Overview of the management of chronic kidney disease in adults

Author
Mark Rosenberg, MD

Section Editor
Gary C Curhan, MD, ScD

Deputy Editor
Alice M Sheridan, MD

All topics are updated as new evidence becomes available and our peer review process is complete.
Literature review current through: Mar 2015. | **This topic last updated:** May 16, 2014.

INTRODUCTION — All patients with renal disease (whether acute or chronic) should undergo an assessment of renal function by estimating the glomerular filtration rate (GFR) from the serum creatinine. This measurement is used clinically to evaluate the degree of renal impairment, to follow the course of the disease, and to assess the response to therapy. An attempt must also be made to obtain a specific diagnosis. The first step in this process is a careful urinalysis, looking for proteinuria, hematuria, and cellular casts. Further evaluation may include quantification of proteinuria, kidney ultrasound, referral to a nephrologist, and a kidney biopsy. Nephrology referral is especially indicated when there is a rapid decline in kidney function, an elevated albumin to creatinine ratio (>300 mg/g), or urinary red blood cell casts. (See "Assessment of kidney function" and "Diagnostic approach to the patient with acute kidney injury (acute renal failure) or chronic kidney disease" and "Urinalysis in the diagnosis of kidney disease".)

An overview of the general issues involved in the management of the patient with chronic kidney disease (CKD), including modalities to slow the rate of progression, will be presented here. The specific therapy of patients with particular renal diseases is discussed separately in the appropriate topic reviews.

NATURAL HISTORY OF RENAL DISEASE — The initial injury to the kidney may result in a variety of clinical manifestations, ranging from asymptomatic hematuria to renal failure requiring dialysis. Many individuals fully recover and subsequently suffer from little or no sequelae. Poststreptococcal glomerulonephritis in children, for example, most frequently has a long-term benign prognosis. By comparison, some patients, such as those with lupus nephritis, experience repeated and chronic insults to the renal parenchyma, thereby resulting in lasting damage. Furthermore, others in whom the initial disease is either inactive or cured may still develop progressive renal disease due to hemodynamic and other mechanisms.

In addition to variations in the activity of the individual diseases, these different manifestations are partly due to how the kidney responds to injury. The kidney is able to adapt to damage by increasing the filtration rate in the remaining normal nephrons, a process called adaptive hyperfiltration. As a result, the patient with mild renal insufficiency often has a normal or near-normal serum creatinine concentration. Additional homeostatic mechanisms (most frequently occurring within the renal tubules) permit the serum concentrations of sodium, potassium, calcium, and phosphorous and the total body water to also remain within the normal range, particularly among those with mild to moderate renal failure. (See "Assessment of kidney function".)

Adaptive hyperfiltration, although initially beneficial, appears to result in long-term damage to the glomeruli of the remaining nephrons, which is manifest by proteinuria and progressive renal failure. This process appears to be responsible for the development of renal failure among those in whom the original illness is either inactive or cured [1]. The institution of measures to help prevent this process, such as antihypertensive therapy with an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin II receptor blocker (ARB), may slow progressive disease and even preserve renal function. If these modalities are effective, the benefit is likely to be greatest if begun before a great deal of irreversible scarring has occurred. (See "Secondary factors and progression of chronic kidney disease".)

The gradual decline in function in patients with chronic kidney disease (CKD) is initially asymptomatic. However, as previously mentioned, different signs and symptoms may be observed with advanced renal failure, including volume overload, hyperkalemia, metabolic acidosis, hypertension, anemia, and mineral and bone disorders (MBD). The

onset of end-stage renal disease (ESRD) results in a constellation of signs and symptoms referred to as uremia.

Manifestations of the uremic state include anorexia, nausea, vomiting, pericarditis, peripheral neuropathy, and central nervous system abnormalities (ranging from loss of concentration and lethargy to seizures, coma, and death). No direct correlation exists between the absolute serum levels of blood urea nitrogen (BUN) or creatinine and the development of these symptoms. Some patients have relatively low levels (eg, a BUN of 60 mg/dL [21.4 mmol/L] in an older patient), but are markedly symptomatic, while others have marked elevations (eg, a BUN of 140 mg/dL [50 mmol/L]), but remain asymptomatic. To continue life, uremic patients require the institution of renal replacement therapy with hemodialysis, peritoneal dialysis, or renal transplantation. (See "Uremic toxins".)

Not all individuals have progressive loss of kidney function. Some studies show a high rate of progression, while others report relatively stable disease [2-4]. The rate of progression of CKD from one major stage to another varies based upon the underlying disease, presence or absence of comorbid conditions, treatments, socioeconomic status, individual genetics, ethnicity, and other factors. Episodes of acute kidney injury (AKI) may cause more rapid progression to ESRD in individual patients. (See "Renal and patient outcomes after acute tubular necrosis".)

Using epidemiologic data, general estimates for the rate of transition from an estimated glomerular filtration rate (eGFR) between 15 to 60 mL/min per 1.73 m^2 to end-stage disease may be approximately 1.5 percent per year, while the rate of transition from an eGFR >60 to <60 mL/min per 1.73 m^2 is approximately 0.5 percent per year [5,6].

The combination of both a low eGFR plus dipstick-positive proteinuria, versus either parameter alone, is associated with a significantly increased risk of progressive renal disease. This was shown in a retrospective study of the association between these measures and the 25-year incidence of ESRD of middle-aged men originally studied in the Multiple Risk Factor Intervention Study (MRFIT) [7]. The presence of 1+ dipstick proteinuria, 2+ dipstick proteinuria, eGFR <60 mL/min per 1.73 m^2, and a low eGFR plus 2+ proteinuria was associated with hazard ratios of 3.1, 15.7, 2.4, and 41, respectively, for the development of ESRD over a 25-year period.

DEFINITION AND CLASSIFICATION — Chronic kidney disease (CKD) is defined as the presence of kidney damage (usually detected as urinary albumin excretion of ≥30 mg/day, or equivalent) **or** decreased kidney function (defined as estimated glomerular filtration rate [eGFR] <60 mL/min per 1.73 m^2) **for three or more months**, irrespective of the cause. The persistence of the damage or decreased function for at least three months is necessary to distinguish CKD from acute kidney disease (AKI).

Classification, or staging, of CKD provides a guide to management, including stratification of risk for progression and complications of CKD. Risk stratification is used to inform appropriate treatments and the intensity of monitoring and patient education. We agree with the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) guidelines that state that among patients who are diagnosed using the criteria described above, staging of CKD should be done according to the following (table 1) [8]:

- Cause of disease
- Six categories of eGFR (G stages)
- Three categories of albuminuria (A stages)

Staging patients with CKD according to cause, eGFR, and albuminuria enhances risk stratification for the major complications of CKD (figure 1 and figure 2). As seen in these figures, increasing albuminuria is associated with a higher risk of adverse events at every level of eGFR.

A more detailed discussion of the definition and classification of CKD is provided separately. (See "Definition and staging of chronic kidney disease in adults".)

ASSOCIATION WITH CARDIOVASCULAR DISEASE, END-STAGE RENAL DISEASE, AND MORTALITY — There is a large body of evidence that patients with chronic kidney disease (CKD) have a substantial increase in cardiovascular risk that can be in part explained by an increase in traditional risk factors

such as hypertension, diabetes, and the metabolic syndrome. CKD alone is also an independent risk factor for cardiovascular disease. Among patients with CKD, the risk of death, particularly due to cardiovascular disease, is much higher than the risk of eventually requiring dialysis. This is discussed separately. (See "Chronic kidney disease and coronary heart disease".)

Close attention to the prevention and management of cardiovascular disease should occur among patients identified with CKD [9]. As an example, the increased intake of calcium (which is commonly given to treat hyperphosphatemia and may result in a high calcium-phosphorus product) may enhance coronary arterial calcification. Although controversial, this is thought by some to be associated with the development of coronary atherosclerosis and is related to the presence and/or consequences of elevated serum phosphorus, calcium, and parathyroid hormone (PTH) levels. (See 'Mineral and bone disorders (MBD)' below and "Vascular calcification in chronic kidney disease".)

These and other observations have suggested that CKD should be considered a coronary equivalent and that aggressive risk factor reduction should be part of standard therapy of patients with CKD. (See "Chronic kidney disease and coronary heart disease", section on 'CKD as a CHD risk equivalent' and "Chronic kidney disease and coronary heart disease", section on 'Reduction of CHD risk in patients with CKD'.)

Patients with CKD are also at increased risk for the development of end-stage renal disease (ESRD) as well as all-cause mortality. The competing risks of cardiovascular and ESRD vary depending on the population of patients studied and factors such as age, proteinuria, and type of kidney disease. (See "Chronic kidney disease and coronary heart disease", section on 'Competing risks of cardiovascular and end-stage renal disease'.)

GENERAL MANAGEMENT OF CHRONIC KIDNEY DISEASE — The general management of the patient with chronic kidney disease (CKD) involves the following issues [10]:

- Treatment of reversible causes of renal failure
- Preventing or slowing the progression of renal disease
- Treatment of the complications of renal failure
- Adjusting drug doses when appropriate for the level of estimated glomerular filtration rate (eGFR)
- Identification and adequate preparation of the patient in whom renal replacement therapy will be required

Reversible causes of renal failure — In addition to exacerbation of their original renal disease, patients with CKD with a recent decrease in renal function may be suffering from an underlying reversible process, which, if identified and corrected, may result in the recovery of function.

Decreased renal perfusion — Hypovolemia (such as vomiting, diarrhea, diuretic use, bleeding); hypotension (due to myocardial dysfunction or pericardial disease); infection (such as sepsis); and the administration of drugs which lower the eGFR (such as nonsteroidal antiinflammatory drugs [NSAIDs] and angiotensin-converting enzyme [ACE] inhibitors) are common causes of potentially reversible declines in renal function.

The normal response to renal hypoperfusion is to lower the urine sodium concentration (<25 mEq/L) and the fractional excretion of sodium (<1 percent in patients with advanced renal failure) to very low levels. However, the superimposition of a prerenal process among patients with CKD may not result in the expected low values since the tubules in the diseased kidney are unable to reabsorb sodium so efficiently. As a result, hypovolemia in these patients should be diagnosed by the history and physical examination, including the presence of relative hypotension, and a low jugular venous pressure. In this setting, a judicious trial of fluid repletion may result in the return of renal function to the previous baseline. (See "Fractional excretion of sodium, urea, and other molecules in acute kidney injury (acute renal failure)".)

Administration of nephrotoxic drugs — The administration of drugs or diagnostic agents that adversely affect renal function are a frequent cause of worsening renal function. Among patients with CKD, common offenders include aminoglycoside antibiotics (particularly with unadjusted doses), NSAIDs, and radiographic contrast material, particularly in diabetics. The administration of such drugs should therefore be avoided or used with caution

in patients with underlying CKD. (See "Manifestations of and risk factors for aminoglycoside nephrotoxicity" and "NSAIDs: Acute kidney injury (acute renal failure)" and "Pathogenesis, clinical features, and diagnosis of contrast-induced nephropathy".)

Certain drugs also interfere with either creatinine secretion or the assay used to measure the serum creatinine. These include cimetidine, trimethoprim, cefoxitin, and flucytosine. In these settings, there will be no change in the true GFR; the clinical clue that this has occurred is the absence of a concurrent elevation in the blood urea nitrogen (BUN). (See "Drugs that elevate the serum creatinine concentration".)

