Disease Progression and the Application of Evidence-Based Treatment Guidelines

Diagnose It Early: A Case for Screening and Appropriate Management

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ABSTRACT

BACKGROUND: Screening processes to identify patients who have chronic kidney disease (CKD) early in the disease allow time to manage its comorbidities and complications effectively and aggressively. The Kidney Early Evaluation Program (KEEP), sponsored by the National Kidney Foundation (NKF), is a free screening program that targets people who have diabetes, hypertension, and parents, grandparents, or siblings with diabetes, hypertension, or CKD.

OBJECTIVES: To (1) introduce KEEP and its objectives and (2) review population data and progress with goals to date.

SUMMARY: The KEEP goals are to raise awareness of CKD, especially in high-risk patients, provide free testing, and encourage dialogue between patients and their physicians, leading to a treatment plan. Of the 55,000 patients who have been screened through KEEP, approximately 13,000 (29%), or nearly 1 in 3 patients, have been identified as having CKD. Once a patient has been diagnosed with CKD, clinicians must address risk factors such as diabetes, hypertension, and kidney-specific diseases (e.g., glomerular diseases) that contribute to the process of renal decline. The NKF through the Kidney Disease Outcomes Quality Initiative has assembled a series of guidelines addressing dialysis adequacy, vascular access, anemia, nutrition, CKD, bone and mineral metabolism, dyslipidemia, hypertension, cardiovascular disease, and diabetes.

CONCLUSION: CKD is quite common but often unrecognized and under-treated, even though rigorous guidelines for diagnosis and care have been developed. Ten areas have been identified as important for optimal care of the CKD patient. Each of these areas should be addressed and closely monitored in this population: hypertension, anemia, glucose control, lipid control, smoking cessation, aspirin prophylaxis and use of a beta-blocker post-myocardial infarction, use of angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, diet, exercise, and weight control.

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The Kidney Early Evaluation Program (KEEP), sponsored by the National Kidney Foundation (NKF), is a free screening program that targets people who have diabetes, high blood pressure, and parents, grandparents, or siblings with diabetes, hypertension, or chronic kidney disease (CKD).¹ Patients can refer themselves after learning about KEEP from magazines, newspaper articles, or other media, or can be referred by a health care provider. Although KEEP is administered by the NKF, the actual screening events are organized by 52 NKF affiliates. KEEP is staffed by lay and professional volunteers who are trained by the NKF. The program's goals are to raise awareness of CKD, especially in high-risk patients; provide free testing; and encourage dialogue between patients and their physicians, leading to a treatment plan. Educating and empowering patients is also a goal in order to prevent or delay CKD, initiate appropriate referrals for follow-up care, and provide ongoing information and support.¹

During a KEEP screening, volunteer health care professionals (e.g., physicians, nurses, and pharmacists) monitor blood pressure, record weight, and coordinate lab work (e.g., blood glucose, hemoglobin, urine dipstick for microalbuminemia and hematuria, albumin, and serum creatinine). Albumin to creatinine ratio is employed to determine serum creatinine and estimate glomerular filtration rate (eGFR) using a Modification of Diet in Renal Disease equation. Clinicians notify patients of the screening results and may refer them to their primary care physicians for follow-up if abnormal results were identified.

Abnormal results identified during a KEEP screening are not considered diagnostic but rather, indicative of increased risk. Overall, patient participation in the KEEP screening process takes approximately 30 minutes. At the conclusion of the screening, the clinician sends data collected to the NKF.¹ Aggregate data are published yearly in the KEEP Annual Data Report. Of the 55,000 patients who have been screened through the KEEP process since its inception in 2000, approximately 13,000 (29%), or nearly 1 in 3 patients, have been identified as having CKD, with stage 3 being identified most frequently.²

CKD: Progression and Comorbidities

Once a patient has been diagnosed with CKD, clinicians must identify and address risk factors associated with disease progression. Risk factors may be divided into 3 descriptive categories:

1. **Susceptibility factors**, such as advanced age, racial/ethnic minorities, family history, and low income or education, may put a patient at an increased risk of developing CKD. For example, approximately 50 million Americans are more than 60 years old and should be monitored for progressive renal function decline.² Thirty-four million black Americans and 35 million Hispanics or Latinos are also at increased risk for CKD.²

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2. *Initiators* are factors such as diabetes, hypertension, and kidney-specific diseases (e.g., glomerular diseases) that are strongly associated with the beginning of renal decline.
3. *Progression factors* contribute to the advancement of CKD and include hyperglycemia, hypertension, proteinuria, and smoking.² Each of these factors is modifiable through patient behaviors and drug therapy. Addressing them is critical. Diabetes is the primary cause of end-stage renal disease (ESRD). However, the presence of hypertension is also a strong risk factor and is more common, affecting 43 million Americans.² Most often, diabetes and hypertension are comorbid and must both be addressed and managed.

Evaluation includes diagnosing the underlying cause of CKD, staging for severity, identifying comorbid conditions and complications, and assessing risk of cardiovascular disease (CVD). The results of evaluation should drive specific therapy (see Table 1) with an overall goal of preventing further loss of kidney function. Glomerular disease should be treated, if possible, and if diabetes and/or hypertension are present, controlling glycosylated hemoglobin (A1c) and blood pressure is crucial. Early detection and aggressive management of CKD and its comorbidities may slow or arrest progression to ESRD. Employing medications that may reduce glucose or blood pressure and simultaneously reduce proteinuria; prescribing an erythropoiesis-stimulating agent (ESA) and/or an iron product for anemia; starting a lipid-lowering product; and using primary prevention medications such as aspirin are part of the CKD management principles.

Medication review is critical for patients who have CKD. There are several areas where patients require guidance or where medications require adjustment. Renally cleared medications often require dosage adjustment as kidneys fail and some medications accumulate, making them more difficult to use. It may be necessary to increase therapeutic drug monitoring and a host of new medications may need to be added. New medications added as renal decline progresses must be compatible with the current regimen. A patient with stage 3 or 4 CKD is prescribed an average of 6 to 8 medications.³ A patient at end-stage CKD is prescribed about 10 to 12 medications.⁴ Therapeutic drug monitoring should prevent most drug-drug interactions and some adverse drug events, while patient education may help to make adverse events more manageable for the patient and provide continual encouragement for patient adherence to the treatment regimen.

■ Kidney Disease Outcomes Quality Initiative Guidelines

The CKD patient population tends to experience a number of adverse outcomes and comorbidities, and the NKF has attempted to help clinicians address these concerns. The Kidney Disease Outcomes Quality Initiative (KDOQI), developed by a multidisciplinary team, was created to provide comprehensive diagnosis and management guidelines for CKD.⁵ Within

TABLE 1 Management Principles for CKD

Delay or stop CKD progression	<ul style="list-style-type: none"> • Treat underlying conditions if possible. • Address blood pressure control, aggressively targeting JNC 7's target values. • Use ACEIs as tolerated, monitoring for renal deterioration and hyperkalemia. • Follow the American Diabetes Association recommendations for glycemic control (target A1c < 7%). • Consider protein restriction. • Treat hyperlipidemia. • Avoid nephrotoxins (nonsteroidal anti-inflammatory agents, aminoglycosides).
Treat CKD's pathologic manifestations	<ul style="list-style-type: none"> • Anemia (erythropoietin-stimulating agents) • Hyperphosphatemia (dietary phosphate binders and dietary phosphate restriction) • Hypocalcemia (calcium supplements and/or calcitriol) • Hyperparathyroidism (calcitriol or vitamin D analogs) • Volume overload (loop diuretics or ultrafiltration) • Metabolic acidosis (oral alkali supplementation) • Uremic manifestations with chronic renal replacement therapy (hemodialysis, peritoneal dialysis, or renal transplantation) • Cardiovascular complications using standard of care
Plan for chronic renal replacement therapy	<ul style="list-style-type: none"> • Educate patients early and frequently about disease progression, potential dialysis modalities, renal transplantation, and the option to refuse or discontinue chronic dialysis. • Place permanent vascular access (arteriovenous fistula) at least 6 months in advance of anticipated date of dialysis. • Arrange elective peritoneal dialysis catheter insertion. • Refer for renal transplantation early.
Establish a multi-disciplinary team early	<ul style="list-style-type: none"> • Refer to nephrology early. • Involve a renal dietitian. • Schedule vascular surgery for permanent vascular access. • Schedule general surgery for peritoneal catheter placement. • Enroll the patient in a renal transplant center.
Address dietary changes	<ul style="list-style-type: none"> • Restrict protein as the patient approaches CKD stage 5 to delay onset of uremic symptoms. • Assess malnutrition risk and implement strategies to correct or address it. • Restrict phosphate, starting early in CKD. • Restrict potassium. • Restrict sodium and water as necessary to avoid volume overload.

