ORDINE DEI MEDICI CHIRURGHI
E DEGLI ODONTOIATRI
DELLA PROVINCIA DI PARMA

MICROALBUMINURIA
COME MARCATORE DI RISCHIO CARDIOVASCOLARE

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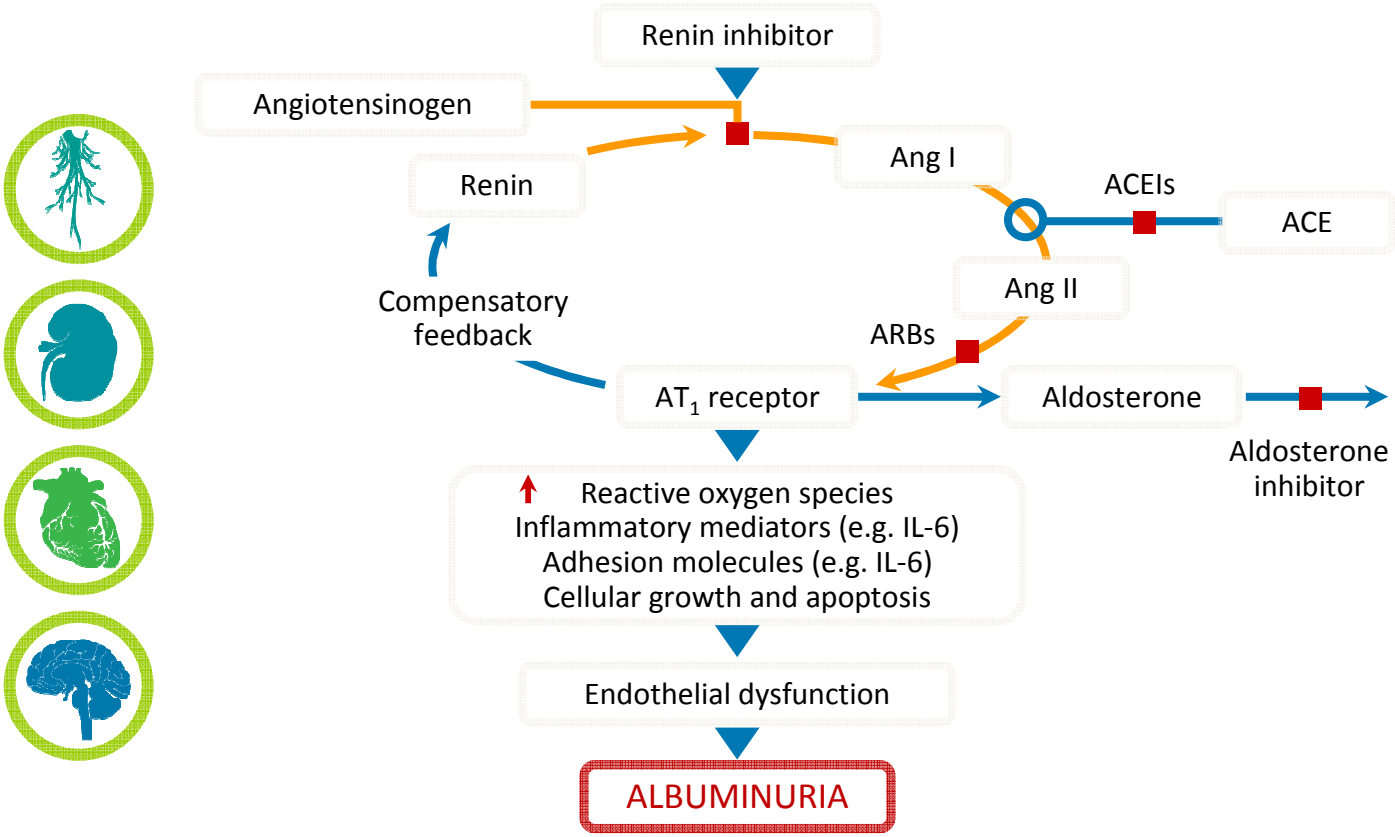
- Evidence points to a major role for the RAAS in pathophysiological changes that lead to progressive renal and cardiovascular disease



Basi S , et al. Am J Kidney Dis. 2006

Albuminuria

	24-H Urine Albumin (mg/24 h)	Overnight Urine Albumin (μg/min)	Spot Urine			
			Albumin (mg/L)	Albumin/Creatinine Ratio		
				Gender	mg/mmol	mg/g
Normal	<15	<10	<10	M	<1.25	<10
				F	<1.75	<15
High normal	15 to <30	10 to <20	10 to <20	M	1.25 to <2.5	10 to <20
				F	1.75 to <3.5	15 to <30
Microalbuminuria	30 to <300	20 to <200	20 to <200	M	2.5 to <25	20 to <200
				F	3.5 to <35	30 to <300
Macroalbuminuria	>300	>200	>200	M	>25	>200
				F	>35	>300

De Jong PE, Curhan GC. J Am Soc Nephrol 17:2110-2126, 2006

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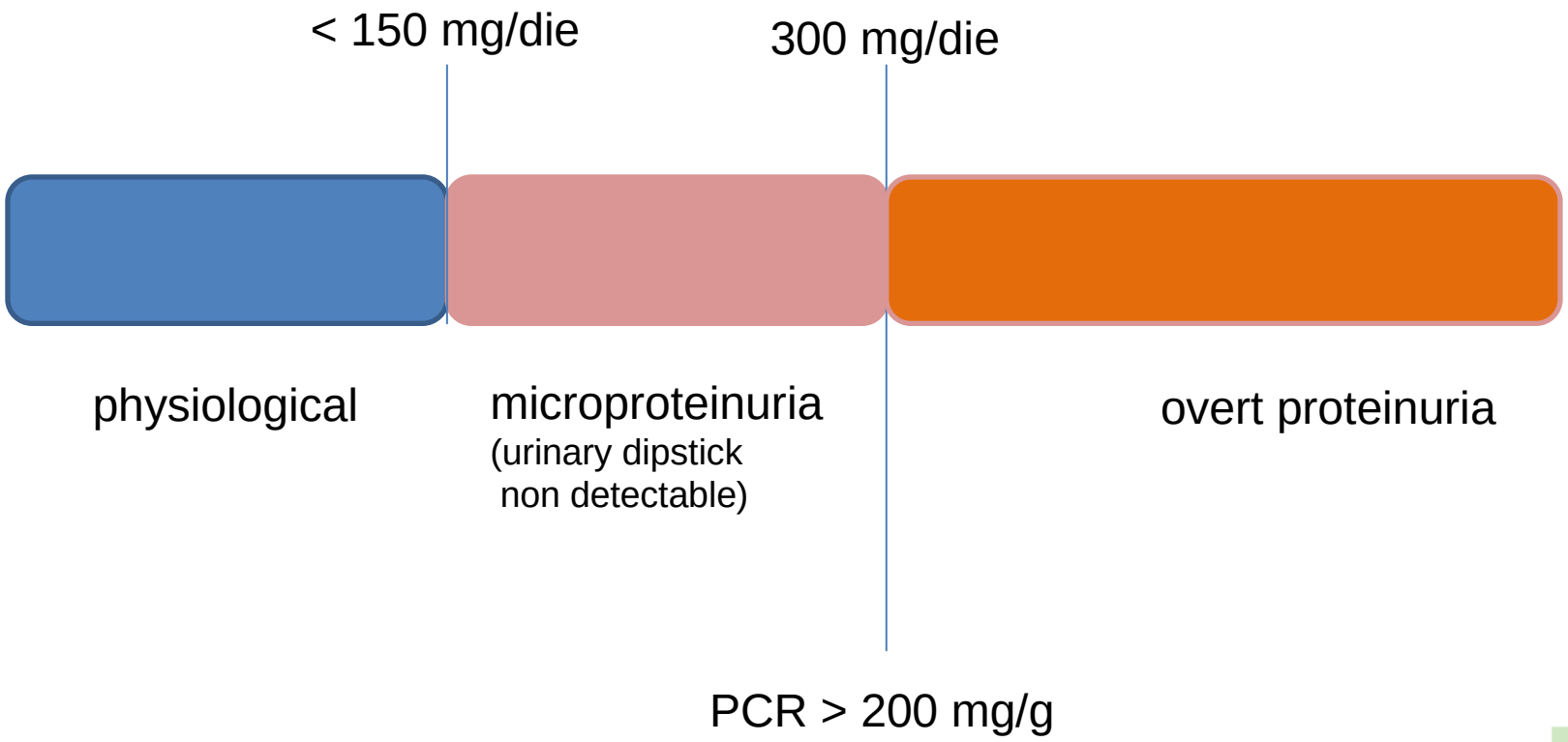
Urinary PROTEIN excretion



De Jong PE, Curhan GC. J Am Soc Nephrol 17:2110-2126, 2006

Quando ricercare albuminuria e proteinuria?

- L'escrezione urinaria di albumina e di proteine deve essere quantificata, sia nei diabetici che nei non diabetici, **quando eGFR < 60 mL/min/1.73 m^2**; il primo risultato anomalo dev'essere confermato con un campione mattutino

- Stesso atteggiamento nei confronti dei soggetti con **eGFR > 60 mL/min/1.73 m^2** ma per i quali si ha sospetto di nefropatia cronica

Linee Guida ISS - Min Sal - SIN 2012

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Banche dati consultate	Cochrane, Medline, Embase
Tipologia di studi inclusi	revisioni sistematiche, RCT, studi osservazionali
Studi reperiti	1.609
Studi selezionati	37
Studi estratti	26

- **Mortalità per tutte le cause e per malattie cardiovascolari**
- **Fragilità e cognitive impairment**

ACR ≥ 265 mg/g oppure PCR ≥ 442 mg/g

p

Stages of Chronic Kidney Disease

Stage	Description	GFR (mL/min/1.73 m^2)
1	Kidney damage with normal or ↑ GFR	≥90
2	Kidney damage with mild ↓ GFR	60–89
3	Moderate ↓ GFR	30–59
4	Severe ↓ GFR	15–29
5	Kidney failure	<15 (or dialysis)

3a: 45 – 59 mL/min/1.73 mq
3b: 30 – 44 mL/min/1.73 mq

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- Mortalità per tutte le cause e per malattie cardiovascolari
- Fragilità e cognitive impairment

STADIO 3 — Incremento di rischio per eventi cardiovascolari

STADIO 3b — Incremento di mortalità generale e di mortalità per malattie cardiovascolari (eccesso di rischio)

Incremento di rischio per fragilità e declino cognitivo

p — Fattore di rischio indipendente per mortalità generale

Fattore di rischio indipendente per stroke

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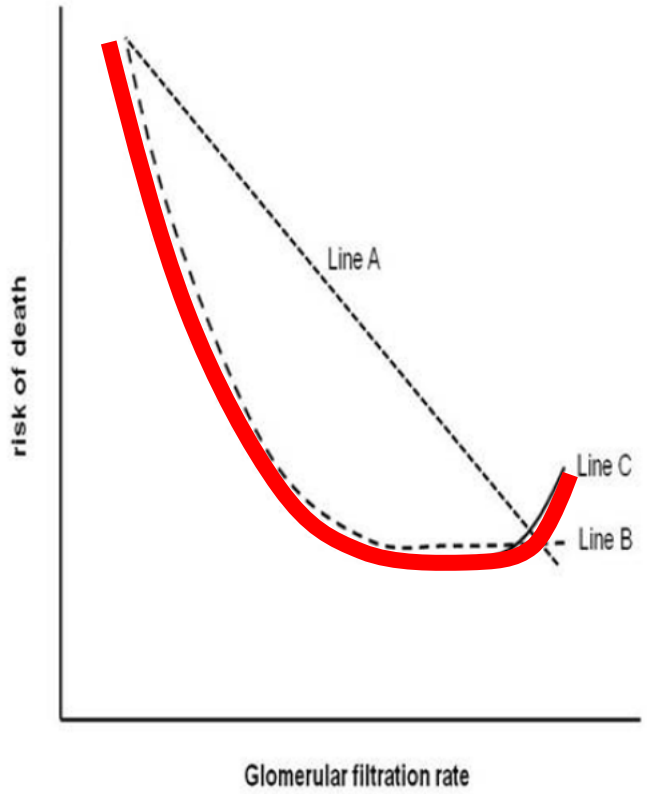
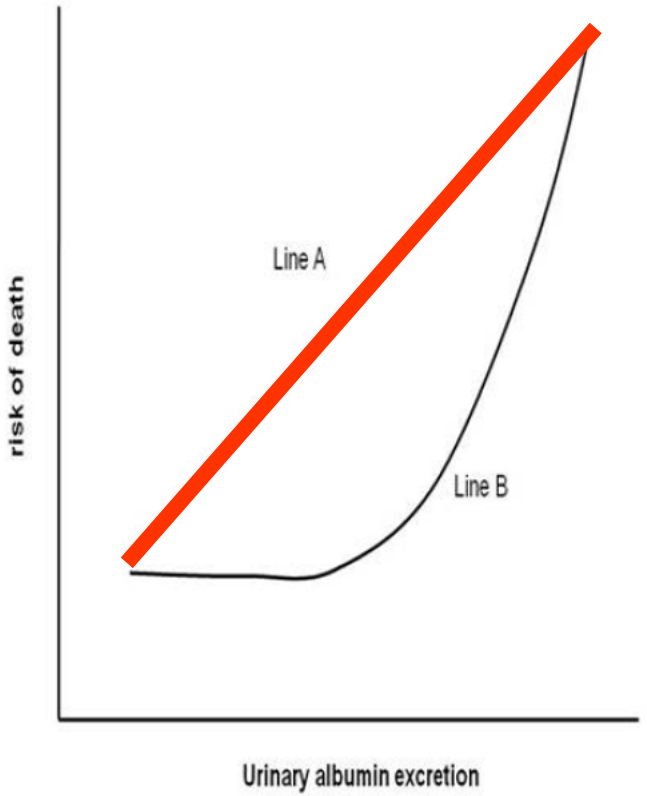
PUBLIC HEALTH AND PREVENTIVE NEPHROLOGY JNEPHROL 2012; 25(01): 7-12
DOI:10.5301/jn.5000045

A population-based approach for the definition of chronic kidney disease: the CKD Prognosis Consortium

Association with all-cause mortality of GFR and UAE





Cirillo M et al, J Nephrol 2012

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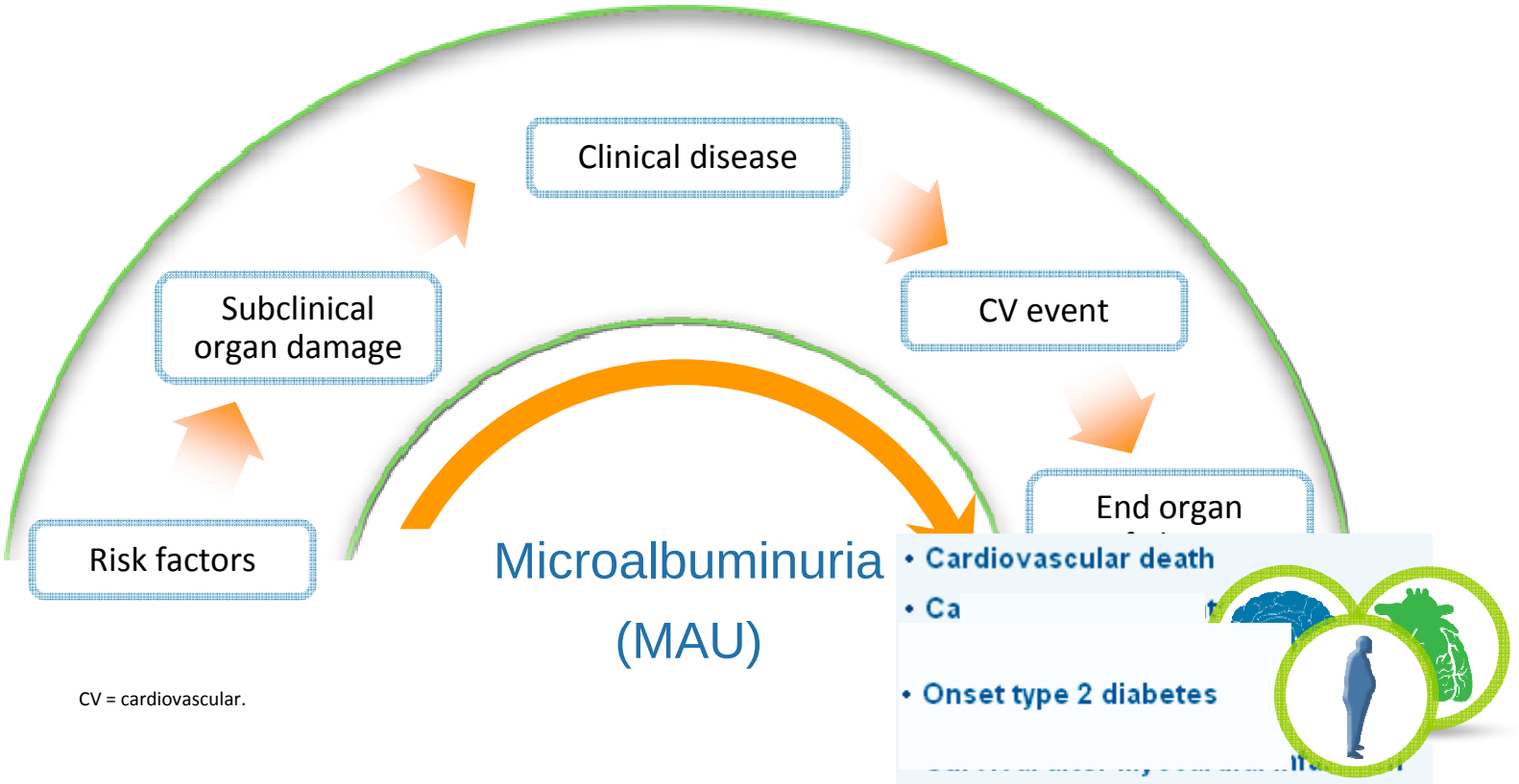
MAU is an early, sub-clinical sign of target-organ damage and is correlated with specific cardio-renal outcomes



CV = cardiovascular.

Dzau VJ, et al. Circulation. 2006

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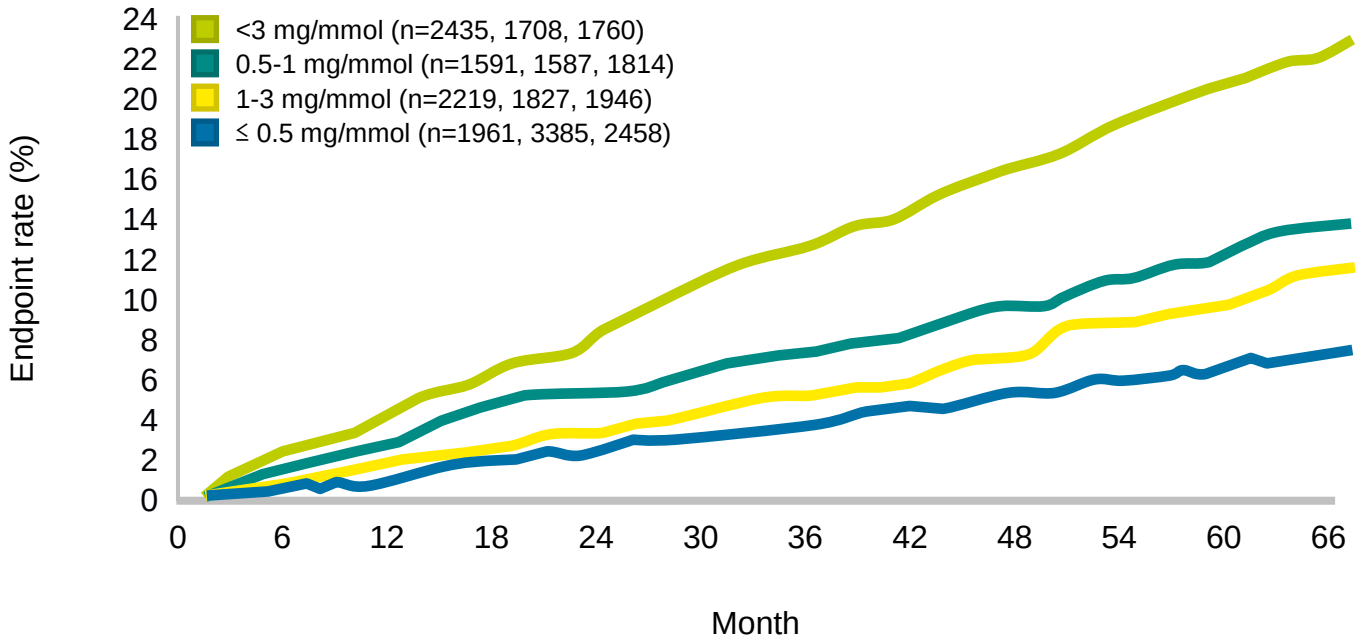
Key clinical studies evaluating the predictive value of MAU on CV risk

MAU as a predictor

Year	Study name	Author/s	Title	Patient #
2000	**WESDM**	Valmadrid CT, et al.	The risk of CV disease mortality associated with microalbuminuria and gross proteinuria in persons with older-onset diabetes mellitus.	N=840
2001	**HOPE**	Gerstein HC, et al.	Albuminuria and risk of CV events, death, and heart failure in diabetic and non-diabetic individuals.	N=3498
2002	**PREVEND**	Hillege HL, et al.	Prevention of Renal and Vascular End Stage Disease (PREVEND) Study Group. Urinary albumin excretion predicts CV and non CV mortality in the general population.	N=85,421
2003	**UKPDS**	Adler AI, et al.	Development and progression of nephropathy in type 2 diabetes: The UK Prospective Diabetes Study (UKPDS 64).	N=5,097
2005	**LIFE**	Ibsen H, et al.	Reduction in albuminuria translates to reduction in CV events in hypertensive patients: losartan intervention for endpoint reduction in hypertension study.	N=8,206
2005	**Framingham Heart Study**	Arnlöv J, et al.	Low-grade albuminuria and incidence of CV disease events in non-hypertensive and non-diabetic individuals.	N=1,568
2009	**CHARM**	Jackson CE, et al.	Albuminuria in chronic heart failure: prevalence and prognostic importance.	N=2,310
2010	**MAGIC**	Viazzi F, et al.	Microalbuminuria is a predictor of chronic renal insufficiency in patients without diabetes and with hypertension: the MAGIC study.	N=917
2010	**ONTARGET**	Schmieder R, et al.	Changes in albuminuria predict mortality and morbidity in patients with vascular disease.	N=23,480

Composite CV endpoint rates stratified baseline albuminuria measurement (UACR)

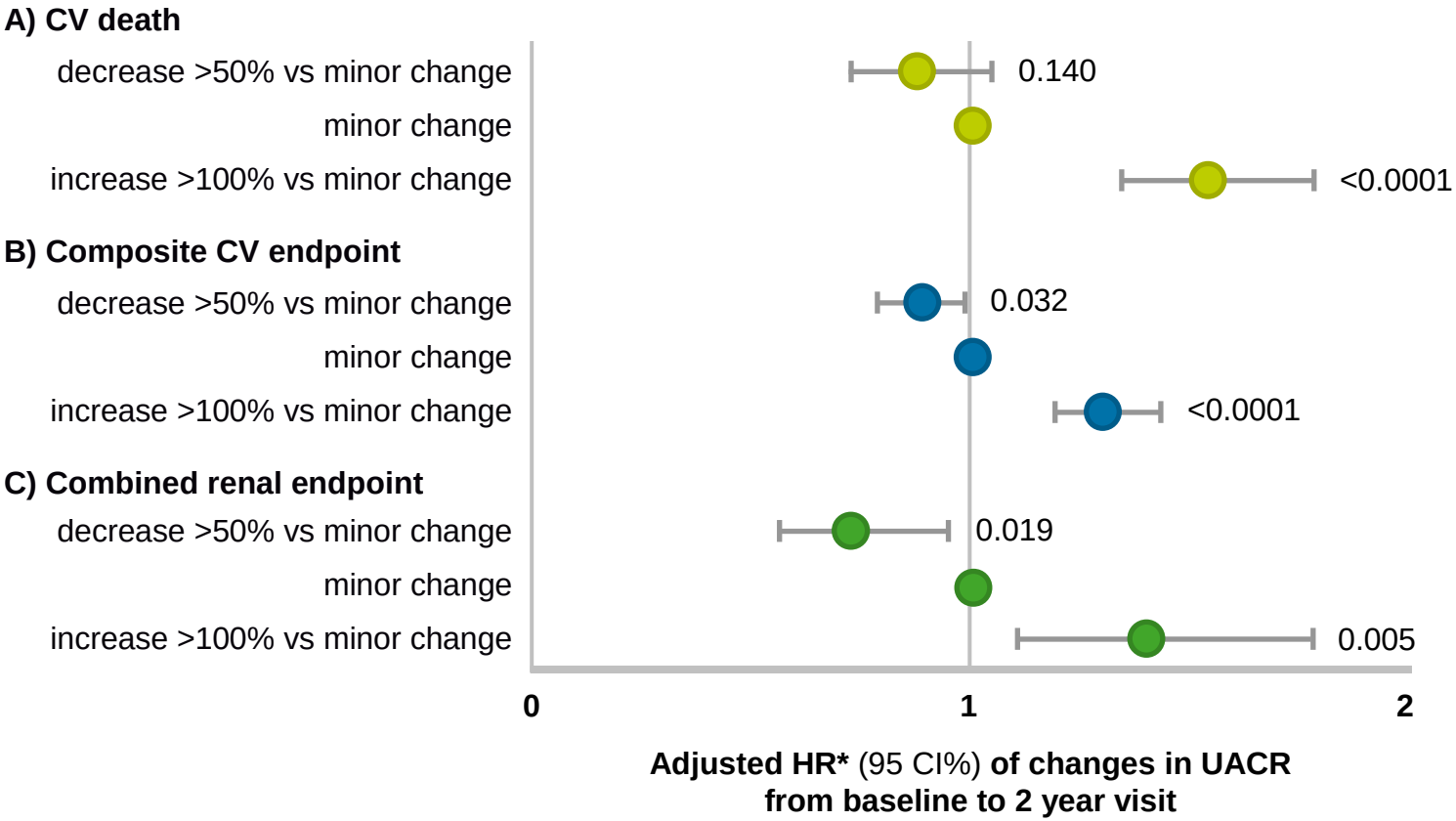
The LIFE study



Reducing UACR is associated with a reduction in CV events in patients with hypertension

Ibsen H, et al. Hypertension. 2005;45:198-202.

The ONTARGET/TRANSCEND study programme



The risk of CV and renal outcomes is increased significantly if MAU is increased and is decreased if MAU is reduced

Schmieder RE, et al. JASN 2011

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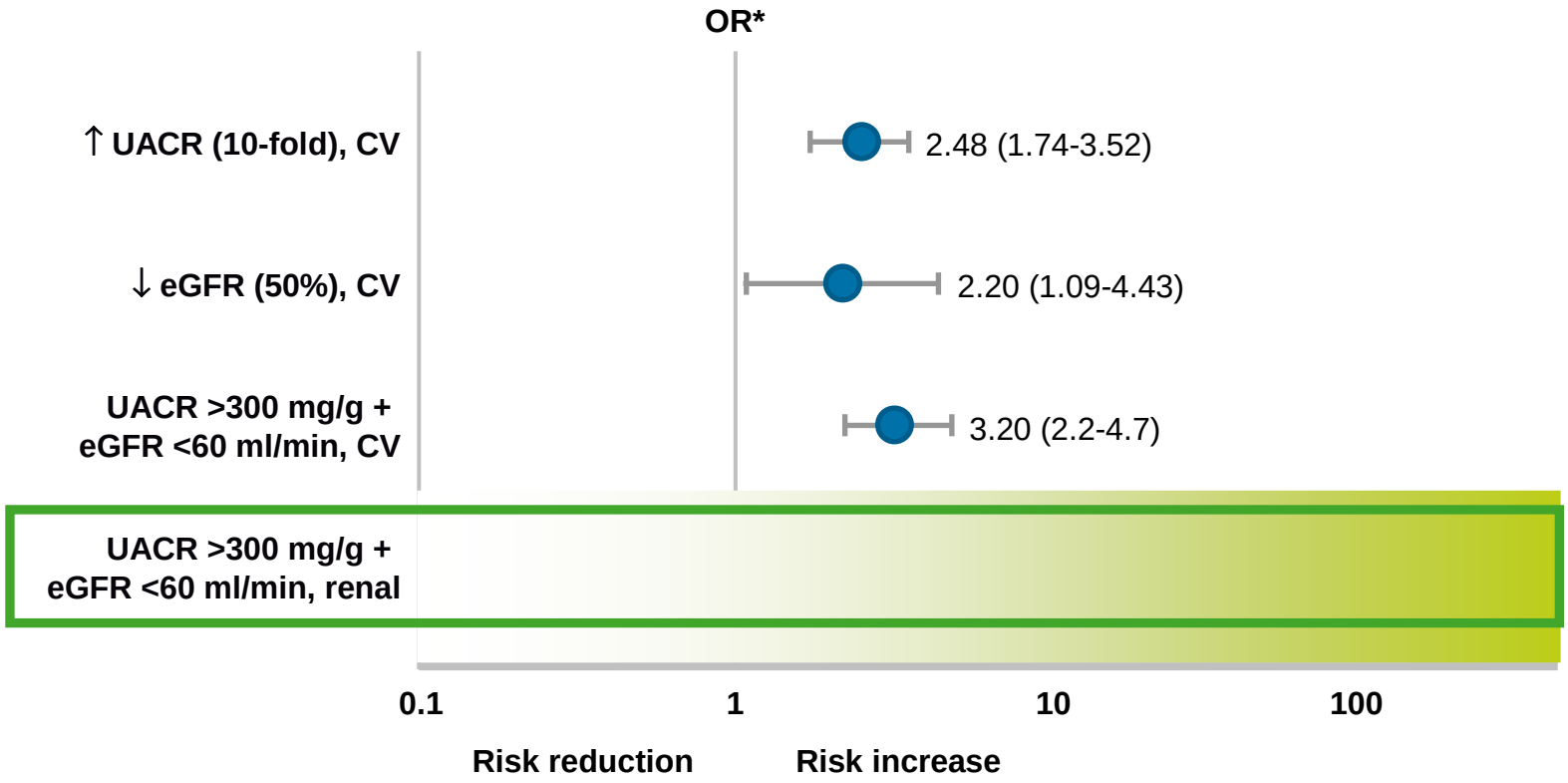
Increase in risk according to renal variables in ADVANCE

Impact of renal variables on risk of CV and renal events



* Multivariate adjusted (also for regression dilution).

CV = cardiovascular; UACR = urinary albumin:creatinine ratio; eGFR = estimated glomerular filtration rate.

Ninomiya T, et al. ADVANCE Collaborative Group. J Am Soc Nephrol. 2009;20:1813-21.

Understanding the clinical and epidemiological implications of MAU

- The RAAS plays a major role in development of albuminuria
- MAU is a strong and independent risk factor for cardio-renal disease
- UACR and eGFR are multiplicatively and independently associated with mortality risk without evidence of interaction
- Albumin is a continuous predictor of mortality starting at low levels, whereas eGFR is predictive only above a certain threshold
- Reducing proteinuria/MAU leads to a decreased risk in CV and renal outcomes and all-cause mortality

When to screen?
Guideline recommendations for MAU testing

Organisation	Patient Group	Frequency
ESH-ESC Guidelines 2009 Reappraisal	All people with: • **Hypertension** (SBP 140 mmHg or DBP 90 mmHg) • **Metabolic syndrome & high-normal BP** (SBP 130–139 mmHg or DBP 80–85 mmHg)	• Routine assessment at screening for CV risk and during treatment • Patient should be assessed routinely using: – Serum creatinine – Estimated creatinine clearance – Urinalysis (complemented by MAU via dipstick test and microscopic examination) – Electrocardiogram • MAU should be examined during treatment as well as during screening

Current ESH-ESC guidelines recommend routine testing for MAU in patients with hypertension and in metabolic syndrome with high-normal BP

1. Mancia G, et al. J Hypertens. 2007;25:1105-87. 2. Mancia G, et al. J Hypertens. 2009;27:2121-58.

Availability, prognostic value and cost of some markers of organ damage (scored from 0 to 4 pluses)

Markers	CV predictive val	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. GFR or ClCr	+++	++++	+
Microalbuminuria	+++	++++	+

ESH/ESC Hypertension Guidelines, 2007

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- Il 21% della popolazione generale dispone di un GFR calcolato
- L'11% dei pazienti diabetici e ipertesi dispone di un rapporto Alb/Creat

SIN/SIMG, 2007

courtesy by Stefano Bianchi, Livorno, Italy

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