recommendation 5: Request for repeat urine albumin and serum creatinine (for GFR estimation) based on individual risk for progression and HbA1c to assess for glycemic control (Strong SOR, Moderate QOE)

The goal of treatment in adults with T2DM and CKD is improvement of signs and symptoms of CKD and prevention of progression of disease. Monitoring must be done with diagnostic levels to be seen as constant, if not improving, in mind. In order to monitor for treatment response, testing should be done at least annually regardless of ongoing management[37,7]. However, monitoring can be more frequent based on the individual risk for progression. KDIGO recommends at least twice per year for patients at high risk and at least thrice per year for those who are at very high risk (Figure 1).

Green reflects CKD with normal eGFR and ACR and requires follow-up measurements annually. Cautious measurement is required in yellow and is for testing at least once a year. As eGFR and ACR progress, more frequent testing is advised such as twice a year for orange, three times per year for red, and four times per year for dark red[38].

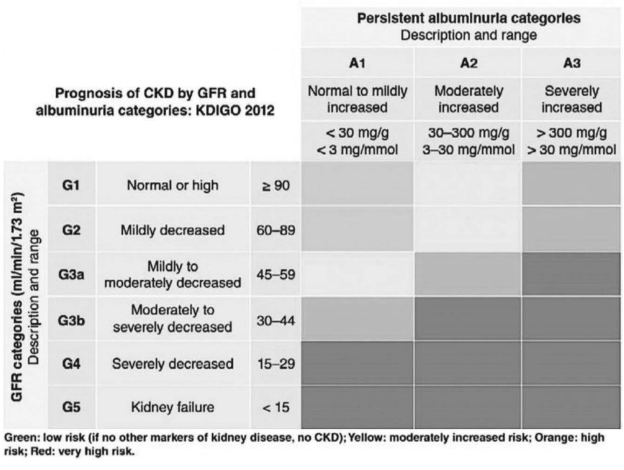


Figure 1. Prognosis of CKD by GFR and Albuminuria Category

For patients on Metformin, eGFR is monitored annually if it is more than or equal to 60 ml/min per 1.73 m^2 and at least every 3-6 months when the eGFR is 30-59 ml/min per 1.73 m^2.[37] For those on SGLT-2 inhibitors, routine assessment of renal function (creatinine and/or eGFR) is not recommended within 6-8 weeks of SGLT-2 initiation since there is likely to be a transient deterioration[42]. Testing for serum potassium during the first visit is beneficial for patients who will be started on certain medications (such as nonsteroidal MRA)[37]. Patients with CKD are at increased risk to develop cardiovascular conditions.

Glycemic control is associated with delay in progression of chronic kidney disease and reduction in risk of other micro and macrovascular complications in patients with T2DM. KDIGO (2022)[41] recommends using hemoglobin A1C (HbA1C) to monitor glycemic control at least twice a year. As CKD progresses, the presence of anemia should be considered and assessed for when using HbA1c to evaluate glycemic control.[42]

KQ6: Among adults with T2DM and CKD, what tests should be used to assess for comorbidities and complications?

Recommendation 6: Offer the following laboratory tests to assess for comorbidities and complications of CKD in adults with type 2 diabetes and CKD:

A. Total cholesterol, LDL, HDL and triglycerides to guide with management and to assess for presence of other comorbidities. (Strong SOR, Low QOE)

Lipid profile testing during the first visit serves to establish diagnosis of severe hypercholesterolemia or hypertriglyceridemia, which may be factors in assessment of cardiovascular risk of a patient[43]. Fasting triglyceride (FT) levels above 11.3mmol/L (1000 mg/dL) or LDL-C above 4.9mmol/L (190 mg/dL) should prompt referral to specialist for further evaluation[37].

There is no direct evidence that routine measurement and monitoring of fasting lipids will improve treatment outcomes, and are therefore not recommended[37]. Since cardiovascular risk assessment (done annually) is now the primary indication to initiate or adjust lipid-lowering agents, testing after initial measurement may not be needed in most patients. However, if warranted, lipid profile may be rechecked after 4-12 weeks of initiation or change of lipid lowering agents, then annually after for monitoring of response to therapy or, may be reassessed after 6-8 weeks for those who were just started with statins according to Philippine Dyslipidemia Guidelines, 2020 7,[44].

B. Hemoglobin level to assess for anemia. (Strong SOR, Moderate QOE)

In the absence of use of erythropoiesis-stimulating agents (ESAs), there may be a gradual decline in Hb over time in patients with CKD as the level of GFR declines, suggesting the need for regular surveillance of Hb concentration. As kidney function

declines and in patients with more advanced CKD stages, the incidence and prevalence of anemia increases[37]. Anemia is considered as hemoglobin <12 g/dL in men; <11 g/dL in women in patients with eGFR <60 ml/min/1.73m^2. Checking for anemia is also recommended when using HBa1C as a measure of glycemic control7. Once a year testing may be done to screen for anemia, and more frequent if abnormal[45].

C. eGFR and serum electrolytes regularly, in patients concurrently on potentially nephrotoxic agents. (Strong SOR, Moderate QOE)

There are medicines whose toxicity is worsened in acute illness particularly in a setting of dehydration such as diarrhea and vomiting. General advice about appropriate dosing and when to restart these agents should be given to people taking these drugs during intercurrent illness, together with a recommendation for consultation with a health-care professional as soon as possible[37]. Other cases where eGFR must be checked are with patients who are taking nephrotoxic drugs, and patients who underwent radiocontrast. Especially with patients with <60 ml/min/1.73m^2, GFR must be measured 48-96 hrs after the procedure[37].

D. Serum calcium, phosphate, PTH and alkaline phosphatase activity in patients with GFR <60 ml/min/1.73m^2 (G3a or lower) to establish a possibility of bone and mineral disorder. (Strong SOR, Moderate QOE)

As kidney function declines, abnormalities of serum calcium, phosphate, and circulating hormones related to CKD-Mineral and Bone Disorder progress[7]. Calcium and phosphate levels should be monitored once for stage 3a/b, and once every 12 months for stage 4 and 5[42]. Abnormalities in calcium and phosphate levels occur relatively later during the course of nephropathy. Patients with elevated levels of calcium and phosphate have higher mortality with or without elevation in PTH levels. Alkaline phosphatase levels should be maintained within the local laboratory range values[37]. Testing for alkaline phosphatase should be done once for stage 3a/b, and once every 12 months for stage 4 and 5[7,44].

It is suggested that for patients with PTH above the normal upper limit should be evaluated for hyperphosphatemia, hypocalcemia, and vitamin D deficiency, all of which can be life threatening for patients with chronic kidney conditions. Testing for PTH levels should be done once as indicated for stage 3a/b, every 3 to 6 months for stage 4, and every 1 to 3 months for stage 5[7,44].

Decreased bone mass and changes in bone microarchitecture occur early in CKD and worsen with progression of disease such that patients with CKD are at increased risk of bone fracture. Although fracture rates and fracture-related mortality are elevated in CKD, bone densitometry does not reliably predict fracture risk in patients with GFR <45 ml/min/1.73 m^2.[37] Clinicians are encouraged to use clinical tools If considering osteoporosis such as FRAX score. If renal mineral and bone disorder are highly suspected, refer instead to a nephrologist and/or endocrinologist[44].

E. Diagnostic work-up for underlying cardiac disease in those with related signs and symptoms, that follows recommendations from locally accepted guidelines. (Strong SOR, Moderate QOE)

Patients who come in for the first visit with cardiovascular risks must be advised for assessment for conditions affecting the heart and other organs. Clinicians must be aware of local guidelines and the accordant timing of requesting for procedures (such as electrocardiogram, exercise ECG, and/or echocardiography). Cardiovascular risk should be assessed annually in most patients with CKD since benefits to treatment are likely to accrue over years rather than months[37]. Routine screening for coronary artery disease is not recommended for asymptomatic patients as it does not improve outcomes[7]. Consider investigation for coronary artery diseases in DM patients with: 1. atypical cardiac symptoms (chest discomfort or unexplained dyspnea); 2. symptoms associated with vascular diseases (presence of bruit, claudication, transient ischemic attack, stroke, or peripheral arterial disease); and 3. abnormal electrocardiogram findings (Q waves). Testing may be done by using exercise ECG with or without Echocardiography.

Testing for coronary artery calcium (an independent predictor of ASCVD events) is also reasonable for adults $\geq$ 40 years of age with diabetes but not recommended routinely due to radiation exposure. It must be advised that for adult patients with CKD who would undergo BNP/N-terminal-proBNP (NT-proBNP) and troponin testing, interpretations of results must be done with caution prior to diagnosing heart failure and acute coronary syndrome[37].

F. Repeat serum creatinine and potassium 2-4 weeks after initiation or increase in dose of RASi (ACEi or ARBs), MRA, nsMRA, and diuretics. (Strong SOR, Very Low QOE)

For type 2 diabetic patients with nephropathy and being treated with ACEi or ARB, test for serum creatinine and serum potassium within 2–4 weeks of initiation or increase in the dose of an ACEi or ARB[7,38]. If serum creatinine increases by 30% from baseline within 4 months, it is advisable to discontinue ACEi or ARBs[7,38]. An imaging study (doppler ultrasound) may be advisable to check for renal artery stenosis in cases of elevation of creatinine after initiation of ACEi or ARBS[37]. If mineralocorticoid receptor antagonists are used, monitor for serum potassium regularly to check for hyperkalemia[37]. If diuretics are used, monitor for serum potassium to check for hypokalemia[7].

G. Vit B level for those on Metformin for 4 years or longer, if available (Moderate SOR, Low QOE)

Metformin treatment was associated with a mean reduction of vitamin B12 concentration compared to placebo after approximately 4 years[7]. Initial lab tests for vitamin B12 deficiency may include CBC with peripheral blood smear, serum B12, and folate levels.[46] However, consequences of vitamin B12

deficiency and metformin treatment is uncommon and judgement for management will not change. One consensus panel member raised the use of RBC indices, being more available and less costly, in assessing for Vit B deficiency, with enlarged RBCs (high Mean Corpuscular Volume) possibly indicating megaloblastic anemia.

