



Guideline on CKD

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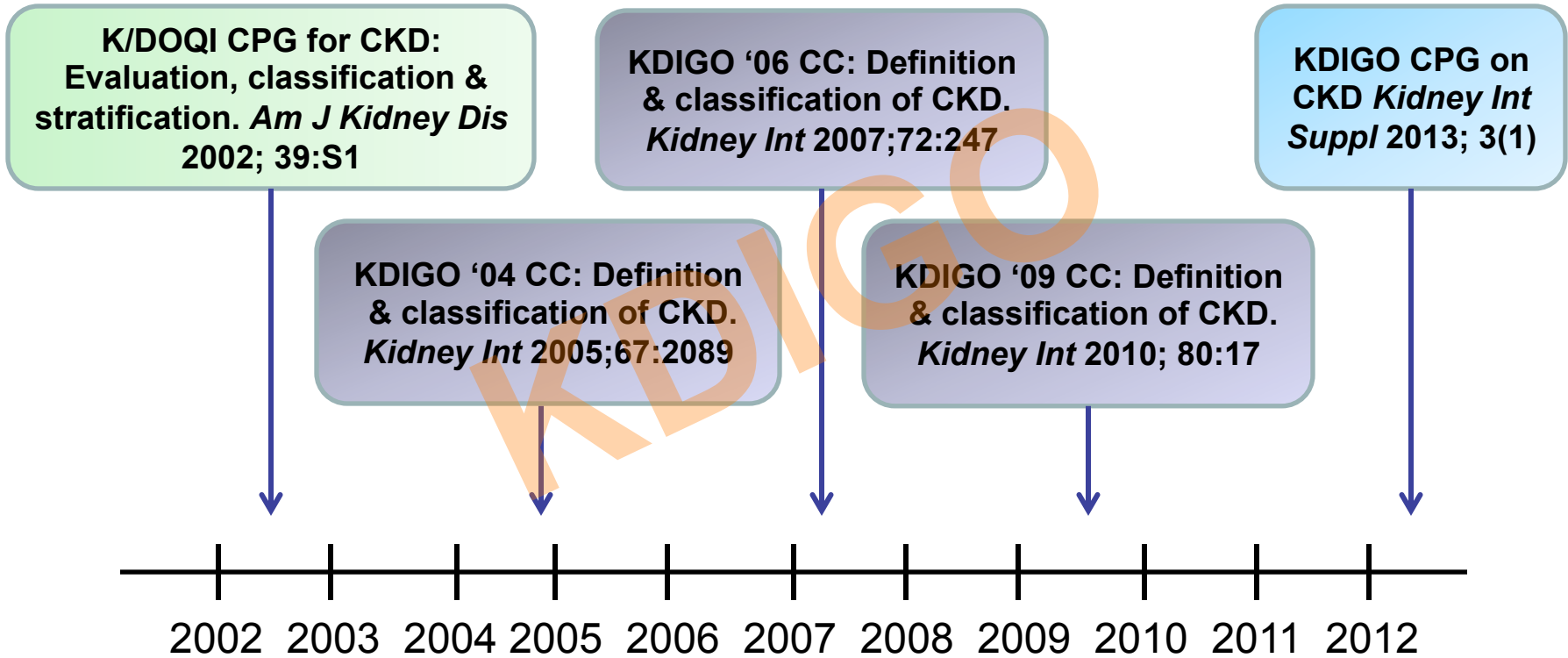
What is CKD?

“When bubbles settle on the surface of the urine, they indicate disease of the kidneys, and that the complaint will be protracted.” -- Hippocrates 400 BCE



Kidney Disease: Improving Global Outcomes

A decade of efforts to define CKD



Kidney Disease: Improving Global Outcomes

KDOQI 2002 definition and staging

Definition: Kidney damage for ≥ 3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR or GFR < 60 mL/min/1.73m² for ≥ 3 months, with or without kidney damage.

Stage	Description	GFR (ml/min/1.73 m ²)
1	Kidney damage with normal or \uparrow GFR	> 90
2	Kidney damage with mild \downarrow in GFR	60-89
3	Moderate \downarrow in GFR	30-59
4	Severe \downarrow in GFR	15-29
5	Kidney failure	< 15 (or dialysis)

Am J Kidney Dis 2002; 39:S1

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KDIGO surveys and Controversy Conferences in 2004 and 2006

Two modifications to account for dialysis and transplantation.

Stage	Description	GFR (ml/min/1.73 m ²)	Treatment
1	Kidney damage with normal or ↑ GFR	> 90	T if kidney transplant
2	Kidney damage with mild ↓ in GFR	60-89	
3	Moderate ↓ in GFR	30-59	
4	Severe ↓ in GFR	15-29	D if dialysis
5	Kidney failure	< 15 (or dialysis)	

Kidney Int 2005;67:2089
Kidney Int 2007;72:247



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The definition, classification, and prognosis of chronic kidney disease: a KDIGO Controversies Conference report

Andrew S. Levey¹, Paul E. de Jong², Josef Coresh³, Meguid El Nahas⁴, Brad C. Astor³, Kunihiro Matsushita³, Ron T. Gansevoort², Bertram L. Kasiske⁵ and Kai-Uwe Eckardt⁶

On the basis of analyses in 45 cohorts that included 1,555,332 participants from general, high-risk, and CKD populations, the conference recommended retaining the current definition for CKD, and to modify the classification by emphasizing clinical diagnosis, adding albuminuria stage, and subdividing stage 3.

Kidney Int. 2011; 80:17

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The CKD guideline team



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**KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of
Chronic Kidney Disease**

VO
http

VOLUME 3 | ISSUE 1 | JANUARY 2013

<http://www.kidney-international.org>



www.kdigo.org

CKD guideline goal

... to clarify the definition and classification system of CKD, and to develop appropriate guidance as to the management and care of people with CKD ... foster an extended collaborative research agenda



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What the guideline covers

- Target population: all adults and children identified with CKD who are not on renal replacement therapy.
- CKD: any (or unknown) cause.
- Target audience: nephrologists, primary care physicians, non-nephrology specialists, clinical chemists and other practitioners caring for adults and children with CKD.
- Target healthcare settings: primary, secondary and tertiary care.

