

XXIII
Congreso Nacional
de medicina general
y de familia

GRA
NA
DA 2016
26-28 MAYO



SEMG
Sociedad Española de Médicos
Generales y de Familia

FORO DE ACTUALIZACIÓN

Hipertensión Arterial.

Tratamiento en situaciones especiales:

ENFERMEDAD RENAL

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UNIDAD DE HIPERTENSION. HOSPITAL INFANTA
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CATEDRA EXTRAORDINARIA DE RIESGO
CARDIOVASCULAR
FACULTAD DE MEDICINA. UNIVERSIDAD DE
SALAMANCA



CONFLICTO DE INTERESES

El ponente declara poseer 100 acciones de Bayer AG a las que, de momento, le ha perdido un 35% de su valor.

La próxima vez será más cuidadoso con sus inversiones.



GUIAS KDIGO: ENFERMEDAD RENAL NO DIABETICOS

- ✓ **Recomendamos** para todos los pacientes con EUA < 30 una PA < 140/90 (1A)
- ✓ **Sugerimos** para pacientes con EUA \geq 30 y < 300 una PA < 130/80 (2D)
- ✓ **Sugerimos** para pacientes con EUA \geq 300 una PA < 130/80 (2C)
- ✓ **Sugerimos** usar ARA/IECA en los pacientes con EUA \geq 30 y < 300 (2D)
- ✓ **Recomendamos** usar ARA/IECA en los pacientes con EUA \geq 300 (1B)

GUIAS KDIGO: ENFERMEDAD RENAL EN DIABETICOS

- ✓ **Recomendamos** para todos los pacientes con EUA < 30 una PA < 140/90 (1B)
- ✓ **Sugerimos** para pacientes con EUA \geq 30 una PA < 130/80 (2D)
- ✓ **Sugerimos** usar ARA/IECA en los pacientes con EUA \geq 30 y < 300 (2D)
- ✓ **Recomendamos** usar ARA/IECA en los pacientes con EUA \geq 300 (1B)

GUIAS EUROPEAS 2013

Recommendations	Class ^a	Level ^b	Ref. ^c
While initiation of antihypertensive drug treatment in diabetic patients whose SBP is ≥ 160 mmHg is mandatory, it is strongly recommended to start drug treatment also when SBP is ≥ 140 mmHg.	I	A	275, 276 290–293
A SBP goal < 140 mmHg is recommended in patients with diabetes.	I	A	270, 275, 276, 295
The DBP target in patients with diabetes is recommended to be < 85 mmHg.	I	A	290, 293
All classes of antihypertensive agents are recommended and can be used in patients with diabetes; RAS blockers may be preferred, especially in the presence of proteinuria or microalbuminuria.	I	A	394, 513
It is recommended that individual drug choice takes comorbidities into account.	I	C	-
Simultaneous administration of two blockers of the RAS is not recommended and should be avoided in patients with diabetes.	III	B	433

DBP, diastolic blood pressure; RAS, renin–angiotensin system; SBP, systolic blood pressure.

^aClass of recommendation.

^bLevel of evidence.

^cReference(s) supporting levels of evidence.

GUIAS EUROPEAS 2013

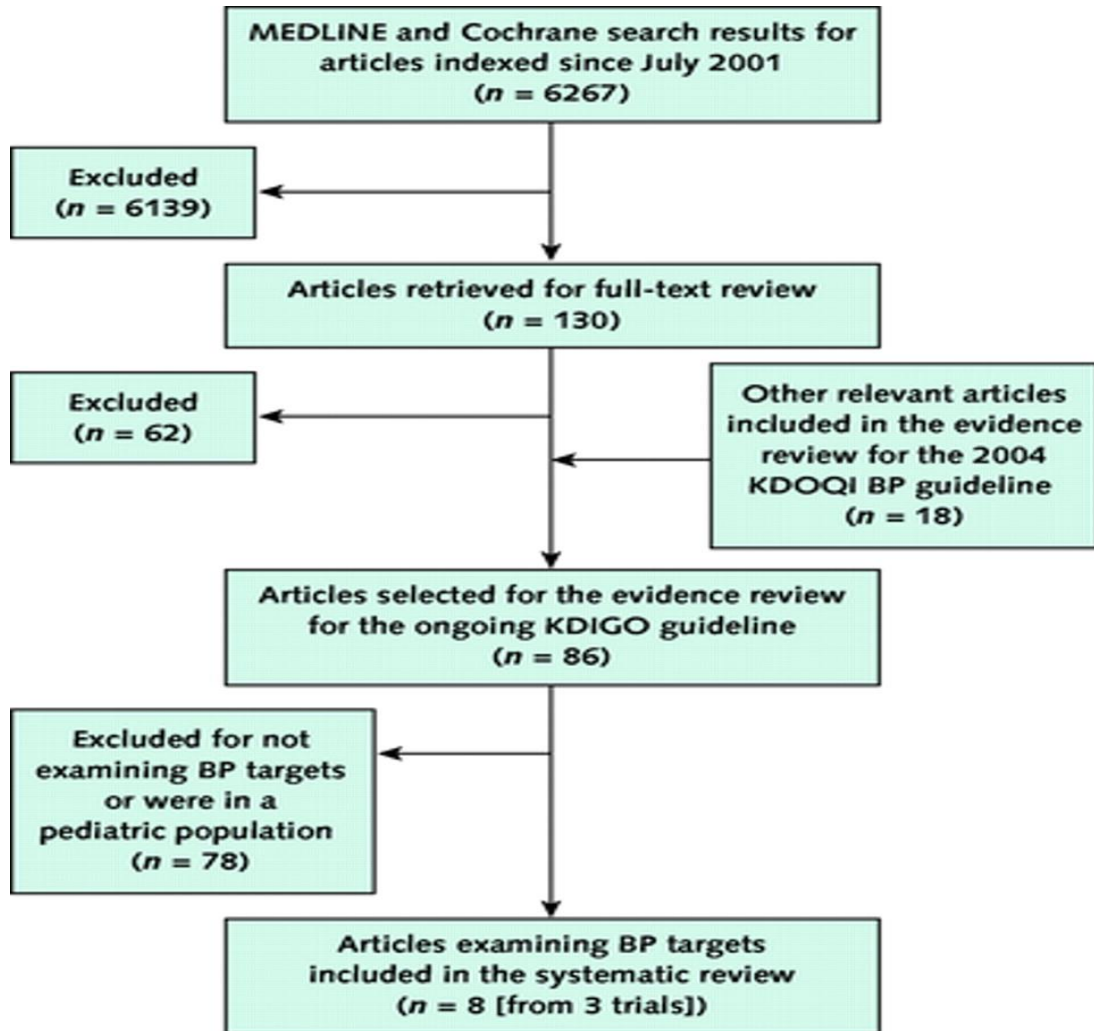
Recommendations	Class ^a	Level ^b	Ref. ^c
Lowering SBP to <140 mmHg should be considered.	IIa	B	303, 313
When overt proteinuria is present, SBP values <130 mmHg may be considered, provided that changes in eGFR are monitored.	IIb	B	307, 308, 313
RAS blockers are more effective in reducing albuminuria than other antihypertensive agents, and are indicated in hypertensive patients in the presence of microalbuminuria or overt proteinuria.	I	A	513, 537
Reaching BP goals usually requires combination therapy, and it is recommended to combine RAS blockers with other antihypertensive agents.	I	A	446
Combination of two RAS blockers, though potentially more effective in reducing proteinuria, is not recommended.	III	A	331, 433, 463
Aldosterone antagonists cannot be recommended in CKD, especially in combination with a RAS blocker, because of the risk of excessive reduction in renal function and of hyperkalaemia.	III	C	-

BP, blood pressure; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; RAS, renin–angiotensin system; SBP, systolic blood pressure.

^aClass of recommendation.

^bLevel of evidence.

^cReference(s) supporting levels of evidence.



Summary of evidence search and selection. BP = blood pressure; KDIGO = Kidney Disease: Improving Global Outcomes; KDOQI = Kidney Disease Outcomes Quality Initiative.

Upadhyay A et al. Ann Intern Med 2011;154:541-548

Annals of Internal Medicine

Blood Pressure Reduction Slows the Progression of Nondiabetic Kidney Disease: The MDRD Study

Study Group	Target Mean Arterial BP* (mm Hg)	Achieved Mean Arterial BP (mm Hg ± SD)	Achieved Systolic BP (mm Hg ± SD)	Achieved Diastolic BP (mm Hg ± SD)	Number with Kidney Failure (%)
Usual BP Control (n=408)	<107 or <113	98.4 ± 7.4	133.8 ± 14.9	80.7 ± 7.2	286 (70)
Tighter BP Control (n=432)	<92 or <98	93.3 ± 6.0	126.2 ± 13.6	76.9 ± 6.4	268 (62)†

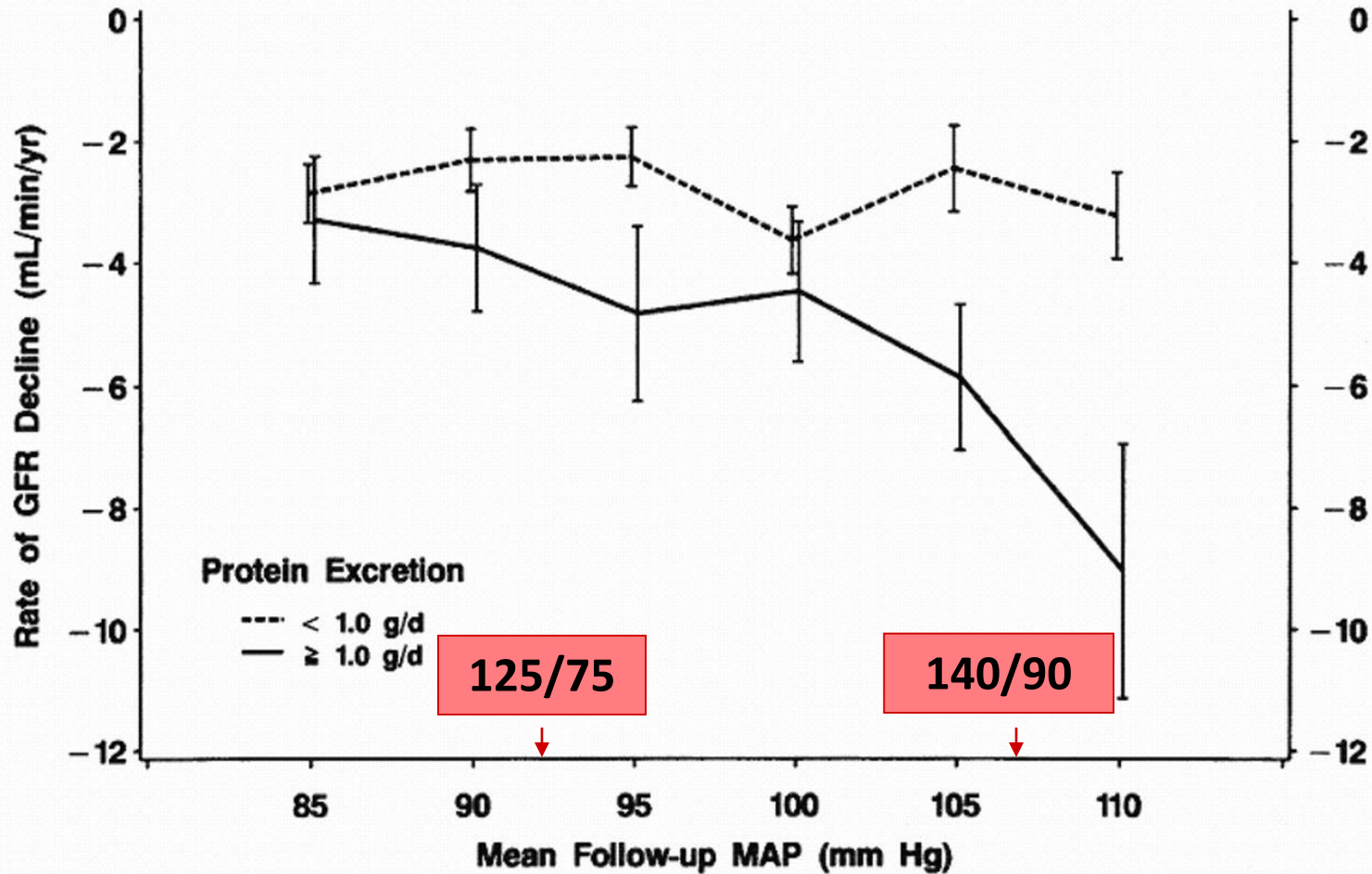
*The lower value was assigned to participants 60 years of age or younger, and the higher value was assigned to participants 61 years of age or older.

†Unadjusted hazard ratio = 0.78 (95% CI, 0.66 to 0.93; $P = 0.0056$); adjusted hazard ratio = 0.68 (95% CI, 0.57 to 0.82; $P < 0.001$).

BP = blood pressure; SD = standard deviation;
MDRD = Modification of Diet in Renal Disease Study

Sarnak MJ, et al. *Ann Intern Med.* 2005;142:342-351.

