

Control de la PA y protección renal en el paciente diabético

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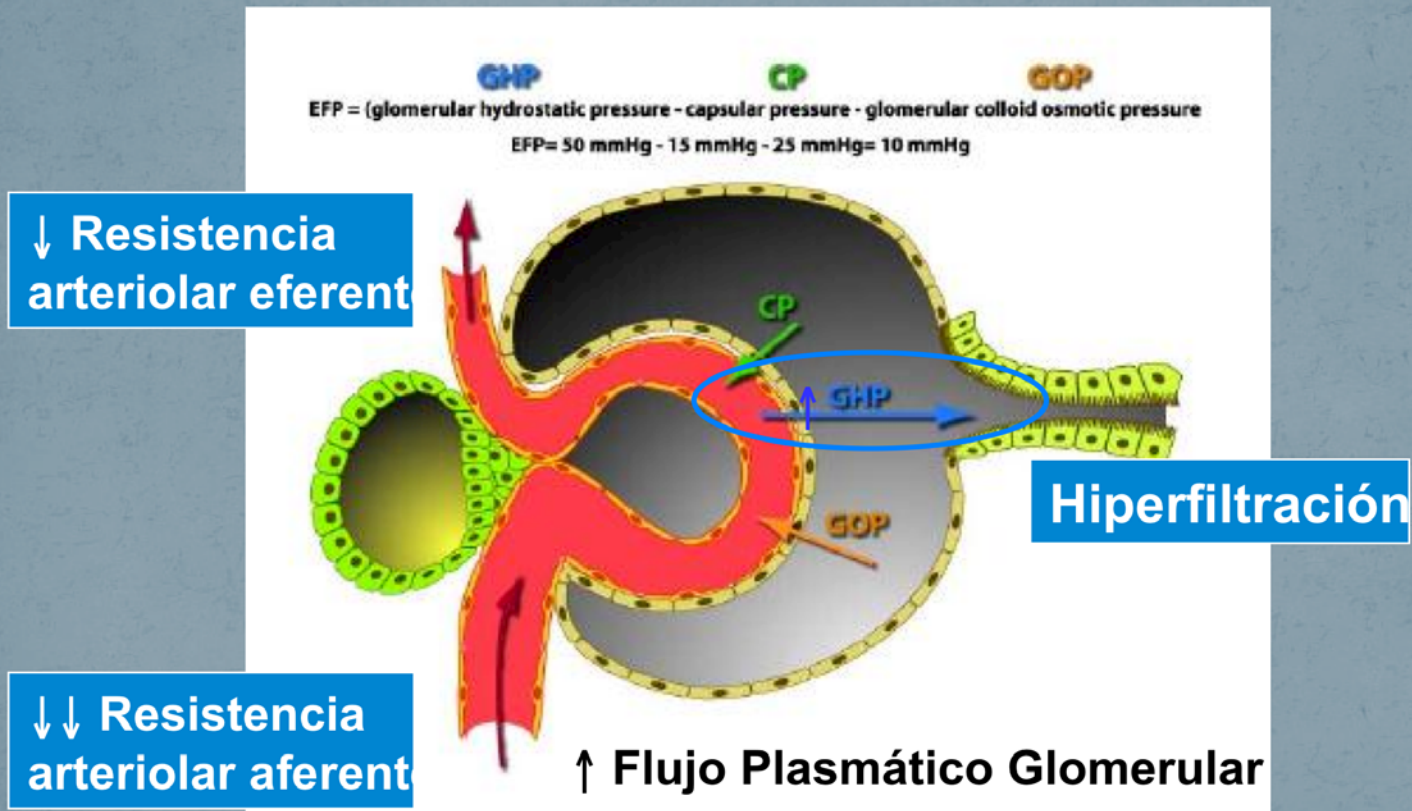


El 30-50% de pacientes con evolución de la DM de 10 a 20 años presenta algún grado de afectación renal

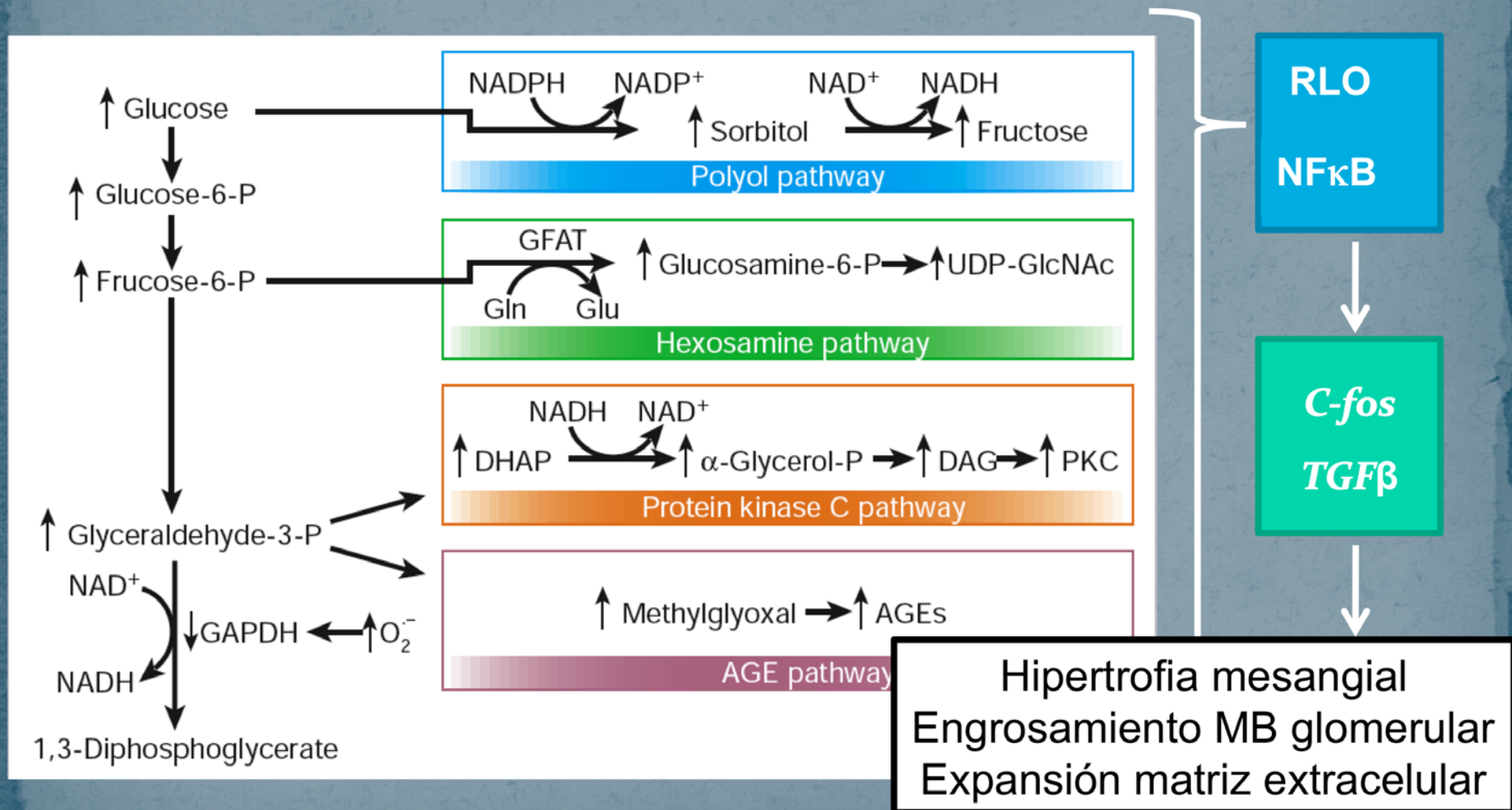
- Prevalencia de microalbuminuria
 - DM1: 13%
 - DM2: 23%
- ... de proteinuria
 - DM1: 4,6%
 - DM2: 5%
- ... y de insuficiencia renal
 - DM1: 4,8%
 - DM2: 8,4%
- 900.000 – 1.500.000 personas con ND en España