What is *not* in the guideline

- Evaluation and management of people receiving renal replacement therapy
- Specific diagnostic approaches to people with AKI, GN or other specific diagnoses
- Treatment of each of the specific causes of CKD
- Management of pregnancy in women with CKD or of pregnant women who develop kidney disease
- Detailed management of complications of CKD

GRADE: an emerging consensus on rating quality of evidence and strength of recommendations

Guidelines are inconsistent in how they rate the quality of evidence and the strength of recommendations. This article explores the advantages of the GRADE system, which is increasingly being adopted by organisations worldwide

Quality of evidence	High	A	Strength of recommendation	1	“We recommend“
	Moderate	B		2	“We suggest“
	Low	C			
	Very low	D			

Grade 1A ... Grade 2D (8 options); plus “Not Graded“

Guyatt GH, et al. *BMJ* 2008; 336:924

Topics

Section 1:

Definition & Classification

Section 2:

Definition, Identification & Prediction of CKD Progression

Section 3:

Management of CKD Progression & Complications

Section 4:

Other Complications

Section 5:

Referral to Specialists & Models of Care

SECTION 1: Definition and Classification

KDIGO



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Audience Response Question 1:

Which of the following would *NOT* meet the KDIGO definition of CKD ≥ 3 months of:

1. GFR 65 & urine albumin 60 mg/24h
2. GFR 65 & urine RBCs with IgA on biopsy
3. GFR 65 after kidney transplant
4. GFR 65 after donating a kidney for transplant
5. GFR 45 at age 75 years

1.1 Definition of CKD

1.1.1: CKD is defined as abnormalities of kidney structure or function, present for ≥ 3 months, with implications for health (Table 2). (*Not Graded*)

Table 2 | Criteria for CKD (either of the following present for ≥ 3 months)

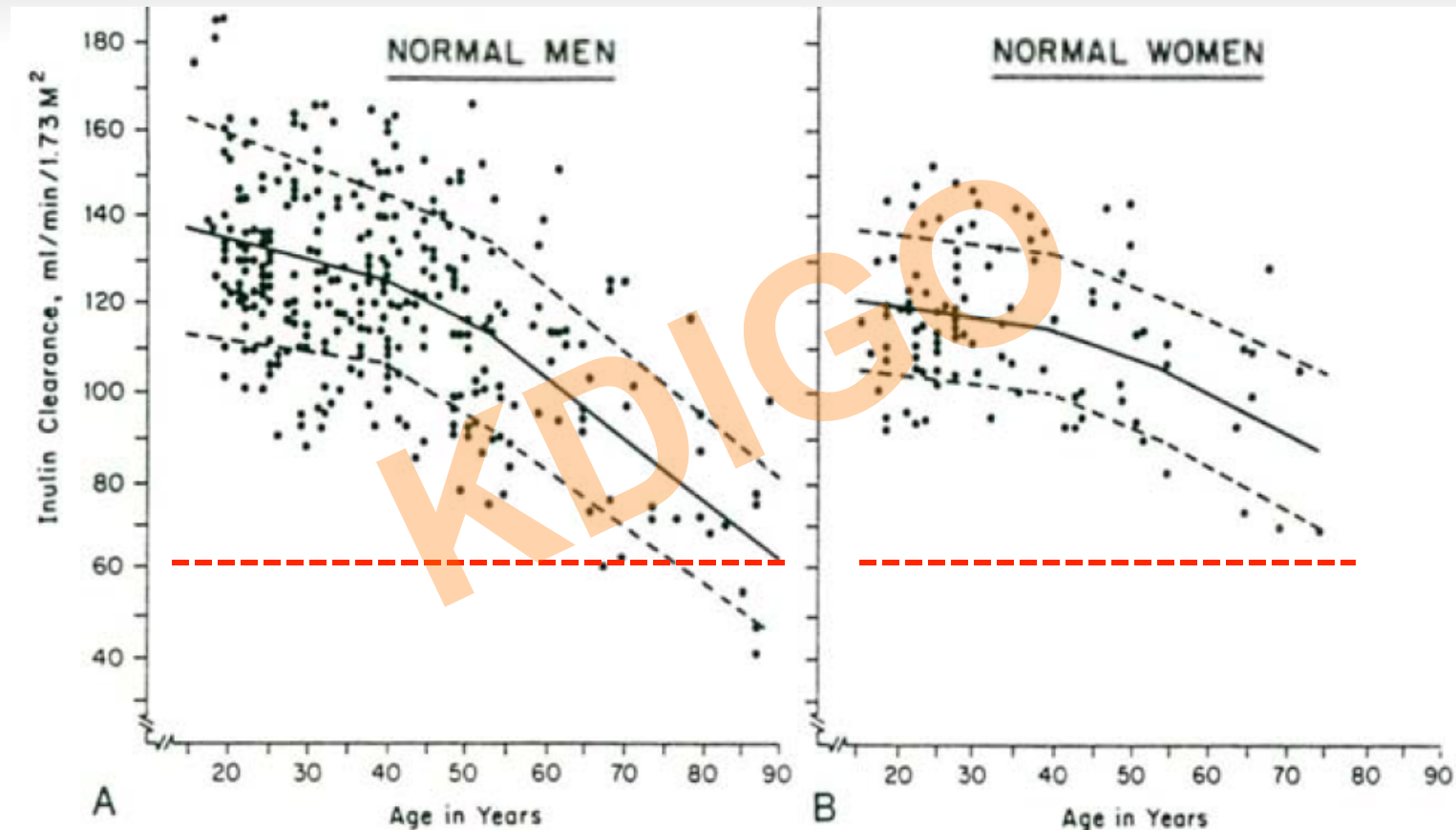
Markers of Kidney Damage	Albuminuria > 30 mg/day
	Urine sediment abnormalities (e.g., hematuria, red cell casts etc)
	Electrolyte and other abnormalities due to tubular disorders
	Abnormalities detected by histology
	Structural abnormalities detected by imaging
	History of kidney transplantation
	Decreased GFR