References 1 through 9 were used to develop this chart.

ACEI=angiotensin-converting enzyme inhibitor; CKD=chronic kidney disease; JNC 7=Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.

FIGURE 1 Association of Level of GFR With Complications

Adapted from K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification. Available at: www.kidney.org/professionals/KDOQI/guidelines_ckd/toc.htm. Accessed on September 17, 2007. GFR=glomerular filtration rate.

KDOQI, separate guidelines have been developed to address each of the following areas: dialysis adequacy, vascular access, anemia, nutrition, CKD, bone and mineral metabolism, dyslipidemia, hypertension, CVD, and diabetes.¹ Although these diagnoses must be addressed in concert, each requires some specialized knowledge on the part of the clinician.

Glomerular Filtration Rate

Glomerular filtration rate (GFR), calculated from blood creatinine, age, race, gender, and other factors, is the best test measure to determine the degree of kidney dysfunction. A declining GFR is associated with additional complications, including anemia, inability to walk a quarter of a mile, low albumin (malnourishment), and electrolyte abnormalities (hypocalcemia and/or hyperphosphatemia)² (Figure 1).

Cardiovascular Disease

Analysis of the Kaiser Permanente database has found that death rate correlates with declining GFR.⁶ Cardiovascular morbidity

and mortality is greater among CKD patients than in the general population, and most patients with CKD will die of CVD before reaching ESRD. A 1999 study by Sarnak and Levey determined that the dialysis population, compared with the general population of people without CKD, experiences a greater annual mortality rate related to cardiovascular events.⁷ In the general population, morbidity rates increase with age. For the dialysis population, risk is high from an early age and remains high. A 35- to 44-year-old dialysis patient, for example, has a cardiovascular risk comparable with that of an 84- or 85-year-old individual who is not on dialysis. CVD mortality rates are 15 times higher in the ESRD population than in people who do not have ESRD. All patients with CKD should be considered the highest risk group for CVD, and all CKD patients should undergo an assessment for traditional or CKD-related cardiovascular risk factors. Patients with CKD are at increased risk for CVD if they have traditional CVD risk factors, but additional risk factors specific to the CKD population can complicate their prognoses (Table 2).

The KDOQI treatment guidelines for CVD and hypertension emphasize that as GFR declines, the incidence of hypertension (defined as blood pressure >140/90 mm Hg) increases from 42% in populations with normal GFR to approximately 75% in people with ESRD (GFR <15 mL per minute per 1.73 m²). Bakris et al. conducted a meta-analysis examining mean arterial blood pressure and GFR decline.⁸ They found that as mean arterial blood pressure increases, GFR decline accelerates.

