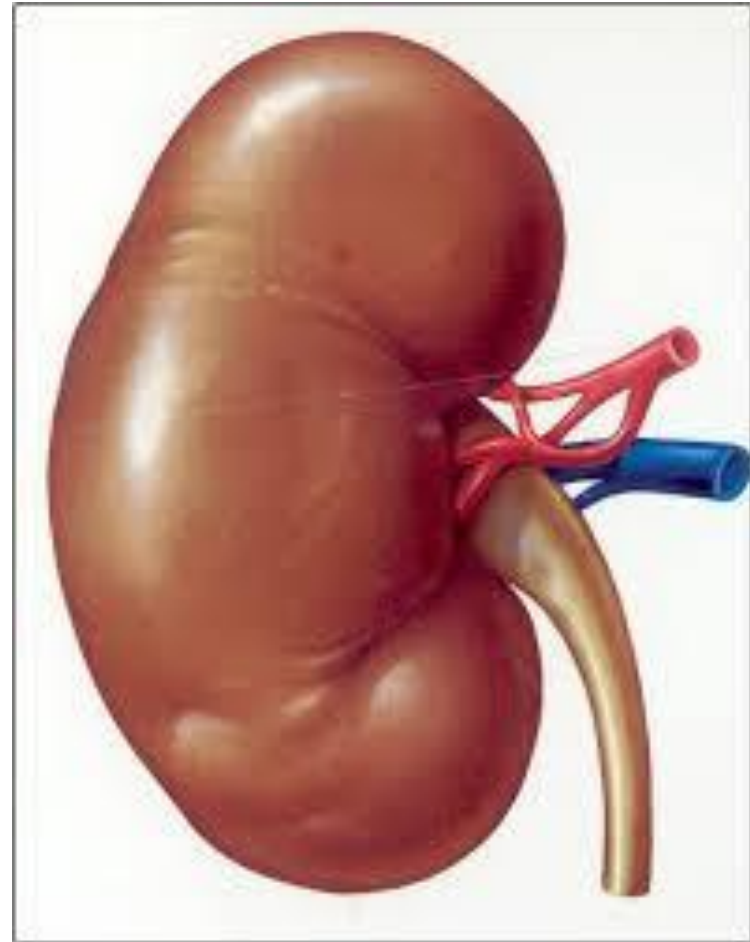
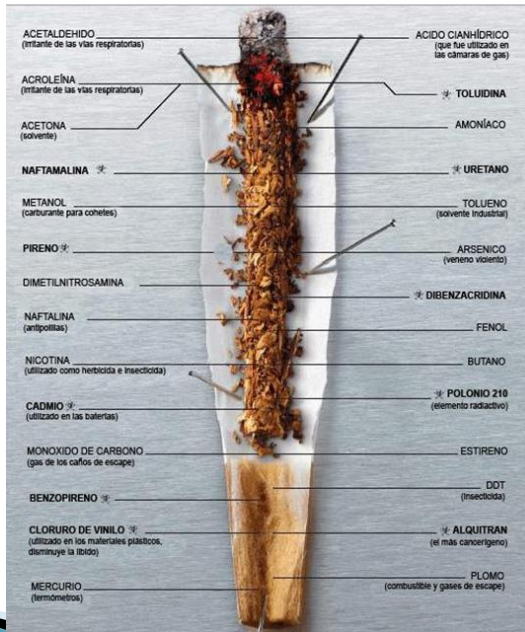


Factores de riesgo y riñón

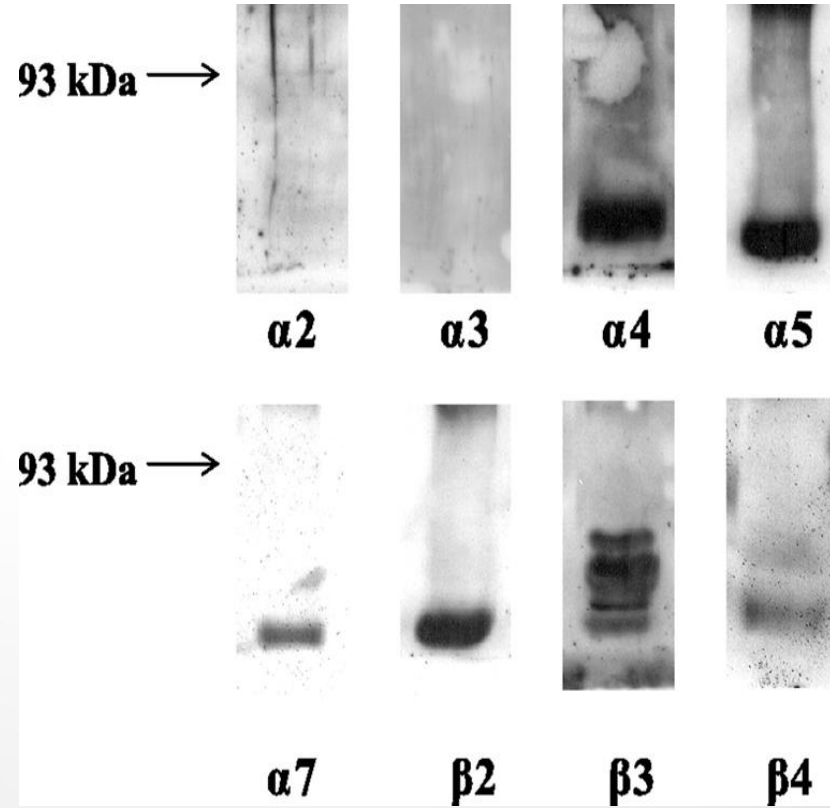
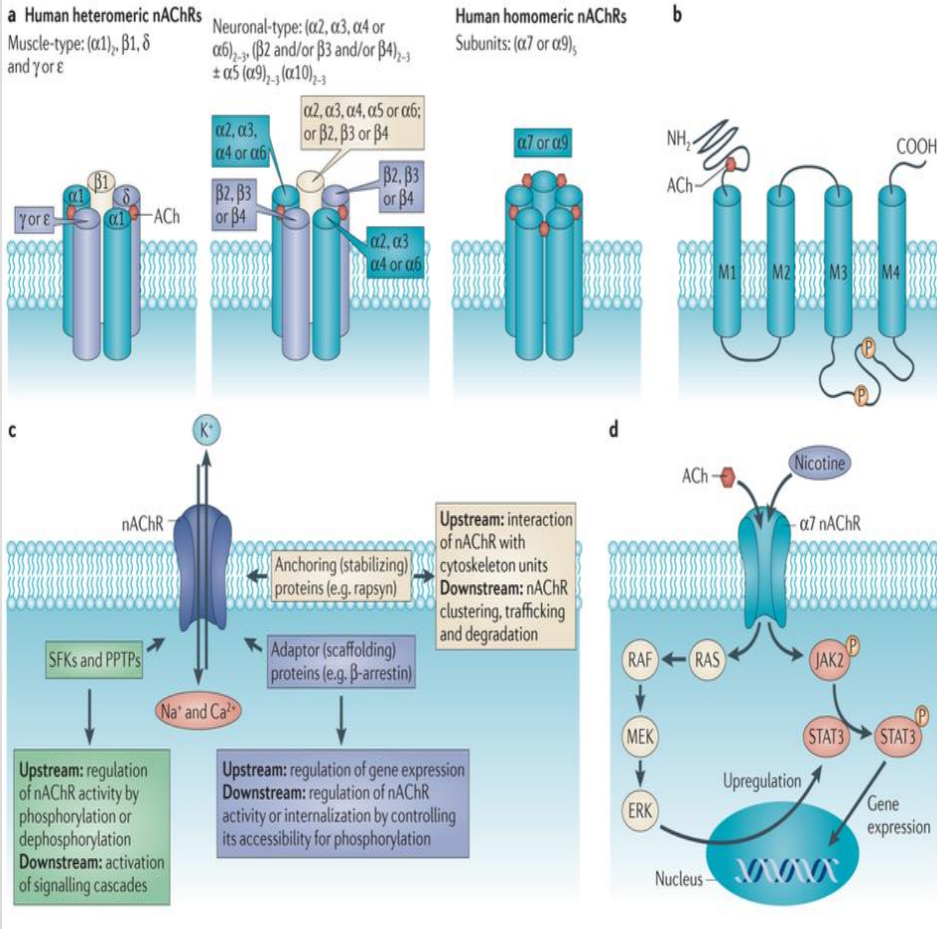
Escuela de verano
Baeza 2016