Urinary tract obstruction — Urinary tract obstruction should always be considered in the patient with unexplained worsening renal function; although, in the absence of prostatic disease, it is much less common than decreased renal perfusion. Patients with slowly developing obstruction typically have no changes in the urinalysis, no symptoms referable to the kidney, and initially maintain their urine output. Given this lack of clinical clues, renal ultrasonography is often performed to exclude urinary tract obstruction in patients with an unexplained elevation in the serum creatinine. (See "Clinical manifestations and diagnosis of urinary tract obstruction and hydronephrosis".)

Slowing the rate of progression — Studies in experimental animals and humans suggest that progression in CKD may be due at least in part to secondary factors that are unrelated to the activity of the initial disease. The major factors are thought to be intraglomerular hypertension and glomerular hypertrophy (which are primarily responsible for the adaptive hyperfiltration described above), leading to glomerular scarring (glomerulosclerosis). Additional causes may include systemic hypertension, hyperlipidemia, metabolic acidosis, and tubulointerstitial disease. (See "Secondary factors and progression of chronic kidney disease".)

The major histologic manifestation of hemodynamically-mediated renal injury is secondary focal segmental glomerulosclerosis [11]. Thus, proteinuria typically is present in patients with progressive CKD, even in primary tubulointerstitial diseases such as reflux nephropathy.

Principal targets for renal protection — Therapy to slow the rate of progression in patients with CKD, independent of treatment of the underlying disease, is centered on attaining the blood pressure goal and, in patients with proteinuric disease, attaining the proteinuria goal. Blood pressure goals for nondiabetic and diabetic patients are discussed in detail elsewhere. (See "Treatment of diabetic nephropathy", section on 'Therapeutic goals' and "Antihypertensive therapy and progression of nondiabetic chronic kidney disease in adults", section on 'Proteinuria goal' and "Antihypertensive therapy and progression of nondiabetic chronic kidney disease in adults", section on 'Blood pressure goal'.)

In addition to blood pressure control, specific goals related to a reduction in urinary protein excretion have been formulated to slow the rate of progression of proteinuric CKD. Proteinuria goals and the use of ACE inhibitors or angiotensin receptor blocker (ARB) agents in patients with proteinuric CKD are discussed elsewhere. (See "Antihypertensive therapy and progression of nondiabetic chronic kidney disease in adults", section on 'Effect of renin-angiotensin system inhibitors on progression of CKD' and "Overview of hypertension in acute and chronic kidney disease", section on 'Choice of antihypertensive therapy'.)

In contrast to their renoprotective effects in proteinuric CKD, angiotensin inhibitors do **not** appear to be more beneficial than other antihypertensive agents in patients with nonproteinuric CKD. Recommendations for antihypertensive treatment of patients with nonproteinuric CKD are discussed elsewhere. (See "Overview of hypertension in acute and chronic kidney disease", section on 'Sequence of antihypertensive therapy in nonproteinuric CKD'.)

When used in patients with CKD, common side effects of angiotensin inhibition include a mild to moderate reduction in GFR, which occurs soon after the initiation of therapy, or an increase in dose and hyperkalemia, which can occur either soon after the initiation of therapy or later, if the patient has progressive CKD. (See "Major side effects of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers".)

Other targets for renal protection — Other therapeutic modalities also may offer some renal protection:

- Protein restriction − Protein restriction may slow the progression of CKD, although the optimal level of protein intake has not been determined. This issue is discussed elsewhere. (See "Protein restriction and progression of chronic kidney disease".)

- Statin therapy − Hyperlipidemia should be treated, in part because there is some evidence that it may enhance the rate of progression of the renal disease (see below). (See "Statins and chronic kidney disease".)

- Smoking cessation − Stopping smoking is associated with a slower rate of progression of CKD [12]. In an increasing number of studies, smoking also appears to correlate with an enhanced risk of developing kidney disease (primarily nephrosclerosis) as well as increasing the rate of progression among those with existing CKD [13].

- Treatment of chronic metabolic acidosis with supplemental bicarbonate may slow the progression to end-stage renal disease (ESRD). (See "Pathogenesis, consequences, and treatment of metabolic acidosis in chronic kidney disease", section on 'Slowing of CKD progression'.)

Treatment of the complications of renal failure — A wide range of disorders may develop as a consequence of the loss of renal function. These include disorders of fluid and electrolyte balance, such as volume overload, hyperkalemia, metabolic acidosis, and hyperphosphatemia, as well as abnormalities related to hormonal or systemic dysfunction, such as anorexia, nausea, vomiting, fatigue, hypertension, anemia, malnutrition, hyperlipidemia, and bone disease. Attention needs to be paid to all of these issues.

One recommended diet, including suggestions for protein, fat, mineral, and water, is presented (table 2). This should be modified based upon the needs of the individual patient.

Volume overload — Sodium and intravascular volume balance are usually maintained via homeostatic mechanisms until the eGFR falls below 10 to 15 mL/min per 1.73 m^2. However, the patient with mild to moderate CKD, despite being in relative volume balance, is less able to respond to rapid intake of sodium and is therefore prone to fluid overload.

Patients with CKD and volume overload generally respond to the combination of dietary sodium restriction and diuretic therapy, usually with a loop diuretic given daily. Some investigators have claimed that limiting sodium intake may also help decrease progression of CKD by lowering intraglomerular pressure [14]. We agree with the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) guidelines that, among all adults with CKD, sodium intake should be restricted to <2 g/day unless contraindicated [8]. (See "Loop diuretics: Maximum effective dose and major side effects" and "Treatment of refractory edema in adults".)

Hyperkalemia — The ability to maintain potassium excretion at near normal levels is generally maintained in patients with renal disease as long as both aldosterone secretion and distal flow are maintained [15,16]. Thus, hyperkalemia generally develops in the patient who is oliguric or who has an additional problem such as a high-potassium diet, increased tissue breakdown, or hypoaldosteronism (due in some cases to the administration of an ACE inhibitor or ARB) [17]. Impaired cell uptake of potassium also may contribute to the development of hyperkalemia in advanced CKD. (See "Causes and evaluation of hyperkalemia in adults".)

Hyperkalemia due to ACE inhibitor or ARB therapy is most likely to occur in patients in whom the serum potassium concentration is elevated or in the high-normal range prior to therapy. This is discussed in detail separately. (See "Treatment and prevention of hyperkalemia in adults".)

There are several measures that may help prevent hyperkalemia in patients with CKD. These include ingestion of a low-potassium diet (eg, <40 to 70 mEq/day [1500 to 2700 mg/day]) and avoiding, if possible, the use of drugs that raise the serum potassium concentration, such as NSAIDs [18]. Nonselective beta blockers may result in a postprandial rise in the serum potassium concentration, but do not cause persistent hyperkalemia. (See "Causes and evaluation of hyperkalemia in adults", section on 'Beta blockers' and "Patient information: Low-potassium diet (Beyond the Basics)".)

Metabolic acidosis — There is an increasing tendency to retain hydrogen ions among patients with CKD [19-21]. This can lead to a progressive metabolic acidosis, with the serum bicarbonate concentration tending to stabilize between 12 and 20 mEq/L and rarely falling below 10 mEq/L [20,22]. The treatment of metabolic acidosis in CKD patients is discussed elsewhere. Metabolic acidosis may be treated with bicarbonate supplementation. Bicarbonate supplementation requires careful monitoring of volume status because bicarbonate is administered with sodium. (See "Pathogenesis, consequences, and treatment of metabolic acidosis in chronic kidney disease", section on 'Treatment of metabolic acidosis in CKD'.)

Mineral and bone disorders (MBD) — Hyperphosphatemia is a common complication of CKD. A tendency toward phosphate retention begins early in renal disease due to the reduction in the filtered phosphate load. Although this problem is initially mild, with hyperphosphatemia being a relatively late event, phosphate retention is intimately related to the common development of secondary hyperparathyroidism. (See "Overview of chronic kidney disease-mineral bone disease (CKD-MBD)".)

From the viewpoint of calcium and phosphate balance, the hypersecretion of parathyroid hormone (PTH) is initially appropriate since PTH can correct both hyperphosphatemia and hypocalcemia. As a result, phosphate balance and a normal serum phosphate concentration are generally maintained in patients with an eGFR of >30 mL/min per 1.73 m^2 [23]. The price paid is secondary hyperparathyroidism and the development of renal osteodystrophy. (See "Overview of chronic kidney disease-mineral bone disease (CKD-MBD)".)

Dietary phosphate restriction and oral phosphate binders may limit the development of secondary hyperparathyroidism in patients with CKD (table 3A-B). Our approach, including the choice of phosphate binder, is discussed elsewhere (See "Treatment of hyperphosphatemia in chronic kidney disease", section on 'Treatment'.)

The increased intake of calcium may enhance coronary arterial calcification in this setting. This is thought by some to be associated with the development of coronary atherosclerosis and may be related to the presence and/or consequences of elevated serum phosphorus, calcium, and PTH levels. Detailed discussions of these issues, including specific KDIGO guidelines, can be found separately (see "Vascular calcification in chronic kidney disease"). The KDIGO clinical practice guidelines for MBD in CKD, as well as other KDIGO guidelines, can be accessed through the KDIGO website (www.kdigo.org).

Changes in bone structure are an almost universal finding with progressive CKD [24]. The principal types of renal bone disease include osteitis fibrosa, osteomalacia, and adynamic bone disease. (See "Overview of chronic kidney disease-mineral bone disease (CKD-MBD)".)

Osteitis fibrosa results from secondary hyperparathyroidism. Although an exact relationship is unclear, PTH levels appear to increase when renal function decreases beyond a certain threshold value, with evidence suggesting that hormone levels begin to rise when the creatinine clearance is <40 to 70 mL/min [25,26].

To help guide preventive measures, PTH levels should therefore be assessed among such patients as hormonal abnormalities are one of the earliest markers of abnormal mineral and bone metabolism with progressive CKD. Prevention and/or treatment of osteitis fibrosis in patients with predialysis CKD are primarily based upon dietary phosphate restriction, the administration of oral phosphate binders, and the administration of calcitriol (or vitamin D analogs) to directly suppress the secretion of PTH.

Circulating calcitriol (1,25-dihydroxyvitamin D), the most active metabolite of vitamin D, is principally synthesized in the kidney. Circulating calcitriol levels begin to fall when the eGFR is <40 mL/min per 1.73 m^2 and are typically markedly reduced in patients with ESRD. In addition to the loss of functioning renal mass, calcitriol production is also reduced by phosphate retention. (See "Overview of chronic kidney disease-mineral bone disease (CKD-MBD)".)

Calcimimetics are agents that allosterically increase the sensitivity of the calcium-sensing receptor in the parathyroid gland to calcium. The calcium-sensing receptor is the principal factor regulating parathyroid gland PTH secretion and hyperplasia. The separate target offers the potential to suppress PTH secretion by mechanisms

complementary and potentially synergistic with vitamin D analogs that target the vitamin D receptor. Although not approved for patients with CKD not yet on dialysis, cinacalcet, the only currently available calcimimetic, is an emerging option in the treatment of secondary hyperparathyroidism in predialysis patients with CKD. (See "Management of secondary hyperparathyroidism and mineral metabolism abnormalities in dialysis patients", section on 'Calcimimetics'.)