Pharmacologic Treatment

KQ7: Among adults with T2DM and CKD, what medications are effective in achieving glycemic targets and preventing or delaying progression of CKD?

Recommendation 7.1: Initiate the following to achieve glycemic targets and prevent or delay the progression of CKD (Strong SOR, Moderate QOE):

a. Sodium-glucose cotransporter 2 inhibitors (SGLT2i) with primary evidence of reducing CKD progression for patients with eGFR ≥20 ml/min per 1.73 m²

b. Metformin for patients with T2D, CKD with an eGFR ≥30 ml/min per 1.73 m²

SGLT2 inhibitors are recommended to reduce chronic kidney disease progression and cardiovascular events in patients with an estimated glomerular filtration rate ≥20 ml/min per 1.73 m² and with urine ACR ≥200 mg/g (≥20 mg/mmol)[38]. Several significant cardiovascular trials conducted on individuals with type 2 diabetes who are at a high risk for cardiovascular disease (CVD) or already have CVD, investigated the impact on the kidneys as a secondary outcome. The trials mentioned are EMPA-REG OUTCOME and CANVAS. EMPA-REG OUTCOME is the Empagliflozin Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients. Compared to a placebo, empagliflozin reduced the risk of incident or worsening nephropathy by 39%. This composite outcome included progression to UACR >300 mg/g creatinine, doubling of serum creatinine, end-stage renal disease (ESRD), or death from ESRD. It also lowered the risk of doubling of serum creatinine accompanied by a decreased estimated glomerular filtration rate (eGFR) ≤45 mL/min/1.73 m² by 44%. CANVAS is the Canagliflozin Cardiovascular Assessment Study. Canagliflozin decreased the risk of progression of albuminuria by 27%. Albuminuria often indicates kidney damage or dysfunction. Additionally, it reduced the risk of reduction in eGFR, ESRD, or death from ESRD by 40%. Each of these medications showed statistically significant reductions in various aspects of kidney-related complications among individuals with type 2 diabetes when compared to a placebo[47].

Metformin can be used in patients with diabetic nephropathy, but its use is limited to those with an eGFR ≥30 mL/min/1.73 m², with dose adjustments for eGFR 30–44 mL/min/1.73 m², and it should be discontinued if eGFR falls below 30 mL/min/1.73 m² (See Figure 1)[41]. While metformin is effective in glycemic control and cardiovascular risk reduction, there is no direct evidence from the mentioned resources that it delays the progression of nephropathy.

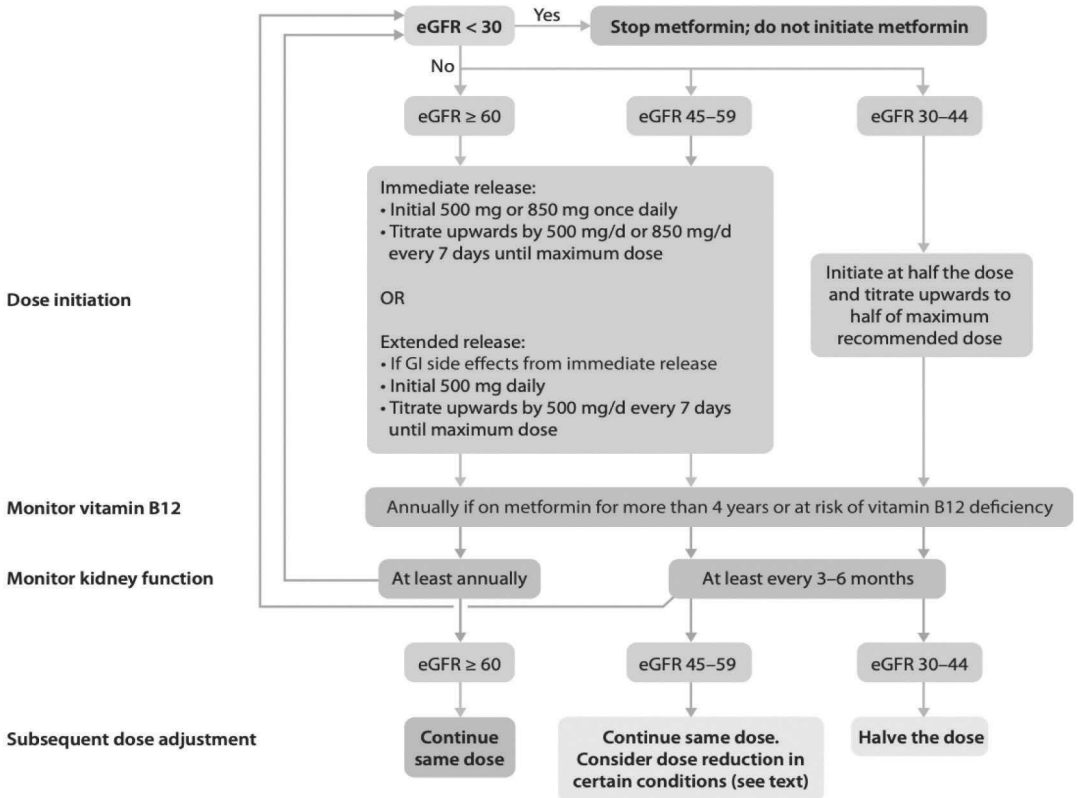


Figure 2. Suggested approach in dosing metformin based on the level of kidney function (KDIGO, 2022)

KQ8: Among adults with T2DM and CKD who have not achieved individualized glycemic targets despite the use of metformin and SGLT2i, what additional medication/s are effective in achieving glycemic targets and preventing or delaying the progression of CKD?

Recommendation 8.1: Offer Long acting GLP-1 RA with proven CKD benefit 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. (Strong SOR, High QOE)

Several clinical trials, such as the LEADER and SUSTAIN-6 trials, have demonstrated cardiovascular and renal benefits of long-acting GLP-1 RAs in patients with T2D and CKD[38,47]. Long-acting GLP-1 Ras are additional treatment options for patients with T2D and CKD who have not achieved their glycemic targets despite using metformin and SGLT2 inhibitors. They have shown efficacy in reducing blood glucose levels, promoting weight loss, and improving cardiovascular outcomes, including reducing the risk of major adverse cardiovascular events.

LEADER is the Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results. Liraglutide mitigated the risk of new or worsening nephropathy by 22%. This composite outcome encompassed persistent macroalbuminuria, doubling of serum creatinine, ESRD, or death from ESRD. SUSTAIN-6 is the Trial to Evaluate Cardiovascular and Other Long-term Outcomes With Semaglutide in Subjects With Type 2 Diabetes 1. Semaglutide decreased the risk of new or worsening nephropathy by 36%. This composite outcome included persistent high levels of urinary albumin, doubling of serum creatinine, or ESRD.

KQ9. Among adults with T2DM and CKD, what additional medications are effective in reducing cardiovascular risk and delay progression of CKD?

Recommendation 9.1: Offer ACE inhibitor or angiotensin receptor blocker for treatment of hypertension to reduce cardiovascular risk and delay progression of CKD (*Strong SOR, High QOE*)

According to 2023 ADA Standard of Care for Diabetes, ACE inhibitors or angiotensin receptor blockers (ARBs) are recommended for patients with modestly elevated urinary albumin to creatinine ratio (30-299 mg/g creatinine). They are strongly recommended for patients with a urinary albumin to creatinine ratio of 300 mg/g creatinine or higher and/or an estimated glomerular filtration rate (eGFR) less than 60 mL/min/1.73 m^2. These medications should be titrated to the highest approved dose that is tolerated. ACE inhibitors and ARBs are commonly used in patients with chronic kidney disease (CKD) due to their reno-protective effects, exerted by blocking the renin-angiotensin-aldosterone system, which plays a crucial role in regulating blood pressure and kidney function. These two (2) drugs are the recommended first-line treatment for hypertension in people with diabetes and urinary albumin-to-creatinine ratio ≥300 mg/g creatinine (A) or 30-299 mg/g creatinine. This range indicates the presence of mild to moderate albuminuria, which is an early sign of kidney damage. They have been shown to reduce proteinuria, slow the progression of CKD, and decrease the risk of cardiovascular events. Treatment with ACE inhibitors or ARBs can help reduce proteinuria and potentially slow the progression of CKD in this population. These medications have been shown to also have substantial reno-protective effects in patients with advanced kidney disease[47].

It is recommended to titrate ACE inhibitors or ARBs to the highest approved dose that is tolerated by the patient. This allows for optimal reno-protective effects and may further reduce proteinuria and slow the progression of CKD. However, dose adjustments should be made based on individual patient factors, including blood pressure control and tolerability. Nevertheless, it is not recommended to use combinations of ACE inhibitors and angiotensin receptor blockers, as well as combinations of ACE inhibitors or angiotensin receptor blockers with direct renin inhibitors because of associated increased occurrence of adverse events, specifically hyperkalemia, syncope, and acute kidney injury (AKI)[47]. If hypertension remains uncontrolled despite maximizing medications, referral to appropriate specialists is warranted.

KQ10: Among adults with T2DM, CKD, and established ASCVD or heart failure, what medications are recommended for cardiovascular and kidney risk reduction?

