



Complete Summary

GUIDELINE TITLE

K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification.

BIBLIOGRAPHIC SOURCE(S)

K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Kidney Disease Outcome Quality Initiative. Am J Kidney Dis 2002 Feb; 39(2 Suppl 1):S1-246. [667 references] [PubMed](#)

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SCOPE

DISEASE/CONDITION(S)

Chronic kidney disease

GUIDELINE CATEGORY

Evaluation
Management
Prevention
Risk Assessment
Screening

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Nephrology

Pediatrics
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Clinical Laboratory Personnel
Health Care Providers
Managed Care Organizations
Nurses
Patients
Physician Assistants
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

- The ultimate objectives of the National Kidney Foundation (NKF) Dialysis Outcome Quality Initiative (DOQI) are to improve the quality of care and outcomes of all individuals with kidney disease and to reduce the risk of developing kidney disease.

The objectives of the Chronic Kidney Disease Work Group are:

- To define and classify chronic kidney disease, irrespective of underlying cause
- To evaluate laboratory measurements for the clinical assessment of kidney disease
- To evaluate the association of the level of kidney function with complications of chronic kidney disease
- To stratify the risk for loss of kidney function and development of cardiovascular disease

TARGET POPULATION

Individuals with chronic kidney disease or at risk of developing chronic kidney disease. The majority of topics focus on adults (≥ 18 years).

INTERVENTIONS AND PRACTICES CONSIDERED

Definition and Classification of Stages of Chronic Kidney Disease

1. Establishing presence of chronic kidney damage based on level of kidney function (glomerular filtration rate [GFR])
2. Assigning stage of disease based on level of kidney function according to Kidney Disease Outcomes Quality Initiative Chronic Kidney Disease (K/DOQI CKD) classification

Evaluation and Treatment

1. Evaluation to determine diagnosis, comorbid conditions, severity, complications, and risks for loss of kidney function and cardiovascular disease

2. Treatment including specific therapy, evaluation and management of comorbid conditions, slowing the loss of kidney function, prevention and treatment of cardiovascular disease, prevention and treatment of complications, preparation of kidney failure and replacement therapy, and dialysis and transplantation
3. Development of a clinical action plan based on disease stage
4. Medication review
5. Incorporation of self-management behaviors into treatment plan
6. Referral to a specialist, as necessary

Individuals at Increased Risk of Chronic Kidney Disease

1. Assessment for increased risk based on clinical and sociodemographic factors
2. Testing for markers of kidney damage and estimating level of GFR
3. Treatment according to standard regimen
4. Risk factor reduction

Estimation of GFR

1. Use of the Modification of Diet in Renal Disease (MDRD) Study and Cockcroft-Gault equations in adults
2. Use of the Schwartz and Counahan-Barratt equations in children
3. Serum creatinine measurements
4. Estimating GFR through prediction equations
5. Use of international standards for calibrating serum creatinine assays
6. 24-hour urine sampling for measuring creatinine clearance

Assessment of Proteinuria

1. Use of untimed "spot" urine samples
2. Timed urine collection (overnight or 24-hour)
3. Screening with urine dipsticks (standard and albumin-specific)
4. Quantitative measurement (protein-to-creatinine ratio or albumin-to-creatinine ratio)
5. Special considerations for screening in adults and children, including children with diabetes

Markers of Chronic Kidney Disease Other than Proteinuria

1. Urine sediment examination
2. Dipstick for red blood cells and white blood cells
3. Imaging studies
4. Urinary markers (considered but not recommended)

Association of Level of GFR with Hypertension

1. Blood pressure monitoring
2. Treatment of high blood pressure including specification of target blood pressure levels, nonpharmacologic therapy, and specific antihypertensive agents for the prevention of progression of kidney disease and development of cardiovascular disease

Association of Level of GFR with Anemia

1. Measurement of hemoglobin level
2. Evaluation and treatment of anemia

Association of Level of GFR with Nutritional Status

1. Assessment of dietary protein and energy intake and nutritional status
2. Dietary modification, counseling and education, or specialized nutrition therapy

Bone Disease and Disorders of Calcium and Phosphorus Metabolism

1. Evaluation and treatment according to forthcoming K/DOQI guidelines

Neuropathy

1. Assessment for central and peripheral neurologic involvement (signs and symptoms)
2. Specialized laboratory testing

Association of Level of GFR with Indices of Functioning and Well-being

1. Assessment for impairment of functioning and well-being
2. Assessment of effects of interventions

Factors Associated with Loss of Kidney Function in Chronic Kidney Disease

1. Assessment and estimation of rate of GFR decline
2. Interventions to slow the progression including strict glucose control in diabetes, strict blood pressure control, angiotensin-converting enzyme (ACE) inhibition or angiotensin-2 receptor blockade, dietary protein restriction, lipid-lowering therapy, and partial correction of anemia
3. Prevention and/or correction of acute decline of GFR by prevention of frequent causes such as volume depletion, intravenous radiographic contrast, selected nephrotoxic medications, and obstruction of the urinary tract.
4. Serum creatinine measurements at least yearly