TABACO Y RIÑÓN

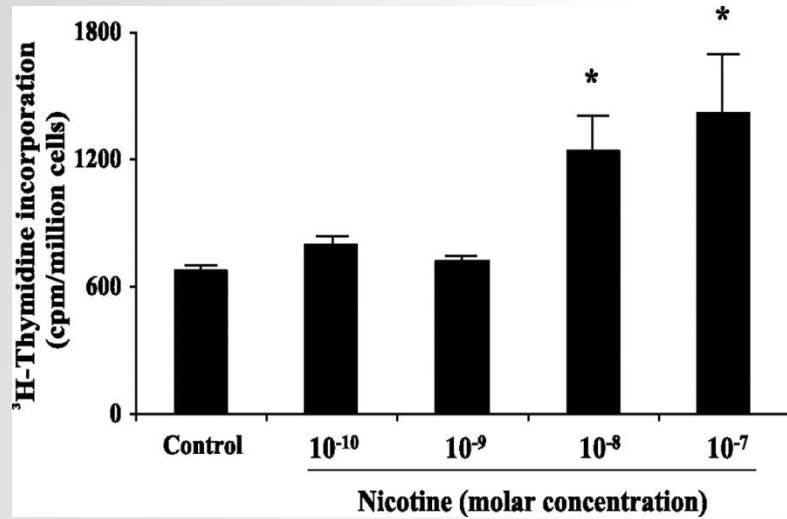


Estructura y función de nAChRs.

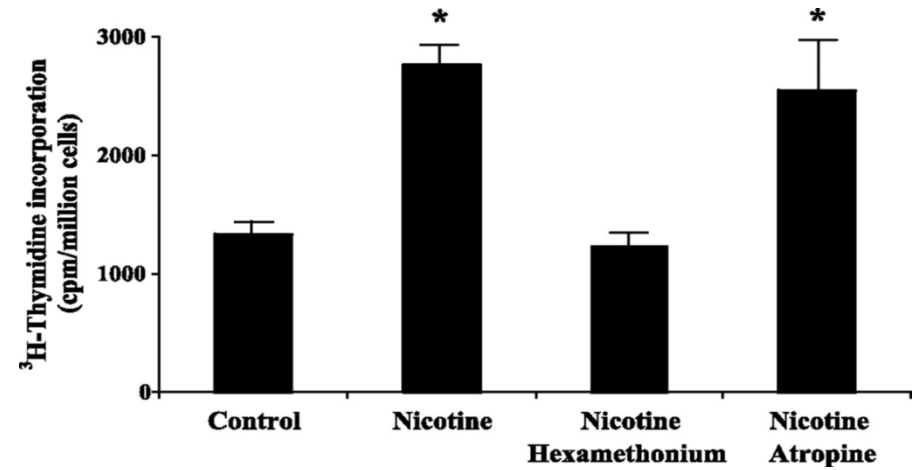
Expression of nicotine ACh receptor (nAChR) subunits in human mesangial cells.



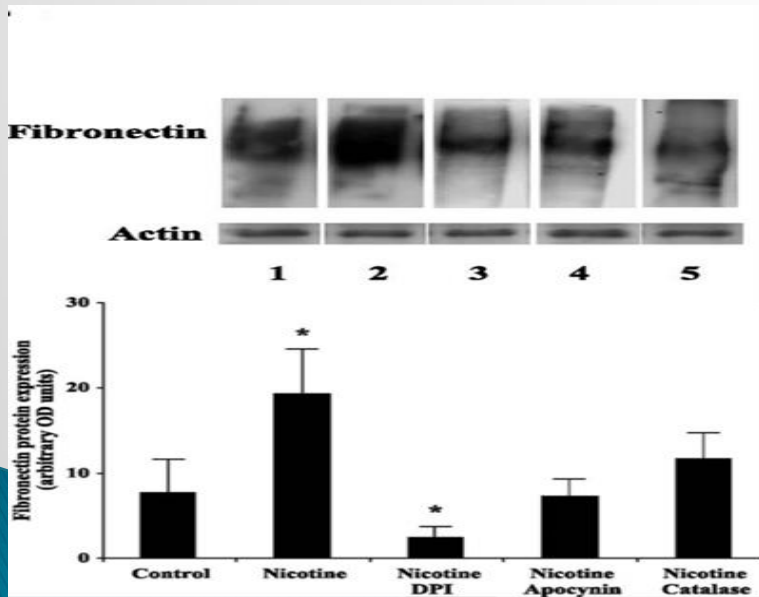
Nicotine (10^{-7} to 10^{-10} M) induced mesangial cell proliferation in a dose-dependent manner.



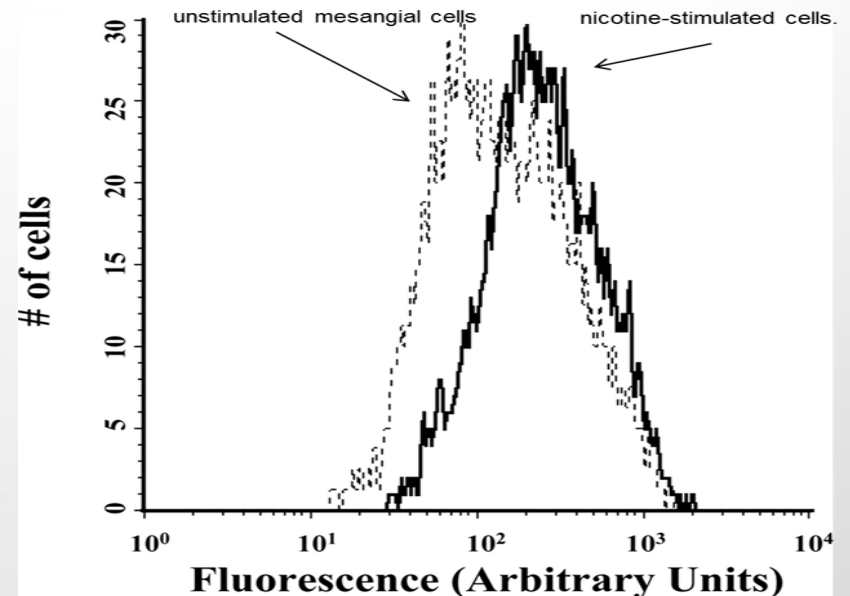
Nicotine-induced mesangial cell proliferation is prevented by the nonspecific nAChR blocker hexamethonium (10^{-4} M) but not by the muscarinic receptor blocker atropine (10^{-7} M).



Nicotine increases fibronectin production in human mesangial cells.



Nicotine increases reactive oxygen species production as assessed by flow cytometric analysis

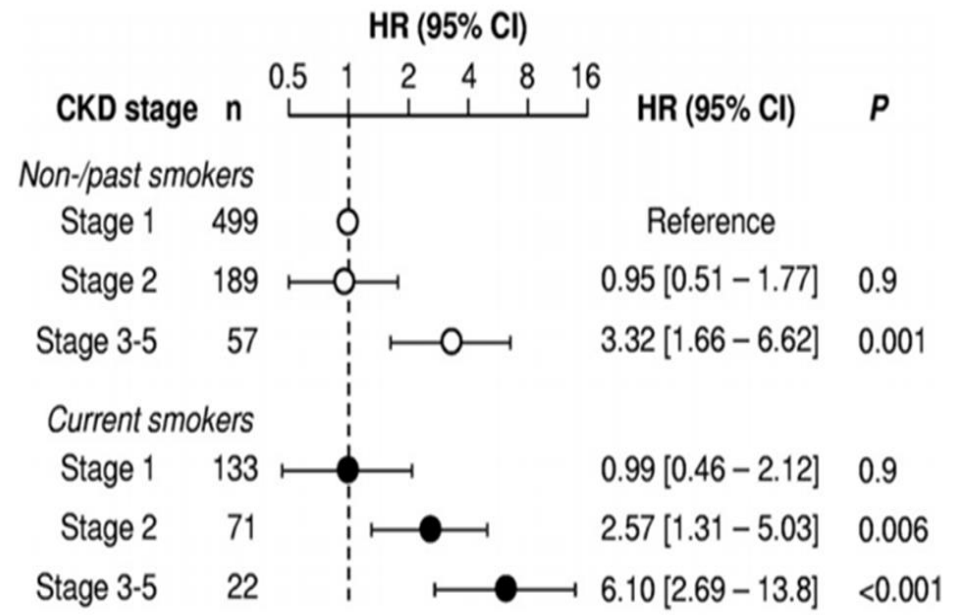
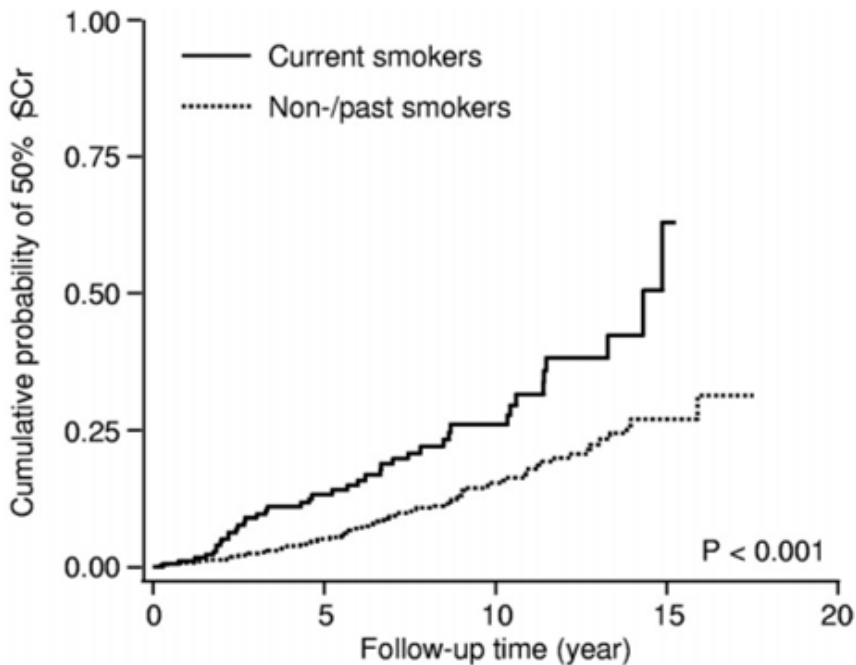