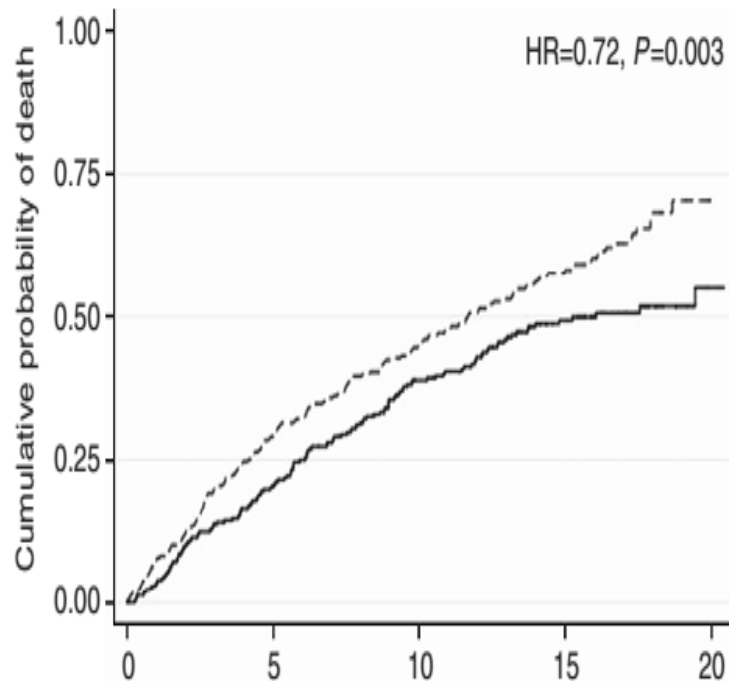
Mean glomerular filtration rate (GFR) decline and achieved follow-up blood pressure in MDRD study



RISK OF DEATH DURING LONG-TERM EXTENDED FOLLOW-UP OF MDRD TRIAL PARTICIPANTS.

a

Risk of death after ESRD onset by BP arm

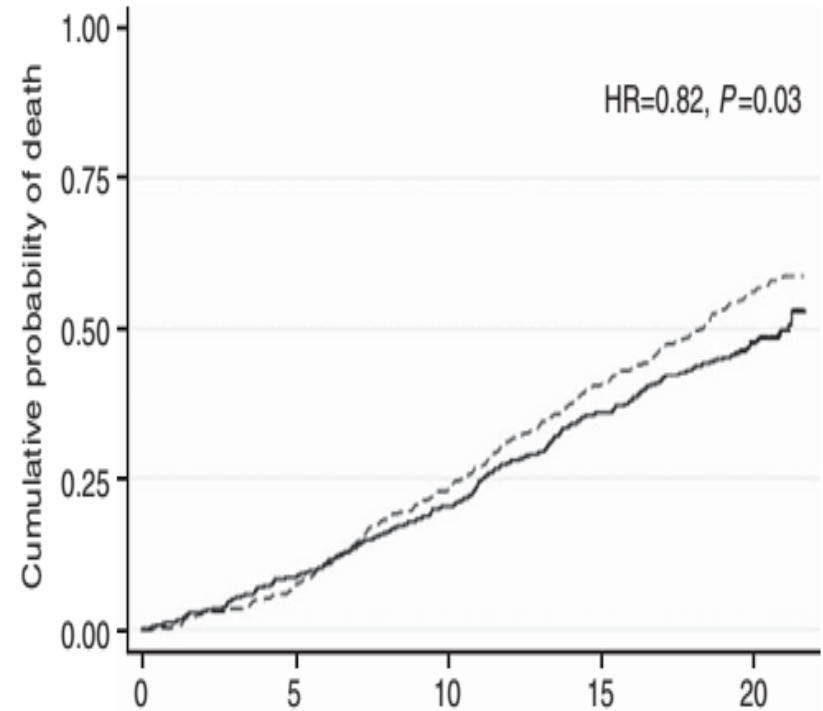


Number at risk	Years after ESRD onset				
	0	5	10	15	20
Usual BP	319	210	153	82	1
Strict BP	308	235	160	89	5

----- Usual BP ——— Strict BP

b

Risk of death regardless of ESRD status by BP arm



Number at risk	Years after randomization in MDRD				
	0	5	10	15	20
Usual BP	408	379	312	241	135
Strict BP	432	395	344	276	162

----- Usual BP ——— Strict BP

RISK OF DEATH DURING LONG-TERM EXTENDED FOLLOW-UP OF MDRD TRIAL PARTICIPANTS.

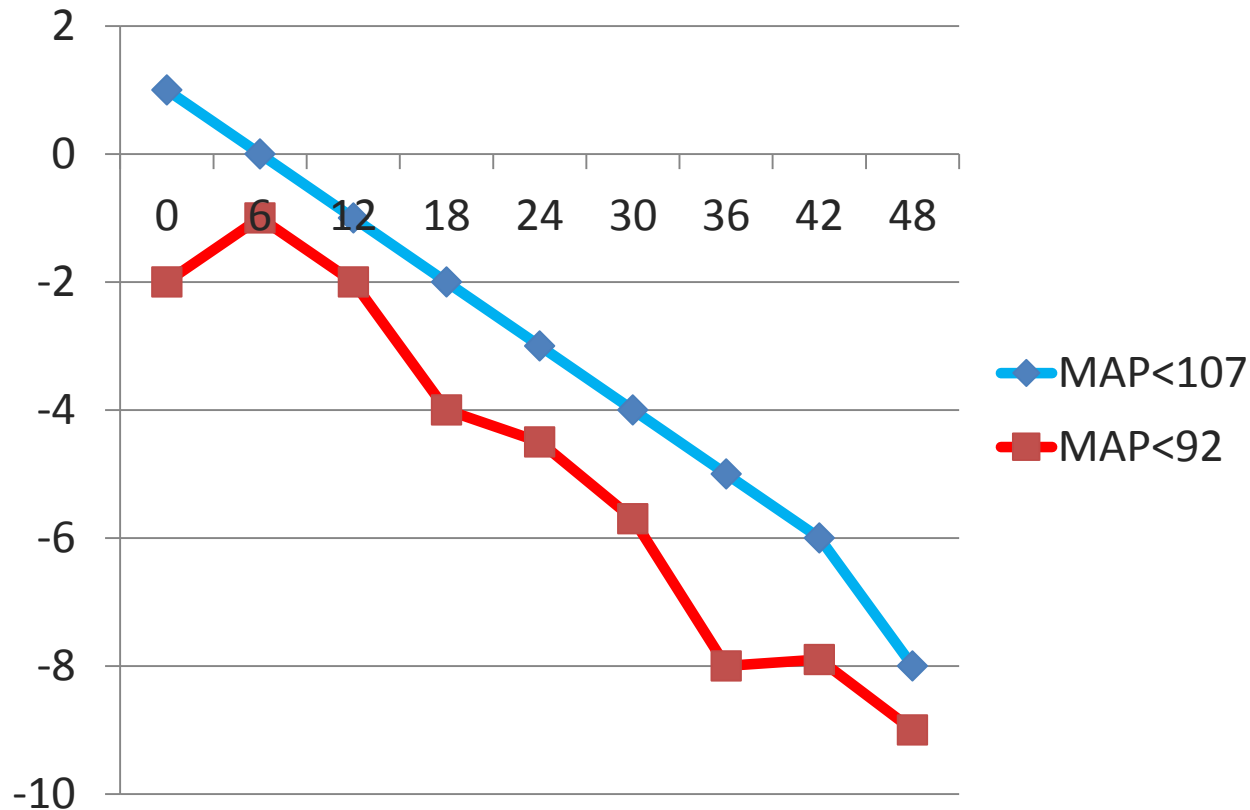
Table 2 | Characteristics at ESRD onset in the subset of patients with available data according to the Medical Evidence form

Characteristics	Strict blood pressure N = 171	Usual blood pressure N = 153	P-value
<i>Comorbidities</i>			
Congestive heart failure	9 (5.3%)	20 (13.1%)	0.02
Coronary artery disease	14 (8.2%)	29 (19.0%)	0.004
Diabetes	19 (11.1%)	19 (12.4%)	0.72
Cerebrovascular disease	4 (2.3%)	7 (4.6%)	0.36
Hypertension	139 (81.3%)	131 (85.6%)	0.30
<i>Laboratory data</i>			
Albumin ^a (g/dl) (± s.d.)	3.7 ± 0.6	3.7 ± 0.6	0.78
Hemoglobin ^b (g/dl) (± s.d.)	10.6 ± 1.5	10.3 ± 1.8	0.21

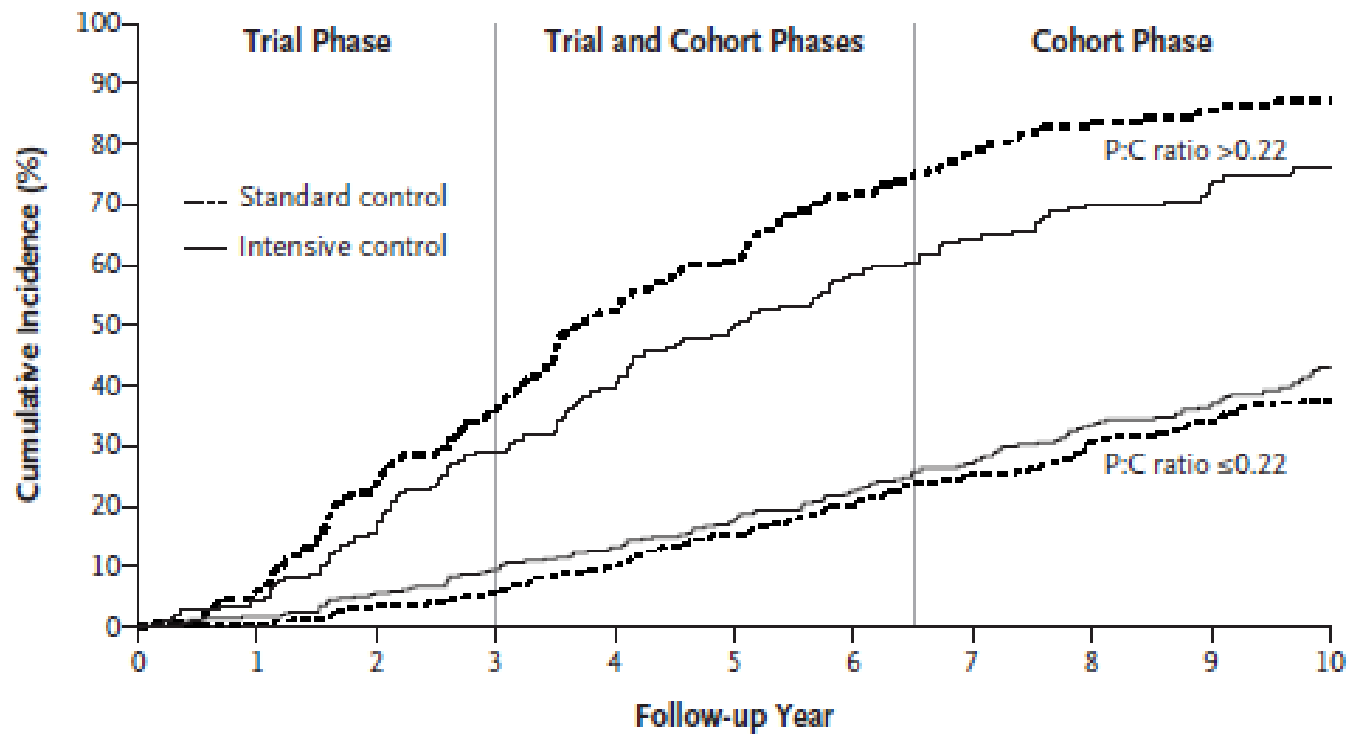
^aFor albumin, N = 133 for strict blood pressure arm and N = 122 for usual blood pressure arm.

^bFor hemoglobin, N = 145 for strict blood pressure arm and N = 133 for usual blood pressure arm.

Figure 2. Mean Change in Glomerular Filtration Rate by Randomized Group Shown are the estimated mean changes (SE) in glomerular filtration rate (GFR) (mL/min per 1.73 m²) from baseline through follow-up in the 2 blood pressure goal interventions (A) and in the 3 drug interventions (B).



AASK: CONTROL INTENSIVO DE LA P.A.



P:C Ratio >0.22

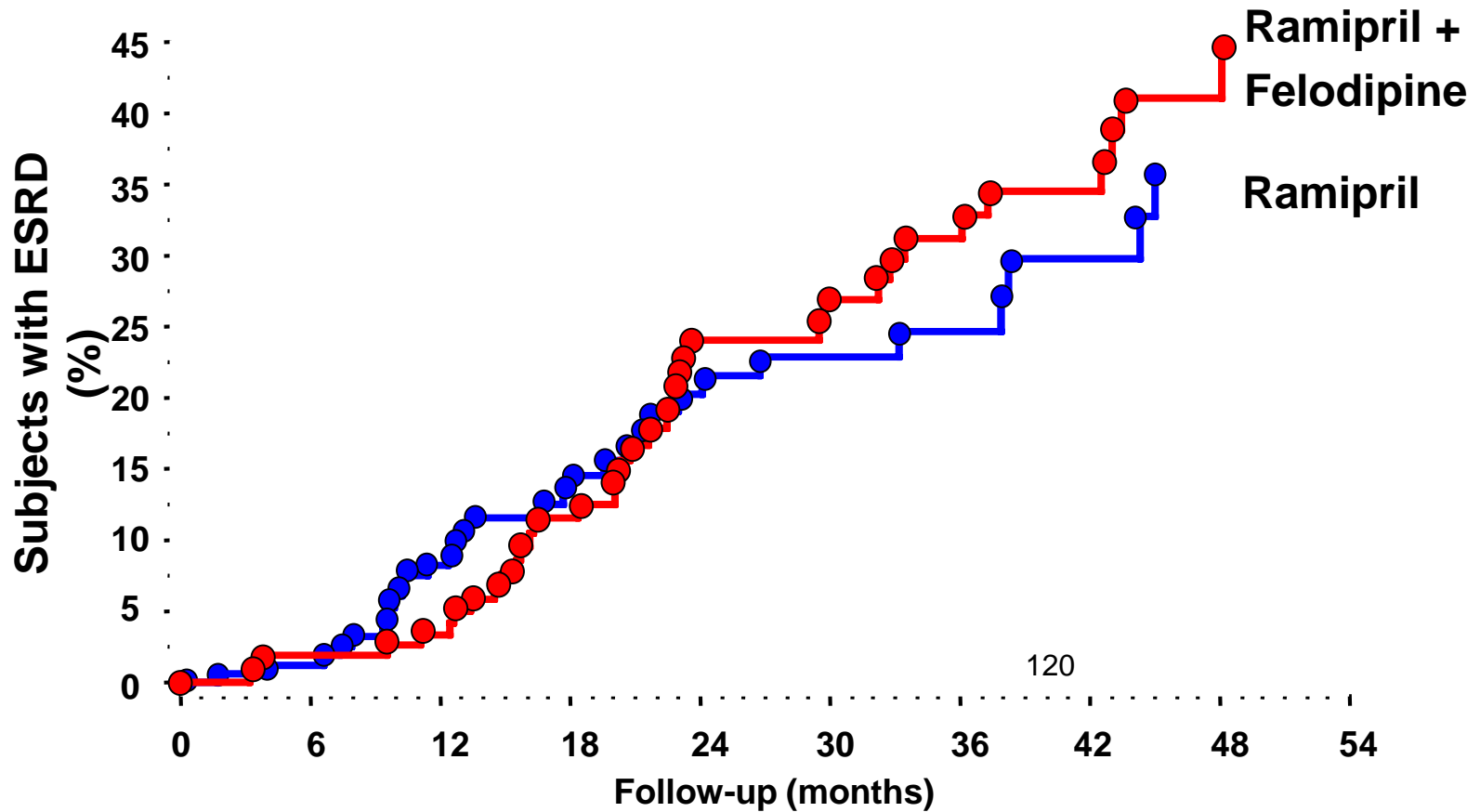
Standard control	176	165	134	113	81	66	45	32	26	22	13
Intensive control	181	172	151	128	109	87	67	56	47	40	25