Audience Response Question 2:

Which of the following justifies including GFR <60 mL/min/1.73m² in defining CKD:

1. increased risk for CVD
2. increased risk of all-cause mortality
3. increased risk of drug dosing errors
4. increased risk of metabolic complications
5. all of the above

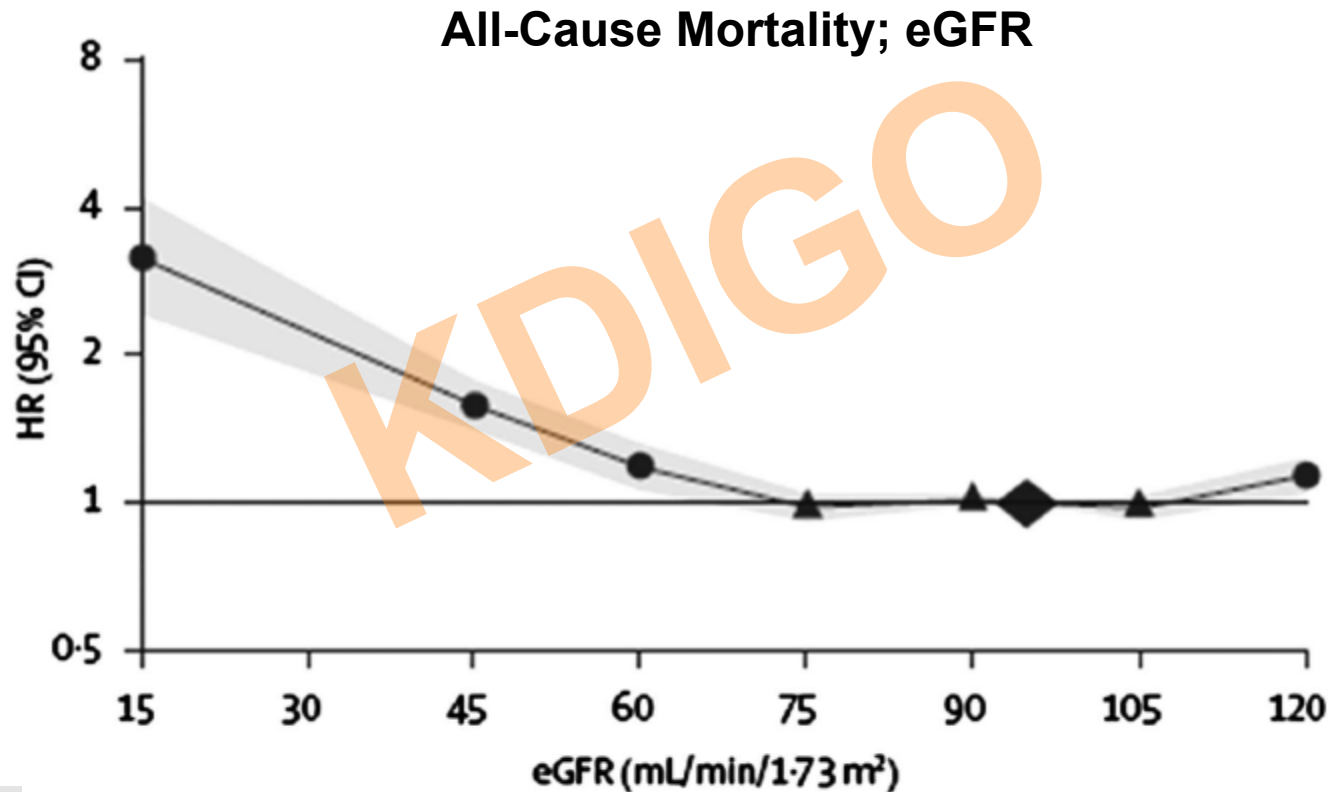
Rationale for defining CKD by GFR <math><60 \text{ mL}/\text{min}/1.73\text{m}^2</math>



Wesson L. Physiology of the human kidney. New York: Grune & Stratton. 1969

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Rationale for defining CKD by GFR <60 mL/min/1.73m²

