KDIGO Guidelines on CKD Evaluation and Management

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Goals of Presentation

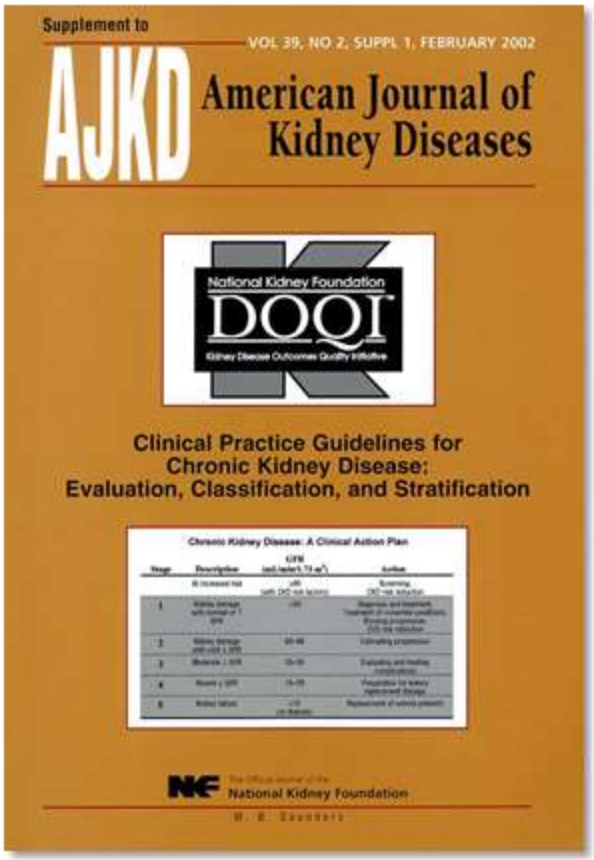
- Clarify the definition and classification system of CKD (KDIGO 2012)
- Provide guidance to improve the diagnosis, evaluation, and classification of CKD worldwide

Outline

- Background
- Definition of chronic kidney disease (CKD)
- Classification of CKD
- Evaluation of CKD
- Risk stratification
- Summary
- Conclusion

BACKGROUND

KDOQI CKD Evaluation, Classification and Stratification (2002)



- Defined 2 independent criteria for CKD:
  - Glomerular filtration rate (GFR) <60 ml/min per 1.73 m^2 for ≥3 months
  - Presence of kidney damage [structural, functional, or pathological abnormality; markers (e.g., albuminuria)] for ≥3 months
- Classified CKD by severity according to GFR
- Provided a common language for kidney disease that would:
  - Facilitate new research
  - Provide clinicians with a stage-specific clinical action plan
  - Provide a framework for developing a public health approach toward resolution

KDOQI CKD Classification (2002)

Endorsed by KDIGO (Kidney Disease: Improving Global Outcomes) with minimal modifications in 2004

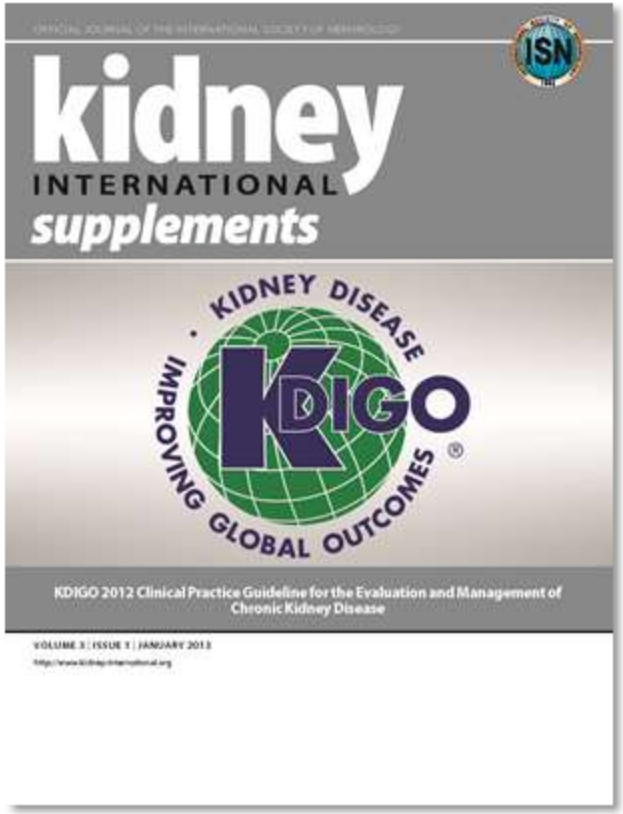
Concerns with KDOQI Definition and Classification (2002)

- New information on albuminuria and GFR and their association with mortality has emerged since publication of the KDOQI CKD definition and staging

- Increased recognition of limitations of the KDOQI CKD definition and classification initiated debate that:
  - Reflects changing knowledge
  - Provides opportunities for improvement

KDIGO 2012 CPG for Evaluation and Management of Chronic Kidney Disease*

- Serves to update the 2002 KDOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification and Stratification
- Follows a decade of focused research and clinical practice in CKD



*Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney inter., Suppl.* 2013; 3: 1-150.

Definition and classification of CKD

Definition of CKD

CKD is defined as:

- Abnormalities of kidney structure or function, present for >3 months, with implications for health

How does the definition compare with 2002 KDOQI?