DPI: difenilyodonium (inhibidor de NADPH oxidasa)
Apocinina: inhibidor específico de NADPH oxidasa

Cumulative probability of primary outcome (50% increase in serum creatinine level) for non-/past and current smokers

Estudio :STOP-IgA N
 N: 971; IgA: Biopsia
 Seg. (5,8 años (mediana))

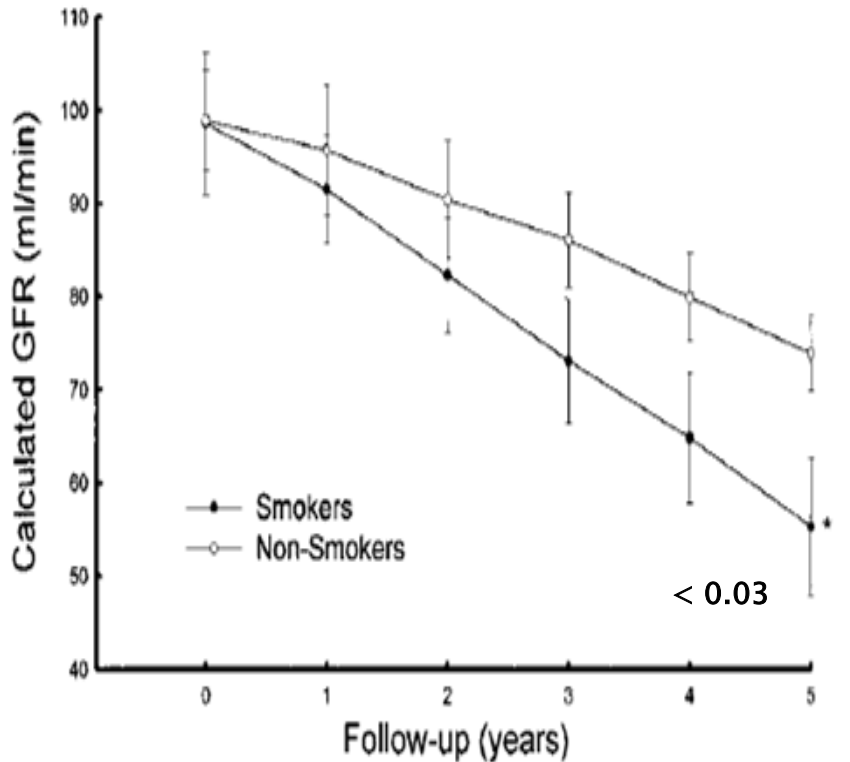
HR de ↑ 50% creatinina según estadio de ERC



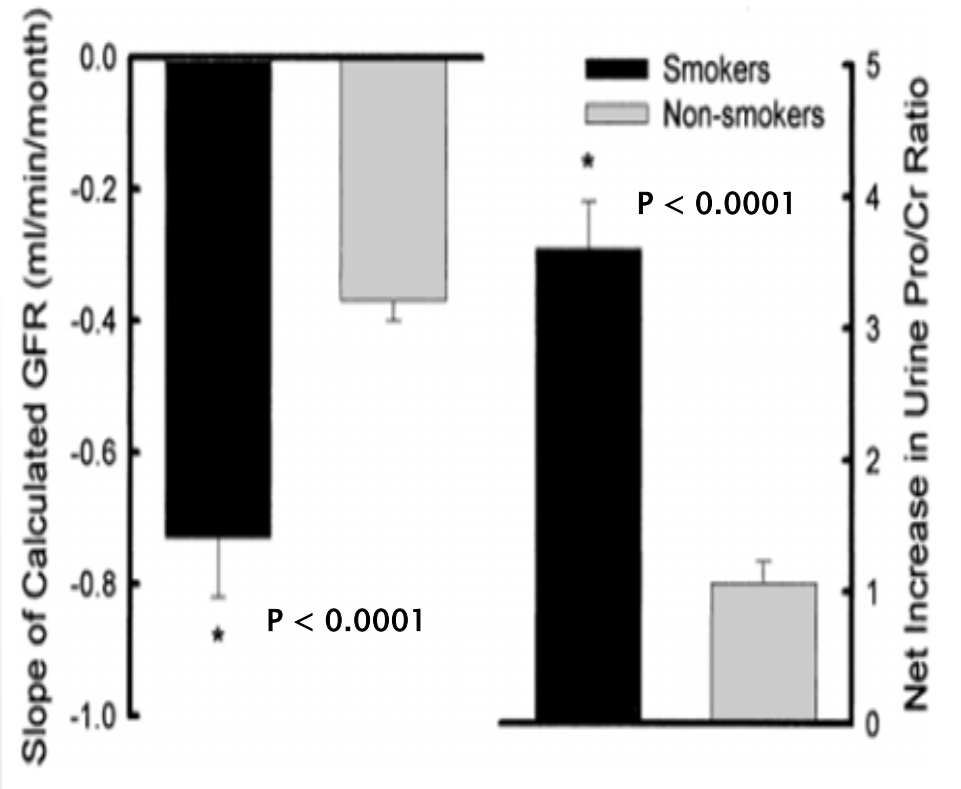
Cigarette Smoking Predicts Faster Progression of Type 2 Established Diabetic Nephropathy Despite ACE Inhibition

N 33
Seg 5 años

Mean calculated glomerular filtration rate (GFR) at each year after study entry during the 5-year follow-up in smokers versus nonsmokers



Mean slope of the calculated glomerular filtration rate (GFR) and net increase in urine protein-to-creatinine (Pro/Cr) ratio during follow-up in smokers and nonsmokers..



Smoking Increases Serum Levels of Transforming Growth Factor- in Diabetic Patients