Recommendation 10.1: Initiate a sodium-glucose cotransporter 2 inhibitor with proven benefit in patients with type 2 diabetes and established heart failure to reduce the risk of worsening heart failure and cardiovascular death. Offer combined therapy with a sodium-glucose co-transporter 2 inhibitor (SGLT2i) and a glucagon-like peptide 1 receptor agonist (GLP1 RA) with demonstrated cardiovascular benefit in patients with type 2 diabetes and CKD and established atherosclerotic cardiovascular disease (ASCVD) or multiple risk factors for atherosclerotic cardiovascular disease. (*Strong SOR, High QOE*)

Heart failure which may develop in as many as 50% of patients with type 2 diabetes, is associated with increased morbidity and mortality and thus, contribute independently to adverse outcomes. Several large clinical trials have shown benefit with use of SGLT2 inhibitors in terms of reduction in cardiovascular death and hospitalization for heart failure.[7] In particular, the CREDENCE trial with Canagliflozin showed a 39% reduction in hospitalization for heart failure and a 31% reduction in composite outcomes of hospitalization for heart failure and cardiovascular death, in a population of patients with diabetic kidney disease with albuminuria.[7]

A combined therapy approach with a sodium-glucose co-transporter 2 inhibitor (SGLT2i) with demonstrated cardiovascular benefit and a glucagon-like peptide 1 receptor agonist (GLP1 RA) with demonstrated cardiovascular benefit may be considered for reducing the risk of adverse cardiovascular and kidney events in patients with type 2 diabetes and established atherosclerotic cardiovascular disease (ASCVD) or multiple risk factors for ASCVD for additive reduction in the risk of adverse cardiovascular and kidney events.[7] Multiple clinical trials, such

as EMPA-REG OUTCOME, CANVAS Program, and DECLARE-TIMI 58, have demonstrated that SGLT2 inhibitors reduce the risk of major adverse cardiovascular events (MACE) in patients with type 2 diabetes and established ASCVD or multiple risk factors for ASCVD. These medications have shown significant benefits in reducing the risk of cardiovascular death, heart failure hospitalization, and renal events. Likewise, several clinical trials, including LEADER, SUSTAIN-6, and REWIND, have shown that GLP1 receptor agonists provide cardiovascular benefits in patients with type 2 diabetes. These medications have been associated with a reduction in MACE, cardiovascular death, and stroke. Combining an SGLT2 inhibitor with demonstrated cardiovascular benefit and a GLP1 receptor agonist with demonstrated cardiovascular benefit has shown potential for additive reduction in the risk of adverse cardiovascular and kidney events. The complementary mechanisms of action of these two classes of medications may provide additional benefits beyond what each medication offers individually. However, long term studies are still needed to strengthen the claim[48].

Table 10. Summary of drugs with known benefits among with patients with CKD with concomitant heart failure and ASCVD risk

	Outcome with Known Benefit	
Drug Class	Heart Failure	ASCVD Risk
SGLT2is	Empagliflozin Canagliflozin Dapagliflozin Ertugliflozin	Empagliflozin Canagliflozin
GLP-1	-	Dulaglutide Liraglutide Semaglutide

Recommendation 10.2: Offer non-steroidal Mineralocorticoid Receptor Antagonists (eg. Finerenone) to adults with type 2 diabetes and CKD with concomitant heart failure who are at increased risk for cardiovascular events or chronic kidney disease progression and unable to use an SGLT2 inhibitor. (*Strong SOR, High QOE*)

The FIDELIO-DKD and FIGARO-DKD trials, have demonstrated that finerenone, a non-steroidal mineralocorticoid receptor antagonist, reduces the risk of cardiovascular events and slows the progression of kidney disease in patients with CKD and type 2 diabetes. A pooled analysis of more than 10,000 patients with type 2 diabetes and CKD from the 2 trials showed a significant reduction in composite outcomes of cardiovascular death, non-fatal MI, nonfatal stroke and hospitalization for heart failure as well as in sustained decrease in eGFR or renal death[7]. The availability of finerenone or other specific mineralocorticoid receptor antagonists may vary depending on the region and specific regulatory approvals. It is important to consult local formularies, guidelines, and healthcare providers to determine the availability and access to these medications in a particular healthcare setting.

KQ11: Among adults with T2DM with CKD, what additional medication/s therapy (based on intensity) is indicated for the primary prevention of atherosclerotic cardiovascular diseases?

Recommendation 11: Initiate statin therapy, in addition to lifestyle therapy among patients with T2DM and CKD, to achieve target levels. Titration and target reduction are individualized based on clinical profile and risk stratification (*Strong SOR, Moderate QOE*)

The use of statins has been extensively studied in individuals with T2DM[44,47]. Statins have been shown to reduce LDL cholesterol levels, decrease the risk of cardiovascular events, and improve overall cardiovascular outcomes in this population. Hence, ADA recommended starting statin therapy among patients with diabetes but intensity differs based on target reduction. The intensity of statin therapy refers to the magnitude of LDL cholesterol reduction achieved with a specific statin dosage. High-intensity statin therapy is associated with greater LDL cholesterol reduction and cardiovascular risk reduction compared to moderate-intensity statin therapy. Table 11 below categorizes different statins according to intensity.

Table 11. List of Statin drugs with associated intensity based on the Philippine guidelines for dyslipidemia

Treatment Intensity	**%LDL-C reduction**	**Drug Regimen**
Low Intensity	<30%	Fluvastatin 20-40 mg Pravastatin 10-20 mg Simvastatin 10 mg
Moderate Intensity	30%-50%	Atorvastatin 10-20 mg Fluvastatin 80 mg Rosuvastatin 5-10 mg Simvastatin 20-40 mg Pravastatin 40-80 mg Pitavastatin 2-4 mg
High Intensity	>50%	Atorvastatin 40-80 mg Rosuvastatin 20-40 mg

Treatment decisions regarding statin therapy should be based on a comprehensive assessment of each patient's cardiovascular risk factors, including age, presence of ASCVD, and estimated 10-year ASCVD risk. The individual's tolerance, potential side effects, and preferences should also be considered. For the Filipino population, the 2020 clinical practice guidelines for the management of dyslipidemia outlines individualized targets for different populations (Table 12).

It is important for patients to engage in shared decision-making with their healthcare provider to determine the most appropriate statin therapy regimen based on their specific clinical characteristics, risk factors, and treatment goals. Regular monitoring and follow-up are essential to assess treatment response and make any necessary adjustments.

KQ12. Among adults with T2DM and CKD, what additional medications are effective in delaying progression of CKD?

Recommendation 12.1: Offer Ketoanalogue supplementation with low protein diet to patients with higher eGFR (≥30ml/ min/1.73m2) to delay progression of CKD (*Strong SOR, Moderate QOE*)

Keto-analogues (also called alpha-keto acids) are often prescribed as part of a low-protein diet (LPD) or very-low-protein diet (VLPD) in chronic kidney disease (CKD), including diabetic nephropathy. They aim to reduce the burden of nitrogenous waste while providing essential amino acid precursors.

Ketoanalogue (KA) supplementation helps preserve kidney function in CKD patients, particularly those with higher eGFR levels. In a meta-analysis of 10 randomized controlled trials, early ketoanalogue (KA) supplementation significantly improves kidney function in patients with chronic kidney disease (CKD) who have an eGFR above 18 mL/min/1.73 m^2.[49] However, in patients with an eGFR below 18 mL/ min/1.73 m^2, KA supplementation did not appear to offer the same benefit. Adding KA to a very-low-protein diet (KAVLP), however, did not show clear benefit over a low-protein diet (KALP). While KA added to low-protein diet (KALP) led to significant delay in progression of CKD compared to placebo, there was no significant difference between KAVLP and KALP in preventing kidney function decline. Overall, KA supplementation significantly slows the decline in kidney function in CKD patients.

Although most of the published protocols focus on CKD in general, the principles apply to adult patients with diabetes and CKD with special attention to glycemic control and potential adjustments in the following:

Dosing Recommendations

Most clinical protocols use 1 tablet per 5 kg body weight per day (equivalent to approximately 0.1 g keto-analogues/kg/day).

Administration

Divide the total daily dose into 3 meals (e.g., breakfast, lunch, dinner). Keto-analogue tablets are usually taken with meals, as they rely on transamination with dietary nitrogen to form essential amino acids.

Protein Intake

In diabetic nephropathy (especially CKD stages 3–5), the keto-analogues are typically combined with a low-protein diet (0.6 g/kg/ day) or a very-low-protein diet (0.3–0.4 g/kg/day), depending on the severity of renal dysfunction. Ensure adequate caloric intake (often 30–35 kcal/kg/day) to avoid malnutrition.

Frequency and Duration

Keto-analogues are usually given three times daily. This aligns with the main meals of the day to maximize the utilization of dietary

Table 12. Cholesterol targets for different patient groups based on the Philippine guidelines for dyslipidemia

Patient Group	LDL-C Target (mg/dL)	HDL-C Target (mg/dL)	Triglyceride Target (mg/dl)
Individuals with no clinical ASCVD	<130	>40 in males/ >50 in females	<150
Individuals with DM **With ≥ 1 risk factors/ target organ damage** **With ASCVD**	<100 <70 <55		
Individuals with clinical ASCVD	<55		
Familial Hypercholesterolemia without ASCVD or without major risk factor/target organ damage	<70		
Familial Hypercholesterolemia with ASCVD or with ≥ 1 risk factors/ target organ damage	<55		

amino nitrogen and improve the overall protein balance. Therapy is typically continued until dialysis initiation or as long as patients can maintain adequate nutrition, metabolic control, and stable acid–base status.

Adjustments in Patients with T2DM and CKD[50-52]

Glycemic Control: Reduction in dietary protein and total nitrogen intake may alter insulin requirements. Close monitoring of blood glucose is essential and adjust insulin or oral hypoglycemic doses as needed to avoid hypoglycemia.

Renal Function and Metabolic Parameters: Monitor serum potassium, phosphate, and acid–base balance, as well as urea and creatinine. In advanced CKD or if hyperkalemia occurs, more frequent monitoring and dietary adjustments (e.g., potassium restriction) may be necessary.

Nutritional Status: Protein-energy wasting is a concern in diabetic patients with CKD. Regular assessment of BMI, albumin, pre-albumin, and muscle mass is recommended. If signs of malnutrition develop, diet modification or supplementation may be required.

Combination with Other Nephroprotective Measures: Continue optimal glycemic control, blood pressure control (e.g., ACE inhibitors/ARBs), and lipid management. The keto-analogue–supplemented LPD or VLPD is adjunctive to standard diabetic nephropathy management, not a stand-alone intervention.

