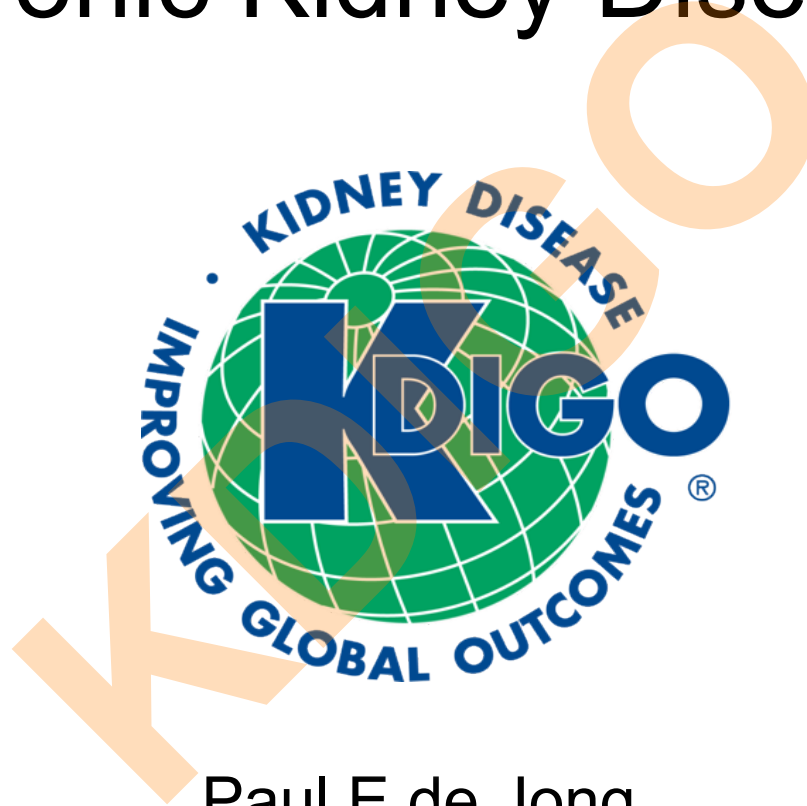# Evaluation of Chronic Kidney Disease

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Evaluation and Management of CKD

1. Definition and classification of CKD
2. Definition and impact of progressive CKD
3. The association between CKD and CVD
4. The treatment of progressive CKD
   early, later and pre – end stage interventions
5. Referral to specialist care

Evaluation and Management of CKD

1. **Definition and classification of CKD**
2. Definition and impact of progressive CKD
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4. The treatment of progressive CKD
   early, later and pre – end stage interventions
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Definition and classification of CKD

At present many health care systems advocate screening for CKD, especially in the elderly. Which percentage of the people with CKD is detected in 2011 (US data)?

1. 5% of the cases <65yr, and 12.5% of the cases >65yr

2. 10% of the cases <65yr, and 25% of the cases >65yr

3. 20% of the cases <65yr, and 50% of the cases >65yr

4. 30% of the cases <65yr, and 75% of the cases >65yr

Definition and classification of CKD

In elderly with diabetes, information on the level of albuminuria is available …

  1. twice as often as info on the level of GFR

  2. as frequent as info on the level of GFR

  3. in 2 out of the 3 subjects with info on GFR

  4. in 1 out of the 3 subjects with info on GFR

Definition and classification of CKD

With information on the level of GFR, but without info on the level of albuminuria, the risk associated with CKD can correctly be defined in

1. about 2 out of the 3 cases

2. about half of the cases

3. about 20% of the cases

4. less than 10% of the cases

CKD: abnormalities of kidney structure or function for >3 months, with implications for health

Criteria for CKD (either of the following present for >3 months)	
Markers of kidney damage (one or more)	Albuminuria (AER ≥30 mg/d; ACR ≥30 mg/g [≥3 mg/mmol])
	Urine sediment abnormalities
	Electrolyte and other abnormalities due to tubular disorders
	Abnormalities detected by histology
	Structural abnormalities detected by imaging
	History of kidney transplantation
Decreased GFR	GFR <60 ml/min/1.73 m^2

Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate.

Use the following albuminuria categories

		Albuminuria categories in CKD		
Category	AER	ACR (approximate equivalent)		Terms
	(mg/d)	(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/d [ACR >2220 mg/g; >220 mg/mmol]).

Use the following albuminuria categories

Albuminuria categories in CKD

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*Relative to young adult level.
**Including nephrotic syndrome (albumin excretion usually >2200 mg/d [ACR >2220 mg/g; >220 mg/mmol]).

The term "microalbuminuria" should no longer be used

Evaluation of CKD
measurement of albuminuria

We suggest the following measurement for initial screening on proteinuria in a morning spot urine sample (2B)

1. albumin-creatinine ratio (ACR)
2. protein-creatinine ratio (PCR)
3. strip for total protein with automatic reading
4. strip for total protein with manual reading

Evaluation of CKD
measurement of albuminuria

Confirm reagent strip positive albuminuria and proteinuria by quantitative measurement of ACR or PCR

Confirm ACR ≥30mg/g (≥3mg/mmol) in a random spot urine sample in a subsequent early morning urine sample