Patient characteristics and TGF- β levels

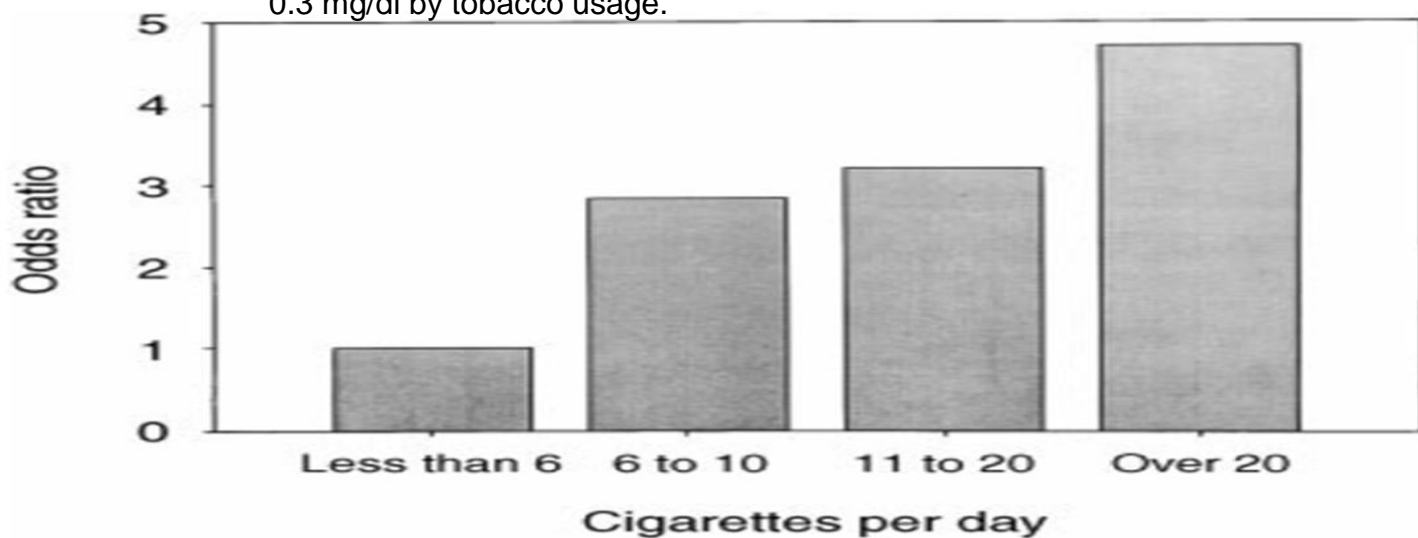
	Diabetic patients		Control subjects	
	Smokers	Nonsmokers	Smokers	Nonsmokers
<i>n</i>	8	8	9	10
Age (years)	34 \pm 4	30 \pm 3	36 \pm 4	36 \pm 7
Sex (% male)	50	40	70	65
Diabetes duration (years)	10 \pm 5	12 \pm 7	—	—
BMI (kg/m ²)	23.1 \pm 1.5	22.3 \pm 1.8	24.1 \pm 1.7	24.2 \pm 1.9
HbA _{1c} (%)	7.0 \pm 1.1	7.1 \pm 0.9	—	—
Urinary cotinine (ng/ml)	1,427 \pm 893	17 \pm 45	1,218 \pm 683	3 \pm 6
Urinary albumin excretion (μ g/min)	5.1 \pm 3.5	4.1 \pm 2.6	—	—
TGF- β (ng/ml)	17.9 \pm 6.2*	8.6 \pm 5.1	3.1 \pm 2.4	3.6 \pm 1.7

Data are means \pm SD. **P* < 0.05 (diabetic smokers vs. other groups) by analysis of variance.

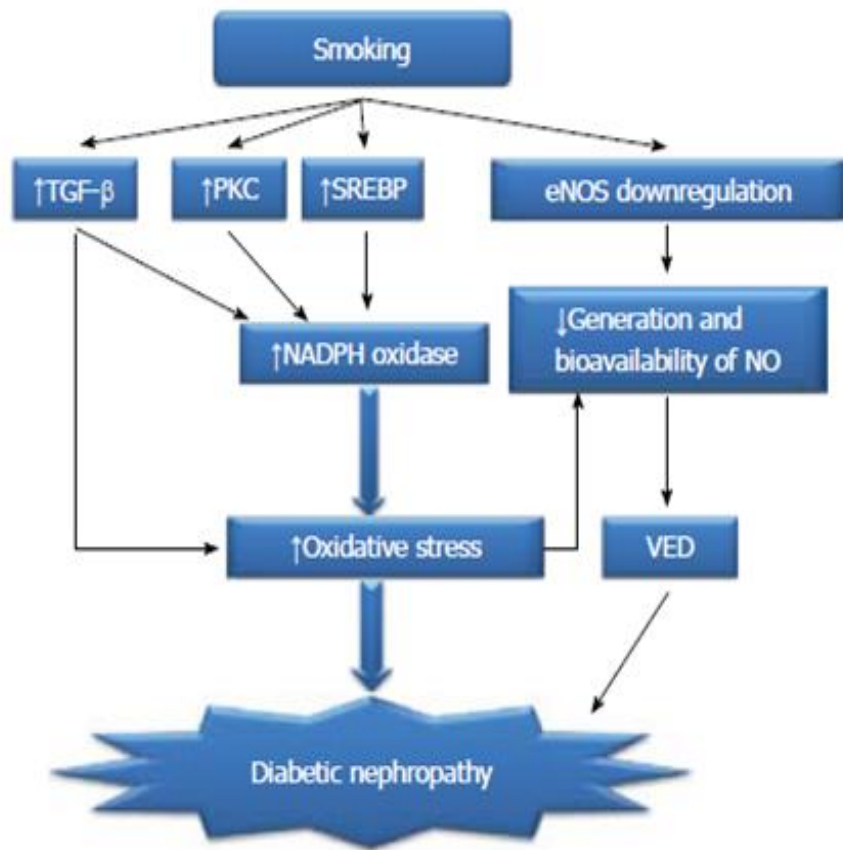
“Best fit” logistic regression model for changes in serum creatinine ≥ 0.3 mg/dL with gender, age, weight, and baseline serum creatinine included in the model

Parameter	Reference group	Risk group	Odds ratio (95% confidence interval)	P value
Gender	Male	Female	0.87 (0.56-1.35)	0.53
Weight		↑ by 10 lb.	1.12 (1.05-1.20)	0.0005
Age		↑ by 5 y	1.66 (1.40-1.97)	0.0001
Baseline serum creatinine		↑ by 1 mg/dL	1.12 (1.06-1.19)	0.0001
Carotid intimal thickness		↑ by 0.1 mm	1.52 (1.01-1.08)	0.011
Systolic blood pressure		↑ of 10 mm Hg	1.16 (1.07-1.26)	0.0003
Number of cigarettes smoked		↑ by 5 cigarettes/day	1.31 (1.12-1.52)	0.0011

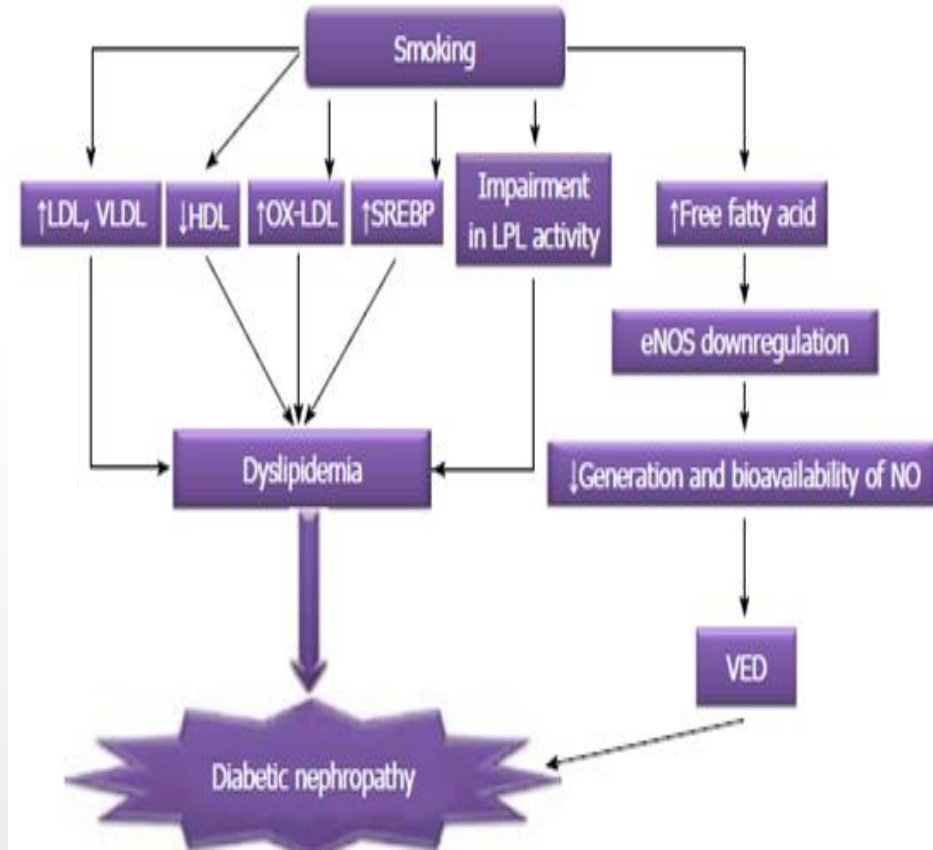
Adjusted odds ratios of a serum creatinine increase of at least 0.3 mg/dl by tobacco usage.