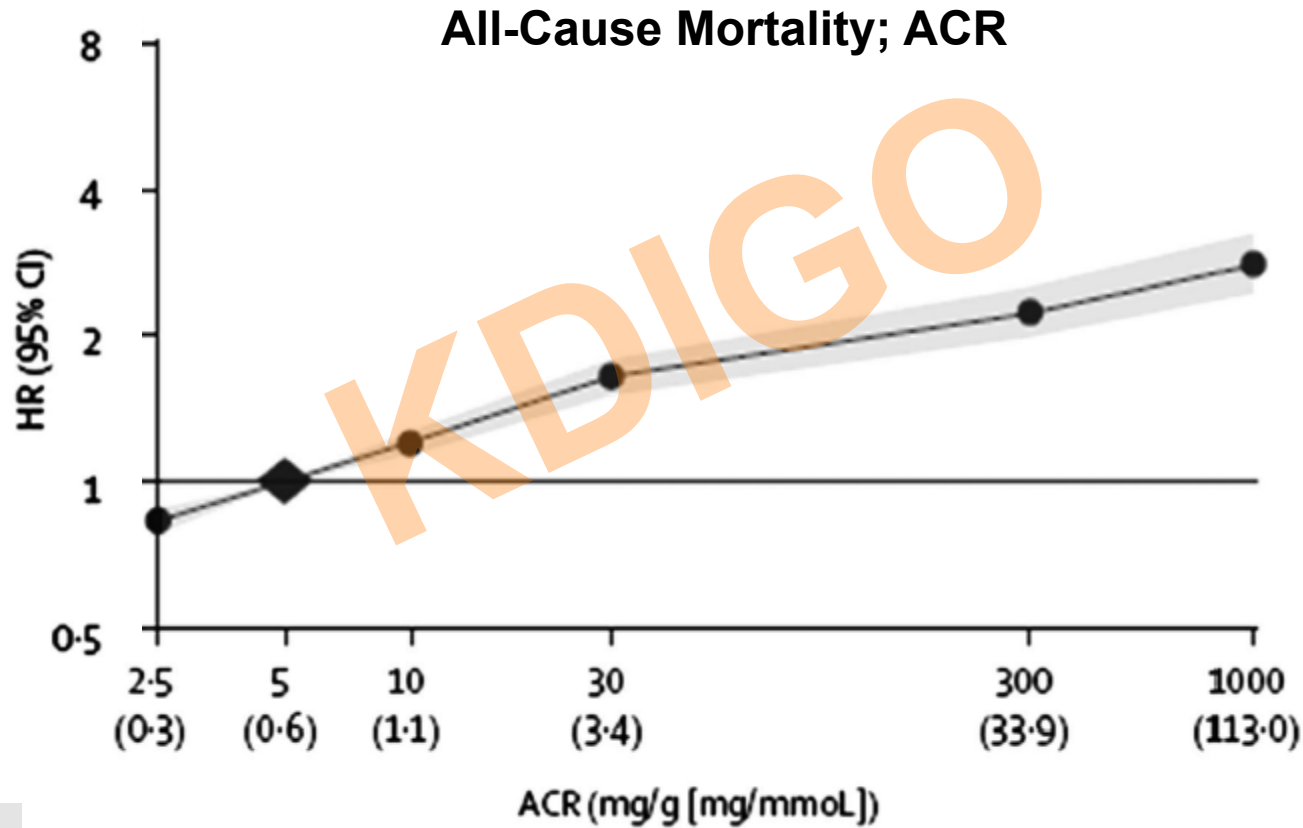


Rationale for defining CKD by GFR <60 mL/min/1.73m²

GFR <60 mL/min/1.73m² is associated with a higher risk of complications of CKD:

- Drug toxicity
- Metabolic and endocrine complications
- CVD and death

Rationale for defining CKD by ACR <30 mg/g



1.2 Staging of CKD

- 1.2.1:** We recommend that CKD is classified based on cause, GFR category and albuminuria category (CGA). (1B)
- 1.2.2:** 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. (*Not graded*)

GFR categories

1.2.3: Assign GFR categories as follows [Table 5]
(*Not Graded*):

Table 5 | GFR categories in CKD

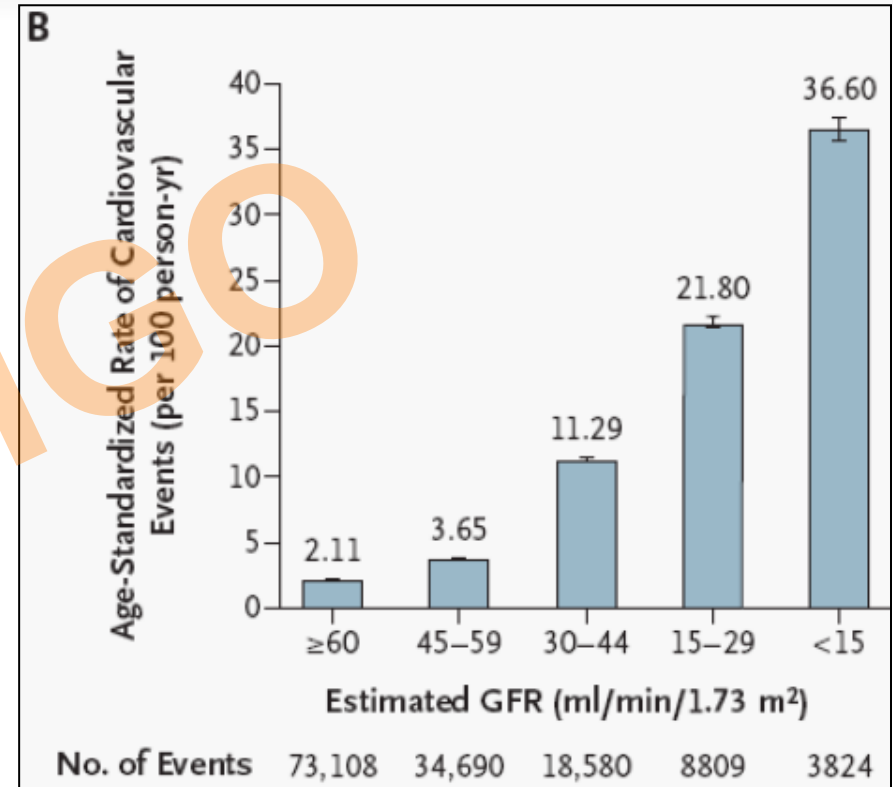
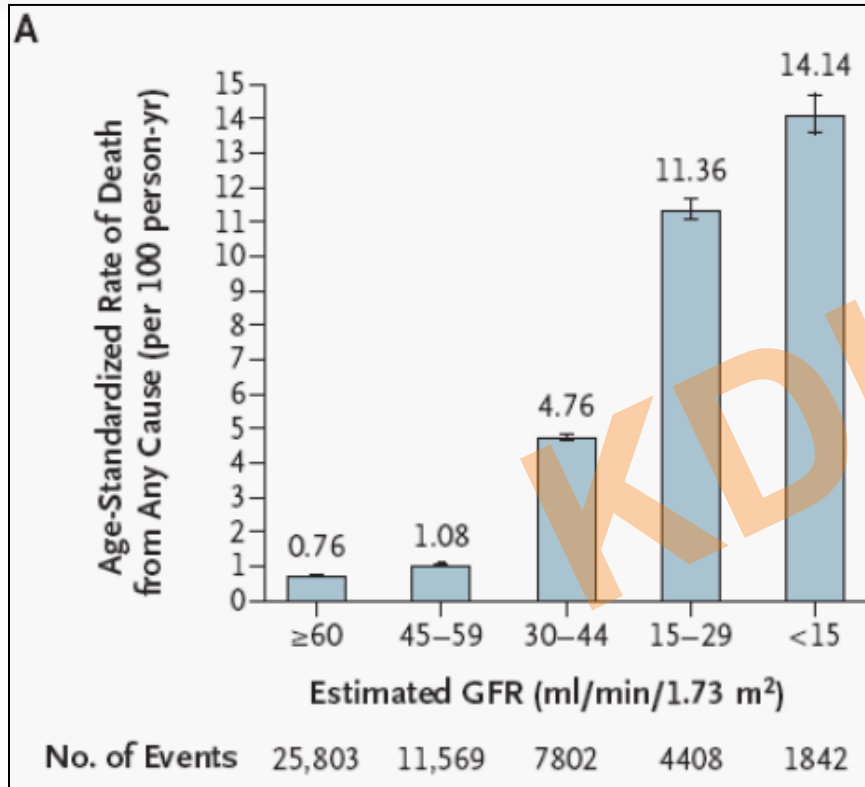
GFR category	GFR (ml/min/1.73 m ²)	Terms
G1	≥ 90	Normal or high
G2	60–89	Mildly decreased*
G3a	45–59	Mildly to moderately decreased
G3b	30–44	Moderately to severely decreased
G4	15–29	Severely decreased
G5	< 15	Kidney failure