- Definition remains intact but includes "with implications for health"
  - Reflects notion that a variety of abnormalities of kidney structure or function may exist, but not all have implications for health of individuals, and therefore need to be contextualized

Criteria for CKD

Either of the following present for >3 months

- Markers of kidney damage (one or more)
- Decreased GFR (GFR <60 ml/min/1.73 m^2)

Duration >3 months, based on documentation or inference

- Duration is necessary to distinguish chronic from acute kidney disease
- Clinical evaluation will often enable documentation or inference of duration
- Documentation of duration is usually not declared in epidemiologic studies

Criteria for CKD

Markers of kidney damage (one or more)

- Albuminuria (albumin-to-creatinine ratio ≥30 mg/g; ≥3 mg/mmol)
- Urine sediment abnormalities
- Electrolyte and other abnormalities due to tubular disorders
- Pathological abnormalities detected by histology or inferred
- Structural abnormalities detected by imaging
- History of kidney transplantation

Criteria for CKD

Decreased glomerular filtration rate (GFR) <60 ml/min/1.73 m^2

- GFR is the best overall index of kidney function in health and disease
- The normal GFR in young adults is approximately 125 ml/min/1.73 m^2
- GFR <15 ml/min/1.73 m^2 is defined as kidney failure
- Can be detected by current estimating equations for GFR based on serum creatinine or cystatin C (estimated GFR) *but not by serum creatinine or cystatin C alone*
- Decreased eGFR can be confirmed by measured GFR, if required

Criteria for CKD

Implications for Health

- CKD is associated with a wide range of complications
- Recent epidemiologic studies have linked decreased GFR and albuminuria to the risk of adverse health outcomes not previously identified as CKD complications

GFR categories (ml/min/ 1.73 m²) Description and range				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
	G1	Normal or high	≥90		Monitor	Refer*
	G2	Mildly decreased	60–89		Monitor	Refer*
	G3a	Mildly to moderately decreased	45–59	Monitor	Monitor	Refer
	G3b	Moderately to severely decreased	30–44	Monitor	Monitor	Refer
	G4	Severely decreased	15–29	Refer*	Refer*	Refer
	G5	Kidney failure	<15	Refer	Refer	Refer

Referral decision making by GFR and albuminuria. *Referring clinicians may wish to discuss with their nephrology service depending on local arrangements regarding monitoring or referring.

Pediatric Considerations

Generally applies to children (birth-18 years) with the following exceptions or allowances:

- Duration >3 months does not apply to newborns or infants ≤3 mo
- Criteria of GFR <60 ml/min/1.73 m^2 does not apply to children <2 years of age in whom an age appropriate value should be applied
- Urinary total protein or albumin excretion rate above the normal value for age may be substituted for albuminuria ≥30 mg/24 hours
- Electrolyte abnormalities are to be defined in light of age normative values

EVALUATION

KDIGO 2012

1.4.3: Evaluation of GFR

1.4.3.1: We recommend using serum creatinine and a GFR estimating equation for initial assessment. (1A)

1.4.3.2: We suggest using additional tests (such as cystatin C or a clearance measurement) for confirmatory testing in specific circumstances when eGFR based on serum creatinine is less accurate. (2B)

1.4.3.3: We recommend that clinicians (1B):

- **use a GFR estimating equation to derive GFR from serum creatinine (eGFRcreat) rather than relying on the serum creatinine concentration alone.**
- **understand clinical settings in which eGFRcreat is less accurate.**

Evaluation of GFR

Sources of Error in GFR Estimating Equations using Creatinine

Source of Error	Example
Non-steady state	• AKI
Non-GFR determinants of SCr that differ from study populations in which equations were developed	

Factors affecting creatinine generation	• Race/ethnicity other than US and European black and white
	• Extremes of muscle mass
	• Extremes of body size
	• Diet and nutritional status
	  • High protein diet
	  • Creatine supplements
	• Muscle wasting diseases
	• Ingestion of cooked meat

Factors affecting tubular secretion of creatinine	• Decrease by drug-induced inhibition
	  • Trimethoprim
	  • Cimetidine
	  • Fenofibrate

Factors affecting extra-renal elimination of creatinine	• Dialysis • Decrease by inhibition of gut creatininase by antibiotics • Increased by large volume losses of extracellular fluid
Higher GFR	Higher biological variability in non-GFR determinants relative to GFR • Higher measurement error in SCr and GFR
Interference with creatinine assay	• Spectral interferences (e.g., bilirubin, some drugs) • Chemical interferences (e.g., glucose, ketones, bilirubin, some drugs)

Abbreviations: AKI, acute kidney injury; GFR, glomerular filtration rate; SCr, serum creatinine.

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Evaluation of GFR

Measure cystatin C in adults with $eGFR_{creat}$ 45-59* who do not have markers of kidney damage if confirmation of CKD is required:

- Use an estimating equation to derive GFR from serum cystatin C rather than relying on cystatin C concentration alone
  - If $eGFR_{cys}$ / $eGFR_{creat\text{-}cys}$ is also <60*, diagnosis of CKD is confirmed
  - If $eGFR_{cys}$ / $eGFR_{creat\text{-}cys}$ ≥60*, diagnosis of CKD is not confirmed
- Understand clinical setting where $eGFR_{cys}$ and $eGFR_{creat\text{-}cys}$ are less accurate

*expressed as ml/min/1.73 m^2

For Labs Reporting eGFR

When measuring serum creatinine:

- Use a specific assay with calibration traceable to the international standard reference materials and minimal bias compared to isotope-dilution mass spectrometry (IDMS) reference methodology
- Report $eGFR_{creat}$ in addition to the serum creatinine and specify the equation used
- Use the 2009 CKD-EPI creatinine equation to report eGFR in adults
  - An alternative creatinine-based equation is acceptable if shown to improve accuracy of GFR estimates compared to the 2009 CKD-EPI creatinine equation