Fenómenos hemodinámicos

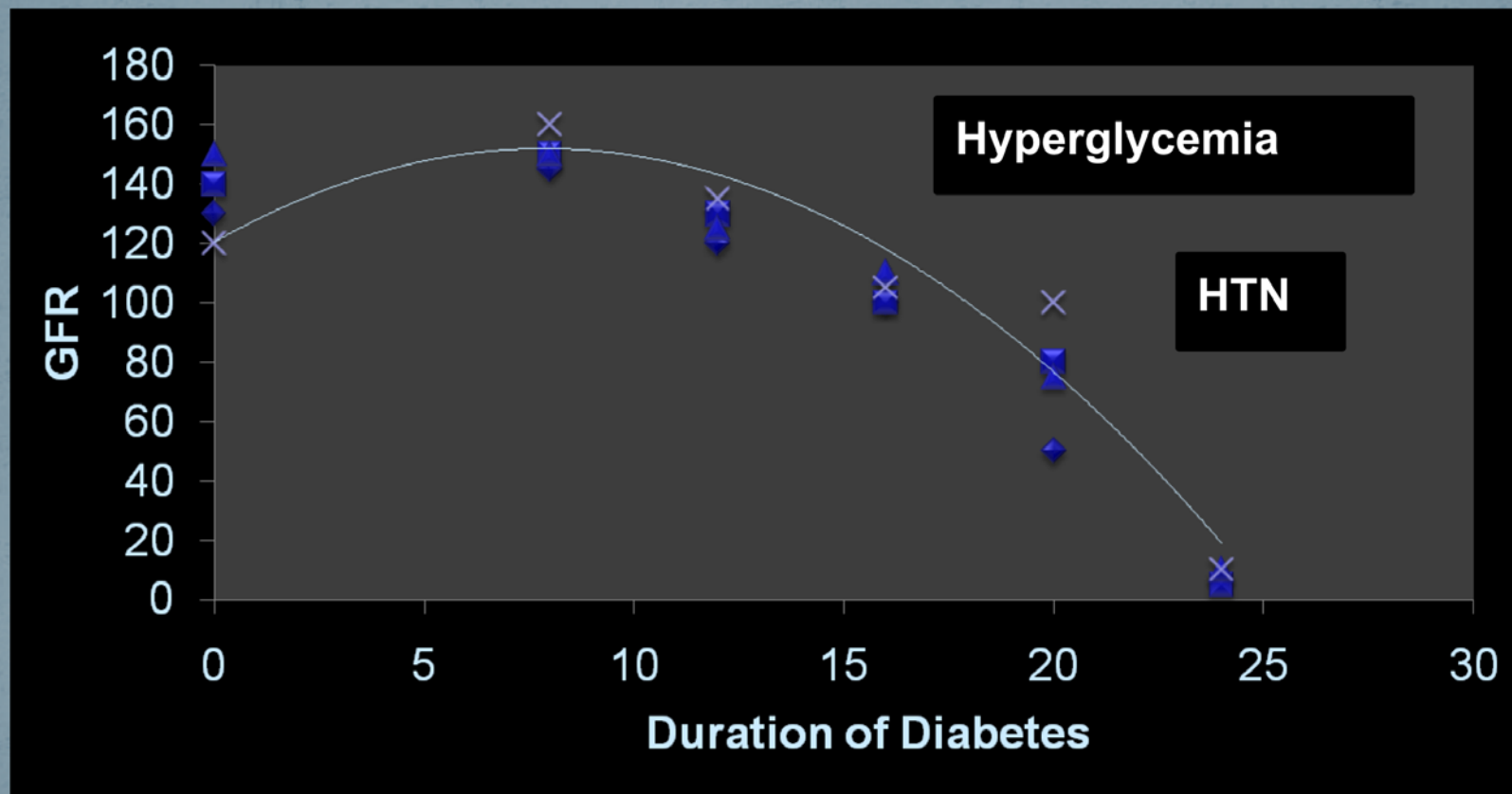
Alteración de la autorregulación



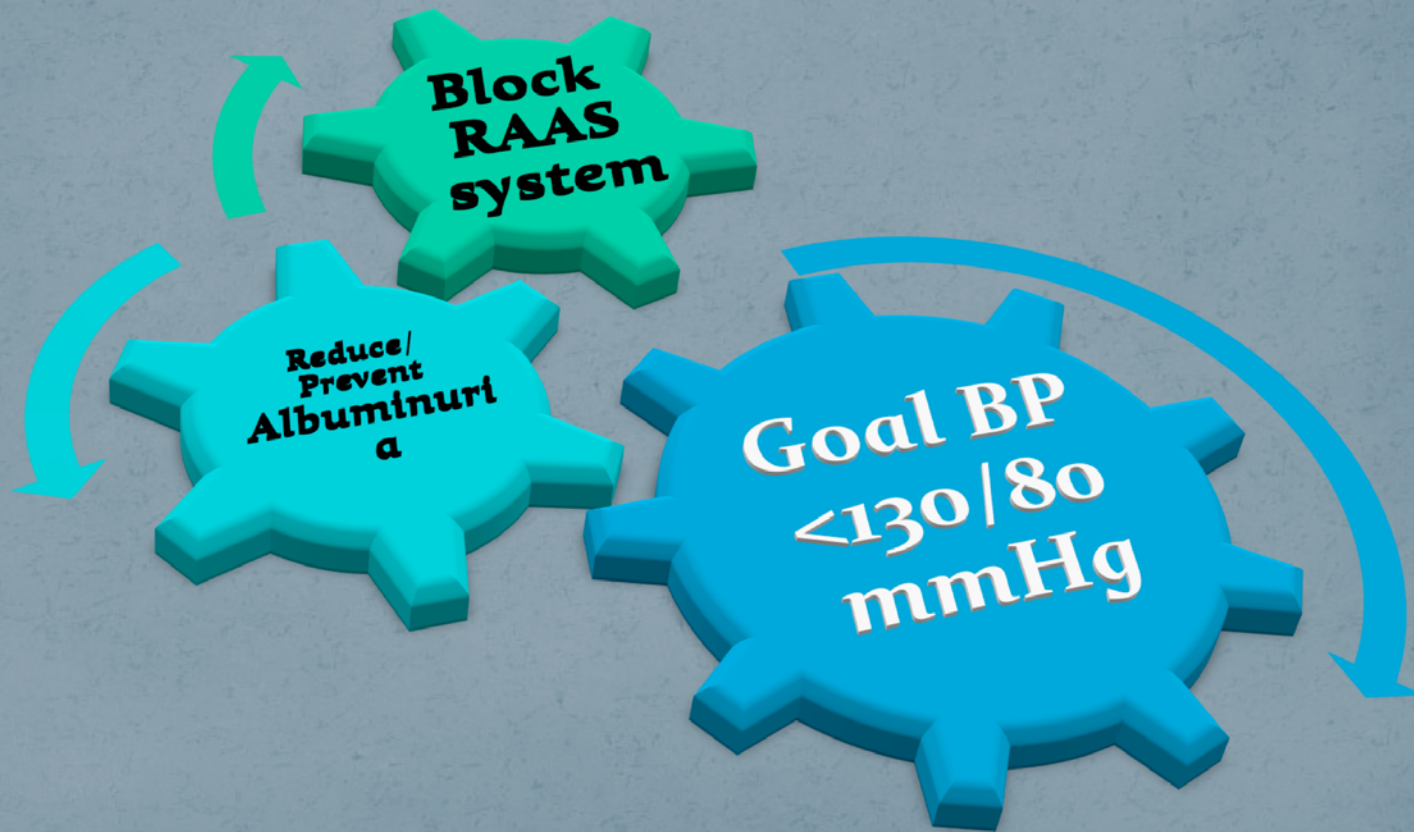
Fenómenos no-hemodinámicos



Evolución del filtrado glomerular en DM

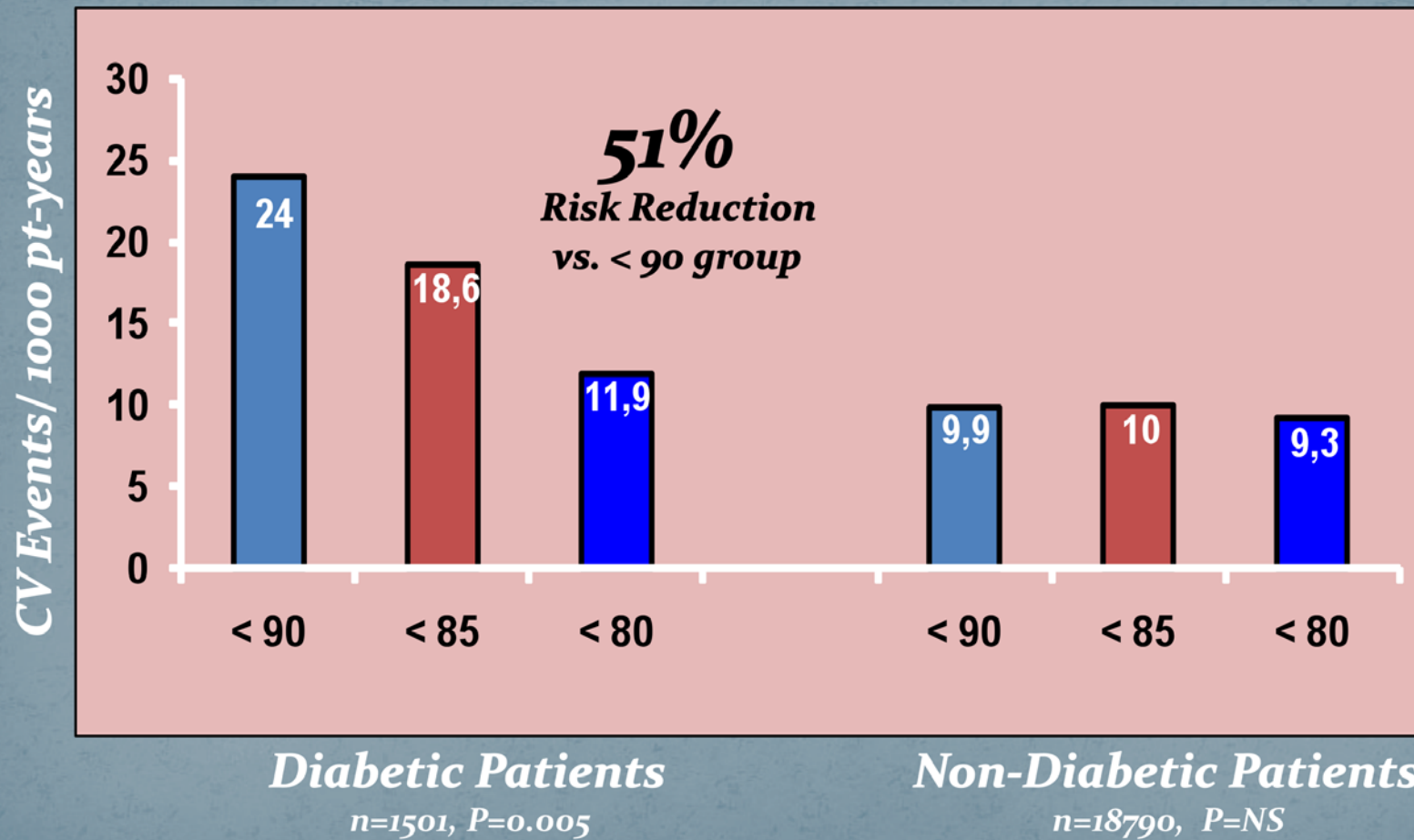


Presión arterial y protección renal en diabetes



PA en el paciente diabético

Estudio HOT



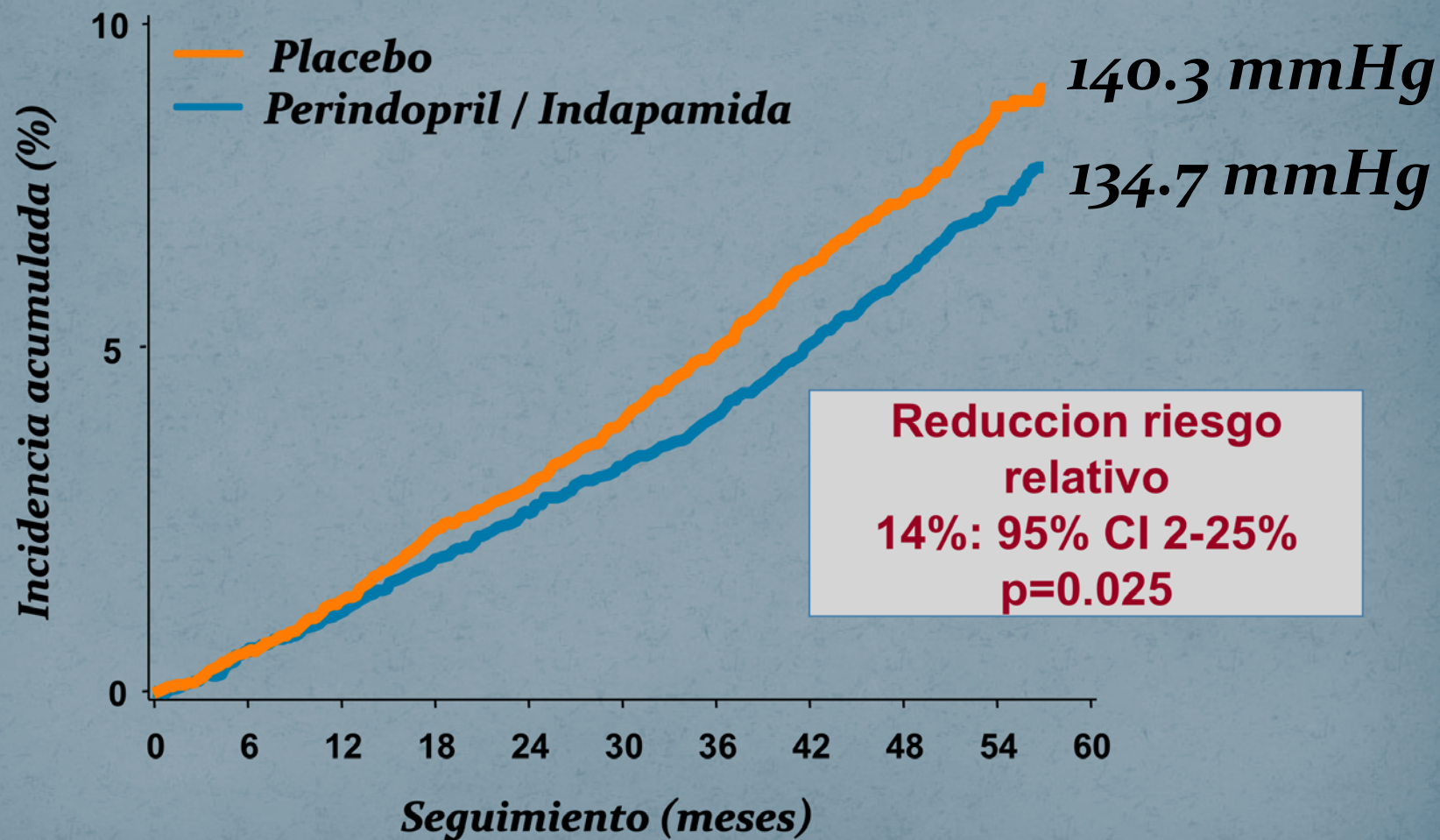
Hansson L, et al. Lancet 1998; 351: 1755-62

Antihypertensive treatment UK Prospective Diabetes Study (1998)

Intensive blood pressure control policy achieved 144/82 mmHg
Less tight control achieved 154/87 mmHg
Median follow-up of 8.4 years

	RR	p	NNT
Any diabetes-related endpoint	21%	0.005	9
Diabetes-related deaths	32%	0.02	17
Myocardial infarction	20%	0.13	23
Stroke	44%	0.013	12
Microvascular endpoints	37%	0.01	18

ADVANCE - Mortalidad



Patel A, et al. Lancet 2007; 370: 829-40

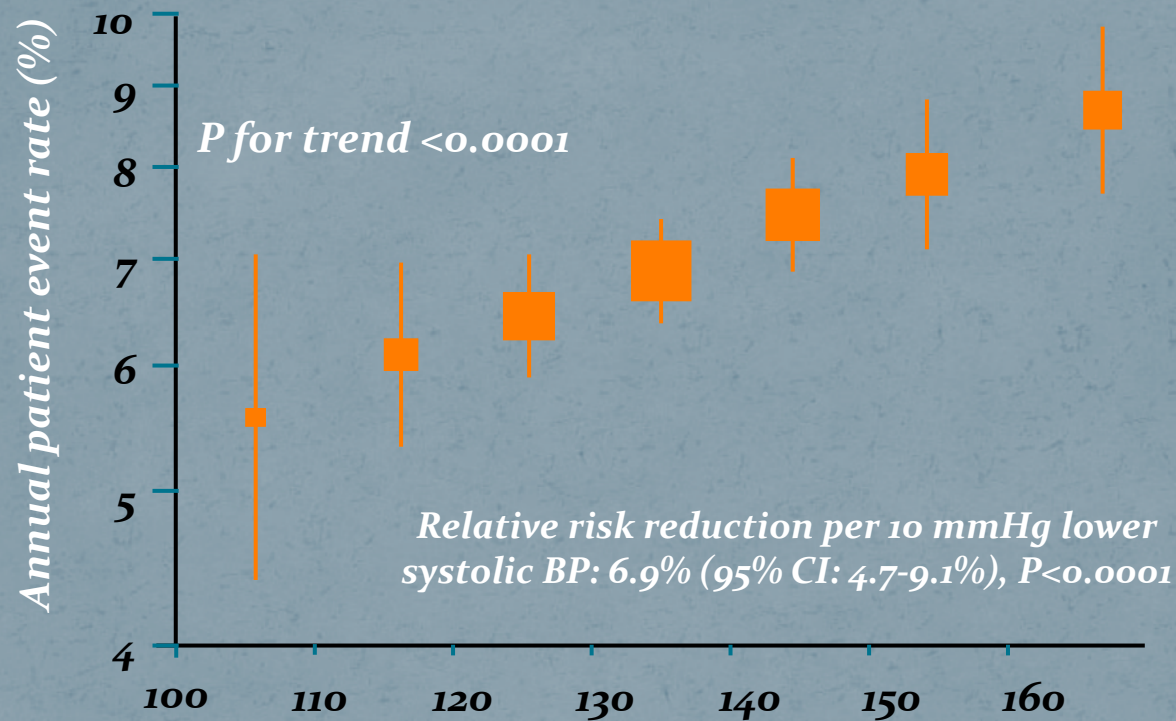
ADVANCE – PB lowering arm Summary of Renal events

● Routine administration of the fixed combination of perindopril-indapamide:

- Reduced the major renal outcome by 21%***
- Reduced progression of albuminuria by 22%***
- Promoted regression of albuminuria by 16%***

Patel A, et al. Lancet 2007; 370: 829-40

ADVANCE - Major renal outcomes by SBP achieved during follow-up*

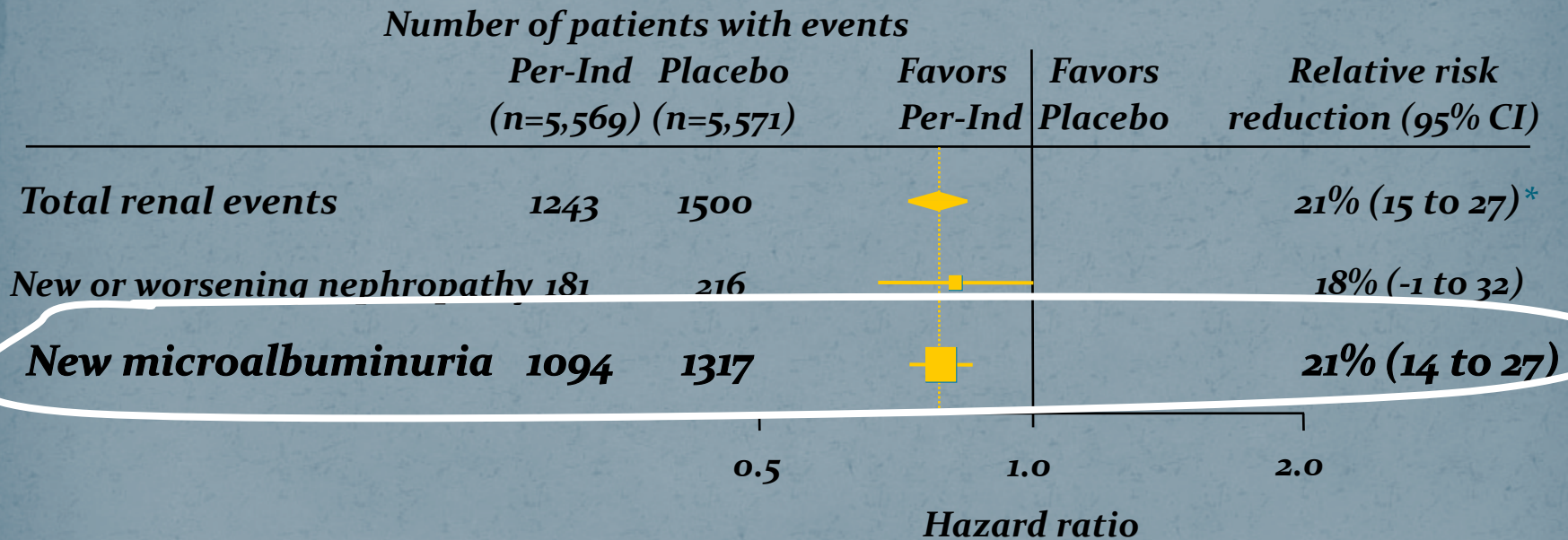


	106	116	125	135	144	154	168
Median systolic BP	106	116	125	135	144	154	168
No. of person-years	1431	4266	8974	11983	9138	4942	3470
	Achieved systolic blood pressure (mmHg)						