Possible mechanism involved in smoking-induced oxidative stress

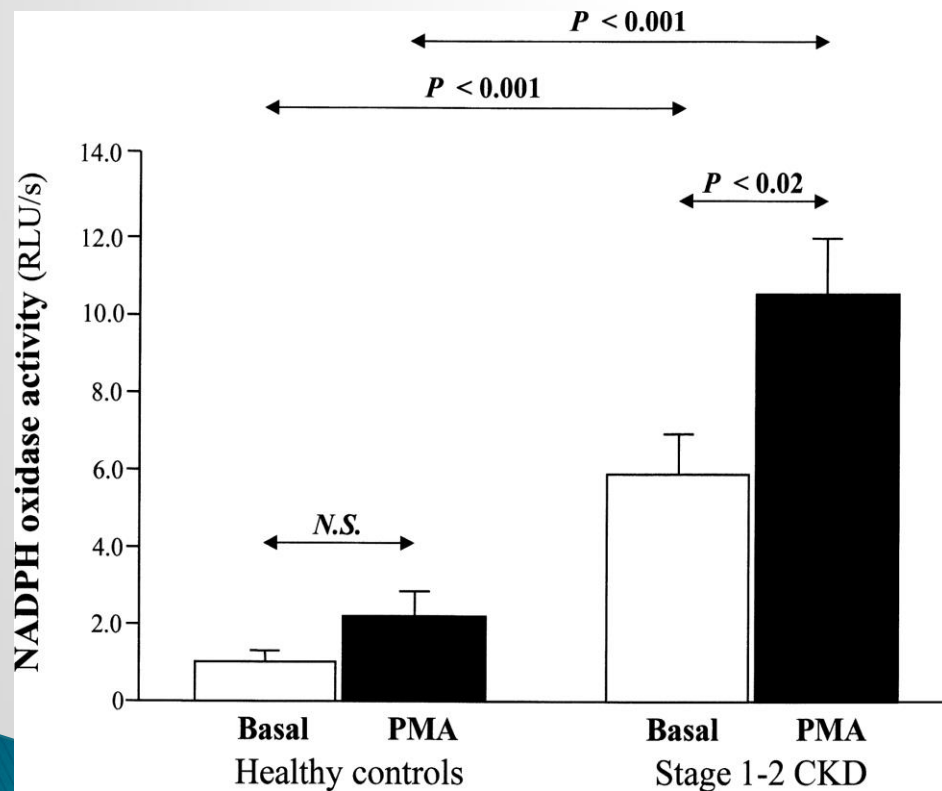


Possible mechanisms involved in smoking-induced dyslipidemia

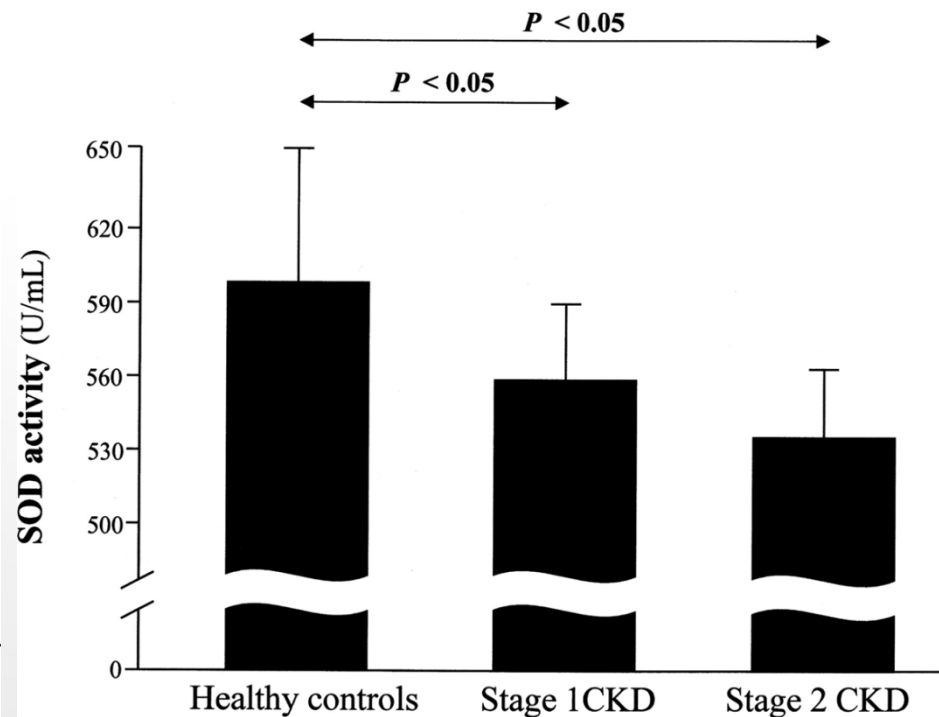


Mayor actividad oxidativa y menor actividad antioxidante en ERC

Phagocytic nicotinamide adenine dinucleotide phosphate (NADPH) oxidase activity in control subjects and patients with stages 1–2 chronic kidney disease (CKD) measured in basal conditions (open bars) and after stimulation with phorbol myristate acetate (PMA) (closed bars).

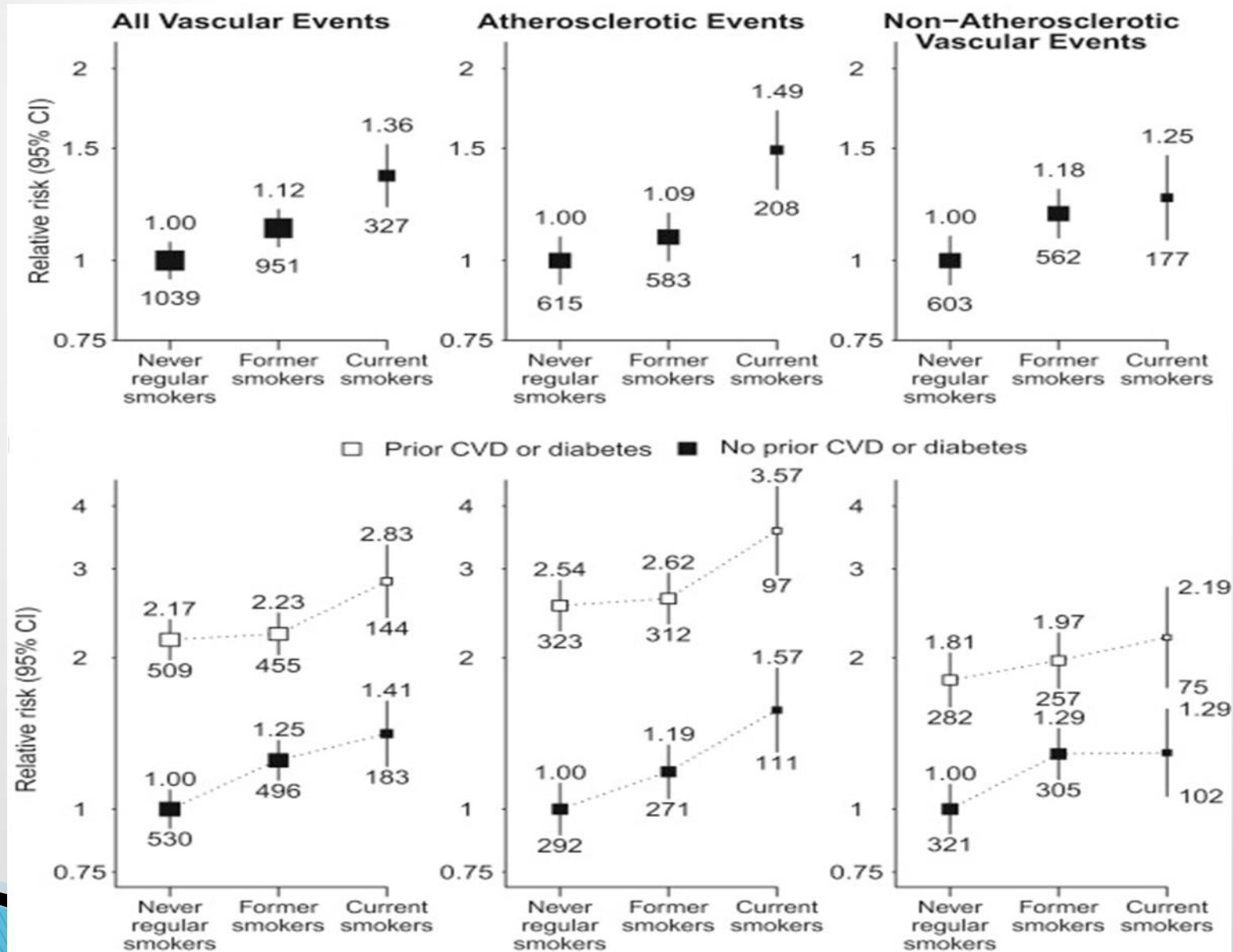


Erythrocyte superoxide dismutase (SOD) activity in control subjects and patients with stages 1 and 2 chronic kidney disease (CKD).