If a more accurate estimate is required, measure albumin or total protein excretion rate in a timed urine collection
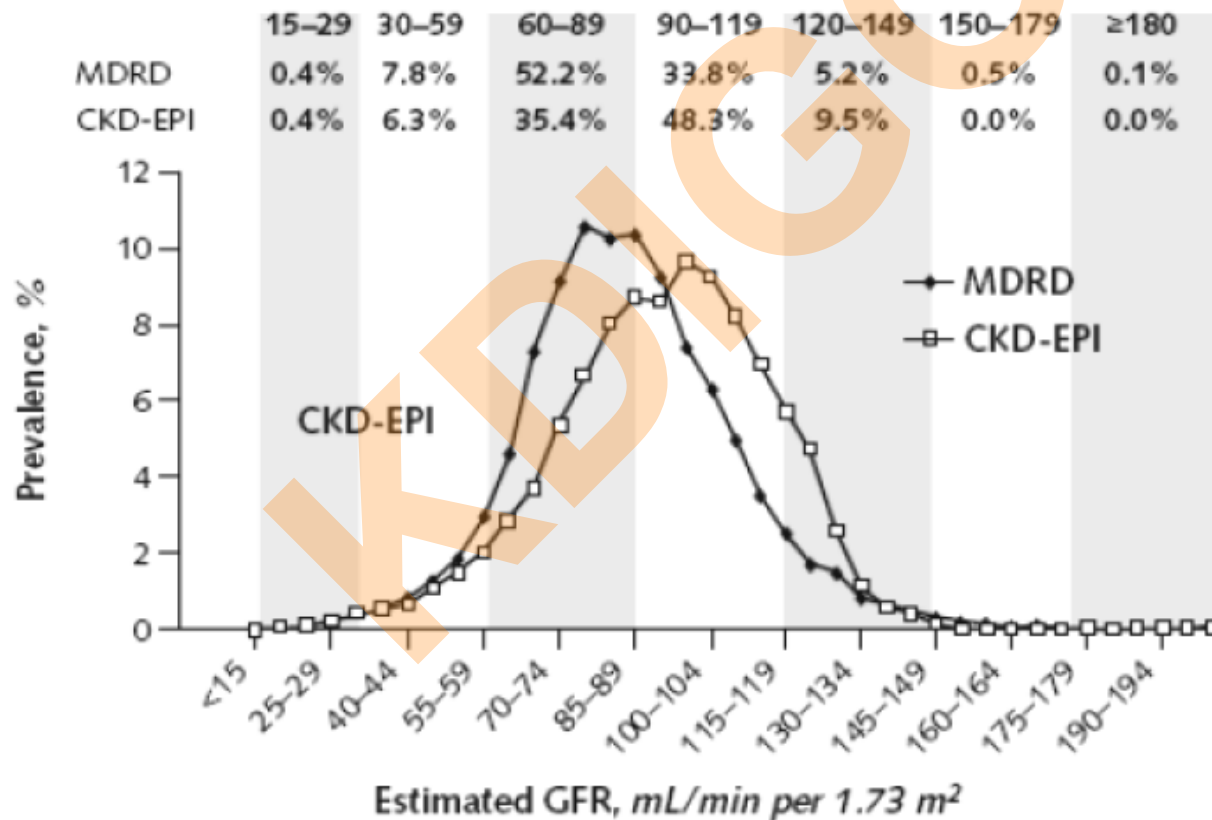
Use the following GFR categories

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

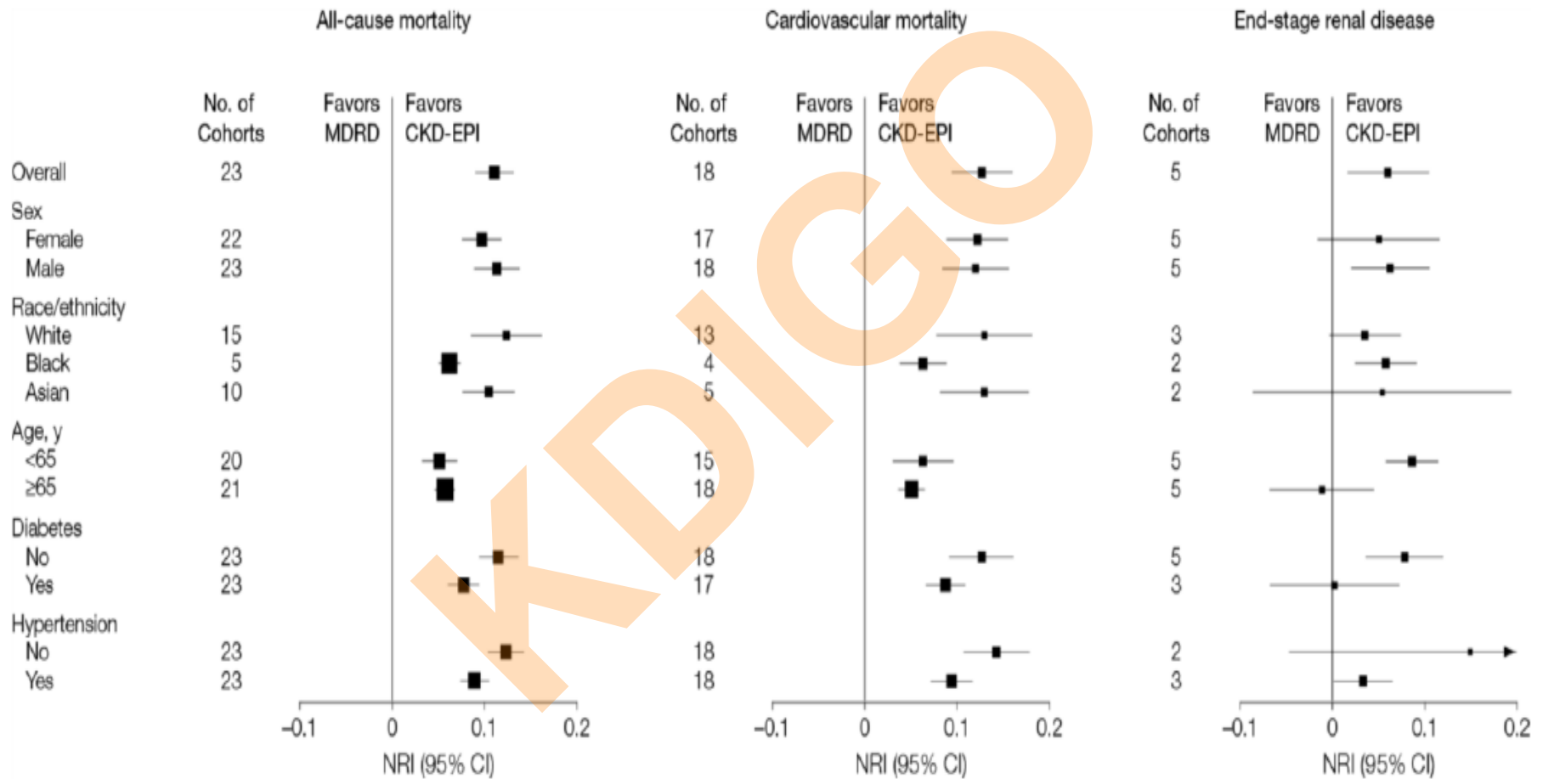G1 and G2 is defined CKD only in case of moderately or severely increased albuminuria

Evaluation of CKD - measurement of GFR

We recommend that laboratories report eGFR using the CKD-EPI creatinine equation (1B).