Association of Chronic Kidney Disease with Diabetic Complications

1. Prevention, detection, evaluation, and treatment according to published guidelines
2. Angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers
3. Application of published guidelines

Association of Chronic Kidney Disease with Cardiovascular Disease

1. Assessment of cardiovascular disease risk factors
2. Cardiovascular risk factor reduction

MAJOR OUTCOMES CONSIDERED

- Incidence and prevalence of earlier stage and end-stage kidney disease
- Sensitivity and specificity of clinical markers for kidney damage
- Accuracy of different estimates of glomerular filtration rate (GFR)
- Glomerular filtration rate
- Loss of kidney function
- Disease progression
- Adverse outcomes of kidney disease (kidney failure, cardiovascular disease, premature death)
- Predictive value of high blood pressure, anemia, malnutrition, bone disease, and neuropathy for kidney disease

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The Work Group and Evidence Review Team decided in advance that a systematic process would be followed to obtain information on topics that relied on primary articles. In general, only full journal articles of original data were included. Review articles, editorials, letters, or abstracts were not included (except as noted). Though reports of formal studies were preferred, case series were also included. No systematic process was followed to obtain textbooks and review articles.

Studies for the literature review were identified primarily through Medline searches of English language literature conducted between February and June 2000. These searches were supplemented by relevant articles known to the domain experts and reviewers.

The Medline literature searches were conducted to identify clinical studies published from 1966 through the search dates. Separate search strategies were developed for each topic. Development of the search strategies was an iterative process that included input from all members of the Work Group. Search strategies were designed to yield approximately 1,000 to 2,000 titles each. The text words or MeSH headings for all topics included kidney or kidney diseases or kidney function tests. The searches were limited to studies on humans and published in English and focused on either adults or children, as relevant. In general, studies that focused on hemodialysis or peritoneal dialysis were excluded. The Medline search strategies are included in the Evidence Report.

Medline search results were screened by clinicians on the Evidence Review Team. Potential papers for retrieval were identified from printed abstracts and titles, based on study population, relevance to topic, and article type. In general, studies with fewer than 10 subjects were not included (except as noted). After retrieval, each paper was screened to verify relevance and appropriateness for review, based primarily on study design and ascertainment of necessary variables. Some

articles were relevant to two or more topics. A goal was set of approximately 30 articles per topic. In many cases, the goal was exceeded. Domain experts made the final decision for inclusion or exclusion of articles. All articles included were abstracted and contained in the evidence tables. Table 154 in the original guideline document details the literature search and review for each topic.

NUMBER OF SOURCE DOCUMENTS

Abstracts screened = 18,153

Articles reviewed = 1,110

Formal structured review of content and methodology = 367

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

S – Analysis of individual patient data from a single large, generalizable study of high methodological quality (for example, Third National Health and Nutrition Examination Survey [NHANES III])

C – Compilation of original articles (evidence tables)

R – Review of reviews and selected original articles

O – Opinion

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Data Extraction and Construction of Evidence tables

Data extraction forms were designed to capture information on various aspects of the primary articles. Forms for all topics included study setting and demographics, eligibility criteria, causes of kidney disease, numbers of subjects, study design, study funding source, population category, study quality (based on criteria appropriate for each study design), appropriate selection and definition of measures, results, and sections for comments and assessment of biases.

The various steps involved in development of the guideline statements, rationale statements, tables, and data extraction forms were piloted on one of the topics (bone disease) with a Work Group member at New England Medical Center. The

"in-person" pilot experience allowed more efficient development and refinement of subsequent forms with Work Group members located at other institutions. It also provided experience in the steps necessary for training junior members of the Evidence Review Team to develop forms and to efficiently extract relevant information from primary articles. Training of the Work Group members to extract data from primary articles subsequently occurred by e-mail as well as at meetings.

Two types of evidence tables were prepared. Detailed tables contain data from each field of the components of the data extraction forms. These tables are contained in the evidence report but are not included in the manuscript. Summary tables describe the strength of evidence according to four dimensions: study size, applicability depending on the type of study subjects, results, and methodological quality. Within each table, studies are ordered first by methodological quality (best to worst), then by applicability (most to least), and then by study size (largest to smallest).

Applicability

Applicability (also known as generalizability or external validity) addresses the issue of whether the study population is sufficiently broad so that the results can be generalized to the population of interest at large. The study population is typically defined by the inclusion and exclusion criteria. The target population was defined to include patients with chronic kidney disease and those at increased risk of chronic kidney disease, except where noted. A designation for applicability was assigned to each article, according to a three-level scale. In making this assessment, sociodemographic characteristics were considered, as were the stated causes of chronic kidney disease and prior treatments.

Glomerular Filtration Rate (GFR) Range

For all studies, the range of GFR (or creatinine clearance [CCr]) is represented graphically when available. The mean or median GFR is represented by a vertical line, with a horizontal bar showing a range that includes approximately 95% of study participants. Studies without a vertical or horizontal line did not provide data on the mean/median or range, respectively. When GFR or creatinine clearance measurements are not available, serum creatinine levels are listed as text.