*Adjusted for age, sex, HbA_{1c}, serum lipids, BMI, smoking, alcohol use, and study drug

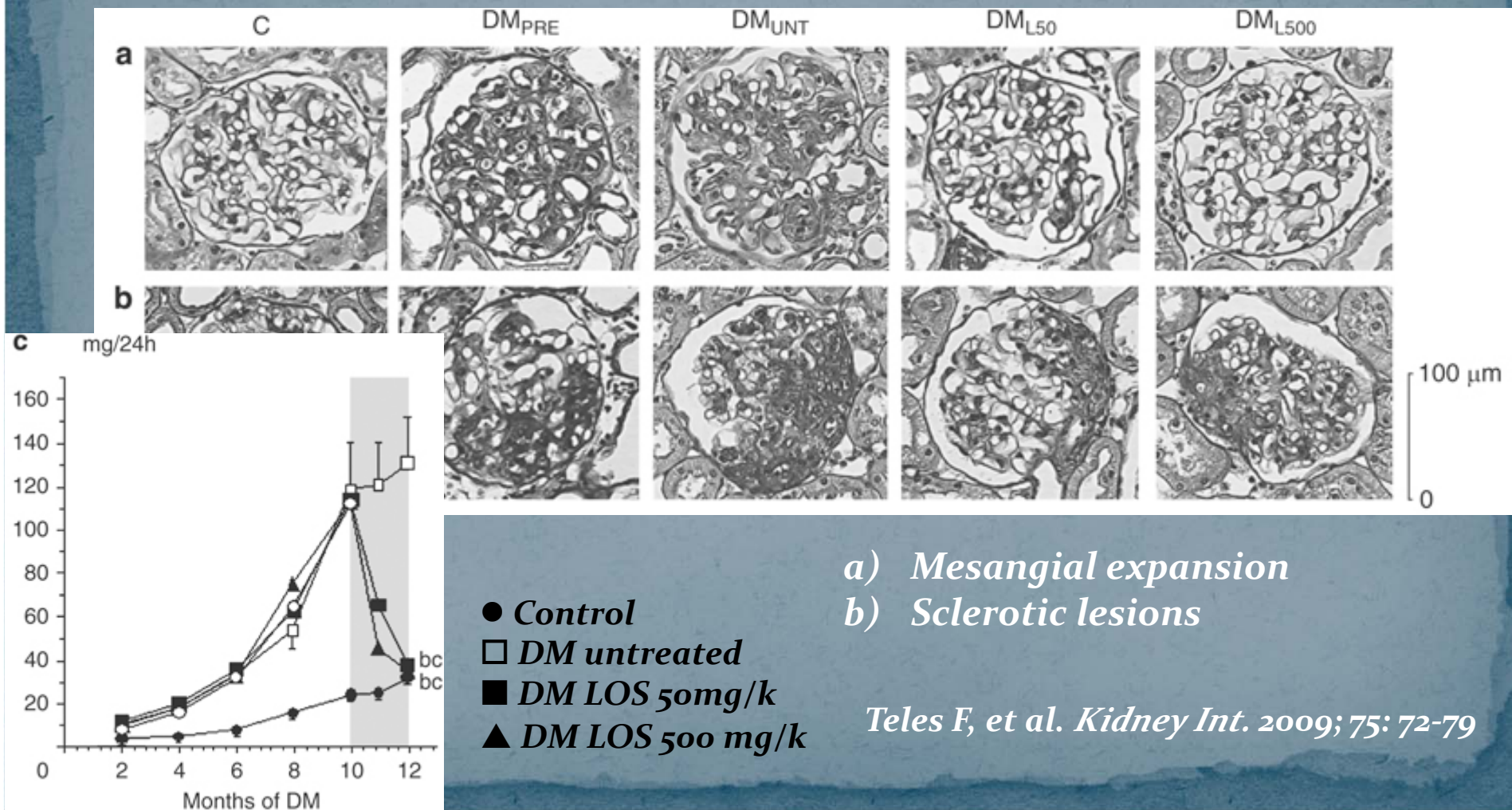
ADVANCE – PB lowerig arm

Renal events

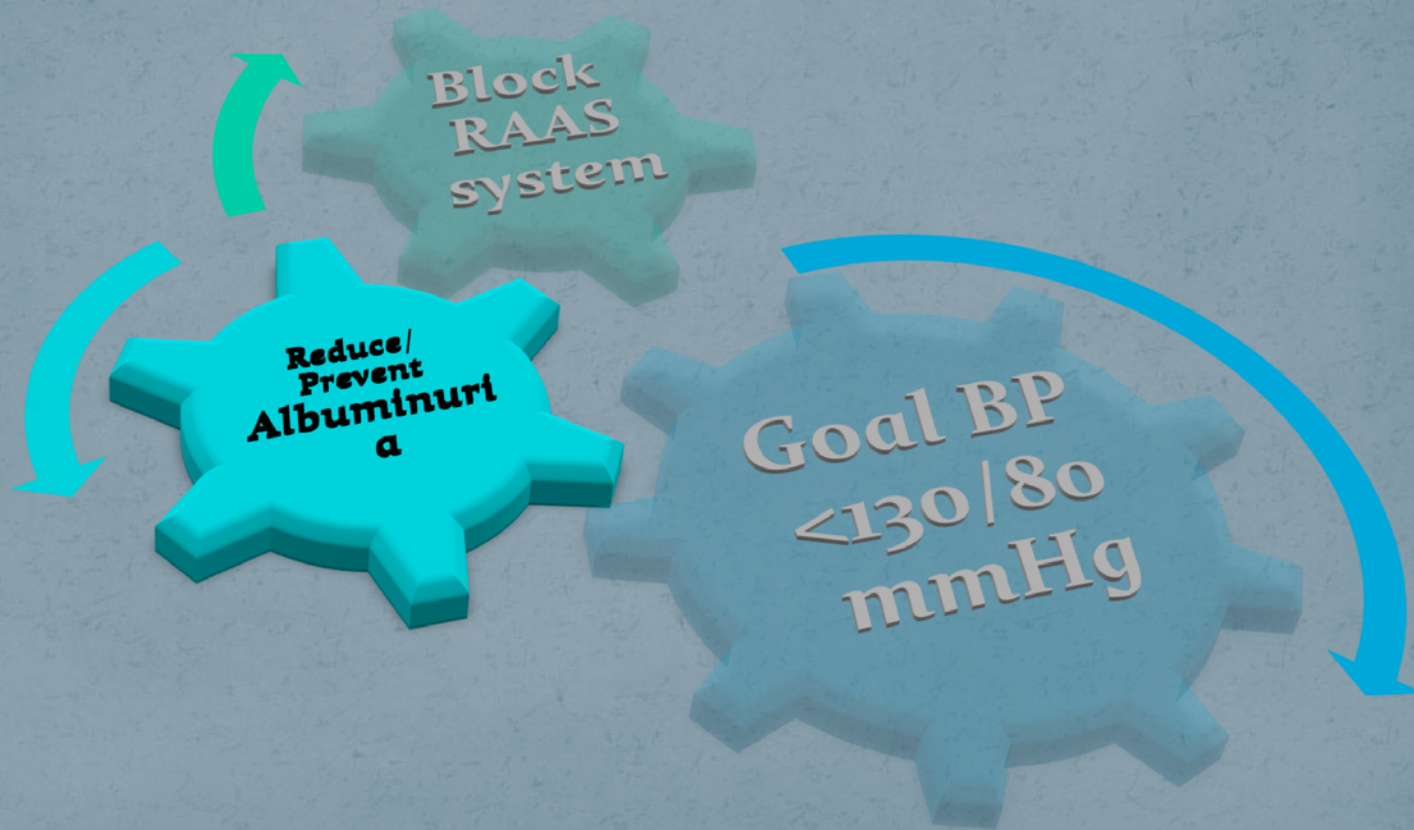


Patel A, et al. Lancet 2007; 370: 829-40

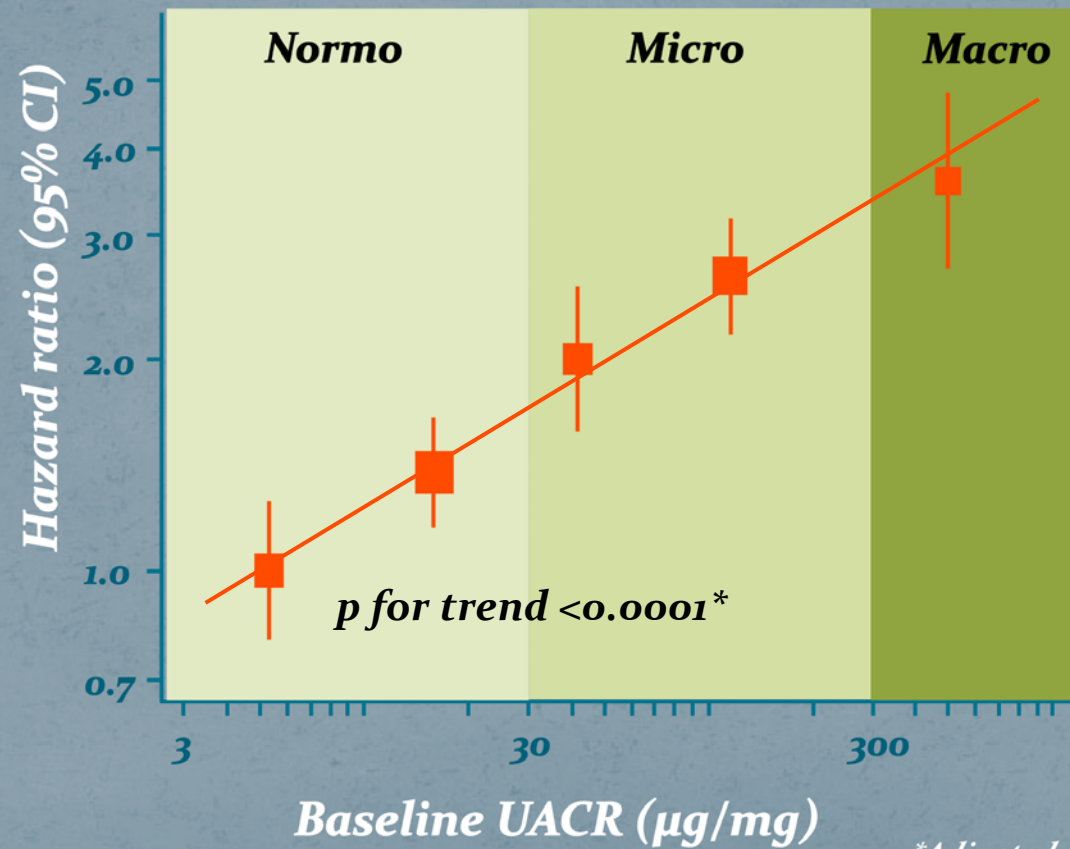
Regression of glomerular injury by losartan in experimental diabetic nephropathy



Presión arterial y protección renal en diabetes



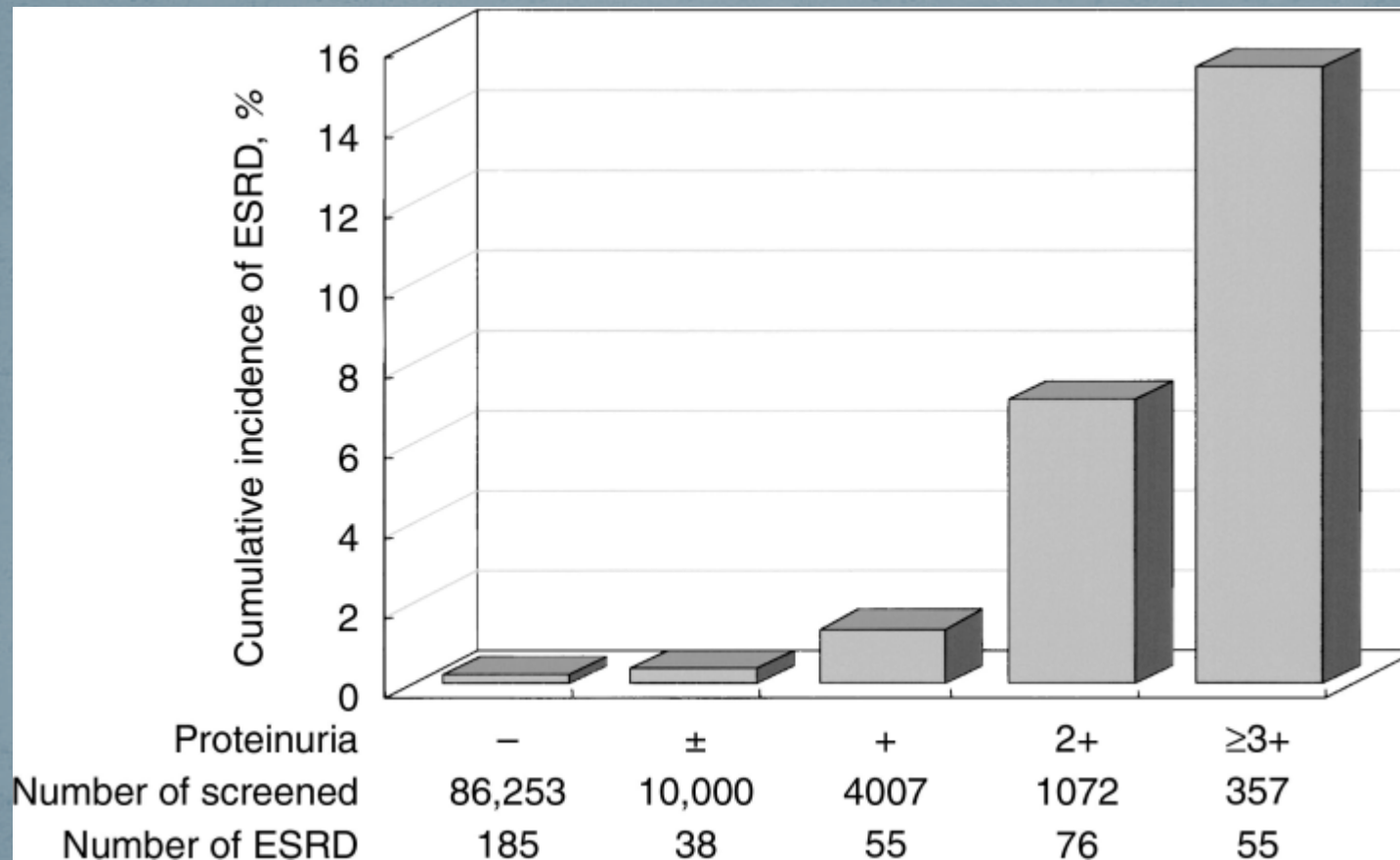
Riesgo de mortalidad CV según albuminuria basal (ADVANCE)