	15–29	30–59	60–89	90–119	120–149	150–179	≥180
MDRD	0.4%	7.8%	52.2%	33.8%	5.2%	0.5%	0.1%
CKD-EPI	0.4%	6.3%	35.4%	48.3%	9.5%	0.0%	0.0%

Levey AS et al. Ann Int Med 2009;150:604-612

Evaluation of CKD - measurement of GFR

Matsushita K et al. JAMA 2012;307:1941-51

The staging of CKD since 2002

GFR	normoalbuminuria	micro/macroalbuminuria
>90	No CKD	Stage 1
60-75	No CKD	Stage 2
30-60	Stage 3	Stage 3
15-30	Stage 4	Stage 4
<15	Stage 5	Stage 5

In 2002 no data on prognosis of the various stages

Risk perception in the old CKD staging system

GFR	normoalbuminuria	micro/macroalbuminuria
>90	No CKD	Stage 1
60-75		Stage 2
30-60	Stage 3	
15-30	Stage 4	
<15	Stage 5	

Stage 3 is expected to have higher risk than stage 1 and 2

Ranking for adjusted relative risk

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

Levey AS et a; Kidney Int 2011

*Meta-analysis of 45 cohorts
n=1.500.000 with 5 years of follow-up*

Staging of CKD since 2012

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

			Persistent albuminuria categories Description and range		
			A1	A2	A3
			Normal to mildly increased	Moderately increased	Severely increased
			<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
GFR categories (ml/min/ 1.73 m²) Description and range	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		

Levey AS et al. Kidney Int 2011;80:17-28

Better risk stratification with new CKD classification

KDOQI 2002

	normal <30 mg/g	micro 30-300 mg/g	macro ≥300 mg/g
≥90		stage 1	
60-89		stage 2	
45-59			
30-44		stage 3	
15-29		stage 4	
<15		stage 5	

KDIGO 2012

	normal <30 mg/g	moderate↑ 30-300 mg/g	severe ↑ ≥300 mg/g
≥90			
60-89		moderate risk	
45-59		high risk	
30-44			
15-29		very high risk	
<15			

% of US population by GFR and albuminuria classes according to 2012 classification

Risk class		normal <30 mg/g	moderate↑ 30-300 mg/g	severe ↑ ≥300 mg/g
Risk class	≥90		1.9	0.4
moderate (yellow) 7.7% (~70%)	60-89		2.2	0.3
	45-59	3.6	0.8	0.2
high (orange) 2.5% (~20%)	30-44	1.0	0.4	0.2
very high (red) 1.3% (~10%)	15-29	0.2	0.1	0.1
	<15	0.0	0.0	0.1

Levey AS et al. Kidney Int 2011;80:17-28

Overall CKD prevalence 11.5%

Probability of eGFR and albuminuria testing in Medicare patients at risk for CKD

USRDS, CKD Atlas 2013
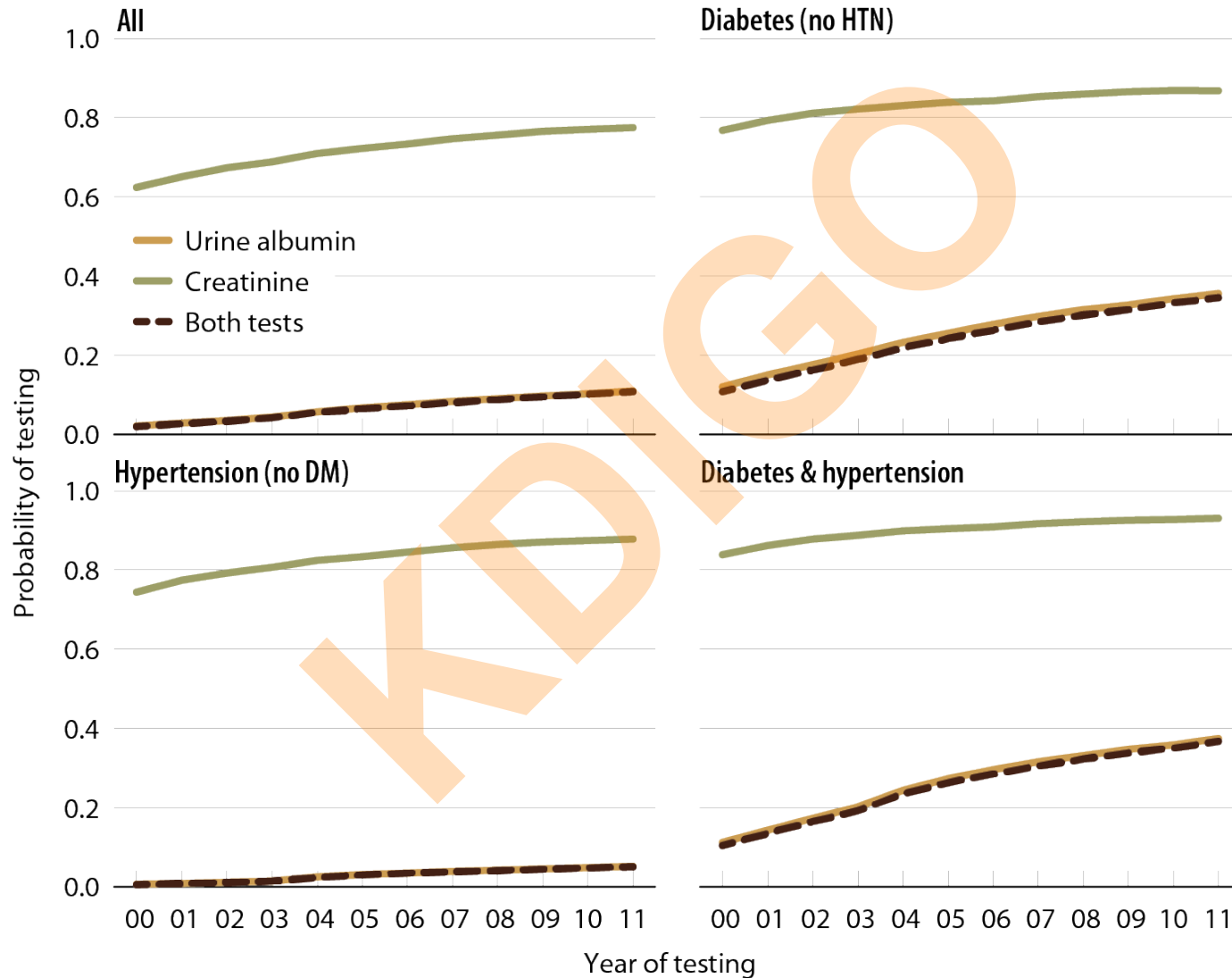
Prevalence (%) of recognized CKD is rising