Evaluation of GFR

Measure cystatin C in adults with $eGFR_{creat}$ 45-59* who do not have markers of kidney damage if confirmation of CKD is required:

- Use an estimating equation to derive GFR from serum cystatin C rather than relying on cystatin C concentration alone
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  - If $eGFR_{cys}$ / $eGFR_{creat\text{-}cys}$ ≥60*, diagnosis of CKD is not confirmed
- Understand clinical setting where $eGFR_{cys}$ and $eGFR_{creat\text{-}cys}$ are less accurate

*expressed as ml/min/1.73 m^2

Evaluation of GFR

For initial assessment:

- Use serum creatinine and a GFR estimating equation to derive $eGFR_{creat}$
- Do not rely on serum creatinine concentration alone
- Understand clinical settings in which $eGFR_{creat}$ is less accurate

Confirmatory tests:

- Confirmation may be needed when eGFR based on serum creatinine is thought to be less accurate or when more accurate estimation is required
  - Cystatin C-based equations
  - Clearance measurement

Evaluation of GFR

Measure GFR using an exogenous filtration marker under circumstances where more accurate ascertainment of GFR will impact on treatment decisions

When reporting serum creatinine:

- **We recommend that serum creatinine concentration be reported and rounded to the nearest whole number when expressed as standard international units (lmol/l) and rounded to the nearest 100th of a whole number when expressed as conventional units (mg/dl)**

When reporting eGFRcreat:

- **We recommend that eGFRcreat should be reported and rounded to the nearest whole number and relative to a body surface area of 1.73 m2 in adults using the units ml/min/1.73 m2 . K We recommend eGFRcreat levels less than 60 ml/min/1.73 m2 should be reported as ‘‘decreased.’’**

1.4.3.4: We recommend that clinical laboratories should (1B):

- **measure serum creatinine using a specific assay with calibration traceable to the international standard reference materials and minimal bias compared to isotope-dilution mass spectrometry (IDMS) reference methodology.**
- **report eGFRcreat in addition to the serum creatinine concentration in adults and specify the equation used whenever reporting eGFRcreat.**
- **report eGFRcreat in adults using the 2009 CKD-EPI creatinine equation. An alternative creatinine-based GFR estimating equation is acceptable if it has been shown to improve accuracy of GFR estimates compared to the 2009 CKD-EPI creatinine equation.**

1.4.4: Evaluation of albuminuria

1.4.4.1: We suggest using the following measurements for initial testing of proteinuria (in descending order of preference, in all cases an early morning urine sample is preferred) (2B):

1) **urine albumin-to-creatinine ratio (ACR);**
2) **urine protein-to-creatinine ratio (PCR);**
3) **reagent strip urinalysis for total protein with automated reading;**
4) **reagent strip urinalysis for total protein with manual reading.**

1.4.4.2: We recommend that clinical laboratories report ACR and PCR in untimed urine samples in addition to albumin concentration or proteinuria concentrations rather than the concentrations alone. (1B)

1.4.4.2.1: The term microalbuminuria should no longer be used by laboratories. (Not Graded)

Evaluation of Albuminuria

- Understand settings that may affect interpretation of measurements of albuminuria and order confirmatory tests as indicated
- Confirm reagent strip positive albuminuria and proteinuria by quantitative laboratory measurement and express as a ratio to creatinine wherever possible
- Confirm ACR ≥30 mg/g (ACR ≥3 mg/mmol) on a random untimed urine with a subsequent early morning sample of urine
- If a more accurate estimate of albuminuria or total proteinuria is required, measure albumin excretion rate or total protein excretion rate in a timed urine sample

Evaluation of Albuminuria

For initial testing (in order of preference):

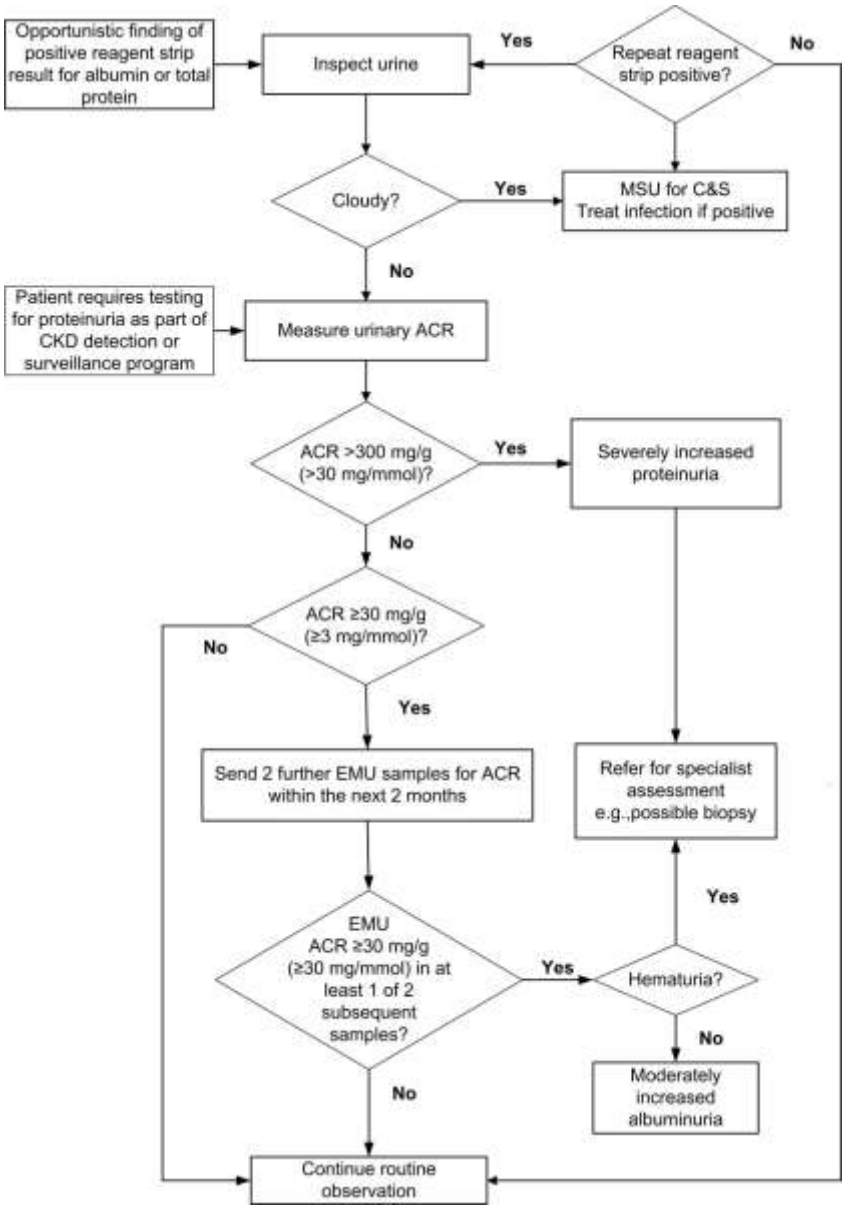
Adults:

- urine albumin-to-creatinine ratio (ACR)
- urine protein-to-creatinine ratio (PCR)
- reagent strip urinalysis for total protein with automated reading
- reagent strip urinalysis for total protein with manual reading

Children:

- urine PCR, early morning urine sample preferred
- urine ACR, early morning urine sample preferred
- reagent strip urinalysis for total protein with automated reading
- reagent strip urinalysis for total protein with manual reading

Evaluation of Albuminuria



Adapted from Lamb EJ, Price CP. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics, p. 669-708, 2012.

Evaluation of Albuminuria

- If significant non-albumin proteinuria is suspected, use assays for specific urine proteins (e.g., α1-microglobulin, monoclonal heavy or light chains, [known in some countries as “Bence Jones” proteins]

For Labs Reporting Albuminuria

Clinical laboratories should:

- Report ACR and PCR in untimed urine samples in addition to albumin concentration or proteinuria concentrations rather than the concentrations alone
- No longer use prefixes “normo,” “micro,” or “macro” when referring to albuminuria because these terms are antiquated, non-descriptive definitions
- Use current terminology for albuminuria:

Category	(mg/g)	(mg/mmol)
A1: Normal to mildly increased	<30	<3
A2: Moderately increased	30-300	3-30
A3: Severely increased	>300	>30

CLASSIFICATION OF CKD

KDIGO 2012

1.4: EVALUATION OF CKD

1.4.1: Evaluation of chronicity

1.4.1.1: In people with GFR o60 ml/min/1.73 m2 (GFR categories G3a-G5) or markers of kidney damage, review past history and previous measurements to determine duration of kidney disease. (Not Graded)

- **If duration is 43 months, CKD is confirmed. Follow recommendations for CKD.**
- **If duration is not 43 months or unclear, CKD is not confirmed. Patients may have CKD or acute kidney diseases (including AKI) or both and tests should be repeated accordingly.**

Classification of CKD

- It is recommended that CKD be classified by:
  - Cause
  - GFR category
  - Albuminuria category
- This is collectively referred to as “CGA Staging”
- Represents a revision of the previous KDOQI CKD guidelines, which included staging only by level of GFR

CGA Staging

Cause

Assign cause of CKD based on presence or absence of systemic disease and the location within the kidney of observed or presumed pathologic-anatomic findings

	Examples of systemic diseases or conditions affecting the kidney	Examples of primary kidney diseases (absence of systemic diseases affecting the kidney)
Glomerular disease	Diabetes, systemic autoimmune diseases, systemic infections, drugs, neoplasia (including amyloidosis)	Diffuse, focal or cresentic proliferative glomerulonephritis; focal and segmental glomerulosclerosis; membranous nephropathy; minimal change disease
Tubulointerstitial disease	Systemic infections, autoimmune, sarcoidoisis, drugs, urate, environmental toxins (lead, aristolochic acid), neoplasia (myeloma)	Urinary-tract infections, stones, obstruction
Vascular disease	Atherosclerosis, hypertension, ischemia, cholesterol emboli, systemic vasculitis, thrombotic microangiopathy, systemic sclerosis	ANCA-associated renal liimited vasculitis; fibromuscular dysplasia
Cystic and congenital disease	Polycystic kidney disease, Alport's syndrome, Fabry's disease	Renal dysplasia, medullary cystic disease, podocytopathies

Abbreviations: ANCA, antineutrophil cytoplasmic antibody; CKD, chronic kidney disease, GN, glomerulonephritis
Genetic diseases are not considered separately because some diseases in each category are now recognized as having genetic determinants.
*Note that there are many different ways in which to classify CKD. This method of separating systemic diseases and primary kidney diseases is only one, proposed by the KDIGO Work Group, to aid in conceptual approach.