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.

Rationale for GFR categories

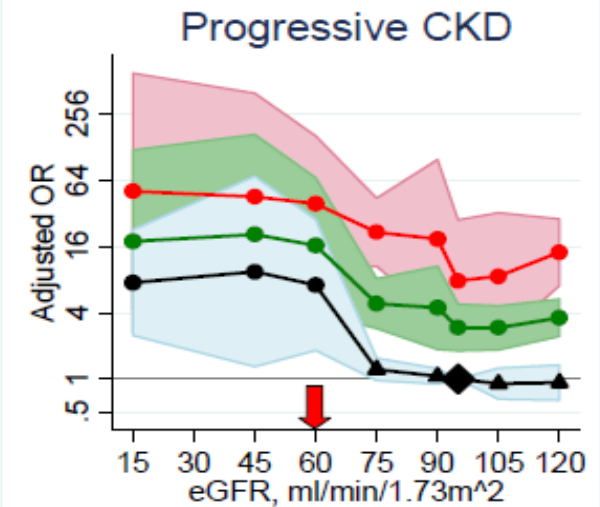
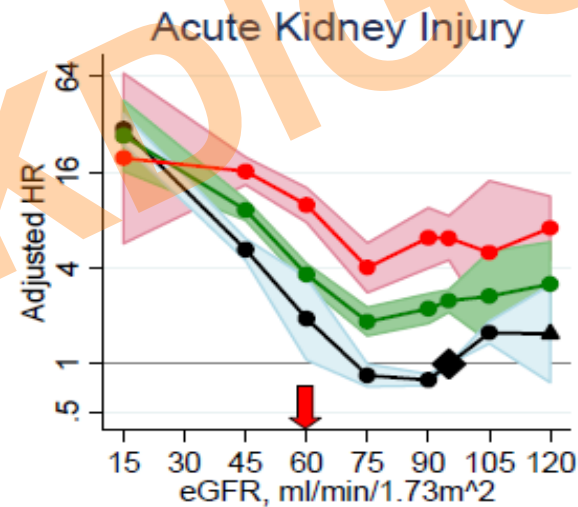
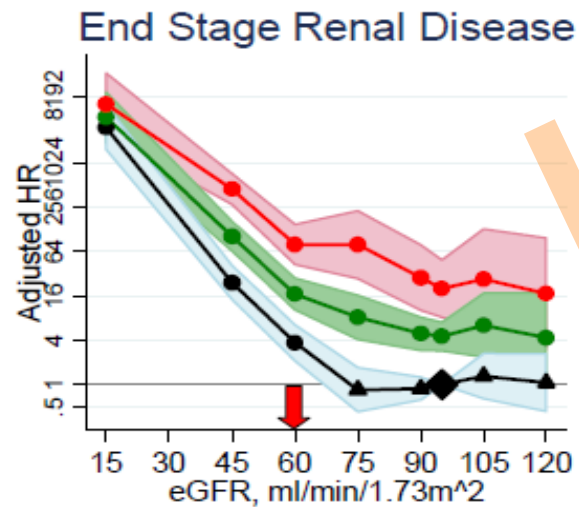
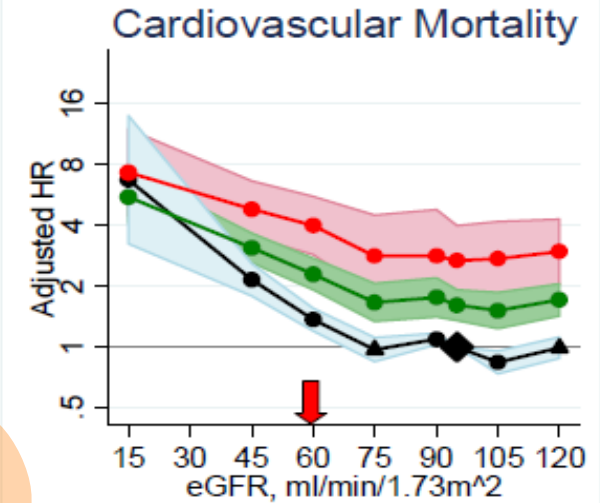
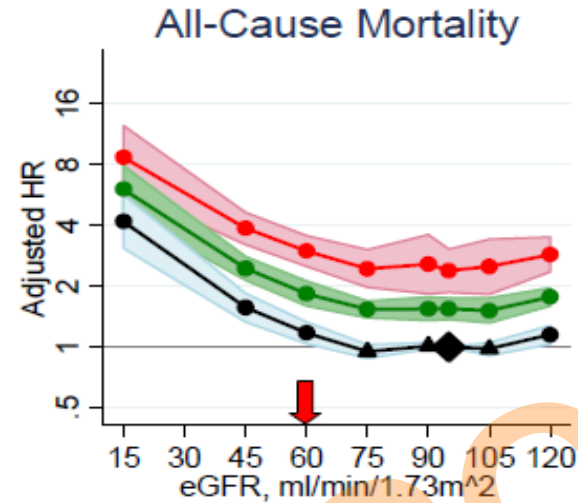


AS Go, et al. *New Engl J Med* 2004; 351:1296



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Summary of Relative Risks from Continuous Meta-Analysis



AS Levey, et al. *Kidney Int* 2011; 80:17

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Summary of Relative Risks from Categorical Meta-Analysis

(dipstick 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

AS Levey, et al. *Kidney Int* 2011; 80:17

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Albuminuria categories

1.2.4: Assign albuminuria* categories as follows (*Not Graded*):

Category	AER	Approximately Equivalent		Terms
	(mg/d)	ACR	ACR	
		(mg/mmol)	(mg/g)	
A1	<30	<3	<30	Normal to mildly increased
A2	30-299	3-29	30-299	Moderately increased*
A3	≥300	>30	≥300	Severely increased**

*note that where albuminuria measurement is not available, urine reagent strip results can be substituted.