Reducing a blood pressure from 140/90 mm Hg to 130/80 mm Hg can slow progressive renal disease. A blood pressure reduction of 10mm Hg can reduce renal disease progression by 65%. For example, a 35-year-old female with CKD and a serum creatinine of 1.5 mg per dL, an estimated GFR of 60 mL per minute per 1.73 m², and a current blood pressure of 150/100 mm Hg could delay her progression to ESRD by 8 to 9 years by reducing blood pressure to 140/90 mm Hg. Further blood pressure reduction to 130/80 mm Hg could delay progression by 15 years. If, however, her blood pressure remains uncontrolled at 150/100 mm Hg, she can expect to need dialysis in 5 years. The importance of tight blood pressure control in CKD patients has also been identified by the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7).⁹ This paradigm applies to all CKD patients in stages 1 through 4.

The average number of antihypertensive medications needed to control high blood pressure can be calculated, at least in the clinical setting, by looking at large antihypertensive trials.^{8,10} Most patients will require 3 or more medications to control blood pressure adequately. When choosing antihypertensive therapy for a patient with CKD, clinicians need to consider compelling comorbid indications, such as heart failure with systolic dysfunction, post-myocardial infarction with or without systolic dysfunction, chronic stable angina, high-risk coronary artery

disease, recurrent stroke prevention, or supraventricular tachycardia. Depending on the comorbidities, certain antihypertensive medications are recommended for first-line use. Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs) are preferred in the diabetic and nondiabetic/high protein excretion populations. No particular antihypertensive medication is preferred in the nondiabetic/low protein excretion and transplant populations.² Both the KDOQI guidelines and JNC 7 recommend that clinicians prescribe the best agent for the patient's unique mix of comorbidities.

Diabetes

Diabetes, a CVD risk factor, also poses special challenges in the CKD patient. For each 1% increase in A1c, the cardiovascular hazard ratio increases 15% in the patient with type 1 diabetes and 18% in the patient with type 2 diabetes. Three fourths of patients with diabetes die of CVD as opposed to one third of the general population.⁵ Steno et al. followed 160 type 2 diabetic patients with microalbuminuria for almost 8 years to determine if targeted, intensified, multifactorial intervention would lead to better outcomes than would conventional treatment.¹¹ Study participants received either conventional therapy or intensive therapy. Intensive therapy stressed A1c control, employed aspirin therapy, and controlled lipids and blood pressure. In the intensive-therapy group, A1c values, systolic and diastolic blood pressure, serum cholesterol, and triglyceride levels were measured after an overnight fast. Findings included that the urinary albumin excretion rate declined to a greater extent than in the conventional-therapy group. Patients receiving intensive therapy reduced their risk of CVD by 53%, nephropathy by 61%, and retinopathy by 63%. Target-driven, long-term, intensified intervention aimed at multiple risk factors in patients with type 2 diabetes and microalbuminuria reduces the incidence of CKD and prevents complications.

If a choice must be made between tight blood pressure control and tight glucose control in CKD patients, tight blood pressure control is more likely to reduce risk of stroke, any diabetic endpoint, diabetes mellitus death, or microvascular complications.⁸ Regardless, overall outcome will be better if all surrogate markers of CKD are addressed.⁷

Anemia

As kidney function declines during CKD progression from stage 1 to stage 5, the risk of developing anemia increases dramatically (see Figure 2).¹² Anemic patients with CKD usually have left ventricular hypertrophy, which may exacerbate heart failure. Furthermore, patients with CKD and anemia report reduced aerobic capacity, overall well-being, sexual function, and cognition. Body mechanisms, in attempting to fix or account for the damaged state caused by the triad of CKD, heart failure, and anemia, lead to a continuing promulgating cycle of worsening CKD, heart failure, and anemia.¹³

TABLE 2 Traditional CVD Risk Factors and CKD-Specific CVD Risk Factors

Traditional CVD Risk Factors	CKD-Specific CVD Risk Factors
Older age	Type of CKD
Male gender	Decreased GFR
White race	Proteinuria
Hypertension	RAS activity
Elevated LDL	ECF volume overload
Decreased HDL	Abnormal serum calcium and phosphate
Diabetes mellitus	Pronounced dyslipidemia
Tobacco use	Anemia
Physical inactivity	Malnutrition
Menopause	Inflammation
Psychosocial stress	Infection
Family history of CVD	Thrombogenic factors
	Elevated homocysteine
	Uremic toxins

National Kidney Foundation (2006).⁵

CKD=chronic kidney disease; CVD=cardiovascular disease; ECF=extracellular fluid; GFR=glomerular filtration rate; HDL=high-density lipoprotein; LDL=low-density lipoprotein; RAS=renin-angiotensin system.