P:C Ratio ≤0.22

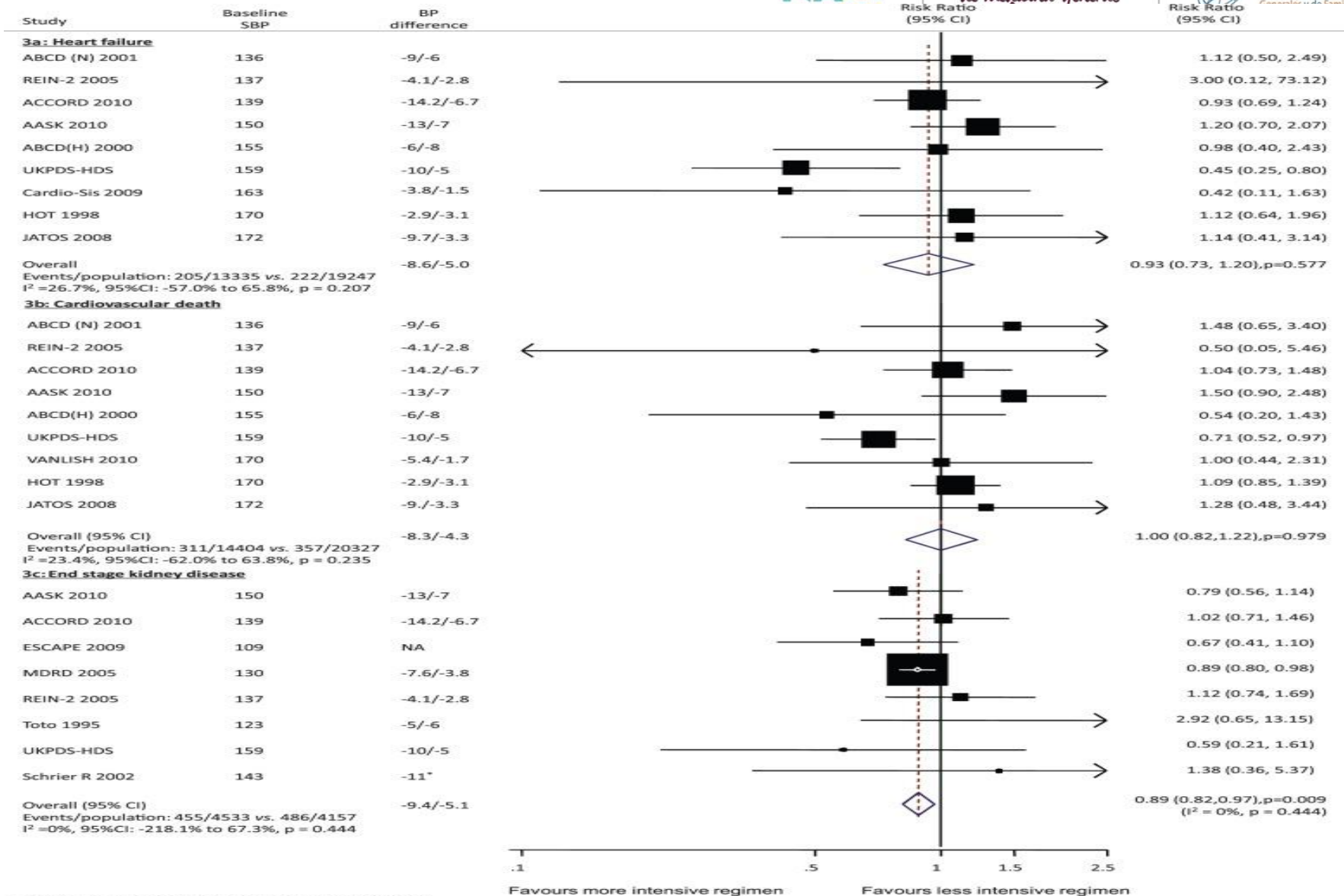
Standard control	376	373	362	353	332	302	267	234	214	196	128
Intensive control	357	350	335	321	306	282	254	228	206	189	128

Figure 2. Cumulative Incidence of the Composite Primary Outcome, According to Baseline Proteinuria Status.

REIN-2

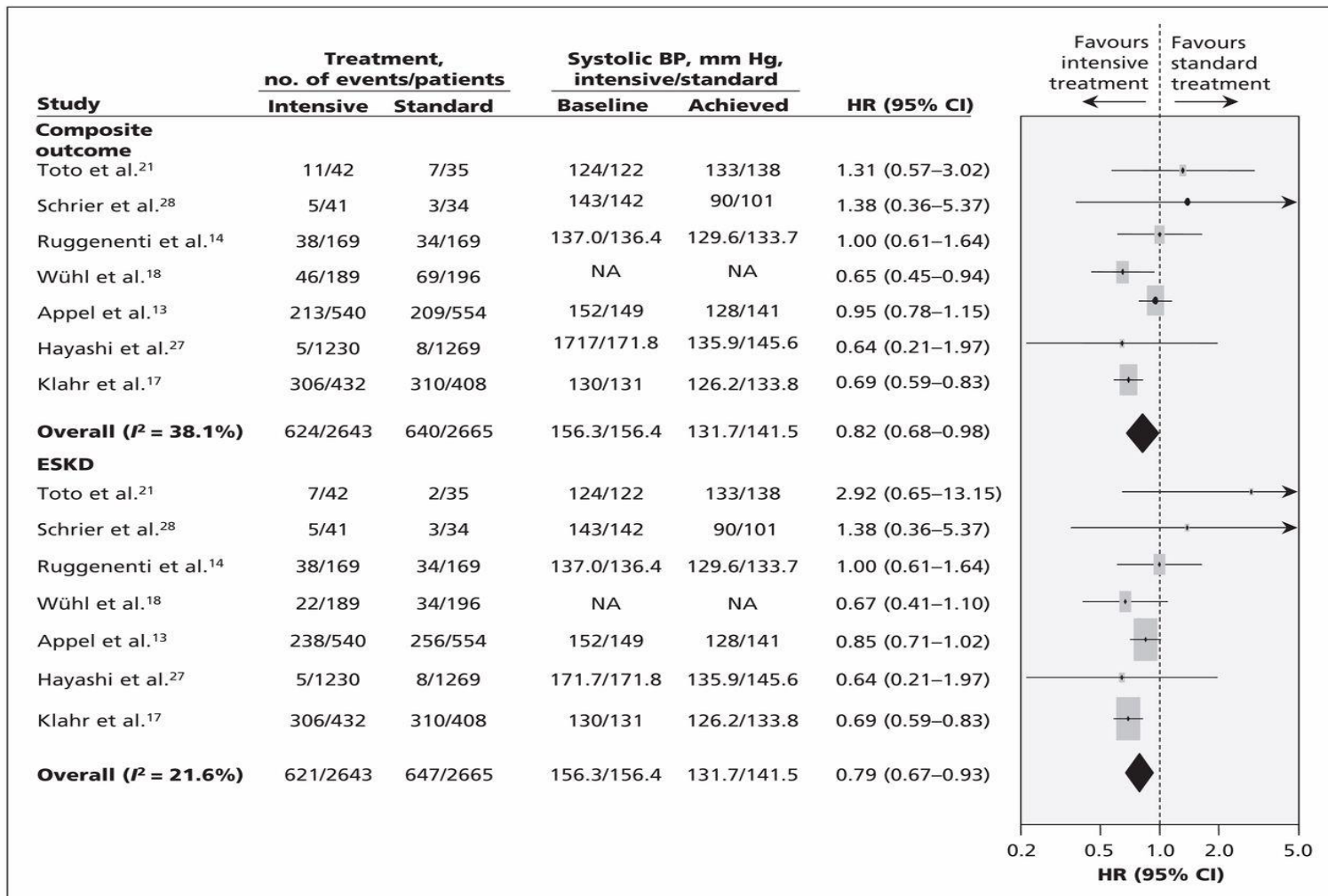


EFFECTS OF INTENSIVE BLOOD PRESSURE LOWERING ON CARDIOVASCULAR AND RENAL OUTCOMES

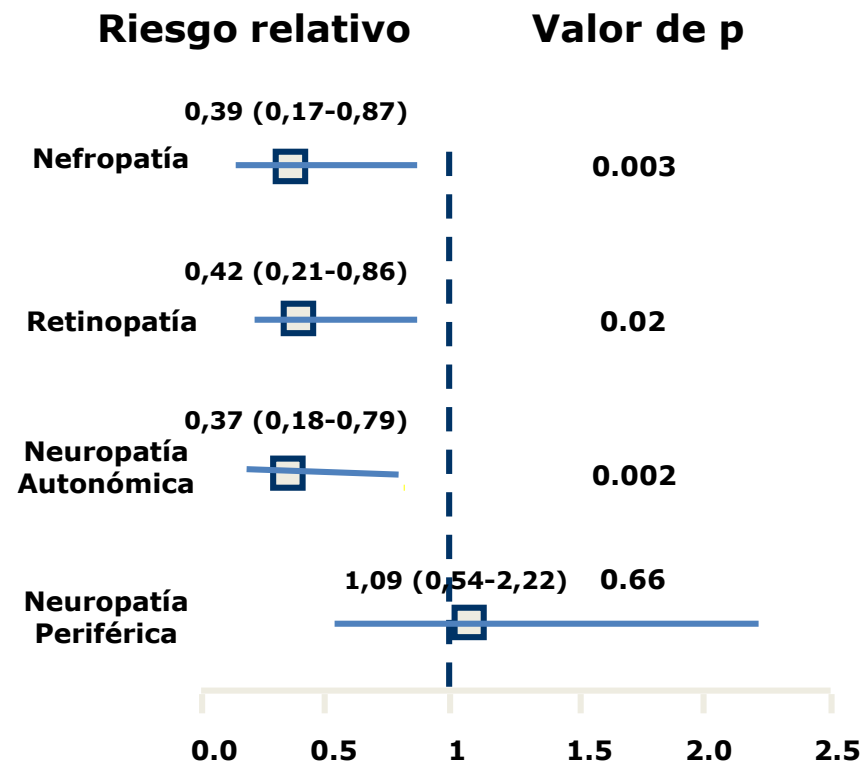
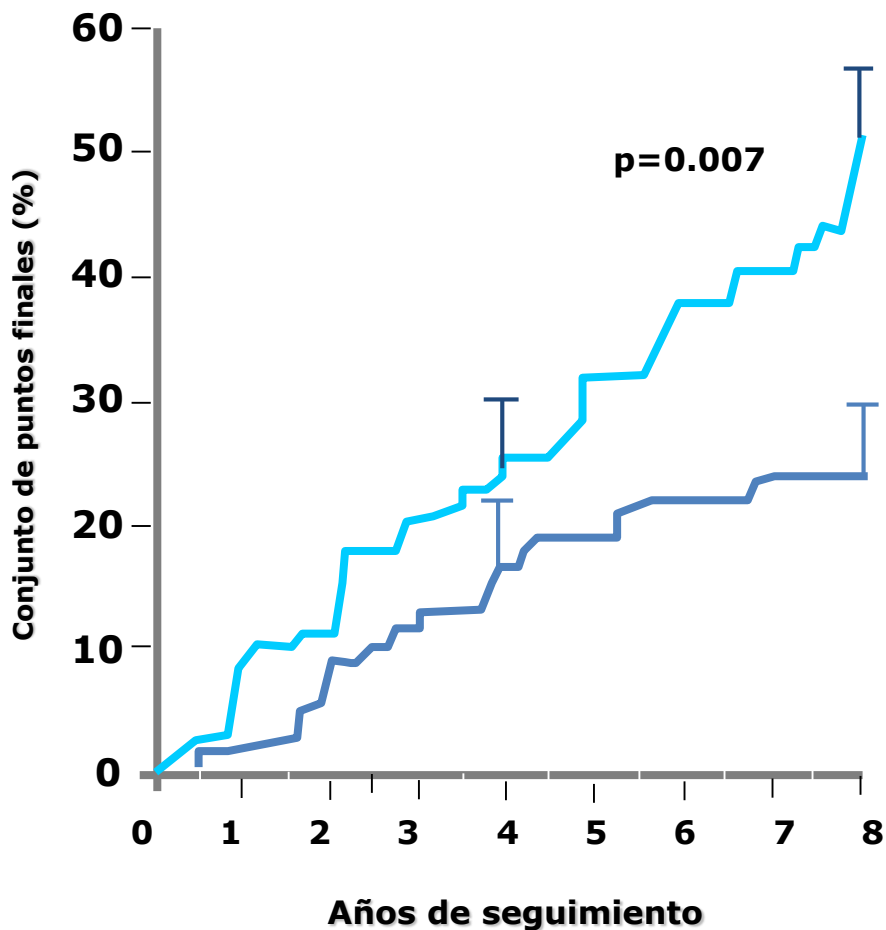


BP: blood pressure, SBP: systolic blood pressure (mmHg)
* Mean arterial pressure difference

Effects of intensive blood pressure lowering on progressive kidney failure.