**Adjusted for age, sex, HbA_{1c}, serum lipids, BMI, smoking, alcohol use, and study drug*

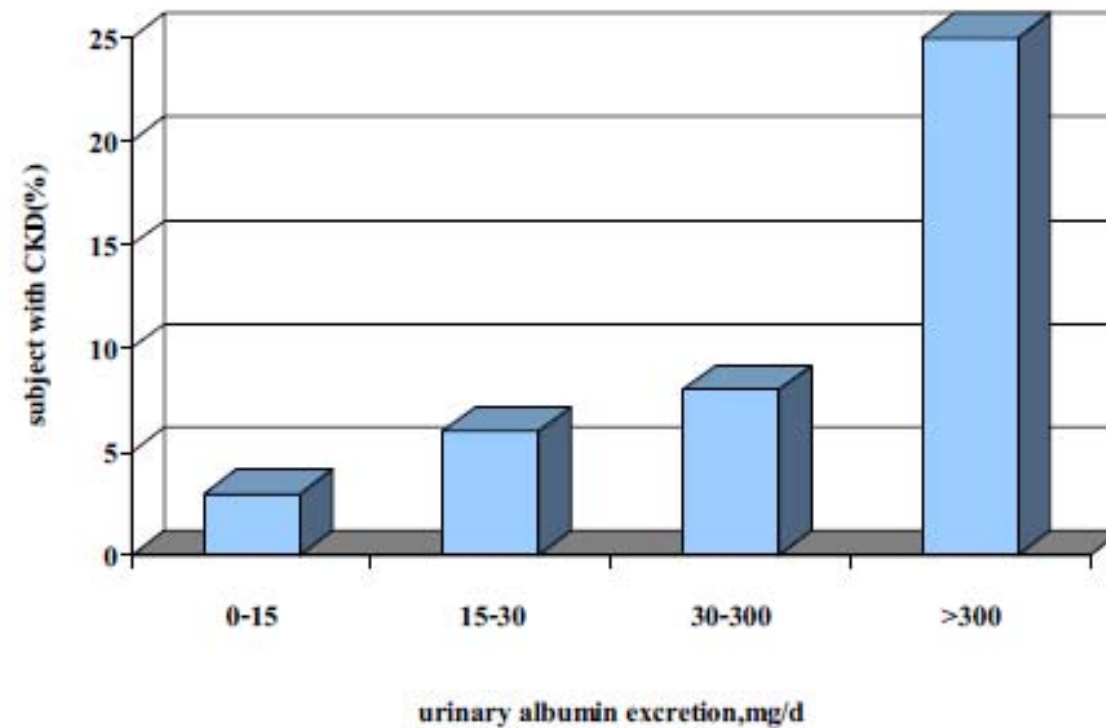
Incidencia de IR terminal según proteinuria basal

N = 106.177
Seg. 17 años

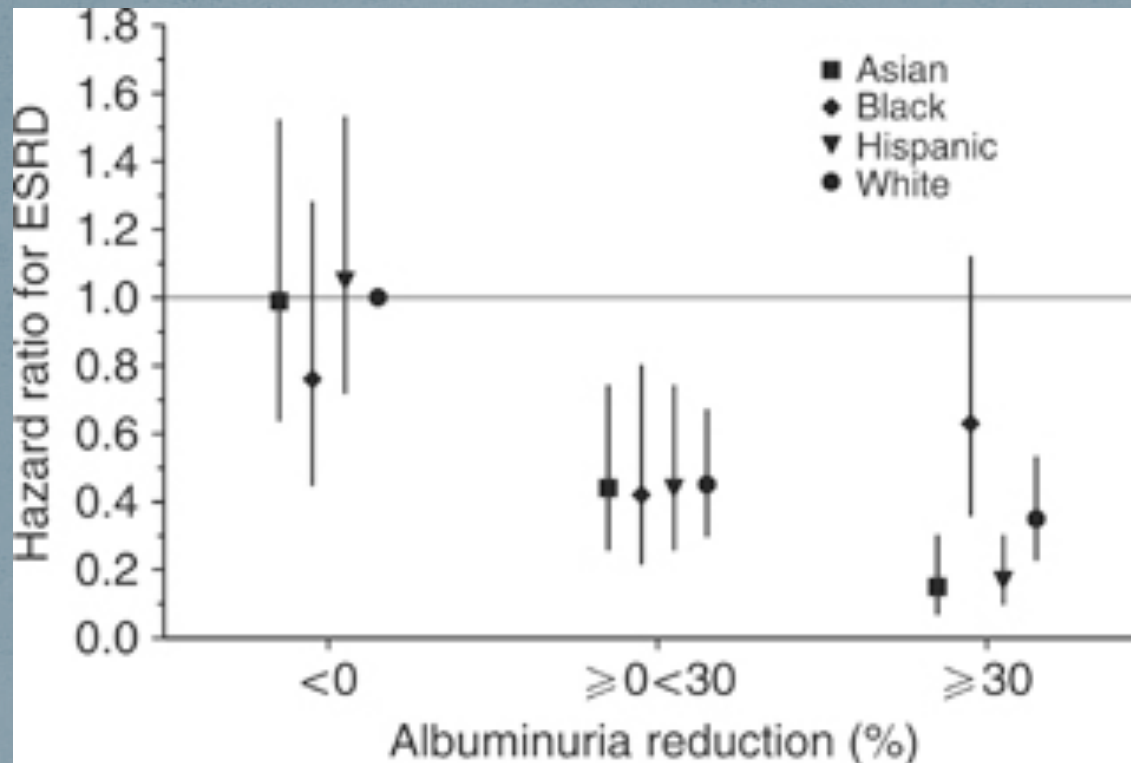


Iseki K, et al. Kidney Int. 2003; 63: 1468-74

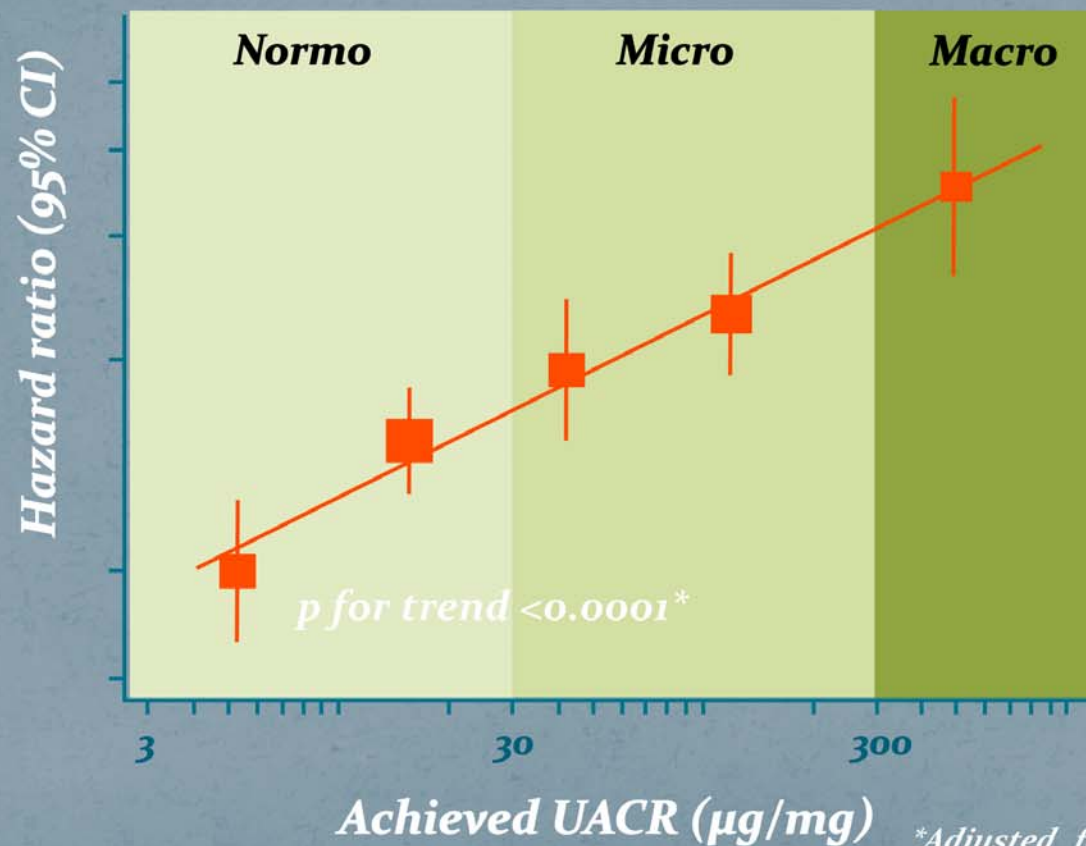
New stage 3 CKD and albuminuria after 4.2 years follow up



IR terminal según reducción de albuminuria basal en DM2 – Estudio RENAAL

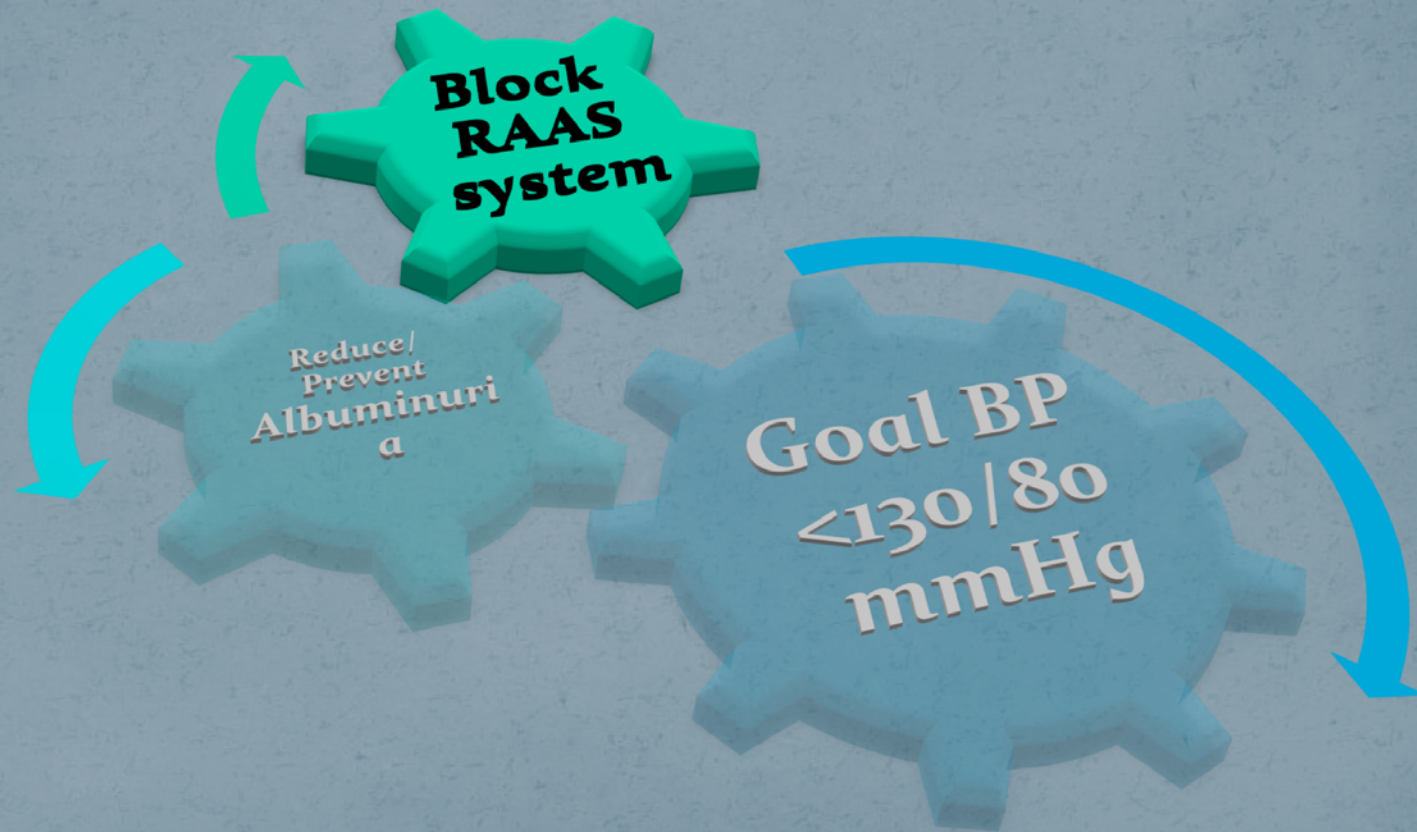


Mortalidad CV según reducción de albuminuria basal en DM2 (ADVANCE)