FIGURE 2 Anemia Prevalence in CKD

* Keane WF et al.¹²

** United States Renal Data System. USRDS 2005 Annual Data Report: Atlas of End-Stage Renal Disease in the United States. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2005. CKD=chronic kidney disease; GFR=glomerular filtration rate.

The May 2006 KDOQI guidelines recommended a target hemoglobin of between 11 and 13 g per dL for anemia, but the April 2007 revision reduced the target range to 11 to 12 g per dL.¹⁴ The KDOQI guidelines also recommend monitoring serum ferritin, transferrin saturation, and reticulocyte hemoglobin content for hemodialysis and peritoneal dialysis. To meet

KDOQI goals of a target hemoglobin of 11 to 12 g per dL, ESAs and oral or intravenous iron therapy are important pharmacologic therapies.¹⁵ With the recent black box warnings on ESAs emphasizing increased risk for death and serious cardiovascular reactions when administered to target a hemoglobin of ≥ 12 g per dL, dialysis organizations are examining their policies and adjusting algorithms.

In November 2006, 2 studies—CHOIR and CREATE—were published. The Correction of Anemia with Epoetin Alfa in Chronic Kidney Disease (CHOIR) included 1,432 patients with a mean GFR of 27 mL per minute per 1.73 m^2 .¹⁶ Of the study population, 715 patients were randomly assigned to receive a dose of epoetin alfa targeted to achieve a hemoglobin level of 13.5 g per dL, and 717 received a dose targeted to achieve a level of 11.3 g per dL. The groups attained average hemoglobin levels of 11.3 g per dL and 12.6 g per dL, respectively, a difference of about 1 g per dL, but the high-hemoglobin group required more erythropoietin to reach that level.

Two hundred twenty-two composite events occurred: 65 deaths (29.3%), 101 hospitalizations for heart failure (45.5%), 25 myocardial infarctions (11.3%), and 23 strokes (10.4%). Of these, 125 events occurred in the high-hemoglobin group and 97 events occurred in the low-hemoglobin group. Seven patients (3.2%) were hospitalized for heart failure and myocardial infarction combined, and 1 patient (0.5%) died after having a stroke. Improvements in quality of life were similar between the 2 groups. The probability of death was significantly less in the low-hemoglobin group. The use of a target hemoglobin level of 13.5 g per dL was associated with an increased risk of serious adverse events.¹⁶

Drueke et al. conducted a similar study, CREATE, (Cardiovascular Risk Reduction in Early Anemia Treatment with Epoetin Beta) to study whether correction of anemia in patients with stage 3 or 4 CKD improves cardiovascular outcomes.¹⁷ CKD patients with GFRs averaging 27 mL per minute per 1.73 m^2 were randomized to ESA therapy to achieve a hemoglobin of 13 to 15 g per dL or 10.5 to 11.5 g per dL. Survival was similar between the groups over 48 months. One of the study conclusions was that early complete correction of anemia in CKD patients does not reduce the risk of cardiovascular events.