MICROALBUMINURIA: ESTUDIO STENO



Landmark Trials in Diabetics and Non-Diabetics with ESRD/Death as an Endpoint



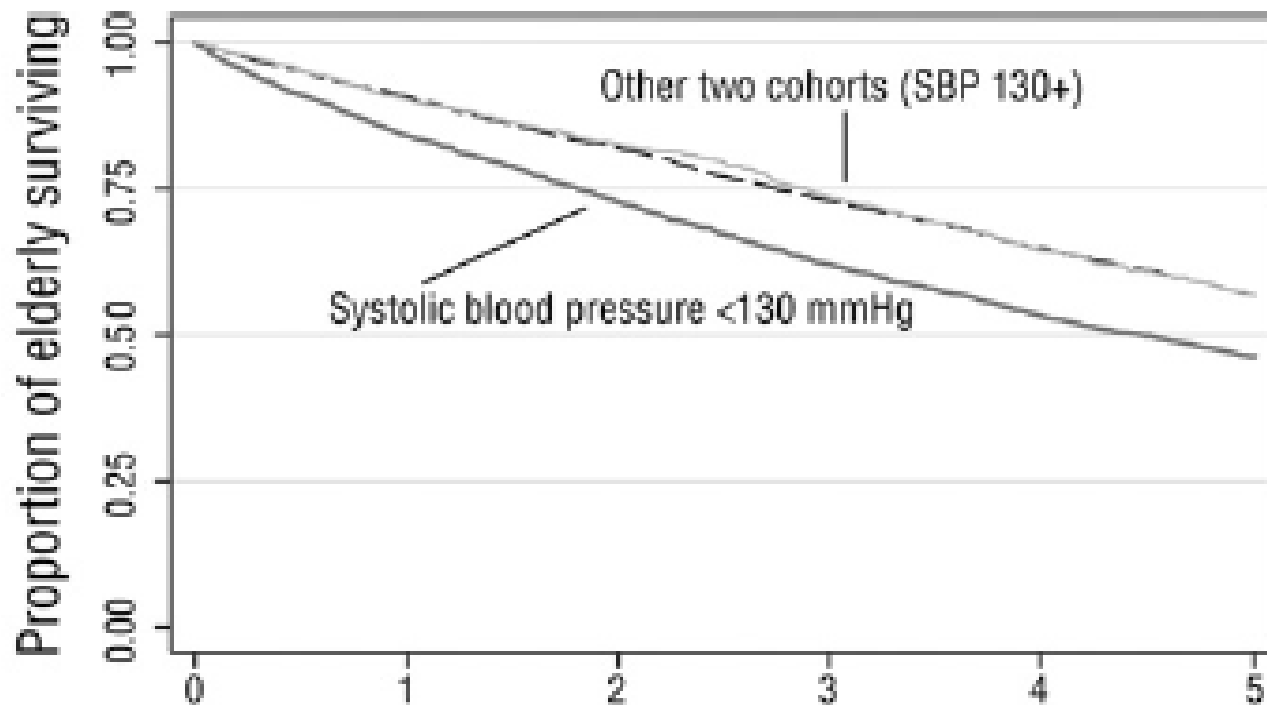
Trial	Year	Endpoint significance	Achieved BP
Captopril	1993	P=0.007	141/82
AIPRI	1996	P<0.001	139/82
REIN	1997	P=0.03	142/84
RENAAL	2001	P=0.01	142/77
IDNT	2001	results pending	141/78

Lewis EJ, et al. N Engl J Med. 1993;329(20):1456-1462.

Maschio G, et al. N Engl J Med. 1996;334(15):939-945.

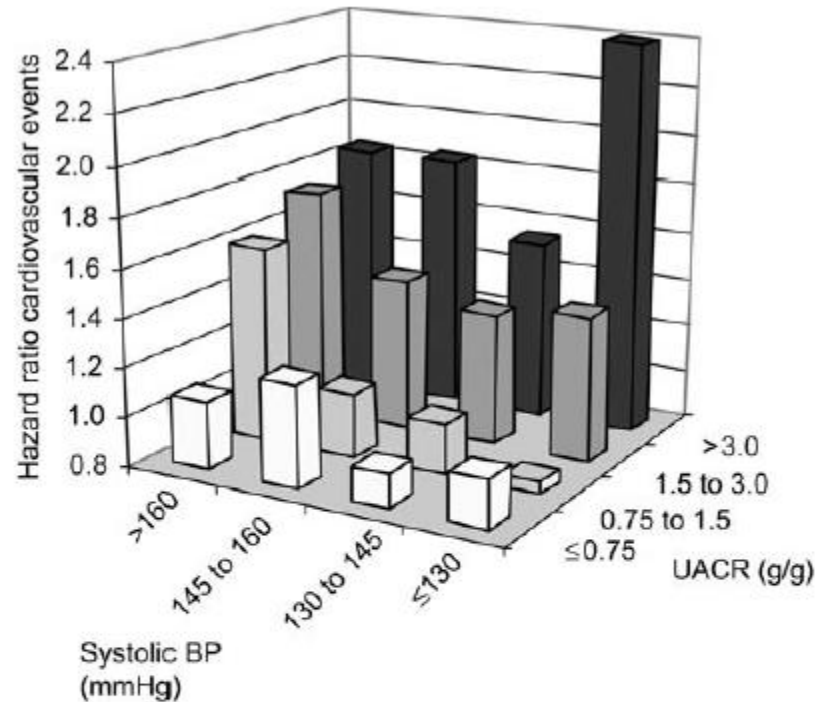
The GISEN Group. Lancet. 1997;349:1857–1863.

J CURVE IN ELDERLY CKD PATIENTS



	Years of follow-up					
Number at risk	0	1	2	3	4	5
SBP < 130	2876	2369	2016	1685	1419	1210
SBP=130-160	3516	3126	2782	2428	2119	1824
SBP>160	1104	975	885	771	661	570

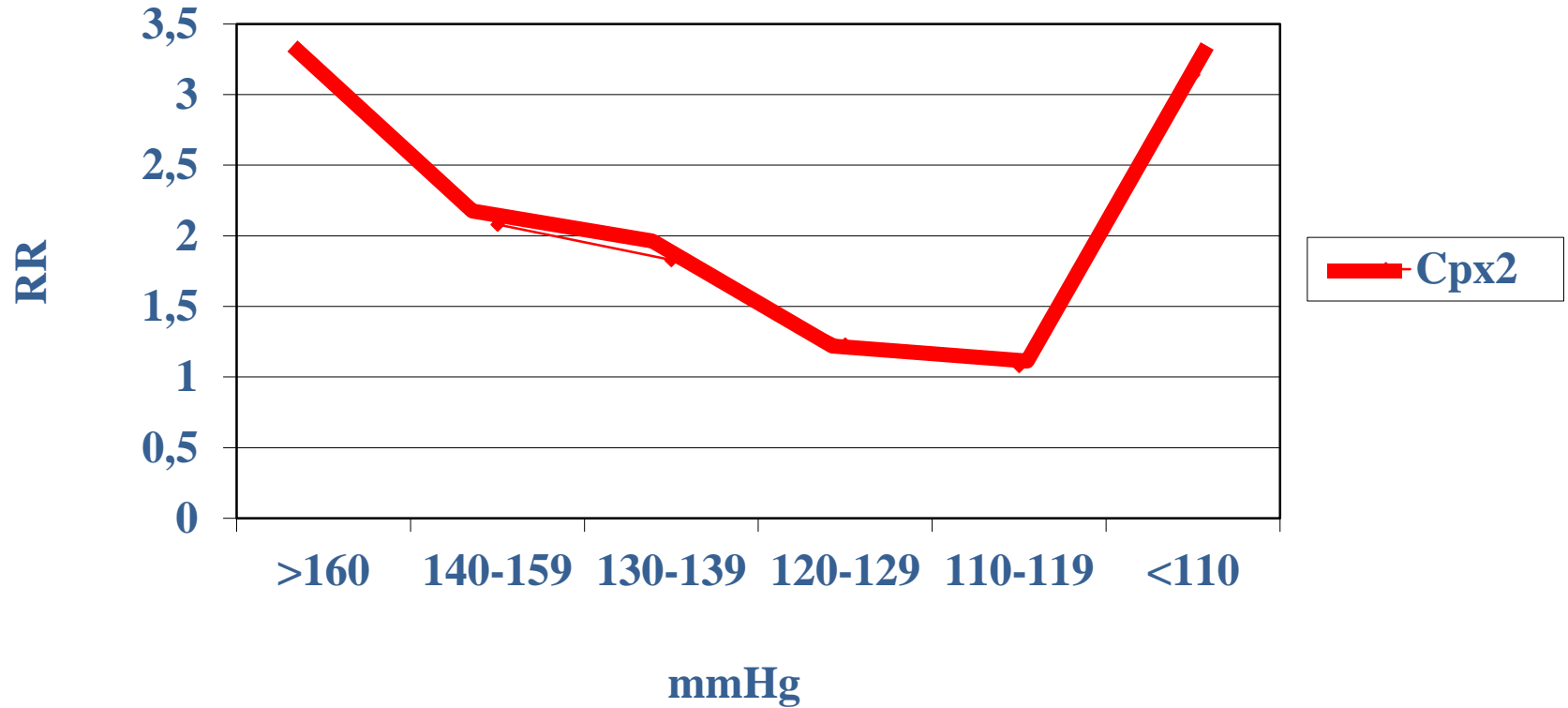
MICROALBUMINURIA Y P.A.: EFECTOS INDEPENDIENTES



Month 6 UACR (g/g)	Month 6 systolic blood pressure (mmHg)			
	≤130	130 to 145	145 to 160	>160
≤0.75	234 (6.9)	472 (7.2)	234 (7.9)	145 (8.8)
0.75 to 1.5	126 (7.6)	223 (7.1)	186 (8.9)	117 (11.6)
1.5 to 3.0	117 (13.4)	243 (9.2)	231 (12.3)	232 (14.0)
>3.0	44 (20.0)	120 (12.2)	111 (13.6)	165 (15.9)

Figure 3 Risk for cardiovascular events by achieved Month 6 albuminuria and systolic blood pressure. The table below the graph shows the number of patients in each category with the corresponding cardiovascular event rate per 100 patients years in brackets.