*Adjusted for age, sex, HbA_{1c}, serum lipids, BMI, smoking, alcohol use, and study drug

Presión arterial y protección renal en diabetes



Clinical Trials and Renal Outcomes

Progression of diabetic nephropathy/ESRD

<i>Protection</i>	<i>No Protection</i>
<ul style="list-style-type: none">• ADVANCE Perindopril• AASK/REIN Ramipril• IDNT Irbesartan• RENAAL Losartan	<ul style="list-style-type: none">• STENO Isradipine• AASK Amlodipine• IDNT Amlodipine

30-35% ↓proteinuria

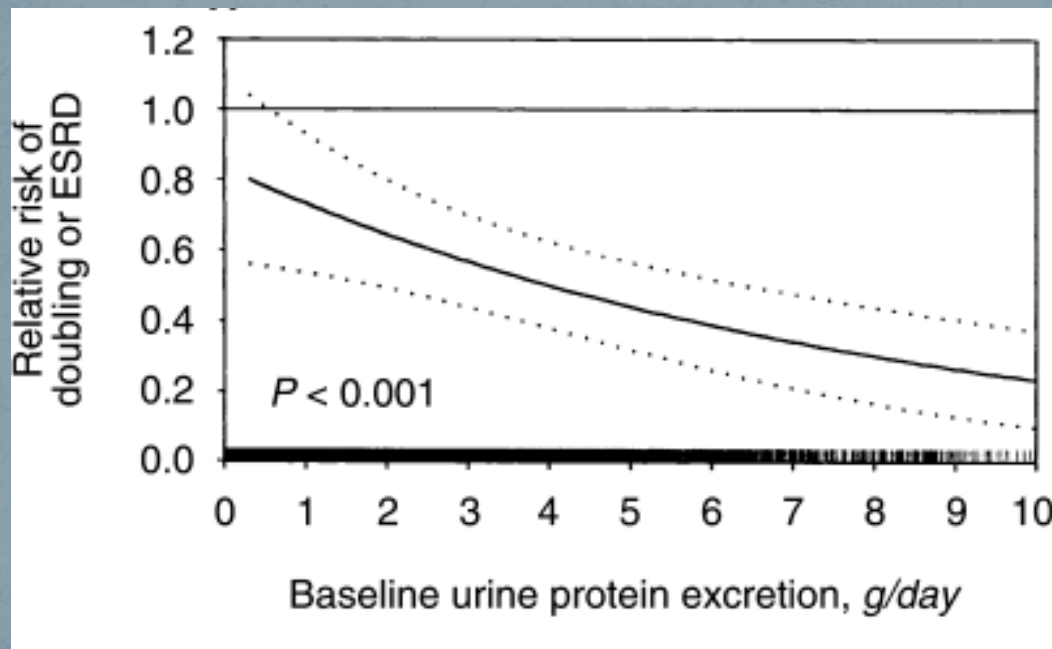
No ↓proteinuria

ESRD = End Stage Renal Disease

Bloqueo SRAA y progresión de ERC

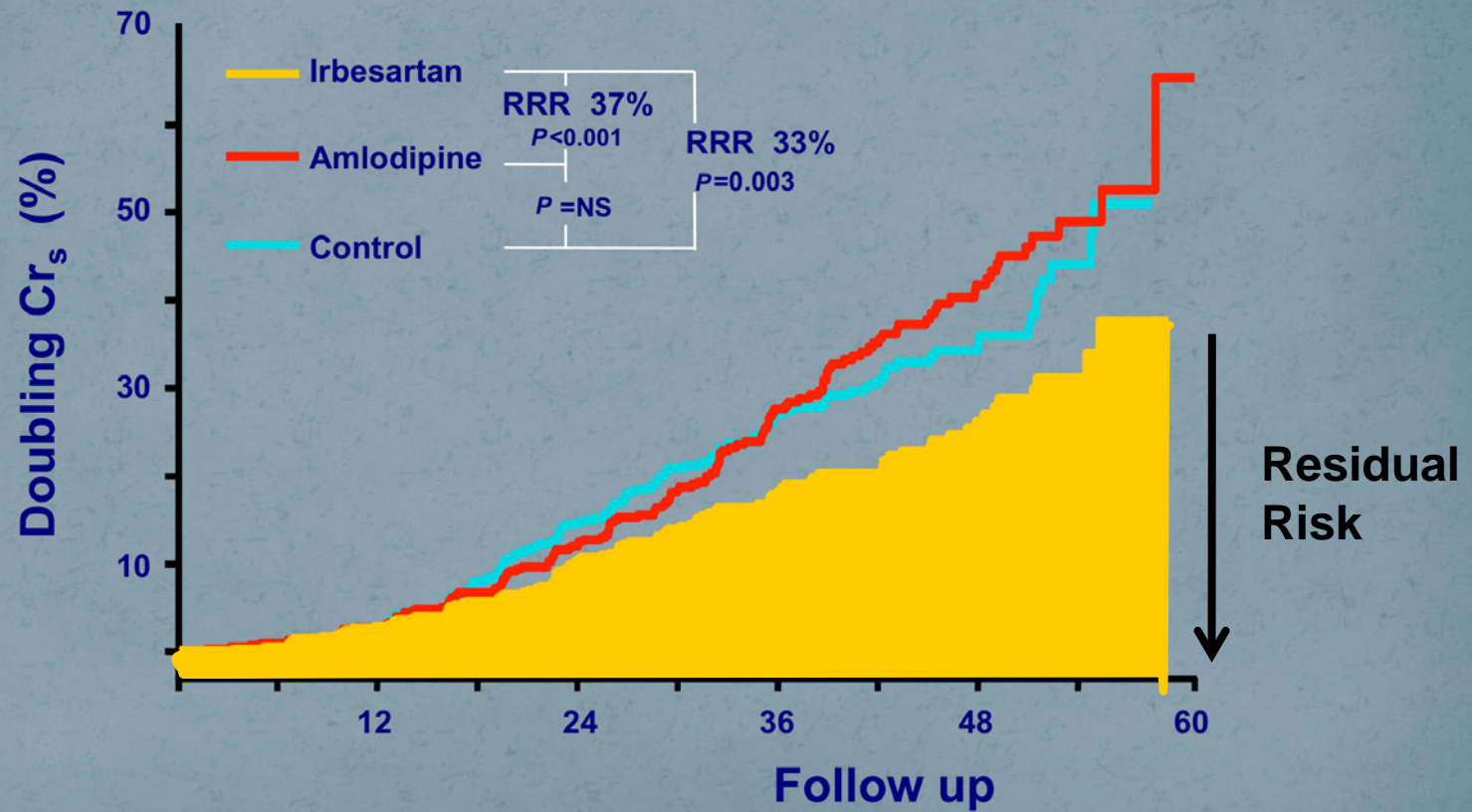
Meta-analysis of 11 randomized controlled trials
1860 patients

