



Definition and staging of chronic kidney disease in adults

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INTRODUCTION

The definition and classification of chronic kidney disease (CKD) guidelines were introduced by the National Kidney Foundation (NKF) Kidney Disease Outcomes Quality Initiative (KDOQI) in 2002, and were subsequently adopted with minor modifications by the international guideline group Kidney Disease Improving Global Outcomes (KDIGO) in 2004 [[1-3](#)].

These CKD guidelines shifted the concept of kidney disease from that of an uncommon life-threatening condition requiring care by nephrologists to that of a common condition with a range of severity meriting attention by general internists, and demanding strategies for prevention, early detection, and management [[4,5](#)]. The guidelines had a major effect on clinical practice, research, and public health, but also generated substantial controversy [[6-11](#)].

The most recent definition and classification of CKD will be addressed here. Discussions pertaining to the assessment of kidney function, the epidemiology of CKD, screening for CKD, evaluation of patients with CKD, overview of the management of CKD, and the association between CKD and cardiovascular disease are presented elsewhere:

- (See "[Assessment of kidney function](#)".)
- (See "[Epidemiology of chronic kidney disease](#)".)
- (See "[Early detection of chronic kidney disease](#)".)
- (See "[Diagnostic approach to adult patients with subacute kidney injury in an outpatient setting](#)".)

- (See ["Chronic kidney disease in children: Overview of management"](#).)
 - (See ["Chronic kidney disease and coronary heart disease"](#).)
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CONTROVERSIES ADDRESSED BY THE GUIDELINES

In 2009, Kidney Disease: Improving Global Outcomes (KDIGO) convened a Controversies Conference to address key areas of controversy and review data on more than 1.5 million individuals from 45 cohorts that was assembled by the CKD Prognosis Consortium [12-16]. The following controversies were among those discussed:

- Should the albuminuria threshold to define CKD continue to be 30 mg/day (or equivalent)?
- Should the glomerular filtration rate (GFR) threshold to define CKD continue to be 60 mL/min per 1.73 m²?
- Should the GFR threshold used to define CKD depend upon age?
- Should patients diagnosed as having CKD be staged based upon albuminuria in addition to GFR?

Conference attendees recommended, by at least a two-thirds majority vote, that the previous Kidney Disease Outcomes Quality Initiative (KDOQI) and KDIGO definitions of CKD be retained, but that the classification be modified to include the cause of disease and albuminuria staging [12]. KDIGO subsequently updated the guidelines in 2012 and adopted the recommendations [17]. The rationale behind these decisions is discussed in the sections that follow.

DEFINITION AND STAGING OF CHRONIC KIDNEY DISEASE

Framework and conceptual model — We agree with Kidney Disease Outcomes Quality Initiative (KDOQI) and Kidney Disease: Improving Global Outcomes (KDIGO) that CKD is a heterogeneous group of disorders characterized by alterations in kidney structure and function, which manifest in various ways depending upon the underlying cause or causes and the severity of disease ([figure 1](#)) [1,4]. Risk factors for CKD include genetic or sociodemographic predisposition, or the presence of diseases which can initiate and propagate kidney disease. Kidney failure is the end-stage of CKD and is defined as severely reduced kidney function or treatment with dialysis. The term "end-stage kidney disease" (ESKD) generally refers to chronic kidney failure treated with either dialysis or transplantation. Acute kidney injury (AKI) may complicate CKD and hasten its progression [18,19]. (See ["Overview of the management of](#)

[chronic kidney disease in adults", section on 'Natural history of kidney disease'](#) and ["Definition and staging criteria of acute kidney injury in adults".](#))

CKD is usually asymptomatic in its early stages. Symptoms appear in later stages in association with complications ([figure 1](#)). In addition to commonly recognized hormonal and metabolic complications such as anemia and hyperparathyroidism, CKD complications include increased risks for systemic drug toxicity, cardiovascular disease, infection, cognitive impairment, and impaired physical function [20-23]. Complications are more likely to occur at later stages, and may lead to death before kidney disease progresses to kidney failure. Complications may also arise from the adverse effects of interventions used to prevent or treat the disease. (See ["Overview of the management of chronic kidney disease in adults", section on 'Treatment of the complications of kidney failure'.](#))

Definition of CKD — We agree with the KDOQI and KDIGO guidelines that CKD is defined by the presence of kidney damage **or** decreased kidney function **for three or more months**, irrespective of the cause ([table 1](#)) [24]. The persistence of the damage or decreased function for at least three months is **necessary** to distinguish CKD from acute kidney disease. Kidney damage refers to pathologic abnormalities, whether established via kidney biopsy or imaging studies, or inferred from markers such as urinary sediment abnormalities or increased rates of urinary albumin excretion. Decreased kidney function refers to a decreased glomerular filtration rate (GFR), which is usually estimated (eGFR) using serum creatinine and one of several available equations. (See ["Chronic kidney disease \(newly identified\): Clinical presentation and diagnostic approach in adults".](#))

A discussion of the limitations of GFR estimation, including problems associated with using the serum creatinine in patients who are not in steady-state (such as hospitalized patients) and those with diminished creatinine generation, is presented elsewhere. (See ["Assessment of kidney function".](#))

An important aspect of the definition is that the criteria are objective and can be ascertained by means of simple laboratory tests. Identifying patients with CKD can therefore be done without identification of the underlying cause and without consultation with a nephrologist. However, many patients should, under the circumstances outlined below, be referred to a nephrologist or other specialist with expertise in evaluating and managing patients with CKD in order to identify the cause of the CKD and to provide recommendations for therapies to reverse the kidney disease, slow progression, or treat complications. (See ["Referral to a specialist"](#) below and ["Overview of the management of chronic kidney disease in adults", section on 'Referral to nephrologists'.](#))

Kidney damage — Kidney damage includes pathologic abnormalities in the native or transplanted kidney. Kidney damage is identified in most cases by the presence of one of the following clinical markers ([table 1](#)):

- Albuminuria – In clinical practice, albuminuria is the most frequently assessed marker of kidney damage. Albuminuria reflects increased glomerular permeability to macromolecules [25]. Albuminuria may reflect primary kidney disease or kidney involvement in systemic disease. In particular, albuminuria may represent widespread endothelial dysfunction, such as can be seen with hypertension, diabetes, hypercholesterolemia, smoking, obesity, and other disorders.

Although a number of different measurement methods have been used to assess and define albuminuria ([table 2](#)), the albumin-to-creatinine ratio (ACR) in an untimed "spot" urine has many advantages ([calculator 1](#)) [26,27]. The generally accepted threshold for an abnormally elevated ACR is 30 mg/g (3.4 mg/mmol) or greater. ACR can be estimated by converting spot urine protein-to-creatinine ratio and dipstick urine protein using various formulas [28,29]. (See "[Moderately increased albuminuria \(microalbuminuria\) in type 1 diabetes mellitus](#)" and "[Moderately increased albuminuria \(microalbuminuria\) in type 2 diabetes mellitus](#)" and "[Assessment of urinary protein excretion and evaluation of isolated non-nephrotic proteinuria in adults](#)" and "[Overview of heavy proteinuria and the nephrotic syndrome](#)".)