B.P. CONTROL AND C.K.D. PROGRESSION: META-ANALYSIS



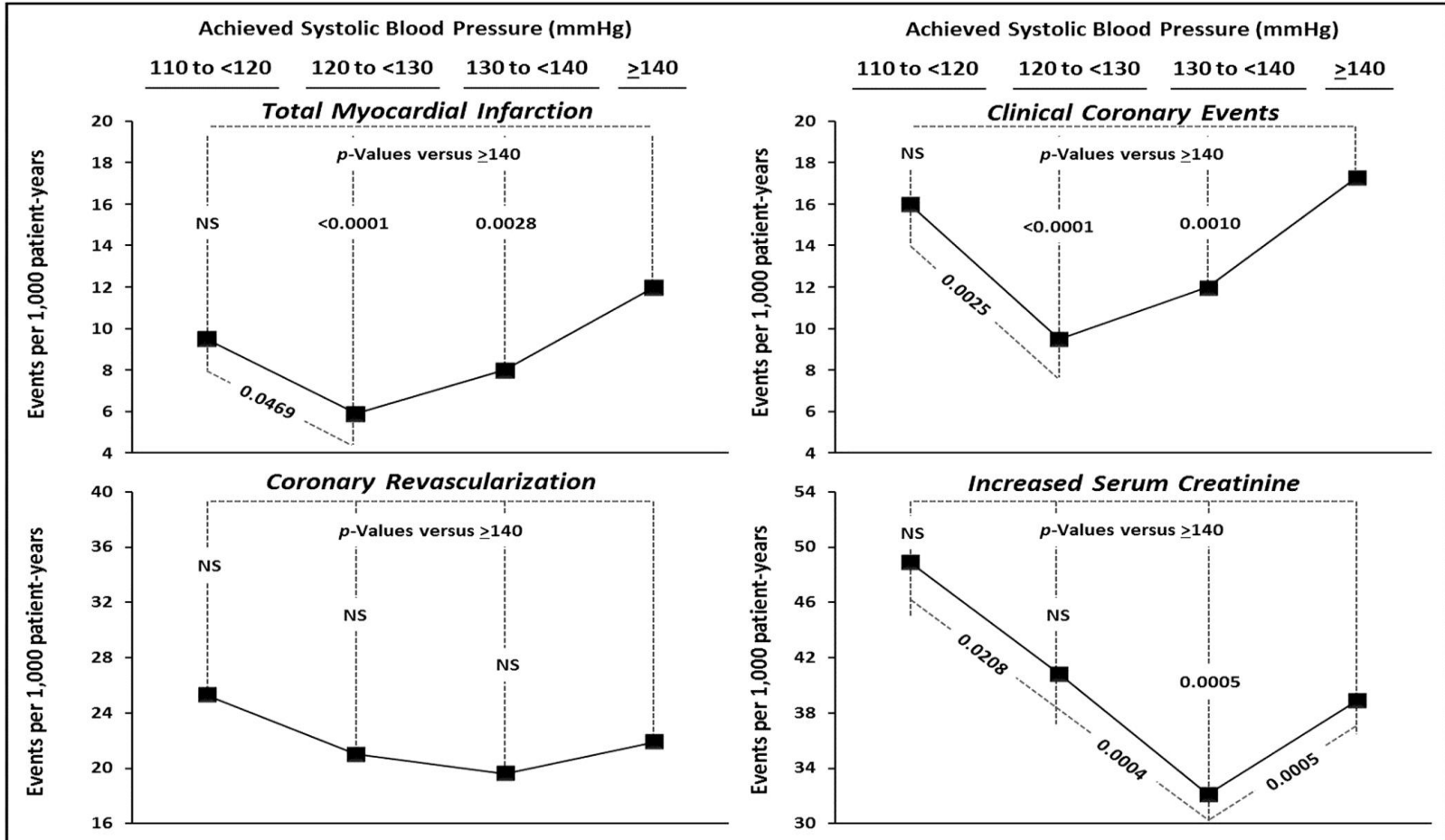
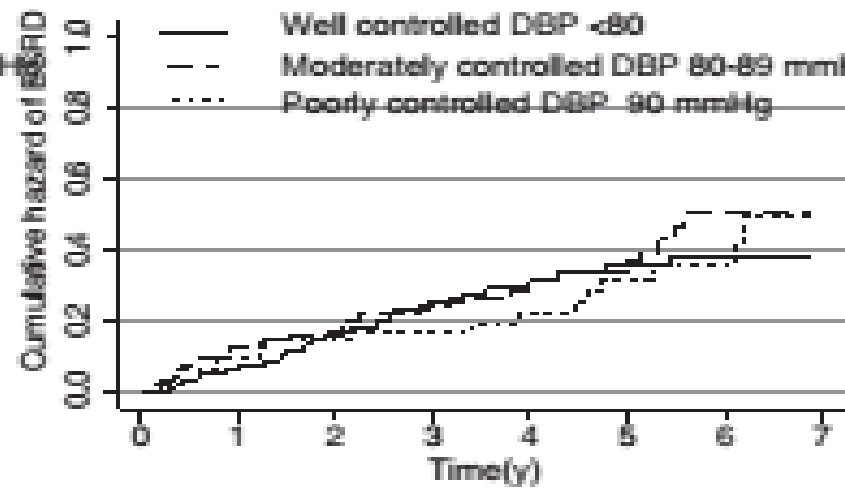
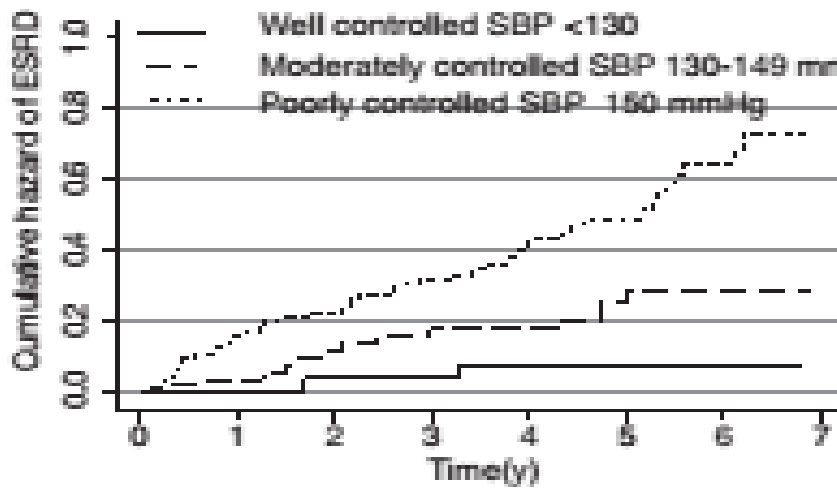
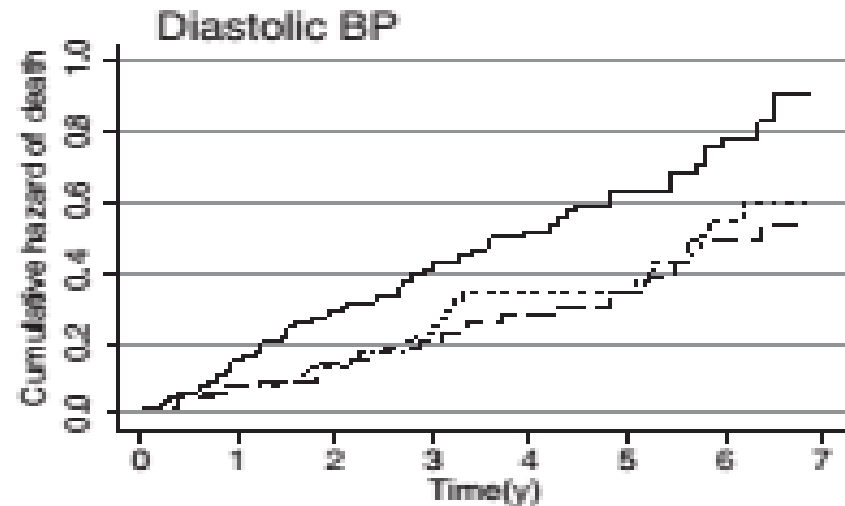
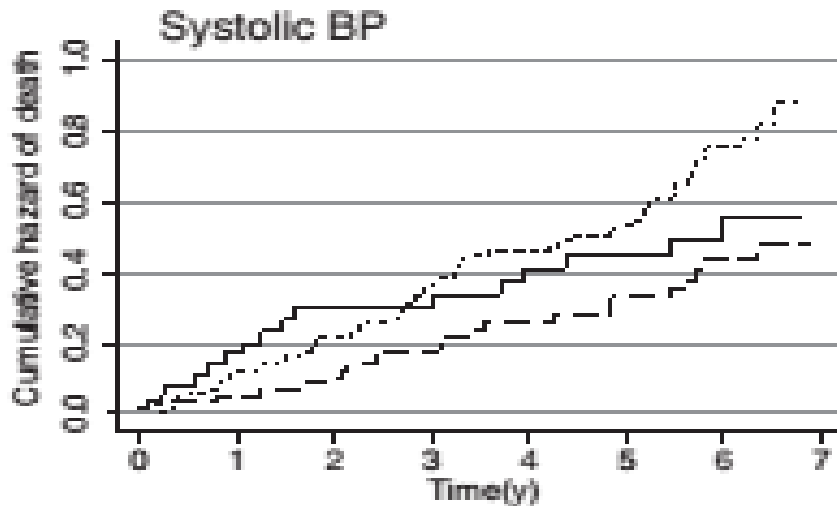


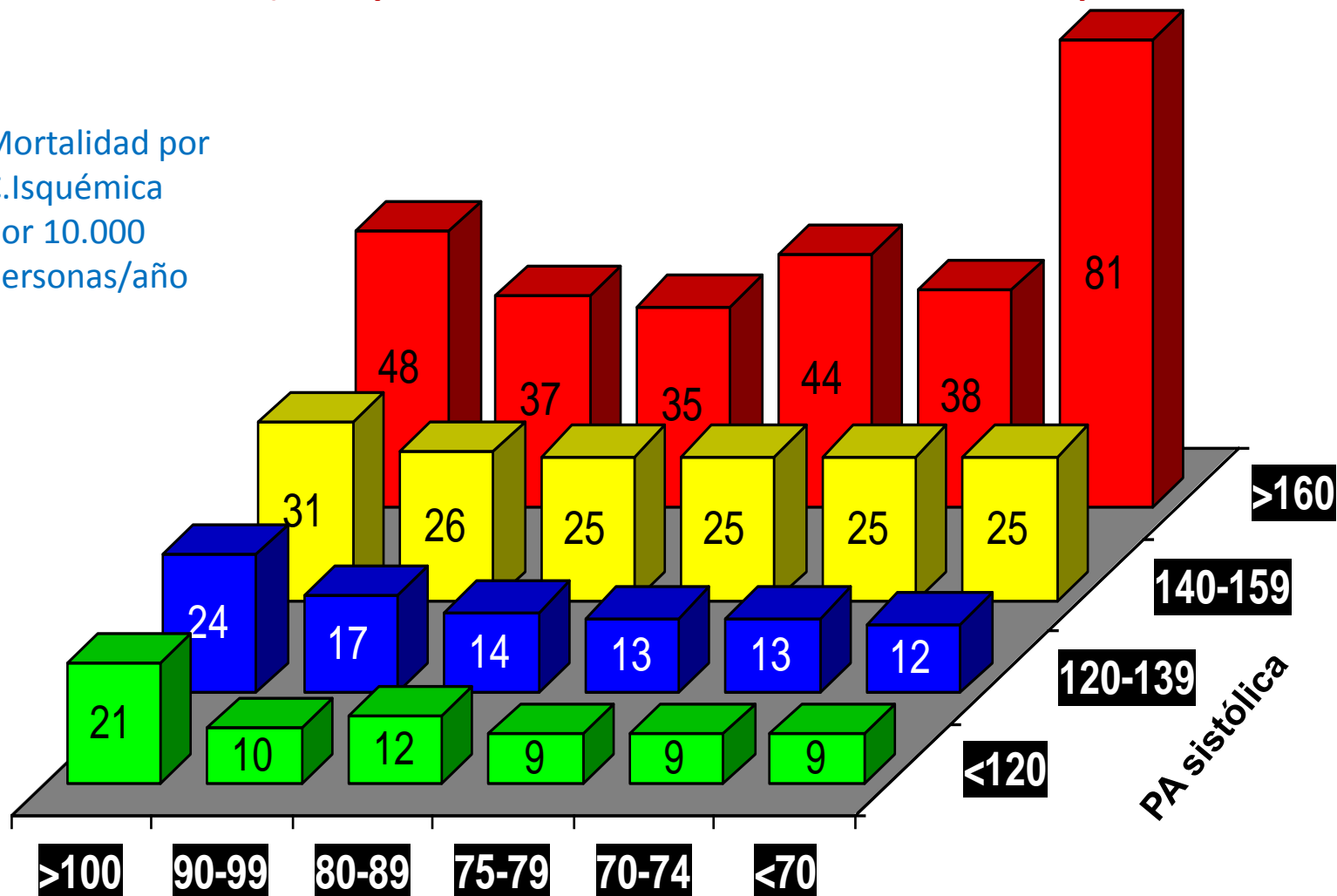
Figure 4 Event rates (per 1000 patient years) for major clinical outcomes in patients in ACCOMPLISH categorized according to their achieved systolic blood pressures. The P values for differences between adjacent groups are shown only if they are significant...



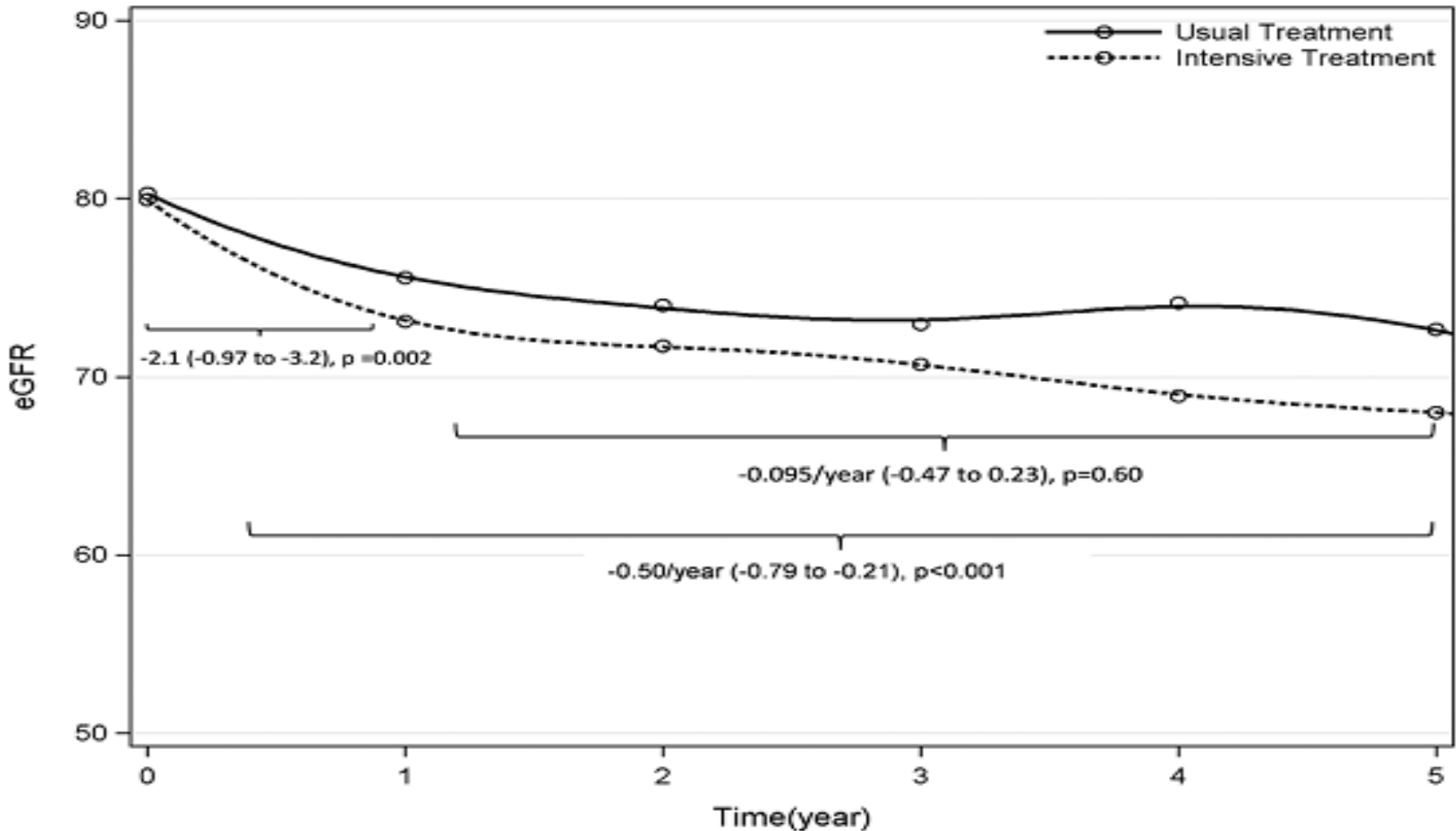
EFECTOS CONJUNTOS PAS Y PAD SOBRE MORTALIDAD CORONARIA