Recommendation 12.2: Evidence on the role of probiotics in delaying the progression of CKD is insufficient to recommend its use (*Moderate SOR, Moderate QOE*)

Current evidence on using probiotics for diabetic kidney disease (DKD) is limited, especially in the earlier stages. Some studies suggest that certain probiotic strains (like specific Lactobacillus and Bifibacterium) may help reduce inflammation, oxidative stress, and potentially slow disease progression. Animal and lab studies have shown promising results (improved kidney function and reduced protein in the urine), but these findings do not always apply to humans. A recent meta-analysis reported that probiotics may significantly delay increases in serum creatinine, BUN, Cystatin C, urinary albumin-to-creatinine ratio, and sodium in DKD, but did not improve GFR, 24-hour total protein or potassium levels. Overall, while probiotics show potential benefits, more high-quality clinical trials are needed to clarify their role in managing early DKD.[53]

Recommendation 12.3: Offer bicarbonate supplementation to patients with CKD stages 4-5 with low serum bicarbonate levels (<22 mmol/L) (*Strong SOR, Low QOE*)

Studies suggest that oral sodium bicarbonate therapy may slow the decline in kidney function among patients with diabetic kidney disease who have metabolic acidosis, although current evidence is based primarily on smaller trials. In a single-center study by Phisitkul and colleagues (2010), patients with type 2 diabetes and CKD who received sodium bicarbonate experienced less progression of nephropathy compared to those who did not receive bicarbonate supplementation; however, larger randomized controlled trials are needed to confirm these findings.[54,55]

Initiation: In patients with diabetic kidney disease (DKD) who have metabolic acidosis (typically defined as a serum bicarbonate <22 mEq/L), oral sodium bicarbonate therapy may be started to help correct acid-base balance.[16,17] Commonly, the initial dose ranges from 650 mg to 1300 mg (1–2 tablets of 650 mg each) taken two to three times daily, depending on the severity of acidosis and the patient's tolerance.[56]

Dosing and Titration: The goal is often to maintain a serum bicarbonate level of 22–24 mEq/L.[55] Titrate the dose every 2–4 weeks based on serum bicarbonate and patient symptoms (e.g., gastrointestinal tolerance, potential edema or hypertension in sodium-sensitive individuals). If adequate correction is not achieved, the dose can be increased gradually in increments of 650 mg per day and distributed into multiple doses to minimize gastrointestinal side effects.

Monitoring

Serum Bicarbonate: Check levels every 2–4 weeks initially, then less frequently (e.g., monthly or quarterly) once the target is reached and stable.[55]

Renal Function: Monitor serum creatinine, eGFR, and electrolytes regularly (e.g., every 3–6 months) to detect any changes in kidney function or complications like hypernatremia.[54]

Blood Pressure and Volume Status: Sodium load from bicarbonate therapy can contribute to fluid retention and elevated blood pressure, requiring periodic monitoring and potential adjustment of antihypertensive medications.[56]

Adjustment of Frequency: If patients develop gastrointestinal side effects or fluid overload, reduce the dose or frequency, or consider switching to alternative bicarbonate formulations. Once bicarbonate levels are stable and the patient tolerates therapy, some clinicians may consolidate dosing to twice daily or even once daily at bedtime, though thrice-daily regimens are more common when higher total doses are needed.[56]

In patients with chronic kidney disease (CKD) and low serum bicarbonate levels, oral bicarbonate supplementation may help slow disease progression and lower the risk of end-stage renal disease (ESRD).[54,55] To effectively incorporate bicarbonate therapy, regular monitoring of renal function—such as serum creatinine, creatinine clearance (CrCl), or estimated GFR—is recommended to gauge its impact and guide any necessary treatment adjustments. Additionally, because bicarbonate supplementation can improve the nutritional status of CKD patients, emphasizing a balanced diet and adequate protein intake is essential to optimize the benefits of therapy and support overall kidney health.

KQ13. Among adults with T2DM and CKD, what medication/s are effective in the management of anemia?

Recommendation 13.1: Initiate oral iron therapy in patients with chronic kidney disease (CKD), including those with type 2 diabetes mellitus, who are not on dialysis, if on initial evaluation hemoglobin (Hb) levels are found to be <13 g/dL in males or <12 g/dL in females, if with serum ferritin <100 ng/mL and transferrin saturation (TSAT) <40%, or Serum ferritin between 100–300 ng/mL and TSAT <25%. (*Strong SOR, High QOL*)

Oral iron supplementation in diabetic nephropathy is typically considered when hemoglobin (Hb) levels are found to be <13 g/dL in males or <12 g/dL in females, and further iron studies indicate deficiency, defined as either: Serum ferritin <100 ng/mL and transferrin saturation (TSAT) <40%, or Serum ferritin between 100–300 ng/mL and TSAT <25%.[57] While many clinicians start with once-daily dosing of oral iron to minimize gastrointestinal (GI) side effects, some patients may require twice-daily (BID) or thrice-daily (TID) dosing if once-daily therapy proves insufficient.[58] However, higher-frequency dosing increases the risk of GI intolerance.

Oral iron supplements come in two main forms: ferrous salts (e.g., ferrous sulfate, ferrous gluconate, ferrous fumarate, ferrous succinate, iron polymaltose) and ferric salts (e.g., ferric citrate, ferric maltol, sucrosomial iron). In CKD, the most commonly used is ferrous sulfate (20% elemental iron), but ferric citrate is the only oral iron supplement specifically approved by the FDA for iron deficiency anemia in CKD. High doses of oral iron (>45 mg/day) can cause significant gastrointestinal side effects (35%–60% of patients), which limits their use, so newer ferric-based options may help improve absorption and tolerance. Table 1 provides a concise overview of the various dosage forms and the estimated amount of elemental iron found in the primary oral iron products now available in the market. Oral iron supplements commonly result in gastrointestinal side effects in a significant percentage of patients, ranging from 35% to 60% especially when taking a daily dose of 45 mg of elemental iron or more, restricting the capacity to replenish iron solely by high doses of oral formulations.[59]

Monitoring Frequency: In people with CKD treated with iron, it is reasonable to test hemoglobin, ferritin, and TSAT every 3 months for those not receiving dialysis.[57,58]

Recommendation 13.2: Initiate epoetin in patients with persistent anemia after iron deficiency has been corrected or ruled out. Correct all reversible causes of anemia—such as iron deficiency and underlying inflammation—before starting treatment with erythropoiesis-stimulating agents (ESAs). (Strong SOR, Moderate QOL)

Epoetin is a synthetic form of the naturally occurring hormone erythropoietin, designed to stimulate red blood cell production in patients with anemia.[57] In diabetic kidney disease, decreased erythropoietin production and other factors contribute to anemia, and the use of epoetin can help raise hemoglobin levels, potentially improving quality of life and reducing transfusion requirements.[60] Oral iron supplementation is generally considered first in patients with diabetic kidney disease (DKD) and anemia, if iron studies (e.g., ferritin, transferrin saturation) indicate iron deficiency. Erythropoiesis-stimulating agents (ESAs), such as epoetin, are typically introduced when hemoglobin remains below 10 g/dL after iron deficiency has been corrected or ruled out, or if the patient's anemia is severe enough to warrant additional therapy.[57]

Criteria for Initiation: Erythropoiesis-stimulating agent (ESA) therapy (e.g., epoetin) is generally considered in adults with chronic kidney disease (CKD) when hemoglobin (Hb) drops below 10 g/dL, provided modifiable causes of anemia (e.g., iron deficiency) have been addressed.[57] Before starting ESA, assess iron status (ferritin, transferrin saturation) to ensure adequate iron stores. For adult CKD non-dialysis with hemoglobin concentration <10.0 g/dl, decision to whether initiation epoetin therapy be individualized based on: 1) rate of fall of Hb concentration 2) Priori response to iron therapy, 3) risk of needing transfusion, 4) risks related to epoetin therapy and 5) presence of symptoms attributable to anemia.[57]

Table 13. Major oral iron supplements available[20]

Supplement	Elemental Iron per Dosage Unit	Frequency
Ferrous sulfate	65 mg/tablet[a]	1 tablet, 1-3 times per day
Ferrous gluconate	38 mg/tablet[a]	1 tablet, 1-3 times per day
Ferrous fumarate	106 mg/tablet[a]	1 tablet, 1-3 times per day
Ferric maltol	30 mg/tablet	1 tablet, twice per day
Ferric citrate	210 mg/tablet	1-2 tablets, 3 times per day
Liposomal iron	30 mg/tablet	1 tablet per day
[a]For 325-mg tablets		

Dosing and Frequency: Epoetin is commonly started at 50–100 IU/kg per week, usually divided into one to three injections (e.g., once weekly, twice weekly, or thrice weekly), depending on the formulation and patient factors.[60] The dose may be increased or decreased (often by 25%) based on hemoglobin response and rate of rise. Long-acting ESAs (e.g., darbepoetin alfa) can be administered less frequently (e.g., every 2 or 4 weeks), but the principle of adjusting for hemoglobin response remains the same.

Hemoglobin Target and Monitoring: KDIGO recommends aiming for a hemoglobin range generally around 10–11.5 g/dL, avoiding hemoglobin levels above 13 g/dL to minimize cardiovascular risks.18 Monitor hemoglobin every 2–4 weeks after starting or changing the dose; once stable, checks can be spaced out according to clinical judgment and the patient's stability. Iron parameters (ferritin, transferrin saturation) should also be monitored periodically to optimize ESA therapy.

Non-pharmacologic Treatment

The patient centered, family-focused, community-oriented non-pharmacological recommendations for diabetic kidney disease (DKD) include general recommendations for better glycemic control, adherence to treatment, delay progression, reduce mortality, and adequately manage co-morbidities.

KQ14: Among adults with T2DM and CKD, what are the recommended non-pharmacologic patient-centered interventions to improve patient outcomes?

Recommendation 14.1: Provide diabetes self-management education and support (*Strong SOR, Moderate QOE*)

Diabetes self-management education and support (DSMES) is part of the general recommendations by the American Diabetes Education Standards of Care. The need for DSMES should be evaluated during four critical times: at diagnosis, annually and/or targets for treatment are not met, development of complicating factors, and during transition in life and care[47]. In a propensity score matching analysis done by Zimbudzi, et al in 2018, self-management among adult patients with diabetes and chronic kidney disease (CKD) has moderate-quality evidence on improving self-care activities (standard mean difference 0.56 + 0.41, 95% CI) and statistically significant at $p<0.007$ as compared to usual care[61]. Improvement on systolic blood pressure and glycated hemoglobin has low-quality evidence with mean differences of 4.25 + 3.56 mmHg (95% CI, $p=0.02$) and 0.8 + 3% (95% CI and $p=0.01$), respectively.