We agree with the KDIGO recommendation that albuminuria above this threshold, regardless of cause, should be considered part of the definition of CKD. Individuals with a urine ACR >30 mg/g (or equivalent) have a significantly increased risk for all-cause and cardiovascular mortality, ESKD, AKI and CKD progression compared with those who have a lower ACR ([figure 2](#) and [figure 3](#)), even when eGFR is normal [12,14-16,24]. As an example, individuals with an ACR of 30 to 299 mg/g (3.4 to 34 mg/mmol) or equivalent and an eGFR of 90 to 105 mL/min per 1.73 m² had an 11-fold higher relative risk for ESKD than those whose eGFR was similar but whose ACR was below 30 mg/g.

In the KDOQI and KDIGO definition, the threshold value for abnormally elevated urine ACR (30 mg/g or higher) is applied to adults of all ages, both men and women, and all racial-ethnic groups, despite potential differences in creatinine excretion rate among these groups. When this single threshold was applied to a population-based cohort in the United States, the prevalence of albuminuria was significantly greater in women compared with men [30]. Although urinary albumin concentrations were similar, women had lower urinary creatinine concentrations. Thus, sex-specific ACR thresholds that better predict a 24-hour urinary albumin excretion of 30 mg or higher (≥ 25 mg/g for women and ≥ 17 mg/g for men)

have been used in some studies [31]. However, we agree with the KDIGO recommendation to use a common albuminuria threshold for all adults due to the ease of widespread implementation. Albumin excretion rate in a timed urine collection can be used for confirmation when clinical circumstances require more accurate measurement.

- Urinary sediment abnormalities – Urinary sediment abnormalities such as red or white blood cell casts may indicate the presence of glomerular injury or tubular inflammation. (See "[Urinalysis in the diagnosis of kidney disease](#)".)
- Imaging abnormalities – Kidney damage may be detected by the presence of imaging abnormalities such as polycystic kidneys, hydronephrosis, and small and echogenic kidneys. (See "[Radiologic assessment of renal disease](#)".)
- Pathologic abnormalities – A kidney biopsy may reveal evidence for glomerular, vascular, or tubulointerstitial disease.
- Kidney transplantation – Patients with a history of kidney transplantation are assumed to have kidney damage whether or not they have documented abnormalities on kidney biopsy or markers of kidney damage.

Decreased GFR — Glomerular filtration rate (GFR) is generally considered to be the best index of overall kidney function, and declining GFR is the hallmark of progressive kidney disease [32]. Measured GFR varies in normal individuals by age and sex ([figure 4](#)) [33], dietary protein intake, and possibly by race-ethnicity, although the magnitude of racial variations are not well known. Based upon clearance measurements in healthy people and in people with kidney disease, the widely accepted threshold defining a decreased GFR is less than 60 mL/min per 1.73 m²; kidney failure is defined as a GFR <15 mL/min per 1.73 m² or treatment by dialysis ([table 1](#)).

We agree with KDIGO that a measured GFR below this threshold should be considered part of the definition of CKD. GFR can be measured directly using the clearance of exogenous filtration markers such as inulin, iothalamate, or [iohexol](#) [34]. However, these measurement methods are complex to implement. Thus, in clinical practice, GFR is typically **estimated** (estimated GFR, or eGFR) from the serum concentration of creatinine, an endogenous filtration marker. Since 2013, the eGFR is reported routinely by 90 percent of clinical laboratories in the United States whenever the serum creatinine is measured [35]. Serum creatinine is measured frequently, and eGFR reporting has led to increased detection of CKD [36,37].

In routine practice, therefore, individuals who have an eGFR below 60 mL/min per 1.73 m² are defined as having CKD. These individuals have a significantly increased risk for all-cause and

cardiovascular mortality, ESKD, AKI and CKD progression in compared with those whose eGFR is 60 mL/min per 1.73 m² or higher ([figure 2](#) and [figure 3](#)), even if the ACR is normal [[12,14-16,24](#)]. As an example, individuals with an eGFR of 45 to 59 mL/min per 1.73 m² and a urine ACR less than 10 mg/g had a fivefold higher relative risk of ESKD compared than those with a similarly normal ACR but with an eGFR of 60 mL/min per 1.73 m² or greater.

However, as noted below, we do not generally recommend that patients who have an isolated decreased eGFR (eg, an eGFR of 45 to 59 mL/min per 1.73 m² without an elevation in albuminuria) be referred for care by a nephrologist or other specialist with expertise in caring for patients with kidney disease. (See '[Referral to a specialist](#)' below.)

Similar thresholds for older adults — Large meta-analyses have also found that the associations between eGFR and adverse events such as death and ESKD do **not** vary substantially with age [[12,38](#)]. In a meta-analysis that included approximately 1.5 million individuals from multiple cohorts, for example, the associations between lower levels of eGFR with the incidence of death, cardiovascular disease, ESKD, and progression of kidney disease were similar among those older and younger than 65 years [[12](#)]:

- All-cause mortality – Compared with individuals who had an eGFR between 90 and 105 mL/min per 1.73 m² and an ACR less than 10 mg/g, the relative risks for all-cause mortality among those who had an eGFR between 45 and 59 mL/min per 1.73 m² and an ACR less than 10 mg/g (ie, those with an "isolated" reduction in eGFR) were 1.9 (95% CI, 1.4-2.5) in those younger than 65 years and 1.2 (95% CI, 1.0-1.5) in those older than 65 years.
- Cardiovascular mortality – Compared with individuals who had an eGFR between 90 and 105 mL/min per 1.73 m² and an ACR less than 10 mg/g, the relative risks for cardiovascular mortality among those who had an eGFR between 45 and 59 mL/min per 1.73 m² and an ACR less than 10 mg/g (ie, those with an "isolated" reduction in eGFR) were 1.3 (95% CI, 0.6-3.2) in those younger than 65 years and 1.4 (95% CI, 1.2-1.8) in those older than 65 years. In addition, absolute rates of cardiovascular mortality were higher in those older than 65 years.
- End-stage kidney disease – Compared with individuals who had an eGFR of 60 mL/min per 1.73 m² or more, the relative risks for ESKD among those who had an eGFR between 45 and 59 mL/min per 1.73 m² were 3.1 (95% CI, 1.1-8.3) in those younger than 65 years and 3.4 (95% CI, 1.6-7.2) in those older than 65 years. In contrast to cardiovascular mortality, absolute rates of ESKD were lower in those older than 65 years.

Thus, for older adults, the relative risk for all-cause mortality associated with a reduction in eGFR is somewhat smaller than it is in younger individuals, but the relative risks are similar for

cardiovascular mortality and ESKD in both younger and older individuals. A more detailed meta-analysis confirmed that the relative risks for all-cause mortality associated with a given eGFR were smaller among older individuals; however, the absolute risks associated with a given eGFR were higher among older individuals due to the elevated baseline risk for mortality [38].

There are limited data evaluating the association of isolated reductions in GFR with death and ESKD in older individuals (ie, age 75 years and older). However, reductions in GFR are associated with other CKD complications in such patients. In a study of 2272 individuals 80 years of age and older from the general population, the prevalences anemia and hyperparathyroidism were both significantly higher in those whose eGFR was between 45 and 59 mL/min per 1.73 m² compared with those whose eGFR was greater than or equal to 60 mL/min per 1.73 m² [39].