Target serum levels for PTH as well as the approach to the management of this issue are discussed separately. (See "Management of secondary hyperparathyroidism and mineral metabolism abnormalities in adult predialysis patients with chronic kidney disease".)

Hypertension — Hypertension is present in approximately 80 to 85 percent of patients with CKD [27]. Treating hypertension can both slow the progression of proteinuric CKD and reduce the rate of cardiovascular complications. (See "Chronic kidney disease and coronary heart disease", section on 'Blood pressure control' and "Overview of hypertension in acute and chronic kidney disease".)

The desired degree of blood pressure control can usually be safely achieved with combined therapy, which usually begins with an ACE inhibitor or ARB (also given to slow disease progression, as noted above) and a diuretic. Issues surrounding the treatment of hypertension among patients with diabetic nephropathy are discussed in detail separately. (See "Treatment of hypertension in patients with diabetes mellitus".)

Volume expansion, often in the absence of overt edema, contributes to the elevation in blood pressure in most forms of CKD. As a result, before other medications are added, the dose of diuretics should be increased until the blood pressure is normalized or the patient has attained "dry weight," which, in the presence of persistent hypertension, is defined as the weight at which further fluid loss will lead either to symptoms (fatigue, orthostatic hypotension) or to decreased tissue perfusion, as evidenced by an otherwise unexplained elevation in the BUN and plasma creatinine concentration. (See "Overview of hypertension in acute and chronic kidney disease".)

A loop diuretic is recommended for the treatment of hypertension and edema in patients with CKD. The thiazide diuretics in conventional dosing become less effective as monotherapy when the eGFR falls below 20 mL/min per 1.73 m^2. They do, however, produce an additive effect when administered with a loop diuretic for refractory edema. (See "Treatment of refractory edema in adults".)

The optimal blood pressure in hypertensive patients with CKD is uncertain. The rate of loss of eGFR appears to be more rapid when the mean arterial pressure remains at or above 100 mmHg (which reflects a diastolic pressure of 80 to 85 mmHg in the absence of systolic hypertension). To slow progression of CKD, the optimal blood pressure depends in part on the degree of proteinuria. (See "Antihypertensive therapy and progression of nondiabetic chronic kidney disease in adults", section on 'Blood pressure goals depend upon protein excretion'.)

Our recommendations for blood pressure goals in patients with proteinuric CKD are discussed elsewhere. (See "Antihypertensive therapy and progression of nondiabetic chronic kidney disease in adults" and 'Slowing the rate of progression' above.)

Our recommendations for blood pressure goals in patients with nonproteinuric CKD are discussed elsewhere. (See "Antihypertensive therapy and progression of nondiabetic chronic kidney disease in adults", section on 'Blood pressure goals depend upon protein excretion' and "Overview of hypertension in acute and chronic kidney disease", section on 'Sequence of antihypertensive therapy in nonproteinuric CKD'.)

Blood pressure targets should be individualized based on such factors as age, comorbidities, presence of underlying cardiovascular disease, risk of progression of kidney disease, and patient tolerance to treatment.

Anemia — The anemia of CKD is, in most patients, normocytic and normochromic, and is due primarily to reduced production of erythropoietin by the kidney (a presumed reflection of the reduction in functioning renal mass) and to shortened red cell survival [28]. Anemia is a common feature in many patients with CKD who do not yet require dialysis, with anemia becoming increasingly common as eGFRs decline below 60 mL/min per 1.73 m^2 [29,30], particularly among diabetics [31]. As an example, based upon over 15,000 participants in the National

Health and Nutrition Examination Survey (NHANES), the prevalence of anemia (hemoglobin [Hgb] <12 g/dL in men and <11 g/dL in women) increased from 1 percent at an eGFR of 60 mL/min per 1.73 m^2 to 9 percent at an eGFR of 30 mL/min per 1.73 m^2 and to 33 to 67 percent at an eGFR of 15 mL/min per 1.73 m^2 [29]. (See "Erythropoietin for the anemia of chronic kidney disease among predialysis and peritoneal dialysis patients".)

The 2012 KDIGO guidelines suggest that, among patients who do not have anemia, the Hgb concentration should be checked when it is clinically indicated and at least yearly among all patients with stage 3 CKD (ie, eGFR 30 to 59 mL/min per 1.73 m^2); at least every six months among patients with stage 4 to 5 CKD (ie, eGFR ≤29 mL/min per 1.73 m^2); and at least every three months among patients who are on dialysis [8,32]. Among patients who are known to have anemia and are not treated with erythropoietin-stimulating agents (ESAs), Hgb should be checked when it is clinically indicated and at least every three months among patients with stage 3 to 5 (ie, eGFR ≤59 mL/min per 1.73 m^2) who are not on hemodialysis (including patients who are on peritoneal dialysis); patients on hemodialysis should be monitored monthly. (See "Definition and staging of chronic kidney disease in adults", section on 'Staging of CKD'.)

As stated in the 2012 KDIGO guidelines, the evaluation of anemia in those with CKD should begin when the Hgb level is <12 g/dL in females and <13 g/dL in adult males [8,32]. These values are consistent with the World Health Organization (WHO) definition of anemia [33]. If untreated, the Hgb level of patients with advanced CKD normally stabilizes at approximately 8 g/dL in the absence of bleeding or hemolysis.

The anemia observed with CKD is largely diagnosed by excluding nonrenal causes of anemia in the patient with a suitably decreased eGFR. The evaluation of patients should therefore include red blood cell indices, absolute reticulocyte count, serum iron, total iron-binding capacity, percent transferrin saturation, serum ferritin, white blood cell count and differential, platelet count, B12 and folate concentrations if the mean corpuscular volume (MCV) is increased, and testing for blood in stool. This work-up should be performed prior to administering ESA therapy. (See "Approach to the adult patient with anemia".)

Evaluating the adequacy of iron stores in patients with CKD and issues relating to iron therapy in such patients are presented elsewhere. (See "Diagnosis of iron deficiency in chronic kidney disease" and "Use of iron preparations in hemodialysis patients" and "Iron balance in nondialysis, peritoneal dialysis, and home hemodialysis patients".)

Although primarily used in patients with ESRD, ESAs such as erythropoietin and darbepoetin alfa also correct the anemia in those with CKD who do not yet require dialysis. (See "Erythropoietin for the anemia of chronic kidney disease among predialysis and peritoneal dialysis patients".)

The use of ESAs for the treatment of anemia in patients with CKD, including the 2012 KDIGO guideline recommendations, is discussed in detail separately. (See "Anemia of chronic kidney disease: Target hemoglobin/hematocrit for patients treated with erythropoietic agents".)

Dyslipidemia — Abnormal lipid metabolism is common in patients with renal disease [34]. The primary finding in CKD is hypertriglyceridemia, with the total cholesterol concentration usually being normal (perhaps due in part to malnutrition in some patients). We agree with the 2013 KDIGO guidelines that recommend an initial evaluation with lipid profile, including total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides [35]. As per the KDIGO guidelines, follow-up evaluation of lipid profiles is generally not necessary for patients age ≥50 years since statin therapy is not titrated to the lipid profile. (See "Lipid abnormalities in patients with chronic kidney disease not requiring dialysis", section on 'Treatment with statins' and "Secondary prevention of cardiovascular disease in end-stage renal disease (dialysis)", section on 'Lipid modification' and "Lipid abnormalities after renal transplantation", section on 'Treatment of dyslipidemias'.)

Follow-up testing may be performed among patients who are age <50 years who are not already on a statin in order to assess cardiovascular risk and the need for statin therapy. Follow-up evaluation may also be performed to assess adherence to statin treatment; if there is a change in the modality of renal replacement therapy; or if there is concern about new secondary causes of dyslipidemia (such as nephrotic syndrome, hypothyroidism, diabetes, excessive alcohol consumption, or liver disease).

Among patients with CKD, the degree of hypertriglyceridemia that occurs may not be sufficient to significantly increase coronary risk, but other changes have been found that might contribute to the accelerated atherosclerosis commonly seen in ESRD. The treatment of hypertriglyceridemia in CKD patients, including the 2013 KDIGO recommendations, is discussed elsewhere. (See "Lipid abnormalities in patients with chronic kidney disease not requiring dialysis", section on 'Treatment of hypertryglyceridemia' and "Lipid abnormalities after renal transplantation", section on 'Treatment of dyslipidemias' and "Secondary prevention of cardiovascular disease in end-stage renal disease (dialysis)", section on 'Hypertriglyceridemia'.)

In the patient with hypercholesterolemia, a statin can effectively and safely lower the plasma cholesterol concentration to or near acceptable levels. A related issue is the goal LDL-C level. Given evidence that mild to moderate degrees of CKD are associated with an adverse cardiovascular prognosis, CKD is considered a coronary heart disease equivalent [36]. (See "Chronic kidney disease and coronary heart disease".)

The goal LDL-C is discussed elsewhere. (See "Lipid abnormalities in patients with chronic kidney disease not requiring dialysis", section on 'Treatment with statins'.)

Limited data suggest that lipid lowering may have an additional benefit in patients with CKD, which is slowing the rate of progression of the underlying renal disease. (See "Lipid abnormalities in patients with chronic kidney disease not requiring dialysis" and "Statins and chronic kidney disease" and "Chronic kidney disease and coronary heart disease".)

Sexual dysfunction — Significant abnormalities in sexual and reproductive function are frequently observed in patients with advanced renal disease. As an example, >50 percent of uremic men complain of symptoms that include erectile dysfunction, decreased libido, and marked declines in the frequency of intercourse [37]; in addition, disturbances in menstruation and fertility are commonly encountered in women with CKD, usually leading to amenorrhea by the time the patient reaches ESRD. (See "Reproductive and sexual dysfunction in uremic women" and "Sexual dysfunction in uremic men".)

An important clinical implication of these abnormalities is that pregnancy that is carried to term is uncommon in women with a plasma creatinine concentration of ≥3 mg/dL (265 micromol/L) [38]. (See "Pregnancy in women with underlying renal disease".)

Treatment of complications of ESRD — Once the patient has reached the stage of near ESRD (eGFR <15 mL/min per 1.73 m^2), signs and symptoms related to uremia begin to occur, such as malnutrition, anorexia, nausea, vomiting, fatigue, sexual dysfunction, platelet dysfunction, pericarditis, and neuropathy.

Malnutrition — Malnutrition is common in patients with advanced CKD because of a lower food intake (principally due to anorexia), decreased intestinal absorption and digestion, and metabolic acidosis [39-41]. Among participants age ≥60 years in the United States Third NHANES, an eGFR <30 mL/min per 1.73 m^2 was independently associated with malnutrition (odds ratio [OR] 3.6) [40]. Many additional studies have shown a strong correlation between malnutrition and death in maintenance dialysis patients. (See "Indications for initiation of dialysis in chronic kidney disease".)

It is therefore desirable to monitor the nutritional status of patients with CKD. A low plasma concentration of albumin may be indicative of malnutrition. To best assess nutritional status, the serum albumin concentration and body weight should be measured serially; these should be measured approximately every one to three months for those with eGFRs <20 mL/min per 1.73 m^2 and more frequently if necessary for those with eGFRs ≤15 mL/min per 1.73 m^2 [42]. (See "Assessment of nutritional status in end-stage renal disease".)

The desire to maintain adequate nutrition among patients with CKD clearly competes with attempts to slow the progression of renal failure with the use of a low-protein diet. This issue is discussed elsewhere. (See "Protein restriction and progression of chronic kidney disease", section on 'Protein restriction'.)