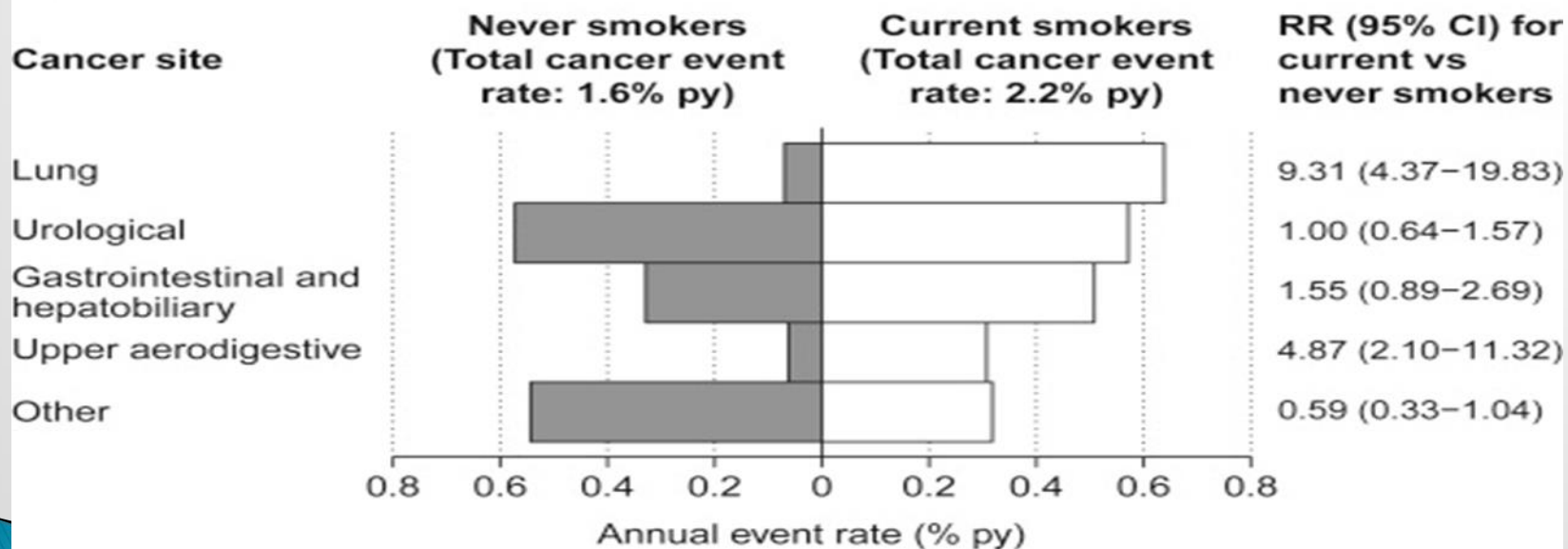
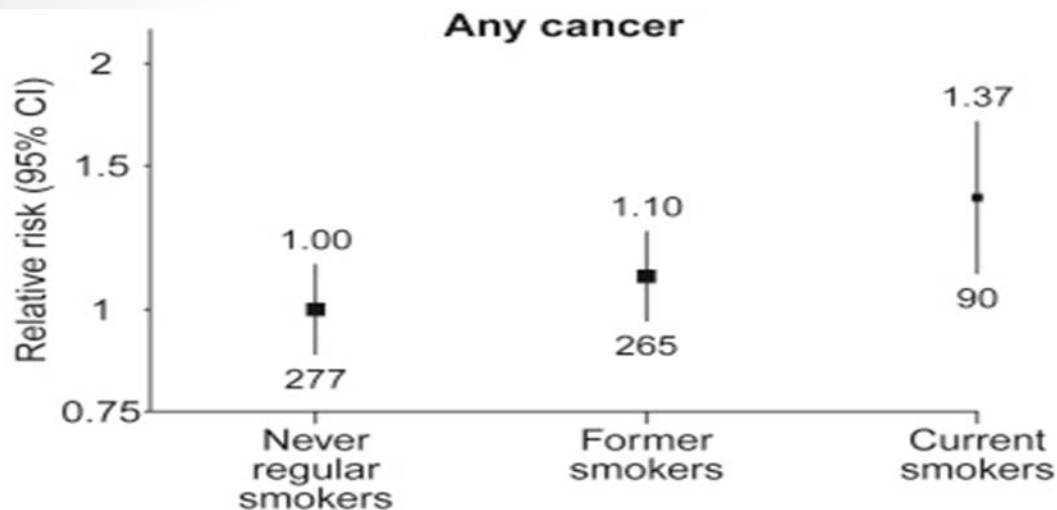


Relevance of baseline smoking status to vascular outcomes

N: 9.270 (51% nunca tabaco)
 Estudio SHARP
 Seg 5 años (mediana)



Relevance of baseline smoking status to cancer incidence and site-specific cancer



Cigarette smoking and second-hand smoking exposure in adolescents with chronic kidney disease

Characteristics of the participating adolescents
N:182

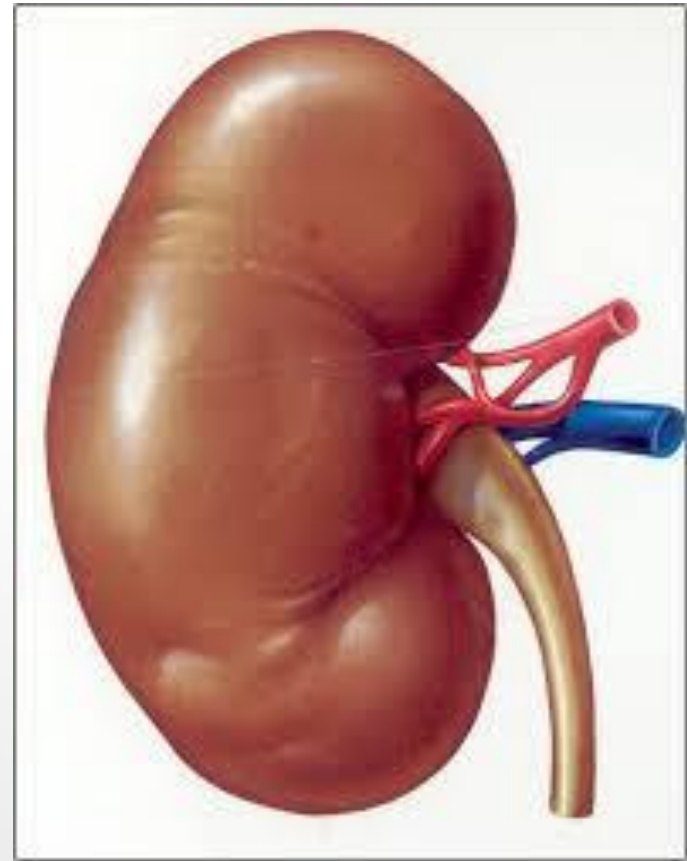
	No. (%)
Gender	
Male	99 (54)
Female	83 (46)
Age (years) (n = 175)	
13–15	82 (47)
16–18	93 (53)
Race (n = 181)	
Black/other	71 (39)
White	110 (61)
Kidney group (n = 178)	
Transplant	60 (34)
Dialysis	25 (14)
Glomerulopathy	93 (52)