Similar thresholds in low-risk groups — Large meta-analyses have also compared risks for all-cause mortality, cardiovascular mortality, and ESKD by eGFR and albuminuria across different risk groups defined by sex, race, and comorbidity. In general, the relative risks for adverse outcomes associated with lower eGFR or higher albuminuria were as high (or higher) among the low-risk groups (ie, women, whites, Asians, non-hypertensives, non-diabetics) [40-43]. These data support similar thresholds for defining CKD irrespective of sex, race, comorbid hypertension, or diabetes.

GFR estimation — The various glomerular filtration rate (GFR) estimating equations use serum creatinine along with some combination of age, sex, race and body size as surrogates for the non-GFR determinants of serum creatinine, and provide more accurate estimates of measured GFR than serum creatinine alone [34,44,45]. Commonly used estimating equations are imperfect, providing GFR estimates that can occasionally be widely disparate from the measured GFR. A detailed discussion of the limitations of GFR estimation is presented elsewhere. (See "[Assessment of kidney function](#)".)

The Modification of Diet in Renal Disease (MDRD) Study equation is the most frequently used GFR estimating equation in the United States [46]. However, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation is more accurate than the MDRD Study equation, especially at a GFR >60 mL/min per 1.73 m², and is replacing the MDRD Study equation [47-50]. Both equations use age, sex, and race in addition to serum creatinine, and assign race as either black (eg, African American) versus non-black. Modifications of the equations for other geographical regions and racial-ethnic groups have been performed [51,52]. (See "[Assessment of kidney function](#)", [section on 'Estimation equations'](#).)

Cystatin C is an alternative endogenous filtration marker that may have advantages over creatinine for GFR estimation because its non-GFR determinants are less affected by race and

muscle wasting, and because it is more predictive of subsequent cardiovascular disease and mortality [53-56]. Use of cystatin C and creatinine together enables more accurate GFR estimates [54,57], and more accurate predictions of risk [53,58,59], although we are not recommending this strategy at this time. (See "[Assessment of kidney function](#)", [section on 'Serum cystatin C'](#) and "[Chronic kidney disease and coronary heart disease](#)", [section on 'Cystatin C and other markers of kidney function'](#).)

Like all diagnostic tests, interpretation of the eGFR should be influenced by the prior probability of disease. An isolated decreased eGFR in an otherwise healthy individual is more likely to be a false positive than in individuals with other markers of kidney damage or who have known risk factors for kidney disease. Confirmation of decreased eGFR by measurement of GFR using an exogenous filtration marker, measurement of creatinine clearance, or estimation of GFR using serum cystatin C is warranted when decisions depend upon more accurate knowledge of GFR, such as determining eligibility for kidney donation or adjusting the dose of toxic drugs that are excreted by the kidneys [44]. In most cases, however, eGFR using serum creatinine is appropriate for diagnosis, staging, and management of CKD.

Confirming the chronicity of damage or decreased function — As noted above, the KDIGO guidelines require that the damage or decreased function be persistent for at least three months in order to make a diagnosis of CKD. Chronicity may be documented or inferred. When evidence of kidney damage or decreased function is first apparent, confirmation of chronicity can be obtained by one of the following:

- Review of past measurements or estimates of GFR
- Review of past measurements of albuminuria or proteinuria
- Review of past urine dipstick and sediment examinations
- Imaging findings, such as reduced kidney volume and reduction in cortical thickness, or presence of multiple cysts
- Obtaining repeat measurements within and beyond the three-month point

In clinical practice, it is usually not difficult to evaluate chronicity. For patients without evidence of chronicity, repeat testing is **essential** to rule out acute kidney disease. In addition, repeat testing is necessary in patients who have an eGFR or ACR near the threshold values for the CKD definition (ie, an eGFR just below 60 mL/min per 1.73 m² or an ACR just above 30 mg/g [3.4 mg/mmol]). In patients with these borderline values, both biological and analytical variations in serum creatinine and urinary albumin may result in the diagnosis of CKD not being confirmed [27,60].

Several studies have demonstrated the importance of repeat testing when evidence for chronicity is not already available at the time damage or decreased function is first recognized [61-64]:

- In a study of approximately 14,000 individuals from the general population with an eGFR greater than or equal to 60 mL/min per 1.73 m² who had repeated ACR measurements after a two-week interval, persistence of an ACR between 30 and 300 mg/g (3.4 to 34 mg/mmol) and an ACR greater than 300 mg/g at two weeks was 54 and 73 percent, respectively [62].
- In another general population cohort of 18,066 individuals with repeat measurements of serum creatinine separated by a mean of three years, 1169 (6.5 percent) had an eGFR less than 60 mL/min per 1.73 m² at baseline [64]. At three years, 891 of these individuals (76 percent) still had a reduced eGFR. The risk of subsequent adverse cardiovascular events was higher in those with persistently low eGFR than in those whose eGFR rose to above 60 mL/min per 1.73 m² at three years.

Staging of CKD — The purpose of CKD staging is to guide management, including stratification of risk for progression and complications of CKD. Risk stratification is used as a guide to inform appropriate treatments and the intensity of monitoring and patient education [1,4]. In patients who are diagnosed with CKD using the criteria described above, staging of the CKD is done according to ([table 3](#)) [24]:

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

Staging patients with CKD according to cause, GFR, and albuminuria enhances risk stratification for the major complications of CKD ([figure 2](#) and [figure 3](#) and [table 4](#)). Low GFR is a stronger predictor of CKD complications than high albuminuria [65]. An overview of the management of patients with according to stage of CKD is provided elsewhere. (See "[Overview of the management of chronic kidney disease in adults](#)".)

Cause of disease — Identifying the cause of kidney disease (eg, diabetes, drug toxicity, autoimmune diseases, urinary tract obstruction, kidney transplantation, etc.) enables specific therapy directed at preventing further injury. In addition, the cause of kidney disease has implications for the rate of progression and the risk of complications ([table 4](#)).

It can be difficult to ascertain the cause of kidney disease. In clinical practice, CKD is most often discovered as decreased eGFR during the evaluation and management of other medical

conditions. The evaluation of patients diagnosed with CKD is discussed elsewhere. (See ["Diagnostic approach to adult patients with subacute kidney injury in an outpatient setting".](#))

GFR — The glomerular filtration rate (GFR; G-stages) follow the original CKD classification scheme ([table 3](#)):

- G1 – GFR >90 mL/min per 1.73 m²
- G2 – GFR 60 to 89 mL/min per 1.73 m²
- G3a – GFR 45 to 59 mL/min per 1.73 m²
- G3b – GFR 30 to 44 mL/min per 1.73 m²
- G4 – GFR 15 to 29 mL/min per 1.73 m²
- G5 – GFR <15 mL/min per 1.73 m² or treatment by dialysis

Since the original KDOQI classification was published, stage 3 CKD (a GFR of 30 to 59 mL/min per 1.73 m²) has been subdivided into GFR stages 3a and 3b to more accurately reflect the continuous association between lower GFR and risk for mortality and adverse kidney outcomes ([figure 2](#)). Patients receiving treatment with dialysis are subclassified as GFR stage 5D to highlight the specialized care that they require.