Overall, the diet of most patients with CKD should provide approximately 30 to 35 kcal/kg per day [43]. One recommended diet, including suggestions for protein, fat, mineral, and water, is presented in the table (table 2). The

Kidney Disease Outcomes Quality Initiative (K/DOQI) clinical practice guidelines for nutrition in chronic renal failure (CRF), as well as other K/DOQI guidelines, can be accessed through the National Kidney Foundation's website (www.kidney.org/professionals/kdoqi/guidelines.cfm).

Uremic bleeding — An increased tendency to bleeding is present in both acute and CKD. This appears to correlate most closely with prolongation of the bleeding time due primarily to impaired platelet function. (See "Platelet dysfunction in uremia".)

No specific therapy is required in asymptomatic patients. However, correction of the platelet dysfunction is desirable in patients who are actively bleeding or who are about to undergo a surgical or invasive procedure (such as a renal biopsy). A number of different modalities can be used in this setting, including the correction of anemia, the administration of desmopressin (dDAVP), cryoprecipitate, estrogen, and the initiation of dialysis. (See "Platelet dysfunction in uremia".)

Pericarditis — Advances in management have decreased the incidence of pericarditis in patients with CKD, but this problem is still associated with significant morbidity and occasional mortality. (See "Pericarditis in renal failure".)

Fever, pleuritic chest pain, and a pericardial friction rub are the major presentations of uremic pericarditis. One relatively characteristic feature of uremic pericarditis is that the electrocardiogram does not usually show the typical diffuse ST and T wave elevation, presumably because this is a metabolic pericarditis, and epicardial injury is uncommon. Thus, the finding of these abnormalities suggests some other cause for the pericarditis. The occurrence of pericarditis in a patient with mild to moderate CKD is another clue that the renal disease is probably not responsible.

The development of otherwise unexplained pericarditis in a patient with advanced renal failure is an indication to institute dialysis (providing there is no circulatory compromise or evidence of impending tamponade) (see below). Most patients with uremic pericarditis respond rapidly to dialysis, with resolution of chest pain as well as a decrease in the size of the pericardial effusion. (See "Pericarditis in renal failure".)

Uremic neuropathy — Dysfunction of the central and peripheral nervous system, including encephalopathy (impaired mental status progressing, if untreated, to seizures and coma), polyneuropathy, and mononeuropathy are important complications of ESRD. They have become much less common because of the current tendency to earlier initiation of dialysis.

Sensory dysfunctions, characterized by the restless leg or burning feet syndromes, are frequent presentations of uremic neuropathy. These complications are usually absolute indications for the initiation of dialysis. The extent of recovery from uremic neuropathy is directly related to the degree and extent of dysfunction prior to the initiation of dialysis. (See "Uremic polyneuropathy".)

Thyroid dysfunction — The kidney normally plays an important role in the metabolism, degradation, and excretion of several thyroid hormones. It is not surprising, therefore, that impairment in kidney function leads to disturbed thyroid physiology. However, the overlap in symptomatology between the uremic syndrome and hypothyroidism requires a cautious interpretation of the tests of thyroid function.

It is usually possible in the individual patient with CKD to assess thyroid status accurately by physical diagnosis and thyroid function testing. The disturbances that can occur include low serum-free and total T3 concentrations and normal reverse T3 and free T4 concentrations. The serum thyrotropin (TSH) concentration is normal, and most patients are euthyroid. (See "Thyroid function in chronic kidney disease".)

Infection and vaccination — Patients with CKD are at increased risk for infection [44-46]. The risk of bacterial infection (particularly pulmonary and genitourinary) increases with the decline in kidney function [45,47]. In one study, compared with an eGFR ≥90 mL/min per 1.73 m^2, eGFRs between 60 to 89, 45 to 59, and 15 to 44 mL/min per 1.73 were associated with 16, 37, and 64 percent greater risks of all-cause infection related hospitalization, respectively [45].

Careful attention should be paid to preventive measures such as influenza and pneumococcal immunization [48,49]. (See "Preventive care in adults: Recommendations".)

We agree with the following 2012 KDIGO guidelines [8]:

- Adults with all stages of CKD should be offered annual vaccination with influenza virus, unless contraindicated.
- Adults with stage 4 and 5 CKD who are at high risk of progression of CKD should be immunized against hepatitis B, and the response confirmed by immunologic testing.
- Adults with CKD stages 4 and 5 should be vaccinated with polyvalent pneumococcal vaccine, unless contraindicated. Patients who have received pneumococcal vaccination should be offered revaccination within five years.

The United States Advisory Committee on Immunization Practices (ACIP) has recommended two forms of pneumococcal vaccine, including pneumococcal polysaccharide vaccine (PPSV23 [Pneumovax or Pnu-Immune]) and the 13-valent pneumococcal conjugate pneumococcal vaccine (PCV13 [Prevnar 13]) for individuals aged ≥19 years with an immunocompromising condition, including CKD [50]. Specific recommendations regarding the schedule of administration of both vaccines are discussed elsewhere. (See "Pneumococcal vaccination in adults", section on 'Indications'.)

REFERRAL TO NEPHROLOGISTS — Patients with chronic kidney disease (CKD) should be referred to a nephrologist when the estimated glomerular filtration rate (eGFR) is <30 mL/min per 1.73 m^2 in order to discuss and potentially plan for renal replacement therapy. There is less consensus about referral for patients with higher eGFR. This issue and other indications for referral to a nephrologist are discussed elsewhere. (See "Definition and staging of chronic kidney disease in adults", section on 'Referral to a specialist'.)

Lower costs and/or decreased morbidity and mortality may be associated with early referral and care by nephrologists [51-61]. (See "Late referral to nephrologists of patients with chronic kidney disease", section on 'Consequences of late referral'.)

Co-management of the patient with the primary care provider is a common strategy at early stages of CKD. Institution of renoprotective therapy (eg, angiotensin-converting enzyme [ACE] inhibitor, angiotensin receptor blocker [ARB], and rigorous blood pressure control) should be done as early as possible after identifying the presence of progressive CKD. Protective therapy has the greatest impact if it is initiated before the plasma creatinine concentration exceeds 1.2 (106 micromol/L) and 1.5 mg/dL (133 micromol/L) in women and men, respectively, or when the eGFR is <60 mL/min per 1.73 m^2. At this point, most patients have already lost more than one-half of their eGFR. Waiting until the disease progresses further diminishes the likelihood of a successful response, but still should be attempted. (See "Antihypertensive therapy and progression of nondiabetic chronic kidney disease in adults" and 'Slowing the rate of progression' above.)

Multidisciplinary CKD clinic — The optimal medical care of CKD patients may be best provided by a team of healthcare professionals who practice at a single site (ie, a CKD clinic), following the principles of the chronic disease model of care [62]. Such CKD clinics focus on guideline-driven nephrology care, management of comorbidities, lifestyle modification, and patient education in order to optimize patient outcomes. Observational and nonrandomized prospective studies have suggested that, compared with standard nephrology care, patients who attend a multidisciplinary CKD clinic have fewer hospitalizations, are more likely to have an arterial-venous fistula rather than graft or catheter, are more likely to start dialysis as an outpatient, and are more likely to adhere to established CKD anemia or mineral and bone disease (MBD) goals [63-67]. One retrospective study has suggested that a multidisciplinary approach may improve survival [67]. The 2012 Kidney Disease: Improving Global Outcomes (KDIGO) CKD guidelines suggest management of CKD patients in a multidisciplinary setting, with access to dietary counseling, renal replacement therapies, transplant options, vascular access surgery, and ethical, psychological and social care [68].

PREPARATION FOR AND INITIATION OF RENAL REPLACEMENT THERAPY — It is important to identify patients who may eventually require renal replacement therapy since adequate preparation can decrease morbidity and perhaps mortality. Early identification enables dialysis to be initiated at the optimal time with a functioning chronic access and may also permit the recruitment and evaluation of family members for the placement of a renal allograft prior to the need for dialysis. In addition, the ability of the individual to psychologically accept the requirement of lifelong renal replacement therapy is often diminished if inadequate time has elapsed between the time of recognition of end-stage renal disease (ESRD) and the initiation of dialysis.

Chronic kidney disease (CKD) progresses at a variable rate due to differences in the clinical course of the underlying diseases (particularly between individuals) and the recognition that the natural history of progressive renal disease can be altered by various therapeutic interventions, particularly strict blood pressure control with an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) (see 'Slowing the rate of progression' above). As a result, exactly if and when a patient may require dialysis or renal transplantation is unclear. In addition, some patients refuse renal replacement therapy until the onset of absolute indications, while others desire early initiation to avoid the complications of severe CKD, such as malnutrition.

Choice of renal replacement therapy — Once it is determined that renal replacement therapy will eventually be medically indicated, the patient should be counseled to consider the advantages and disadvantages of hemodialysis (in-center or at home), peritoneal dialysis (continuous or intermittent modalities), and renal transplantation (living or deceased donor) [69,70]. The option of conservative management should also be discussed among patients who are unwilling or unable to undergo renal replacement therapy. The 2006 Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines recommend that patients with an estimated glomerular filtration rate (eGFR) <30 mL/min per 1.73 m^2 should be educated concerning these issues [70].

Kidney transplantation is the treatment of choice for ESRD. A successful kidney transplant improves the quality of life and reduces the mortality risk for most patients when compared with maintenance dialysis. To facilitate early transplantation, a 2008 National Kidney Foundation (NKF)/KDOQI conference suggested early education and referral to a transplantation center plus the identification of potential living donors [71].

However, not all patients are appropriate candidates for a kidney allograft because of absolute and/or relative contraindications to this procedure or the subsequent required medications. Referral to a transplant program should occur once renal replacement therapy is thought to be required within the next year [72]. (See "Patient survival after renal transplantation" and "Evaluation of the potential renal transplant recipient".)

Living-donor transplants, if available, have the additional advantage of being performed with minimal delay, thereby permitting preemptive transplantation (transplantation prior to dialysis). Such patients appear to have improved graft survival compared with those who undergo a period of dialysis before transplantation [73]. (See "Dialysis issues prior to and after renal transplantation" and "Risk factors for graft failure in kidney transplantation".)

For these individuals and for those who are suitable transplant recipients, but must wait for an available kidney, the choice between hemodialysis or peritoneal dialysis is influenced by a number of considerations such as availability, convenience, comorbid conditions, home situation, age, gender, and the ability to tolerate volume shifts. (See "Dialysis modality and patient outcome" and "Choosing a modality for chronic peritoneal dialysis" and "Dialysis in diabetic nephropathy".)

In the United States, the universal availability of renal replacement therapy forces the nephrologist to consider its application in every patient in whom it might be indicated. However, the patient, particularly older adults and terminally ill, may decline renal replacement therapy, a choice which is assuming more prominence as patients and physicians grapple with the increasing use of advance directives and the laudable goals of death with dignity and life with quality. We agree with the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) guidelines that conservative management of ESRD should be an option for such patients [68]. (See 'Conservative management of ESRD' below and "Withdrawal from and withholding of dialysis".)

Preparation for hemodialysis — Hemodialysis requires a stable access to the bloodstream to permit dialysis to

be performed (see "Overview of the hemodialysis apparatus"). The access should generally be placed in the nondominant upper extremity because of the increased risk of infection and more severe consequences of arterial steal syndrome with lower extremity grafts. Venipuncture should therefore be restricted to the arm not chosen for eventual access placement so that the veins in the other arm will be preserved.