(Multiple Risk Factor Intervention Trial -MRFIT)

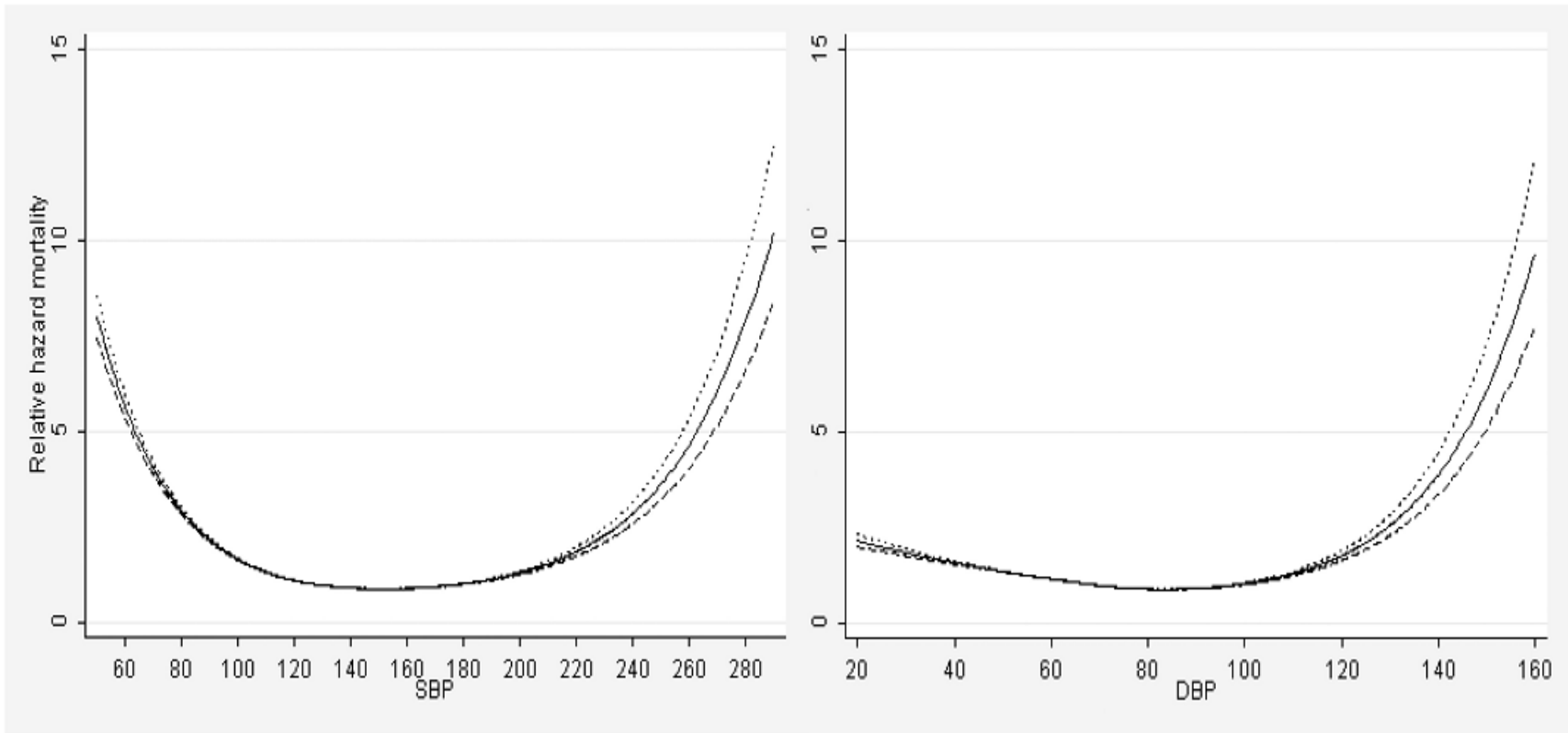
Mortalidad por
C. Isquémica
por 10.000
personas/año



BLOOD PRESSURE CONTROL AND KIDNEY FUNCTION: SPS3



Blood Pressure and Mortality in US Veterans with C.K.D.



Kovesdy C. et al. *Ann Intern Med.* 2013 ;159: 233–242.

Blood Pressure and Mortality in US Veterans with C.K.D.

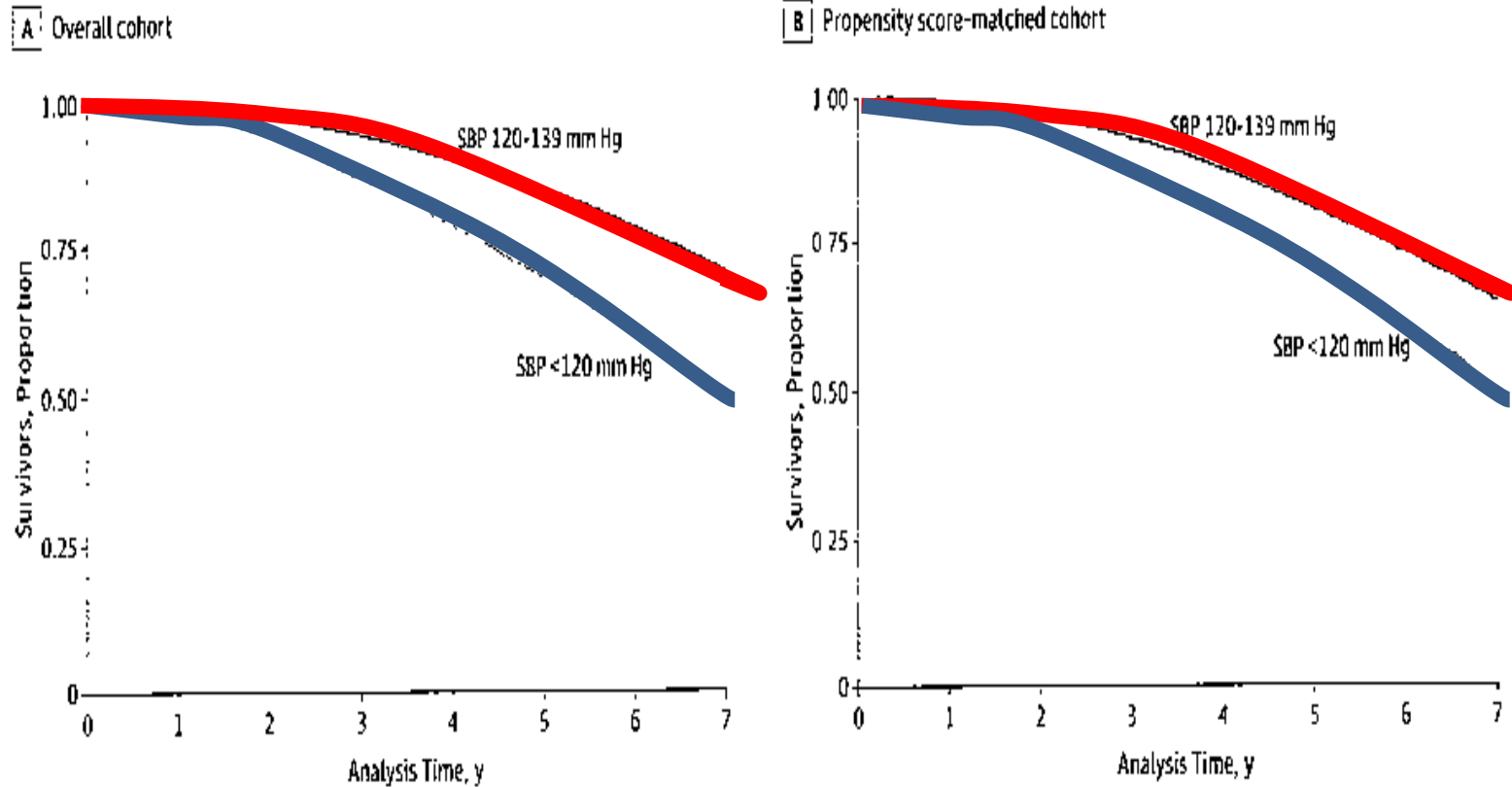
Table 2

HRs of All-Cause Mortality Associated With Hypertension Categories*

Model [†]	HR (95% CI)			
	Patients With SBP <120 mm Hg and DBP <80 mm Hg	Patients With SBP of 120–139 mm Hg or DBP of 80–89 mm Hg	Patients With SBP of 140–159 mm Hg or DBP of 90–99 mm Hg	Patients With SBP ≥160 mm Hg or DBP ≥100 mm Hg
1	1.62 (1.61–1.64)	1.00 (reference)	0.94 (0.93–0.95)	1.08 (1.06–1.10)
2	1.59 (1.58–1.61)	1.00 (reference)	0.93 (0.92–0.95)	1.04 (1.02–1.06)
3	1.48 (1.46–1.49)	1.00 (reference)	0.94 (0.93–0.95)	1.06 (1.04–1.07)
4	1.44 (1.42–1.45)	1.00 (reference)	0.95 (0.94–0.96)	1.05 (1.03–1.07)
5	1.42 (1.41–1.43)	1.00 (reference)	0.95 (0.94–0.96)	1.05 (1.03–1.07)

DBP = diastolic blood pressure; HR = hazard ratio; SBP = systolic blood pressure.

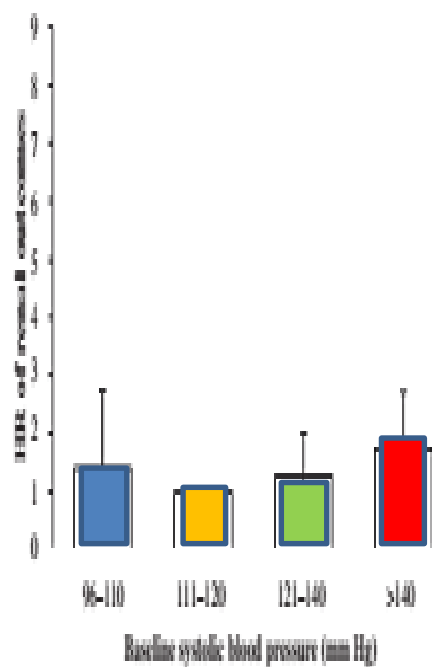
Figure 3. Kaplan-Meier Survival Curves of Patients With Follow-up Systolic Blood Pressure (SBP) Less Than 120 vs 120 to 139 mm Hg



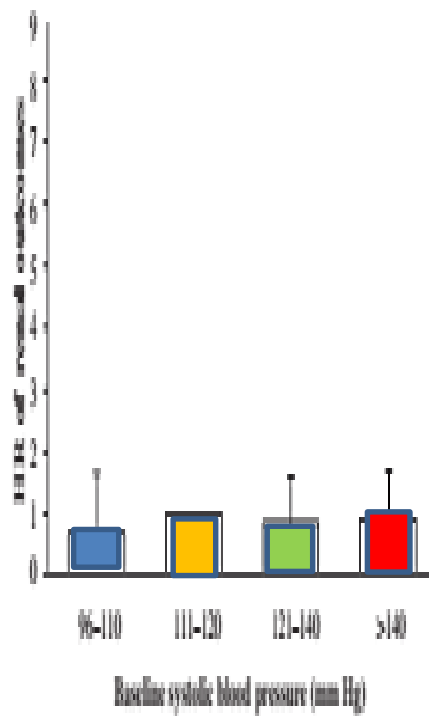
Systolic Blood Pressure and Outcomes in Stage 3–4 Chronic Kidney Disease Patients: Evidence from a Taiwanese Cohort

b)

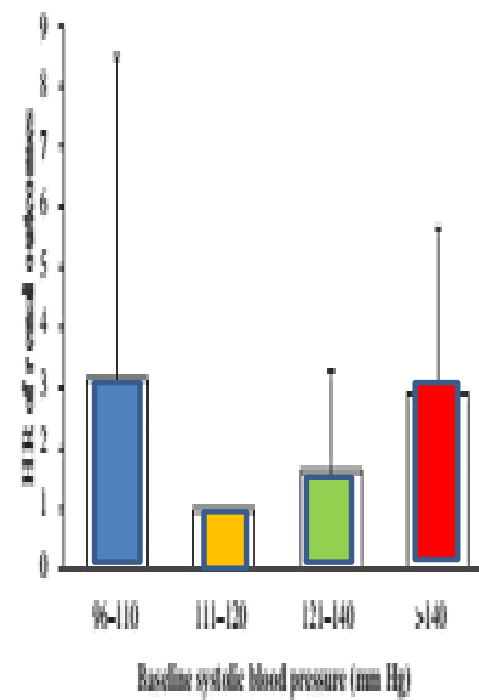
TOTAL



NO DIABETICOS



DIABETICOS



Blood pressure lowering and major cardiovascular events in people with and without chronic kidney disease: meta-analysis of randomised controlled trials