Albuminuria — The three albuminuria stages follow familiar definitions of normal, moderately increased (formerly called "microalbuminuria"), and severely increased (formerly called "macroalbuminuria" and nephrotic range) albuminuria ([table 3](#)) ([calculator 1](#)):

- A1 – ACR <30 mg/g (<3.4 mg/mmol)
- A2 – ACR 30 to 299 mg/g (3.4 to 34.0 mg/mmol)
- A3 – ACR ≥300 mg/g (>34.0 mg/mmol)

The addition of albuminuria staging to GFR staging is new since the original KDOQI classification scheme was published [\[1-3\]](#). Albuminuria staging has been added because of the graded increase in risk for mortality, progression of CKD, and ESKD at higher levels of albuminuria, independent of eGFR, without an apparent threshold value ([figure 2](#) and [figure 3](#)) [\[12,24\]](#). The increase in risk is significant for urine ACR values ≥30 mg/g, even when GFR is >60 mL/min per 1.73 m², consistent with the current threshold value for albuminuria (≥30 mg/g) as a marker of kidney damage. An increased risk is also apparent with urine ACR levels between 10 and 29 mg/g ("high normal" albuminuria), suggesting that levels below 30 mg/g may also warrant increased attention.

Purpose for and implications of CKD staging — The staging system for CKD is intended to aid clinicians in the management of patients with CKD by identifying those with the most severe disease who are, therefore, at greatest risk for progression and complications. Staging

according to cause, GFR, and albuminuria allows for a more complete description of risk for the major adverse outcomes of CKD.

CKD staging is **not** meant to imply that there are GFR or albuminuria thresholds in CKD severity, or that all patients in the same GFR and albuminuria category will have the same prognosis. As an example, a patient with a GFR of 15 mL/min per 1.73 m² likely has more severe kidney disease, and may be at higher risk for complications, than someone with a GFR of 29 mL/min per 1.73 m², even though both patients have GFR stage G4.

Patients with already diagnosed CKD can now be staged according to the cause of kidney disease and then into 18 separate categories with differing degrees of risk for progression to all-cause mortality, cardiovascular mortality, ESKD, CKD progression, and acute kidney injury. The relative risk for each outcome is higher with more severe GFR and ACR stages. Based upon these findings, a "heat map" can be constructed that divides patients with CKD into the following three broad risk categories based upon the likelihood of developing future kidney and cardiovascular complications (eg, ESKD, cardiovascular death) ([figure 5](#)); the proportion of the population in the United States with CKD (ascertained by eGFR and albuminuria) that falls into these risk categories is also given [\[8\]](#):

- Moderate risk (yellow) – 73 percent of patients with CKD
- High risk (orange) – 18 percent of patients with CKD
- Very high risk (red) – 9 percent of patients with CKD

These three broad risk categories may help clinicians decide whether or not to refer their patients to a nephrologist or specialist with expertise in caring for patients with CKD, and to develop a clinical action plan. A similar definition of risk categories was proposed based upon analysis of a large cohort in Canada [\[66\]](#). (See '[Referral to a specialist](#)' below and '[Clinical action plan](#)' below.)

However, the heat map must be considered in the appropriate context:

- First, it is derived from a meta-analysis in which approximately 1.5 million individuals were followed for a mean of five years. If a patient with CKD is staged initially as low risk, this does **not** mean the he or she will remain low risk and not progress over the next several decades. As an example, a patient with autosomal dominant polycystic kidney disease (ADPKD) who is diagnosed by imaging at a young age and who has a normal eGFR and no proteinuria may be low risk for developing ESKD in the short term, but has a high long-term risk of progressive CKD.

- Second, the heat map applies to patients who have been diagnosed with CKD. Individuals who fall into the low risk (green) categories have CKD based upon markers of kidney damage other than albuminuria. Such individuals are generally not identified in population surveys.
- Third, the risk graduation displayed in the heat map is meant to compare patients with the same cause of CKD.

Additional details describing the association between CKD and risk for cardiovascular disease are presented elsewhere. (See "[Chronic kidney disease and coronary heart disease](#)".)

IMPLICATIONS FOR CLINICAL PRACTICE AND PUBLIC HEALTH

The definition and classification of CKD has several important implications for public health and clinical practice.

Prevalence of CKD — Because patients with CKD have a high rate of end-stage kidney disease (ESKD), cardiovascular disease, and death, CKD is an appropriate target for prevention, early detection, and management by non-nephrologist clinicians and public health agencies [67,68]. Using the current definitions, the prevalence of CKD in the United States during the interval from 1999 to 2006 was 11.5 percent (42 percent in glomerular filtration rate [GFR] stages 1-2 and 58 percent in GFR stages 3-4), equivalent to approximately 23 million adults [48]. This was similar to the prevalence of other chronic non-communicable diseases in the United States at that time, such as diabetes (10.6 percent, 23.4 million) [67]. The age-standardized global prevalence of CKD in 2010 was estimated as 10.4 percent in men and 11.8 percent in women, although there was heterogeneity across regions [69].

In 2013, reduced GFR was associated with 4 percent of deaths worldwide or 2.2 million deaths. More than one-half of these attributable deaths were cardiovascular deaths (1.2 million), whereas 0.96 million were ESKD-related deaths. Compared with other risk factors, reduced GFR ranked below hypertension, overweight-obesity, and high plasma glucose, but similarly with high cholesterol, as a risk factor for disability-adjusted life years in both developed and developing world regions [70].

Application to older adults — The prevalence of CKD in people 70 years and older in the United States is high (approximately 45 percent) [48,71]. It is possible that the association between advancing age and lower eGFR and higher albuminuria may be due to vascular disease rather than a natural aging process [71-73]. The fact that lower eGFR values are associated with increased kidney and cardiovascular disease rates in older as well as younger

individuals is not consistent with the interpretation that decreased eGFR with aging is "normal" or "physiological." Rather, it suggests that decreased eGFR in older adults is evidence of disease. Similarly, the increased risk for adverse kidney outcomes for individuals whose urine albumin-to-creatinine ratio (ACR) is between 30 and 299 mg/g (3.4 to 34 mg/mmol) in older as well as younger adults is not consistent with the interpretation that moderately increased albuminuria (formerly called "microalbuminuria") is only a marker for increased cardiovascular disease risk.

As in diabetes, hypertension, or hypercholesterolemia, selecting a threshold value to define the disease must balance the risk of "labeling" low-risk individuals against the benefit of early detection of high-risk individuals [74-77]. As an example, the systolic blood pressure threshold for the definition of hypertension, previously higher in older adults than in the young, is now the same for all ages. We agree with the position of KDIGO that definition of CKD should be the same for all ages, although the evaluation and management should be adapted for age [78,79].