Percentage of US Population by eGFR and Albuminuria Category: KDIGO 2012 and NHANES 1999-2006

				Persistent Albuminuria Categories, Description and Range			All
				A1	A2	A3	
				normal to mildly increased	moderately increased	severely increased	
				<30 mg/g <3 mg/mmol	30-299 mg/g 3-29 mg/mmol	≥300 mg/g ≥30 mg/mmol	
GFR Categories, Description and Range (mL/min/1.73 m ²)	G1	normal or high	>90	55.6	1.9	0.4	57.9
	G2	mildly decreased	60-89	32.9	2.2	0.3	35.4
	G3a	mildly to moderately decreased	45-59	3.6	0.8	0.2	4.6
	G3b	moderately to severely decreased	30-44	1.0	0.4	0.2	1.6
	G4	severely decreased	15-29	0.2	0.1	0.1	0.4
	G5	kidney failure	<15	0.0	0.0	0.1	0.1
				93.2	5.4	1.3	100.0

1.3 Predicting prognosis of CKD

1.3.1: In predicting risk for outcome of CKD, identify the following variables:

- 1) cause of CKD;
- 2) GFR category;
- 3) albuminuria category;
- 4) other risk factors and comorbid conditions. (*Not Graded*)

Prognosis of CKD by GFR
and Albuminuria
Categories:
KDIGO 2012

Albuminuria Categories, Description and Range		
A1	A2	A3
normal to mildly increased	moderately increased	severely increased
<30 mg/g <3 mg/mmol	30-299 mg/g 3-29 mg/mmol	≥300 mg/g ≥30 mg/mmol

GFR Categories, Description and Range (mL/min/ 1.73 m ²)	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			

1.4 Evaluation of CKD: chronicity

1.4.1: *Evaluation of Chronicity*

1.4.1.1: In people with GFR <60 mL/min/1.73m² or markers of kidney damage, review past history and previous measurements to determine duration (*Not Graded*).

- If duration is >3 months, CKD is confirmed. Follow recommendations for CKD.
- If duration is not >3 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.

1.4 Evaluation of CKD: cause

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*)

Audience Response Question 3:

Which does KDIGO recommend for defining & classifying CKD:

- 1. measure GFR with plasma or urine clearance of an inert tracer (inulin, iohexol, etc.) whenever possible**
- 2. use a cystatin C rather than a Cr formula for eGFR**
- 3. use the “CKD-EPI” formula for eGFR**
- 4. use the best available formula for estimating GFR with serum Cr**



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1.4 Evaluation of CKD: 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)

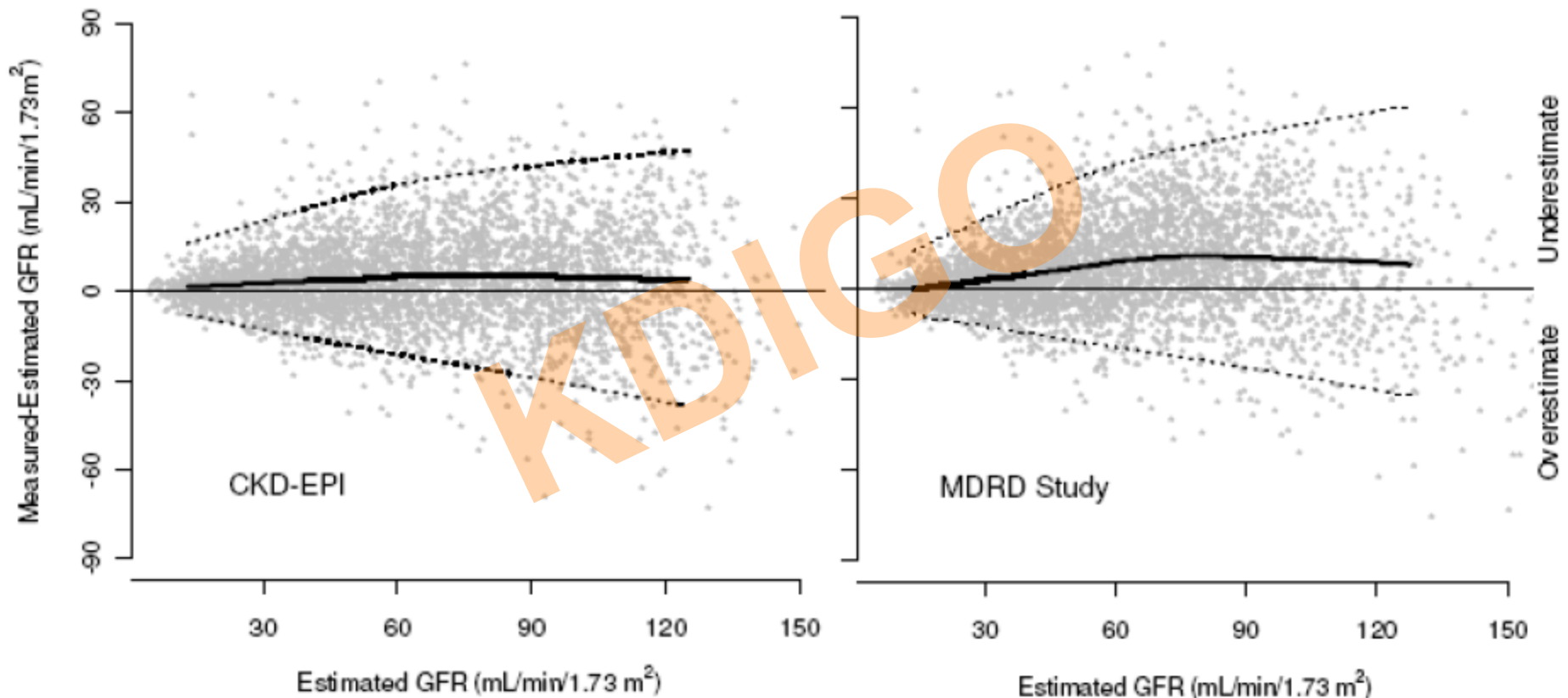
1.4.3.3: We recommend that clinicians (1B):