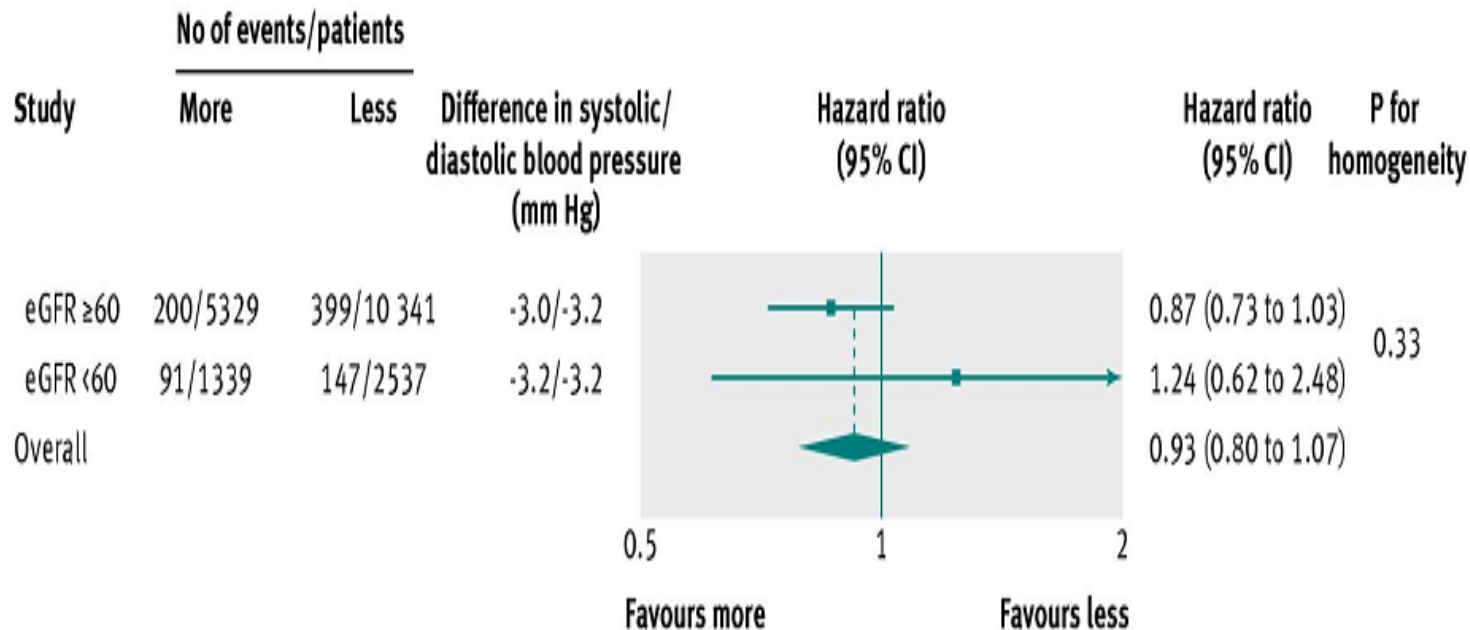


Fig 3 Effects of more intensive v less intensive blood pressure lowering regimens for risk of major cardiovascular events according to kidney function status

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Randomized Trial of Intensive versus Standard Blood-Pressure Control

The SPRINT Research Group*

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*A complete list of the members of the Systolic Blood Pressure Intervention Trial (SPRINT) Research Group is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on November 9, 2015, at NEJM.org.

DOI: [10.1056/NEJMoa1511939](https://doi.org/10.1056/NEJMoa1511939)

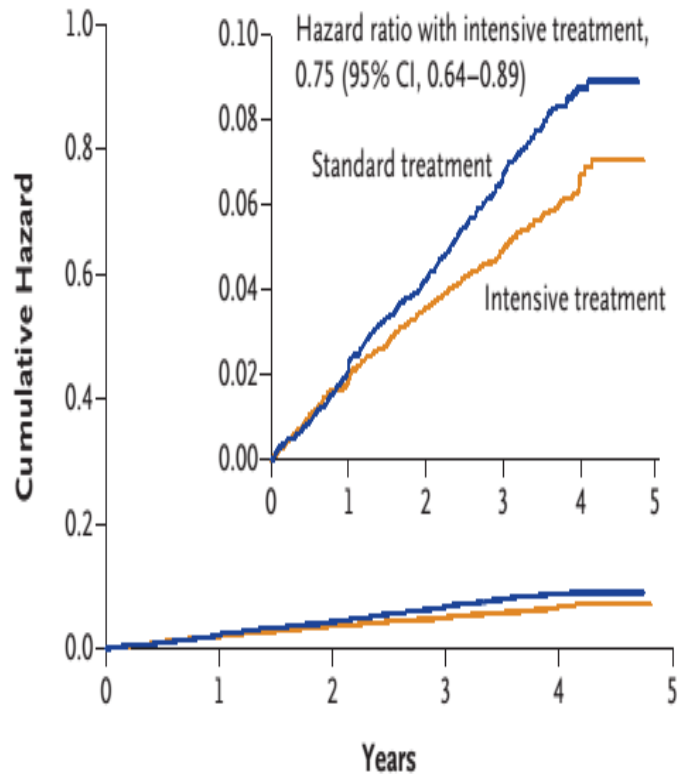
Table 1. Baseline Characteristics of the Study Participants.*

Characteristic	Intensive Treatment (N = 4678)	Standard Treatment (N = 4683)
Criterion for increased cardiovascular risk — no. (%)†		
Age ≥75 yr	1317 (28.2)	1319 (28.2)
Chronic kidney disease‡	1330 (28.4)	1316 (28.1)
Cardiovascular disease	940 (20.1)	937 (20.0)
Clinical	779 (16.7)	783 (16.7)
Subclinical	247 (5.3)	246 (5.3)
Framingham 10-yr cardiovascular disease risk score ≥15%	2870 (61.4)	2867 (61.2)
Female sex — no. (%)	1684 (36.0)	1648 (35.2)
Age — yr		
Overall	67.9±9.4	67.9±9.5
Among those ≥75 yr of age	79.8±3.9	79.9±4.1
Race or ethnic group — no. (%)§		
Non-Hispanic black	1379 (29.5)	1423 (30.4)
Hispanic	503 (10.8)	481 (10.3)
Non-Hispanic white	2698 (57.7)	2701 (57.7)
Other	98 (2.1)	78 (1.7)
Black race¶	1454 (31.1)	1493 (31.9)
Baseline blood pressure — mm Hg		
Systolic	139.7±15.8	139.7±15.4
Diastolic	78.2±11.9	78.0±12.0
Distribution of systolic blood pressure — no. (%)		
≤132 mm Hg	1583 (33.8)	1553 (33.2)
>132 mm Hg to <145 mm Hg	1489 (31.8)	1549 (33.1)
≥145 mm Hg	1606 (34.3)	1581 (33.8)

Table 1. Baseline Characteristics of the Study Participants.*

Serum creatinine — mg/dl	1.07±0.34	1.08±0.34
Estimated GFR — ml/min/1.73 m ²		
Among all participants	71.8±20.7	71.7±20.5
Among those with estimated GFR ≥60 ml/min/1.73 m ²	81.3±15.5	81.1±15.5
Among those with estimated GFR <60 ml/min/1.73 m ²	47.8±9.5	47.9±9.5
Ratio of urinary albumin (mg) to creatinine (g)	44.1±178.7	41.1±152.9
Fasting total cholesterol — mg/dl	190.2±41.4	190.0±40.9
Fasting HDL cholesterol — mg/dl	52.9±14.3	52.8±14.6
Fasting total triglycerides — mg/dl	124.8±85.8	127.1±95.0
Fasting plasma glucose — mg/dl	98.8±13.7	98.8±13.4
Statin use — no./total no. (%)	1978/4645 (42.6)	2076/4640 (44.7)
Aspirin use — no./total no. (%)	2406/4661 (51.6)	2350/4666 (50.4)
Smoking status — no. (%)		
Never smoked	2050 (43.8)	2072 (44.2)
Former smoker	1977 (42.3)	1996 (42.6)
Current smoker	639 (13.7)	601 (12.8)
Missing data	12 (0.3)	14 (0.3)

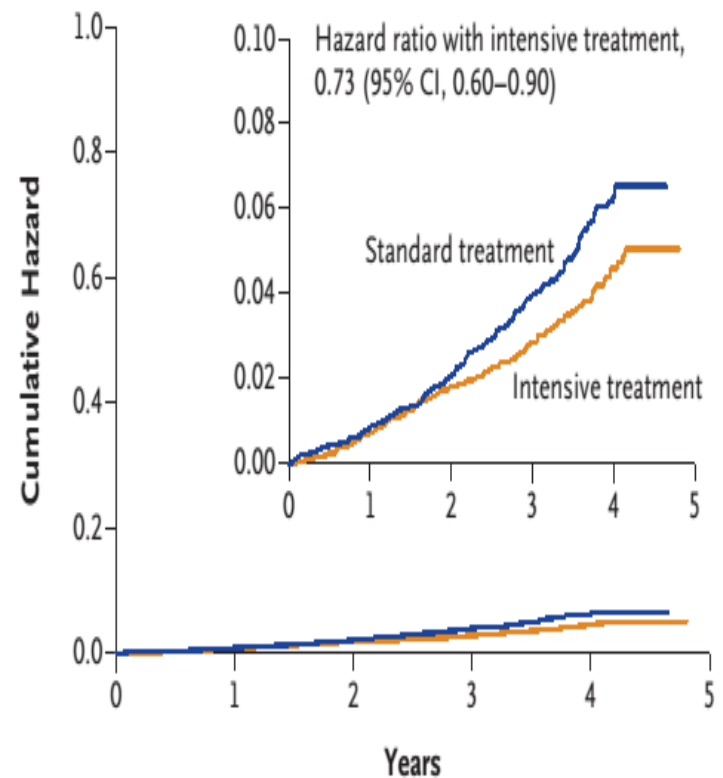
A Primary Outcome



No. at Risk

Standard treatment	4683	4437	4228	2829	721
Intensive treatment	4678	4436	4256	2900	779

B Death from Any Cause



No. at Risk

Standard treatment	4683	4528	4383	2998	789
Intensive treatment	4678	4516	4390	3016	807

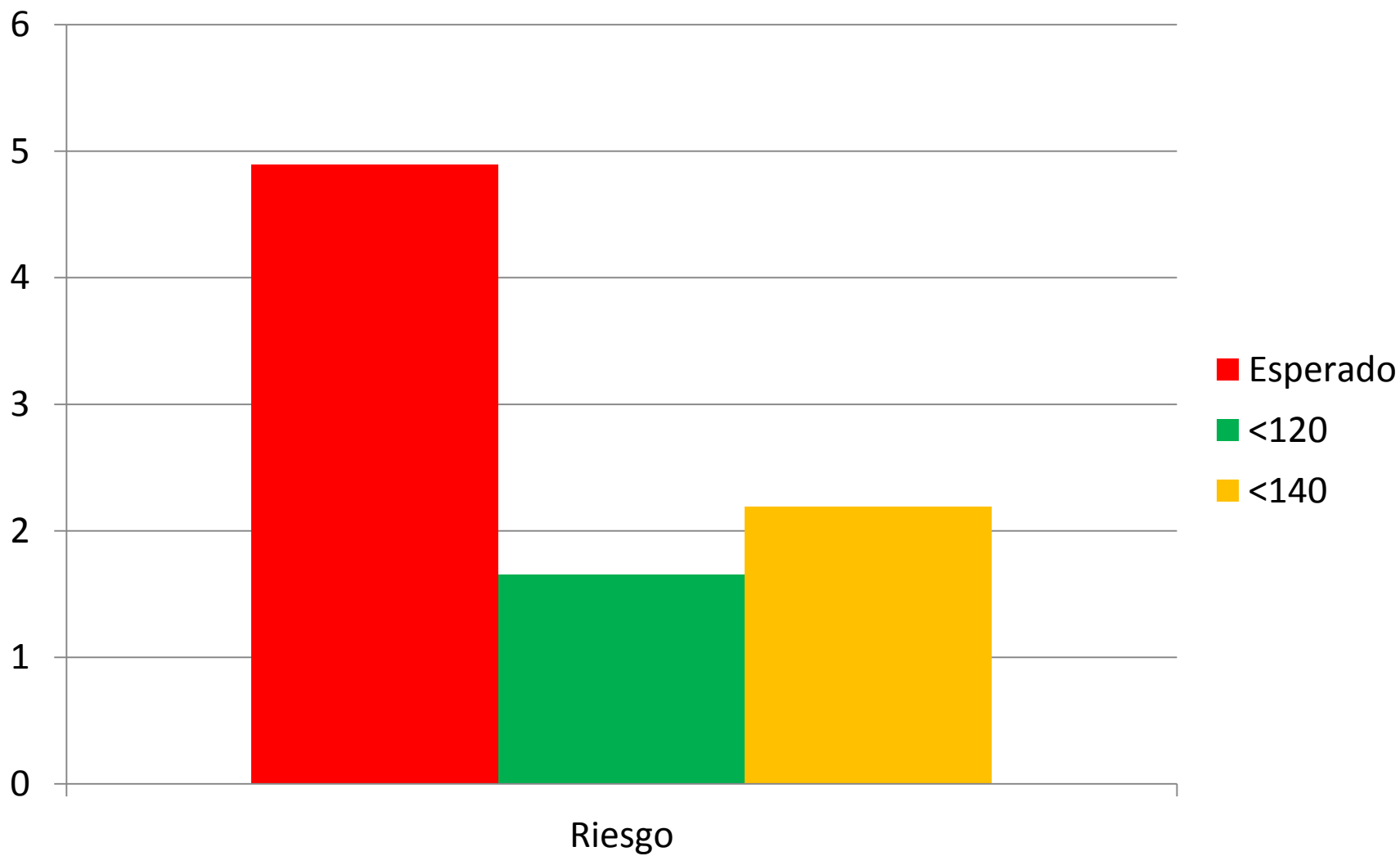
Table 3. Serious Adverse Events, Conditions of Interest, and Monitored Clinical Events.