CKD classification to assign prognosis for individuals — The staging system will help clinicians to determine how and how intensely to treat and monitor patients with established CKD. More accurate risk prediction for an individual patient can be accomplished by the development of risk-prediction instruments. In addition to eGFR and albuminuria, the cause of kidney disease, as well as other factors (eg, age, sex, race, cholesterol levels, smoking status, and others), should be considered in estimating prognosis. As examples, one instrument for predicting risk of progression of CKD from eGFR <60 mL/min per 1.73 m² to ESKD that used age, sex, eGFR, and albuminuria was developed from a large cohort of patients referred to nephrologists and has been extensively validated [80,81]. Another instrument for predicting risks for development of ESKD, cardiovascular disease, and mortality in patients with eGFR <30 mL/min per 1.73 m² used additional variables (race, systolic blood pressure, smoking status, diabetes mellitus, and history of cardiovascular disease) and has also undergone extensive validation [82]. We think such models could eventually be useful tools to help guide decision-making for individual patients.

REFERRAL TO A SPECIALIST

Referral depends upon practice patterns, which are not uniform across healthcare systems or geographic regions, even within countries. As a result, there are numerous recommendations that propose indications for referral to nephrologists, and none have been universally adopted [83-87]. However, one indication that is common to most guidelines is that all patients with severely decreased glomerular filtration rate (GFR; estimated GFR [eGFR] less than 30 mL/min per 1.73 m², GFR stage 4) should be referred for co-management with a nephrologist. Patients

at or below this level of eGFR have already demonstrated that they have progressive kidney disease, and therefore are at high risk for progression to end-stage kidney disease (ESKD). In such patients, late referral to a nephrologist (ie, less than three months before the start of dialysis therapy) is associated with higher mortality after the initiation of dialysis [88,89].

Patients with severely decreased eGFR require preparation for the possible onset of ESKD. Preparation involves a discussion regarding kidney replacement therapy (dialysis and transplantation), and conservative therapy for those not willing or unable to undergo kidney replacement therapy. In patients electing replacement therapy, timely creation of vascular access for hemodialysis, home dialysis training, and donor evaluation for preemptive transplantation should occur. Several studies have demonstrated that patients who are referred to nephrology late are less likely to initiate dialysis with a functioning fistula [85,90,91].

There is less consensus about referral for patients with higher eGFR. Based in part upon current guidelines [24,84,85], we recommend that, in addition to referral of all patients who have an eGFR less than 30 mL/min per 1.73 m², patients with CKD who meet one or more of the following criteria be referred to a nephrologist or other clinician skilled in managing patients with CKD:

- Urine albumin-to-creatinine ratio (ACR) \geq 300 mg/g (34 mg/mmol), including nephrotic syndrome
- Hematuria not secondary to urological conditions
- Inability to identify a presumed cause of CKD
- eGFR decline of more than 30 percent in fewer than four months without an obvious explanation
- Difficult to manage complications such as anemia requiring erythropoietin therapy, and abnormalities of bone and mineral metabolism requiring phosphorus binders or vitamin D preparations
- Serum potassium greater than 5.5 mEq/L
- Difficult to manage drug complications
- Patients under the age of 18 years
- Resistant hypertension
- Recurrent or extensive nephrolithiasis

- Confirmed or presumed hereditary kidney disease, such as polycystic kidney disease, Alport syndrome, or autosomal dominant interstitial kidney disease:
 - (See ["Autosomal dominant polycystic kidney disease \(ADPKD\): Treatment".](#))
 - (See ["Clinical manifestations, diagnosis, and treatment of Alport syndrome \(hereditary nephritis\)".](#))
 - (See ["Autosomal dominant tubulointerstitial kidney disease \(medullary cystic kidney disease\)".](#))

Nephrologists can assist primary care clinicians and other specialists in the diagnosis and care of patients at all stages of CKD. These functions include determination of the cause of CKD, recommendations for specific therapy, suggestions for treatments to slow progression in patients who have not responded to conventional therapies, identification and treatment for kidney disease-related complications, and preparation for dialysis. Because patients with CKD are at risk for a diverse set of adverse outcomes (not just kidney failure), referral to other appropriate specialists (eg, cardiologists for those with complex cardiovascular disease) should also be considered.

CLINICAL ACTION PLAN

Suggestions for the treatment and monitoring of patients who are diagnosed with CKD vary according to the stage of CKD based upon cause, glomerular filtration rate (GFR), and albuminuria. A discussion of the recommended clinical action plan according to CKD stage is presented elsewhere. (See ["Overview of the management of chronic kidney disease in adults".](#))

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See ["Society guideline links: Chronic kidney disease in adults".](#))

SUMMARY

- Chronic kidney disease (CKD) is a heterogeneous group of disorders characterized by alterations in kidney structure and function, which manifest in various ways depending upon the underlying cause or causes and the severity of disease ([figure 1](#)). The term

"end-stage kidney disease" (ESKD) generally refers to CKD treated with either dialysis or transplantation. (See ['Framework and conceptual model'](#) above.)

- CKD is usually asymptomatic in its early stages. Symptoms appear in later stages in association with complications ([figure 1](#)). In addition to commonly recognized hormonal and metabolic complications such as anemia and hyperparathyroidism, CKD complications include increased risks for systemic drug toxicity, cardiovascular disease, infection, cognitive impairment, and impaired physical function. (See ['Framework and conceptual model'](#) above.)
- CKD is defined by the presence of kidney damage **or** decreased kidney function **for three or more months**, irrespective of the cause ([table 1](#)). The persistence of the damage or decreased function for at least three months is **necessary** to distinguish CKD from acute kidney disease. Kidney damage refers to pathologic abnormalities, whether established via kidney biopsy or imaging studies or inferred from markers such as urinary sediment abnormalities or increased rates of urinary albumin excretion. Decreased kidney function refers to a decreased glomerular filtration rate (GFR), which is usually estimated (eGFR) using serum creatinine and one of several available equations. (See ['Definition of CKD'](#) above.)
 - Kidney damage is identified in most cases by the presence of albuminuria, urinary sediment abnormalities, anatomic abnormalities discovered with imaging studies, pathologic abnormalities discovered with kidney biopsy, or a history of kidney transplantation ([table 1](#)). (See ['Kidney damage'](#) above.)
 - Decreased kidney function is identified in most cases by an eGFR less than 60 mL/min per 1.73 m² ([table 1](#)). Estimation of GFR is discussed in more detail elsewhere. (See ['Decreased GFR'](#) above and ['Assessment of kidney function'](#).)
- Confirmation of chronicity can be obtained by one of the following (see ['Confirming the chronicity of damage or decreased function'](#) above):
 - Review of past measurements or estimates of GFR
 - Review of past measurements of albuminuria or proteinuria
 - Review of past urine dipstick and sediment examinations
 - Imaging findings, such as reduced kidney volume and reduction in cortical thickness, or presence of multiple cysts
 - Obtaining repeat measurements within and beyond the three-month point