Results

Results are represented by prevalence levels, proportions (percents) for categorical variables, mean levels for continuous variables, and associations between study measures. Symbols indicate the type and significance of associations between study measures:

The specific meanings of these symbols are explained in the footnotes of tables where they appear in the original guideline. Some informative studies reported only single point estimates of study measures (e.g., mean data) rather than associations. Where data on associations were limited, evidence tables provide these point estimates. Studies that provide data on associations and studies that

provide only point estimates are listed and ranked separately, with shading used to distinguish them.

Quality

Methodological quality (or internal validity) refers to the design, conduct, and reporting of the clinical study. Because studies with a variety of types of design were evaluated, a three level classification of study quality was devised: least bias (results are valid); susceptible to some bias, but not to invalidate the results; and significant bias that may invalidate the results.

Strength of Evidence

Each rationale statement has been graded according the level of evidence on which it is based.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

A state-of-the-art evidence-based approach is used for the development of each of the Kidney Disease Outcomes Quality Initiative (K/DOQI) guideline components. To ensure methodologic rigor, an independent consultant is used to conduct an exhaustive literature search to uncover current medical opinion. The resulting evidence report is then submitted to the multidisciplinary Work Group for critical appraisal and grading. Based on the consensus of the Work Group, a set of guidelines are developed to address areas supported by key findings in the evidence report.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guideline was subjected to a three-stage review process.

Stage One: Internal Review

The proposed guidelines are reviewed by the Kidney Disease Outcomes Quality Initiative (K/DOQI) Advisory Board, Kidney Disease Outcomes Quality Initiative Support Group, and various National Kidney Foundation Committees.

Stage Two: Organizational Review

The proposed guidelines are submitted for comment to individuals designated by key allied health professional associations and organizations involved in the care of patients with kidney disease.

Stage Three: Open Review

The guidelines are made available to the public for comment.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Excerpted by the National Guideline Clearinghouse™ (NGC™):

Guideline 1. Definition and Stages of Chronic Kidney Disease

Adverse outcomes of chronic kidney disease can often be prevented or delayed through early detection and treatment. Earlier stages of chronic kidney disease can be detected through routine laboratory measurements.

- The presence of chronic kidney disease should be established, based on presence of kidney damage and level of kidney function (glomerular filtration rate [GFR]), irrespective of diagnosis.
- Among patients with chronic kidney disease, the stage of disease should be assigned based on the level of kidney function, irrespective of diagnosis, according to the Kidney Disease Outcomes Quality Initiative Chronic Kidney Disease (K/DOQI CKD) classification:

Stages of Kidney Disease

Stage 1 - Kidney damage with normal or increased GFR, $GFR \geq 90$ mL/min/1.73 m²

Stage 2 - Kidney damage with mild decrease in GFR, $GFR = 60-89$ mL/min/1.73 m²

Stage 3 - Moderate decrease in GFR, $GFR = 30-59$ mL/min/1.73 m²

Stage 4 - Severe decrease in GFR, $GFR = 15-29$ mL/min/1.73 m²

Stage 5 - Kidney failure, $GFR < 15$ mL/min/1.73 m² or dialysis

Note: Chronic kidney disease is defined as either kidney damage or GFR <60 mL/min/1.73 m² for ≥3 months. Kidney damage is defined as pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.

Guideline 2. Evaluation and Treatment

The evaluation and treatment of patients with chronic kidney disease requires understanding of separate but related concepts of diagnosis, comorbid conditions, severity of disease, complications of disease, and risks for loss of kidney function and cardiovascular disease.

- Patients with chronic kidney disease should be evaluated to determine:
 - Diagnosis (type of kidney disease)
 - Comorbid conditions
 - Severity, assessed by level of kidney function
 - Complications, related to level of kidney function
 - Risk for loss of kidney function
 - Risk for cardiovascular disease
- Treatment of chronic kidney disease should include:
 - Specific therapy, based on diagnosis
 - Evaluation and management of comorbid conditions
 - Slowing the loss of kidney function
 - Prevention and treatment of cardiovascular disease
 - Prevention and treatment of complications of decreased kidney function
 - Preparation for kidney failure and kidney replacement therapy
 - Replacement of kidney function by dialysis and transplantation, if signs and symptoms of uremia are present
- A clinical action plan should be developed for each patient, based on the stage of disease as defined by the K/DOQI CKD classification:

Stages of Chronic Kidney Disease: A Clinical Action Plan*

Stage 1 -- Diagnosis and treatment, treatment of comorbid conditions, slowing progression, cardiovascular disease risk reduction

Stage 2 -- Estimating progression

Stage 3 -- Evaluating and treating complications

Stage 4 -- Preparation for kidney replacement therapy

Stage 5 -- Replacement (if uremia present)

*Each action includes actions from preceding stages.

- Review of medications should be performed at all visits for the following:
 - Dosage adjustment based on level of kidney function
 - Detection of potentially adverse effects on kidney function or complications of chronic kidney disease

- Detection of drug interactions
 - Therapeutic drug monitoring, if possible
- Self-management behaviors should be incorporated into the treatment plan at all stages of chronic kidney disease.
- Patients with chronic kidney disease should be referred to a specialist for consultation and co-management if the clinical action plan cannot be prepared, the prescribed evaluation of the patient cannot be carried out, or the recommended treatment cannot be carried out. In general, patients with GFR <30 mL/min/ 1.73 m² should be referred to a nephrologist.