There are three major types of vascular access for maintenance hemodialysis: primary arteriovenous (AV) fistulas; synthetic arteriovenous fistulas (AV grafts); and double-lumen, cuffed tunneled catheters. To facilitate placement of a permanent vascular access, the 2008 Society for Vascular Surgery (SVS) guidelines recommend that patients be referred to an access surgeon when the patient has late stage 4 CKD, defined by an eGFR of <20 to 25 mL/min per 1.73 m^2 [74]. (See "Arteriovenous fistulas and grafts for chronic hemodialysis access".)

Primary AV fistulas — Primary AV fistulas are the preferred form of vascular access given their significantly higher long-term patency rates and lower rate of complications. Since a primary AV fistula requires months to mature and is the access of choice, patients should be referred for surgery to attempt access construction when it is estimated that the patient is within one year of the anticipated need for dialysis, as manifested by an eGFR <25 mL/min per 1.73 m^2, a plasma creatinine concentration >4 mg/mL (354 micromol/L), or a rapid rate of progression. The 2006 K/DOQI guidelines recommend that a fistula be placed at least six months prior to the anticipated start of hemodialysis [70].

Primary AV fistulas are typically constructed with an end-to-side vein-to-artery anastomosis of the cephalic vein and the radial artery. These fistulas have good long-term patency and infrequently develop infectious complications. A well-constructed radial cephalic fistula that functions for the first six months can be expected to function for up to 20 years.

The evaluation of non-maturing AV fistulas may require an assessment with procedures that involve the administration of iodinated radiocontrast agents, thereby possibly resulting in radiocontrast-induced nephropathy and required early dialysis. In one study of 65 endovascular procedures among 34 patients with stage 4 CKD and non-maturing AV fistulas, contrast-induced nephropathy (25 percent increase in serum creatinine concentration) occurred in only 5 percent of patients at one week post-procedure, and no one required acute dialysis [75]. The mean contrast volume was small (mean of 7.8 mL per procedure).

The administration of gadolinium during magnetic resonance imaging (MRI) has been linked to an often severe disease called nephrogenic systemic fibrosis among patients with moderate to severe renal disease, particularly those requiring dialysis. As a result, it is recommended that gadolinium-based imaging be avoided, if possible, in patients with an eGFR <30 mL/min per 1.73 m^2. There is no consensus among experts concerning the decision to administer gadolinium among patients with an eGFR between 30 and 60 mL/min per 1.73 m^2. (See "Nephrogenic systemic fibrosis/nephrogenic fibrosing dermopathy in advanced renal failure".)

The patient should be instructed in the care of the fistula. Such care includes routinely checking for a thrill and notifying the nephrologist if this is not present. The arm that has the fistula should not be used for blood drawing or for blood pressure checks. Patients should avoid sleeping on the access arm, avoid tight clothing on the access, and not carry anything that weighs more than 5 pounds with that arm.

Synthetic AV access (bridge grafts) — AV fistulas constructed with synthetic material, most commonly polytetrafluoroethylene (PTFE), provide excellent vascular access in patients who fail endogenous AV fistula placement. PTFE has good surgical handling characteristics, and grafts of this material usually mature in two weeks. Synthetic grafts have a higher long-term complication rate (eg, infection, thrombosis) than primary fistulas. The 2006 K/DOQI guidelines recommend that a synthetic graft be placed at least three to six weeks prior to the anticipated start of hemodialysis [70].

As for a fistula, the patient should be instructed in the care of the AV graft. Such care includes routinely checking for a thrill and notifying the nephrologist if this is not present. The arm that has the graft should not be used for blood drawing or for blood pressure checks. Patients should avoid sleeping on the access arm, avoid tight clothing on the access, and not carry anything that weighs more than 5 pounds with that arm.

Cuffed tunneled catheters — These central venous catheters, which can be used immediately after placement, are primarily used as intermediate-duration vascular access to allow maturation of endogenous fistulas. They can also provide acceptable long-term access in patients who have exhausted all available sites. Nevertheless, these central venous catheters are inferior to AV access as long-term access since they provide lower flows and have higher rates of infection and other complications. (See "Overview of central catheters for acute and chronic hemodialysis access".)

Preparation for peritoneal dialysis — Peritoneal dialysis catheters, which are placed into the abdominal cavity, can be used immediately after placement [76]. However, to minimize the risk of fluid leak, it is preferable to wait at least 10 to 14 days before beginning dialysis. If dialysis is required less than 10 days following catheter placement, small volume exchanges performed in the recumbent position can be performed with little risk of leak. (See "Placement and maintenance of the peritoneal dialysis catheter", section on 'Postoperative catheter care'.)

Preparation for renal transplantation — Preparation for renal transplantation, which principally involves evaluation of the potential renal transplant recipient and the living donor, is discussed in detail separately. Referral of patients with CKD to a transplant center should occur when the eGFR decreases to <30 mL/min per 1.73 m^2 [77]. (See "Evaluation of the potential renal transplant recipient" and "Living unrelated donors in renal transplantation".)

Indications for renal replacement therapy — There are a number of clinical indications to initiate dialysis in patients with CKD. These include [70,78,79]:

- Pericarditis or pleuritis (urgent indication).
- Progressive uremic encephalopathy or neuropathy, with signs such as confusion, asterixis, myoclonus, wrist or foot drop, or, in severe, cases, seizures (urgent indication).
- A clinically significant bleeding diathesis attributable to uremia (urgent indication).
- Fluid overload refractory to diuretics.
- Hypertension poorly responsive to antihypertensive medications.
- Persistent metabolic disturbances that are refractory to medical therapy. These include hyperkalemia, hyponatremia, metabolic acidosis, hypercalcemia, hypocalcemia, and hyperphosphatemia.
- Persistent nausea and vomiting.
- Evidence of malnutrition.

Relative indications for the initiation of dialysis include decreased attentiveness and cognitive tasking, depression, persistent pruritus, or the restless leg syndrome.

We suggest that, among patients with progressive CKD, clinicians must be vigilant for the presence of symptoms and/or signs of uremia, and patients should also be fully informed of any symptoms of uremia to be able to contact their physicians appropriately. Dialysis should be considered based upon clinical factors plus the eGFR. Dialysis should be initiated in the patient with symptoms and/or signs due to uremia.

Among asymptomatic patients with progressive CKD, the timing of initiation of dialysis is unclear, and there is no specific threshold eGFR level that has been established for the initiation of dialysis. To help avoid the onset of possible life-threatening complications of uremia, the initiation of dialysis should be considered in the asymptomatic patient with an extremely low eGFR, such as an eGFR of approximately 8 to 10 mL/min per 1.73 m^2. However, some clinicians may choose to closely monitor (weekly) asymptomatic patients with progressive CKD, even when the eGFR is less than 8 to 10 mL/min per 1.73 m^2, with the initiation of dialysis upon the onset of uremic signs/symptoms. The 2012 KDIGO guidelines suggest that dialysis be initiated when there are signs or symptoms attributable to kidney failure (such as serositis, acid-base or electrolyte disorders not easily corrected medically, pruritus); an inability to control volume status or blood pressure; a progressive deterioration in nutritional status that

is refractory to dietary interventions; or cognitive impairment [8]. The 2012 KDIGO guidelines state that such signs and symptoms often, but not invariably, occur when the eGFR is between 5 and 10 mL/min per 1.73 m^2.

All approaches require close follow-up, early nephrology referral, and adequate advance dialysis planning (including the presence of a functioning peritoneal or vascular access and referral for transplantation). A detailed discussion of the indications for dialysis in the patient with CKD can be found elsewhere. (See "Indications for initiation of dialysis in chronic kidney disease".)

CONSERVATIVE MANAGEMENT OF ESRD — Patients may elect to withhold dialysis [80-82]. We agree with the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) guidelines that conservative management of end-stage renal disease (ESRD) should be an option for all patients who decide not to pursue renal replacement therapy [68]. Conservative care includes the management of symptoms, advance-care planning, and provision of appropriate palliative care. (See "Withdrawal from and withholding of dialysis" and "Palliative care: End-stage renal disease".)

INFORMATION FOR PATIENTS — UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient information: Chronic kidney disease (The Basics)" and "Patient information: Peritoneal dialysis (The Basics)" and "Patient information: Dialysis and diet (The Basics)" and "Patient information: Bone problems caused by kidney disease (The Basics)" and "Patient information: Medicines for chronic kidney disease (The Basics)")

- Beyond the Basics topics (see "Patient information: Chronic kidney disease (Beyond the Basics)" and "Patient information: Dialysis or kidney transplantation — which is right for me? (Beyond the Basics)" and "Patient information: Hemodialysis (Beyond the Basics)" and "Patient information: Peritoneal dialysis (Beyond the Basics)" and "Patient information: Protein in the urine (proteinuria) (Beyond the Basics)" and "Patient information: Split urine collection for orthostatic proteinuria (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- Chronic kidney disease (CKD) is defined as the presence of kidney damage (usually detected as urinary albumin excretion of 30 mg/day or more, or equivalent) **or** decreased kidney function (defined as an estimated glomerular filtration rate [eGFR] <60 mL/min/1.73 m^2) **for three or more months**, irrespective of the cause. The persistence of the damage or decreased function for at least three months is necessary to distinguish CKD from acute kidney disease. Classification, or staging, of CKD provides a guide to management. (See 'Definition and classification' above.)

- CKD is associated with a higher risk of cardiovascular disease, end-stage renal disease (ESRD), infection, malignancy, and mortality. (See 'Association with cardiovascular disease, end-stage renal disease, and mortality' above and 'Infection and vaccination' above.)

- The management of CKD includes treatment of reversible causes of renal dysfunction and preventing or slowing the progression of renal disease. (See 'Reversible causes of renal failure' above and 'Slowing the rate of progression' above.)

- Complications of the loss of renal function include disorders of fluid and electrolyte balance, such as volume

overload, hyperkalemia, metabolic acidosis, and hyperphosphatemia, as well as abnormalities related to hormonal or systemic dysfunction, such as anorexia, nausea, vomiting, fatigue, hypertension, anemia, malnutrition, hyperlipidemia, and bone disease. Attention needs to be paid to all of these issues. (See 'Treatment of the complications of renal failure' above.)

- Patients with CKD should be referred to a nephrologist when eGFR is <30 mL/min per 1.73 m^2 in order to discuss and potentially plan for renal replacement therapy. Co-management of the patient with the primary care provider is a common strategy at early stages of CKD, The optimal medical care of later stage CKD patients may be best provided by a team of healthcare professionals who practice at a single site (ie, a CKD clinic), following the principles of the chronic disease model of care. (See 'Referral to nephrologists' above.)
- It is important to identify patients who may eventually require renal replacement therapy since adequate preparation can decrease morbidity and perhaps mortality. Such patients should be counseled to consider the advantages and disadvantages of hemodialysis (in-center or at home), peritoneal dialysis (continuous or intermittent modalities), and renal transplantation (living or deceased donor). The option of conservative management should also be discussed among patients who are unwilling or unable to undergo renal replacement therapy. (See 'Preparation for and initiation of renal replacement therapy' above and 'Conservative management of ESRD' above.)
- Clinical indications to initiate dialysis in patients with CKD include (see 'Indications for renal replacement therapy' above and "Indications for initiation of dialysis in chronic kidney disease"):
    - Pericarditis or pleuritis (urgent indication).
    - Progressive uremic encephalopathy or neuropathy, with signs such as confusion, asterixis, myoclonus, wrist or foot drop, or, in severe, cases, seizures (urgent indication).
    - A clinically significant bleeding diathesis attributable to uremia (urgent indication).
    - Fluid overload refractory to diuretics.
    - Hypertension poorly responsive to antihypertensive medications.
    - Persistent metabolic disturbances that are refractory to medical therapy. These include hyperkalemia, hyponatremia, metabolic acidosis, hypercalcemia, hypocalcemia, and hyperphosphatemia.
    - Persistent nausea and vomiting.
    - Evidence of malnutrition.
    - Relative indications include decreased attentiveness and cognitive tasking, depression, persistent pruritus, or the restless leg syndrome.
- Conservative management of ESRD should be an option for all patients who decide not to pursue renal replacement therapy. Conservative care includes the management of symptoms, advance-care planning, and provision of appropriate palliative care. (See 'Conservative management of ESRD' above and "Withdrawal from and withholding of dialysis" and "Palliative care: End-stage renal disease".)