CGA Staging

Albuminuria

Assign albuminuria† categories

Category	AER	ACR (Approximate equivalent)		Terms
	(mg/24h)	(mg/mmol)	(mg/g)	
A1	<30	<3	<30	Normal to mildly increased
A2	30-300	3-30	30-300	Moderately increased*
A3	>300	>30	>300	Severely increased**

Abbreviations: AER, albumin excretion rate; ACR, albumin-to-creatinine ratio; CKD, chronic kidney disease
*Relative to young adult level.
**Including nephrotic syndrome (albumin excretion usually >2200 mg/24 hours [ACR >2220 mg/g; >220 mg/mmol])

†Note that where albuminuria measurement is not available, urine reagent strip results can be substituted

CGA Staging

GFR

Assign GFR categories

GFR category	GFR (ml/min/1.73 m^2)	Terms
G1	≥90	Normal or high
G2	60-89	Mildly decreased*
G3a	45-59	Mildly to moderately decreased
G3b	30-44	Moderately to severely decreased
G4	15-29	Severely decreased
G5	<15	Kidney failure

Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate.
*Relative to young adult level
In the absence of evidence of kidney damage, neither GFR category G1 nor G2 fulfill the criteria for CKD.

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1.4.2: Evaluation of cause

1.4.2.1: Evaluate the clinical context, including personal and family history, social and environmental factors, medications, physical examination, laboratory measures, imaging, and pathologic diagnosis to determine the causes of kidney disease. (Not Graded)

Evaluation of Cause

Evaluate the clinical context to determine the cause(s) of kidney disease

- Personal and family history
- Social and environmental factors
- Medications
- Physical examination
- Laboratory measures
- Imaging
- Pathologic diagnosis

Evaluation of Chronicity

In people with GFR <60 ml/min/1.73 m^2 or markers of kidney damage:

- Review past history and previous measurements to determine duration of kidney disease
  - If duration is >3 months, CKD is confirmed
  - If duration is ≤3 months or unclear, CKD is not confirmed. Patients may have CKD or acute kidney disease (including acute kidney injury) or both and tests should be repeated accordingly

Predicting Prognosis of CKD

- In predicting risk outcomes, identify:
  - Cause of CKD
  - GFR category
  - Albuminuria category
  - Other risk factors and comorbid conditions
- Use estimated risk of concurrent complications and future outcomes to guide decisions for testing and treatment for CKD complications
- In populations with CKD, group GFR and albuminuria categories with similar relative risk for CKD outcomes into risk categories

Prognosis of CKD by GFR and Albuminuria Categories

Extensive work by the CKD Prognosis Consortium defined the relative risks across GFR and albuminuria categories for:

- All-cause mortality
- Cardiovascular mortality
- Kidney failure
- Acute kidney injury
- Progressive CKD

Levels of risk can be identified and grouped into categories, but they may differ somewhat for each outcome.

CURRENT CHRONIC KIDNEY DISEASE (CKD) NOMENCLATURE USED BY KDIGO

CKD is defined as abnormalities of kidney structure or function, present for >3 months, with implications for health and CKD is classified based on cause, GFR category, and albuminuria category (CGA).

Prognosis of CKD by GFR and albuminuria category

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

GFR categories (ml/min/ 1.73 m²) Description and range				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
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

Examples of CGA Staging

Cause	GFR category	Albuminuria category	Criterion for CKD
Diabetic kidney disease	G5	A3	Decreased GFR, Albuminuria
Idiopathic focal sclerosis	G2	A3	Albuminuria
Kidney transplant recipient	G2	A1	History of kidney transplantation
Polycystic kidney disease	G2	A1	Imaging abnormality
Vesicoureteral reflux	G1	A1	Imaging abnormality
Distal renal tubular acidosis	G1	A1	Electrolyte abnormalities
Hypertensive kidney disease	G4	A2	Decreased GFR, Albuminuria
CKD presumed due to diabetes and hypertension	G4	A1	Decreased GFR
CKD presumed due to diabetes and hypertension	G2	A3	Albuminuria
CKD presumed due to diabetes and hypertension	G3a	A1	Decreased GFR
CKD cause unknown	G3a	A1	Decreased GFR

Summary of Relative Risks from Categorical Meta-Analysis

(reagent strip included [-, ±, +, ≥++])