Guideline 3. Individuals at Increased Risk of Chronic Kidney Disease

Some individuals without kidney damage and with normal or elevated GFR are at increased risk for development of chronic kidney disease.

- All individuals should be assessed, as part of routine health encounters, to determine whether they are at increased risk of developing chronic kidney disease, based on clinical and sociodemographic factors.
- Individuals at increased risk of developing chronic kidney disease should undergo testing for markers of kidney damage and to estimate the level of GFR.
- Individuals found to have chronic kidney disease should be evaluated and treated as specified in Guideline 2.
- Individuals at increased risk, but found not to have chronic kidney disease, should be advised to follow a program of risk factor reduction, if appropriate, and undergo repeat periodic evaluation.

Guideline 4. Estimation of GFR

Estimates of GFR are the best overall indices of the level of kidney function.

- The level of GFR should be estimated from prediction equations that take into account the serum creatinine concentration and some or all of the following variables: age, gender, race and body size. The following equations provide useful estimates of GFR:
 - In adults, the Modification of Diet in Renal Disease (MDRD) Study and Cockcroft-Gault equations;
 - In children, the Schwartz and Counahan-Barratt equations.
- The serum creatinine concentration alone should not be used to assess the level of kidney function.
- Clinical laboratories should report an estimate of GFR using a prediction equation, in addition to reporting the serum creatinine measurement.
- Autoanalyzer manufacturers and clinical laboratories should calibrate serum creatinine assays using an international standard.
- Measurement of creatinine clearance using timed (for example, 24-hour) urine collections does not improve the estimate of GFR over that provided by prediction equations. A 24-hour urine sample provides useful information for:
 - Estimation of GFR in individuals with exceptional dietary intake (vegetarian diet, creatinine supplements) or muscle mass (amputation, malnutrition, muscle wasting)
 - Assessment of diet and nutritional status
 - Need to start dialysis

Guideline 5. Assessment of Proteinuria

Normal individuals usually excrete very small amounts of protein in the urine. Persistently increased protein excretion is usually a marker of kidney damage. The excretion of specific types of protein, such as albumin or low molecular weight globulins, depends on the type of kidney disease that is present. Increased excretion of albumin is a sensitive marker for chronic kidney disease due to diabetes, glomerular disease, and hypertension. Increased excretion of low molecular weight globulins is a sensitive marker for some types of tubulointerstitial disease. In this guideline, the term "proteinuria" refers to increased urinary excretion of albumin, other specific proteins, or total protein; "albuminuria" refers specifically to increased urinary excretion of albumin. "Microalbuminuria" refers to albumin excretion above the normal range but below the level of detection by tests for total protein. Guidelines for detection and monitoring of proteinuria in adults and children differ because of differences in the prevalence and type of chronic kidney disease.

Guidelines for Adults and Children:

- Under most circumstances, untimed ("spot") urine samples should be used to detect and monitor proteinuria in children and adults.
- It is usually not necessary to obtain a timed urine collection (overnight or 24-hour) for these evaluations in either children or adults.
- First morning specimens are preferred, but random specimens are acceptable if first morning specimens are not available.
- In most cases, screening with urine dipsticks is acceptable for detecting proteinuria:
 - Standard urine dipsticks are acceptable for detecting increased total urine protein.
 - Albumin-specific dipsticks are acceptable for detecting albuminuria.
- Patients with a positive dipstick test (1+ or greater) should undergo confirmation of proteinuria by a quantitative measurement (protein-to-creatinine ratio or albumin-to-creatinine ratio) within 3 months.
- Patients with two or more positive quantitative tests temporally spaced by 1 to 2 weeks should be diagnosed as having persistent proteinuria and undergo further evaluation and management for chronic kidney disease as stated in Guideline 2.
- Monitoring proteinuria in patients with chronic kidney disease should be performed using quantitative measurements.

Specific Guidelines for Adults:

- When screening adults at increased risk for chronic kidney disease, albumin should be measured in a spot urine sample using either:
 - Albumin-specific dipstick
 - Albumin-to-creatinine ratio
- When monitoring proteinuria in adults with chronic kidney disease, the protein-to-creatinine ratio in spot urine samples should be measured using:
 - Albumin-to-creatinine ratio
 - Total protein-to-creatinine ratio is acceptable if albumin-to-creatinine ratio is high (>500 to 1,000 mg/g)

Specific Guidelines for Children Without Diabetes:

- When screening children for chronic kidney disease, total urine protein should be measured in a spot urine sample using either:
 - Standard urine dipstick
 - Total protein-to-creatinine ratio
- Orthostatic proteinuria must be excluded by repeat measurement on a first morning specimen if the initial finding of proteinuria was obtained on a random specimen.
- When monitoring proteinuria in children with chronic kidney disease, the total protein- to-creatinine ratio should be measured in spot urine specimens.