age	65+	20-64	20-64
	Medicare	Truven Health MS	Clinformatics DataMart
2000	2.7	0.3	
2001	3.1	0.4	0.3
2002	3.4	0.5	0.4
2003	3.8	0.5	0.4
2004	4.2	0.5	0.5
2005	4.8	0.5	0.5
2006	5.9	0.6	0.6
2007	6.8	0.6	0.7
2008	7.6	0.7	0.7
2009	8.5	0.8	0.8
2010	9.2	0.8	0.9
2011	10.0	0.9	0.9

USRDS, CKD Atlas 2013

Prevalence of recognized CKD still insufficient

2011	65+ Medicare	20-64 Truven	20-64 Clinformatics	NHANES
20-44		0.4	0.4	6.5
45-54		0.8	1.0	8.4
55-64		1.9	2.1	15.3
65-74	6.9			29.1
75-74	12.2			49.5
85+	16.0			65.5

CKD is recognized in 10% of the cases <65yr, and in 25% of the cases >65yr (US data)

USRDS, CKD Atlas 2013

Prevalences of moderate (yellow), high (orange), and very high (red) risk

	<30 mg/g	30-300	≥300 mg/g
≥90		4.1	
60-89			0.7
45-59	3.6	0.8	0.2
30-44	1.0	0.4	0.2
15-29		0.5	
<15			

No albuminuria info: 4.8/11.5 (42%)
CKD will be missed

	<30 mg/g	30-300	≥300 mg/g
≥90			
60-89		4.1	0.7
45-59	3.6	0.8	0.2
30-44	1.0	0.4	0.2
15-29		0.5	
<15			

No albuminuria info: no risk classification in GFR 30-60

	<30 mg/g	30-300	≥300 mg/g
≥90		4.1	
60-89			0.7
45-59	3.6	0.8	0.2
30-44	1.0	0.4	0.2
15-29		0.5	
<15			

No albuminuria info: only GFR ≤30 well classified

	<30 mg/g	30-300	≥300 mg/g
≥90		4.1	
60-89			0.7
45-59	3.6	0.8	0.2
30-44	1.0	0.4	0.2
15-29		0.5	
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Definition and classification of CKD

At present many health care systems advocate screening for CKD, especially in the elderly. Which percentage of the people with CKD is detected in 2011 (US data)?

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4. 30% of the cases <65yr, and 75% of the cases >65yr

Definition and classification of CKD

In elderly with diabetes, information on the level of albuminuria is available …

1. twice as often as info on the level of GFR

2. as frequent as info on the level of GFR

3. in 2 out of the 3 subjects with info on GFR

4. in 1 out of the 3 subjects with info on GFR

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With information on the level of GFR, but without info on the level of albuminuria, the risk associated with CKD can correctly be defined in

1. about 2 out of the 3 cases

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Evaluation and Management of CKD

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3. The association between CKD and CVD
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   early, later and pre – end stage interventions
5. Referral to specialist care

Definition and impact of progressive CKD

Which of the following statements on progressive CKD is not correct?

1. A fall in GFR >-30% in 2 years is comparable to a slope in GFR >-5 ml/min/1.73m^2/yr

2. A fall in GFR >-30% in 2 years is observed in <5% of the subjects with a baseline GFR <60 ml/min/1.73m^2

3. A fall in GFR >-30% in 2 years is associated with an increased risk for ESRD and for mortality, independent of baseline GFR

4. A fall in GFR >-30% is suggested to be an alternative endpoint in clinical trials on renoprotective therapies

Definition of CKD progression

Assess GFR/albuminuria at least annually in people with CKD, and more often in people with higher risk

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 >30 mg/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).

Levey AS et al. Kidney Int 2011;80:17-28

Progression of CKD

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

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	G5	Kidney failure	<15			

Levey AS et al. Kidney Int 2011;80:17-28

Definition of Progression of CKD

→ a decline in GFR category (per 15ml/min/1.73m^2), accompanied by a 25% or more drop in GFR

or

a slope of minus 5 ml/min/1.73m^2/year or more

→ it is to be studied whether progression should also be defined as a rise in albuminuria category, accompanied by a 100% or more rise in albuminuria