ACEI treatment vs. Antihypertensive non-ACEI regimens



Bloqueo SRAA en nefropatía diabética

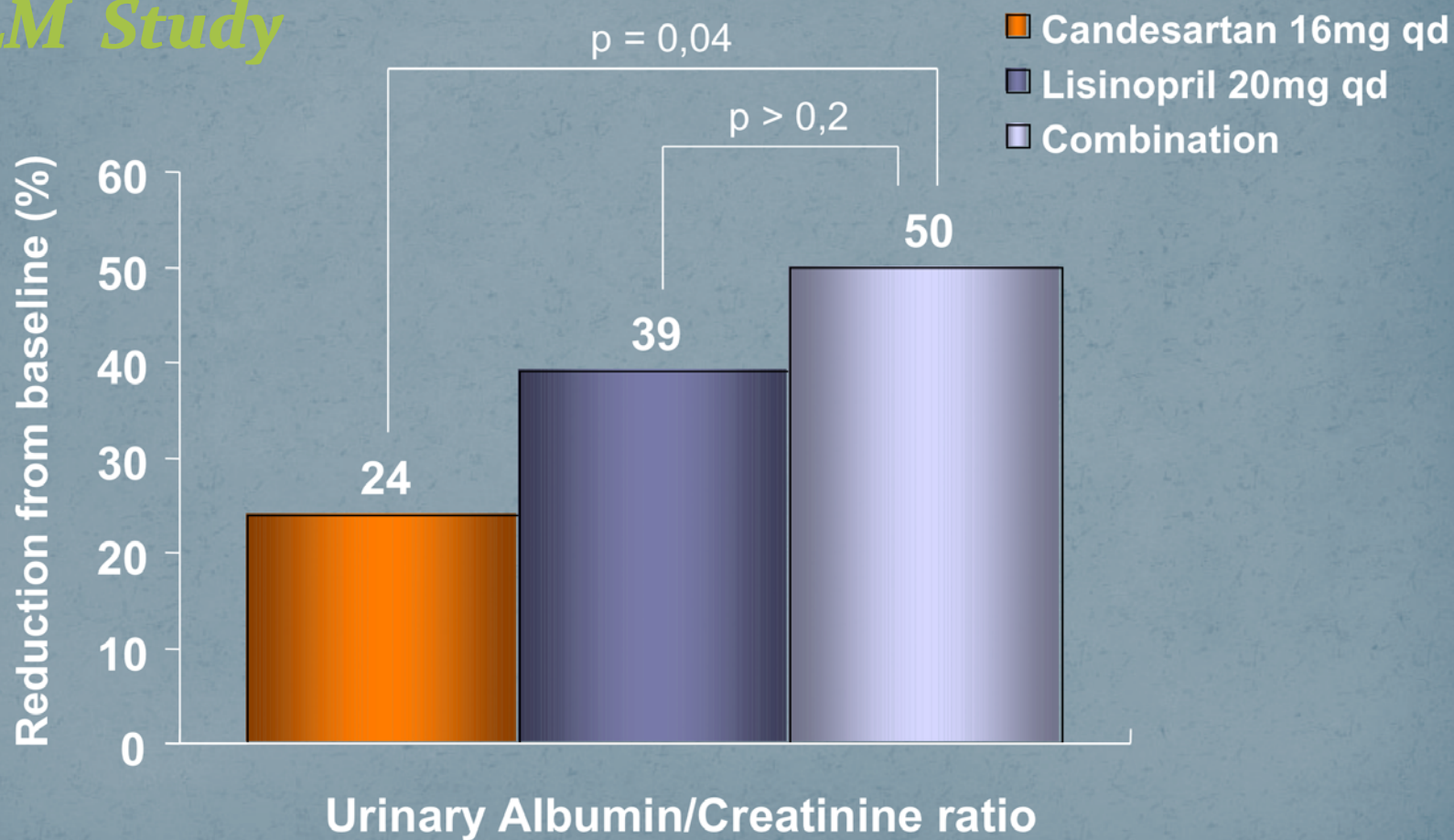
The IDNT Trial



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

Doble bloqueo IECA/ARA₂ en DM

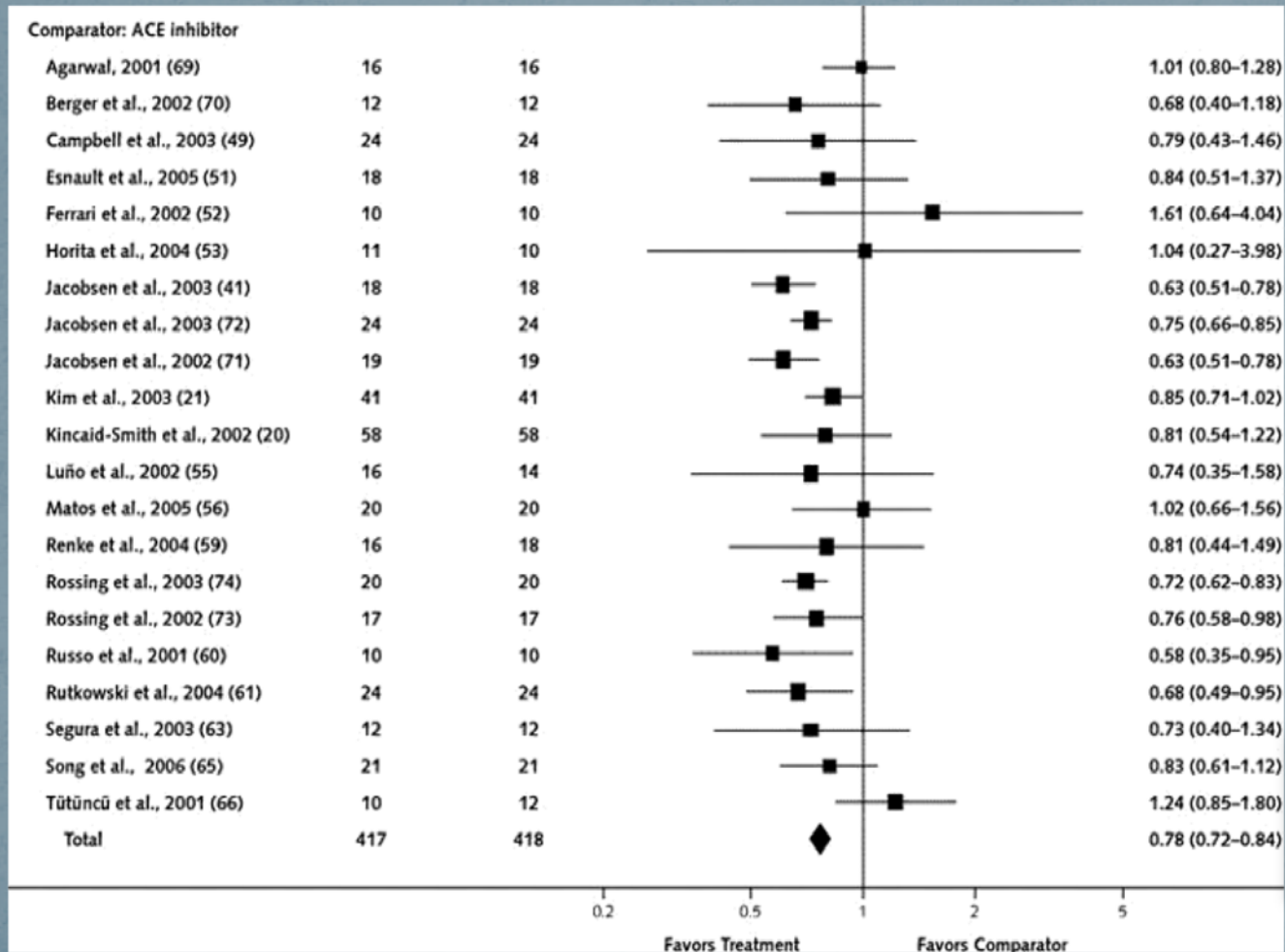
CALM Study



Mogensen CE, et al. *BMJ* 2000; 321: 1440-4

Bloqueo intenso del SRAA

Doble bloqueo IECA/ARA₂

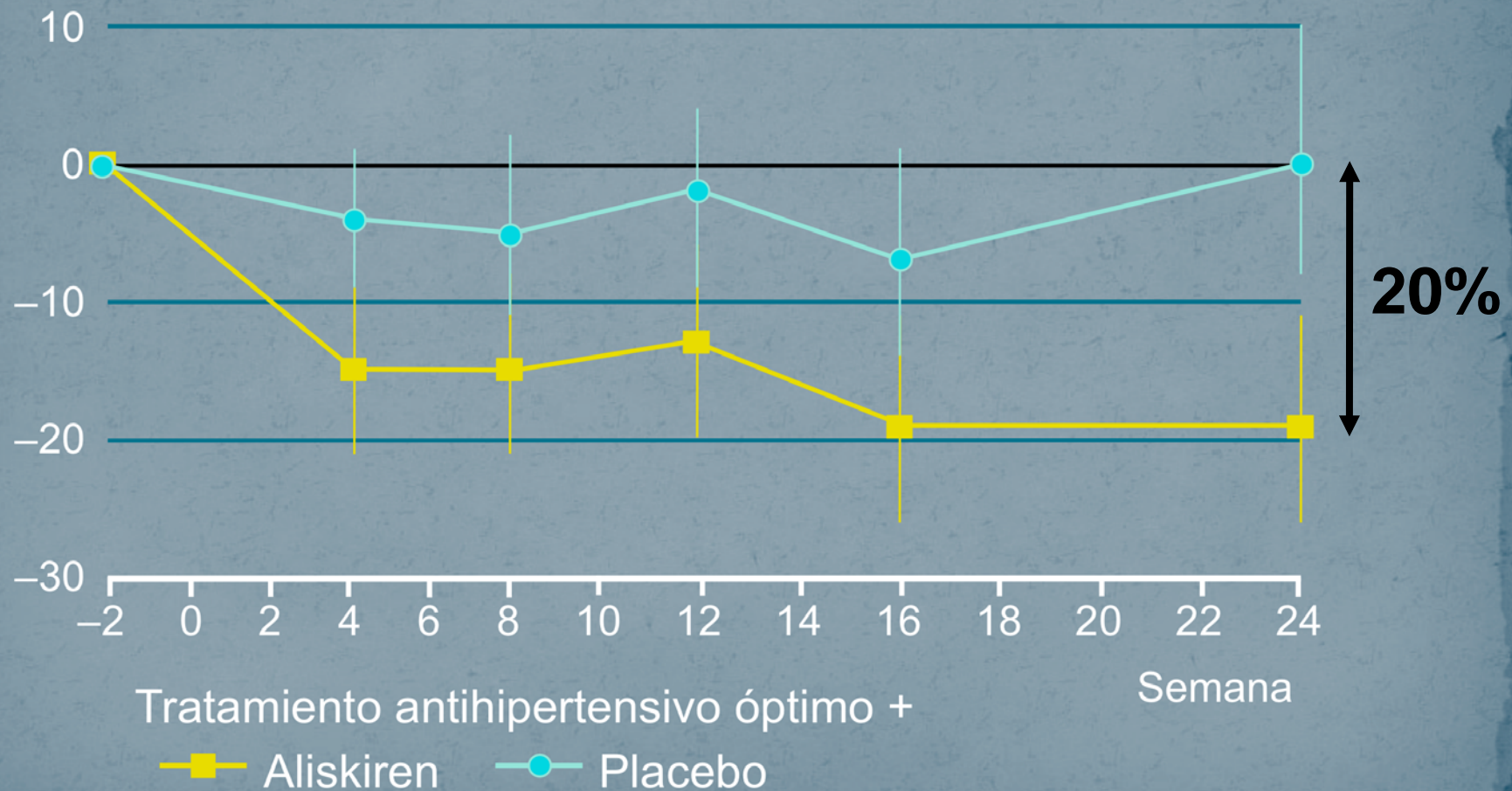


**Reducción
22% vs IECA**

Reducción de proteinuria en DM2

ARA₂ + IDR Estudio AVOID

Media geométrica del cambio de la UACR respecto al valor basal (%)

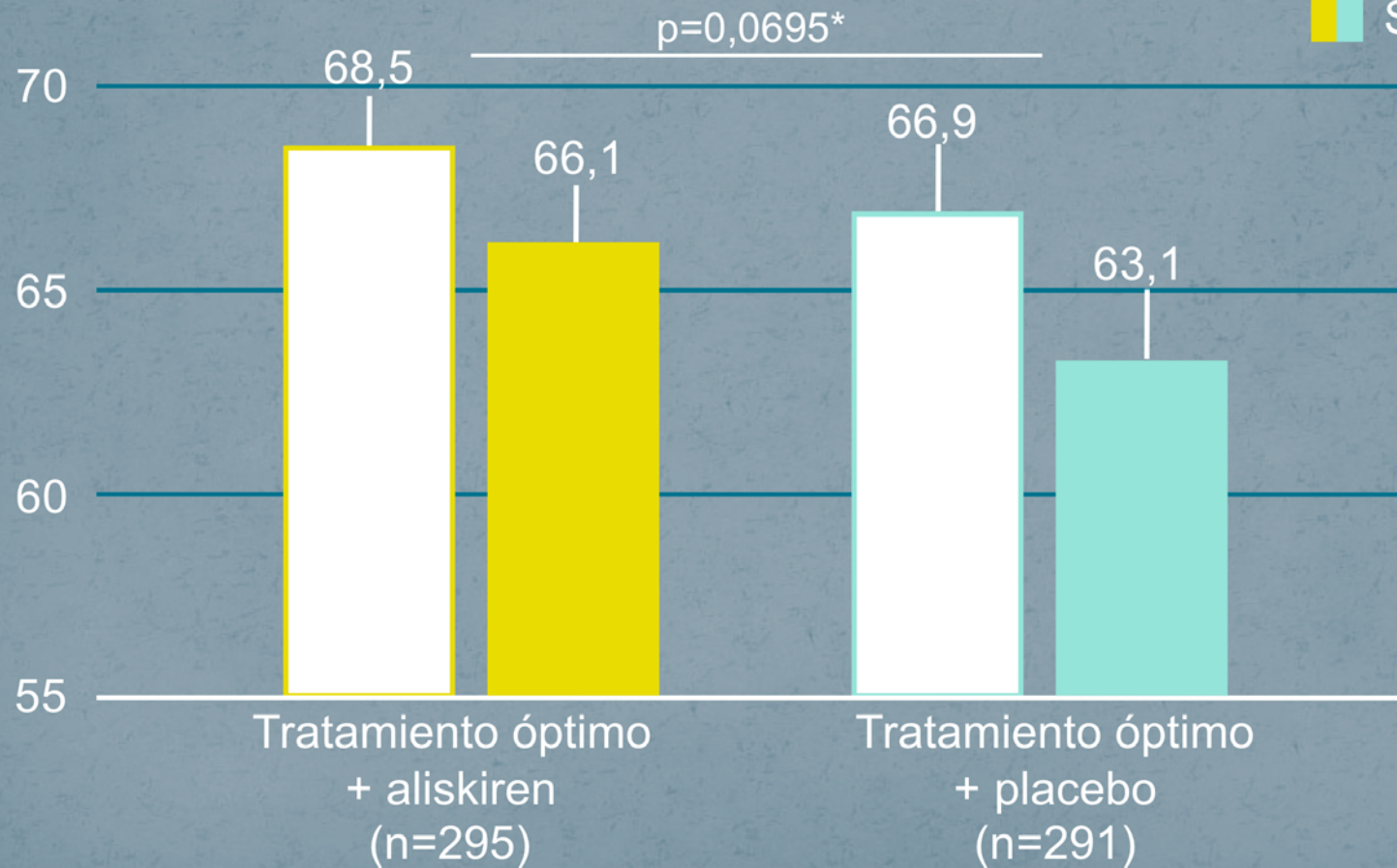


Parving *et al.* *N Engl J Med* 2008; 358: 2433-46

AVOID - Evolución de la función renal

eTFG basal medio y al final de la Semana 24 (ml/min/1,73 m²)

Basal
Semana 24

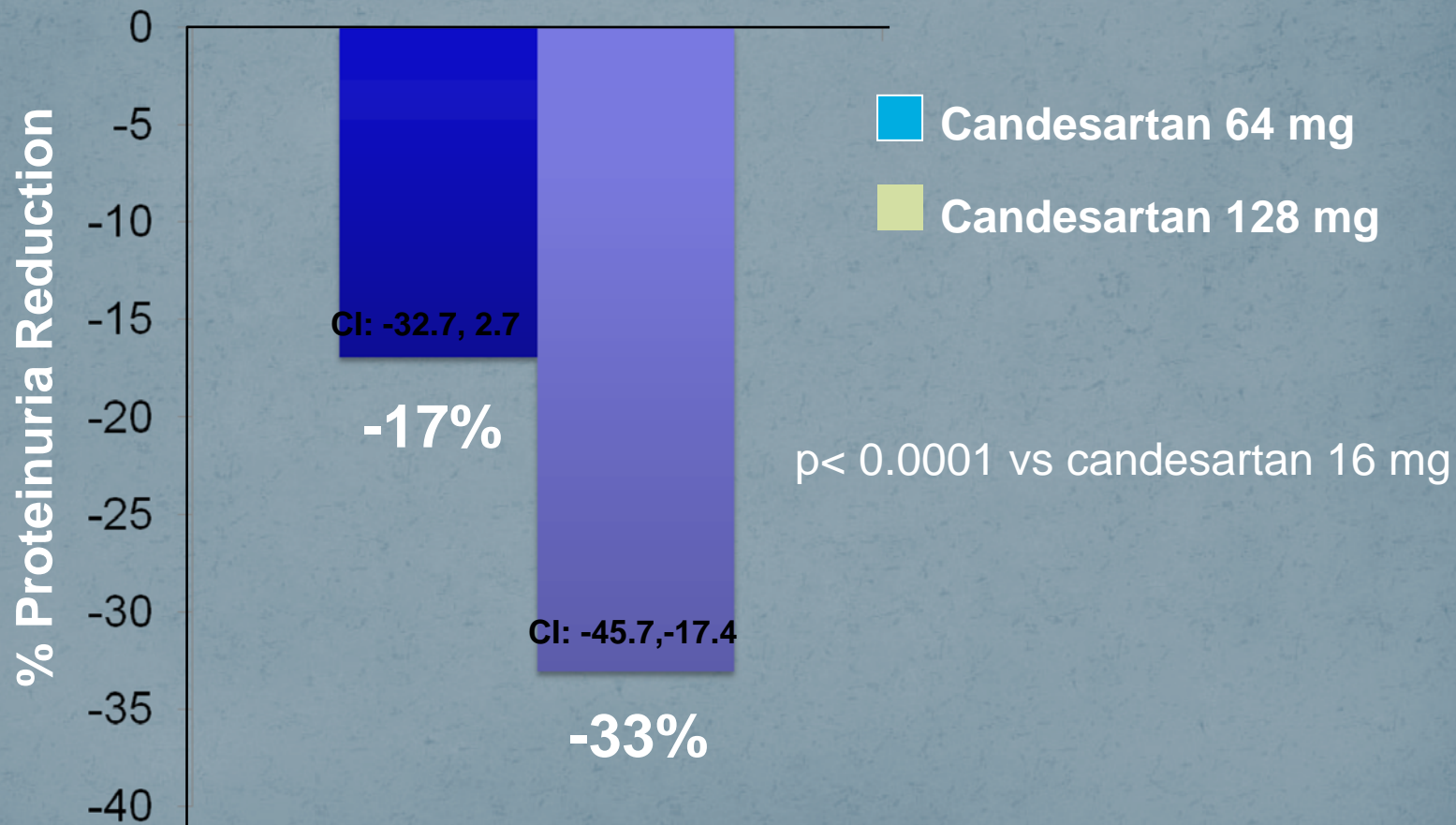


Parving *et al.* *N Engl J Med* 2008; 358: 2433-46

Bloqueo intenso del SRAA

Dosis “supramáximas”