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

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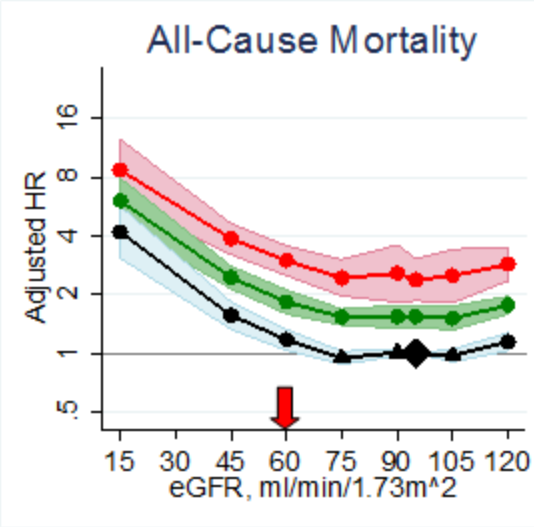
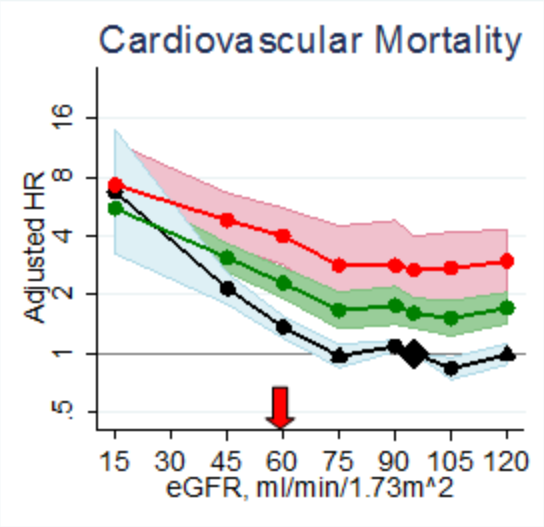
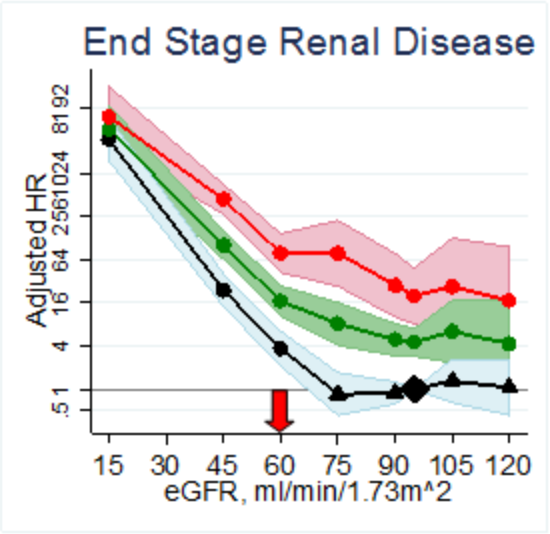
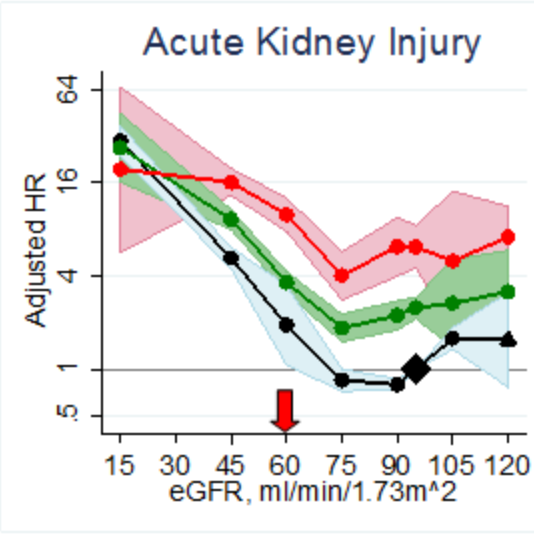
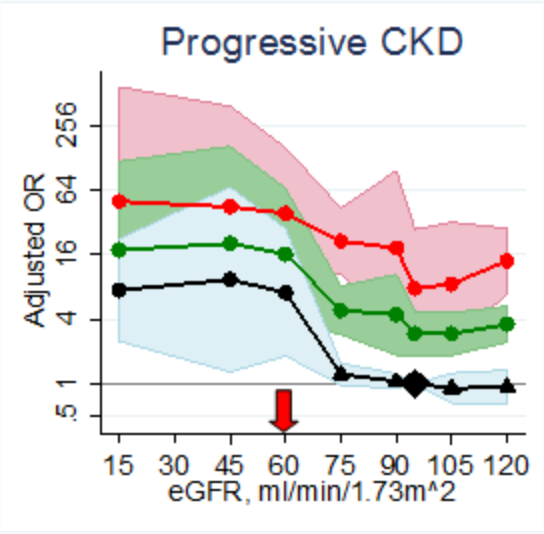
Summary of Relative Risks from Continuous Meta-Analysis











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General Guide to Referral Decisions by GFR and Albuminuria Categories

GFR categories (ml/min/ 1.73 m²) Description and range				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
	G1	Normal or high	≥90		Monitor	Refer*
	G2	Mildly decreased	60–89		Monitor	Refer*
	G3a	Mildly to moderately decreased	45–59	Monitor	Monitor	Refer
	G3b	Moderately to severely decreased	30–44	Monitor	Monitor	Refer
	G4	Severely decreased	15–29	Refer*	Refer*	Refer
	G5	Kidney failure	<15	Refer	Refer	Refer

*Referring clinicians may wish to discuss with their nephrology service depending on local arrangements regarding monitoring or referring.

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2.1: DEFINITION AND IDENTIFICATION OF CKD PROGRESSION

2.1.1: Assess GFR and albuminuria at least annually in people with CKD. Assess GFR and albuminuria more often for individuals at higher risk of progression, and/or where measurement will impact therapeutic decisions (see figure below). (Not Graded)

2.1.2: Recognize that small fluctuations in GFR are common and are not necessarily indicative of progression. (Not Graded)

2.2: PREDICTORS OF PROGRESSION

2.2.1: Identify factors associated with CKD progression to inform prognosis. These include cause of CKD, level of GFR, level of albuminuria, age, sex, race/ethnicity, elevated BP, hyperglycemia, dyslipidemia, smoking, obesity, history of cardiovascular disease, ongoing exposure to nephrotoxic agents, and others. (Not Graded)

2.1.3: Define CKD progression based on one of more of the following (Not Graded):

- **Decline in GFR category (Z90 [G1], 60–89 [G2], 45–59 [G3a], 30–44 [G3b], 15–29 [G4], o15 [G5] ml/min/ 1.73 m2). A certain drop in eGFR is defined as a drop in GFR category accompanied by a 25% or greater drop in eGFR from baseline.**
- **Rapid progression is defined as a sustained decline in eGFR of more than 5 ml/min/1.73 m2 /yr.**
- **The confidence in assessing progression is increased with increasing number of serum creatinine measurements and duration of follow-up**

2.1.4: In people with CKD progression, as defined in Recommendation 2.1.3, review current management, examine for reversible causes of progression, and consider referral to a specialist. (Not Graded)

5.2: CARE OF THE PATIENT WITH PROGRESSIVE CKD

5.2.1: We suggest that people with progressive CKD should be managed in a multidisciplinary care setting. (2B)

5.2.2: The multidisciplinary team should include or have access to dietary counseling, education and counseling about different RRT modalities, transplant options, vascular access surgery, and ethical, psychological, and social care. (Not Graded)

Guide to Frequency of Monitoring (number of times per year) by GFR and Albuminuria Category				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 >30mg/mmol
GFR categories (ml/min/1.73 m²) 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).