Risk of % change/2yr or slope of GFR for ESRD

baseline eGFR <60ml/min/1.73m²
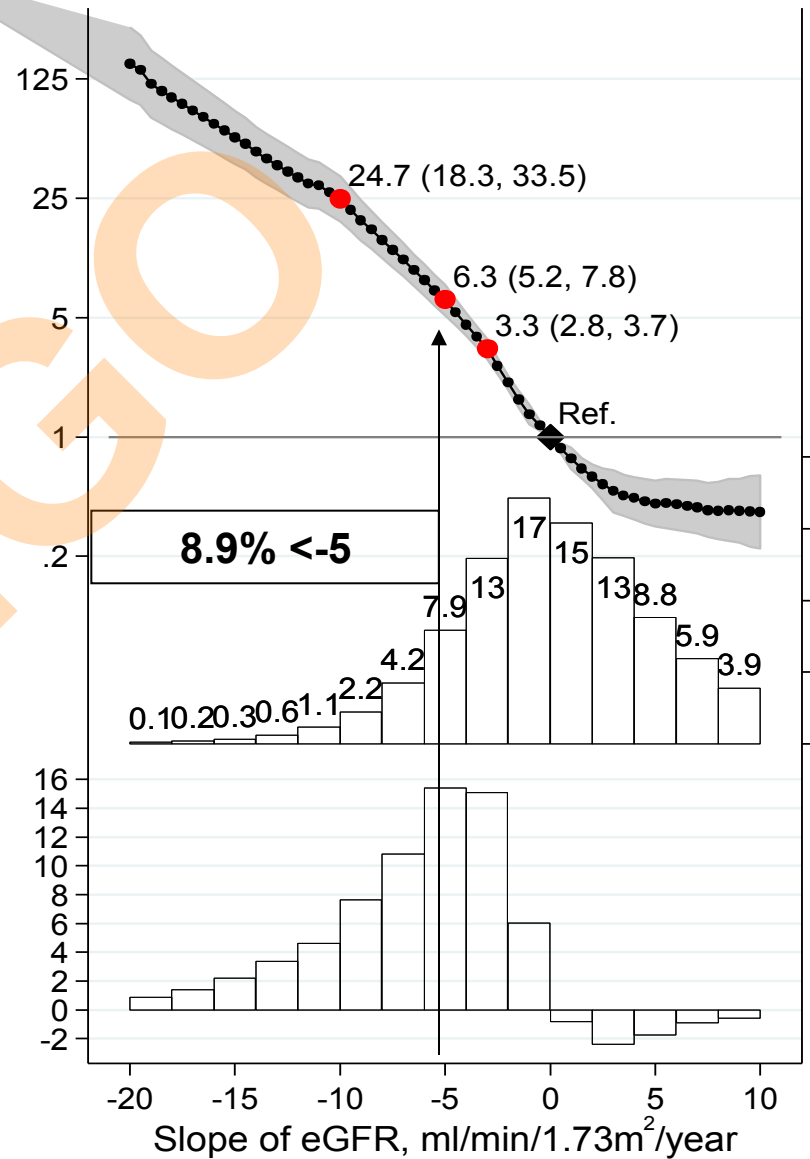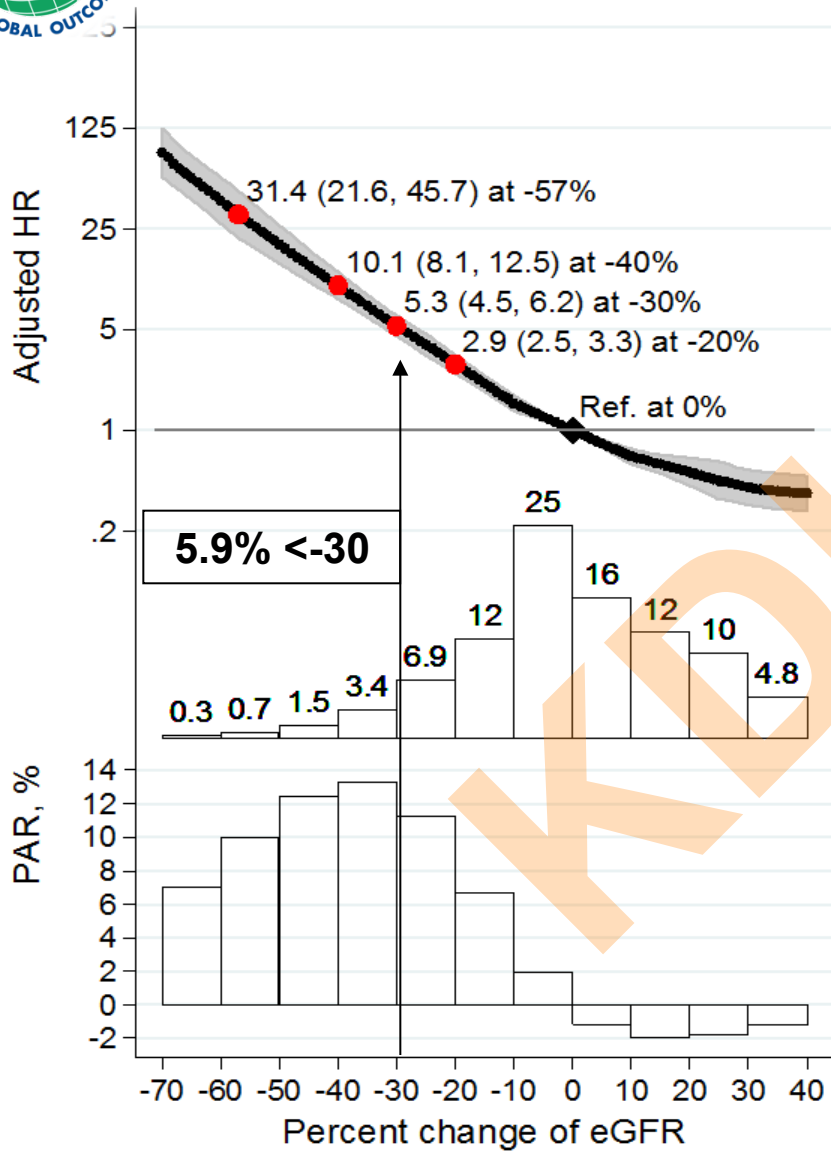
Definition and impact of progressive CKD

Which of the following statements on progressive CKD is <u>not</u> correct?

1. A fall in GFR >-30% in 2 years is comparable to a slope in GFR >-5 ml/min/1.73m^2/yr

2. **A fall in GFR >-30% in 2 years is observed in <5% of the subjects with a baseline GFR <60 ml/min/1.73m^2**

3. A fall in GFR >-30% in 2 years is associated with an increased risk for ESRD and for mortality, independent of baseline GFR

4. A fall in GFR >-30% is suggested to be an alternative endpoint in clinical trials on renoprotective therapies

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The association of CKD and CVD

Which of the following statements is correct?

1. GFR and albuminuria are independently associated with an increased risk for both ESRD and CVD

2. The above associations are more steep for CVD than for ESRD

3. The above associations depend on the presence of diabetes and/or hypertension

4. The above associations depend on age and ethnicity

CV/renal prognosis related to GFR and ACR

Summary of Relative Risks from Continuous Meta-Analysis

Matsushita K et al, Lancet 2010;375:2073-81 and Gansevoort RT et al Kidney Int 2011;80:93-104
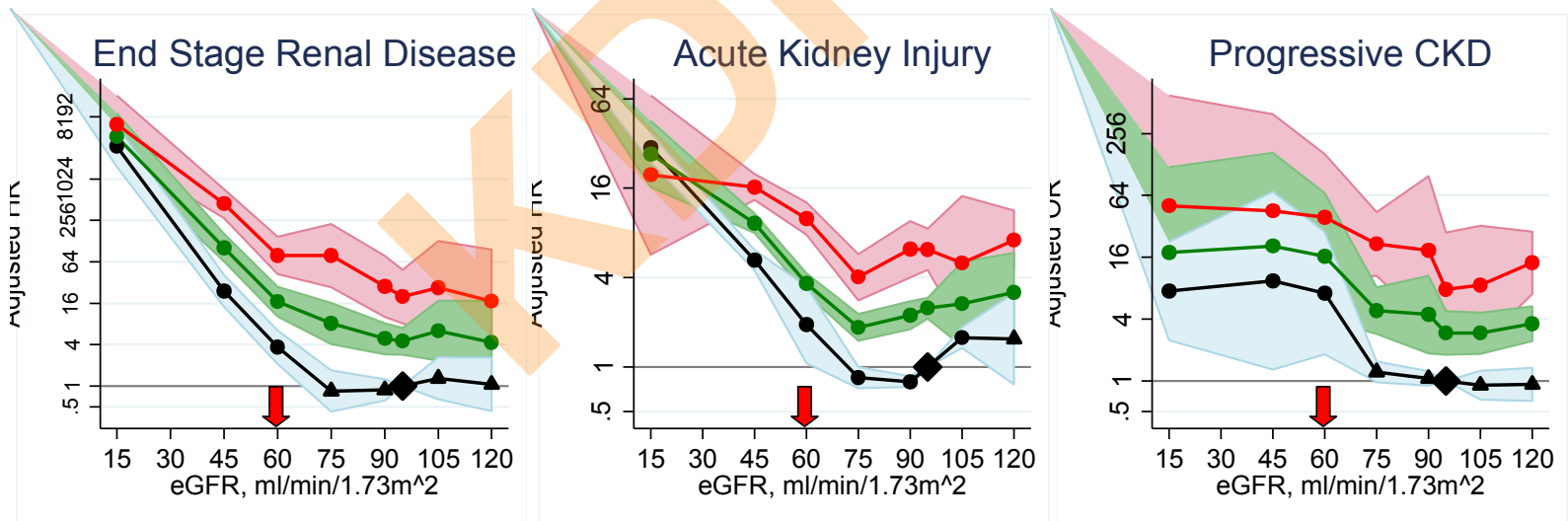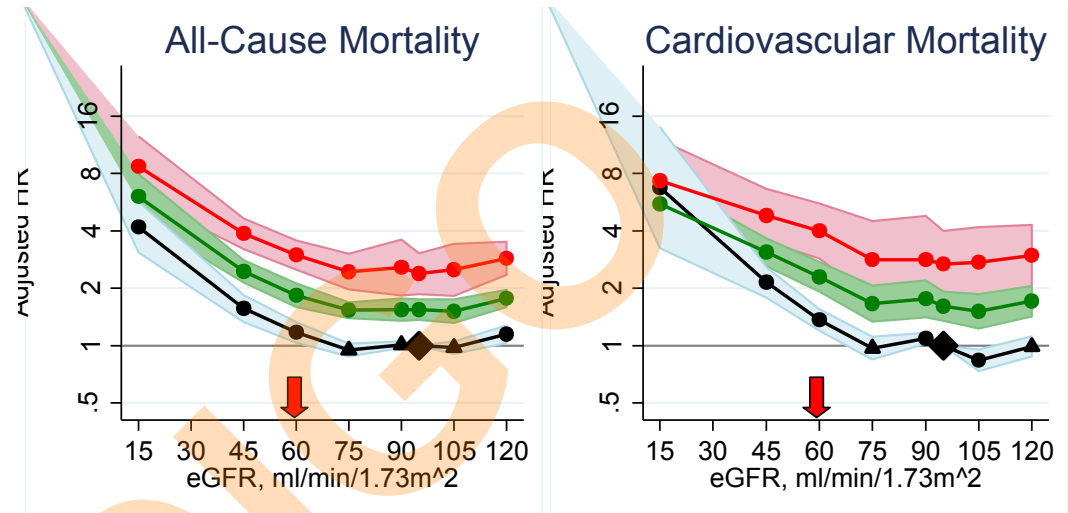
Mortality Rates (top) and adjusted HR (bottom) of GFR (left) and ACR (right) in age subgroups

Hallan SI et al for the CKD-PC consortium, JAMA 2012; 308:2349-60
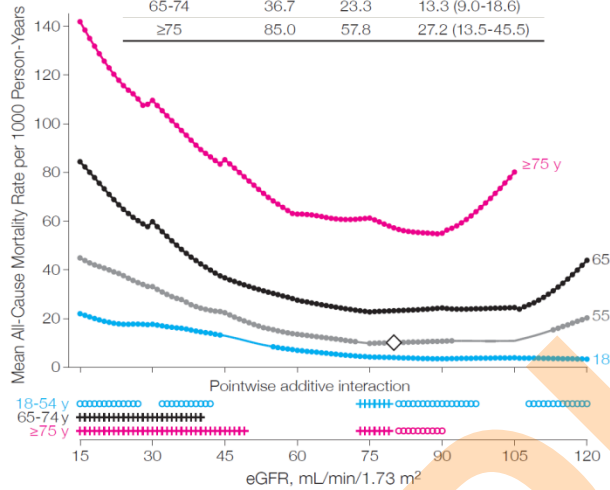
Adjusted HR of GFR and ACR with mortality in Asians (green), Whites (black) and Blacks (red)
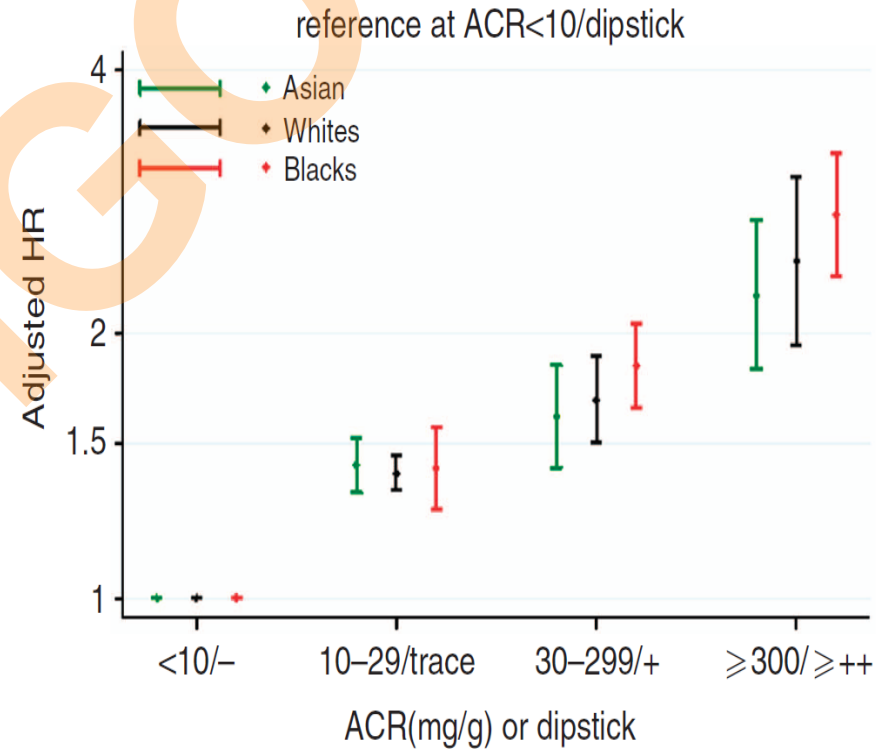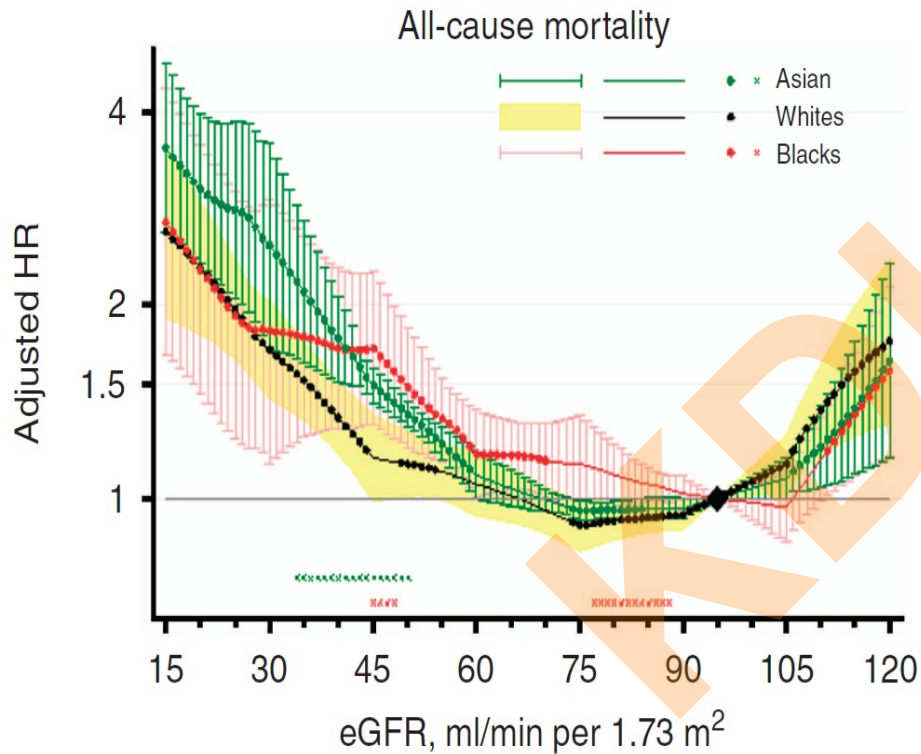
Associations of GFR and ACR with ESRD in diabetes vs non diabetes

Fox et al. for the CKD-PC consortium. Lancet 2012;380:1662-73
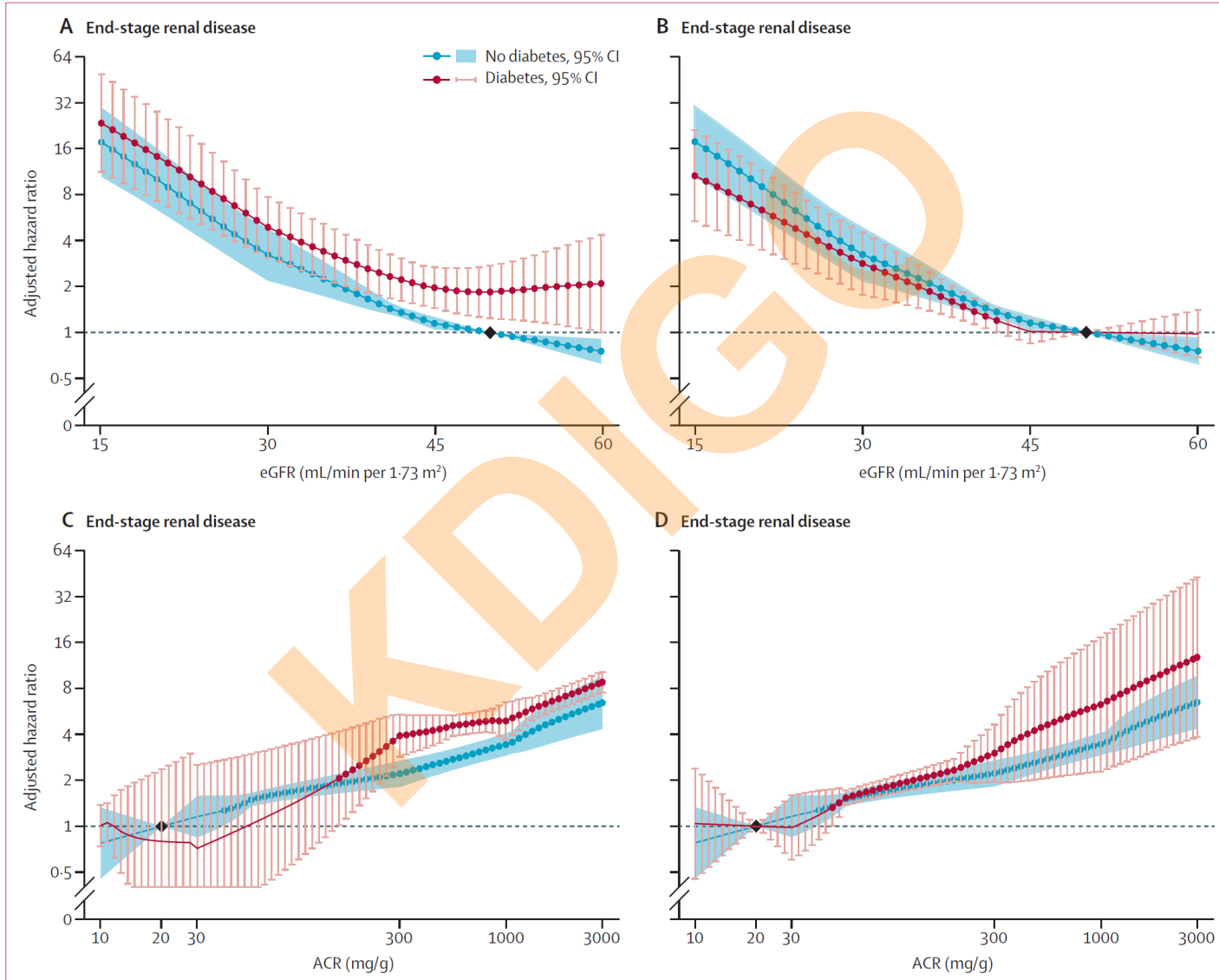
Associations of GFR and ACR with ESRD in hypertensives vs non-hypertensives
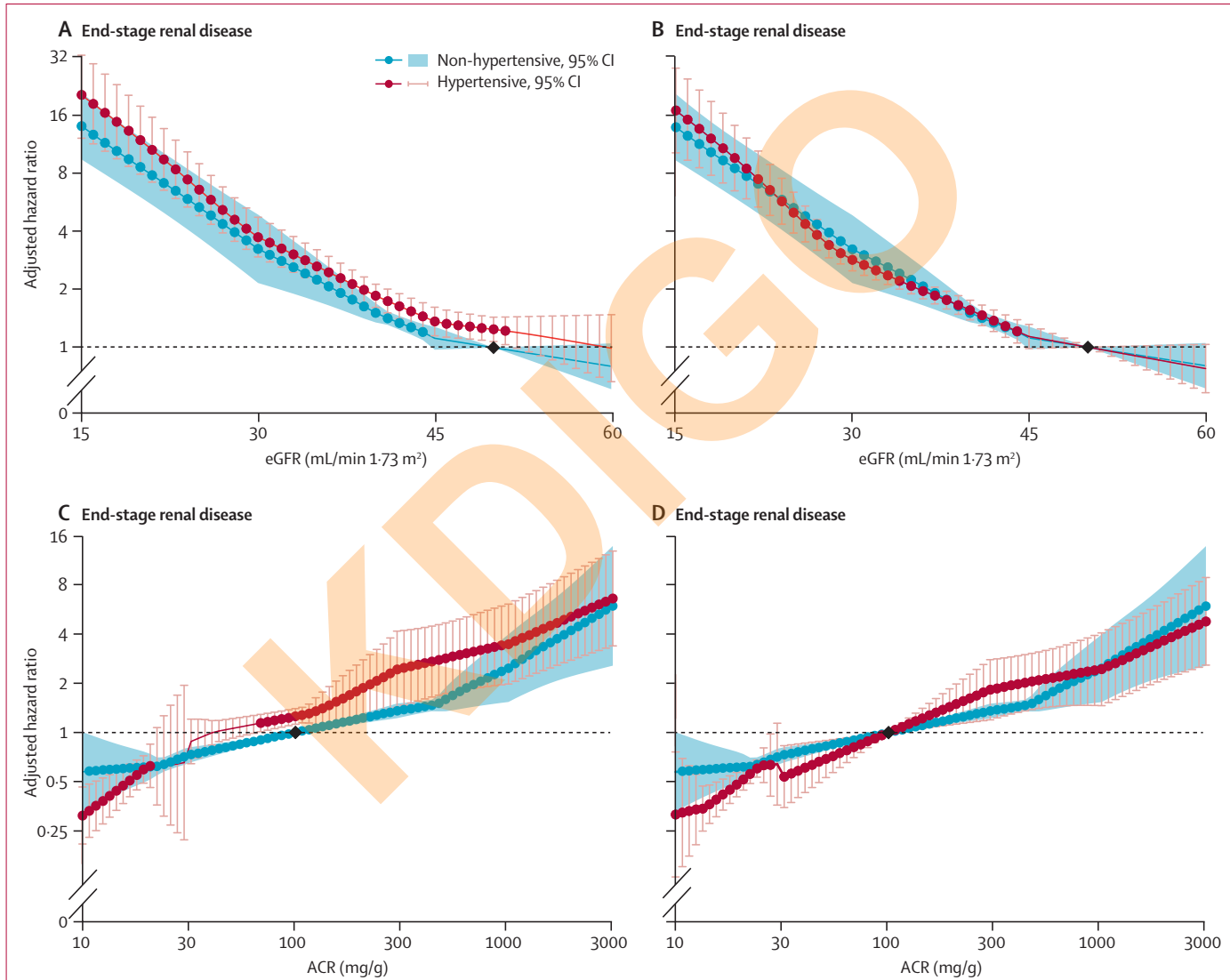
Mahmoodi et al for the CKD-PC Consortium. Lancet 2012; 380: 1649–61

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4. The above associations depend on age and ethnicity

Take home messages

- The new CKD classification includes 3 albuminuria classes in all GFR strata

- This classification affords better risk stratification

- However, detection of increased albuminuria thusfar stays far behind detection of impaired GFR

- Progression of CKD can be defined as a 30% loss of GFR

- CKD is associated with a worse CV and renal prognosis, in all ages, in all ethnicities, in diabetes and non-diabetes, and in hypertension and non-hypertension

Thanks for your attention

www.kdigo.org

The KDIGO grading system

	Patients	**Clinicians**	**Policy**
Grade 1 **We recommend**	Most people in your situation want the action,	Most patients should receive the action, only a few not	The recommendation can be used as policy or performance measure
Grade 2 **We suggest**	The majority of people in your situation want the action, but many not	Different choices are appropriate Decide in line with patient preferences	Debate is required before recommendation can be used as policy or performance measure

Grade	Evidence	Meaning
A	**high**	the true effect lies close to the estimate of the effect
B	**moderate**	the true effect may be close to the estimate, but may be different
C	**low**	the true effect may be substantially different from the estimate
D	**very low**	the estimate of effect is very uncertain, and often far from truth