- The purpose of CKD staging is to guide management, including stratification of risk for progression and complications of CKD ([figure 2](#) and [figure 3](#) and [table 4](#)). Risk stratification is used as a guide to inform appropriate treatments and the intensity of monitoring and patient education. In patients who are diagnosed with CKD using the criteria described above, staging of the CKD is done according to ([table 3](#)) (see '[Staging of CKD](#)' above):
 - Cause of disease – Identifying the cause of kidney disease (eg, diabetes, drug toxicity, auto-immune diseases, urinary tract obstruction, kidney transplantation, etc.) enables specific therapy directed at preventing further injury and has implications for the rate of progression and the risk of complications ([table 4](#)). (See '[Cause of disease](#)' above.)
 - Six categories of GFR (G stages) – The GFR (G-stages) are shown in the table ([table 3](#)). Since the original Kidney Disease Outcomes Quality Initiative (KDOQI) classification was published, stage 3 CKD (a GFR of 30 to 59 mL/min per 1.73 m²) has been subdivided into GFR stages 3a and 3b to more accurately reflect the continuous association between lower GFR and risk for mortality and adverse kidney outcomes. (See '[GFR](#)' above.)
 - Three categories of albuminuria (A stages) – The three albuminuria stages follow familiar definitions of normal, moderately increased (formerly called "microalbuminuria"), and severely increased (formerly called "macroalbuminuria" and nephrotic range) albuminuria ([table 3](#)) ([calculator 1](#)). Albuminuria staging has been added because of the graded increase in risk for mortality, progression of CKD, and ESKD at higher levels of albuminuria, independent of eGFR. (See '[Albuminuria](#)' above.)
- Based upon this staging, a "heat map" can be constructed that divides patients with CKD into three broad risk categories (moderate, high, and very high) based upon the likelihood of developing future kidney and cardiovascular complications (eg, ESKD, cardiovascular death) ([figure 5](#)). (See '[Purpose for and implications of CKD staging](#)' above.)
- We recommend that, in addition to referral of all patients who have an eGFR less than 30 mL/min per 1.73 m², patients with CKD who meet one or more of the following criteria be referred to a nephrologist or other clinician skilled in managing patients with CKD (see '[Referral to a specialist](#)' above):
 - Urine albumin-to-creatinine ratio (ACR) ≥300 mg/g (34 mg/mmol), including nephrotic syndrome
 - Hematuria not secondary to urological conditions
 - Inability to identify a presumed cause of CKD

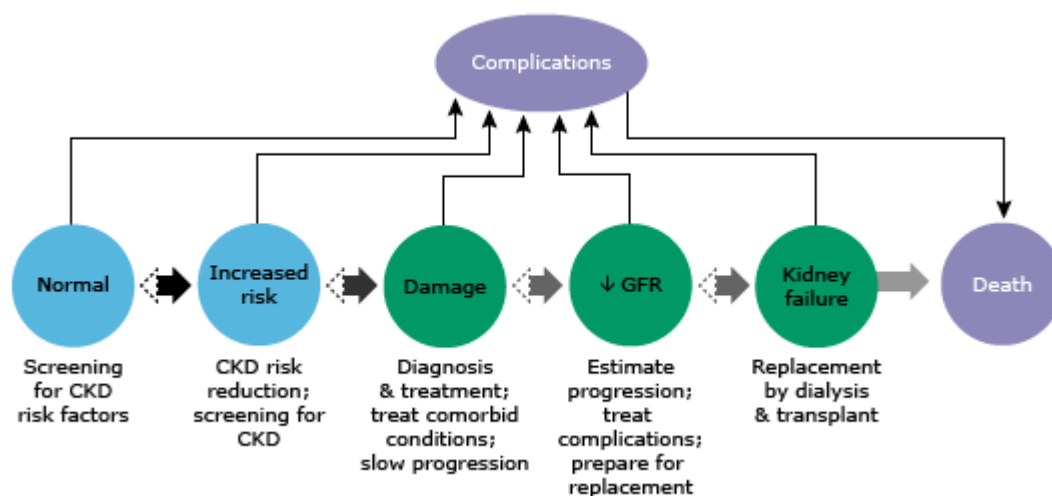
- eGFR decline of more than 30 percent in fewer than four months without an obvious explanation
- Difficult to manage complications such as anemia requiring erythropoietin therapy, and abnormalities of bone and mineral metabolism requiring phosphorus binders or vitamin D preparations
- Serum potassium greater than 5.5 mEq/L
- Difficult to manage drug complications
- Patients under the age of 18 years
- Resistant hypertension
- Recurrent or extensive nephrolithiasis
- Confirmed or presumed hereditary kidney disease

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GRAPHICS

Conceptual model for chronic kidney disease



This diagram presents the continuum of development, progression and complications of chronic kidney disease (CKD) and strategies to improve outcomes. Green circles represent stages of CKD; aqua circles represent potential antecedents of CKD, lavender circles represent consequences of CKD; and thick arrows between circles represent the development, progression and remission of CKD. "CKD" is defined as the presence of either kidney damage or decreased kidney function for three or more months, irrespective of cause (underlying illness and pathology). "Complications" refers to all complications of CKD, including complications of decreased GFR, albuminuria and cardiovascular disease. Complications may also arise from adverse effects of interventions to prevent or treat the disease. The horizontal arrows pointing from left to right emphasize the progressive nature of CKD. Dashed arrowheads pointing from right to left signify that remission is less frequent than progression.

Original figure modified for this publication. From: Levey AS, Stevens LA, Coresh J. Conceptual model of CKD: applications and implications. Am J Kidney Dis 2009; 53:S4. Illustration used with the permission of Elsevier Inc. All rights reserved.

Definition and criteria for chronic kidney disease

Definition:	
Chronic kidney disease is defined based on the presence of either kidney damage or decreased kidney function for three or more months, irrespective of cause.	
Criteria	Comment
Duration ≥ 3 months, based on documentation or inference	<p>Duration is necessary to distinguish chronic from acute kidney diseases.</p> <ul style="list-style-type: none"> Clinical evaluation can often suggest duration Documentation of duration is usually not available in epidemiologic studies
Glomerular filtration rate (GFR) < 60 mL/min/1.73 m ²	<p>GFR is the best overall index of kidney function in health and disease.</p> <ul style="list-style-type: none"> The normal GFR in young adults is approximately 125 mL/min/1.73 m²; GFR < 15 mL/min/1.73 m² is defined as kidney failure Decreased GFR can be detected by current estimating equations for GFR based on serum creatinine (estimated GFR) but not by serum creatinine alone Decreased estimated GFR can be confirmed by measured GFR, measured creatinine clearance, or estimated GFR using cystatin C
Kidney damage, as defined by structural abnormalities or functional abnormalities other than decreased GFR	<p>Pathologic abnormalities (examples). Cause is based on underlying illness and pathology. Markers of kidney damage may reflect pathology.</p> <ul style="list-style-type: none"> Glomerular diseases (diabetes, autoimmune diseases, systemic infections, drugs, neoplasia) Vascular diseases (atherosclerosis, hypertension, ischemia, vasculitis, thrombotic microangiopathy) Tubulointerstitial diseases (urinary tract infections, stones, obstruction, drug toxicity) Cystic disease (polycystic kidney disease)
	<p>History of kidney transplantation. In addition to pathologic abnormalities observed in native kidneys, common pathologic abnormalities include the following:</p> <ul style="list-style-type: none"> Chronic allograft nephropathy (non-specific findings of tubular atrophy, interstitial fibrosis, vascular and glomerular sclerosis) Rejection Drug toxicity (calcineurin inhibitors) BK virus nephropathy Recurrent disease (glomerular disease, oxalosis, Fabry disease)
	<p>Albuminuria as a marker of kidney damage (increased glomerular permeability, urine albumin-to-creatinine ratio [ACR] > 30 mg/g).*</p> <ul style="list-style-type: none"> The normal urine ACR in young adults is < 10 mg/g. Urine ACR categories 10-29, 30-300 and > 300 mg are termed "mildly increased, moderately increased, and severely increased" respectively. Urine ACR > 2200 mg/g is accompanied by signs and symptoms of nephrotic syndrome (low serum albumin, edema and high serum cholesterol). Threshold value corresponds approximately to urine dipstick values of trace or 1+, depending on urine concentration High urine ACR can be confirmed by urine albumin excretion in a timed urine collection
	<p>Urinary sediment abnormalities as markers of kidney damage, for example:</p> <ul style="list-style-type: none"> RBC casts in proliferative glomerulonephritis WBC casts in pyelonephritis or interstitial nephritis Oval fat bodies or fatty casts in diseases with proteinuria Granular casts and renal tubular epithelial cells in many parenchymal diseases (non-specific)
	<p>Imaging abnormalities as markers of kidney damage (ultrasound, computed tomography and magnetic resonance imaging with or without contrast, isotope scans, angiography).</p> <ul style="list-style-type: none"> Polycystic kidneys Hydronephrosis due to obstruction