Urine cotinine/creatinine ratios for non-smokers grouped by SHS exposure

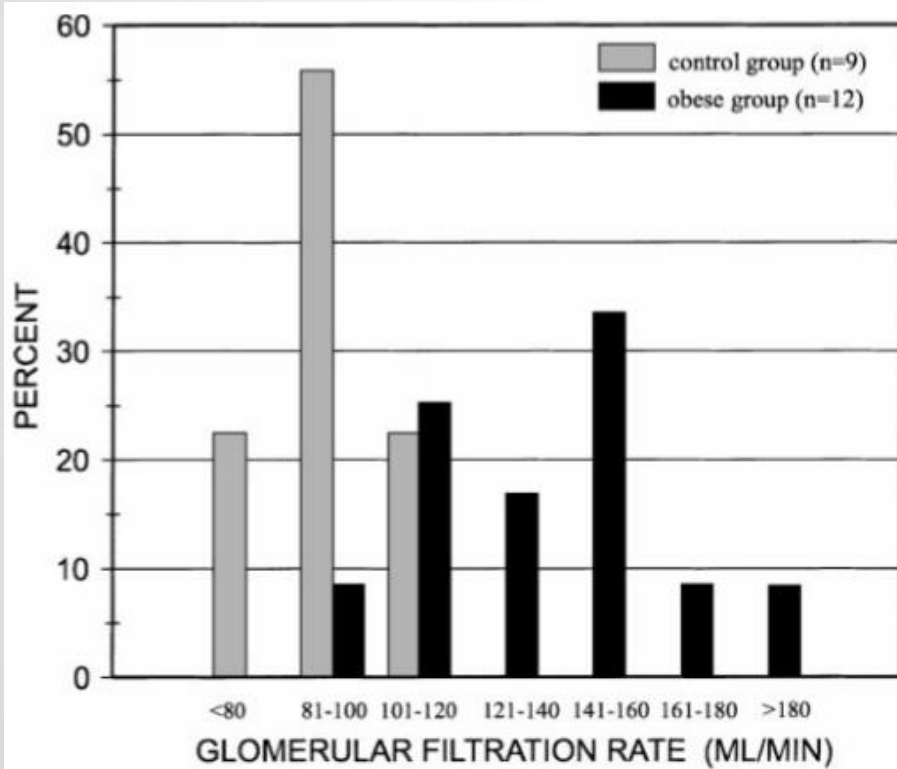
Group	Cotinine/creatinine ratio (ng/mg)
Have friend(s) who smoke = No	0.8 (2.5) (n = 48)
Have friend(s) who smoke = Yes	1.5 (7.2) (n = 49)
P-value	0.007
Live with smoker(s) = No	0.5 (1.1) (n = 54)
Live with smoker(s) = Yes	3.0 (8.4) (n = 43)
P-value	<0.001
Friend(s) = No; Live with = No	0.3 (0.8) (n = 28)
Friend(s) = Yes; Live with = No	0.9 (1.1) (n = 26)
Friend(s) = No; Live with = Yes	1.3 (7.7) (n = 20)
Friend(s) = Yes; Live with = Yes	5.0 (17.7) (n = 22)
P-value	<0.001

The median and IQR (in parentheses) values are reported.

OBESIDAD Y RIÑÓN



Obesidad y hemodinámica glomerular



Filtration dynamics in control and obese subjects

	Control Group	Obese Group	P Value
<i>n</i>	9	12	
GFR, ml/min	90 ± 5	136 ± 8	<0.0005
RPF, ml/min	610 ± 41	801 ± 34	<0.005
FF	0.15 ± 0.01	0.17 ± 0.01	<0.05
MAP, mmHg	86 ± 2	98 ± 3	<0.02
I _{la} , mmHg	26.0 ± .8	26.4 ± 0.7	NS

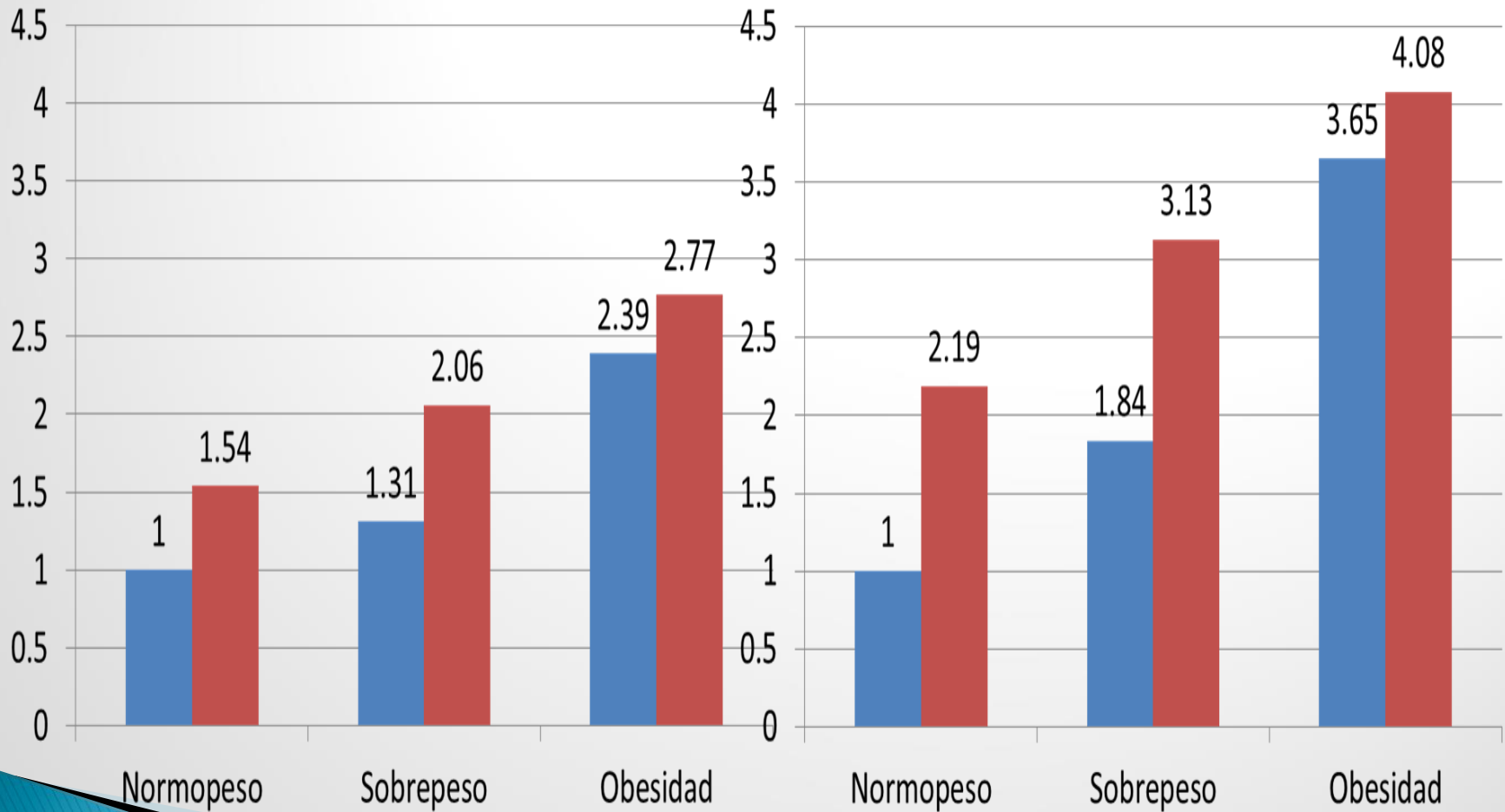
Values are means ± SE. *n*, No. of subjects; GFR, glomerular filtration rate; RPF, renal plasma flow; FF, filtration fraction; MAP, mean arterial pressure; I_{la}, oncotic pressure.

Riesgo de ERC ,peso y SM

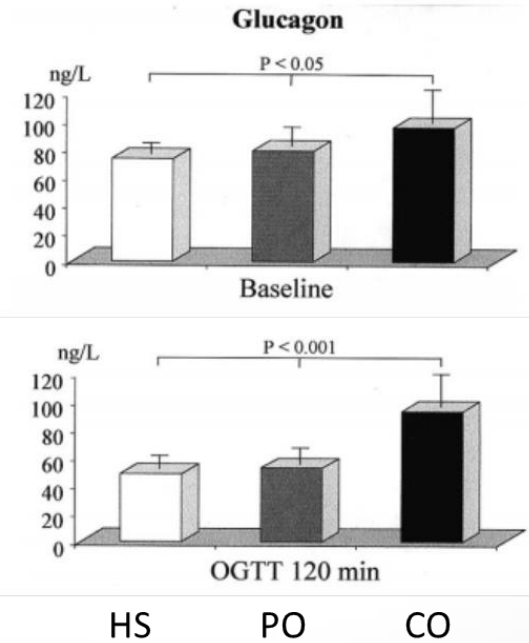
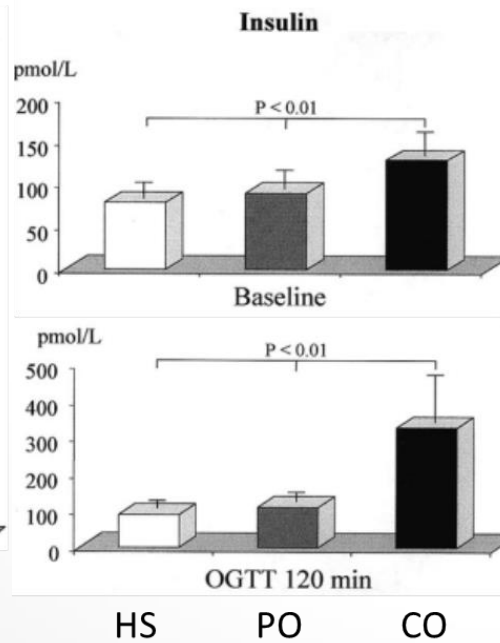
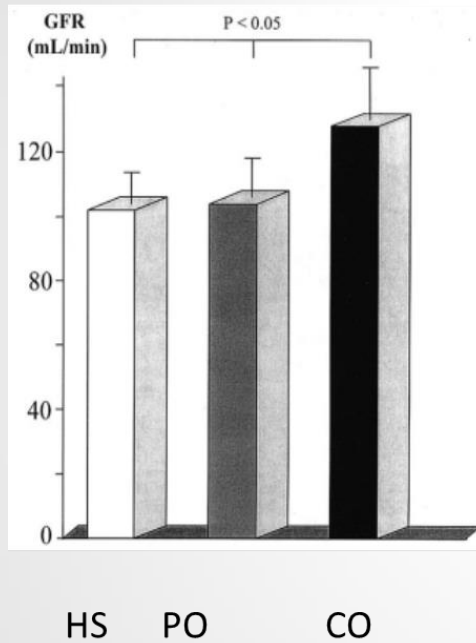
N 6852