Other studies have examined hemoglobin's influence on outcomes. Besarab et al. studied more than 1,200 CKD patients receiving dialysis who were randomized to a normal hematocrit of $42 \pm 3\%$ or a lower hematocrit of $30 \pm 3\%$, equivalent to a hemoglobin of 12 g per dL and 10 g per dL, respectively.¹⁸ After 29 months, patients in the normal-hematocrit group experienced 183 deaths and 19 first nonfatal myocardial infarctions. Those in the low-hematocrit group had 150 deaths and 14 nonfatal myocardial infarctions. The difference in event-free survival between the 2 groups did not reach the prespecified statistical stopping point, but the researchers halted the study early for safety concerns. Adequacy of dialysis declined for

patients in the normal-hematocrit group, and they received more intravenous iron dextran than did low-hematocrit patients. The researchers concluded that hemodialysis patients with clinically evident heart failure or ischemic heart disease should be treated to lower hematocrit or hemoglobin targets.

In 2000, a KDOQI work group recommended targeting a hemoglobin concentration of 11 to 12 g per dL in CKD patients; they increased it to 11 to 13 g per dL in 2006. CHOIR and CREATE were published, suggesting that lower hemoglobins are safer than those exceeding approximately 12.6 g per dL. Consequent to the U.S. Food and Drug Administration's requirement for a black box warning, the KDOQI work group reconvened and published revised guidelines in September 2007 stating, "In the opinion of the Work Group, in dialysis and non-dialysis patients with CKD receiving ESA therapy, the selected hemoglobin target should generally be in the range of 11 to 12 g per dL."¹⁹

■ Bone Disease Parameters

KDOQI has also established targets for serum phosphorous, corrected calcium, the calcium-phosphorous product (a multiplication product of phosphorous and calcium levels), and intact parathyroid hormone in patients with CKD (Table 3). Once calcium-phosphorous product exceeds the reference range of between 40 and 45 mg^2 per dL^2 , the relative risk of death increases. Patients with secondary hyperparathyroidism or bone and mineral metabolism abnormalities often have bone pain, fractures, and joint pain and swelling. Their soft tissues may start to calcify and muscle weakness may occur. Pruritis, exacerbation or worsening of left ventricular hypertrophy, or worsening of anemia can also occur.

■ Dyslipidemia

Dyslipidemia is common in patients with CKD, and the lipid profile varies widely depending on the level of kidney function and the degree of proteinuria. All stages of CKD are considered a coronary heart disease (CHD) risk equivalent (similar to diabetes mellitus); therefore, all patients with CKD should be considered in the highest risk group for CHD. The common pattern of late-stage CKD includes hypertriglyceridemia, low or normal levels of low-density lipoprotein (LDL), low lipoprotein (a), and low high-density lipoprotein (HDL). KDOQI recommends initiating treatment when triglycerides exceed >500 mg per dL, LDL is >100 mg per dL, non-HDL >130 mg per dL, or HDL falls <40 mg per dL.⁵

Generally, HMG-CoA reductase agents (statins) are used to lower LDL; fibrates, including fenofibrates, are used to lower triglycerides; and niacin is used to increase HDL. In the CKD population, HMG-CoA reductase agents (statins) are preferred, with gemfibrozil and niacin used periodically. The complete NKF algorithm for treating dyslipidemia in CKD is available at www.kidney.org/professionals/kdoqi/guidelines_lipids/iii.htm#Fig7.

Smoking

In the CKD population, smoking confers a dose-dependent risk for CKD progression, with diabetic women at particular risk. After 20 years of smoking, males have 2.5 times the risk of CKD, and women have 2.9 times greater risk than nonsmokers.²⁰ Smoking represents one of the modifiable risk factors to improve patient outcomes in the CKD patient (Table 4).

Progress Report

Using Table 4 as a guide of optimal patient management, most patients are not managed to goal and there are many gaps to achieving optimal care. Among diabetics, only 7% of patients achieve their goals of A1c <7, a blood pressure <130/80 mm Hg, and total cholesterol <200 mg per dL.²¹ Ninety-three percent of all patients have 1 or more of these risk factors for CKD development. One in 3 diabetics has hypertension, 1 in 2 has hyperlipidemia, and 1 in 6 is a smoker.²¹