- | | |
|--|---|
| | <ul style="list-style-type: none">▪ Cortical scarring due to infarcts, pyelonephritis or vesicoureteral reflux▪ Renal masses or enlarged kidneys due to infiltrative diseases▪ Renal artery stenosis▪ Small and echogenic kidneys (common in later stages of CKD due to many parenchymal diseases) |
|--|---|

* Albumin-to-creatinine ratio (ACR) conversion factor 1.0 mg/g = 0.113 mg/mmol.

Reproduced from: Levey A, Coresh J. Chronic kidney disease. Lancet 2011. DOI: 10.1016/S0140-6736(11)60178-5. Table used with the permission of Elsevier Inc. All rights reserved.

Graphic 80632 Version 3.0

Categories for albuminuria and proteinuria

	Normal to mildly increased	Moderately increased	Severely increased
AER (mg/day)	<30	30 to 300	>300
PER (mg/day)	<150	150 to 500	>500
ACR (mg/g)	<30	30 to 300	>300
PCR (mg/g)	<150	150 to 500	>500
Protein dipstick	Negative to trace	Trace to 1+	>1+

Normal urine contains small amounts of albumin, low-molecular-weight serum proteins, and proteins derived from renal tubules and the lower urinary tract. Albuminuria and proteinuria can be measured using excretion rates in timed urine collections, ratio of concentrations to creatinine concentration in spot urine samples, and semiquantitative dipsticks in spot urine samples. Relationships among measurement methods within a category are not exact.

Normal albumin and protein excretion rates are <10 mg/day and <50 mg/day, respectively. In most kidney diseases, albumin is the predominant urine protein, comprising approximately 60 to 90 percent of urine protein when protein excretion rate is very high. Urine albumin excretion rate of 30 to 300 and >300 mg/day correspond to moderately increased albuminuria (formerly "microalbuminuria") and severely increased albuminuria (formerly "macroalbuminuria"), respectively. Urine albumin and protein excretion rates of >2200 mg/day and >3500 mg/day are usually accompanied by signs and symptoms of nephrotic syndrome (hypoalbuminemia, hypercholesterolemia, and edema).

Albuminuria and proteinuria may be assessed from ACR and PCR. ACR and PCR are best determined by repeated measurement in morning first voided urine. In general, for clinical decision-making, ACR and PCR are sufficient, but AER and PER can be measured as a confirmatory test. Relationships between AER and ACR and between PER and PCR are based on the assumption that average creatinine excretion rate is 1 g/day. Creatinine excretion varies with age, sex, race and diet; therefore, the relationship among these categories is approximate only. ACR <10 mg/g (<1.1 mg/mmol) is considered normal; ACR 10 to 29 mg/g (1.1 to 3.3 mg/mmol) is considered "mildly increased."





Proteinuria may be assessed from semiquantitative urine dipsticks. The relationship between urine dipstick results and other measures depends upon urine concentration. In particular, a "trace" result can correspond to the "normal to mildly increased" category or low range of the "moderately increased" category. Positive dipstick tests can be confirmed by ACR, PCR, AER, or PER. For ACR and PCR, to convert from mg/g creatinine to mg/mmol of creatinine, multiply by 0.113.

AER: albumin excretion rate; PER: protein excretion rate; ACR: albumin/creatinine ratio; PCR: protein/creatinine ratio.

Data from: KDIGO. Summary of recommendation statements. Kidney Int 2013; 3(Suppl):5.

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 rank 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.)

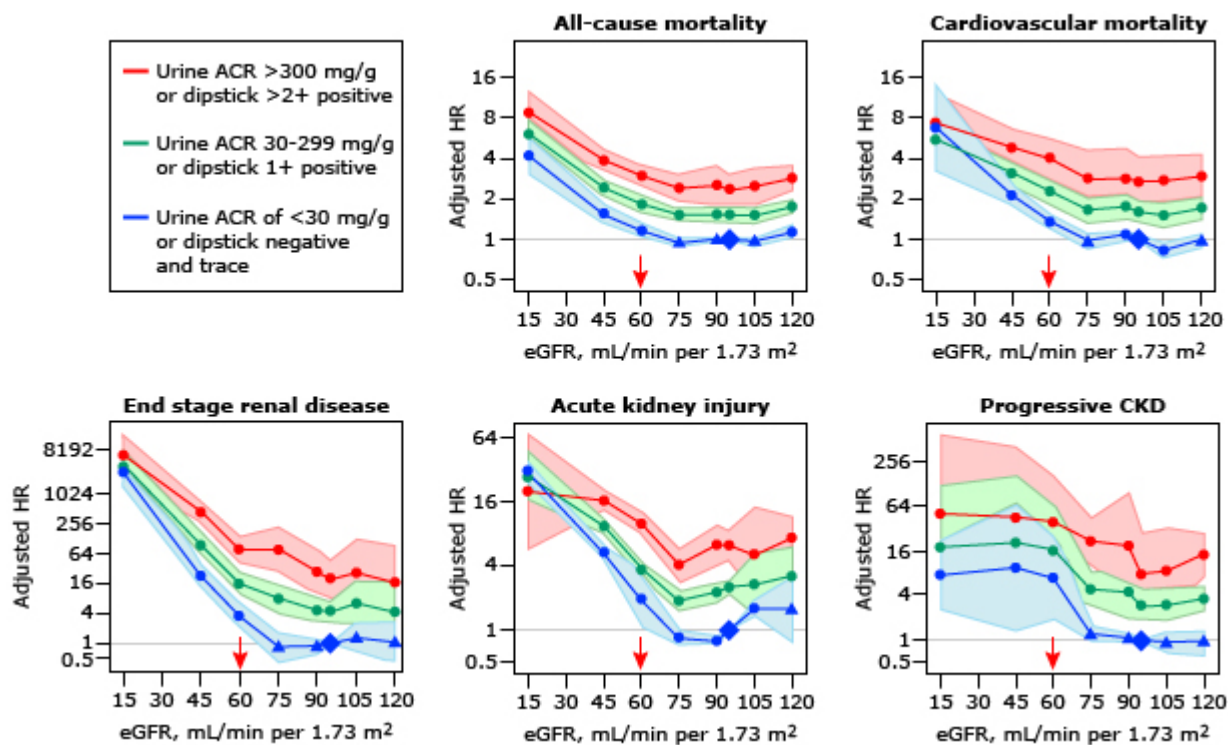
RR: relative risk; ACR: albumin creatinine ratio; eGFR: estimated glomerular filtration rate; Ref: reference cell; ESRD: end-stage renal disease; AKI: acute kidney injury; CKD: chronic kidney disease; CVD: cardiovascular disease.