Specific Guidelines for Children With Diabetes:

- Screening and monitoring of post-pubertal children with diabetes of 5 or more years of duration should follow the guidelines for adults.
- Screening and monitoring other children with diabetes should follow the guidelines for children without diabetes.

Guideline 6. Markers of Chronic Kidney Disease Other Than Proteinuria

Markers of kidney damage in addition to proteinuria include abnormalities in the urine sediment and abnormalities on imaging studies. Constellations of markers define clinical presentations for some types of chronic kidney disease. New markers are needed to detect kidney damage that occurs prior to a reduction in GFR in other types of chronic kidney diseases.

- Urine sediment examination or dipstick for red blood cells and white blood cells should be performed in patients with chronic kidney disease and in individuals at increased risk of developing chronic kidney disease.
- Imaging studies of the kidneys should be performed in patients with chronic kidney disease and in selected individuals at increased risk of developing chronic kidney disease.
- Although several novel urinary markers (such as tubular or low-molecular weight proteins and specific mononuclear cells) show promise of future utility, they should not be used for clinical decision-making at present.

Guideline 7. Association of Level of GFR With Hypertension

High blood pressure is both a cause and a complication of chronic kidney disease. As a complication, high blood pressure may develop early during the course of chronic kidney disease and is associated with adverse outcomes—in particular, faster loss of kidney function and development of cardiovascular disease.

- Blood pressure should be closely monitored in all patients with chronic kidney disease.
- Treatment of high blood pressure in chronic kidney disease should include specification of target blood pressure levels, nonpharmacologic therapy, and specific antihypertensive agents for the prevention of progression of kidney disease (see Guideline 13) and development of cardiovascular disease (see Guideline 15).

Guideline 8. Association of Level of GFR With Anemia

Anemia usually develops during the course of chronic kidney disease and may be associated with adverse outcomes.

- Patients with GFR <60 mL/min/1.73 m² should be evaluated for anemia. The evaluation should include measurement of hemoglobin level.
- Anemia in chronic kidney disease should be evaluated and treated (see the National Guideline Clearinghouse [NGC] summary of the K/DOQI [NKF-K/DOQI clinical practice guidelines for anemia of chronic kidney disease: update 2000, Guidelines 1-4](#)).

Guideline 9. Association of Level of GFR With Nutritional Status

Protein energy malnutrition develops during the course of chronic kidney disease and is associated with adverse outcomes. Low protein and calorie intake is an important cause of malnutrition in chronic kidney disease.

- Patients with GFR <60 mL/min/1.73 m² should undergo assessment of dietary protein and energy intake and nutritional status (see the National Guideline Clearinghouse [NGC] summary of the K/DOQI [Clinical Practice Guidelines for Nutrition in Chronic Renal Failure, Guidelines 23 and 26](#)).
- Patients with decreased dietary intake or malnutrition should undergo dietary modification, counseling and education, or specialized nutrition therapy (see the National Guideline Clearinghouse [NGC] summary of the K/DOQI [Clinical Practice Guidelines for Nutrition in Chronic Renal Failure, Guidelines 24 and 25](#)).

Guideline 10. Bone Disease and Disorders of Calcium and Phosphorus Metabolism

Bone disease and disorders of calcium and phosphorus metabolism develop during the course of chronic kidney disease and are associated with adverse outcomes.

- Patients with GFR <60 mL/min/1.73 m² should be evaluated for bone disease and disorders of calcium and phosphorus metabolism.
- Patients with bone disease and disorders of bone metabolism should be evaluated and treated (see forthcoming K/DOQI Clinical Practice Guidelines on Bone Metabolism and Disease in Chronic Kidney Disease).

Guideline 11. Neuropathy

Neuropathy develops during the course of chronic kidney disease and may become symptomatic.

- Patients with chronic kidney disease should be periodically assessed for central and peripheral neurologic involvement by eliciting symptoms and signs during routine office visits or exams.
- Specialized laboratory testing for neuropathy in patients with chronic kidney disease is indicated only in the presence of symptoms.

Guideline 12. Association of Level of GFR With Indices of Functioning and Well-Being

Impairments in domains of functioning and well-being develop during the course of chronic kidney disease and are associated with adverse outcomes. Impaired functioning and well-being may be related to sociodemographic factors, conditions causing chronic kidney disease, complications of kidney disease, or possibly directly due to reduced GFR.

- Patients with GFR <60 mL/min/1.73 m² should undergo regular assessment for impairment of functioning and well-being:
 - To establish a baseline and monitor changes in functioning and well-being over time;
 - To assess the effect of interventions on functioning and well-being.

Guideline 13. Factors Associated With Loss of Kidney Function in Chronic Kidney Disease

The level of kidney function tends to decline progressively over time in most patients with chronic kidney diseases.