Table 14. The 7 key components of DSMES according to CDC

Eating healthy
Being active
Taking medicine as prescribed
Monitoring blood sugar levels, activity, and eating habits
Reducing risks to lower the chances of diabetes complications
Healthy coping with diabetes and emotional well-being
Problem solving to find solutions and take action

Recommendation 14.2: Discuss initial medical nutrition therapy with focus on appropriate protein and salt intake and/or referral to nutritionist-dietician for individualized medical nutrition therapy (MNT) (*Strong SOR, Low QOE*)

The cornerstone of multidisciplinary management of DKD is medical nutrition therapy (MNT)[62]. The American Diabetes Association recommends individualized MNT done by a dietician-nutritionist. This improves outcomes on reducing HbA1c, weight, and cholesterol. Increased dietary protein intake (DPI) is associated with increased albuminuria and rapid kidney function loss caused by exacerbated glomerular hyperfiltration. High DPI is also linked to increased cardiovascular mortality. Hence, an intake of 0.6-0.8g/kg/day is recommended among patients with non-dialysis chronic kidney disease (CKD)[47]. This can slow the decline of glomerular filtration rate (GFR) overtime. Better blood pressure control and reduction of cardiovascular risk is achievable by restricting dietary sodium intake to <2,300mg/ day. Better glycemic control can all be achieved by reducing carbohydrate intake and avoiding sources of simple sugars.

Referral to nutritionist-dietician for individualized medical nutrition therapy is also recommended by ADA. However, if a nutritionist-dietician is not available, the healthcare provider should be able to ensure MNT advice is given.

Recommendation 14.3: Discuss weight management and physical activity based on general recommendations among patients with diabetes mellitus (*Strong SOR, Low QOE*)

The American Diabetes Association recommends at least 150 minutes of cumulative moderate-intensity physical activity per week or to compatible physical activities with a patient's physical and cardiovascular tolerance. Physical activity decreases cardiovascular risk and all-cause mortality by improving insulin sensitivity, reducing inflammatory markers, and improving endothelial function leading to slower decline of GFR. It is also recommended that intentional weight loss has benefits among patients with obesity, diabetes, and CKD Stage IIIb and above by reducing albuminuria and improving blood pressure which may have potential kidney benefits. The recommendation by ADA is a minimum weight loss of 5%.

Exercise prescription must also be individualized based on the patient's clinical profile and capacity to engage in physical activity.

Recommendation 14.4: Screen for tobacco and vape use and discuss, assess and identify barriers on smoking cessation among T2DM patients with nephropathy using tobacco products (*Strong SOR, Low QOE*)

Tobacco use is an established risk factor in macro and microvascular diseases. Hence, screening for use and encouraging cessation are key recommendations from the latest KDIGO clinical practice guidelines to prevent premature mortality from CVD. Smoking cessation can also slow down CKD progression and decrease proteinuria[63]. Moreover, the use of electronic cigarettes (e-cigs) or vape has also increased throughout the years. Laboratory studies showed volatile organic compounds

contained in vapes or e-cigs are associated with kidney injury; however, human data is still limited[64]. Nevertheless, vaping is now known to be a risk factor for cardiovascular diseases[65]. Given the increased CV risk and possible association to kidney injury, patients with CKD should be screened for tobacco and vape use; and should be counselled towards cessation. Clinicians can use various strategies as motivational counseling or the 5A technique - Ask, Advise, Assess, Assist, and Arange, as smoking cessation strategies among patients with identified tobacco or vape use. Referral to appropriate specialists can also be done if indicated.

Recommendation 14.5: Offer teleconsultation for monitoring control, adherence to management, and lifestyle modification (*Strong SOR, Very Low QOE*)

Telemedicine allows remote monitoring of patients with diabetes mellitus in general66. It improves access to care while decreasing travel requirements. It can be cost-effective and has shown to improve A1c control. It is a good complement to conventional methods of consultations and can be sustainable in monitoring non-communicable diseases[67]. However, acceptability and accessibility must also be considered when offering it.

KQ15: Among adults with T2DM and CKD, what are the recommended non-pharmacologic family-focused interventions to improve patient outcomes?

Recommendation 15.1: Provide family directed health education on diabetes and CKD (address family misperceptions and lifestyle) (*Strong SOR, Very Low QOE*)

The optimal management of diabetes and its complications involves multifaceted daily self-management routines and often complex interactions with healthcare professionals[68]. Health supporters may assist with day-to-day decisions about medication and routine symptom management, help coordinate health care among multiple providers, and facilitate healthy behavior changes such as improvements in diet or self-monitoring[69].

Recommendation 15.2: Involve a family member or a caregiver on DM2 nephropathy management and education (*Strong SOR, Very Low QOE*)

Social support from family and friends has great potential to help people with chronic illnesses better manage their conditions[68,69]. Positive social support from family and friends has been linked with increased patient self- efficacy, better self-management behavior, better patient-doctor communication, and better health outcomes. There is significant potential for family members and friends to influence the health and health management of adults with chronic illness[68,69]. Both in and out-of-home supporters spend an average of approximately two hours helping with health care on days that they provide help. Time spent providing support to family and friends with chronic health conditions might be leveraged to improve disease self-management and health outcomes[8]. These supporters are frequently focused on patient concerns about their health conditions and health care that could directly impact patients' health and safety, such as bothersome symptoms, medication side effects and confusion about health care provider instructions. Supporters experiencing negative conversations with support recipients might benefit from training in positive communication techniques.

When used by healthcare providers, autonomy supportive communication techniques increase support recipients' motivation and self-directed problem-solving to improve health behaviors[8]. Autonomy supportive communication skills include empathy, support for patient agency, and collaborative goal setting. Family members and friends of adults with chronic illnesses spend a substantial amount of time providing health related support, and engage in critical discussions about health with support recipients. These supporters express difficulties communicating with their support recipients as well as a need for more information about their support recipients' health conditions and current health care. Family psychoeducation can increase caregiver support in the treatment of diabetes mellitus patients[69]. Family education positively affects glycemic control, self-management, and family support in patients with type 2 diabetes mellitus. Improving family awareness through education is mandatory to be done by health care professionals in addition to providing usual care. Lastly, It is recommended that family exercise intervention programmes should be formulated according to 30–60 min per session, more than three times per week, for more than six months of aerobic exercise or aerobic combined with resistance exercise[70].

KQ16: Among adults with T2DM and CKD, what are the recommended non-pharmacologic community-oriented interventions to improve patient outcomes?

Recommendation 16.1: Navigate patients through existing community resources as one strategy in addressing barriers to care (*Strong SOR, Very Low QOE*)

Patient navigation refers to "a process where a navigator engages with a patient to determine barriers to care and provides information to improve access to components of the health system, not just primary care"[71]. Navigation is one strategy to address social determinants of health in which family physicians are also known to do so[72]. Knowledge on existing community resources allows a family physician to connect a patient to the appropriate channel in the healthcare system. Hence, family physicians are recommended to navigate patients as part of their care. This entails that the clinician must also be knowledgeable of existing community resources. Family assessment tools such as SCREEM and Ecomap can also be used in the navigation.

Recommendation 16.2: Encourage patients to participate in existing community lifestyle programs such as DM club and other related support groups. (*Strong SOR, Very Low QOE*)

Individuals are advised enrollment to community lifestyle programs. In a study of a 12-month community lifestyle modification

program for high-risk individuals of developing T2DM, there were significant weight reduction, diet improvement, physical activity, and waist circumference reduction among participants[73].

Recommendation 16.3: Encourage patients to participate in existing credible online/virtual support groups and communities. (*Strong SOR, Very Low QOE*)

Patients with diabetes are encouraged to join credible community-based peer-support groups for self-management, self-care, diabetes education, and peer support. Type 2 diabetes patients participating in peer support for self-management have a significant decline of HbA1c levels after 6 months and improvement of quality of life[74]. In a cross-sectional study by Litchman, et al. (2018), patients with type 2 diabetes have better glycemic control when they highly engage in an online community[75]. This is supported by a scoping review in 2019 by Litchman et al.. After reviewing 47 articles, participating in an online community may be beneficial for patients with diabetes in terms of social support in information, emotion, appraisal, and diabetes-related instruments[78]. Contradictory, there are lower levels of diabetes self-care management among Type 2 DM patients engaged to a diabetes-related online support group[77]. There are no studies yet on other health outcomes

Patient Outcomes

KQ17: What are the desired clinical and non-clinical outcomes following treatment among adults with T2DM and CKD?

Adults with type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD) are at increased risk of progression of CKD, especially those with albuminuria, and cardiovascular disease. Thus, the treatment of adult type 2 with diabetes and nephropathy is directed primarily at delaying the progression of kidney disease and reducing the risk of cardiovascular events.[41,78,79] Additional therapies are also often necessary to improve the intermediate risk factors namely hyperglycemia, hypertension and dyslipidemia, which also contribute to both CKD progression and CVD. Evidence on desired clinical outcomes following treatment for type 2 diabetes comes from clinical trials and observational studies that were conducted to evaluate the effectiveness of both pharmacologic and non-pharmacologic therapies. Non-clinical outcomes include quality of life, self-efficacy and patient satisfaction based on observational studies.

Recommendation 17.1: Aware of the importance of adherence to treatment regimen (*Strong SOR, Low QOE*)

Poor medication adherence in T2DM is well documented to be very common with non-adherent diabetic patients having significantly worse glycemic control.[80,81] Poor adherence was also associated with increased morbidity and mortality and increased costs of outpatient care, emergency room visits, hospitalization, and managing complications of diabetes. Poor medication adherence is linked to key nonpatient factors (eg, lack of integrated care in many health care systems and clinical inertia among health care professionals), patient demographic factors (eg, young age, low education level, and low income level), critical patient beliefs about their medications (eg, perceived treatment inefficacy), and perceived patient burden regarding obtaining and taking their medications (eg, treatment complexity, out-of-pocket costs, and hypoglycemia) in observational studies.[82,83] It should be, therefore, emphasized during consultation, among patients with diabetes, the importance of medication adherence.