Variable	Intensive Treatment (N = 4678)	Standard Treatment (N = 4683)	Hazard Ratio	P Value
	<i>no. of patients (%)</i>			
Serious adverse event*	1793 (38.3)	1736 (37.1)	1.04	0.25
Conditions of interest				
Serious adverse event only				
Hypotension	110 (2.4)	66 (1.4)	1.67	0.001
Syncope	107 (2.3)	80 (1.7)	1.33	0.05
Bradycardia	87 (1.9)	73 (1.6)	1.19	0.28
Electrolyte abnormality	144 (3.1)	107 (2.3)	1.35	0.02
Injurious fall†	105 (2.2)	110 (2.3)	0.95	0.71
Acute kidney injury or acute renal failure‡	193 (4.1)	117 (2.5)	1.66	<0.001
Emergency department visit or serious adverse event				
Hypotension	158 (3.4)	93 (2.0)	1.70	<0.001
Syncope	163 (3.5)	113 (2.4)	1.44	0.003
Bradycardia	104 (2.2)	83 (1.8)	1.25	0.13
Electrolyte abnormality	177 (3.8)	129 (2.8)	1.38	0.006
Injurious fall†	334 (7.1)	332 (7.1)	1.00	0.97
Acute kidney injury or acute renal failure‡	204 (4.4)	120 (2.6)	1.71	<0.001
Monitored clinical events				
Adverse laboratory measure§				
Serum sodium <130 mmol/liter	180 (3.8)	100 (2.1)	1.76	<0.001
Serum sodium >150 mmol/liter	6 (0.1)	0		0.02
Serum potassium <3.0 mmol/liter	114 (2.4)	74 (1.6)	1.50	0.006
Serum potassium >5.5 mmol/liter	176 (3.8)	171 (3.7)	1.00	0.97
Orthostatic hypotension¶				
Alone	777 (16.6)	857 (18.3)	0.88	0.01
With dizziness	62 (1.3)	71 (1.5)	0.85	0.35

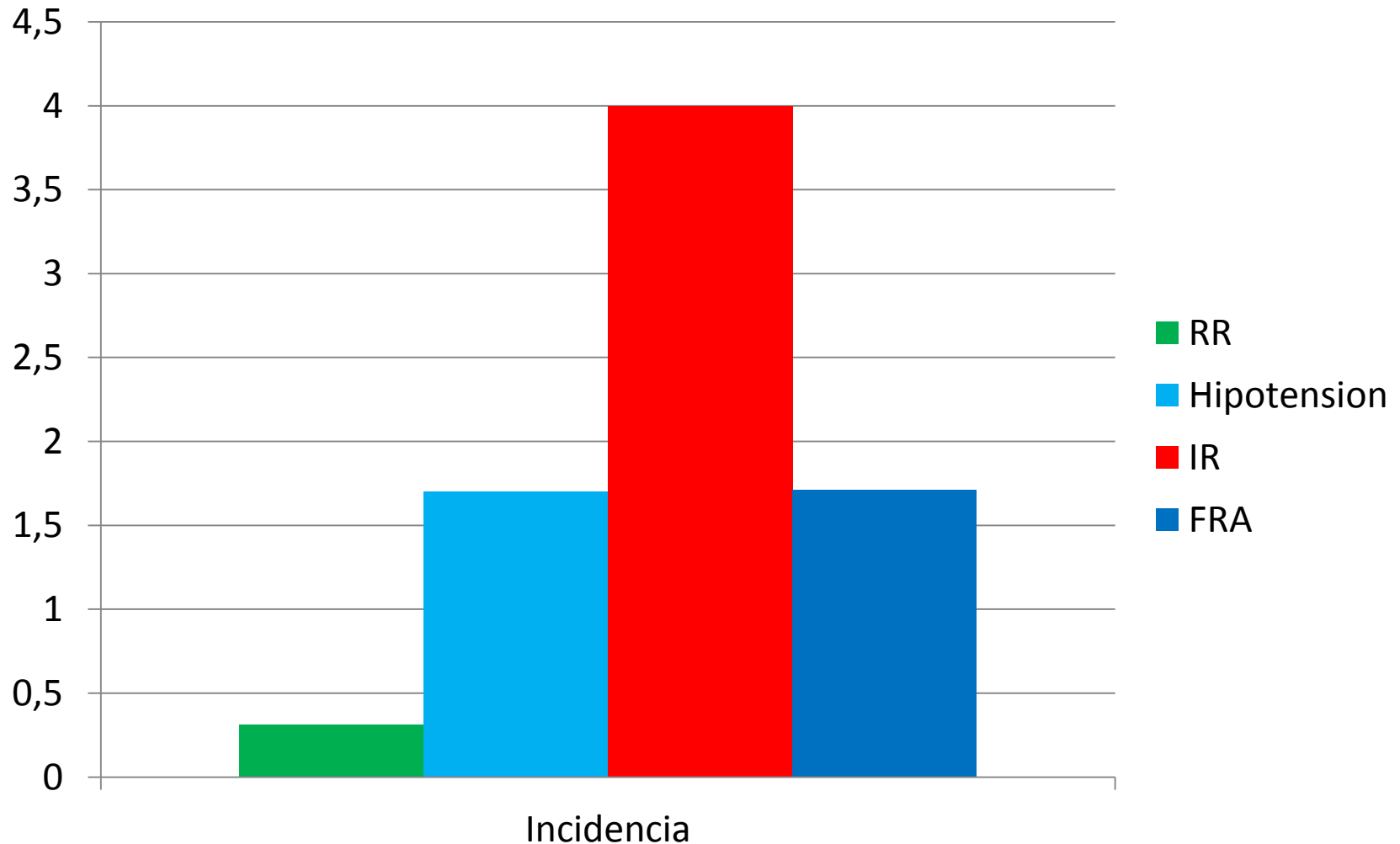
Table 2. Primary and Secondary Outcomes and Renal Outcomes.*

Outcome	Intensive Treatment		Standard Treatment		Hazard Ratio (95% CI)	P Value
	no. of patients (%)	% per year	no. of patients (%)	% per year		
All participants	(N = 4678)		(N = 4683)			
Primary outcome†	243 (5.2)	1.65	319 (6.8)	2.19	0.75 (0.64–0.89)	<0.001
Secondary outcomes						
Myocardial infarction	97 (2.1)	0.65	116 (2.5)	0.78	0.83 (0.64–1.09)	0.19
Acute coronary syndrome	40 (0.9)	0.27	40 (0.9)	0.27	1.00 (0.64–1.55)	0.99
Stroke	62 (1.3)	0.41	70 (1.5)	0.47	0.89 (0.63–1.25)	0.50
Heart failure	62 (1.3)	0.41	100 (2.1)	0.67	0.62 (0.45–0.84)	0.002
Death from cardiovascular causes	37 (0.8)	0.25	65 (1.4)	0.43	0.57 (0.38–0.85)	0.005
Death from any cause	155 (3.3)	1.03	210 (4.5)	1.40	0.73 (0.60–0.90)	0.003
Primary outcome or death	332 (7.1)	2.25	423 (9.0)	2.90	0.78 (0.67–0.90)	<0.001
Participants with CKD at baseline	(N = 1330)		(N = 1316)			
Composite renal outcome‡	14 (1.1)	0.33	15 (1.1)	0.36	0.89 (0.42–1.87)	0.76
≥50% reduction in estimated GFR§	10 (0.8)	0.23	11 (0.8)	0.26	0.87 (0.36–2.07)	0.75
Long-term dialysis	6 (0.5)	0.14	10 (0.8)	0.24	0.57 (0.19–1.54)	0.27
Kidney transplantation	0		0			
Incident albuminuria¶	49/526 (9.3)	3.02	59/500 (11.8)	3.90	0.72 (0.48–1.07)	0.11
Participants without CKD at baseline 	(N = 3332)		(N = 3345)			
≥30% reduction in estimated GFR to <60 ml/min/1.73 m ² §	127 (3.8)	1.21	37 (1.1)	0.35	3.49 (2.44–5.10)	<0.001
Incident albuminuria¶	110/1769 (6.2)	2.00	135/1831 (7.4)	2.41	0.81 (0.63–1.04)	0.10

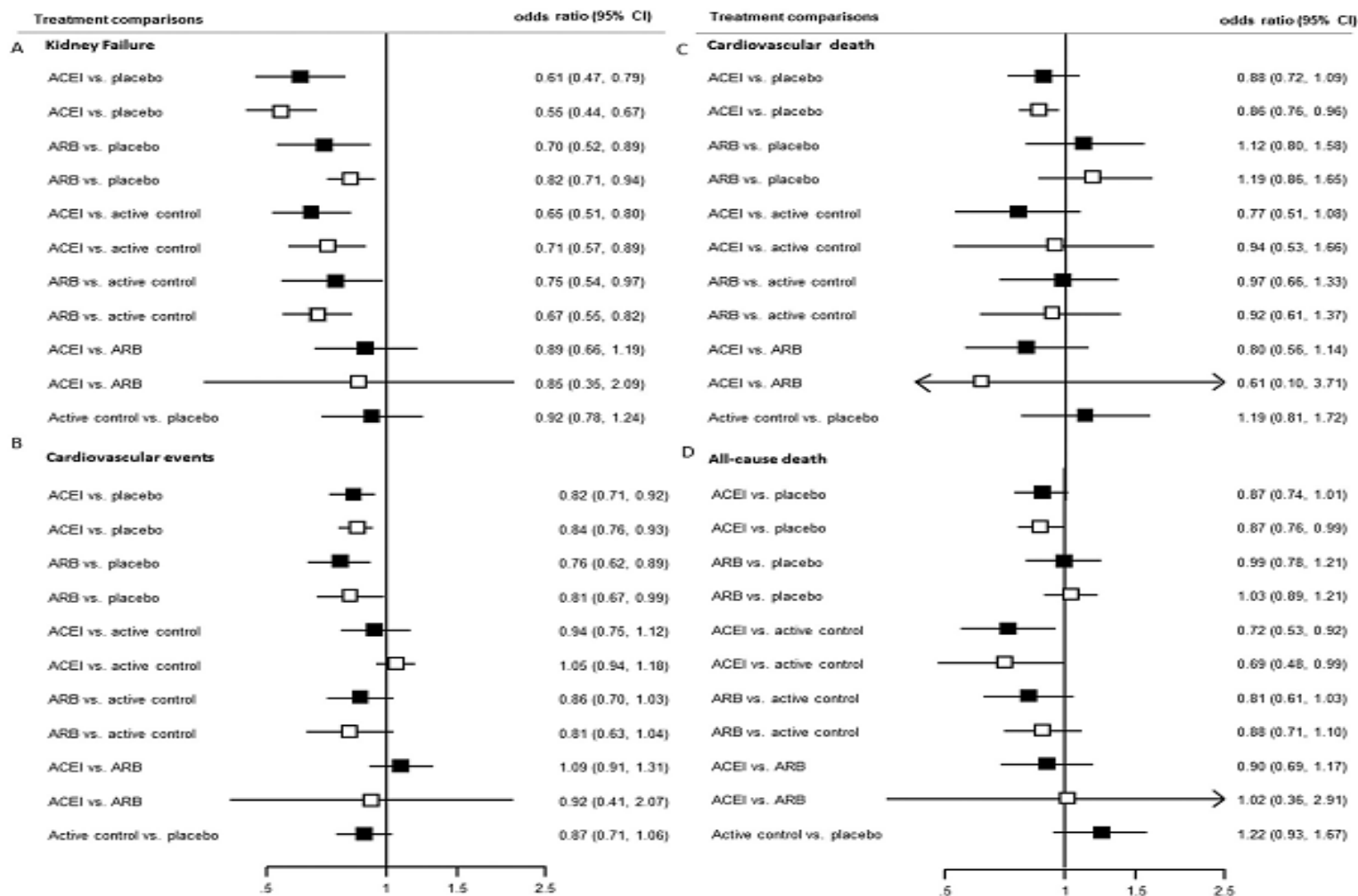
REDUCCION DE RIESGO



BALANCE TERAPEUTICO



Renin-Angiotensin System Inhibitors and Kidney and Cardiovascular Outcomes in Patients With CKD: A Bayesian Network Meta-analysis of Randomized Clinical Trials



CONCLUSIONES

- Una PA < 140/90 mmHg reduce la progresion de la enfermedad renal.
- Un objetivo más intensivo (cercano, pero no por debajo de 130/80 mmHg) podría mejorar los resultados.
- Una PA <130/80 mmHg podría ser el objetivo en pacientes proteinuricos.
- No hay evidencias para indicar este objetivo en MICROALBUMINURIA.

- La CURVA J existe también en pacientes con ERC.
- Disminuciones excesivas de la PA inducidas por la medicación hipotensora pueden tener un efecto contraproducente.
- El beneficio obtenido en el estudio SPRINT –aunque significativo desde el punto de vista estadístico- es una reducción marginal del riesgo individual (0,0035 por paciente) a cambio hay un gran aumento de efectos secundarios.
- Desde el punto de vista renal no se consiguieron beneficios sino solo complicaciones.

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Muchas gracias y
Buenas Tardes