- The rate of GFR decline should be assessed in patients with chronic kidney disease to:
 - Predict the interval until the onset of kidney failure
 - Assess the effect of interventions to slow the GFR decline
- Among patients with chronic kidney disease, the rate of GFR decline should be estimated by:
 - Computing the GFR decline from past and ongoing measurements of serum creatinine
 - Ascertaining risk factors for faster versus slower GFR decline, including type (diagnosis) of kidney disease and nonmodifiable and modifiable factors
- Interventions to slow the progression of kidney disease should be considered in all patients with chronic kidney disease.
 - Interventions that have been proven to be effective include:
 - (1) Strict glucose control in diabetes
 - (2) Strict blood pressure control
 - (3) Angiotensin-converting enzyme inhibition or angiotensin-2 receptor blockade
 - Interventions that have been studied, but the results of which are inconclusive, include:
 - (1) Dietary protein restriction
 - (2) Lipid-lowering therapy
 - (3) Partial correction of anemia
- Attempts should be made to prevent and correct acute decline in GFR. Frequent causes of acute decline in GFR include:
 - Volume depletion
 - Intravenous radiographic contrast
 - Selected antimicrobial agents (for example, aminoglycosides and amphotericin B)

- Nonsteroidal anti-inflammatory agents; including cyclo-oxygenase type 2 inhibitors
- Angiotensin-converting enzyme inhibition and angiotensin-2 receptor blockers
- Cyclosporine and tacrolimus
- Obstruction of the urinary tract
- Measurements of serum creatinine for estimation of GFR should be obtained at least yearly in patients with chronic kidney disease and more often in patients with:
 - GFR <60 mL/min/1.73 m²
 - Fast GFR decline in the past ≥ 4 mL/min/1.73 m² per year)
 - Risk factors for faster progression
 - Ongoing treatment to slow progression
 - Exposure to risk factors for acute GFR decline

Guideline 14. Association of Chronic Kidney Disease With Diabetic Complications

The risk of cardiovascular disease, retinopathy, and other diabetic complications is higher in patients with diabetic kidney disease than in diabetic patients without kidney disease.

- Prevention, detection, evaluation, and treatment of diabetic complications in patients with chronic kidney disease should follow published guidelines and position statements.
- Guidelines regarding angiotensin-converting enzyme inhibitors or angiotensin receptor blockers and strict blood pressure control are particularly important since these agents may prevent or delay some of the adverse outcomes of both kidney and cardiovascular disease.
- Application of published guidelines to diabetic patients with chronic kidney disease should take into account their "higher risk" status for diabetic complications.

Guideline 15. Association of Chronic Kidney Disease With Cardiovascular Disease

Patients with chronic kidney disease, irrespective of diagnosis, are at increased risk of cardiovascular disease (CVD), including coronary heart disease, cerebrovascular disease, peripheral vascular disease, and heart failure. Both "traditional" and "chronic kidney disease related (nontraditional)" CVD risk factors may contribute to this increased risk.

- All patients with chronic kidney disease should be considered in the "highest risk" group for CVD, irrespective of levels of traditional CVD risk factors.
- All patients with chronic kidney disease should undergo assessment of CVD risk factors, including:
 - Measurement of "traditional" CVD risk factors in all patients
 - Individual decision-making regarding measurement of selected "CVD-related" CVD risk factors in some patients
- Recommendations for CVD risk factor reduction should take into account the "highest-risk" status of patients with chronic kidney disease.

CLINICAL ALGORITHM(S)

The following algorithms are provided in the original guideline document:

- Anemia work-up for patients with chronic kidney disease
- Evaluation of proteinuria in patients not known to have kidney disease

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

These guidelines are based on a systematic review of the literature and the consensus of the Work Group.

The original guideline document contains 15 guidelines. The rationale for each guideline contains definitions and classifications of markers of disease (if appropriate) followed by a series of specific "rationale statements", each supported by evidence. Each rationale statement has been graded according to the level of evidence on which it is based. Table 8 of the original guideline document summarizes the method of evidence review and types of studies used for the various sections of the guideline.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Prevention of the loss of kidney function
- Slow the progression of disease
- Amelioration of organ dysfunction and comorbid conditions in those who progress to kidney failure and end stage renal disease
- Prevention or delay of adverse outcomes of chronic kidney disease such as kidney failure, cardiovascular disease, and premature death
- Initiation of treatment for cardiovascular risk factors at earlier stages of chronic kidney disease should be effective in reducing cardiovascular disease events both before and after the onset of kidney failure.
- Uniform definitions of terms and stages would improve communication between patients and providers, enhance public education, and promote dissemination of research results. In addition, it was believed that uniform definitions would enhance conduct of clinical research.
- Expressing the level of kidney function on a continuous scale allows development of patient and public education programs that encourage individuals to "know your numbers".
- Replacement therapy (dialysis and transplantation) is effective in improving the most serious features of uremia, irrespective of the type of chronic kidney disease.
- In addition to lowering systemic blood pressure, angiotensin-converting enzyme inhibitors and angiotensin receptor antagonists also lower glomerular capillary blood pressure and protein filtration, which may contribute to their beneficial effect in slowing progression. They may also have a beneficial effect in reducing angiotensin II mediated cell proliferation and fibrosis.

Subgroups Most Likely to Benefit:

Those at greatest risk for chronic kidney diseases, i.e., individuals with diabetes, hypertension, autoimmune diseases, systemic infections, exposure to drugs or procedures associated with acute decline in kidney function, recovery from acute kidney failure, age > 60 years, family history of kidney disease, reduced kidney mass (includes kidney donors and transplant recipients).

