HIRSLANDEN
KLINIK LINDE
CLINIQUE DES TILLEULS

DIAGNOSTIC DE L'INSUFFISANCE RÉNALE
DIAGNOSE VON NIERENINSUFFIZIENZ

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LINDE TILLEULS ACADEMY

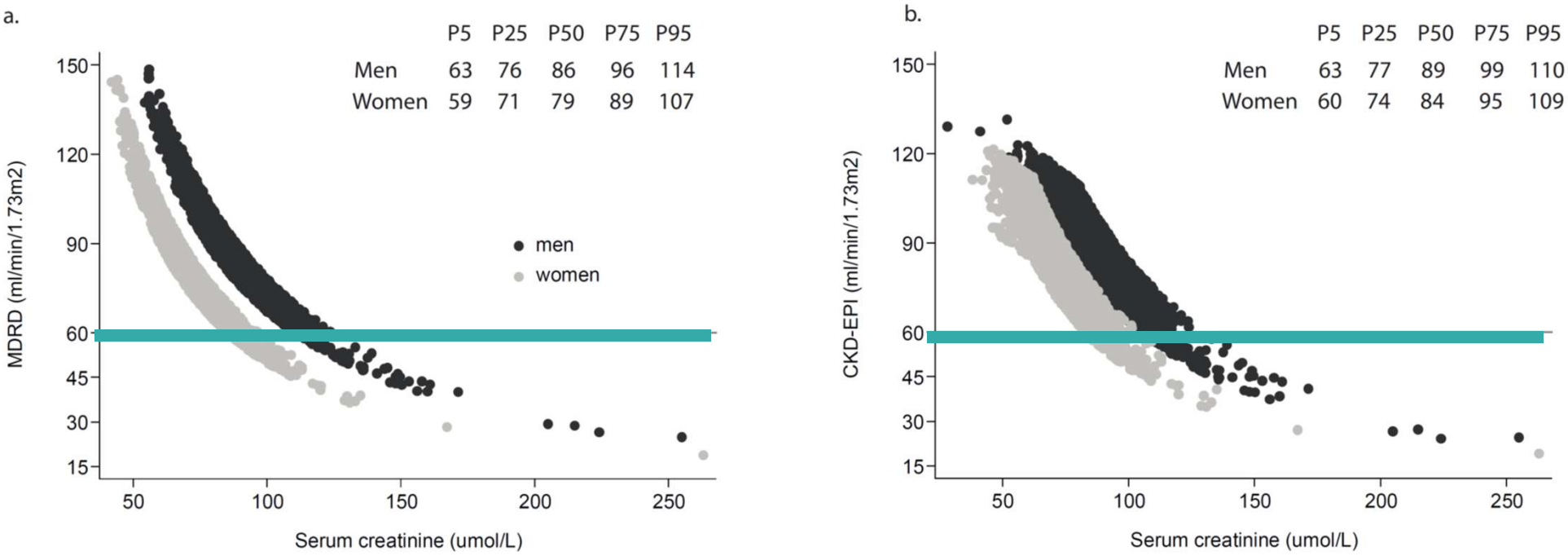
FOCUS ON CKD AND NOT AKI

Stage	Serum creatinine	Urine output
1	1.5–1.9 times baseline OR X0.3 mg/dl (≥ 26.5 mmol/l) increase	<0.5 ml/kg/h for 6–12 hours
2	2.0–2.9 times baseline	<0.5 ml/kg/h for ≥ 12 hours
3	3.0 times baseline OR Increase in serum creatinine to X4.0 mg/dl (X353.6 mmol/l) OR Initiation of renal replacement therapy OR, In patients o18 years, decrease in eGFR to o35 ml/min per 1.73 m	<0.3 ml/kg/h for ≥ 24 hours OR Anuria for X12 hours

DO YOU KNOW THE PREVALENCE OF CKD IN SWITZERLAND

- 50%
- 20 %
- 10%
- 1%

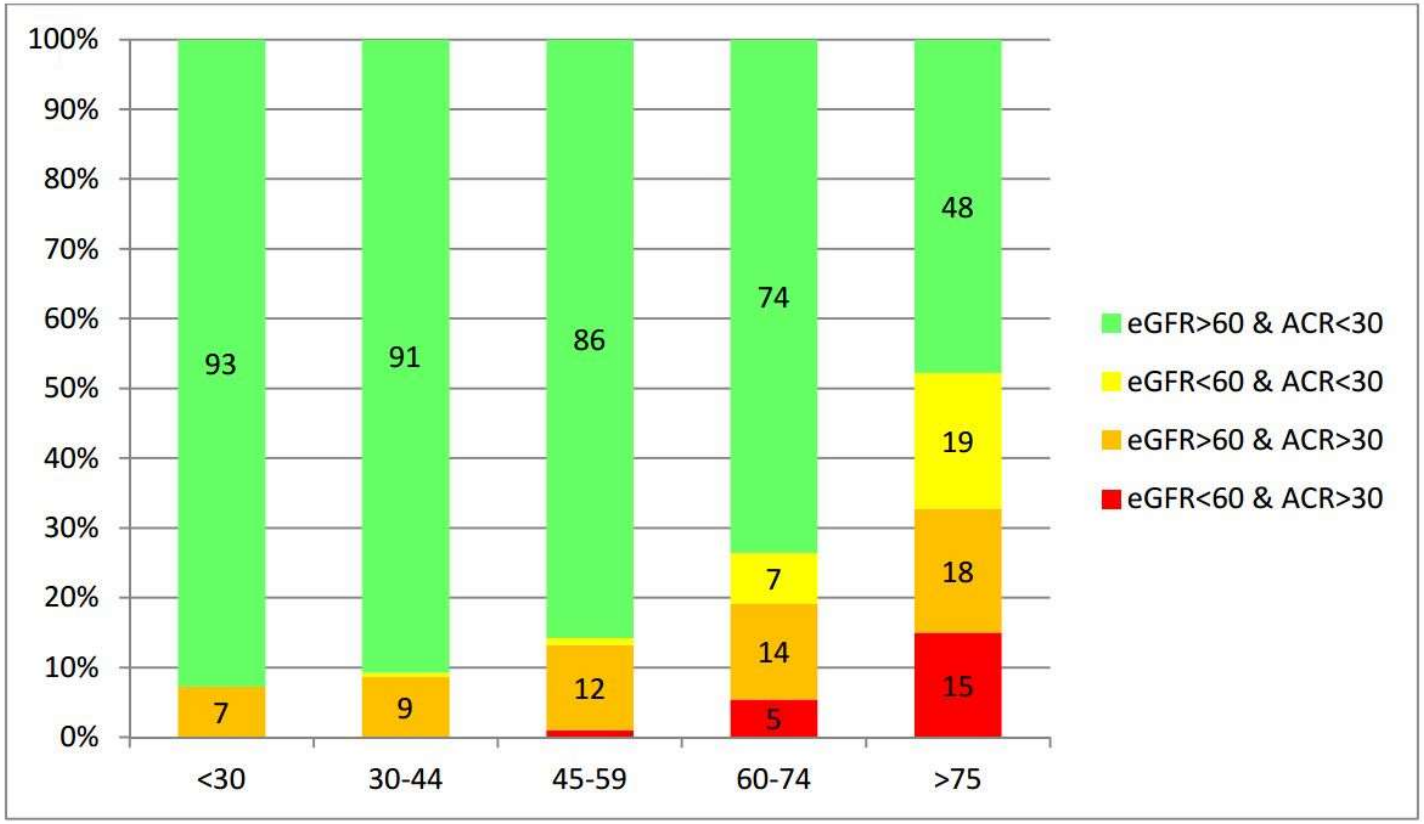
PREVALENCE OF CKD IN LAUSANNE: ÉTUDE COLAUS



Prevalence : ~10%

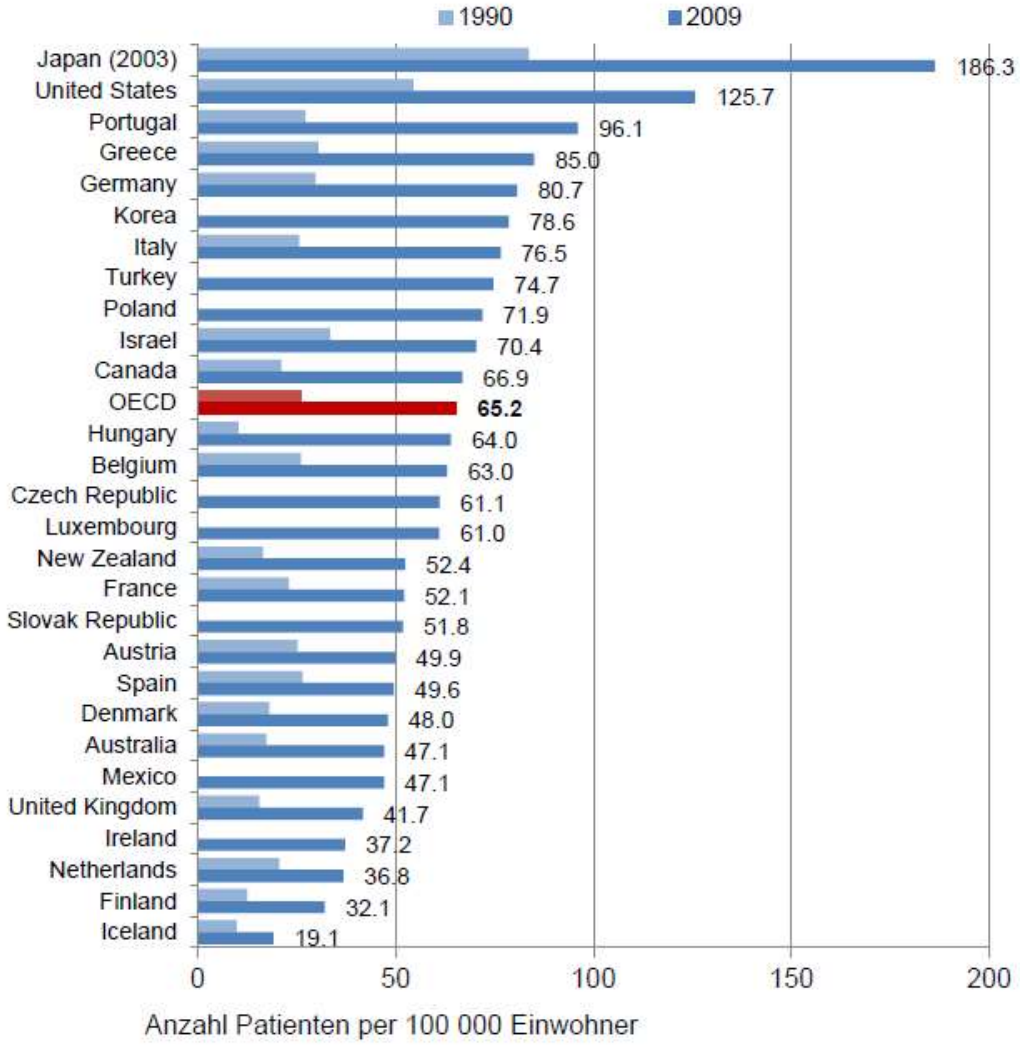
Ponte B, Pruijm M, Bochud M, NDT 2013

PREVALENCE OF CHRONIC KIDNEY DISEASE ACCORDING TO AGE CATEGORY IN A SWISS PRIMARY CARE SETTING



Tomonaga Y et al, PLoS One. 2013 Jul 3;8(7):e67848.

La Suisse:



Nombre de patients dialysés par 100’000

Source: www.svk.ch

CLINICAL CASE

- Status: Poids 92 Kg, taille 1.63 m, TA au cabinet médical : 139/88 mmHg (manchette large, moyenne de 3 mesures)
- Lab: FBC normal, Creatinine 104 µmol/L , K:4.9 mmol/L, HbA1c: 7.8%, Total cholesterol 6.4 mmol/L
- Urinary dipstickBandelette urinaire: protein trace
- UACR: 35.9 mg/mmol

GFR ESTIMATION: WHAT SHOULD YOU USE

- Creatinine ?
- Cystatine C ?
- MDRD ?
- CKD-EPI ?
- CKD-EPI cystatin C ?
- CKD-EPI creatinine cystatin C ?

DEFINITION OF CKD

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

CKD is classified based on cause, GFR category, and albuminuria category (CGA).

1. Kidney damage, with or without decreased GFR, as defined by
    - pathologic abnormalities
    - markers of kidney damage, including abnormalities in the composition of the blood or urine or abnormalities in imaging tests
2. GFR <60 ml/min/1.73 m^2, with or without kidney damage

CLASSIFICATION ACCORDING TO GFR AND ALBUMINURIA CATEGORIES

Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012

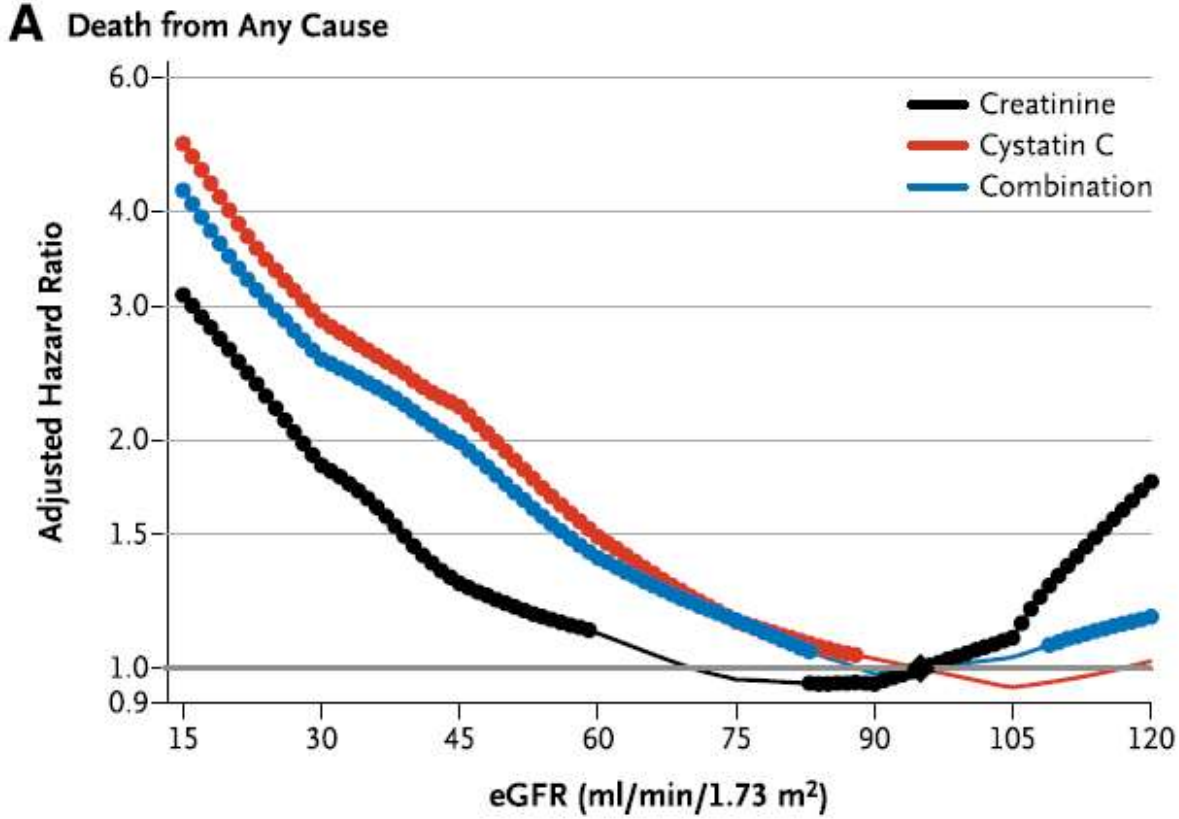
GFR categories (ml/min/1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				< 30 mg/g < 3 mg/mmol	30–300 mg/g 3–30 mg/mmol	> 300 mg/g > 30 mg/mmol
	G1	Normal or high	≥ 90			
	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.

EVALUATION OF GFR

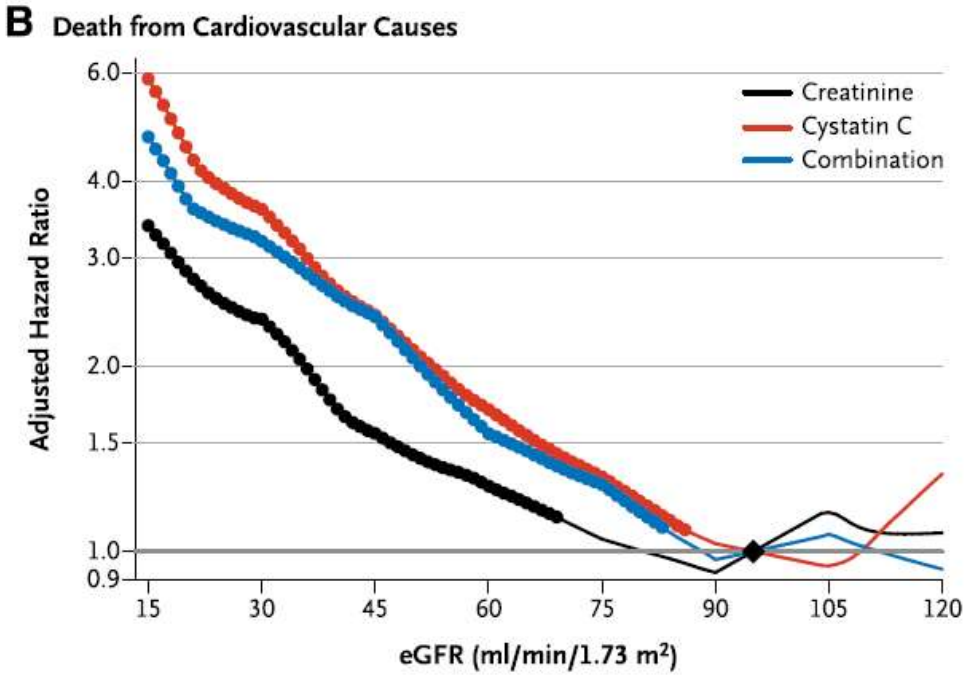
- 1.4.3.1: We recommend using serum creatinine and a GFR estimating equation for initial assessment. (1A)
- 1.4.3.2: We suggest using additional tests (such as cystatin C or a clearance measurement) for confirmatory testing in specific circumstances when eGFR based on serum creatinine is less accurate. (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.

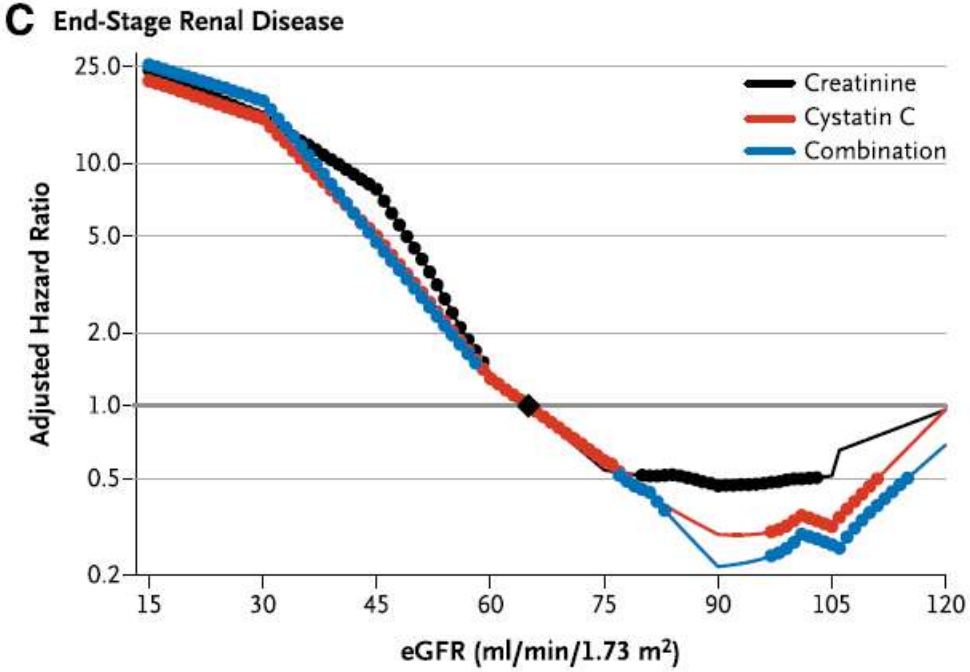
PREDICTIVE RISK OF DEATH: COMPARISON OF 3 CKD-EDI FORMULAS



Shlipak MG et al. N Engl J Med 369: 2459, 2013

PREDICTIVE RISK OF DEATH OF CARDIOVASCULAR CAUSES AND RISK OF END-STAGE RENAL DISEASE





Shlipak MG et al. N Engl J Med 369: 2459, 2013

WHEN SHOULD YOU USE CYSTATIN C

- 1.4.3.5: We suggest measuring cystatin C in adults with eGFRcreat 45–59 ml/min/1.73 m2 who do not have markers of kidney damage if confirmation of CKD is required. (2C)
- If eGFRcys/eGFRcreat-cys is also < 60 ml/min/1.73 m2 , the diagnosis of CKD is confirmed.
- If eGFRcys/eGFRcreat-cys is ≥ 60 ml/min/1.73 m2 , the diagnosis of CKD is not confirmed.

SOURCES OF ERROR IN GFR ESTIMATING 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.

SOURCES OF ERROR IN GFR ESTIMATING USING CYSTATINE C

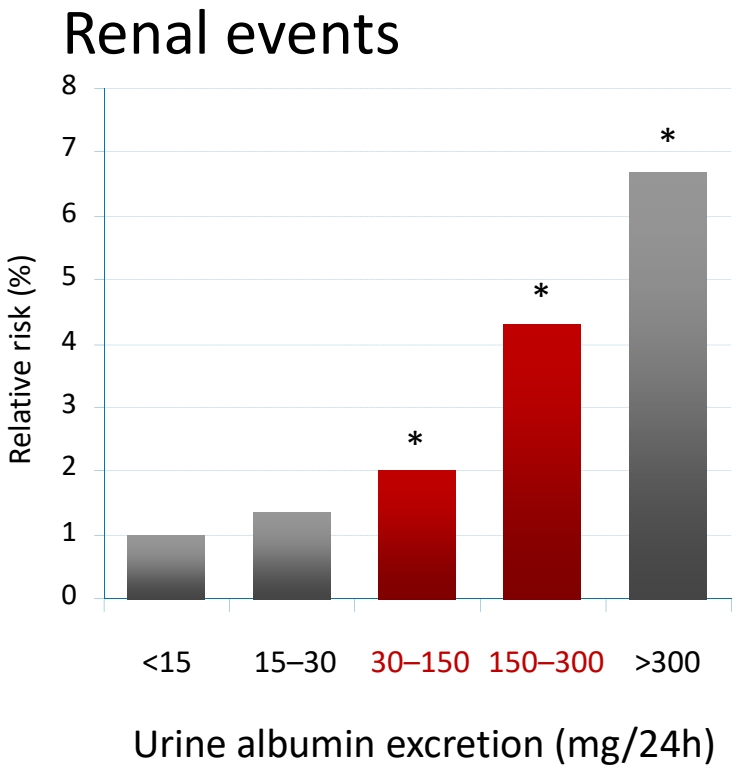
Source of error	Example
Non-steady state	• AKI
Non-GFR determinants of SCysC that differ from study populations in which equations were developed	
Factors affecting cystatin C generation	• Race/ethnicity other than US and European black and white • Disorders of thyroid function • Administration of corticosteroids • Other hypothesized factors based on epidemiologic associations (diabetes, adiposity)
Factors affecting tubular reabosrption of cystatin C	None identified
Factors affecting extra-renal elimination of cystatin C	Increased by severe decrease in GFR
Higher GFR	• Higher biological variability in non-GFR determinants relative to GFR • Higher measurement error in SCysC and GFR
Interference with cystatin C assay	• Heterophilic antibodies

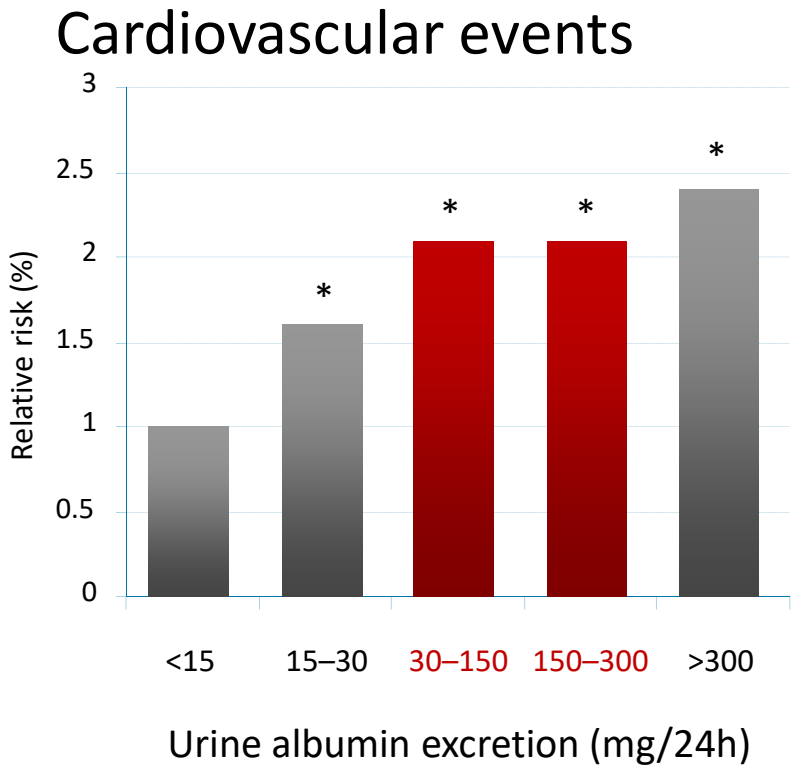
Abbreviations: AKI, acute kidney injury; GFR, glomerular filtration rate, SCysC, serum cystatin C.

FACTORS AFFECTING MICROALBUMINURIA

- Exercise
- Fever
- Elevated meat consumptiom
- Urinary tract infection/ menstruations
- Tobacco smoking

PRESENCE OF MICROALBUMINURIA PREDICTS THE OCCURENCE OF RENAL AND CV ENVENTS





•P < 0.05 vs. UAE <15 mg/24h.

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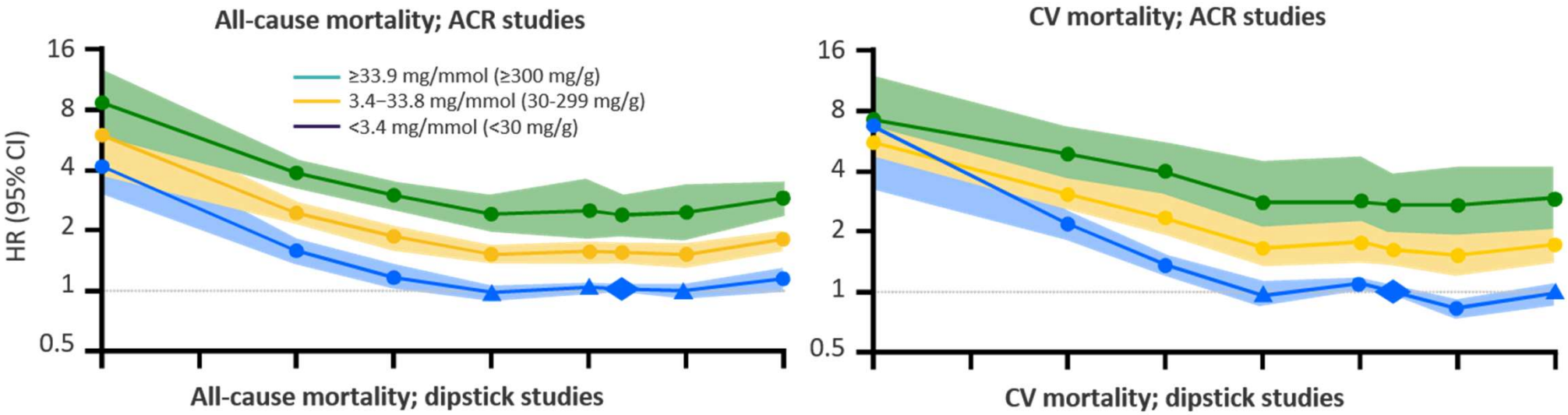
Gansevoort and Jong, JASN. 2009;20:465–468.

HRS AND 95% CIS FOR ALL-CAUSE AND CV MORTALITY ACCORDING TO SPLINE EGFR AND CATEGORICAL ALBUMINURIA



Shaded areas represent 95% CIs. Models included spline eGFR, categorical albuminuria, and their interaction terms as well as adjustment for age, sex, ethnic origin, history of CV disease, SBP, diabetes, smoking, and total cholesterol. The reference (diamond) was eGFR 95 mL/min/1.73 m² plus ACR less than 3.4 mg/mmol (30 mg/g) or dipstick test result negative or trace. Circles represent statistically significant and triangles represent not significant.

Chronic Kidney Disease Prognosis Consortium. Lancet 2010;375:2073–81

AVAILABILITY, PROGNOSTIC VALUE AND COST OF SOME MARKERS OF ORGAN DAMAGE

Markers	CV predicitive value	Availability	Cost
Electrocardiography	++	++++	+
Echocardiography	+++	+++	++
Carotid Intima-Media Thickness	+++	+++	++
Arterial stiffness [Pulse wave velocity]	+++	+	++
Ankle-Brachial index	++	++	+
Coronary calcium content	+	+	++++
Cardiac/Vascular tissue composition	?	+	++
Circulatory collagen markers	?	+	++
Endothelial dysfunction	++	+	+++
Cerebral lacunae/White matter lesions	?		++++
Est. Glomerular Filtration Rate or Creatinine Clearance	+++	++++	+
Microalbuminuria	+++	++++	+

ESH-ESC Practice Guidelines.Journal of Hypertension 2007, 25:1751–1762

FOR OUR PATIENT:
104 ЦMOL/L CRÉATININE, 1.1 MG/L CYSTATINE C

Results

CKD-EPI creatinine equation (2009)	55	mL/min/1.73m^2
CKD-EPI creatinine-cystatin equation (2012)	59	mL/min/1.73m^2
CKD-EPI cystatin C equation (2012)	62	mL/min/1.73m^2
MDRD study equation	55	mL/min/1.73m^2

https://www.kidney.org/professionals/KDOQI/gfr_calculator

TAKE HOME MESSAGES

- CKD is not rare
- Always measure albuminuria in addition to creatinine
- Use the CKD-EPI formula
- Use Cystatine C in some situation
- Remember the limits of creatinine in acute situation

PREVALENCE OF CKD IN US: NKF/KDOQI CLASSIFICATION

Table 1. Stages of Chronic Kidney Disease and Prevalence in Adults.*

Stage	Description	Estimated GFR†	Prevalence	No. of Patients
		ml/min/1.73 m²	%	*millions*
I	Kidney damage with normal or increased GFR	>90	1.78	3.6
II	Kidney damage with small decrease in GFR	60–89	3.24	6.5
III	Kidney damage with moderate decrease in GFR	30–59	7.69	15.5
IV	Kidney damage with large decrease in GFR	15–29	0.35	0.7
V	Kidney failure with need for dialysis (end-stage renal disease)	<15	0.25	0.5

* Data are from National Kidney Foundation guidelines,[1] Coresh et al.,[2] and the U.S. Renal Data System.[3]

† The abbreviated Modification of Diet in Renal Disease (MDRD) formula was used to estimate the glomerular filtration rate (GFR).[1,2,4]

Abboud H, NEJM 2010; 56-65.

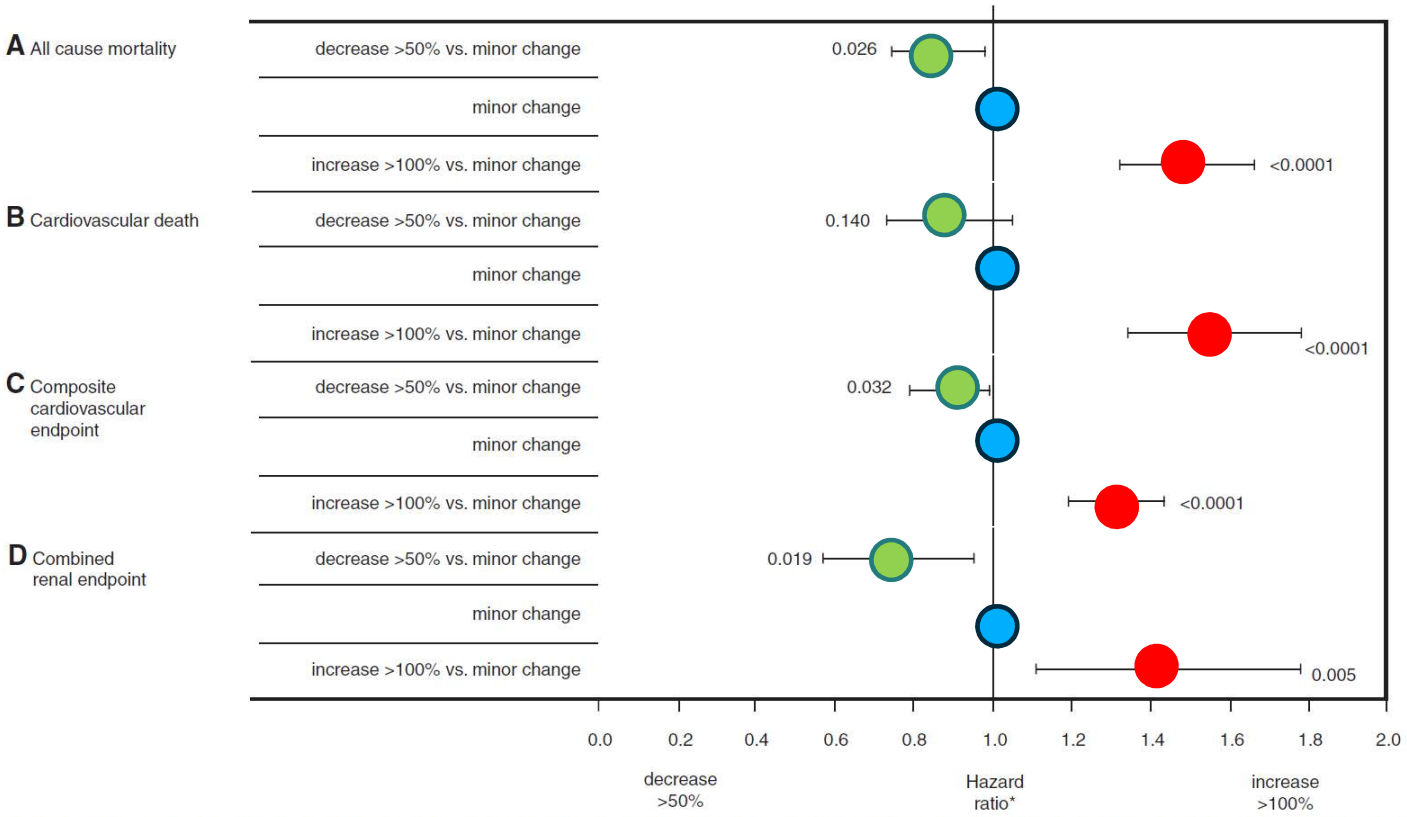
MICROALBUMINURIA AS MARKER OF GENERALIZED VASCULAR DYSFUNCTION

Associated with:

- Lipid abnormalities
- Reduced insulin sensitivity
- Impaired endothelial function
- Peripheral vascular disease
- A prothrombic state

Jones SL et al.Br Med J 1989;298:487–490.
Yip J et al.Lancet 1993;342:883–887.
Stehouwer CD et al. Diabetes 2002;51:1157–1165.
Knobl P et a. Diabetologia 1993;36:1045–1050.

ADJUSTED HR OF CHANGES IN UACR FROM BASELINE TO 2-YEAR VISIT



Schmieder, R. E. et al. (2011). J ASN. **22(7): 1353-1364.**

PREVALENCE OF CKD AND ESTIMATED NUMBER OF ADULTS WITH CKD IN THE US (NHANES 88-94)

Stage	Description	GFR (ml/min/1.73 m^2)	Prevalence*	
			N (1000s)	%
1	Kidney Damage with Normal or ↑ GFR	≥ 90	5,900	3.3
2	Kidney Damage with Mild ↓ GFR	60-89	5,300	3.0
3	Moderate ↓ GFR	30-59	7,600	4.3
4	Severe ↓ GFR	15-29	400	0.2
5	Kidney Failure	< 15 or Dialysis	300	0.1

*Stages 1-4 from NHANES III (1988-1994). Population of 177 million with age ≥20. Stage 5 from USRDS (1998), includes approximately 230,000 patients treated by dialysis, and assuming 70,000 additional patients not on dialysis. GFR estimated from serum creatinine using MDRD Study equation based on age, gender, race and calibration for serum creatinine. For Stage 1 and 2, kidney damage estimated by spot albumin-to-creatinine ratio ≥17 mg/g in men or ≥25 mg/g in women in two measurements.