Recommendation 17.2: Received individual or group-based self-management education to improve blood pressure and glycemic control, self-efficacy and patient satisfaction (*Strong SOR, Low QOE*)

Chronic kidney disease is associated with low health related quality of life. Younger age, women, low education, diabetes, vascular disease, obesity and low eGFR were associated with low baseline HR-QOL in one prospective observational study conducted in 2016. Lower HR-QOL scores were also associated with increased risk for CV events and death.[84,85]

Self-management education is being recommended by the 2022 KDIGO guidelines to improve self-management knowledge and skills among adults with diabetes and CKD. Evidence came from a high-quality systematic review conducted in 2018 and included 8 studies on self-management support interventions in people with CKD. The meta-analysis showed significant benefit in terms of lower systolic blood pressure and HbA1c. No significant benefits were found in the following outcomes: HRQOL, DBP, eGFR and self-management activities. For patients with type 2 diabetes, potential benefits of group-based diabetes self-management education programs include improvement in clinical outcomes (HbA1c, fasting plasma glucose), body weight and psychosocial outcomes such as self-efficacy and patient satisfaction.[41]

Key components of self-management education include diabetes pathophysiology, treatment options, medication usage, monitoring and detecting chronic complications, healthy coping with psychological issues, and problem-solving.

Recommendation 17.3: Albuminuria reduced by >30% or to levels < 300mg/m to delay progression of diabetic kidney disease and decrease cardiovascular risk. (*Strong SOR, Moderate QOE*)

Changes in kidney function can be detected early by increase in urine albumin supporting the clear need for annual determination of urine albumin-to-creatinine ratio for all diabetic patients. Untreated microalbuminuria will gradually worsen, reaching clinical proteinuria or severely increased albuminuria (Grade A3) over 5 to 15 years. The GFR then begins to decline, and without treatment, end-stage renal failure is likely to result in 5 to 7 years.[86]

The American Diabetes Association recommends a reduction of 30% or greater in urinary albumin in diabetic people with CKD who have uACR of ≥ 300 mg/g maintained for at least 2 years to slow the progression of CKD. This initial reduction in uACR is considered as a surrogate for renal benefit in terms of treatment effectiveness.[78,87] This recommendation was based on a statement from the US FDA, Division

of Cardiology and Nephrology after review of prospective cohort studies and randomized controlled trials, where a reduction of 30% uACR over 2 years was associated with reduction in risk of end-stage kidney disease (HR 0.78, 95% CI 0.66-0.95) in prospective cohort studies.[78] In clinical trials on effectiveness of ACE inhibitors and ARB therapy, reducing albuminuria to levels below 300 in mg/g creatinine or by more than 30% from baseline has been associated with improved renal and cardiovascular outcomes.[78,87]

Recommendation 17.4: Achieved glycemic control based on individualized target for HbA1c level among adult diabetic type II patients with CKD or the equivalent plasma glucose to delay progression of kidney disease (*Strong SOR, High QOE*)

Delay in progression of albuminuria and reduction in eGFR are associated with intensive blood sugar control in large randomized trials. However, the benefits of intensive blood sugar lowering are limited and may lead to certain risks in diabetic patients with CKD, particularly hypoglycemia and death.[78,87] Thus, aiming for long-term benefits with glycemic control must be balanced with risks such as hypoglycemia. The American Diabetes Association recommends optimization of blood sugar control, recommending a target baseline of <7% for diabetic patients in general but did not specify particular HbA1c level (or range) as target specifically for those with chronic kidney disease. The 2022 KDIGO41 and 2021 American British Clinical Diabetologists (ABCD and the Renal Association[42] clinical practice guidelines recommend an individualized HbA1c target in diabetic patients with CKD and not treated with dialysis. Specifically, 2022 KDIGO recommends HbA1c target ranging from < 6.5% to <8.0% depending on presence of macrovascular complications, other comorbidities, life expectancy, hypoglycemia awareness and particular treatment that the patient is on, based on low-quality evidence.[41]

The 2021 ABCD and the Renal Association guidelines recommend individualized HbA1c targets for people with diabetes and DKD based on moderate-quality evidence. Presence of anemia should be considered and assessed for when using HbA1c to evaluate glycemic control. With deterioration of kidney function over time, glycemic targets should be adjusted (Table 15).[42]

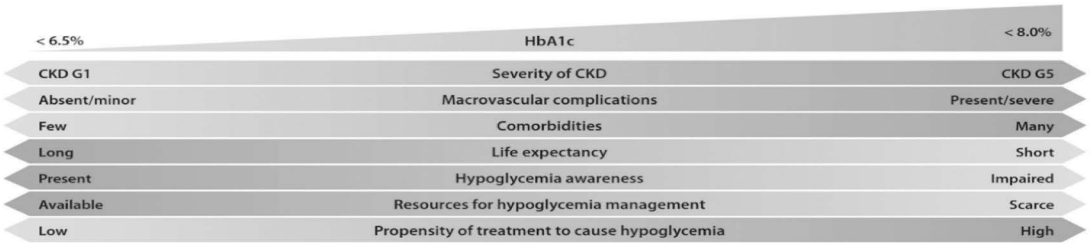


Figure 3. Factors guiding decisions on individual HbA1c targets. From the KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease

Table 15. Glycemic targets for diabetic people with Diabetic Kidney Disease (DKD). From the Association of British Clinical Diabetologists and the Renal Association. Managing hyperglycaemia in people with diabetes and chronic kidney disease

Condition	Glycaemic target	CKD stage and albuminuria	Age
Type 1 diabetes	48–58 mmol/mol (6.5–7.5%)*	CKD stage 2 with variable microalbuminuria	Younger people within 10 years' duration of diabetes
	58–62 mmol/mol (7.5–7.8%)	CKD stages 3–4 and/or albuminuria	The majority of people
	58–68 mmol/mol (7.5–8.5%)	CKD stage 5 – dialysis	Any age
Type 2 diabetes	48–58 mmol/mol (6.5–7.5%)* Aim for <52 mmol/mol (6.9%)	CKD stages 1–2	People who are aged <40 **Diet controlled at any age
	52–58 mmol/mol (6.9–7.5%)	CKD stages 3–4 May be appropriate with a GLP-1 and/ or SGLT-2 inhibitor-based treatment regime without insulin	Any age
	58–68 mmol/mol (7.5–8.5 %)	CKD stages 3–4 and those with CKD stage 5 who are on dialysis. Especially in people with albuminuria who are on an insulin-based regime▽	Any age

*Confirmatory blood glucose or flash glucose monitoring if concern of hypoglycaemia and/or anaemia
▽Recognition of cardiorenal benefits with SGLT-2 inhibitors (and potentially GLP-1 analogue therapy) independent of glycaemic effect
**Over 20% of people with DKD (especially older people aged >75) solely dietary controlled can have HbA1c 42–48 mmol/mol (6–6.5%) without hypoglycaemia

Recommendation 17.5: Achieved blood pressure control with a target BP of < 130/80 mmHg to reduce risk for cardiovascular disease. (*Strong SOR, High QOE*)

The American Diabetes Association recommends use of ACE inhibitors or Angiotensin receptor blockers in type 2 diabetic patients with chronic kidney disease to control hypertension, delay progression of kidney disease and reduce cardiovascular outcomes. Anti-hypertensive therapy reduces the risk of albuminuria and the risk of progression to ESRD, particularly in those with uACR of ≥ 300 mg/g creatinine. Generally, a target BP of <130/80 is recommended to reduce CVD mortality and slow progression to CKD[78,87]. This recommendation is based on results from large randomized clinical trials (ACCORD, UKPDS, RENAAL, HOPE AND MICRO-HOPE studies).78 The 2021 KDIGO guidelines88 on the management of hypertension in patients with CKD recommends a target SBP of < 120 mmHg in patients with CKD with or without diabetes, when tolerated. Evidence included a subgroup analysis from a high-quality large randomized trial (SPRINT) which tested 2 SBP (<120 vs <140mm Hg) and was thus rated as low-quality. Overall, for the entire cohort, there was significant reduction in CV outcomes and all-cause death while in the subgroup of patients with CKD, the reduction in CV outcomes was non-significant (HR: 0.81; 95% CI: 0.63–1.05), while the mortality benefit was nominally significant. This trial however, did not include diabetic patients.[38] When it comes to kidney outcomes, large randomized trials showed a higher rate of decline in the eGFR in the intensive BP control in patients with or without CKD. (ACCORD, SPRINT).[88]

Recommendation 17.6: LDL level reduced to <70 mg/dl to reduce cardiovascular risk. (*Strong SOR, High QOE*)

The American Diabetes Association recommends statin therapy for all adults with diabetes for primary prevention of – moderate intensity for aged 40-75 years without additional CV risk factors and for 20-39 if with additional CV risk factors and high intensity for diabetic patients with 1 or more CV risk factors such as CKD. Treatment is recommended to target at least 50% reduction in LDL-C from baseline or an LDL level of < 70 mg/dl. Evidence includes multiple clinical trials and a meta-analysis of 14 clinical trials that showed significant reduction in ASCVD events, all-cause mortality and vascular mortality.[78]

The 2013 KDIGO guidelines recommends statin therapy or statin/ezetimibe therapy to all patients at least 50 years of age with CKD. The recommendation was based on high-quality clinical trials. However, the guidelines did not include a recommended target for lipid management.[43]

The 2020 Philippine Guidelines on the Management of Dyslipidemia in adult Filipinos from the Philippine Heart Association, PLAS and PSEDM,[44] recommend starting statin in patients with chronic kidney disease to reduce the risk of cardiovascular events. A target of < 70 mg/dl following initiation of statin therapy is recommended for diabetic patients with CKD for the primary prevention of atherosclerotic cardiovascular disease.

KQ18: How should treatment goals be monitored in the care of adults with T2DM and CKD?