The SMART trial

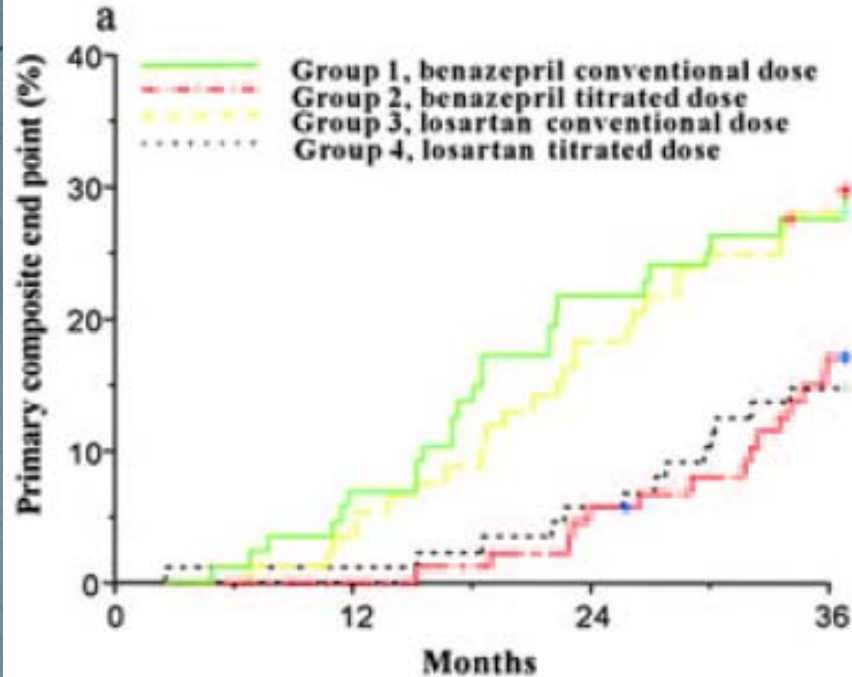


Burgess E et al. *J Am Soc Nephrol* ●●: –, 2009. doi: 10.1681/ASN.2008040416

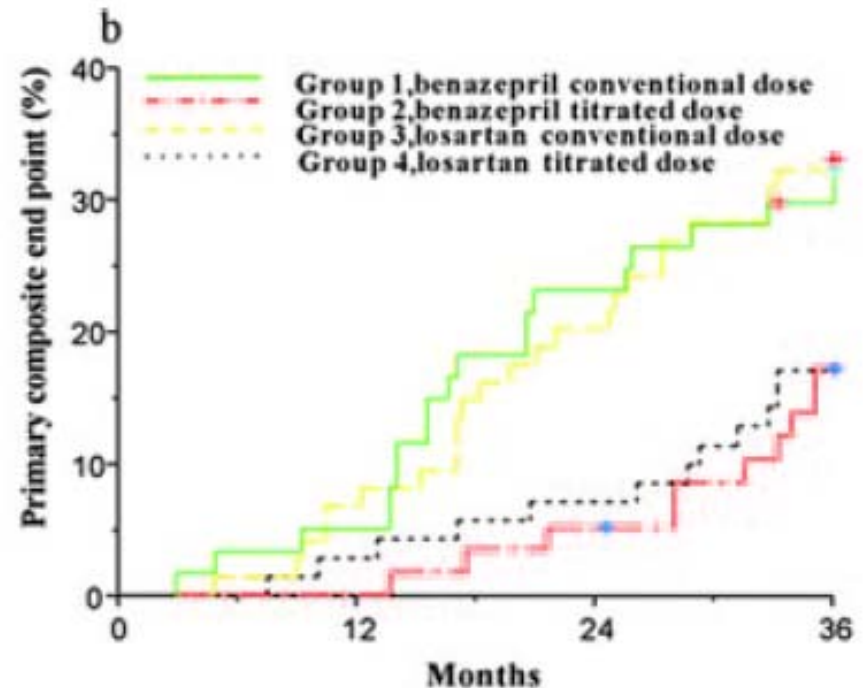
The ROAD Study – Primary Outcome

Doubled Serum Creatinine, ESRD, Death

IntentionToTreat

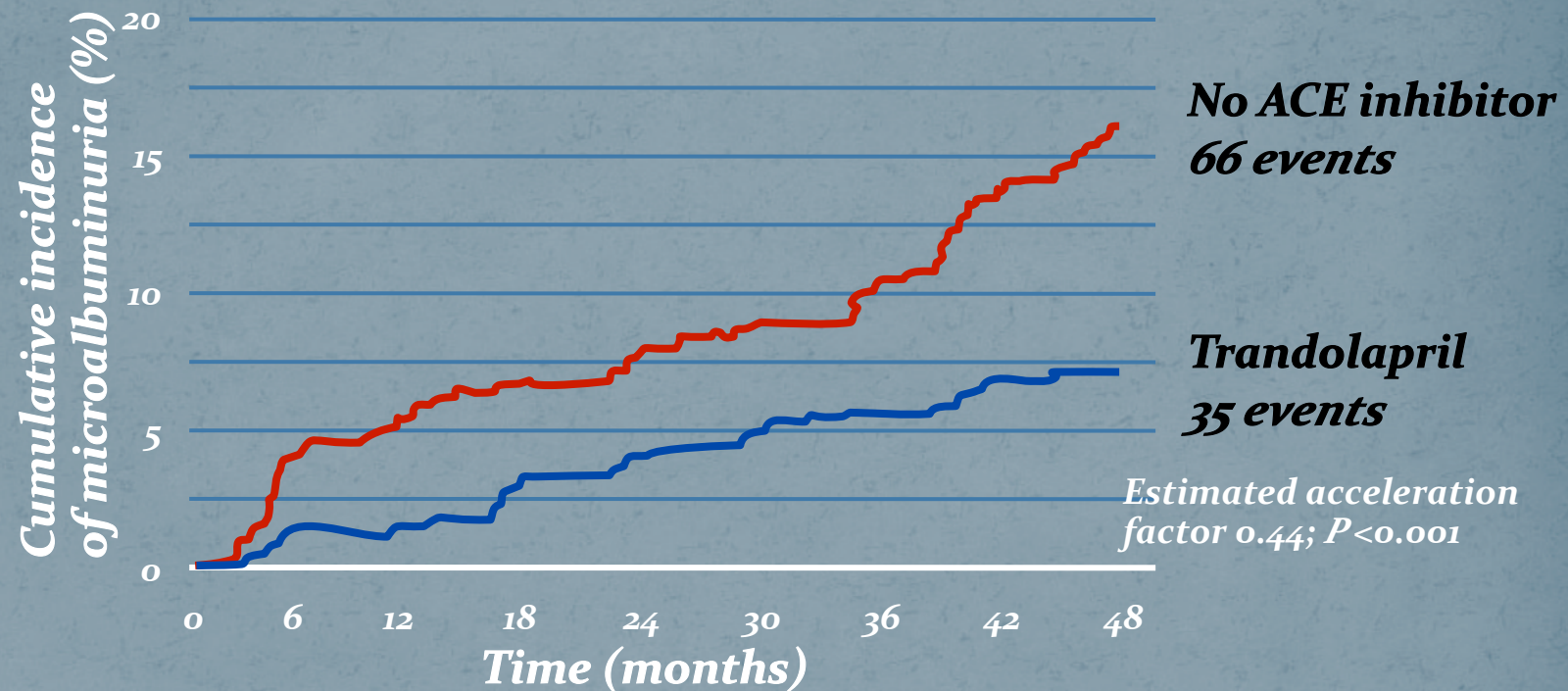


PerProtocol



Prevención primaria de ND: IECA

The BENEDICT trial

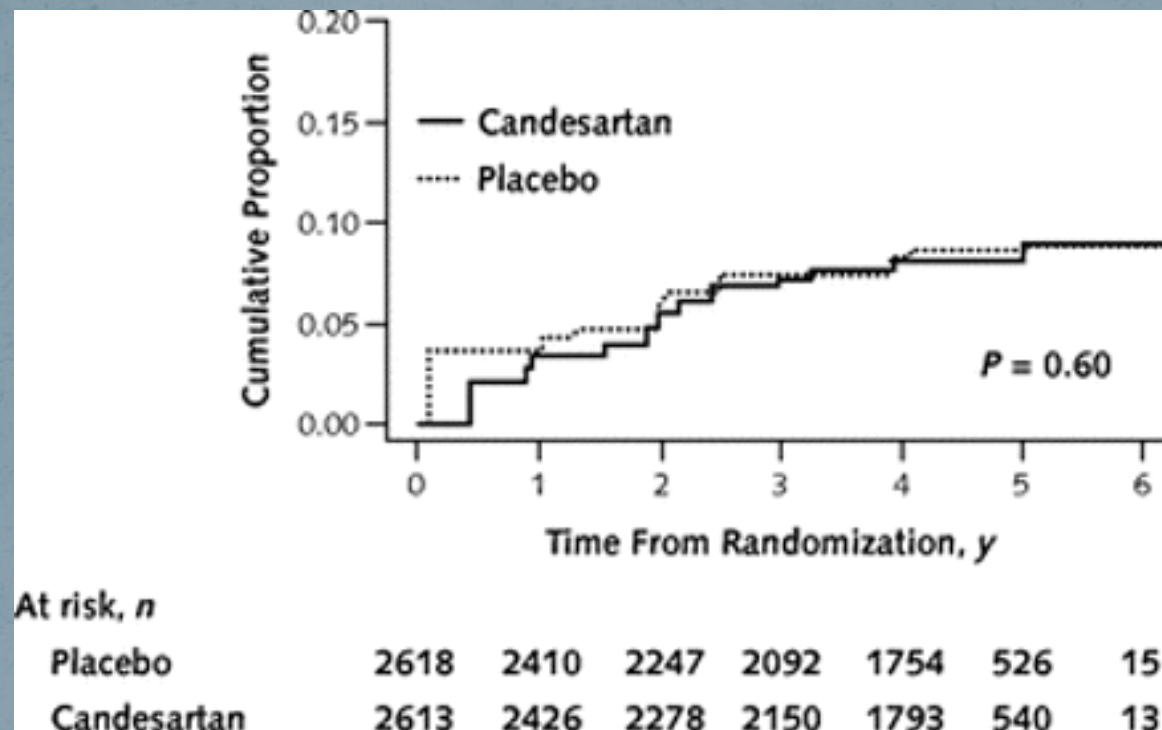


No. at risk	0	6	12	18	24	30	36	42	48
ACE inhibitor	601	503	469	441	417	399	380	311	220
No ACE inhibitor	603	463	424	405	376	357	338	270	188

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

Prevención primaria de ND: ¿ARA₂?

The DIRECT trial



Bilous R, et al. *Ann Intern Med* 2009; 151: 11-20

Prevención primaria de ND: ¿ARA₂?



- The ROADMAP study will establish whether olmesartan can prevent microalbuminuria in patients with type 2 diabetes, and whether this signifies vascular protection
 - First study to examine whether an ARB can prevent or delay the onset of microalbuminuria
- Randomized, double-blind, placebo-controlled, multicentre, multinational, parallel-group trial of olmesartan 40 mg/day vs. placebo
- 4,400 patients with Type-2 diabetes mellitus and normoalbuminuria with at least 1 cardiovascular risk factor



The group randomized to receive olmesartan did have a lower incidence of microalbuminuria. However, they also experienced a 7 mmHg reduction in blood pressure.