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

Cystatin C

- 1.4.3.5:** We suggest measuring cystatin C in adults with $eGFR_{\text{creat}}$ 45-59 who do not have other markers of kidney damage if confirmation of CKD is required. (2C)
- If $eGFR_{\text{cys}} / eGFR_{\text{creat-cys}}$ is also <60 mL/min/1.73 m², the diagnosis of CKD is confirmed
 - If $eGFR_{\text{cys}} / eGFR_{\text{creat-cys}}$ is >60 mL/min/1.73 m², the diagnosis of CKD is not confirmed

Performance of the CKD-EPI and MDRD study equations



AS Levey, et al. *Ann Intern Med* 2009; 150: 604

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Measuring GFR

1.4.3.8: We suggest measuring GFR using exogenous filtration markers under circumstances where more accurate ascertainment of GFR will impact on treatment decisions (e.g. acceptance for kidney donation, dose adaptation of toxic drugs). (2B)

1.4 Evaluation of CKD: 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 Evaluation of CKD: albuminuria

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*)

SECTION 2:

Definition, Identification and Prediction of CKD Progression



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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. (*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 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+

CKD progression

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

- Decline in GFR category (≥ 90 [G1], 60-89 [G2], 45-59 [G3a], 30-44 [G3b], 15-29 [G4], < 15 [G5] ml/min/1.73m²). 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/1.73m²/year.
- The confidence in assessing progression is increased with increasing number of serum creatinine measurements and duration of follow-up.

SECTION 3:

Management of Progression and Complications of CKD



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Audience Response Question 4:

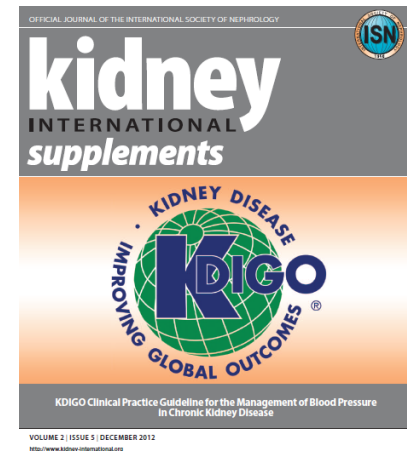
Management of CKD should include all BUT:

1. targeting BP $\leq 140/90$ mm Hg if no proteinuria
2. targeting BP $\leq 130/80$ mm Hg if proteinuria
3. treating hyperuricemia
4. using a statin for increased CVD risk
5. targeting hemoglobin A1c (HbA1c) $\sim 7.0\%$

Blood Pressure

3.1.1: Individualize BP targets and agents according to age, coexistent cardiovascular disease and other comorbidities, risk of progression of CKD, presence or absence of retinopathy (in CKD patients with diabetes), and tolerance of treatment as described in the KDIGO 2012 Blood Pressure Guideline. *(Not Graded)*.

See KDIGO Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease.
Kidney Int Suppl December 2012; Vol. 2 (5)



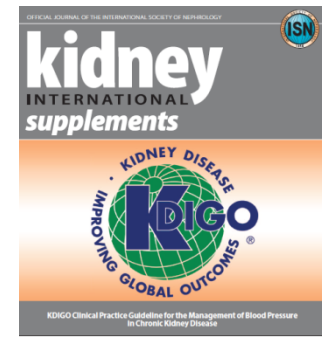
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Blood Pressure

3.1.4: We recommend that in both diabetic and nondiabetic adults with CKD and urine albumin excretion <30 mg/24 hours (or equivalent*) whose office BP is consistently >140 mm Hg systolic or >90 mm Hg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently \leq 140 mm Hg systolic and \leq 90mm Hg diastolic. (1B)



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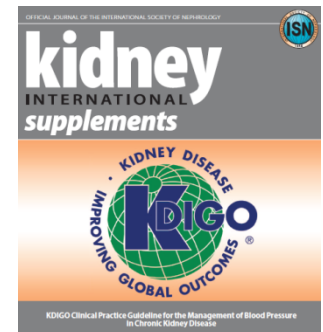


Blood Pressure

3.1.5: We suggest that in both diabetic and non-diabetic adults with CKD and with urine albumin excretion of ≥ 30 mg/24 hours (or equivalent*) whose office BP is consistently >130 mm Hg systolic or >80 mm Hg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently ≤ 130 mm Hg systolic and ≤ 80 mm Hg diastolic. (2D)



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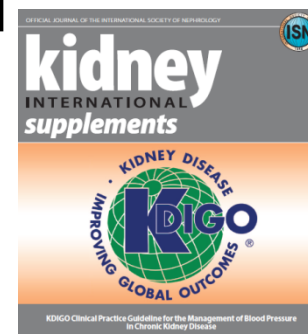


Blood Pressure

- 3.1.6:** We suggest that an ARB or ACE-I be used in diabetic adults with CKD and urine albumin excretion 30-300 mg/24 hours (or equivalent*). (2D)
- 3.1.7:** We recommend that an ARB or ACE-I be used in both diabetic and non-diabetic adults with CKD and urine albumin excretion >300 mg/24 hours (or equivalent*). (1B)
- 3.1.8:** There is insufficient evidence to recommend combining an ACE-I with ARBs to prevent progression of CKD. (*Not Graded*)



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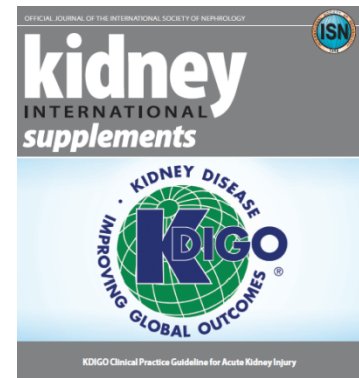
CDK Risk of AKI

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

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

See KDIGO Clinical Practice Guideline for
Acute Kidney Injury.