Other complications of CKD: CVD, medication dosage, patient safety, infections, hospitalizations, and caveats for investigating complications of CKD

4.2: CAVEATS WHEN INTERPRETING TESTS FOR CVD IN PEOPLE WITH CKD

Non-invasive testing

4.2.3: We recommend that people with CKD presenting with chest pain should be investigated for underlying cardiac disease and other disorders according to the same local practice for people without CKD (and subsequent treatment should be initiated similarly). (1B)

4.2.4: We suggest that clinicians are familiar with the limitations of non-invasive cardiac tests (e.g., exercise electrocardiography [ECG], nuclear imaging, echocardiography, etc.) in adults with CKD and interpret the results accordingly. (2B)

4.3: CKD AND PERIPHERAL ARTERIAL DISEASE

4.3.1: We recommend that adults with CKD be regularly examined for signs of peripheral arterial disease and be considered for usual approaches to therapy. (1B)

4.3.2: We suggest that adults with CKD and diabetes are offered regular podiatric assessment. (2A)

Radiocontrast

4.5.2: We recommend that all people with GFR o60 ml/min/1.73 m2 (GFR categories G3a-G5) undergoing elective investigation involving the intravascular administration of iodinated radiocontrast media should be managed according to the KDIGO Clinical Practice Guideline for AKI including:

- **Avoidance of high osmolar agents (1B);**
- **Use of lowest possible radiocontrast dose (Not Graded);**
- **Withdrawal of potentially nephrotoxic agents before and after the procedure (1C);**
- **Adequate hydration with saline before, during, and after the procedure (1A);**
- **Measurement of GFR 48–96 hours after the procedure (1C).**

Gadolinium-based contrast media

4.5.3: We recommend not using gadolinium-containing contrast media in people with GFR o15 ml/min/1.73 m2 (GFR category G5) unless there is no alternative appropriate test. (1B)

4.5.4: We suggest that people with a GFR o30 ml/min/1.73 m2 (GFR categories G4-G5) who require gadoliniumcontaining contrast media are preferentially offered a macrocyclic chelate preparation. (2B)

Bowel preparation

4.5.5: We recommend not to use oral phosphate-containing bowel preparations in people with a GFR o60 ml/min/ 1.73 m2 (GFR categories G3a-G5) or in those known to be at risk of phosphate nephropathy. (1A)

4.6: CKD AND RISKS FOR INFECTIONS, AKI, HOSPITALIZATIONS, AND MORTALITY

CKD and risk of infections

4.6.1: We recommend that all adults with CKD are offered annual vaccination with influenza vaccine, unless contraindicated. (1B)

4.6.2: We recommend that all adults with eGFR o30 ml/min/1.73 m2 (GFR categories G4-G5) and those at high risk of pneumococcal infection (e.g., nephrotic syndrome, diabetes, or those receiving immunosuppression) receive vaccination with polyvalent pneumococcal vaccine unless contraindicated. (1B)

4.6.3: We recommend that all adults with CKD who have received pneumococcal vaccination are offered revaccination within 5 years. (1B)

4.6.4: We recommend that all adults who are at high risk of progression of CKD and have GFR o30 ml/min/1.73 m2 (GFR categories G4-G5) be immunized against hepatitis B and the response confirmed by appropriate serological testing. (1B)

4.6.5: Consideration of live vaccine should include an appreciation of the patient's immune status and should be in line with recommendations from official or governmental bodies. (Not Graded)

4.6.6: Pediatric immunization schedules should be followed according to official international and regional recommendations for children with CKD. (Not Graded)

CKD and risk of AKI

4.6.7: We recommend that all people with CKD are considered to be at increased risk of AKI. (1A)

4.6.7.1: In people with CKD, the recommendations detailed in the KDIGO AKI Guideline should be followed for management of those at risk of AKI during intercurrent illness, or when undergoing investigation and procedures that are likely to increase the risk of AKI. (Not Graded)

CKD and risk of hospitalization and mortality

4.6.8: CKD disease management programs should be developed in order to optimize the community management of people with CKD and reduce the risk of hospital admission. (Not Graded)

4.6.9: Interventions to reduce hospitalization and mortality for people with CKD should pay close attention to the management of associated comorbid conditions and cardiovascular disease in particular. (Not Graded)

Referral to specialists and models of care

5.1: REFERRAL TO SPECIALIST SERVICES

5.1.1: We recommend referral to specialist kidney care services for people with CKD in the following circumstances (1B):