REFERENCES

1. Abboud H, Henrich WL. Clinical practice. Stage IV chronic kidney disease. N Engl J Med 2010; 362:56.
2. Sarnak MJ, Greene T, Wang X, et al. The effect of a lower target blood pressure on the progression of kidney disease: long-term follow-up of the modification of diet in renal disease study. Ann Intern Med 2005; 142:342.

3. Eriksen BO, Ingebretsen OC. The progression of chronic kidney disease: a 10-year population-based study of the effects of gender and age. Kidney Int 2006; 69:375.
4. Hallan SI, Coresh J, Astor BC, et al. International comparison of the relationship of chronic kidney disease prevalence and ESRD risk. J Am Soc Nephrol 2006; 17:2275.
5. Hsu CY, Vittinghoff E, Lin F, Shlipak MG. The incidence of end-stage renal disease is increasing faster than the prevalence of chronic renal insufficiency. Ann Intern Med 2004; 141:95.
6. Fox CS, Larson MG, Leip EP, et al. Predictors of new-onset kidney disease in a community-based population. JAMA 2004; 291:844.
7. Ishani A, Grandits GA, Grimm RH, et al. Association of single measurements of dipstick proteinuria, estimated glomerular filtration rate, and hematocrit with 25-year incidence of end-stage renal disease in the multiple risk factor intervention trial. J Am Soc Nephrol 2006; 17:1444.
8. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int Suppl 2013; 3:5.
9. Snyder JJ, Collins AJ. Association of preventive health care with atherosclerotic heart disease and mortality in CKD. J Am Soc Nephrol 2009; 20:1614.
10. Schieppati A, Pisoni R, Remuzzi G. Pathophysiology and management of chronic kidney disease. In: Primer on Kidney Diseases, Greenberg A (Ed), Elsevier Saunders, Philadelphia 2005. p.444.
11. Rennke HG, Anderson S, Brenner BM. Structural and functional correlations in the progression of renal disease. In: Renal Pathology, Tisher CC, Brenner BM (Eds), Lippincott, Philadelphia 1989. p.43.
12. Orth SR. Effects of smoking on systemic and intrarenal hemodynamics: influence on renal function. J Am Soc Nephrol 2004; 15 Suppl 1:S58.
13. Orth SR, Hallan SI. Smoking: a risk factor for progression of chronic kidney disease and for cardiovascular morbidity and mortality in renal patients--absence of evidence or evidence of absence? Clin J Am Soc Nephrol 2008; 3:226.
14. Weir MR, Fink JC. Salt intake and progression of chronic kidney disease: an overlooked modifiable exposure? A commentary. Am J Kidney Dis 2005; 45:176.
15. Gonick HC, Kleeman CR, Rubini ME, Maxwell MH. Functional impairment in chronic renal disease. 3. Studies of potassium excretion. Am J Med Sci 1971; 261:281.
16. Hsu CY, Chertow GM. Elevations of serum phosphorus and potassium in mild to moderate chronic renal insufficiency. Nephrol Dial Transplant 2002; 17:1419.
17. Gennari FJ, Segal AS. Hyperkalemia: An adaptive response in chronic renal insufficiency. Kidney Int 2002; 62:1.
18. Allon M. Hyperkalemia in end-stage renal disease: mechanisms and management. J Am Soc Nephrol 1995; 6:1134.
19. Uribarri J, Douyon H, Oh MS. A re-evaluation of the urinary parameters of acid production and excretion in patients with chronic renal acidosis. Kidney Int 1995; 47:624.
20. Warnock DG. Uremic acidosis. Kidney Int 1988; 34:278.
21. Widmer B, Gerhardt RE, Harrington JT, Cohen JJ. Serum electrolyte and acid base composition. The influence of graded degrees of chronic renal failure. Arch Intern Med 1979; 139:1099.
22. Wallia R, Greenberg A, Piraino B, et al. Serum electrolyte patterns in end-stage renal disease. Am J Kidney Dis 1986; 8:98.
23. Delmez JA, Slatopolsky E. Hyperphosphatemia: its consequences and treatment in patients with chronic renal disease. Am J Kidney Dis 1992; 19:303.
24. Hruska KA, Teitelbaum SL. Renal osteodystrophy. N Engl J Med 1995; 333:166.
25. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis 2002; 39:S1.
26. Muntner P, Jones TM, Hyre AD, et al. Association of serum intact parathyroid hormone with lower estimated glomerular filtration rate. Clin J Am Soc Nephrol 2009; 4:186.

27. Stefanski A, Schmidt KG, Waldherr R, Ritz E. Early increase in blood pressure and diastolic left ventricular malfunction in patients with glomerulonephritis. Kidney Int 1996; 50:1321.
28. Eschbach JW. Erythropoietin 1991--an overview. Am J Kidney Dis 1991; 18:3.
29. Astor BC, Muntner P, Levin A, et al. Association of kidney function with anemia: the Third National Health and Nutrition Examination Survey (1988-1994). Arch Intern Med 2002; 162:1401.
30. Hsu CY, McCulloch CE, Curhan GC. Epidemiology of anemia associated with chronic renal insufficiency among adults in the United States: results from the Third National Health and Nutrition Examination Survey. J Am Soc Nephrol 2002; 13:504.
31. El-Achkar TM, Ohmit SE, McCullough PA, et al. Higher prevalence of anemia with diabetes mellitus in moderate kidney insufficiency: The Kidney Early Evaluation Program. Kidney Int 2005; 67:1483.
32. KDIGO clinical practice guidelines for anemia in chronic kidney disease. Kidney Int Suppl 2012; 2:288.
33. World Health Organization. Worldwide prevalence of anaemia 1993-2005: WHO global database on anaemia, de Benoist B, McLea E, Egli I, Cogswell M. (Eds), 2008.
34. Appel G. Lipid abnormalities in renal disease. Kidney Int 1991; 39:169.
35. KDIGO Clinical Practice Guideline for Lipid Management in Chronic Kidney Disease. Kidney Int Suppl 2013; 3:263.
36. Sarnak MJ, Levey AS, Schoolwerth AC, et al. Kidney disease as a risk factor for development of cardiovascular disease: a statement from the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. Circulation 2003; 108:2154.
37. Procci WR, Goldstein DA, Adelstein J, Massry SG. Sexual dysfunction in the male patient with uremia: a reappraisal. Kidney Int 1981; 19:317.
38. Hou S. Pregnancy in women with chronic renal disease. N Engl J Med 1985; 312:836.
39. Kopple JD, Greene T, Chumlea WC, et al. Relationship between nutritional status and the glomerular filtration rate: results from the MDRD study. Kidney Int 2000; 57:1688.
40. Garg AX, Blake PG, Clark WF, et al. Association between renal insufficiency and malnutrition in older adults: results from the NHANES III. Kidney Int 2001; 60:1867.
41. Bammens B, Verbeke K, Vanrenterghem Y, Evenepoel P. Evidence for impaired assimilation of protein in chronic renal failure. Kidney Int 2003; 64:2196.
42. Clinical practice guidelines for nutrition in chronic renal failure. K/DOQI, National Kidney Foundation. Am J Kidney Dis 2000; 35:S1.
43. Ahmed K, Kopple J. Nutritional management of renal disease. In: Primer on Kidney Diseases, Greenberg A (Ed), Academic Press, San Diego 1994. p.289.
44. James MT, Quan H, Tonelli M, et al. CKD and risk of hospitalization and death with pneumonia. Am J Kidney Dis 2009; 54:24.
45. Dalrymple LS, Katz R, Kestenbaum B, et al. The risk of infection-related hospitalization with decreased kidney function. Am J Kidney Dis 2012; 59:356.
46. Wu MY, Hsu YH, Su CL, et al. Risk of herpes zoster in CKD: a matched-cohort study based on administrative data. Am J Kidney Dis 2012; 60:548.
47. Naqvi SB, Collins AJ. Infectious complications in chronic kidney disease. Adv Chronic Kidney Dis 2006; 13:199.
48. Coresh J. CKD prognosis: beyond the traditional outcomes. Am J Kidney Dis 2009; 54:1.
49. James MT, Laupland KB. Examining noncardiovascular morbidity in CKD: estimated GFR and the risk of infection. Am J Kidney Dis 2012; 59:327.
50. Centers for Disease Control and Prevention (CDC). Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine for adults with immunocompromising conditions: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep 2012; 61:816.