Kidney Int Suppl March 2012; Vol. 2 (1)



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Protein Intake

- 3.1.13:** We suggest lowering protein intake to 0.8 g/kg/day in adults with diabetes (2C) or without diabetes (2B) and GFR <30 ml/min/1.73m² (GFR categories G4-G5), with appropriate education.
- 3.1.14:** We suggest avoiding high protein intake (>1.3 g/kg/day) in adults with CKD at risk of progression. (2C)

Glycemic Control

- 3.1.15:** We recommend a target hemoglobin A1c (HbA1c) of ~7.0% (53 mmol/mol) to prevent or delay progression of the microvascular complications of diabetes, including diabetic kidney disease. (1A)
- 3.1.16:** We recommend not treating to an HbA1c target of <7.0% (<53 mmol/mol) in patients at risk of hypoglycemia. (1B)
- 3.1.17:** We suggest that target HbA1c be extended above 7.0% (53 mmol/mol) in individuals with comorbidities or limited life expectancy and risk of hypoglycemia. (2C)

Salt Intake

3.1.12: We recommend lowering salt intake to <90 mmol (<2 g) per day of sodium (corresponding to 5 g of sodium chloride) in adults, unless contraindicated. (1C)

KDIGO

Hyperuricemia

3.1.13: There is insufficient evidence to support or refute the use of agents to lower serum uric acid concentrations in people with CKD and either symptomatic or asymptomatic hyperuricemia in order to delay progression of CKD. (*Not Graded*)

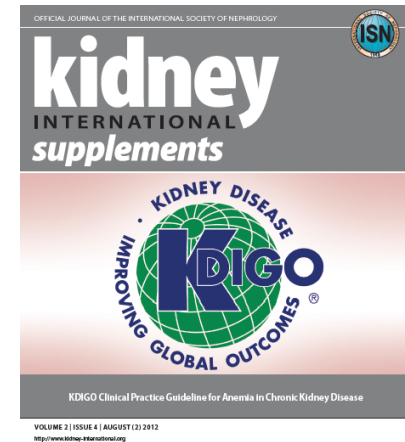
Lifestyle

3.1.14: We recommend that people with CKD be encouraged to take exercise (aiming for at least 30 minutes 5 times per week), achieve a healthy weight (BMI 20-25, according to country specific demographics), and stop smoking. (1D)

Anemia

- 3.2.3:** To identify anemia in people with CKD measure Hb concentration (*Not Graded*):
- when clinically indicated in people with GFR ≥ 60 ml/min/1.73 m² (GFR categories G1-G2);
 - at least annually in people with GFR 30-59 ml/min/1.73 m² (GFR categories G3a-G3b);
 - at least twice per year in people with GFR < 30 ml/min/1.73 m² (GFR categories G4-G5).

See KDIGO Clinical Practice Guideline for Anemia in CKD.
Kidney Int Suppl August 2012; Vol. 2(4)

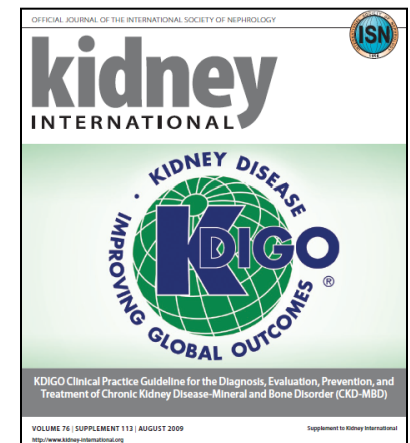


Kidney Disease: Improving Global Outcomes

Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD)

3.3.1: We recommend measuring serum levels of calcium, phosphate, PTH, and alkaline phosphatase activity at least once in adults with GFR <45 ml/min/1.73 m² (GFR categories G3b-G5) in order to determine baseline values and inform prediction equations if used. (1C)

See KDIGO Clinical Practice Guideline for the Diagnosis, Evaluation, Prevention, and Treatment of CKD-MBD 2009.
Kidney Int August 2009; Vol. 76 (Suppl 113)



Kidney Disease: Improving Global Outcomes

Acidosis

3.4.1: We suggest that in people with CKD and serum bicarbonate concentrations <22 mmol/l treatment with oral bicarbonate supplementation be given to maintain serum bicarbonate within the normal range, unless contraindicated. (2B)

SECTION 4: Other Complications of CKD

KDIGO



Kidney Disease: Improving Global Outcomes

Other Complications of CKD

- Cardiac and vascular disease (CVD)
- Medication dosage
- Patient safety
- Infections
- Hospitalizations
- Caveats for investigating complications

SECTION 5: Referral to Specialists and Models of Care



Kidney Disease: Improving Global Outcomes

When to refer to a specialist.

Albuminuria Categories(mg/g)		
A1	A2	A3
normal to increased	moderately increased	severely increased
10-29 mg/g (<3 mg/mmol)	30-299 mg/g (3-29 mg/mmol)	>300 mg/g (>30 mg/mmol)
	monitor	refer*
	monitor	refer*
monitor	monitor	refer
monitor	monitor	refer
refer*	refer*	refer
refer	refer	refer

GFR Categories (mL/min/ 1.73m ²)	G1	high and optimal	≥90
	G2	Mild reduction	60-89
	G3a	mild-moderate reduction	45-59
	G3b	moderate-severe reduction	30-44
	G4	Severe reduction	15-29
	G5	kidney failure	<15

Summary: Key Changes

- Diagnosis and classification:
 - Re-emphasise need for a diagnosis
 - Add albuminuria categories
 - Subdivide GFR category 3
- Define progression & preventive measures
- Interpretation of tests & use of medications
- Models of care



Thank you!