- **AKI or abrupt sustained fall in GFR;**
- **GFR o30 ml/min/1.73 m2 (GFR categories G4-G5)*;**
- **a consistent finding of significant albuminuria (ACR Z300 mg/g [Z30 mg/mmol] or AER Z300 mg/ 24 hours, approximately equivalent to PCR Z500 mg/g [Z50 mg/mmol] or PER Z500 mg/24 hours);**
- **progression of CKD (see Recommendation 2.1.3 for definition);**
- **urinary red cell casts, RBC 420 per high power field sustained and not readily explained;**
- **CKD and hypertension refractory to treatment with 4 or more antihypertensive agents;**
- **persistent abnormalities of serum potassium; K recurrent or extensive nephrolithiasis;**
- **hereditary kidney disease**

5.1.2: We recommend timely referral for planning renal replacement therapy (RRT) in people with progressive CKD in whom the risk of kidney failure within 1 year is 10–20% or higherw , as determined by validated risk prediction tools. (1B)

5.3: TIMING THE INITIATION OF RRT

5.3.1: We suggest that dialysis be initiated when one or more of the following are present: symptoms or signs attributable to kidney failure (serositis, acid-base or electrolyte abnormalities, pruritus); inability to control volume status or blood pressure; a progressive deterioration in nutritional status refractory to dietary intervention; or cognitive impairment. This often but not invariably occurs in the GFR range between 5 and 10 ml/min/1.73 m2 . (2B)

5.3.2: Living donor preemptive renal transplantation in adults should be considered when the GFR is o20 ml/min/ 1.73 m2 , and there is evidence of progressive and irreversible CKD over the preceding 6–12 months. (Not Graded)

5.4: STRUCTURE AND PROCESS OF COMPREHENSIVE CONSERVATIVE MANAGEMENT

5.4.1: Conservative management should be an option in people who choose not to pursue RRT and this should be supported by a comprehensive management program. (Not Graded)

5.4.2: All CKD programs and care providers should be able to deliver advance care planning for people with a recognized need for end-of-life care, including those people undergoing conservative kidney care. (Not Graded)

5.4.3: Coordinated end-of-life care should be available to people and families through either primary care or specialist care as local circumstances dictate. (Not Graded)

5.4.4: The comprehensive conservative management program should include protocols for symptom and pain management, psychological care, spiritual care, and culturally sensitive care for the dying patient and their family (whether at home, in a hospice or a hospital setting), followed by the provision of culturally appropriate bereavement support. (Not Graded)

What's New?

DEFINITION AND CLASSIFICATION OF CKD	
KDOQI 2002	**KDIGO 2012**
CKD is defined as either: • Kidney damage; or • GFR <60 mL/min/1.73 m^2 for ≥3 months	• Definition remains intact • "With implications for health" is added to the definition of CKD
CKD is classified mainly by GFR category	• CKD is now classified by: Cause GFR category (G1-G5) Albuminuria category (A1-A3) • Collectively referred to as CGA Staging
CKD is divided into 5 stages	• GFR level equivalent to previous CKD Stage 3 is now subdivided into 2 GFR categories: 3a and 3b • Terminology changes: GFR levels are now grouped as "categories" • "Categories" are also used to describe extent of albuminuria

What's New?

ALBUMINURIA	
KDOQI 2002	**KDIGO 2012**
Not incorporated into the staging system	Added to the classification system and given 3 categories of severity: • Normal to mildly increased (A1) • Moderately increased (A2) • Severely increased (A3)
Previous terminology: • Normoalbuminuria • Microalbuminuria • Macroalbuminuria	New terminology: • Normal to mildly increased • Moderately increased • Severely increased The term "microalbuminuria" is no longer used and is discouraged
	• Importance of assessment based on the 3 categories of severity is discussed • Guidance on investigation of albuminuria is provided • Algorithm for those with suspected proteinuria is also included

What's New?

EVALUATION & MANAGEMENT	
KDOQI 2002	**KDIGO 2012**
Risk relationship between GFR and albuminuria is not defined	Risk relationship between GFR and albuminuria is defined for : • Overall mortality • CVD • Kidney failure • AKI • CKD progression

• Creatinine-based equations for estimating eGFR are explained
• MDRD equation is recommended as the preferred method (adults)
	• Elaborates on determination of eGFR using creatinine, cystatin C, or both with updated equations (in adults and pediatrics)
	• For initial assessment:
	  • Use a GFR estimating equation to derive GFR from serum creatinine rather than serum creatinine alone
	  • Use the 2009 CKD-EPI creatinine equation for initial assessment
	  • An alternative creatinine-based equation can be used if shown to be more accurate
	• Confirmatory tests:
	  • Use additional tests (such as cystatin C or other clearance measurement) for confirmatory tests in specific circumstances when eGFR based on serum creatinine is less accurate.

Frequency of monitoring: • Based on eGFR	Frequency of monitoring: • Based on eGFR and albuminuria categories

What's New?

MANAGEMENT	
KDOQI 2002	**KDIGO 2012**
	Recognize that small fluctuations in GFR are common and are not necessarily indicative of progression
	Defines CKD progression based on one or more of the following: • Decline in GFR category (a certain drop is a decline in GFR category accompanied by a 25% or greater drop in eGFR) • Rapid progression is a sustained decline of >5 ml/min/1.73 m^2 per yr
Includes management and treatment of CKD complications	Revisits management and treatment of CKD complications
Suggests when to refer for specialist care	Suggests when to refer for specialist care and emphasizes care of patients with progressive CKD under multidisciplinary care setting

Key Messages

- CKD is defined as abnormalities of kidney structure or function, present for >3 months, with implications for health
  - The definition of CKD remains intact but includes "with implications for health"
- It is recommended that CKD be classified by Cause, GFR category, Albuminuria category; this is collectively referred to as the "CGA Staging"
- Prediction of prognosis and frequency of monitoring should be guided by GFR and albuminuria categories