* Dipstick included (-, ±, +, ≥++).

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Graphic 68921 Version 9.0

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

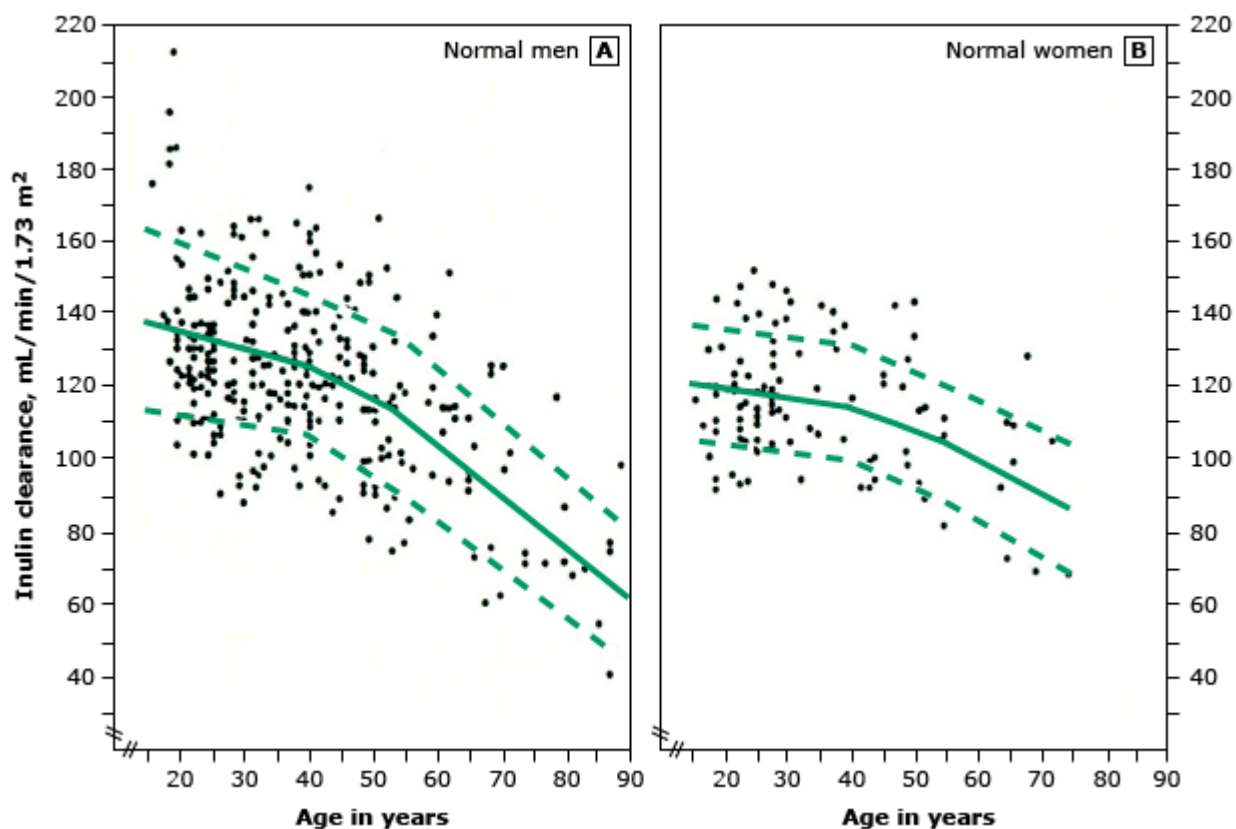


Summary of continuous meta-analysis (adjusted RR) for general population cohorts with ACR. Mortality is reported for general population cohorts assessing albuminuria as urine ACR. Kidney outcomes are reported for general population cohorts assessing albuminuria as either urine ACR or dipstick. eGFR is 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 m² 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 m², 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.

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Normal values for GFR in men and women



Normal values for inulin clearance are shown for men (panel A) and women (panel B) of various ages, with the GFR measured as the urinary clearance of inulin. A GFR <60 mL/min/1.73 m² is the threshold for the definition of chronic kidney disease. Solid lines represent the mean value of GFR per decade of age, and dashed lines represent the value 1 SD from the mean value of GFR per decade of age.

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Graphic 73824 Version 1.0

Chronic kidney disease classification based upon glomerular filtration rate and albuminuria

GFR stages	GFR (mL/min/1.73 m²)	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 nonnephrotic 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.

Relationship of GFR, albuminuria, and cause of kidney disease with future outcomes

Outcomes	Kidney measures			Other measures
	GFR	Albuminuria	Cause	
Kidney outcomes				
Albuminuria rise	+	+++	+++	HBP
CKD progression (chronic GFR decline)	+	+++	+++	HBP, male sex, black race, younger age
Acute kidney injury (acute GFR decline)	+++	++		Age, drug exposure, radiographic contrast
Kidney failure	+++	+	+++	
Complications				
Drug toxicity	+++	+		Drug exposure, liver disease
Metabolic/endocrine	+++	+	+	
CVD and mortality	+++	+++	++	Age, history of CVD, CVD risk factors
Other (infection, cognitive impairment, frailty)	++	++	++	Age, comorbid conditions

+ indicates strength of association of kidney measures to current and future outcomes.

GFR: glomerular filtration rate; CKD: chronic kidney disease; HBP: high blood pressure; CVD: cardiovascular disease.

Courtesy of Andrew S Levey, MD.

Graphic 55646 Version 1.0

Staging of patients who meet the definition of CKD

				Persistent albuminuria categories description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
GFR categories (mL/min/1.73 m ²) description and range	G1	Normal or high	≥90	1 if CKD	1	2
	G2	Mildly decreased	60-89	1 if CKD	1	2
	G3a	Mildly to moderately decreased	45-59	1	2	3
	G3b	Moderately to severely decreased	30-44	2	3	3
	G4	Severely decreased	15-29	3	3	4+
	G5	Kidney failure	<15	4+	4+	4+

GFR and albuminuria grid to reflect the risk of progression by intensity of coloring (green, yellow, orange, red, deep red). The numbers in the boxes are a guide to the frequency of monitoring (number of times per year).

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Graphic 59716 Version 6.0