Recommendation 18.1: Changes in blood pressure, serum creatinine and serum potassium are monitored within 2-4 weeks of initiation or increase in the dose of an ACE inhibitor or ARB. (*Strong SOR, Very Low QOE*)

The 2022 KDIGO guidelines for diabetes management in patients with chronic kidney disease suggested, as a practice point, that diabetic patients with CKD are monitored for symptomatic hypotension, hyperkalemia and excessive rise in serum creatinine within 2-4 weeks from initiation or increase in the dose of an ACEi or ARB. Practice points are consensus-based statements representing the expert judgment of the Work Group and are not graded.[41] ACEis and ARBs counteract the vasoconstrictive effects of Angiotensin II causing vasodilation of the efferent arterioles of the glomeruli resulting in decrease in intraglomerular pressure and decrease in eGFR. Also inhibiting the action of aldosterone, these drugs may also increase the risk of hyperkalemia.[78] In one retrospective study among diabetic patients with albuminuria who were non-adherent to ACEis and ARBs, acute kidney injury (21.7%), hyperkalemia (5.1%) and slight increase in serum creatinine (4.3%) were among the reasons for discontinuing ACEi and ARB.[89]

Recommendation 18.2: Follow-up visits among adult patients with type 2 diabetes nephropathy are advised after 6 months to 1 year, based on the staging of chronic kidney disease to guide therapy and for monitoring . (*Strong SOR, Very Low QOE*)

Adults with type 2 diabetes and CKD patients should be regularly monitored to guide treatment, assess for CKD progression, detect superimposed acute kidney injury and determine whether referral to nephrology is needed. Based on expert opinion, frequency of follow-up measurements for monitoring takes into consideration the patient's stage of CKD and risk of its progression, as shown in Figure 4. Boxes are color coded, suggesting frequency of visits and measurements - (Green) G1A1 or G2A1, annually; (Yellow) G1A2, G2A2 and G3aA1, at least once per year; (Orange) G1 or G2 with A3, G3a with A2 or G3b with A1, twice per year; (Red) G3aA3, G3bA2 and G3bA3, and G4A1 and G4A2, three times per year; and (Dark Red) G4A3 and G5, four times a year[38].

KQ19. What are the indications for referral to Nephrology specialist care among adults with T2DM and CKD?

Recommendation 19.1: Referred for Nephrology specialist care if with CKD G4, G5, A3, or G3bA2. (*Strong SOR, High QOE*)

Also depicted Figure 4, is the recommendation for referral to nephrology services of adult diabetic patients with G4 or G5 with A2 or A3 or G3bA2.[38,87] Consultation with a nephrologist when stage 4 CKD develops (eGFR <30 mL/min/1.73 m^2) has been found to reduce cost, improve blood pressure control, delay dialysis and reduce mortality (RR 0.61, 95% CI 0.55 to 0.67; I^2 = 84%) in a meta-analysis of 40 longitudinal cohort studies (n 63,887 participants)[90].

Urgent referral to a nephrologist is recommended for evaluation of patients with high grade albuminuria (A3) even in lower classification

of staging of CKD(G1 or G2), continuously rising UACR levels and/or continuously declining eGFR, for other possible causes of albuminuria like Primary Glomerulonephritis, if there is uncertainty of diagnosis and for management of difficult complications e.g. resistant hypertension, metabolic bone disease and electrolyte imbalance.[38,87] KDIGO also cites as practice point, additional indications for referral to specialist kidney care including persistent abnormalities in potassium, acidosis, anemia and malnutrition.[38] The goals of early identification and referral include: (1) evaluation and diagnosis, (2) planning and preparation for KRT, and (3) management of CKD-related complications.

Late referral, which has varying definitions, can be detrimental with several consequences, including increased hospitalization and higher mortality (Tables 16 and 17). Most commonly, patients > 75 years old, females, non-Caucasians, uninsured, of lower socioeconomic or educational status, and those with multiple co-morbidities are at risk for late referrals.[38,91]

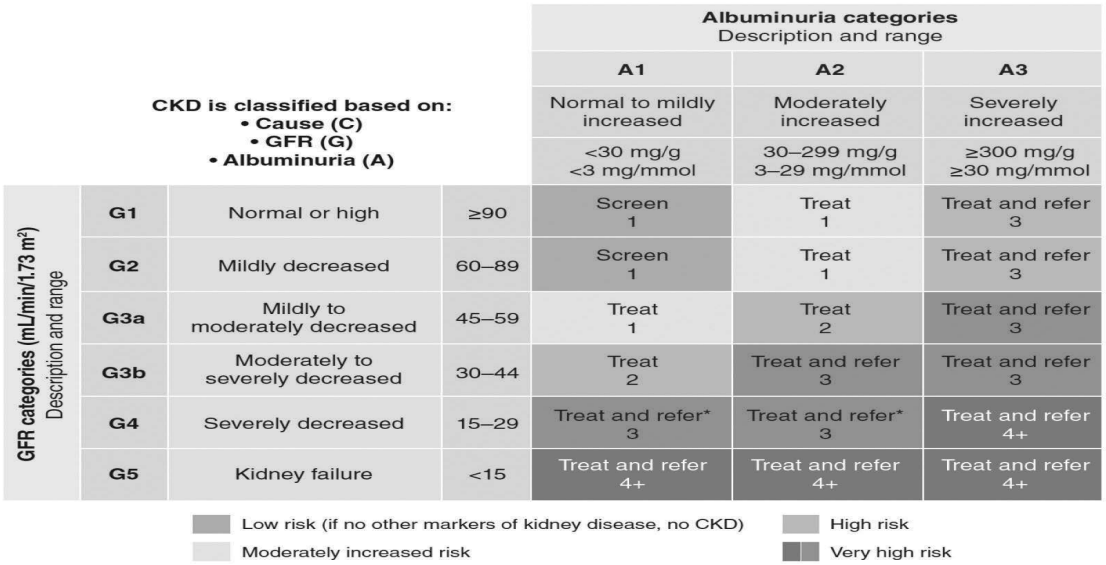


Figure 4. Risk of progression, frequency of visits and referral to nephrology based on eGFR and albuminuria. From 2024 American Diabetes Association Standards of care in Diabetes Chronic Kidney Disease and Risk Management. Adapted from 2024 American Diabetes Association Standards of Care

Table 16. Consequences and benefits of early versus late referrals[38]

Consequences of Late Referrals	Benefits of Early Referrals
Anemia and bone disease	Delay need to initiate RRT
Severe hypertension and fluid overload	Increased proportion with permanent access
Low prevalence of permanent access	Greater choice of treatment options
Delayed referral for transplant	Reduced need for urgent dialysis
Higher initial hospitalization rate	Reduced hospital length of stay and costs
Higher 1-year mortality rate	Improved nutritional status
Less patient choice of RRT modality	Better management of CVD and comorbid conditions
Worse psychosocial adjustment	Improved patient survival

Adapted from Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease

Table 17. Outcomes of early vs late referrals[91]

Variable	Early referral mean (SD)	Late referral mean (SD)	P- value
Overall mortality, %	11 (3)	23 (4)	< 0.0001
1-year mortality, %	13 (4)	29 (5)	0.028
Hospital length of stay, days	13.5 (2.2)	25.3 (3.8)	0.0007
Serum albumin at RRT start, g/dL [d/L]	3.62 (0.05) [36.2 (0.5)]	3.40 (0.03) [34.0 (0.03)]	0.001
Hematocrit at RRT start, %	30.54 (0.18)	29.71 (0.10)	0.013

Adapted from Chan MR, et al. "Outcomes in patients with chronic kidney disease referred late to nephrologists: a meta-analysis." Am J Med 2007; 120(12): 1063-70. doi:10.1016/j.amjmed.2007.04.024

Clinical Pathway

Visit	Pathway Tasks				Patient Outcomes
	History and Physical Examination	**Laboratory**	**Pharmacologic Intervention**	**Non-pharmacologic Interventions**	
First Visit	__ Perform thorough history taking to determine personal medical history, family history, social and environmental factors. __ Perform a thorough physical examination to assess for high blood pressure, weight loss and muscle wasting, anemia, fluid retention and changes in skin color. __Assess for nutrition and protein-energy status by obtaining anthropometric measurements, body composition, and performing hand grip tests __ Evaluate for the presence of possible complications of CKD such as malnutrition, anemia, bone and mineral disorder, acid-base and electrolyte imbalance, risks for infection, peripheral artery diseases, and atherosclerotic cardiovascular disease.	Request for: __Sserum Creatinine __ Spot urine ACR, if available __Offer diagnostic imaging via ultrasound of the kidneys, if clinically warranted and if available Offer the following diagnostic exams to assess for presence of comorbidities or complications: __ Lipid Profile __ Hemoglobin or CBC __ Serum electrolytes __ Serum Calcium, Phosphate, PTH and alkaline phosphatase __ Diagnostic work-up for cardiovascular disease, if clinically warranted __ Vit B level for patients on Metformin for 4 years or longer, if available	__Offer a SGLT2 inhibitor and Metformin to achieve glycemic control and delay the progression of CKD __ Initiate ACE inhibitor or angiotensin receptor blocker for treatment of hypertension to reduce cardiovascular risk and delay progression of CKD __ Initiate statin therapy to achieve individualized target levels. __ Offer combined therapy with a sodium-glucose co-transporter 2 inhibitor (SGLT2i) and a glucagon-like peptide 1 receptor agonist (GLP1 RA) with demonstrated cardiovascular benefit in patients with type 2 diabetes and CKD and heart failure, established atherosclerotic cardiovascular disease or multiple risk factors for atherosclerotic cardiovascular disease. __ Offer Ketoanalogue supplementation to patients with higher eGFR levels to delay CKD progression.	**Patient centered** ___ Provide DM2 self management education and support ___ Discuss medical nutrition therapy with focus on appropriate protein and salt intake ___ Referral to nutritionist-dietician for individualized MNT ___ Discuss recommended physical activity ___ Offer teleconsultation for monitoring control, adherence to management, and lifestyle modification ___ Screen for tobacco and vape use and discuss, assess, and identify barriers on smoking cessation among T2DM patients with nephropathy using tobacco products ___ Discuss complementary options for DM2 patients with nephropathy (if with patient inquiries)	__Aware of the importance of adherence to treatment regimen (Low) __Received individual or group-based self-management education to improve blood pressure and glycemic control, self-efficacy and patient satisfaction. (Low) __Follow-up within 2 weeks, if ARB or ACEi was initiated or dose adjusted or within 6-12 months for treatment guide and for monitoring (Very Low)