POTENTIAL HARMS

- Imaging studies employing iodinated contrast agents can cause acute kidney damage and may present significant risks to some patients with decreased kidney function.
- Angiotensin-converting enzyme (ACE) inhibitors may exacerbate hyperkalemia in patients with advanced renal insufficiency and/or hyporeninemic hypoaldosteronism. In older patients with bilateral renal artery stenosis and in patients with advanced renal disease even without renal artery stenosis, angiotensin-converting enzyme inhibitors may cause a rapid decline in renal function. Cough may also occur.

CONTRAINDICATIONS

CONTRAINDICATIONS

Angiotensin-converting enzyme (ACE) inhibitors are contraindicated in pregnancy and therefore should be used with caution in women of childbearing potential.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- These guidelines are based upon the best information available at the time of publication. They are designed to provide information and assist decision-making. They are not intended to define a standard of care, and should not be construed as doing so. Neither should they be interpreted as prescribing an exclusive course of management.

Variations in practice will inevitably and appropriately occur when clinicians take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every healthcare professional making use of these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation.

The recommendations for research contained within this document are general and not meant to imply a specific protocol.

- The Work Group did not specifically address evaluation and treatment for chronic kidney disease. However, this guideline contains brief reference to diagnosis and clinical interventions and can serve as a "road map", linking

other clinical practice guidelines and pointing out where other guidelines need to be developed. Eventually, Kidney Disease Outcomes Quality Initiative will include interventional guidelines. The first three of these, on bone disease, dyslipidemia, and blood pressure management are currently under development. Other guidelines on cardiovascular disease in dialysis patients and kidney biopsy will be initiated in the Winter of 2001.

- Participation in the review does not necessarily constitute endorsement of the content of the report by the individuals or the organization or institute they represent.
- Limitations of literature searches. While the literature searches were intended to be comprehensive, they were not exhaustive. Medline was the only database searched, and searches were limited to English language publications. Hand searches of journals were not performed, and review articles and textbook chapters were not systematically searched. In addition, search strategies were generally restricted to yield a maximum of about 2,000 titles each. This approach required the exclusion of some topics from searches. However, important studies known to the domain experts that were missed by the literature search were included in the review. In addition, essential studies identified during the review process were also included.

Exhaustive literature searches were hampered by limitations in available time and resources that were judged appropriate for the task. The search strategies required to capture every article that may have had data on each of the questions frequently yielded upwards of 10,000 articles. The difficulty of finding all potentially relevant studies was compounded by the fact that in many studies, the information of interest for this report was a secondary finding for the original studies.

Due to the wide variety of methods of analysis, units of measurements, definitions of chronic kidney disease, and methods of reporting in the original studies, it was often very difficult to standardize the findings for this report.

- Limitations of Evidence Review. The original guideline presents a discussion of limitations of the evidence review pertinent to each guideline topic.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The translation of clinical practice guidelines into clinical practice requires the development of a multi-component long-term implementation plan. A central component of such a plan is the linkage of selected guidelines to continuous quality improvement (CQI) programs to improve outcomes within a given local health care delivery system.

Continuous quality improvement efforts require measurement tools, both to quantify the current process of care and to monitor the success of changing practice patterns on clinical outcomes. Clinical performance measures (CPMs) are such tools. The rationale for CPMs, the essential steps in their development, and the attributes of well-designed CPMs have been described.

The first step in the development of CPMs is the prioritization of clinical practice guidelines, in collaboration with the Work Group that developed the guidelines. Following are guideline statements recommended by the Chronic Kidney Disease Work Group for potential use in continuous quality improvement and clinical performance measures and examples of clinical performance measures that could be developed from them:

Guideline 2

Preparation for kidney replacement therapy (dialysis and transplantation), as well as vascular access care, should be initiated when the estimated glomerular filtration rate (GFR) declines to $< 30 \text{ mL/min/1.73 m}^2$.

Guideline 3

Individuals at increased risk for chronic kidney disease should be tested at the time of a health evaluation to determine if they have chronic kidney disease. These include individuals with diabetes, hypertension, autoimmune diseases, systemic infections, exposure to drugs or procedures associated with acute decline in kidney function, recovery from acute kidney failure, age > 60 years, family history of kidney disease, reduced kidney mass (includes kidney donors and transplant recipients).

Measurements should include serum creatinine for estimation of GFR, assessment of proteinuria, urinary sediment or urine dipstick for red blood cells and white blood cells.

Guideline 4

Estimated GFR should be the parameter used to evaluate the level of kidney function.

Guideline 5

The ratio of protein or albumin to creatinine in spot urine samples should be monitored in all patients with chronic kidney disease.

Guideline 7

Blood pressure should be monitored in all patients with chronic kidney disease.

High blood pressure should be evaluated and treated according to established guidelines, such as the sixth Report of the Joint National Committee for the Prevention, Evaluation, Detection and Treatment of High Blood Pressure (JNC-VI) and the American Diabetes Association (ADA).