51. Bradbury BD, Fissell RB, Albert JM, et al. Predictors of early mortality among incident US hemodialysis patients in the Dialysis Outcomes and Practice Patterns Study (DOPPS). Clin J Am Soc Nephrol 2007; 2:89.
52. Astor BC, Eustace JA, Powe NR, et al. Timing of nephrologist referral and arteriovenous access use: the CHOICE Study. Am J Kidney Dis 2001; 38:494.
53. Winkelmayer WC, Owen WF Jr, Levin R, Avorn J. A propensity analysis of late versus early nephrologist referral and mortality on dialysis. J Am Soc Nephrol 2003; 14:486.
54. Stack AG. Impact of timing of nephrology referral and pre-ESRD care on mortality risk among new ESRD patients in the United States. Am J Kidney Dis 2003; 41:310.
55. Winkelmayer WC, Levin R, Avorn J. The nephrologist's role in the management of calcium-phosphorus metabolism in patients with chronic kidney disease. Kidney Int 2003; 63:1836.
56. Kessler M, Frimat L, Panescu V, Briançon S. Impact of nephrology referral on early and midterm outcomes in ESRD: EPidémiologie de l'Insuffisance REnale chronique terminale en Lorraine (EPIREL): results of a 2-year, prospective, community-based study. Am J Kidney Dis 2003; 42:474.
57. Khan SS, Xue JL, Kazmi WH, et al. Does predialysis nephrology care influence patient survival after initiation of dialysis? Kidney Int 2005; 67:1038.
58. Patwardhan MB, Samsa GP, Matchar DB, Haley WE. Advanced chronic kidney disease practice patterns among nephrologists and non-nephrologists: a database analysis. Clin J Am Soc Nephrol 2007; 2:277.
59. Chan MR, Dall AT, Fletcher KE, et al. Outcomes in patients with chronic kidney disease referred late to nephrologists: a meta-analysis. Am J Med 2007; 120:1063.
60. Tseng CL, Kern EF, Miller DR, et al. Survival benefit of nephrologic care in patients with diabetes mellitus and chronic kidney disease. Arch Intern Med 2008; 168:55.
61. Chow KM, Szeto CC, Law MC, et al. Impact of early nephrology referral on mortality and hospitalization in peritoneal dialysis patients. Perit Dial Int 2008; 28:371.
62. Epping-Jordan JE, Pruitt SD, Bengoa R, Wagner EH. Improving the quality of health care for chronic conditions. Qual Saf Health Care 2004; 13:299.
63. Lim S, Lee JJ, Subramanian S, How P. Multidisciplinary clinic for patients with newly diagnosed chronic kidney disease. Am J Health Syst Pharm 2012; 69:2034.
64. Lee W, Campoy S, Smits G, et al. Effectiveness of a chronic kidney disease clinic in achieving K/DOQI guideline targets at initiation of dialysis--a single-centre experience. Nephrol Dial Transplant 2007; 22:833.
65. Levin A, Lewis M, Mortiboy P, et al. Multidisciplinary predialysis programs: quantification and limitations of their impact on patient outcomes in two Canadian settings. Am J Kidney Dis 1997; 29:533.
66. Wei SY, Chang YY, Mau LW, et al. Chronic kidney disease care program improves quality of pre-end-stage renal disease care and reduces medical costs. Nephrology (Carlton) 2010; 15:108.
67. Curtis BM, Ravani P, Malberti F, et al. The short- and long-term impact of multi-disciplinary clinics in addition to standard nephrology care on patient outcomes. Nephrol Dial Transplant 2005; 20:147.
68. KDIGO. Chapter 1: Definition and classification of CKD. Kidney Int Suppl 2013; 3:19. http://www.kdigo.org/clinical_practice_guidelines/pdf/CKD/KDIGO_2012_CKD_GL.pdf (Accessed on March 04, 2013).
69. Gómez CG, Valido P, Celadilla O, et al. Validity of a standard information protocol provided to end-stage renal disease patients and its effect on treatment selection. Perit Dial Int 1999; 19:471.
70. Hemodialysis Adequacy 2006 Work Group. Clinical practice guidelines for hemodialysis adequacy, update 2006. Am J Kidney Dis 2006; 48 Suppl 1:S2.
71. Abecassis M, Bartlett ST, Collins AJ, et al. Kidney transplantation as primary therapy for end-stage renal disease: a National Kidney Foundation/Kidney Disease Outcomes Quality Initiative (NKF/KDOQITM) conference. Clin J Am Soc Nephrol 2008; 3:471.
72. Knoll G, Cockfield S, Blydt-Hansen T, et al. Canadian Society of Transplantation consensus guidelines on eligibility for kidney transplantation. CMAJ 2005; 173:1181.
73. Mange KC, Joffe MM, Feldman HI. Effect of the use or nonuse of long-term dialysis on the subsequent

survival of renal transplants from living donors. N Engl J Med 2001; 344:726.

74. Sidawy AN, Spergel LM, Besarab A, et al. The Society for Vascular Surgery: clinical practice guidelines for the surgical placement and maintenance of arteriovenous hemodialysis access. J Vasc Surg 2008; 48:2S.
75. Kian K, Wyatt C, Schon D, et al. Safety of low-dose radiocontrast for interventional AV fistula salvage in stage 4 chronic kidney disease patients. Kidney Int 2006; 69:1444.
76. Ghaffari A. Urgent-start peritoneal dialysis: a quality improvement report. Am J Kidney Dis 2012; 59:400.
77. Gaston RS, Basadonna G, Cosio FG, et al. Transplantation in the diabetic patient with advanced chronic kidney disease: a task force report. Am J Kidney Dis 2004; 44:529.
78. Pendse S, Singh A, Zawada E. Initiation of dialysis. In: Handbook of Dialysis, 4th ed., Daugirdas JT, Blake PG, Ing TS (Eds), Lippincott Williams & Wilkins, Philadelphia 2007.
79. K/DOQI Clinical Practice Guidelines for Peritoneal Dialysis Adequacy. Am J Kidney Dis 2006; 47(Suppl 4):S1.
80. Levinsky NG. The organization of medical care. Lessons from the Medicare end stage renal disease program. N Engl J Med 1993; 329:1395.
81. Klahr S. Rationing of health care and the end-stage renal disease program. Am J Kidney Dis 1990; 16:392.
82. United States Renal Data System. USRDS 2009 Annual Data Report. U.S. Department of Health and Human Services. The National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD. Am J Kidney Dis 2010; 55(Suppl 1):S1.

Topic 7172 Version 26.0

GRAPHICS

Revised chronic kidney disease classification based upon glomerular filtration rate and albuminuria

GFR stages	GFR (mL/min/1.73 m^2)	Terms
G1	>90	Normal or high
G2	60 to 89	Mildly decreased
G3a	45 to 59	Mildly to moderately decreased
G3b	30 to 44	Moderately to severely decreased
G4	15 to 29	Severely decreased
G5	<15	Kidney failure (add D if treated by dialysis)
Albuminuria stages	**AER (mg/day)**	**Terms**
A1	<30	Normal to mildly increased (may be subdivided for risk prediction)
A2	30 to 300	Moderately increased
A3	>300	Severely increased (may be subdivided into nephrotic and non-nephrotic for differential diagnosis, management, and risk prediction)

The cause of CKD is also included in the KDIGO revised classification but is not included in this table.

GFR: glomerular filtration rate; AER: albumin excretion rate; CKD: chronic kidney disease; KDIGO: Kidney Disease Improving Global Outcomes.

Data from:

1. *KDIGO. Summary of recommendation statements. Kidney Int 2013; 3 (Suppl):5.*
2. *National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis 2002; 39 (Suppl 1):S1.*

Graphic 70597 Version 14.0

Relative risks of major complications of chronic kidney disease based upon categorical meta-analysis

Ranking of adjusted relative risk

- Rank numbers 1-8
- Rank numbers 9-14
- Rank numbers 15-21
- Rank numbers 22-28

Absolute risk can be computed by multiplying the RRs in each cell by the incidence rate in the reference cell.

All-cause mortality

	ACR <10	ACR 10-29	ACR 30-299	ACR ≥300
eGFR >105	1.1	1.5	2.2	5.0
eGFR 90-105	Ref	1.4	1.5	3.1
eGFR 75-90	1.0	1.3	1.7	2.3
eGFR 60-75	1.0	1.4	1.8	2.7
eGFR 45-60	1.3	1.7	2.2	3.6
eGFR 30-45	1.9	2.3	3.3	4.9
eGFR 15-30	5.3	3.6	4.7	6.6

Cardiovascular mortality

	ACR <10	ACR 10-29	ACR 30-299	ACR ≥300
eGFR >105	0.9	1.3	2.3	2.1
eGFR 90-105	Ref	1.5	1.7	3.7
eGFR 75-90	1.0	1.3	1.6	3.7
eGFR 60-75	1.1	1.4	2.0	4.1
eGFR 45-60	1.5	2.2	2.8	4.3
eGFR 30-45	2.2	2.7	3.4	5.2
eGFR 15-30	14	7.9	4.8	8.1

Kidney failure (ESRD)

	ACR <10	ACR 10-29	ACR 30-299	ACR ≥300
eGFR >105	Ref	Ref	7.8	18
eGFR 90-105	Ref	Ref	11	20
eGFR 75-90	Ref	Ref	3.8	48
eGFR 60-75	Ref	Ref	7.4	67
eGFR 45-60	5.2	22	40	147
eGFR 30-45	56	74	294	763
eGFR 15-30	433	1044	1056	2286

Acute kidney injury (AKI)

	ACR <10	ACR 10-29	ACR 30-299	ACR ≥300
eGFR >105	Ref	Ref	2.7	8.4
eGFR 90-105	Ref	Ref	2.4	5.8
eGFR 75-90	Ref	Ref	2.5	4.1
eGFR 60-75	Ref	Ref	3.3	6.4
eGFR 45-60	2.2	4.9	6.4	5.9
eGFR 30-45	7.3	10	12	20
eGFR 15-30	17	17	21	29

Progressive CKD

	ACR <10	ACR 10-29	ACR 30-299	ACR ≥300
eGFR >105	Ref	Ref	0.4	3.0
eGFR 90-105	Ref	Ref	0.9	3.3
eGFR 75-90	Ref	Ref	1.9	5.0
eGFR 60-75	Ref	Ref	3.2	8.1
eGFR 45-60	3.1	4.0	9.4	57
eGFR 30-45	3.0	19	15	22
eGFR 15-30	4.0	12	21	7.7

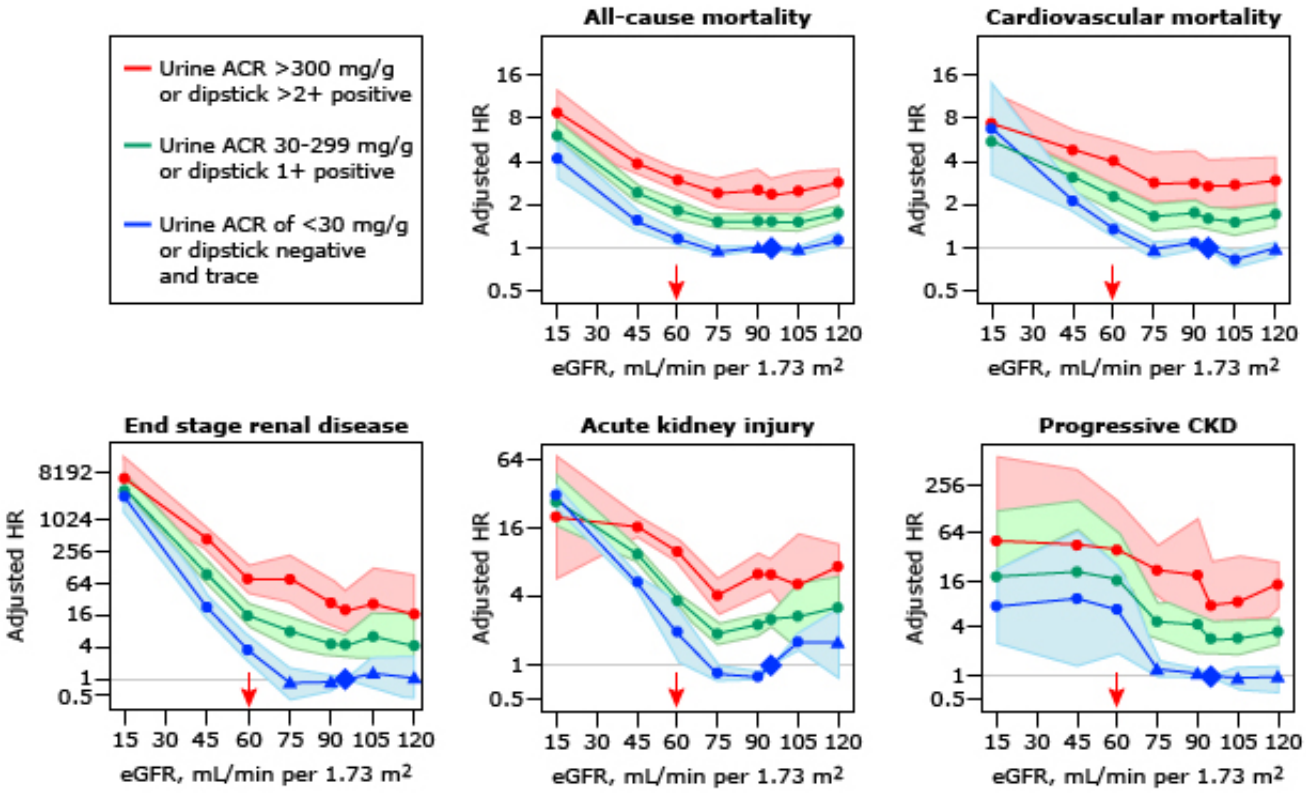
Summary of categorical meta-analysis (adjusted relative risk) for general

population cohorts with ACR. Mortality is reported for general population cohorts assessing albuminuria as urine ACR. Kidney outcomes are reported for general population cohorts assessing albuminuria as either urine ACR or dipstick. eGFR and albuminuria are expressed as categorical variables. All results are adjusted for covariates and compared with the Ref. Each cell represents a pooled RR from a meta-analysis; bold numbers indicate statistical significance at $p<0.05$. Incidence rates per 1000 person-years for the reference cells are 7.0 for all-cause mortality, 4.5 for CVD mortality, 0.04 for kidney failure, 0.98 for AKI, and 2.02 for kidney disease progression. Absolute risk can be computed by multiplying the RRs in each cell by the incidence rate in the reference cell. Colors reflect the ranking of adjusted RR. The point estimates for each cell were ranked from 1 to 28 (the lowest RR having rank number 1, and the highest number 28). The categories with rank numbers 1 through 8 are green; rank numbers 9 through 14 are yellow; rank numbers 15 through 21 are orange; and trank numbers 22 through 28 are colored red. (For the outcome of kidney disease progression, two cells with RR of 1.0 are also green, leaving fewer cells as orange.)