Hipertensión en DM₂ - Tratamiento combinado

ACCOMPLISH

Composite CV mortality/morbidity

Cardiovascular mortality

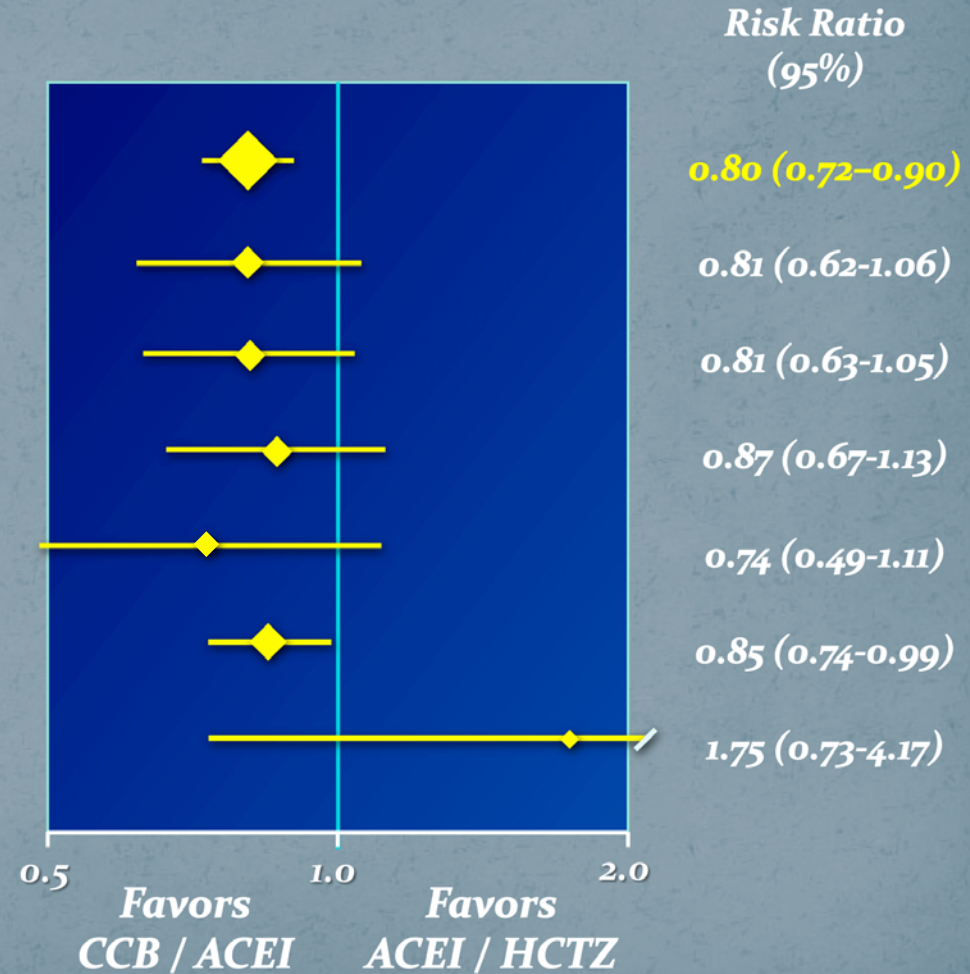
Non-fatal MI

Non-fatal stroke

Hospitalization for unstable angina

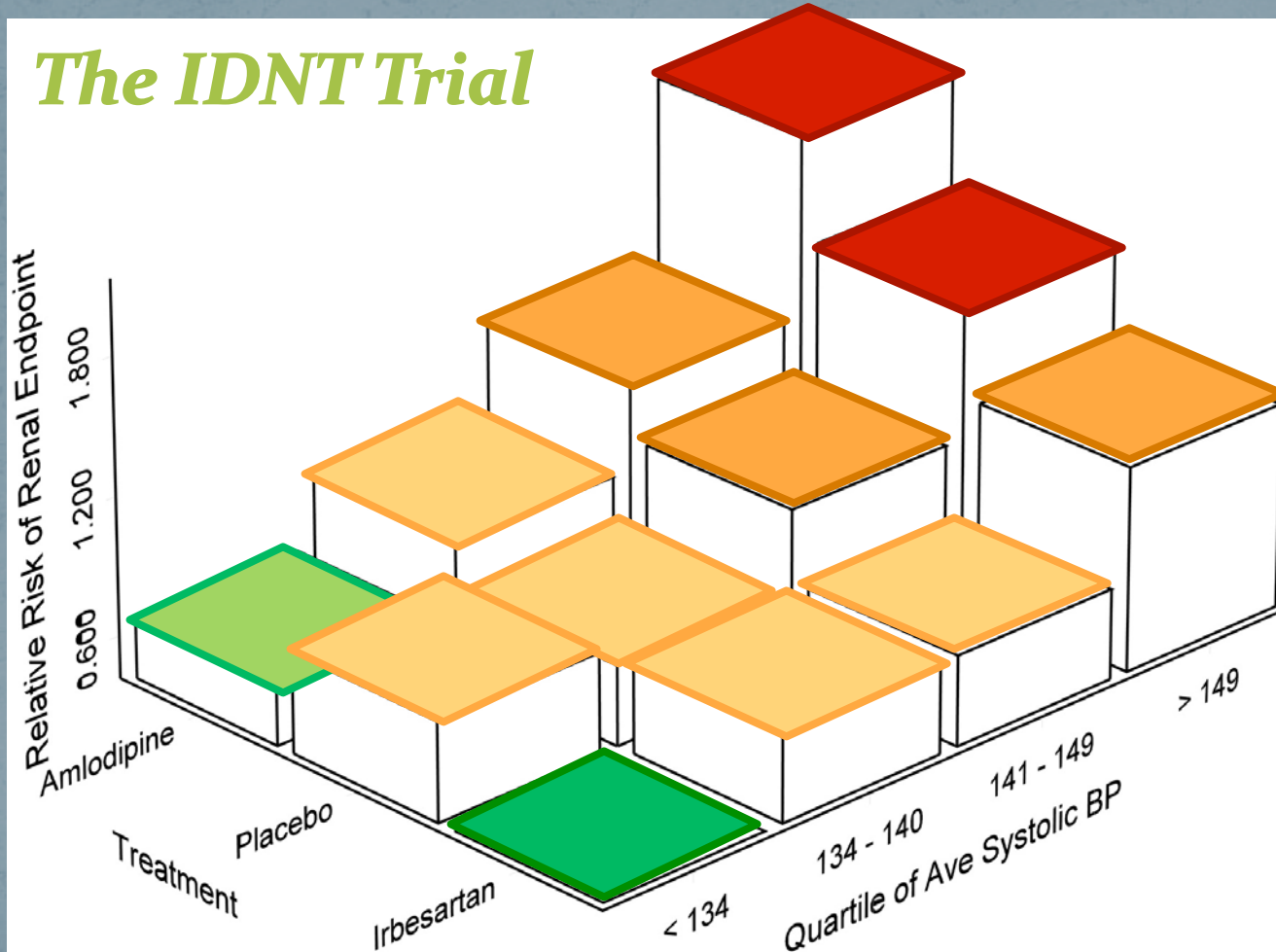
Coronary revascularization procedure

Resuscitated sudden death



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

Riesgo renal y PA por grupos farmacológicos

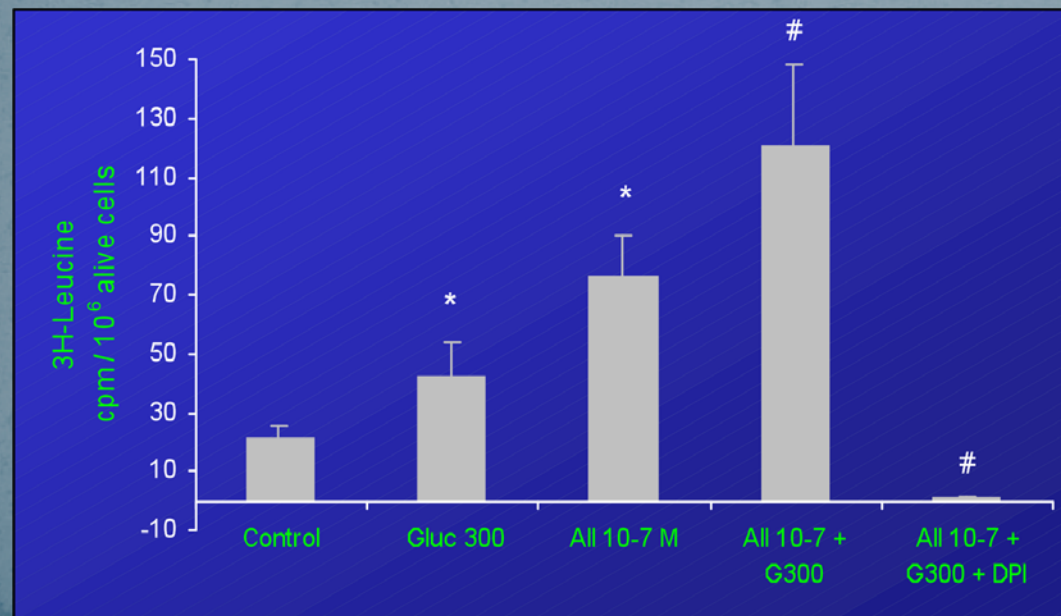
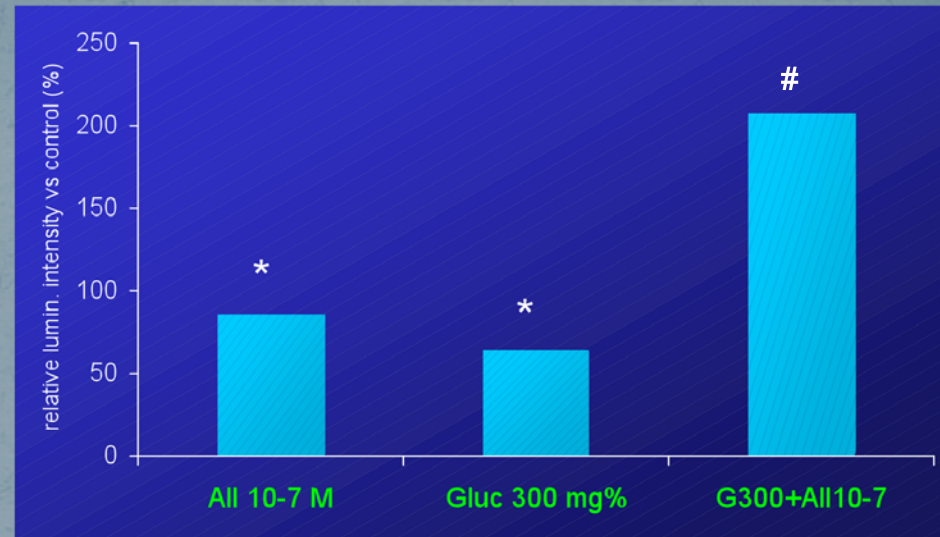


Pohl MA, et al. *J Am Soc Nephrol* 2005; 16: 3027-37

Nefropatía Diabética – Factores de riesgo

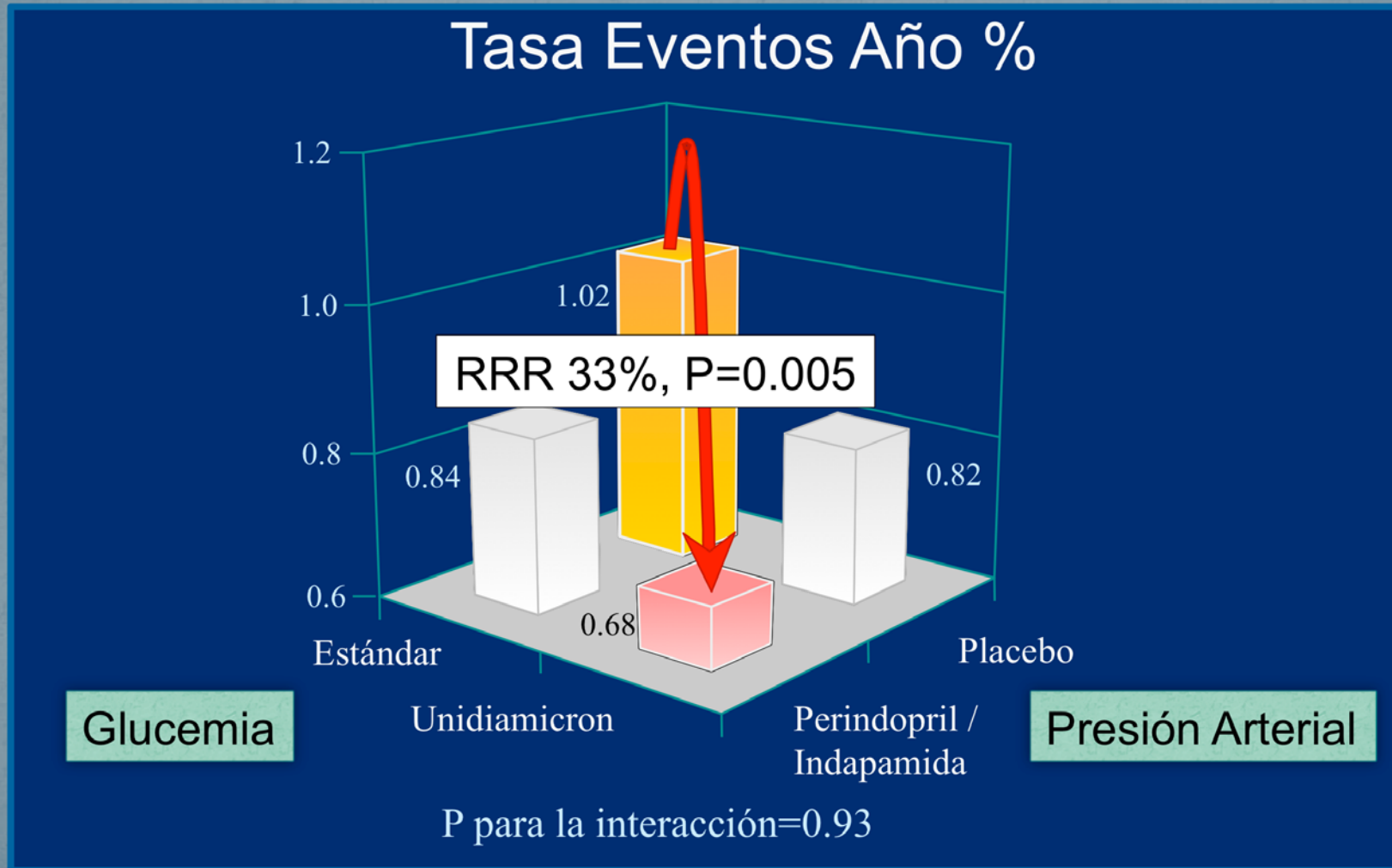
- *Hipertensión arterial*
- *Hiperglicemia*
- *Etnicidad*
- *Sexo masculino*
- *Historia familiar*
- *Tabaquismo*

Co-estimulación de glucosa y Ang II en la hipertrofia mesangial



Galceran JM, et al. Kidney Int
1999

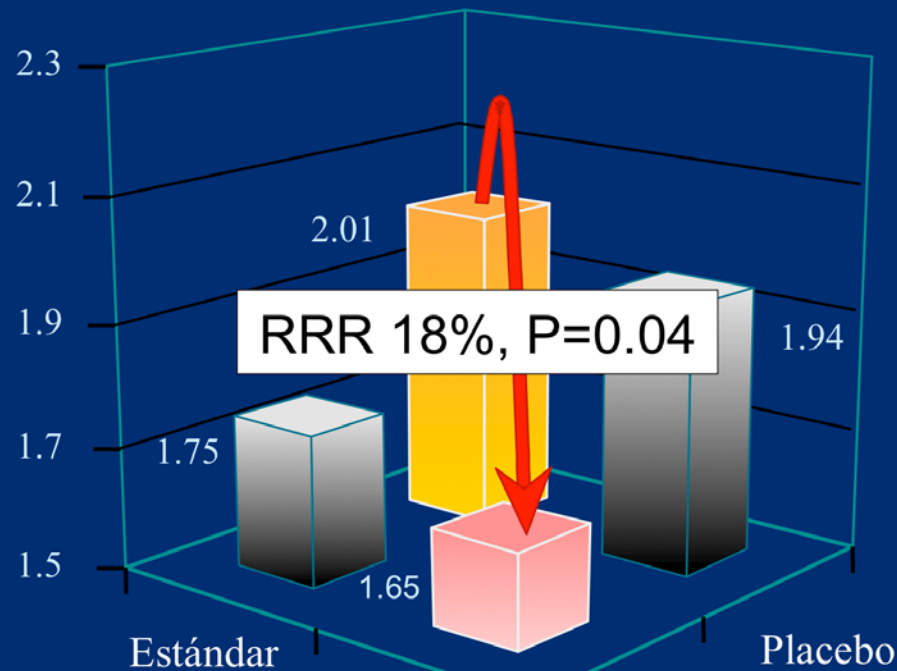
Tratamiento multifactorial y eventos renales en DM₂ - ADVANCE



The ADVANCE collaborative group. EASD 2008

Tratamiento multifactorial y Mortalidad en DM₂ - ADVANCE

Tasa de Eventos Anuales %



Glucemia

Unidiamicron

Perindopril /
Indapamida

Presión Arterial

P para la interacción=0.90

The ADVANCE collaborative group. EASD 2008

CAPÍTULO V

Tratamiento de la hipertensión arterial en el paciente con diabetes mellitus o enfermedad renal crónica

JOSEP M. GALCERAN
Servicio de Nefrología. Fundación Althaia.
Presidente de la Sociedad Catalana de Nefrología.

PROTOCOLOS
HIPERTENSIÓN
ARTERIAL



Sociedad Española de Medicina Interna

Diabetes

Sin Nefropatía

Con Nefropatía

<i>Objetivo de PA</i>	<i>< 130 / 80 mmHg</i>	<i>< 125 / 75 mmHg</i>
<i>Fármaco de elección</i>	<i>Antagonista SRAA</i>	<i>Antagonista SRAA</i>
<i>Primera combinación</i>	<i>Diurético o Calcioantagonista</i>	<i>Diurético o Calcioantagonista *</i>
<i>Posteriores combinaciones</i>	<i>El no utilizado en 1ª combinación. Posteriormente, cualquier otro grupo</i>	<i>El no utilizado en 1ª combinación. Posteriormente, cualquier otro grupo</i>
<i>Otras medidas de prevención cardiovascular</i>	<i>HbA_{1c} < 7% Cese del tabaco cLDL < 100 mg/dl Antiagregación</i>	<i>HbA_{1c} < 7% Cese del tabaco cLDL < 100 mg/dl Antiagregación</i>