Guidelines 8-12

Patients with $\text{GFR} < 60 \text{ mL/min/1.73 m}^2$ should be evaluated and treated for complications of decreased GFR. This includes measurement of: anemia (hemoglobin); nutritional status (dietary energy and protein intake, weight, serum

albumin, serum total cholesterol); bone disease (parathyroid hormone, calcium, phosphorus); functioning and well-being (questionnaires).

Guideline 13

Estimated GFR should be monitored yearly in patients with chronic kidney disease, and more frequently in patients with GFR <60 mL/min/1.73 m², fast GFR decline in the past (4 mL/min/1.73 m²), risk factors for faster progression, ongoing treatment to slow progression, exposure to risk factors for acute GFR decline.

Guideline 14

Individuals with diabetic kidney disease are at higher risk of diabetic complications, including retinopathy, cardiovascular disease, and neuropathy.

They should be evaluated and managed according to established guidelines.

Guideline 15

Individuals with chronic kidney disease are at increased risk of cardiovascular disease.

They should be considered in the "highest risk group" for evaluation and management according to established guidelines.

Implementation Issues for All Guidelines

Implementation issues, including administrative and regulatory issues and barriers to implementation, for individual guidelines are discussed in detail in the original guideline document.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Kidney Disease Outcome Quality Initiative. Am J Kidney Dis 2002 Feb;39(2 Suppl 1):S1-246. [667 references] [PubMed](#)

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2002 Feb

GUIDELINE DEVELOPER(S)

National Kidney Foundation - Disease Specific Society

SOURCE(S) OF FUNDING

National Kidney Foundation

GUIDELINE COMMITTEE

NKF-K/DOQI (National Kidney Foundation-Kidney Disease Outcomes Quality Initiative) Chronic Kidney Disease Work Group

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All work group members completed a disclosure statement certifying that any potential conflict of interest would not influence their judgment or actions concerning the Kidney Disease Outcomes Quality Initiative (K/DOQI).

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Talat Alp Ikizler, MD, is the recipient of several grant (federal and pharmaceutical) awards.

Annamaria Kausz, MD, MS, serves on the Medical Advisory Board of Amgen Inc.

Paul L. Kimmel, MD, has received several grants from the National Kidney Foundation and National Institutes of Health.

Adeera Levin, MD, FRCPC, serves on the Medical Advisory Board for Amgen Canada, Amgen USA, Janssen Cilag International, Ortho Biotech Inc, Canada, and Roche International. She has received grants from the Kidney Foundation of Canada to study comorbidities associated with chronic kidney disease and, more recently, to study the variability in the care delivered across Canada to patients with CKD. She has also received grants from BC Health Research Foundation, BC Transplant Foundation, Janssen Cilag international, Ortho Biotech, Amgen, and Genzyme Inc.

Kenneth Lloyd Minaker, MD, FRCP(C), CSC(GM), UE, has received research funds from Accor Inc. for health promotion research and from BioNebraska Inc. for his work on GHRH and GLP-1.

Michael Steffes, MD, PhD, has reported receiving several grants to conduct research on diabetes, its complications, and macrovascular disease.

Pediatric Work Group

Ronald J. Hogg, MD, has reported receiving research grants from Astra Zeneca, Merck, Novartis, Parke-Davis, and Pfizer.

Kevin V. Lemley, MD, PhD, served on the National Kidney Foundation's PARADE (Proteinuria, Albuminuria, Risk, Assessment, Detection, and Elimination) Initiative Committee and consults for Fibrogen, Inc.

Ronald J. Portman, MD, reports research grants from AstraZenica, Pfizer, and Novartis.

GUIDELINE STATUS

This is the current release of the guideline.

An update is not in progress at this time.

GUIDELINE AVAILABILITY

Electronic copies: Available from the [National Kidney Foundation \(NKF\) Web site](#).

Print copies: Available from NKF, 30 East 33rd St., New York, NY 10016. These guidelines are also available on CD-ROM from NKF.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification. Executive summary. New York (NY): National Kidney Foundation (NKF), 2002. Electronic copies available from the [National Kidney Foundation \(NKF\) Web site](#).
- Guideline development and methodology. New York (NY): National Kidney Foundation (NKF), 2002. Electronic copies available from the [NKF Web site](#).
- Eknoyan G, Levin NW. Impact of the New K/DOQI Guidelines. *Blood Purif* 2002;20(1):103-8.

Print copies: Available from NKF, 30 East 33rd St., New York, NY 10016.

PATIENT RESOURCES

The following is available:

- Are you at increased risk for chronic kidney disease?. New York (NY): National Kidney Foundation (NKF), 1998. Electronic copies available from the [National Kidney Foundation \(NKF\) Web site](#).
- What you need to know about urinalysis. New York (NY): National Kidney Foundation (NKF), 2002. Electronic copies available from the [NKF Web site](#).

Print copies: Available from NKF, 30 East 33rd St., New York, NY 10016.

The following is also available:

- About chronic kidney disease: A guide for patients and their families. New York (NY): National Kidney Foundation (NKF), 2002.

Print copies: Available from NKF, 30 East 33rd St., New York, NY 10016.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI on September 17, 2002. This summary was verified by the guideline developer on November 5, 2002.

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