ACEIs and ARBs are the cornerstone of hypertension therapy. They have been proven to slow kidney and CVD progression in diabetic populations specifically. Yet depending on the datasets employed to measure progress (e.g., National Health and Nutrition Examination Survey [NHANES] III or NHANES from 1999 to 2002), only 35% to 37% of patients who should be prescribed an ACEI or an ARB (patients with diabetes, hypertension, or heart failure) actually receive these renal protective therapies. Underuse of ACEIs and ARBs is also an area that can be improved.²²

Patients with comorbid CKD and diabetes should be taking a glucose-lowering agent (e.g., insulin, thiazolidinediones, secretagogues, or metformin). NHANES has been used for decades to assess nutritional status in the United States. Datasets from NHANES III (1988 to 1994) or NHANES (1999 to 2002) show clear differences in drug regimens between the CKD and non-CKD populations. For example, metformin use reported in NHANES is substantially less in CKD patients than in non-CKD patients (21% vs. 34%), which may be attributed to metformin's propensity to cause lactic acidosis CKD. The manufacturer has recently tightened its recommendation for use of metformin in patients with kidney disease and states that patients whose serum creatinine concentrations exceed the upper limit of normal should not take metformin.

The United States Renal Data System (USRDS) 2007 Medstat dataset compares CKD and ESRD patients' adherence with a variety of drug regimens: ACEIs, ARBs, beta-blockers, statins, and secretagogues. Both CKD and ESRD populations show medication adherence rates of about 80% during the first 6 to 12 months after initiation. However, over the course of 2 years, medication adherence rates decrease steadily to 50%. Patients who are in ESRD take, on average, 10 to 12 medications; CKD patients take 6 to 8 medications. Numerous factors contribute to nonadherence, but the number and timing of medications

TABLE 3 KDOQI Targets for Bone Disease Parameters

Parameter	Target	
	CKD Stages 3-4	CKD Stage 5
Serum P (mg per dL)	2.7-4.6	3.5-5.5
Corrected serum Ca (mg per dL)	Normal range for laboratory used	8.4-9.5
Ca x P product (mg ² per dL ²)	<55	<55
Intact parathyroid hormone (pg per mL)	Stage 3: 35-70 Stage 4: 70-110	150-300

Adapted from K/DOQI Clinical Practice Guidelines for Bone Metabolism and Disease in Chronic Kidney Disease. Available at: www.kidney.org/professionals/KDOQI/guidelines_bone/guide1.htm#table14.

Ca=calcium; CKD=chronic kidney disease; KDOQI=Kidney Disease Outcomes Quality Initiative; P=phosphorus.

TABLE 4 10 Steps to Success

1.	Hypertension control—130/80 mmHg
2.	Hemoglobin target—11-12 g per dL
3.	Glucose control—A1c <7
4.	Lipid control—LDL-C <100 mg per dL, HDL-C >40 mg per dL
5.	Smoking cessation
6.	Aspirin + beta-blocker use post-myocardial infarction
7.	ACEI or ARB therapy
8.	Diet
9.	Exercise
10.	Weight control

ACEI=angiotensin-converting enzyme inhibitor; ARB=angiotensin II receptor blocker; HDL-C=high-density lipoprotein cholesterol; LDL-C=low-density lipoprotein cholesterol.

and the duration of treatment are 2 reasons that can decrease adherence significantly.

Summary

CKD is quite common but is often unrecognized and under-treated. Appropriate screening can identify patients at risk and facilitate early treatment for these patients. One program that has successfully screened patients and referred them for treatment is the NKF's KEEP. To date, more than 90,000 patients have been screened through KEEP, thanks in part to professional volunteers and a broad advertising campaign. When patients are identified as having CKD, this program helps link them with appropriate health care. Patients' specific health care plans should be guided by the NKF's KDOQI clinical practice guidelines, which recommend optimal management therapies for a variety of comorbid conditions to reduce complications in these patients. Early identification and aggressive treatment can prevent progression to ESRD.

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DISCLOSURES

Author Harold J. Manley discloses no potential bias or conflict of interest relating to this article.

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