RR: relative risk; ACR: albumin creatinine ratio; eGFR: estimated glomerular filtration rate; Ref: reference cell; ESRD: end-stage renal disease; AKI: acute kidney injury; CKD: chronic kidney disease; CVD: cardiovascular disease.
* Dipstick included (-, ±, +, ≥++).

Graphic 68921 Version 8.0

Relative risks of major complications of chronic kidney disease based upon a continuous meta-analysis



Summary of continuous meta-analysis (adjusted RR) for general population cohorts with ACR. Mortality is reported for general population cohorts assessing albuminuria as urine ACR. Kidney outcomes are reported for general population cohorts assessing albuminuria as either urine ACR or dipstick. eGFR is expressed as a continuous variable. The three lines represent urine ACR of <30 mg/g or dipstick negative and trace (blue), urine ACR 30-299 mg/g or dipstick 1+ positive (green), and urine ACR >300 mg/g or dipstick >2+ positive (red). All results are adjusted for covariates and compared with reference point of eGFR of 95 mL/min per 1.73 m^2 and ACR of <30 mg/g or dipstick negative (diamond). Each point represents the pooled RR from a meta-analysis. Solid circles indicate statistical significance compared with the reference point ($p<0.05$); triangles indicate non-significance. Red arrows indicate eGFR of 60 mL/min per 1.73 m^2, threshold value of eGFR for the current definition of CKD.

CKD: chronic kidney disease; ACR: albumin creatinine ratio; HR: hazard ratio; eGFR: estimated glomerular filtration rate; RR: relative risk.

Graphic 58089 Version 6.0

Recommended dietary intake for chronic kidney and end-stage renal disease patients*

	Chronic kidney disease•	Maintenance hemodialysis
Protein	0.8 to 1.0 g/kg/dayΔ of high biological value protein	>1.2 to 1.3 g/kg/day
Energy	≥35 kcal/kg/day; if the body weight is greater than 120 percent of normal or the patient is greater than 60 years of age a lower amount may be prescribed	
Fat, percent of total energy intake	30 to 40	30 to 40
Polyunsaturated-to-saturated ratio (fatty acid ratio)	1.0:1.0	1.0:1.0
Carbohydrate	Balance of nonprotein calories	
Total fiber, g/day	20 to 25	20 to 25
Minerals, range of intake		
Sodium, mg/day	<2000	<2000
Potassium, meq/day	40 to 70	40 to 70
Phosphorus, mg/day	600 to 800◇	600 to 800◇
Calcium, mg/day	1400 to 1600	1400 to 1600
Magnesium, mg/day	200 to 300	200 to 300
Iron, mg/day	≥10 to 18§	≥10 to 18§
Zinc, mg/day	15	15
Water, mL/day	Up to 3000 as tolerated	Usually 750 to 1500

* The nutritional intake is adjusted based upon individual needs. This is particularly important for the carbohydrate, lipid, and mineral contents of the diet.

• GFR <70 mL/min/1.73 m2 with evidence for progression.

Δ Some recommend 0.56 to 0.75 g/kg/day, with 0.35 g/kg/day of high biological value protein. The protein intake is increased by 1.0 g/day of high biological value protein for each gram per day of urinary protein loss. This is performed under close supervision and dietary counseling.

◇ Phosphate binders often are also needed to maintain normal serum phosphorus levels.

§ 10 mg/day for males and nonmenstruating females, 18 mg/day for menstruating females.

Data from:

1. *Ahmed, K, Kopple, J. Nutritional management of renal disease. In: Primer on Kidney Diseases, Greenberg, A (Ed). Academic Press, San Diego, CA, 1994, p. 289.*
2. *Ikizler, IA. Nutrition and kidney disease. In: Primer on Kidney Diseases, Greenberg, A (Ed). Elsevier, Philadelphia, 2005, p. 496.*

Graphic 71336 Version 4.0

Table 20. Phosphorus content of protein-containing foods

Food	Common Measure	Phosphorus (mg)	Protein (g)	mg P/ g protein
Beans, Legumes, Tofu				
Beans, Kidney	1 cup	251	15	16.7
Beans, Lima	1 cup	209	15	13.9
Beans, Navy	1 cup	286	16	17.9
Beans, Black	1 cup	241	15	16.1
Beans, Refried	1 cup	217	14	15.5
Soybeans, Boiled	1 cup	421	29	14.5
Soybeans, Roasted	1 cup	624	61	10.2
Sunflower Seeds	1 oz	322	6	53.7
Tofu, Firm	100 g	76	6	12.7
Tofu, Soft	100 g	52	4	13.0
Tofu, Lite	100 g	68	5	13.6
Cheese/Cheese Products				
Cheese, Cheddar	1 oz	145	7	20.7
Cheese, Swiss	1 oz	171	8	21.4
Cottage Cheese, Reg	1 cup	297	28	10.6
Cottage Cheese, 1%	1 cup	151	14	10.8
Cottage Cheese, 2%	1 cup	340	31	11.0
Cottage Cheese, Nonfat	1 cup	151	25	6.0
Cheese, Cream	2 Tb	30	2	15.0
Combination Foods				
Bean/Cheese Burrito, FF	2 small	180	15	12.0
Breakfast Biscuit, FF	1 egg/cheese/bacon	459	16.3	28.2
Cheeseburger, FF	Single w/condiments	310	28.2	11.0
Chicken Sandwich, FF	1 sandwich	405	29.4	13.8
Fried Shrimp, FF	6 to 8 small	344	18.9	18.2
Hot Fudge Sundae	1 small	227	5.6	40.5
Morningstar Breakfast Patty	1 patty	106	9.9	10.7
Pepperoni Pizza, 1 sl	Froz Pepperoni	222	16	13.9
Roast Beef Sandwich	1 sandwich	239	21.5	11.1
Sub Sandwich, FF	1 cold cuts	287	21.8	13.2
Taco, FF	Large	313	31	10.1
Dairy and Milk				
Buttermilk	1 cup	219	8	27.4
Cream Light	1 cup	192	7	27.4
Cream Sour	1 Tb	32	1.2	26.7
Cream, Half and Half	1 cup	230	7	32.9
Cream, Heavy	1 cup	149	5	29.8
Milk, 2%	1 cup	232	8	29.0
Milk, 1%	1 cup	235	8	29.4
Milk, Low-Sodium	1 cup	209	8	26.1
Milk, Nonfat	1 cup	247	8	30.9
Milk, Whole	1 cup	227	8	28.4
Yogurt, Lowfat	4 oz	162	6	27.0
Yogurt, Nonfat	4 oz	177	6	29.5
Yogurt, Reg	4 oz	107	4	26.8

%: percent.

Graphic 79877 Version 5.0

Table 20. Phosphorus content of protein-containing foods (cont'd)

Food	Common Measure	Phosphorus (mg)	Protein (g)	mg P/ g protein
Fish and Seafood				
Crab, Blue	3 oz.	175	17	10.3
Crab, Dungeness	3.oz.	149	19	7.8
Halibut	3 oz.	214	23	9.3
Oysters, Fried	3 oz.	196	13	15.1
Salmon	3 oz.	282	21	13.4
Shrimp	3 oz.	116	18	6.4
Meats/Poultry/Egg				
Beef Liver	3 oz.	392	23	17.0
Beef, Top Sirloin	3 oz.	203	25	8.1
Chicken, breast	3 oz.	196	27	7.3
Chicken, thigh	3 oz.	148	22	6.7
Egg, Large	1 large	86	6	14.3
Ham	3 oz.	239	19	12.6
Lamb Sirloin Chop	3 oz.	190	22	8.6
Pork Loin	3 oz.	146	22	6.6
Turkey	3 oz.	210	28	7.5
Veal Loin	3 oz.	189	22	8.6
Nuts/Nut Butter				
Almonds	1 oz.	139	6	23.2
Macadamia	1 oz.	56	2	28.0
Peanut Butter, Chunky	2 Tb	101	8	12.6
Peanut Butter, Smooth	2 Tb	118	8	14.8
Peanuts, Roasted	1 oz.	147	8	18.4
Walnuts	1 oz.	98	4	24.5
Other Sources of Phosphorus				
Beer	12 oz	43	1	43.0
Chocolate, Milk	1 miniature	95	3	31.7
Chocolate, Semi Sweet	1 oz	37	1	37.0
Coffee, Brewed	1 cup	2.3	0	
Coffee, Instant	1 tsp.	4.5	0	
Cola	12 oz	44	0	
Lemon Lime	12 oz	0	0	
Lemonade	1 cup	5	0.3	16.7
Root Beer	12 oz	0	0	
Tea, Brewed	1 cup	2.4	0	

A common way to determine a dietary phosphorus limit is to use an average of 10 to 12 mg/g of protein (multiply protein goal times 10 to 12 mg phosphorus). Thus, for a 70 kg individual requiring 84 g of protein, the phosphorus range is 840 to 1008 mg.

Considering all common sources of protein, the average phosphorus content per gram of protein is 17.8. If all diary products, nuts, beans, and seeds are eliminated, but meats and tofu are considered, the average phosphorus content per gram of protein is 10.3.

FF: fast food; Tb: tablespoon.

US Department of Agriculture, Agricultural Research Service. 2001. USDA Nutrient Database for Standard Reference, Release 14. Nutrient Data Laboratory Home Page, http://www.nalusda.gov/fnic/foodcomp.

Graphic 56081 Version 8.0

Disclosures

Disclosures: **Mark Rosenberg, MD** Nothing to disclose. **Gary C Curhan, MD, ScD** Consultant/Advisory Boards: AstraZeneca [Gout (Lesir American Society of Nephrology [CJASN Editor-in-Chief]. **Alice M Sheridan, MD** Nothing to disclose.

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a m Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy