SEMI
LA VISIÓN GLOBAL DE LA PERSONA ENFERMA

FEMI

XXXI Congreso Nacional de la Sociedad Española de Medicina Interna

OVIEDO
17-20 Noviembre 2010

Auditorio-Palacio de Congresos
"Príncipe Felipe"

II Congreso Ibérico de Medicina Interna

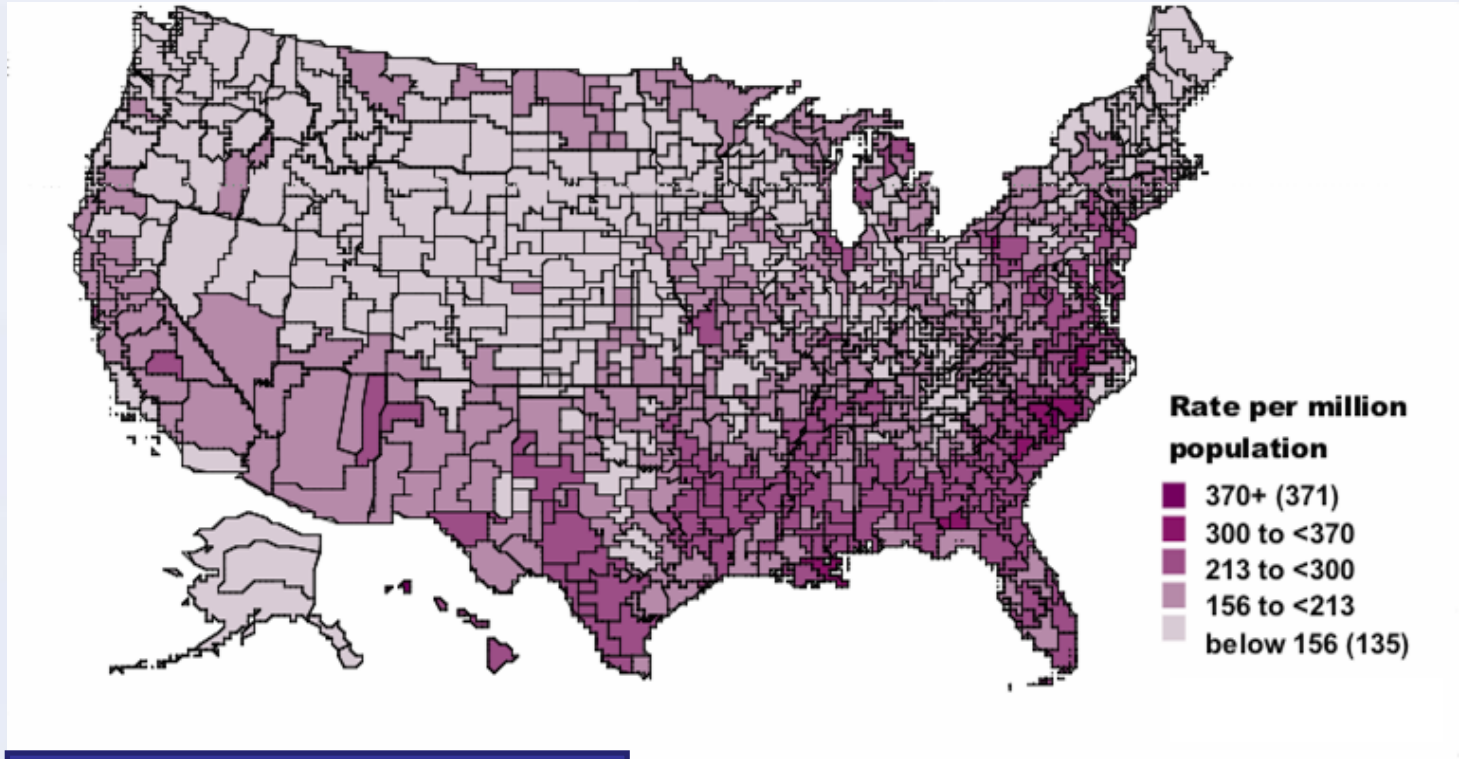
VII Congreso de la Sociedad Asturiana de Medicina Interna

Nefroprotección y riesgo vascular: prevención del daño renal en la HTA

Josep Maria Galcerán
Fundación Althaia, Manresa

althaia

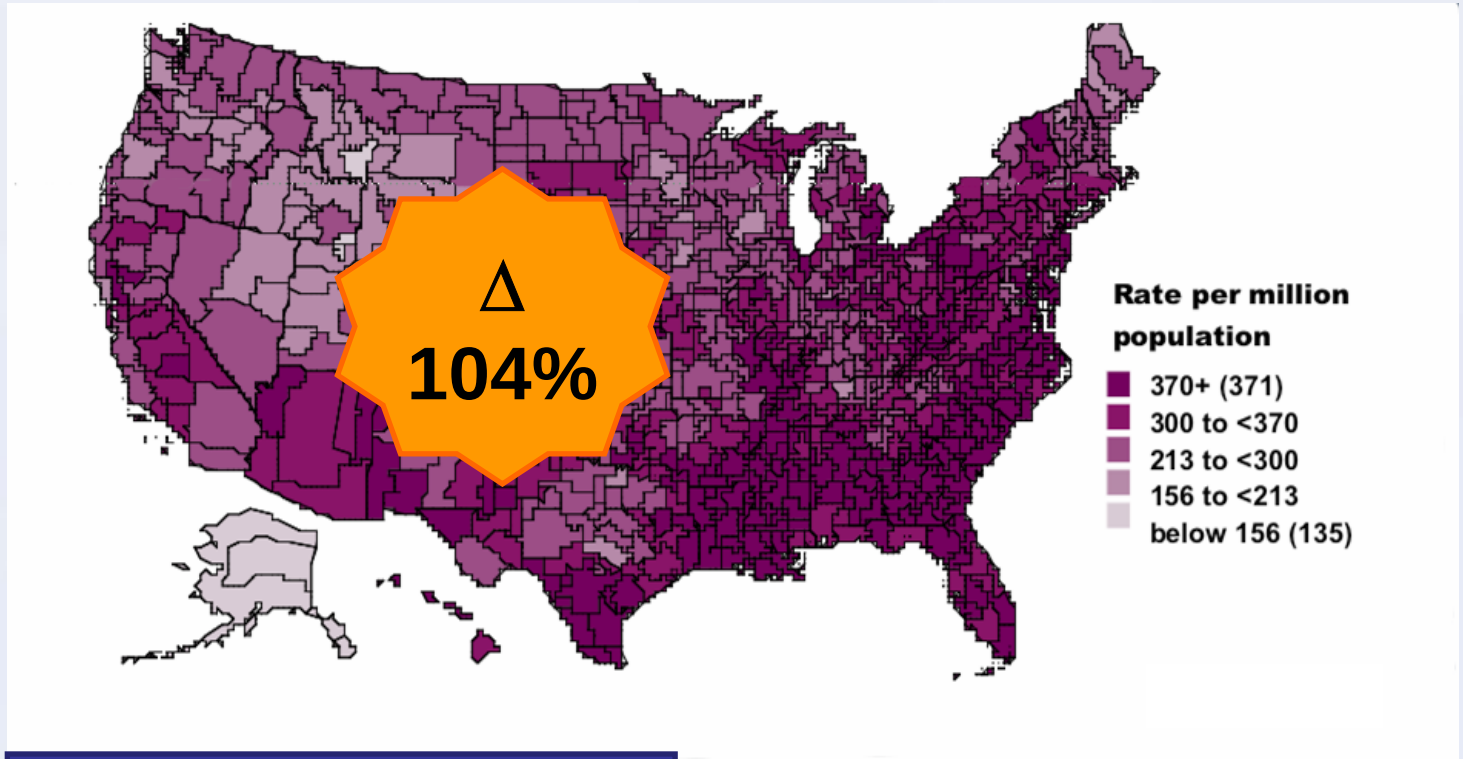
Incidence of Kidney Failure – USA 1990



Prevalence 8,3%

MMWR Morb Mortal Wkly Rep. 2004; 53: 918-20

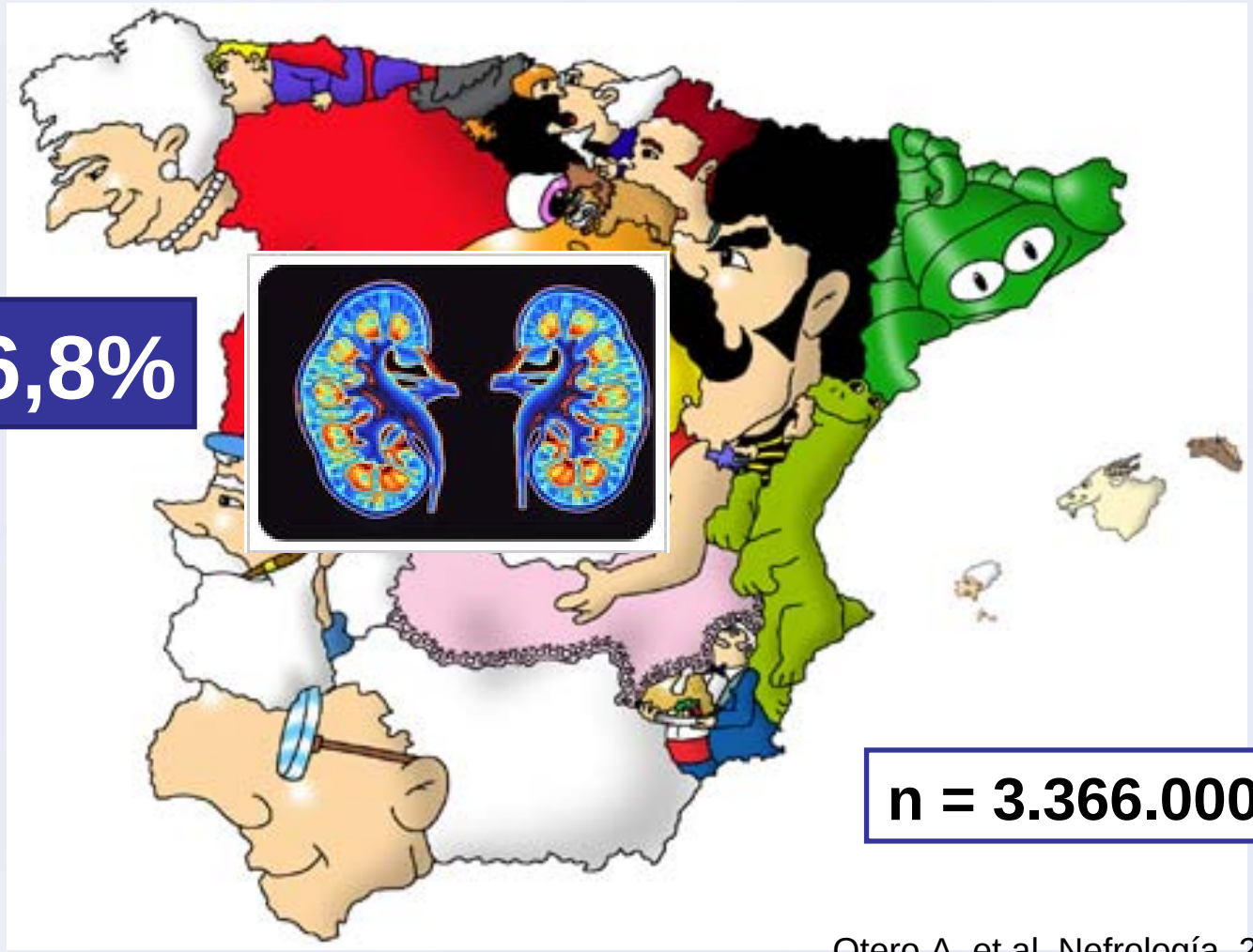
Incidence of Kidney Failure – USA 2000



Prevalence 16,8%

MMWR Morb Mortal Wkly Rep. 2004; 53: 918-20

Prevalencia Insuficiencia Renal España, estudio EPIRCE



Otero A, et al. Nefrología. 2010; 30: 78-86

Función renal y riesgo cardiovascular en pacientes con hipertensión arterial esencial. Estudio FRESHA

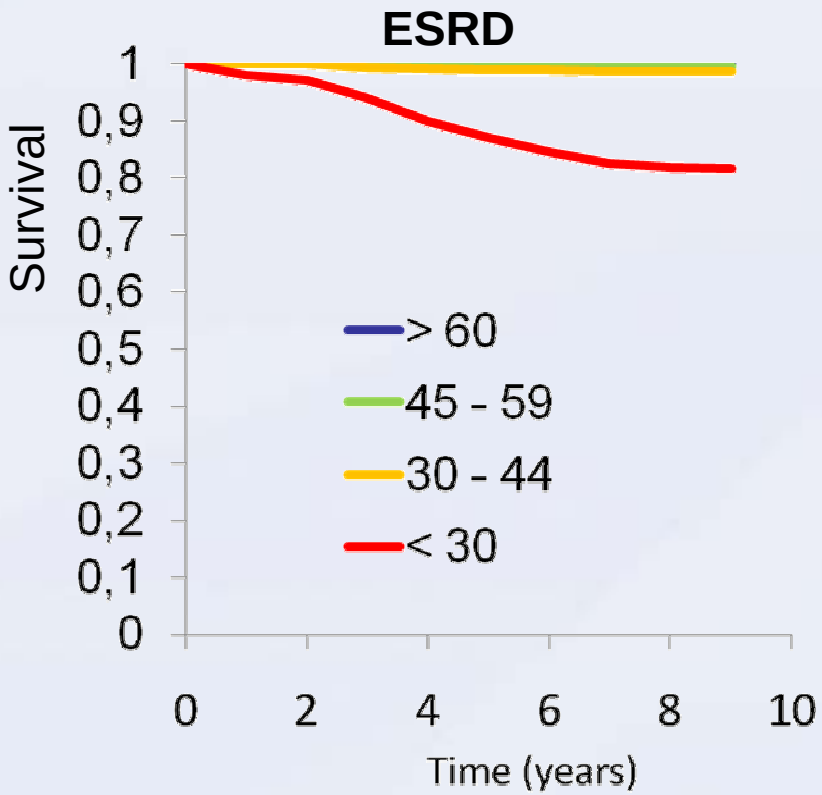
P. Herrero*, R. Marín*, F. Fernández Vega*, M. Gorostidi, A. Riesgo*, J. Vázquez* y B. Díez Ojea*** en representación de los investigadores del estudio FRESHA******

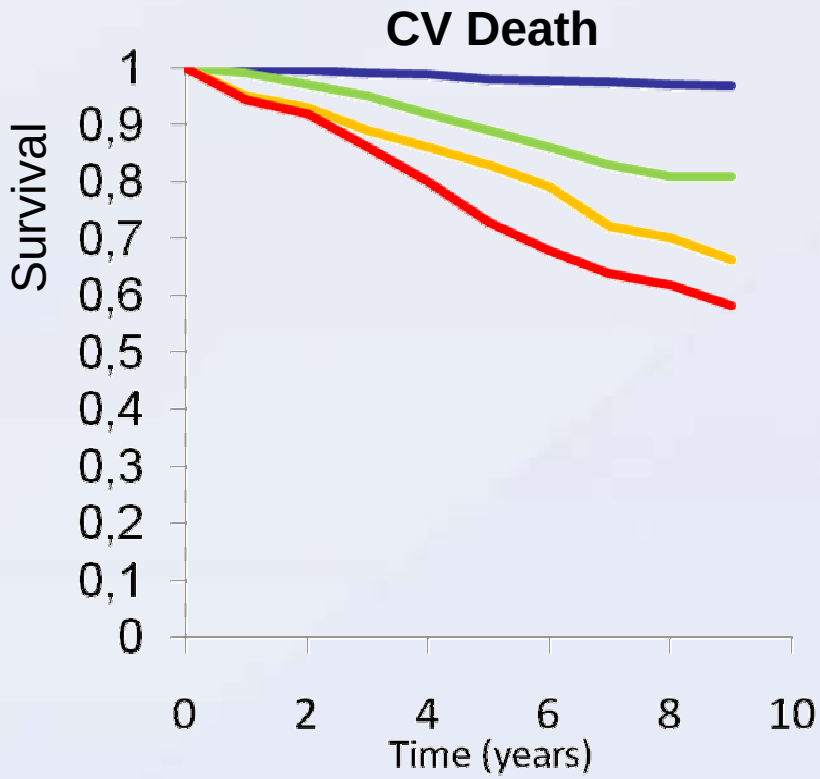
*Unidad de Hipertensión. Servicio de Nefrología. Hospital Universitario Central de Asturias y **Sección de Nefrología. Hospital San Agustín. Avilés (Asturias). ****Los investigadores del estudio FRESHA figuran en el apéndice.

N	2.130
Edad (años)	65,6 ± 11,0
Sexo femenino n (%)	1.136 (53,3)
PA sistólica (mmHg)	145,4 ± 16,3
PA diastólica (mmHg)	83,6 ± 9,9
PA < 140/90 mmHg n (%)	673 (31,6)
Diabetes n (%)	645 (30,3)
Hipercolesterolemia n (%)	977 (45,9)
Fumadores n (%)	348 (16,3)
Obesidad * n (%)	785 (36,9)
Creatinina (mg/dl)	1,00 ± 0,30
eGFR < 60 ml/min/1,73 m² n (%)	691 (32,4%)
Cardiopatía isquémica n (%)	352 (16,5)
Enfermedad cerebrovascular n (%)	159 (7,5)
Insuficiencia cardíaca n (%)	185 (8,7)
Arteriopatía periférica n (%)	223 (10,5)
Hipertrofia ventricular izquierda n (%)	393 (18,5)
Fibrilación auricular n (%)	138 (6,5)
Al menos una enfermedad cardiovascular § n (%)	896 (42,1)

Herrero P, et al. Nefrología 2006; 26: 330-8

Clinical significance of reduced GFR





GFR at screening	>60	45-59	30-44	<30
ESRD	13	9	10	22
Total No	62066	2389	548	120
%	**0,02%**	**0,4%**	**1,3%**	**18,3%**

GFR at screening	>60	45-59	30-44	<30
CV Death	1913	456	185	50
Total No	62066	2389	548	120
%	**3,1%**	**19,1%**	**33,8%**	**41,7%**

Hallan SI, et al. BMJ 2006; 333: 1047-54

CKD and CV disease: a solid association

Culleton BF, Larson MG, Wilson PW, Evans JC, Parfrey PS, Levy D. Cardiovascular disease and mortality in a communitybased cohort with mild renal insufficiency. Kidney Int. 1999;56:2214–9.

Beddhu S, Allen-Brady K, Cheung AK et al. Impact of renal failure on the risk of myocardial infarction and death. *Kidney Int. 2002;62:1776-1783.*

Mann JF, Gerstein HC, Yi QL et al. Development of renal disease in people at high cardiovascular risk: results of the HOPE randomized study. *J Am Soc Nephrol. 2003;14:641-647.*

Santopinto JJ, Fox KA, Goldberg RJ et al. Creatinine clearance and adverse hospital outcomes in patients with acute coronary syndromes: findings from the global registry of acute coronary events (GRACE). *Heart 2003;89:1003-1008.*

Drey N, Roderick P, Mullee M, Rogerson M. A population-based study of the incidence and outcomes of diagnosed chronic kidney disease. Am J Kidney Dis. 2003;42:677-84.

Go AS, Chertow GM, Fan D,McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med. 2004;351:1296-1305.*

Weiner DE, Tighiouart H,Amin MG et al.Chronic kidney disease is a risk factor for cardiovascular disease and all-cause mortality: a pooled analysis of community-based studies. *J Am Soc Nephrol. 2004;15:1307-1315.*

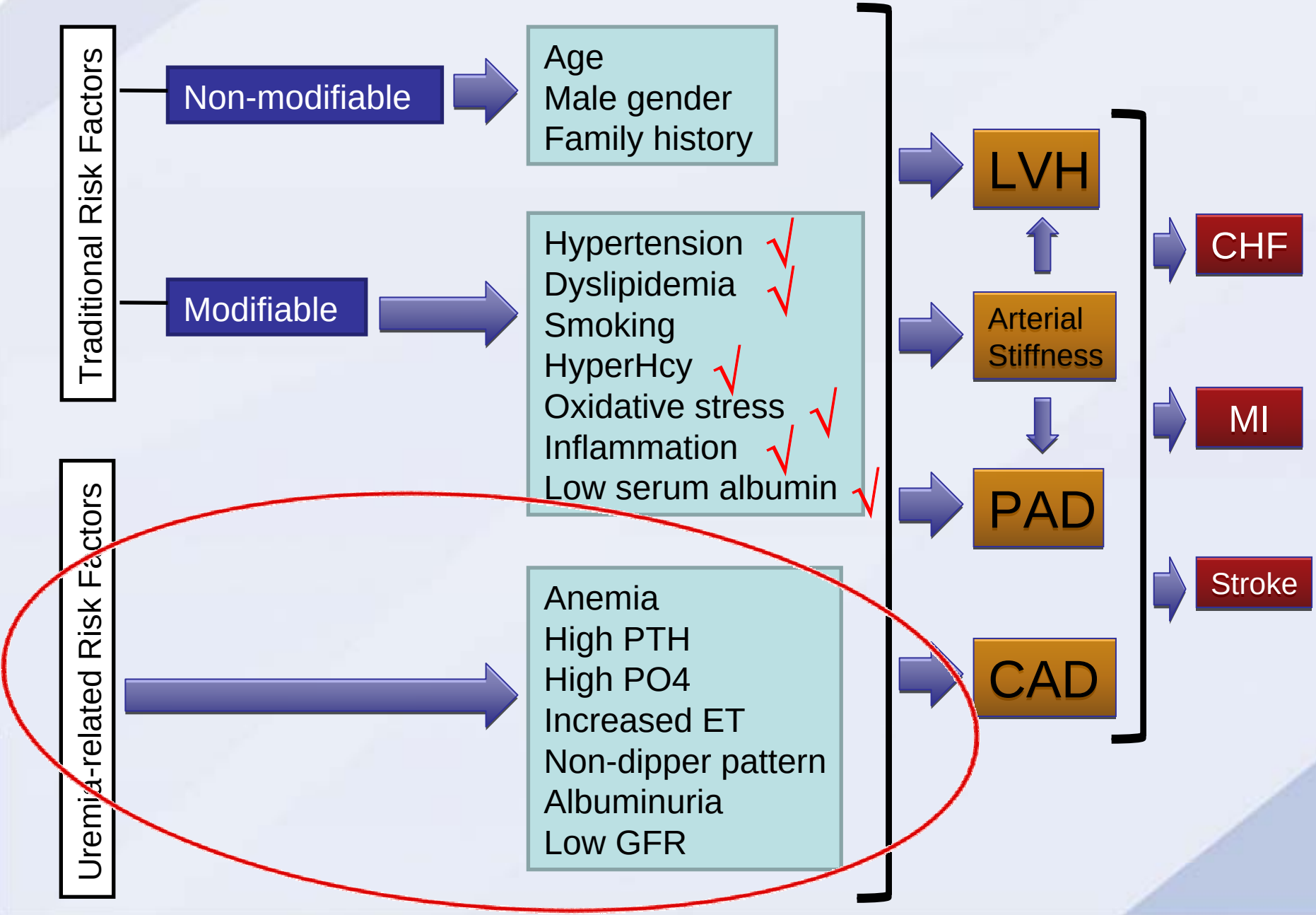
Keith DS, MD, Nichols GA, Gullion CM, et al. Longitudinal Follow-up and Outcomes Among a Population With Chronic Kidney Disease in a Large Managed Care Organization. Arch Intern Med. 2004;164:659-663

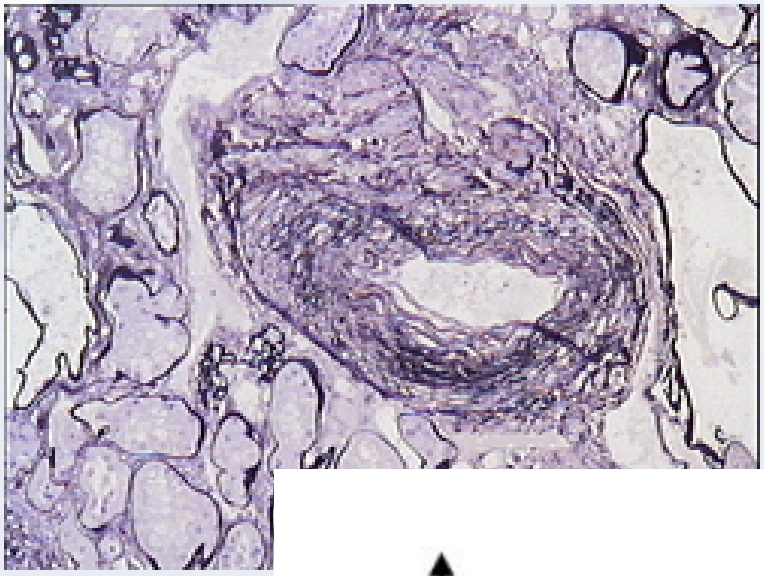
Hallan SI, Dahl K, Oien CM, et al. Screening strategies for chronic kidney disease in the general population: follow-up of cross sectional health survey. *BMJ 2006; 333: 1047-54.*

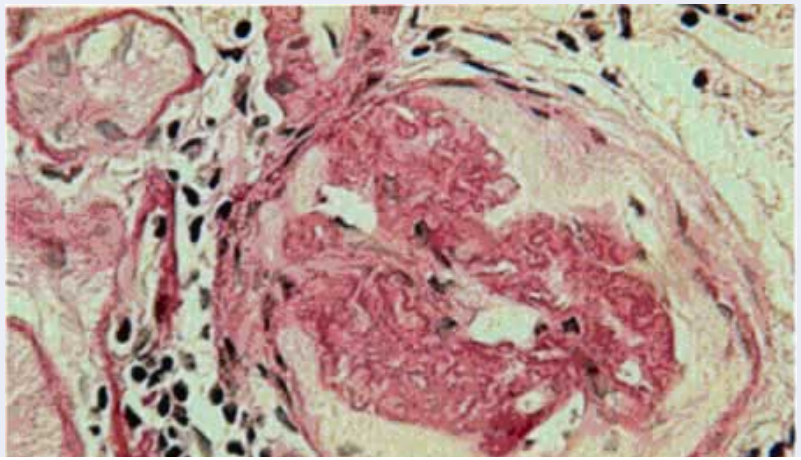
Nakayama N, Metoki H, Terawaki H, et al. Kidney dysfunction as a risk factor for first symptomatic stroke events in a general Japanese population—the Ohasama study. *Nephrol Dial Transplant 2007; 22: 1910-5*

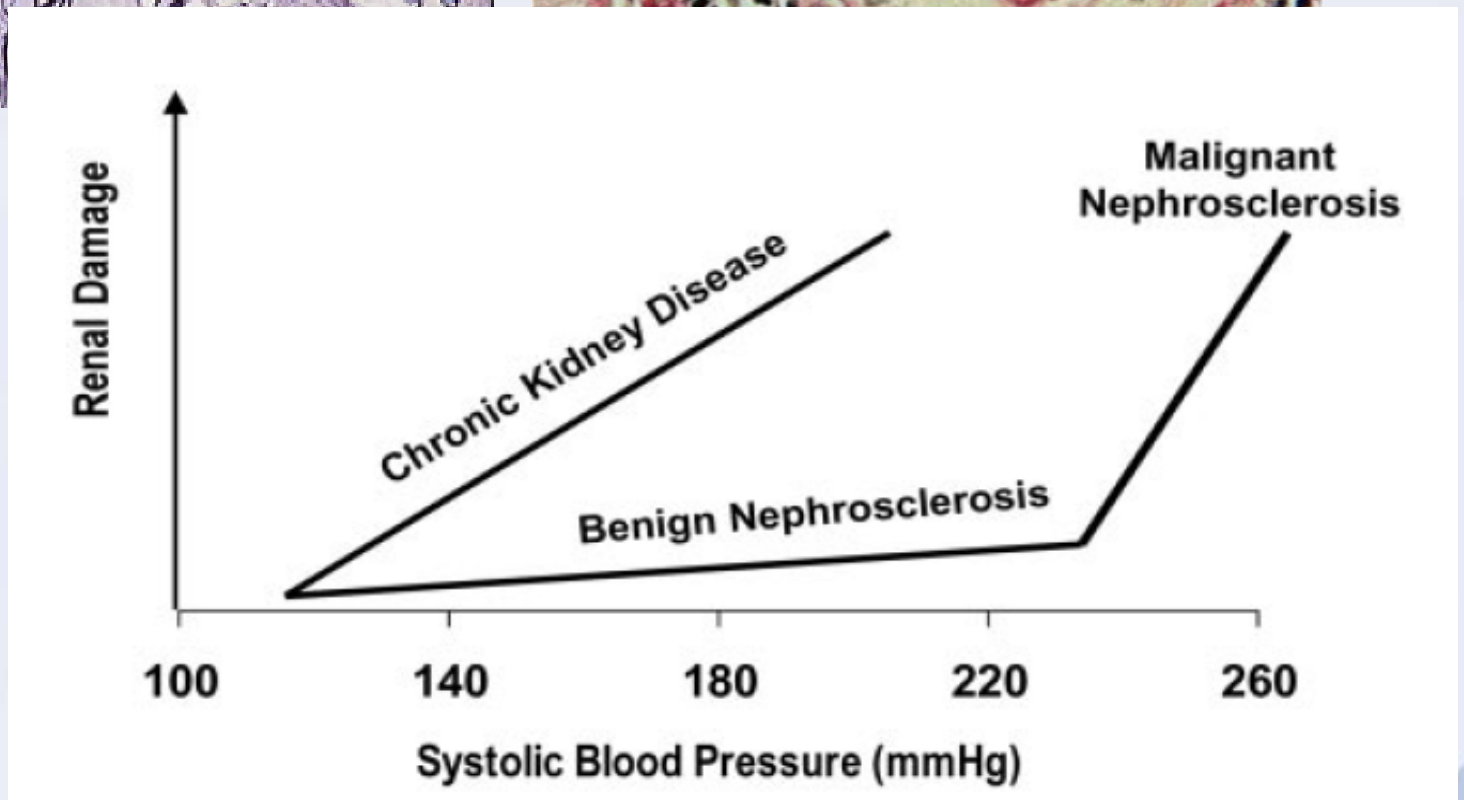
Shlipak MG,Katz R,Kestenbaum B,et al. Rapid decline of kidney function increases cardiovascular risk in the elderly. *J Am Soc Nephrol. 2009;20:2625–30*.

CKD and CV disease: marker or risk factor







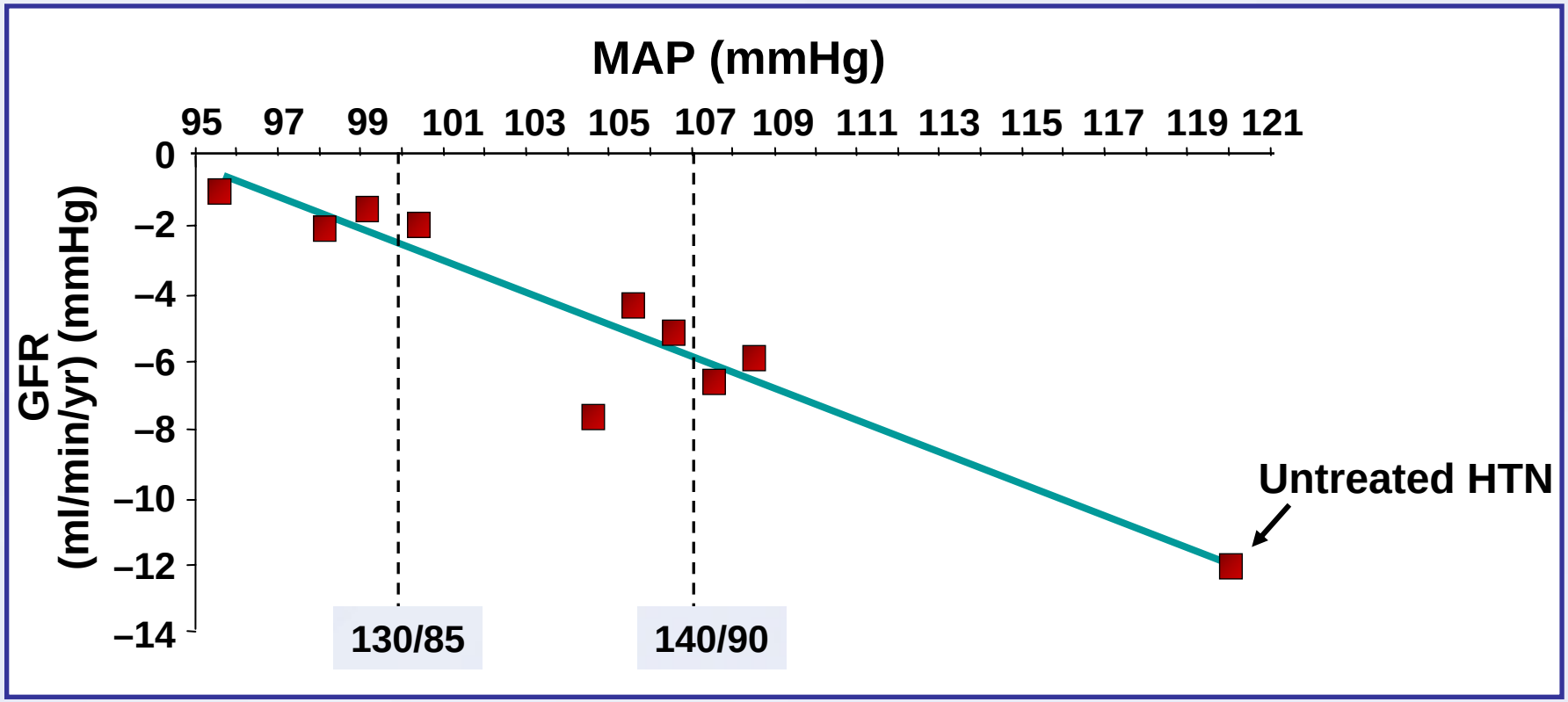


Bidani AK, et al. Hypertension 2004; 44: 595-601

- La reducción de la presión arterial comporta un beneficio renal?

- Algún tipo de fármaco antihipertensivo está más indicado para la preservación de la función renal?

Antihypertensive treatment and CKD progression



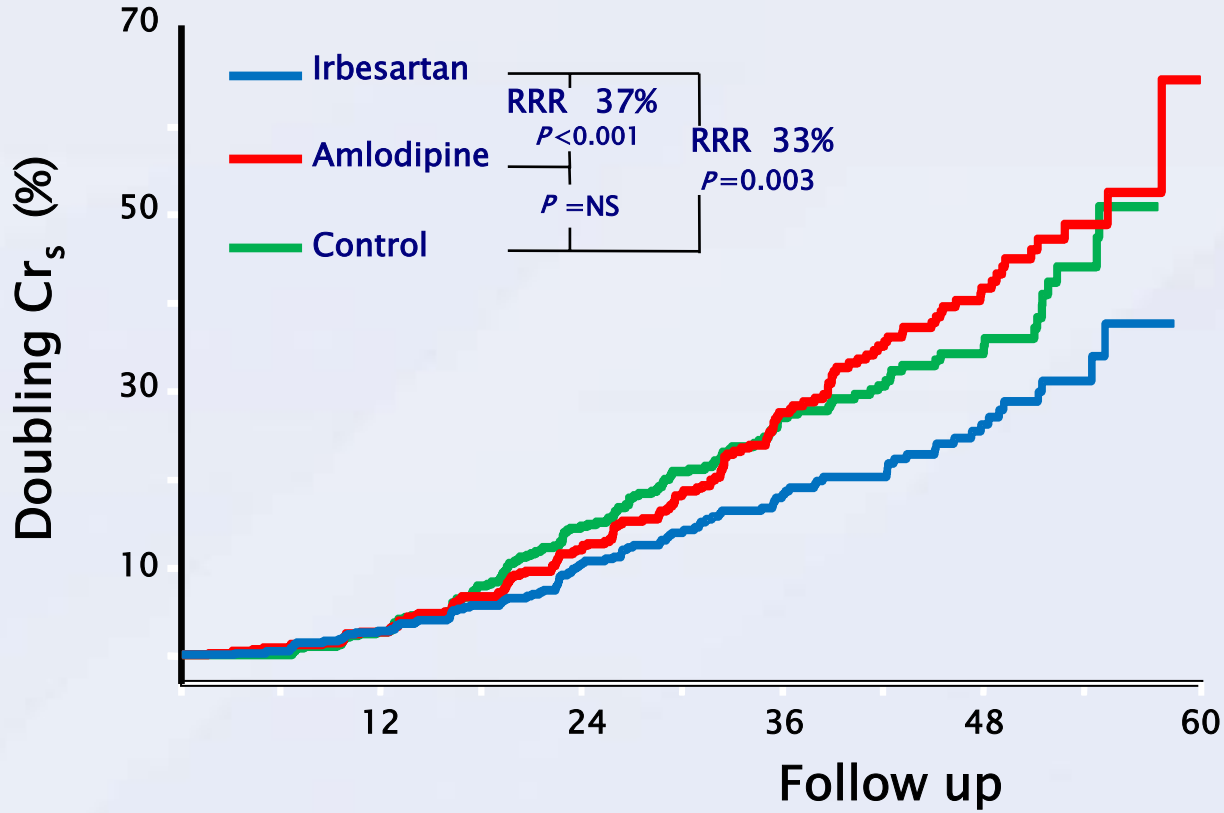
*Trials marked by * are non-diabetic renal disease patients.

Graph: (Bakris GL. *J Clin Hypertens*. 1999)

Trials: (Parving HH, et al. *Br Med J*. 1989) (Viberti GC, et al. *JAMA*. 1993) (Klaur S, et al. *N Engl J Med*. 1993*) (Herbert L, et al. *Kidney Int*. 1994) (Lebovitz H, et al. *Kidney Int*. 1994) (Moschio G, et al. *N Engl J Med*. 1996*) (Bakris GL, et al. *Kidney Int*. 1996) (Bakris GL, et al. *Hypertension*. 1997) (GISEN Group, *Lancet*. 1997)

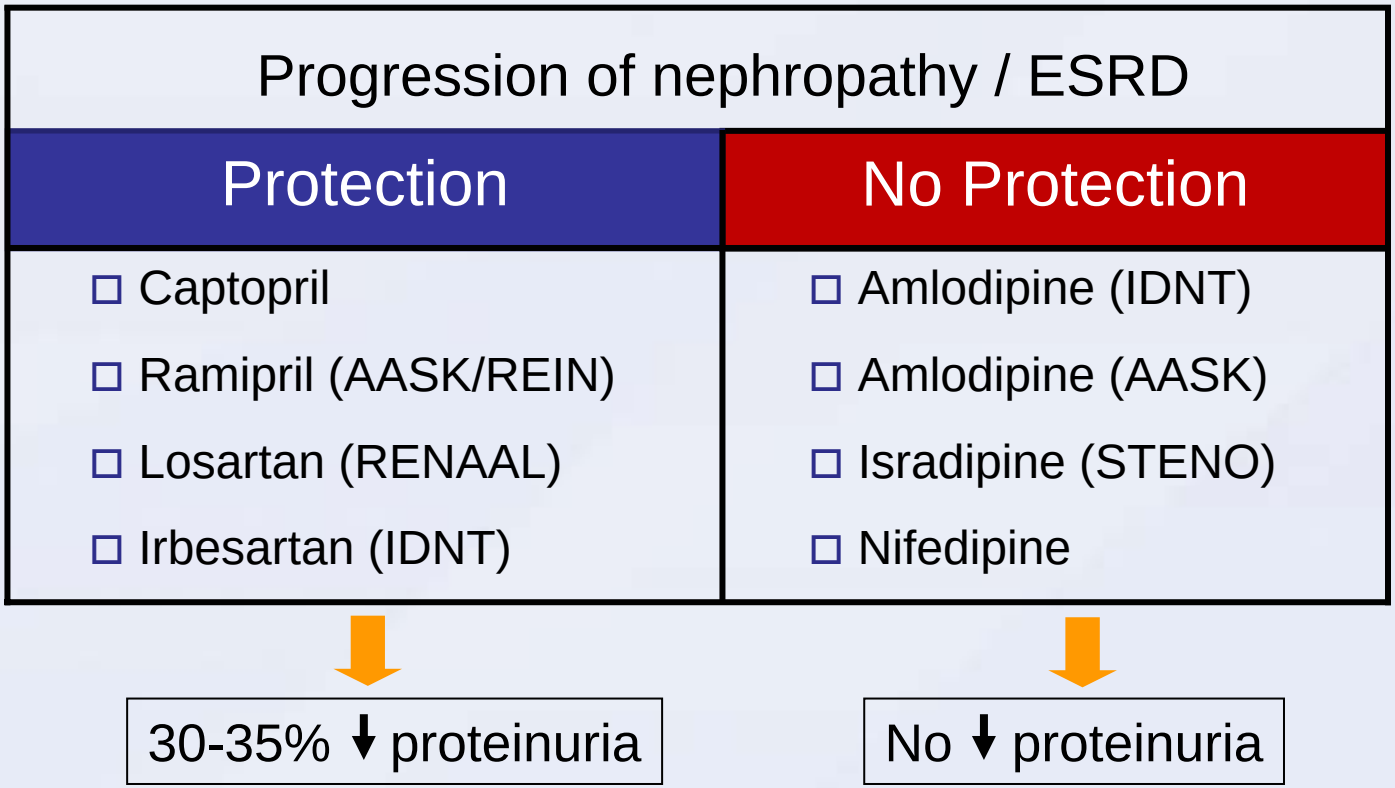
Blocking RAAS promotes better renal protection in proteinuric kidney disease

The IDNT Trial



Lewis EJ et al. NEJM 2001;345:851-60

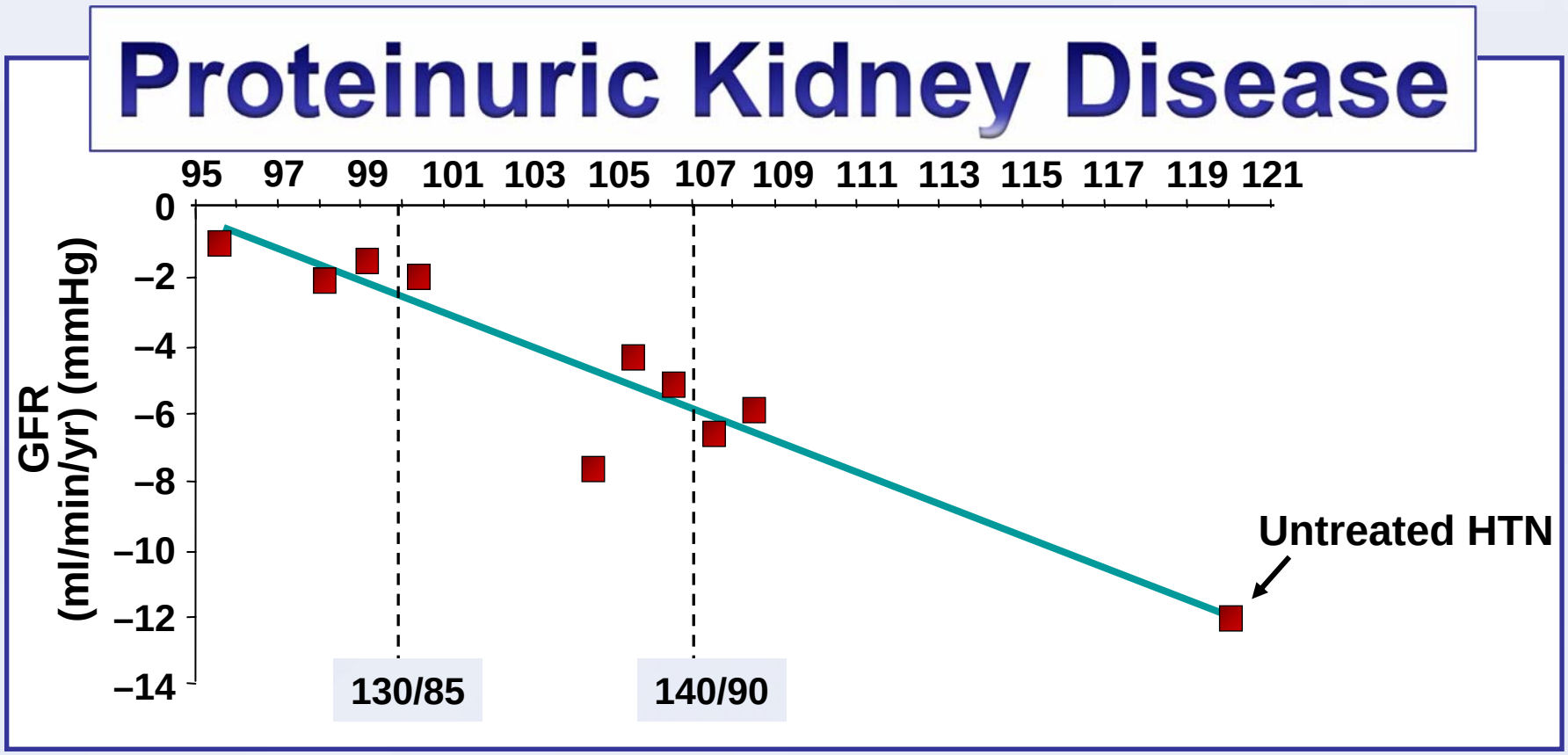
Clinical Trials and renal outcomes



ESRD = End Stage Renal Disease

Lewis EJ et al. *N Engl J Med.* 1993;329:1456-1462; Wright JT et al. *JAMA.* 2002; 288(19):2421-2431; Ruggenenti P et al. *Lancet.* 1999;354(9176):359-364; Brenner BM et al. *N Engl J Med.* 2001;345(12):861-869; Lewis EJ et al. *N Engl J Med.* 2001;345(12):851-860; Norgaard K et al. *Blood Press.*1993;2(4):301-308; Abbott K et al. *J Clin Pharmacol.* 1996;36;274-279.

Antihypertensive treatment and CKD progression



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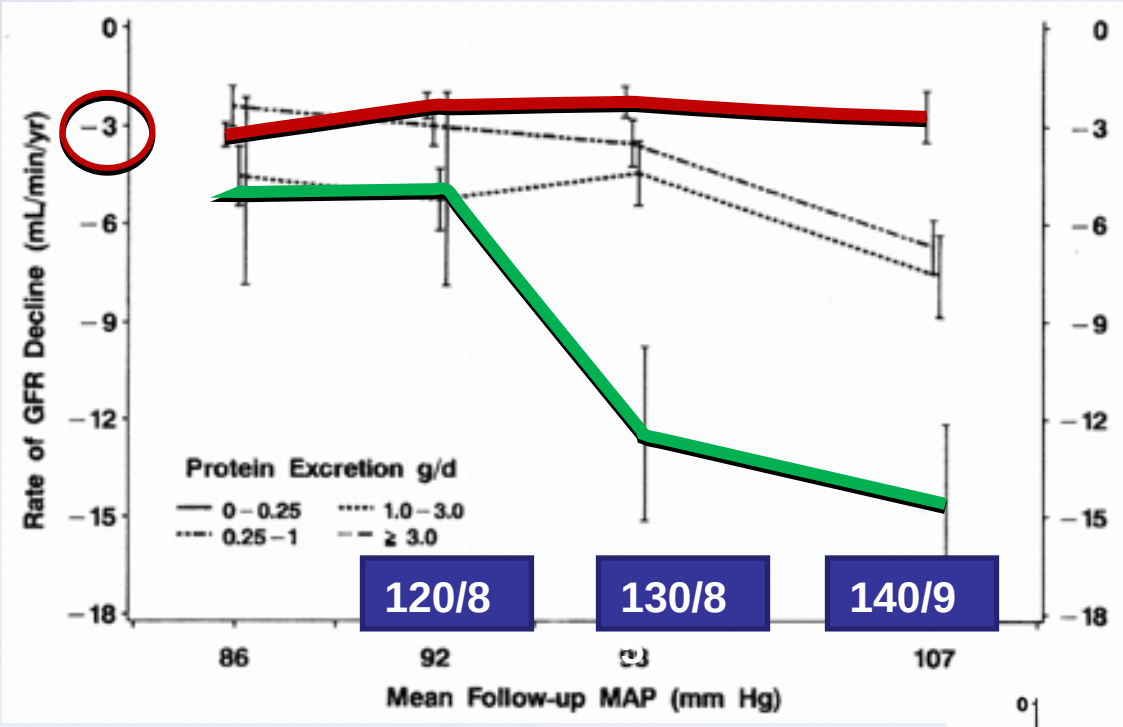
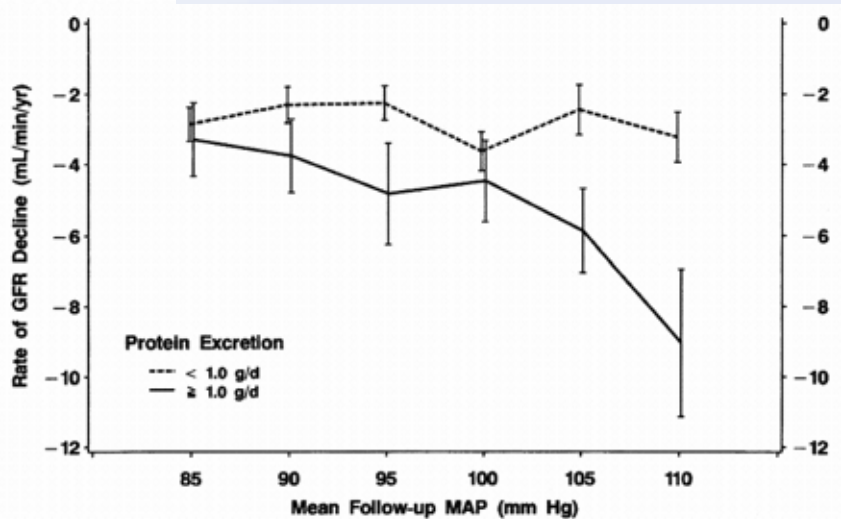
¿Y la insuficiencia renal sin proteinuria?

Mean GFR decline and achieved follow-up blood pressure Modification of Diet in Renal Disease study



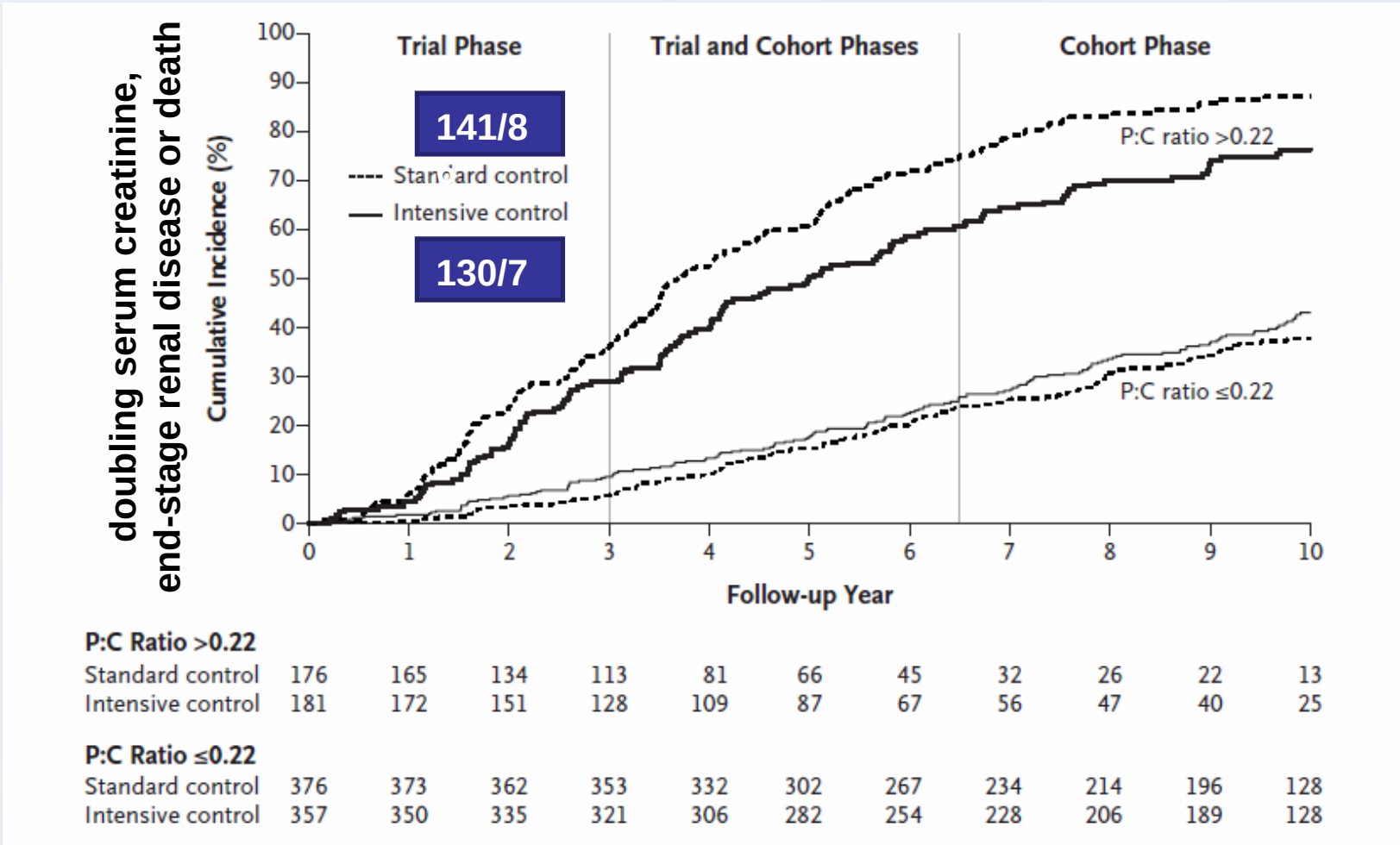
GFR
25-55 mL/min.1.73 m²

GFR
13-24 mL/min.1.73 m²



Peterson JC, et al. Ann Intern Med. 1995; 123: 754-62

Intensive blood pressure control and renal function in hypertensive chronic kidney disease



P:C Ratio >0.22											
Standard control	176	165	134	113	81	66	45	32	26	22	13
Intensive control	181	172	151	128	109	87	67	56	47	40	25
P:C Ratio ≤0.22											
Standard control	376	373	362	353	332	302	267	234	214	196	128
Intensive control	357	350	335	321	306	282	254	228	206	189	128

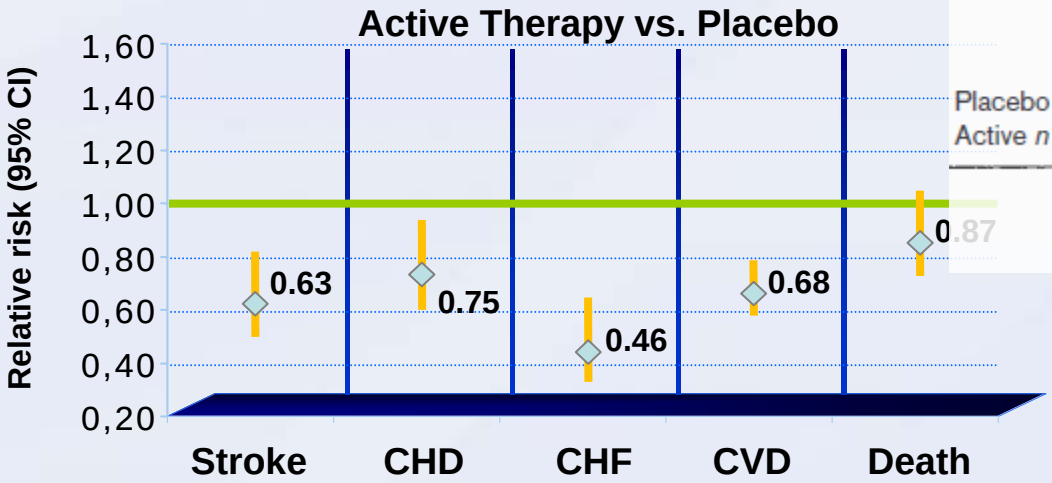
Appel LJ, et al. New Engl J Med. 2010; 363: 918-29

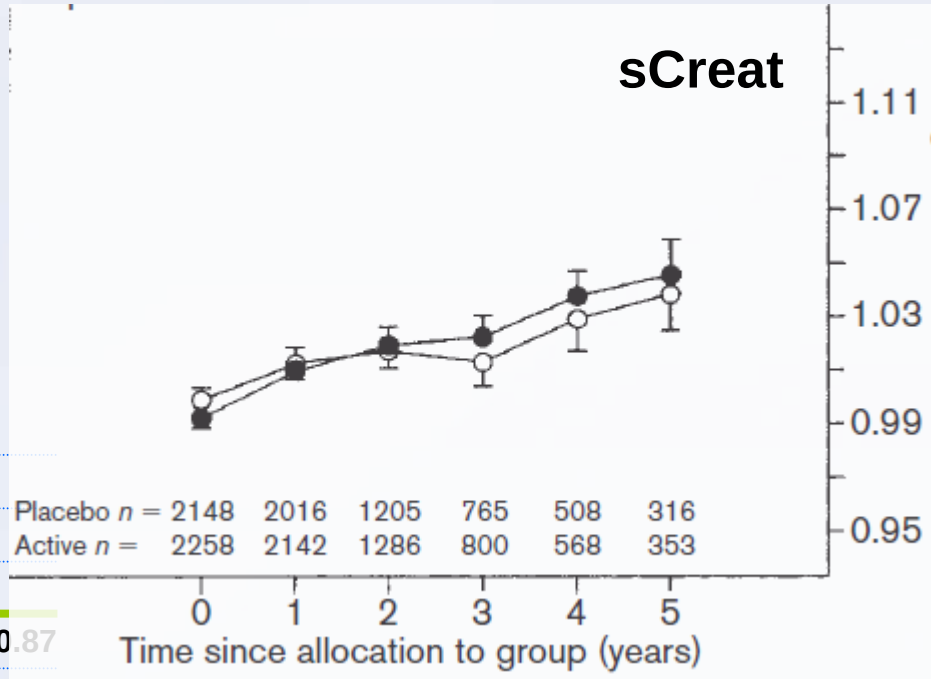
Follow-up of renal function in the Syst-Eur trial

≥60 yr Mean age 72 yr

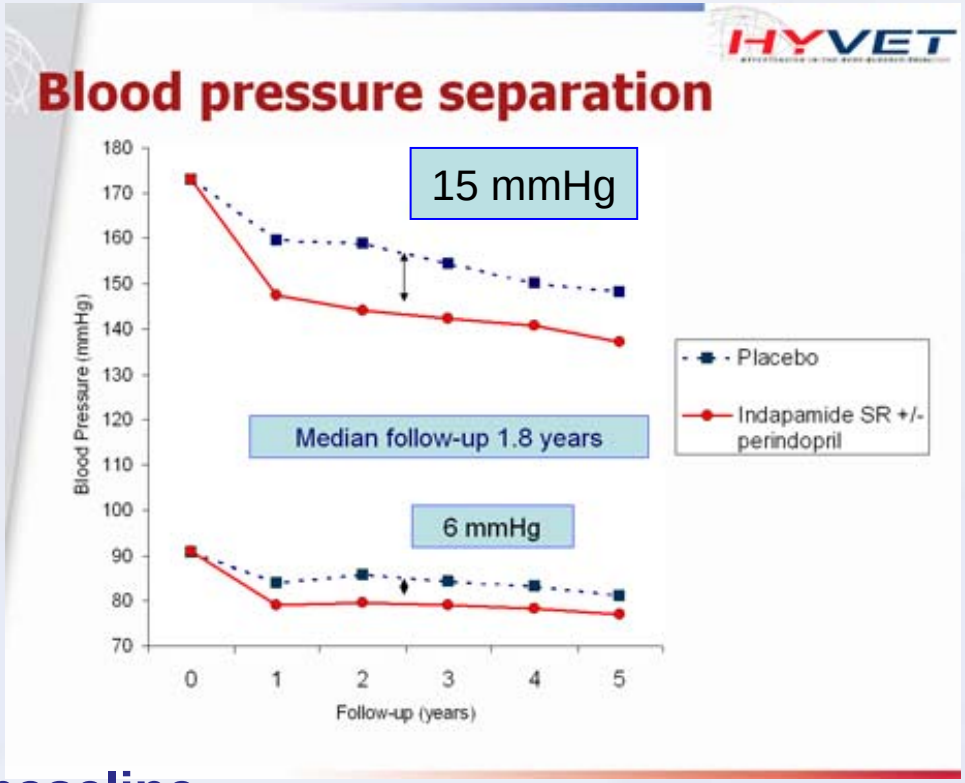
Nitrendipine±Ena±Htz vs. Placebo

ΔBP 10.1/4.5 mHg active vs. placebo





Voyaki SM, et.al. J Hypertens 2001; 19: 511-19



Biochemical changes from baseline

In 2 year cohort there were no significant differences between the groups with regard to change in serum….

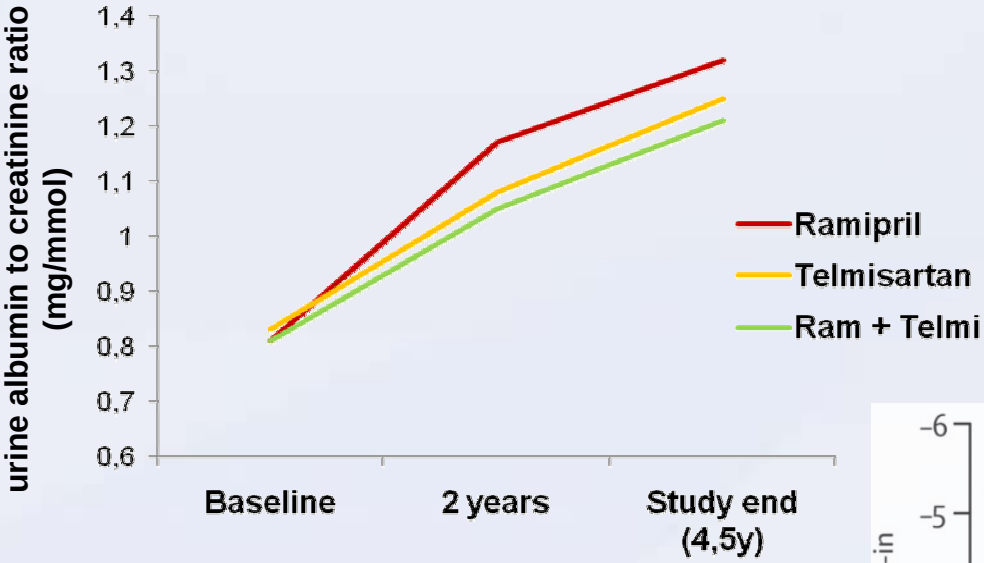
- Potassium
- Uric acid
- Glucose
- **Creatinine**

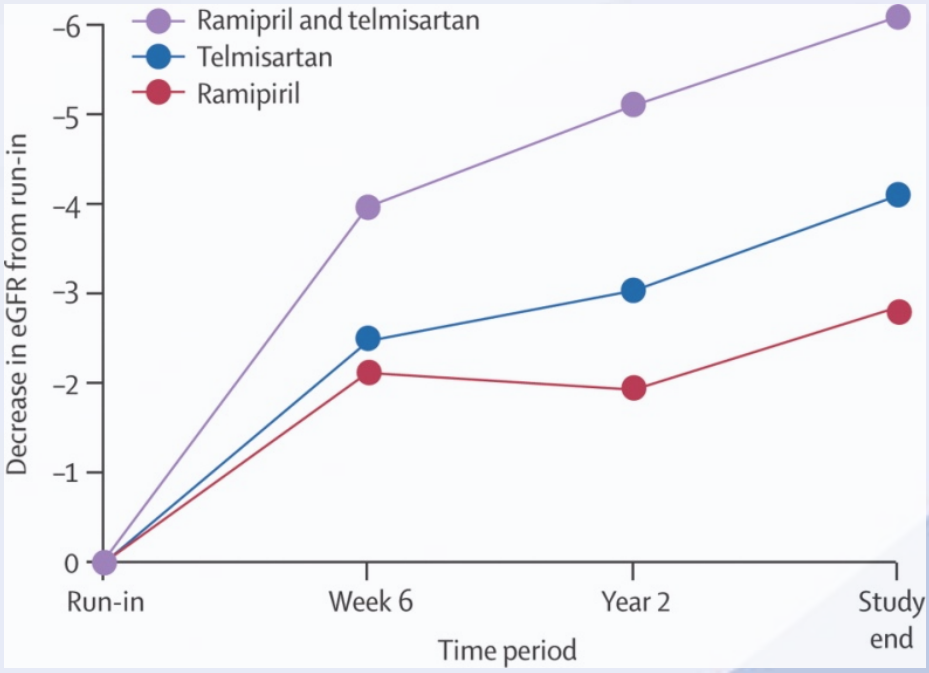
Beckett NS, et al. N Engl J Med. 2008;358

Insuficiencia renal sin proteinuria

- Control de presión arterial?
- Bloqueo del Sistema Renina-Angiotensina?

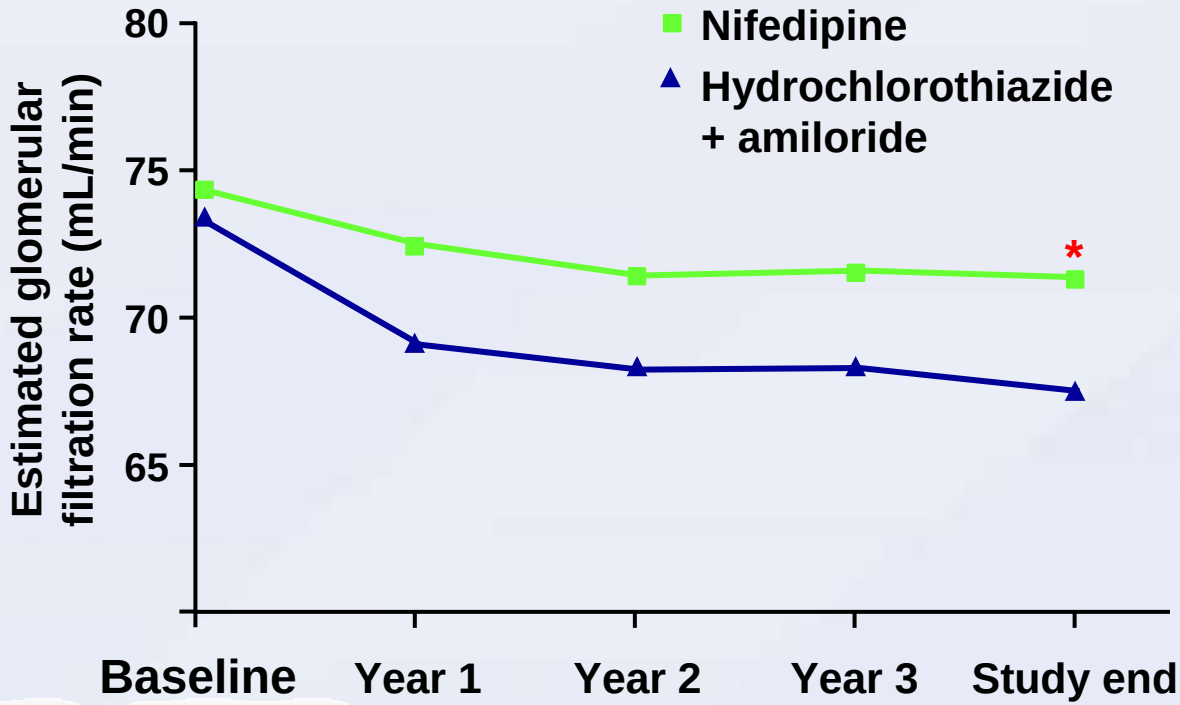
RAS blocking and renal outcomes in the ONTARGET trial





Mann JF, et al. Lancet. 2008; 372: 547-53

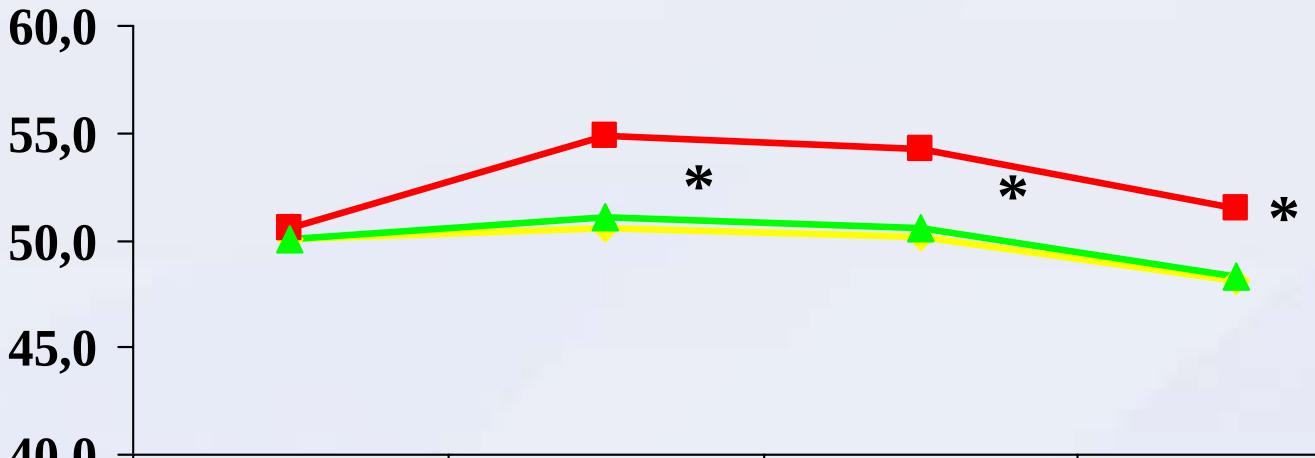
CCB vs Diuretic therapy
eGFR throughout the study - The INSIGHT trial



	Nifedipine (n=3157)		Co-amilozide (n=3164)		p
	n (%)	Number of patients withdrawn	n (%)	Number of patients withdrawn	
Metabolic adverse events					
Hypokalaemia	61 (1·9%)	0	195 (6·2%)	8	<0·0001
Hyponatraemia	8	0	61 (1·9%)	12	<0·0001
Hyperlipidaemia	127 (4·0%)	0	202 (6·3%)	0	<0·0001
Hyperglycaemia	178 (5·6%)	0	244 (7·7%)	4	0·001
Hyperuricaemia	40 (1·3%)	3	201 (6·4%)	1	<0·0001
Impaired renal function	58 (1·8%)	3	144 (4·6%)	18	<0·0001

Brown M, et al. Lancet 2000; 356: 366–72

The ALLHAT trial
Baseline eGFR<60 ml/m



	Baseline (n=5662)	1 Year (n=3583)	2 Year (n=3421)	4 Year (n=2718)
Chlorthalidone	50,1	50,6	50,2	48,1
Amlodipine	50,6	54,9	54,3	51,5
Lisinopril	50,1	51,1	50,6	48,3

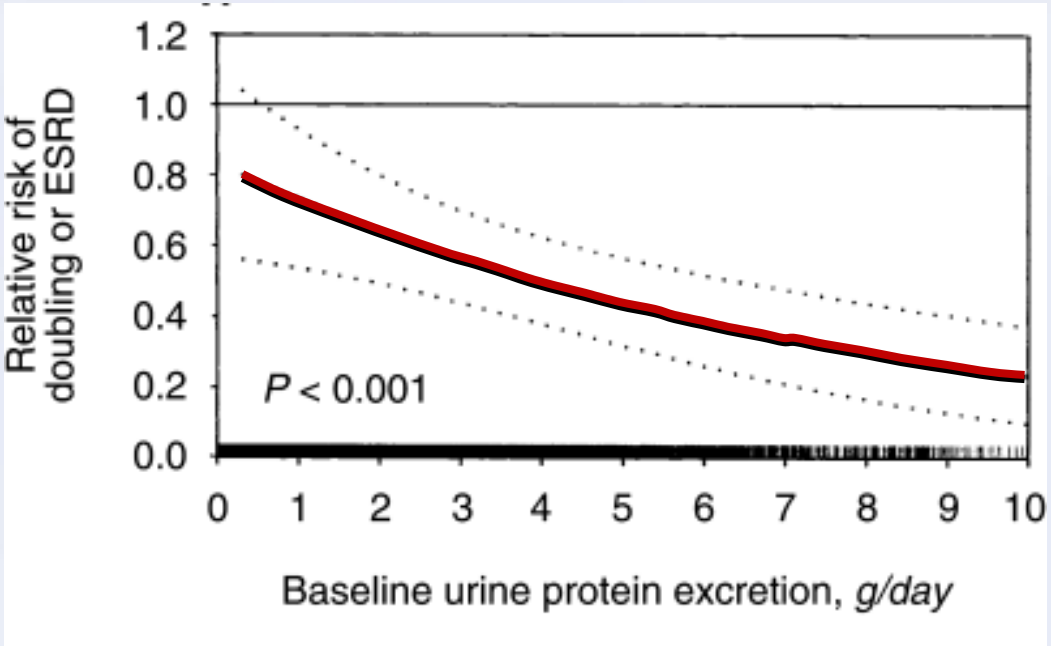
* p<0.05 vs. Chlorthalidone
Estimated GFR (eGFR) calculated from the simplified MDRD equation

Rahman M, et.al. Arch Intern Med 2005; 42: 67-75

ACEI treatment and progression of CKD

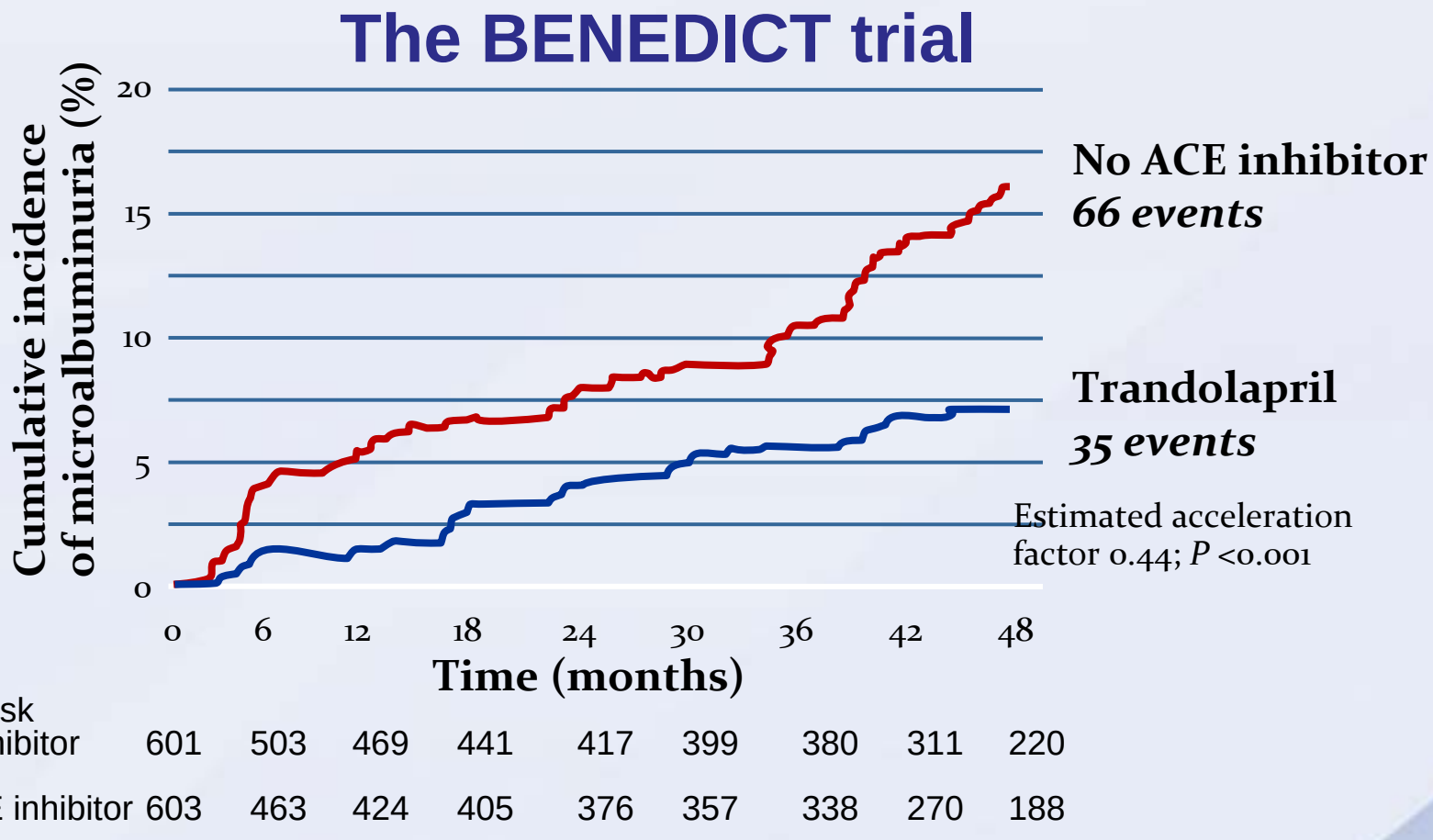
Meta-analysis of 11 randomized controlled trials
1860 patients

ACEI treatment vs. Antihypertensive non-ACEI regimens



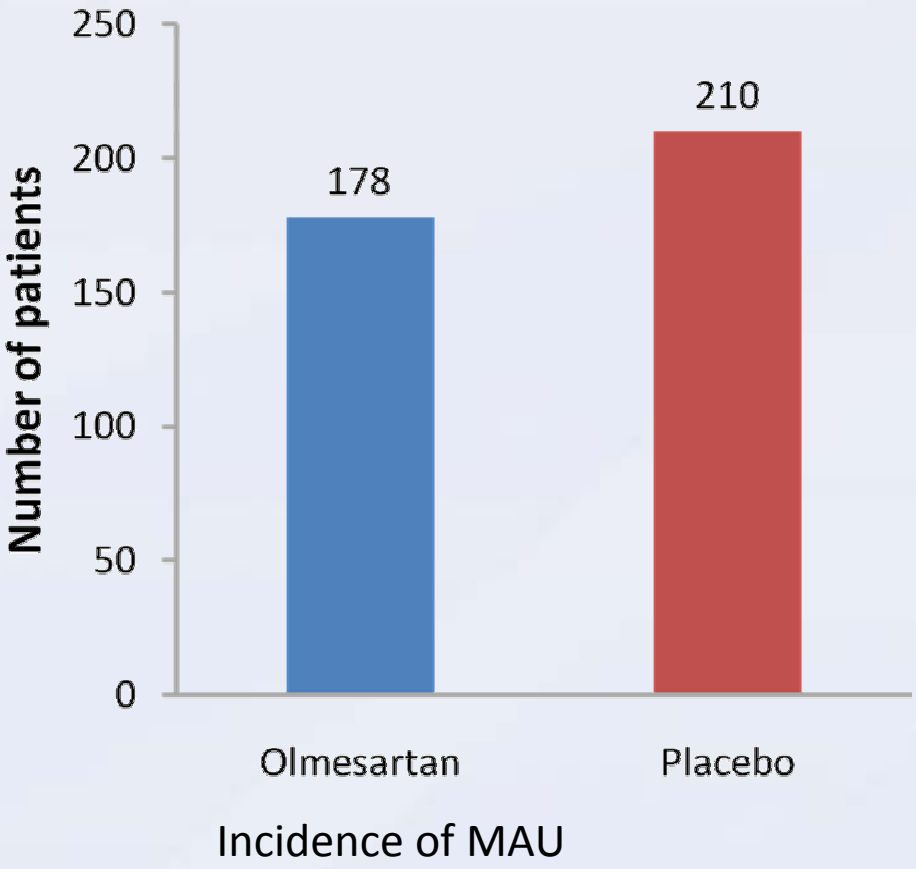
Jafar TH, et al. Kidney Int 2001; 60: 1131-40

Is there a renal benefit in blocking the RAS in non-proteinuric patients?

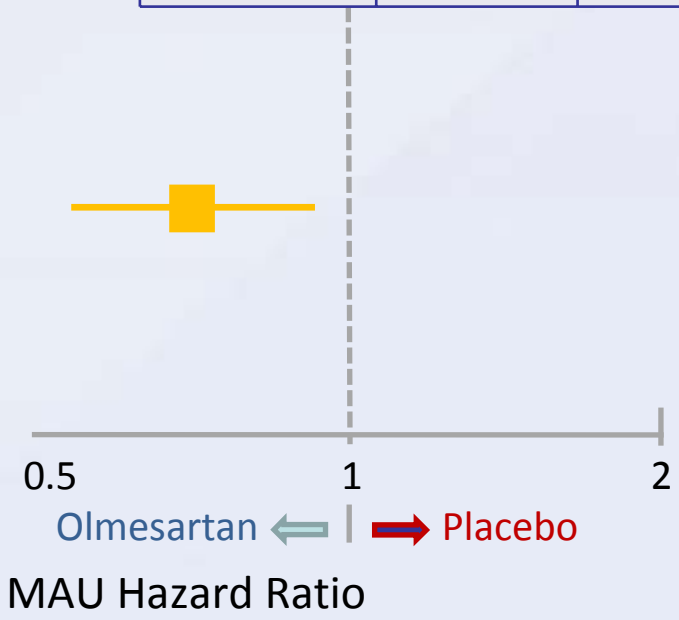


Ruggenenti P, et al. N Engl J Med 2004; **351**: 1941-51.

ROADMAP: Time to First Occurrence of MAU Incidences and Hazard Ratio



Hazard Ratio (95%-CI)	Risk Reduction	p value
0.770 (0.630–0.941)	23%	p=0.010

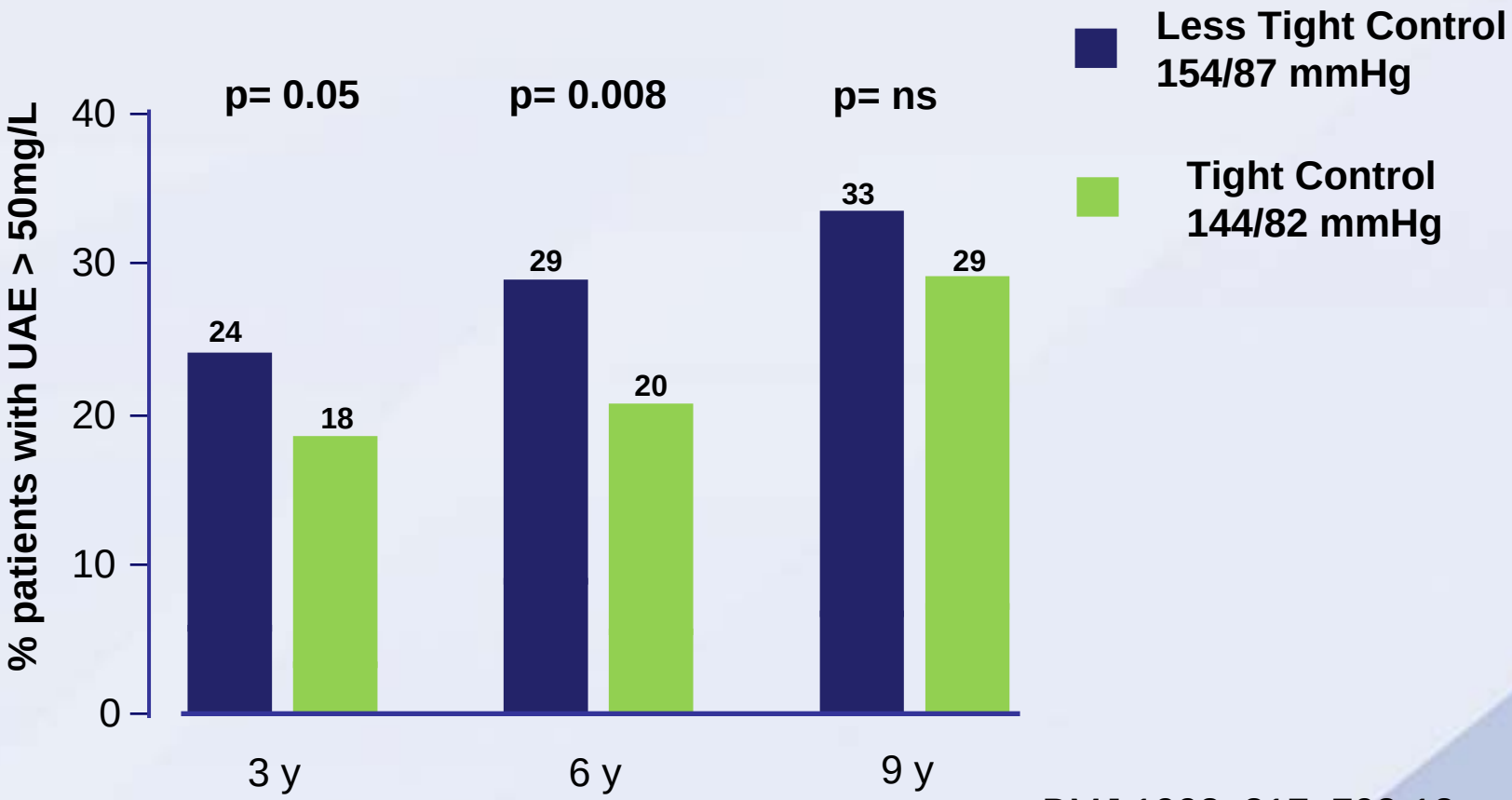


Presented at ASN 2009

Blood pressure control and primary prevention of diabetic nephropathy

UKPDS

DM2 + HTA n=1148



BMJ 1998; 317: 703-13

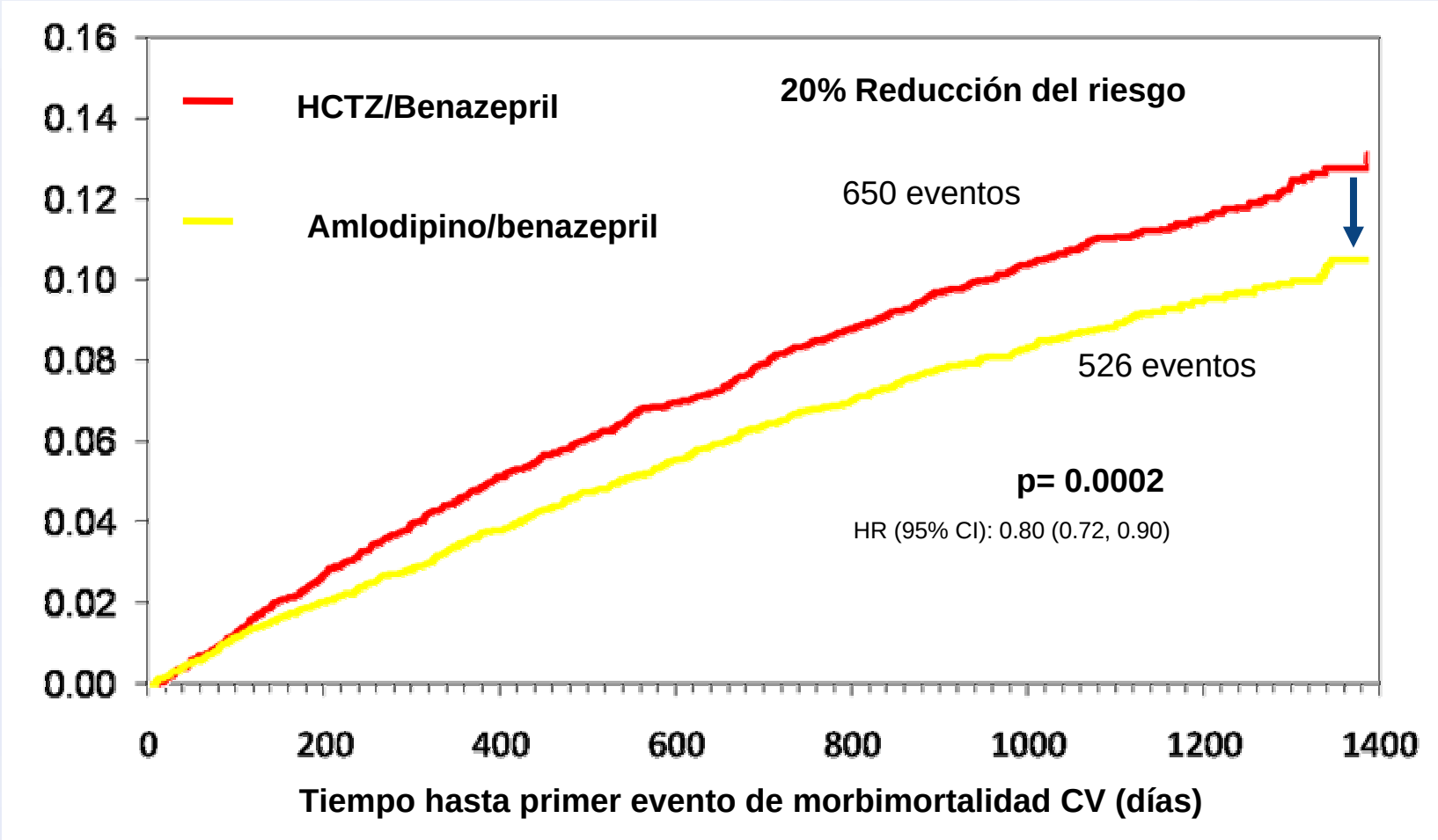
Prevalence and clinical characteristics of microalbuminuria in the Spanish hypertensive population

Med Clin (Barc) 2008; 130: 201-5

Alejandro de la Sierra[a], , , María Isabel Egocheaga[b] and María Teresa Aguilera[c]

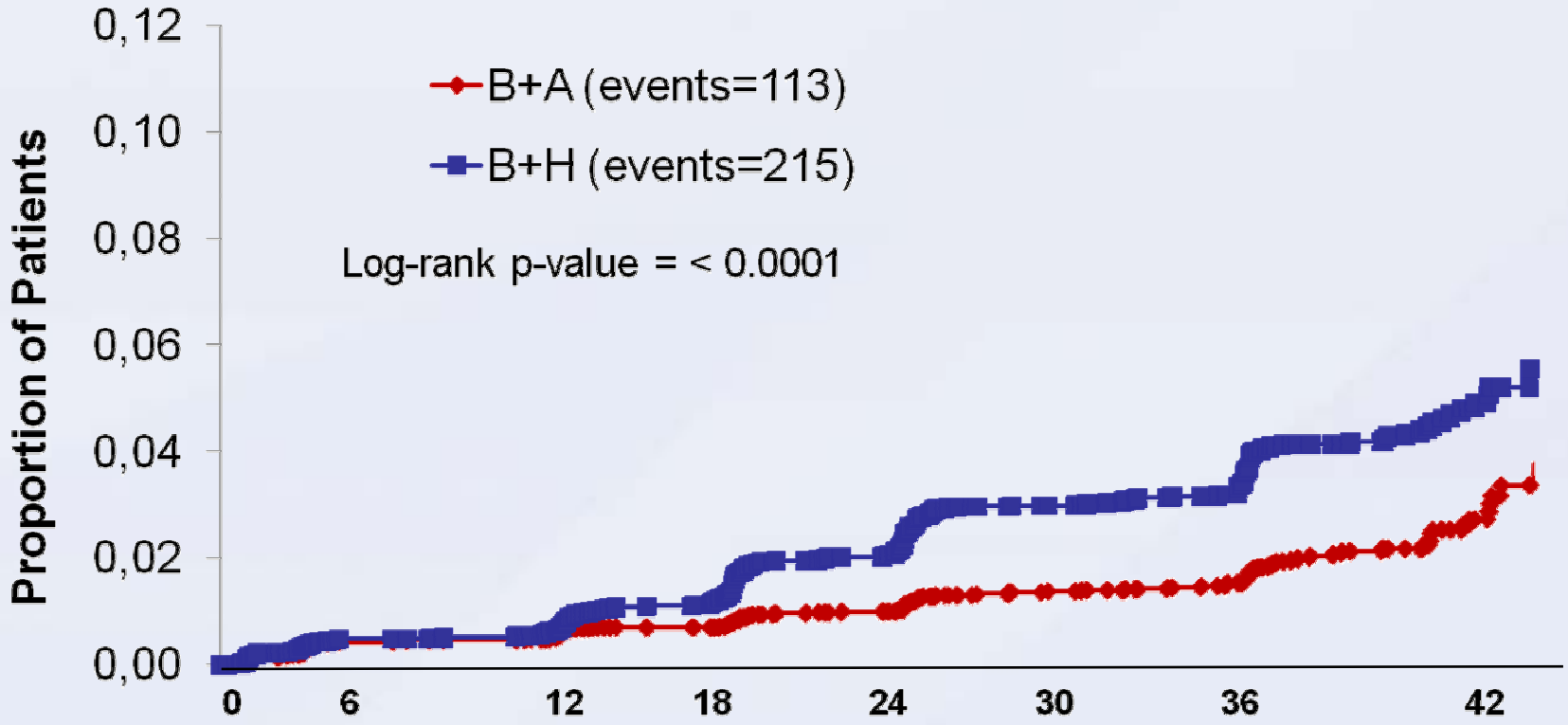
HTA	**40,2%**	**19.698.000**
Diabetes en hipertensos	**34,7%**	**- 6.835.206**
		12.862.794
Proteinuria en hipertensos	**1,8%**	**- 231.530**
		12.631.264

Estudio ACCOMPLISH
Resultados variable principal



Jamerson K, et al. N Engl J Med. 2008; 359: 2417-28

ACCOMPLISH - Kaplan-Meier Curves for Renal Progression - GFR<15+Dialysis+ESRD+2xCr ITT Population

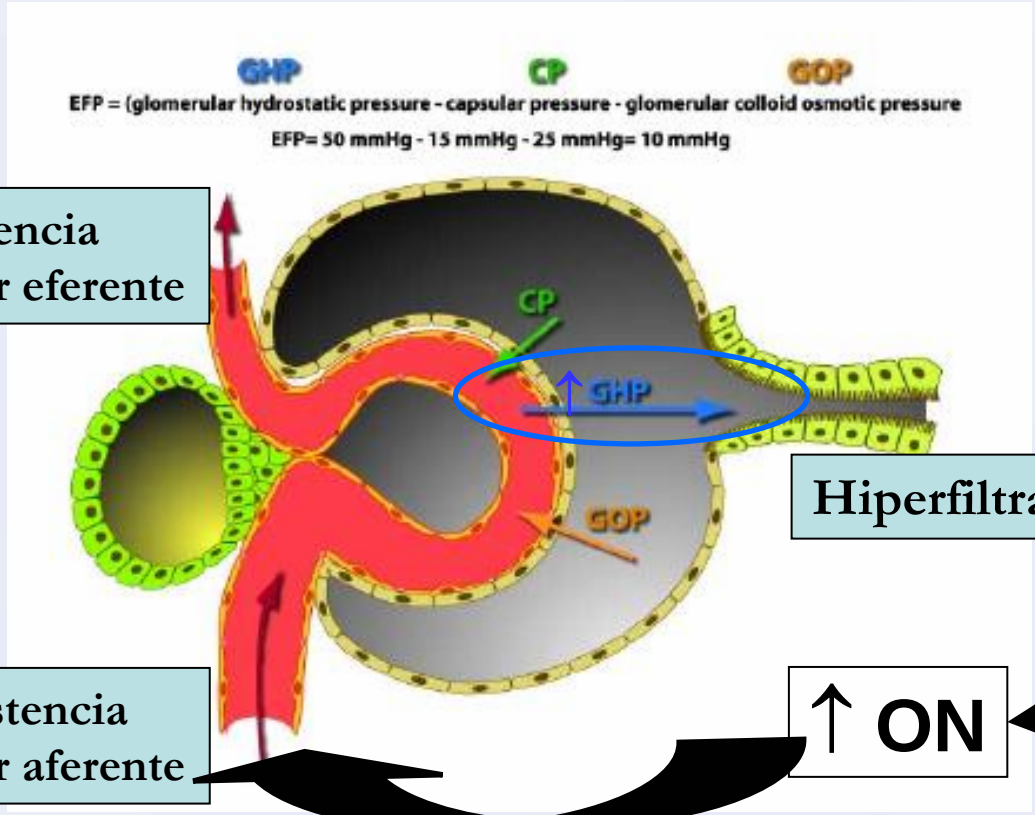


Number at Risk

B+A	5743	5578	5452	5336	5203	5022	3016	1559
B+H	5762	5576	5459	5307	5139	4936	2956	1506

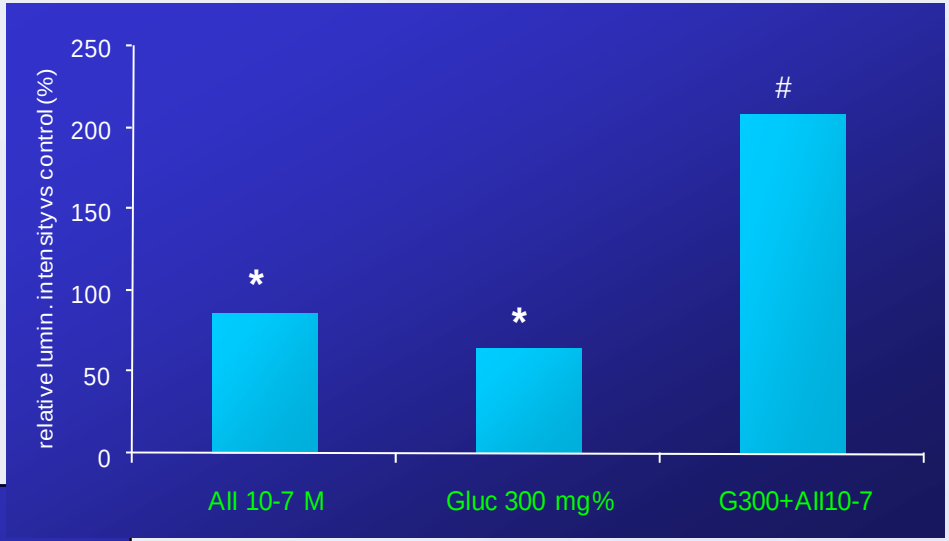
Bakris GL, et.al. Lancet 2010; 375: 1173-81

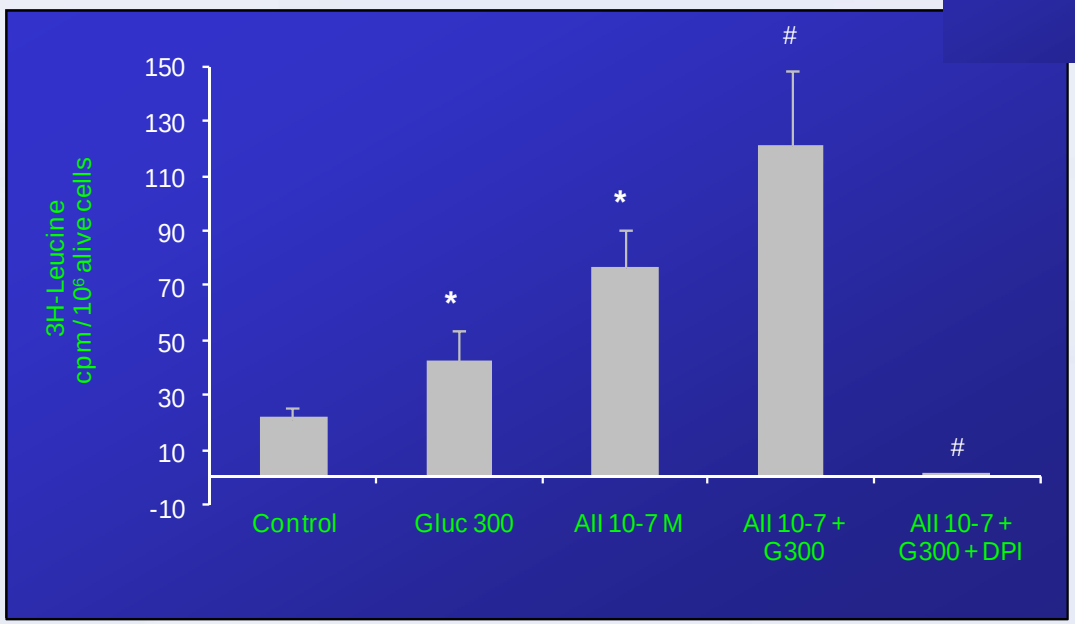
Hemodinamia glomerular en DM



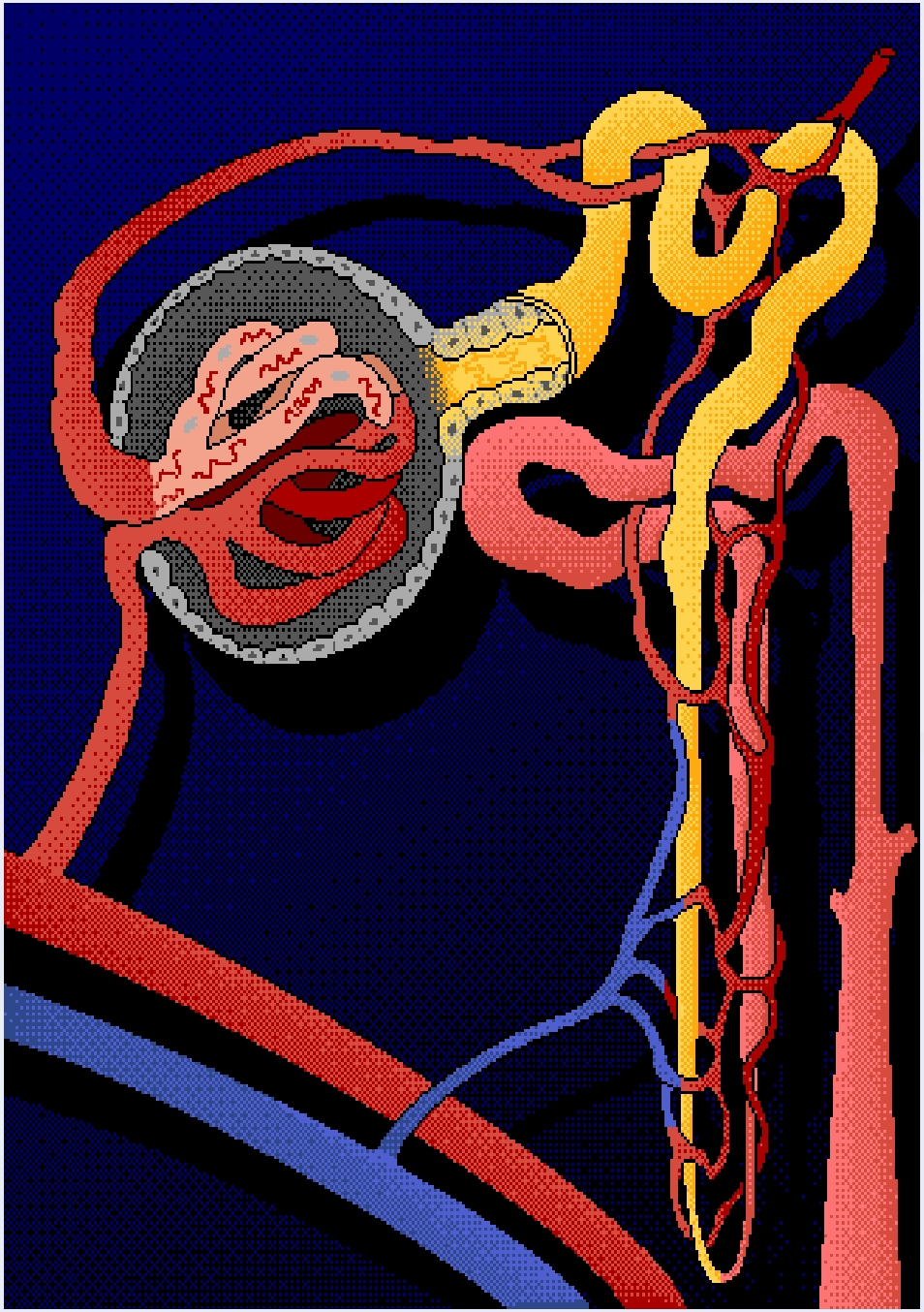
Estrés oxidativo inducido por glucosa e hipertrofia mesangial

Potenciación por Angiotensina II





Galceran JM, et al. Hipertensión 2001; 18: 54



- **La reducción de la presión arterial comporta un beneficio renal?**
  - **Sí, al menos en diabetes y en proteinuria**

- **Algún tipo de fármaco antihipertensivo está más indicado para la preservación de la función renal?**
  - **Sí, bloqueo del SRA en diabetes y en proteinuria**
  - **Probablemente calcioantagonistas, con o sin bloqueo del SRA en el resto**