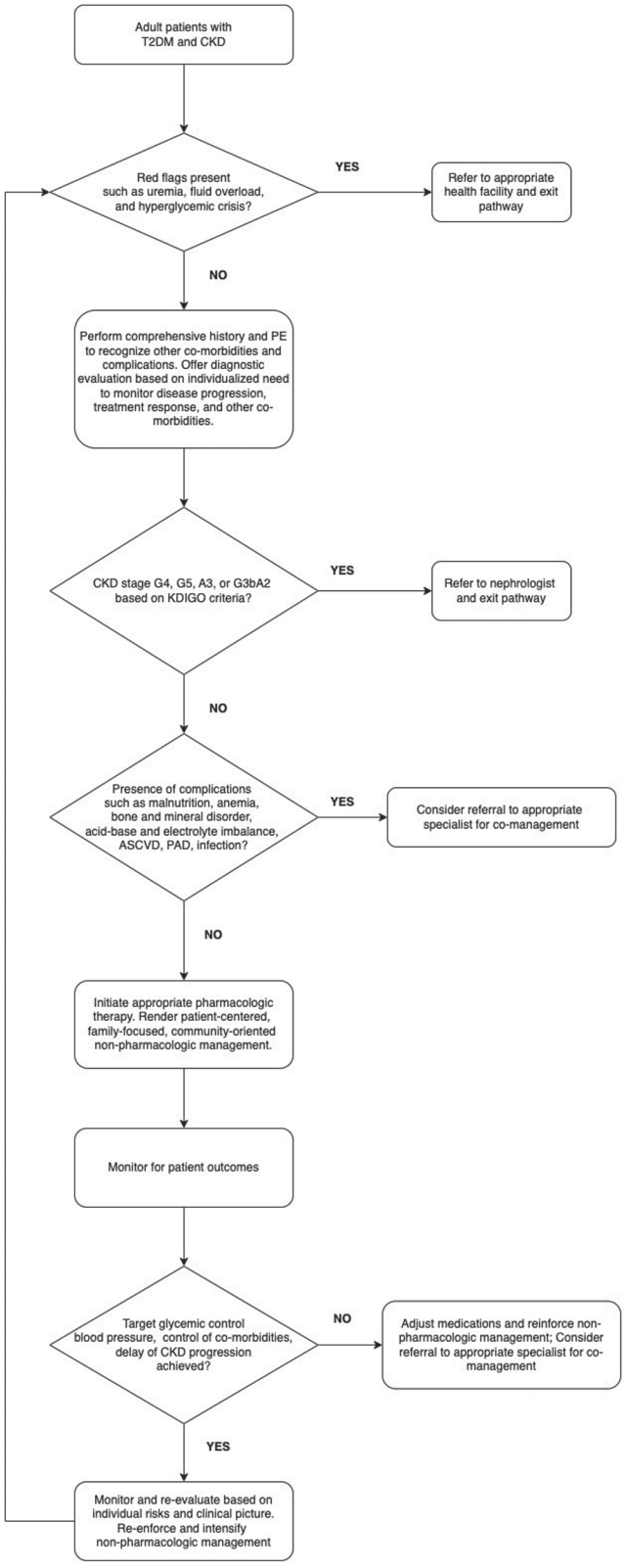
	__ Assess the psychosocial factors related to CKD such as baseline knowledge on CKD, family and community resources, coping mechanisms, and patient preference. __ Utilize appropriate family assessment tools in T2DM patients with CKD to guide in formulating a management plan			**Family focused** ___ Provide family directed health education on DM2 nephropathy (address family misperceptions and lifestyle) ___ Involve a family member or a caregiver on DM2 nephropathy management and education **Community oriented** ___ Assist patients in navigating through existing community resources ___ Encourage patients to participate in existing community lifestyle programs such as DM club and other related support groups ___ Encourage patients to participate in existing credible online/virtual support groups and communities	
Variations	__ Last menstrual period and lactation status of all reproductive age women __ Refer patients with red flags such as uremia, fluid overload, and hyperglycemic crisis to appropriate facility and specialist				

Visit	Pathway Tasks				Patient Outcomes
	History and Physical Examination	**Laboratory**	**Pharmacologic Intervention**	**Non-pharmacologic Interventions**	
Second Visit	__ Reassess status of risk factors identified during the first visit __ Perform complete physical examination including blood pressure, evidence of fluid retention, anemia, bone and mineral disorders, acid-base and electrolyte imbalance, peripheral artery diseases, and atherosclerotic cardiovascular disease. __ Reassess nutrition and protein energy status with anthropometric measurements. Perform body composition and hand-grip tests if not done during the first visit.	__ Request for serum Creatinine and Potassium within 2-4 weeks, if ACEi or ARB is initiated or increased in dose Request for: __ Serum Creatinine __ Spot urine ACR, if available __ HbA1c	__ Adjust dose of medication according to target __ Offer Long acting GLP-1 RA with proven CKD benefit 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. __Offer mineralocorticoid receptor antagonists in patients with CKD who are at increased risk for cardiovascular events or CKD progression, and unable to use an SGLT2i __ Offer appropriate therapy among patients with anemia. __ Offer bicarbonate supplementation among patients with low serum bicarbonate levels	**Patient Centered:** ___ Reinforce DM2 self management education and support, adherence to treatment ___ Reinforce medical nutrition therapy with focus on appropriate protein and salt intake ___ Follow-up referral to nutritionist-dietician for individualized MNT ___ Reinforce recommended physical activity ___ Offer teleconsultation for monitoring control, adherence to management, and lifestyle modification **Family Focused** ___ Reinforce family directed health education on DM2 nephropathy (address family misperceptions and lifestyle) ___ Reinforce Involvement of a family member or a caregiver on DM2 nephropathy management and education	__Received individual or group-based self-management education to improve blood pressure and glycemic control, self-efficacy and patient satisfaction. (Low) __Reduction of 30% or greater in mg/g urinary albumin (Moderate quality) __Reduction in LDL to target < 70 mg/dl (HIGH) __Achieved glycemic control based on individualized target for HbA1c level among adult diabetic type II patients with chronic kidney or the equivalent plasma glucose to delay progression of kidney disease. (HIGH)

				Community Oriented ___ Follow-up and redirect through existing community resources ___ Follow-up participation in existing community lifestyle programs such as DM club and other related support groups. ___ Follow-up participation in existing credible online/virtual support groups and communities	___Achieved blood pressure control with a target BP of < 130/80 mmHg to reduce risk for cardiovascular disease and slow the progression of CKD (HIGH) __Referred to Nephrology care if with CKD G4, G5, A3, or G3bA2.(HIGH) __Follow-up within 2 weeks, if ARB or ACEi was initiated or dose adjusted or within 6-12 months for treatment guide and for monitoring (VERY LOW)
Variations	__ Last menstrual period and lactation status of all reproductive age women __ Refer patients with red flags such as uremia, fluid overload, and hyperglycemic crisis to appropriate facility and specialist				

Visit	Pathway Tasks				Patient Outcomes
	History and Physical Examination	**Laboratory**	**Pharmacologic Intervention**	**Non-pharmacologic Interventions**	
Continuing Visit	__ Reassess status of risk factors identified during the first visit __ Perform complete physical examination including blood pressure, evidence of fluid retention, anemia, bone and mineral disorders, acid-base and electrolyte imbalance, peripheral artery diseases, and atherosclerotic cardiovascular disease. __ Reassess nutrition and protein energy status with anthropometric measurements. Perform body composition and hand-grip tests if not done during the first visit.	__ Request for serum Creatinine and Potassium within 2-4 weeks, if ACEi or ARB is initiated or increased in dose Request for: __Serum Creatinine __ Spot urine ACR, if available __ HbA1c	__ Adjust dose of medication according to target __ Assess for adherence to medication __ Assess for adverse effects of medications __ Prescribe other medications according to presence of other comorbidities and complications	**Patient Centered:** ___ Reinforce DM2 self management education and support, adherence to treatment ___ Reinforce medical nutrition therapy with focus on appropriate protein and salt intake ___ Follow-up referral to nutritionist-dietician for individualized MNT ___ Reinforce recommended physical activity ___ Offer teleconsultation for monitoring control, adherence to management, and lifestyle modification **Family Focused** ___ Reinforce family directed health education on DM2 nephropathy (address family misperceptions and lifestyle) ___ Reinforce Involvement of a family member or a caregiver on DM2 nephropathy management and education	__Received individual or group-based self-management education to improve blood pressure and glycemic control, self-efficacy and patient satisfaction. (Low) __Reduction of 30% or greater in mg/g urinary albumin (Moderate quality) __Reduction in LDL to target < 70 mg/dl (HIGH) __Achieved glycemic control based on individualized target for HbA1c level among adult diabetic type II patients with chronic kidney or the equivalent plasma glucose to delay progression of kidney disease. (HIGH)

				Community Oriented ___ Follow-up and redirect through existing community resources ___ Follow-up participation in existing community lifestyle programs such as DM club and other related support groups. ___ Follow-up participation in existing credible online/virtual support groups and communities	___Achieved blood pressure control with a target BP of < 130/80 mmHg to reduce risk for cardiovascular disease and slow the progression of CKD (HIGH) __Referred to Nephrology care if with CKD G4, G5, A3, or G3bA2.(HIGH) __Follow-up within 2 weeks, if ARB or ACEi was initiated or dose adjusted or within 6-12 months for treatment guide and for monitoring (VERY LOW)
Variations	__ Last menstrual period and lactation status of all reproductive age women __ Refer patients with red flags such as uremia, fluid overload, and hyperglycemic crisis to appropriate facility and specialist				



Algorithm of the diagnosis and management of adults with type 2 diabetes and chronic kidney disease

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