ERC: proteinuria y/o FG <60 ml/min

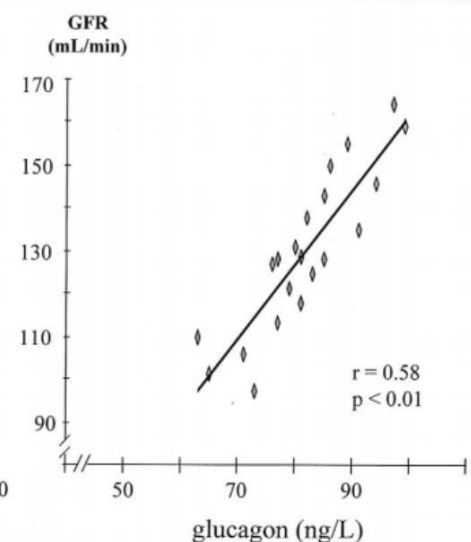
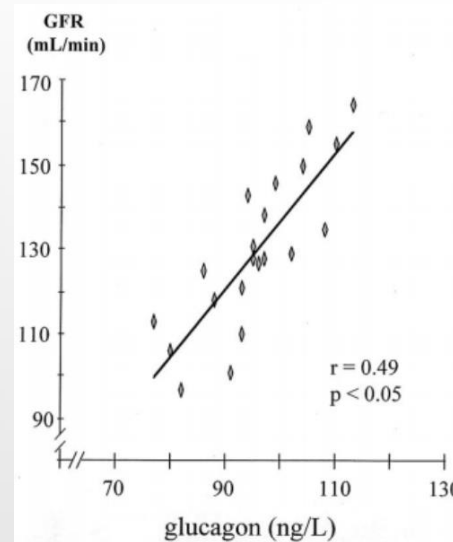
SM -
SM +



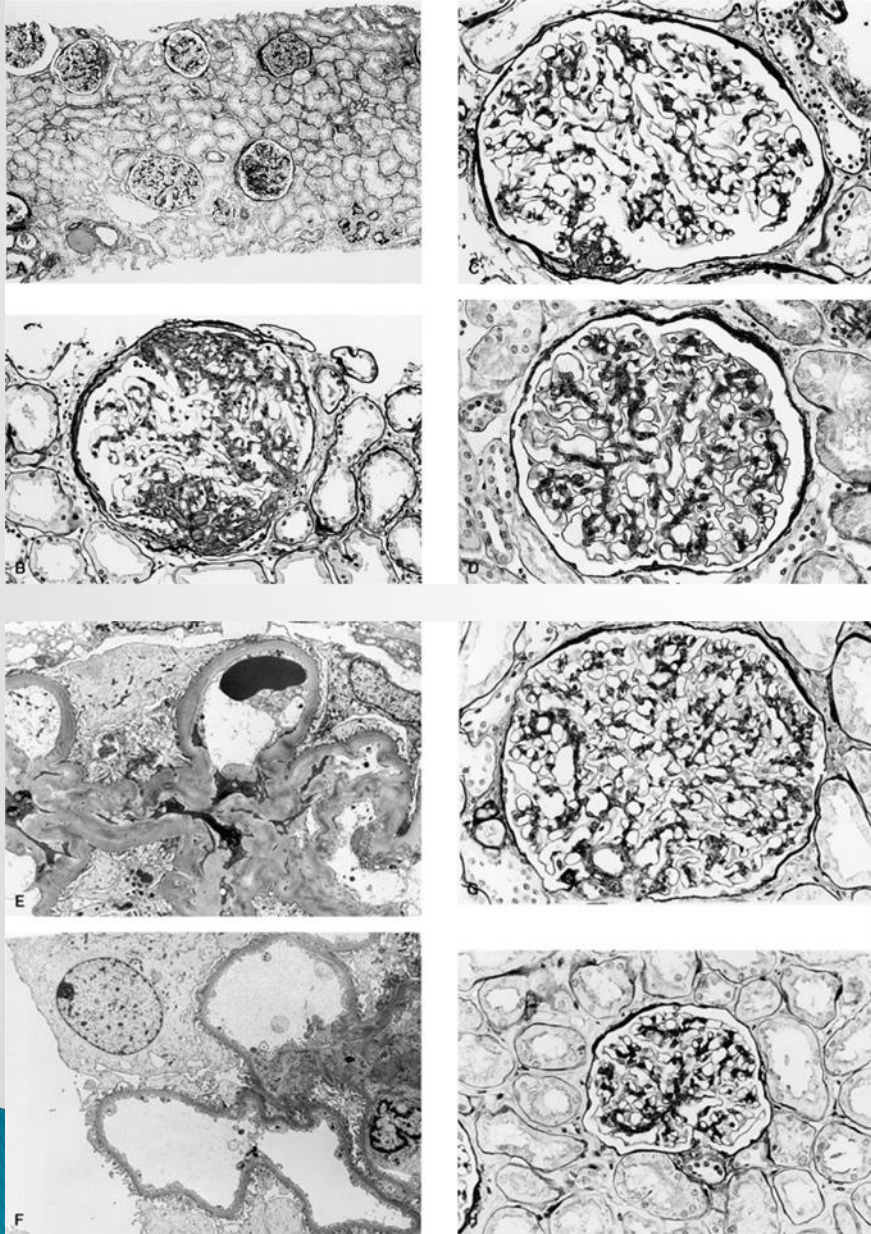
Serum glucagon concentration and hyperinsulinaemia influence renal haemodynamics and urinary protein loss in normotensive patients with central obesity



- healthy subjects(HS)
- peripheral body fat distribution(PO)
- central body fat distribution(CO)

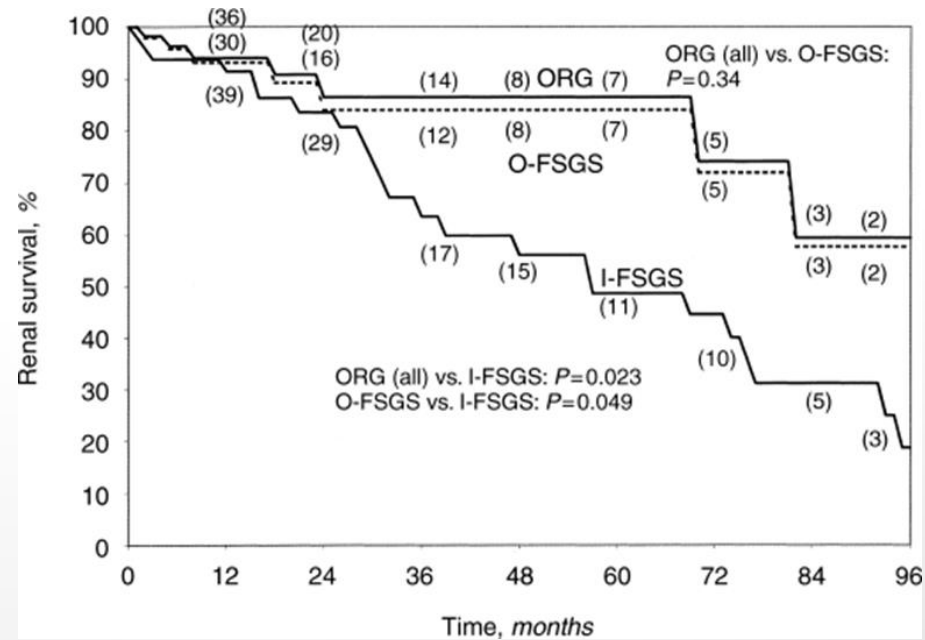


A low power view of ORG shows focal segmental glomerulosclerosis and glomerulomegaly



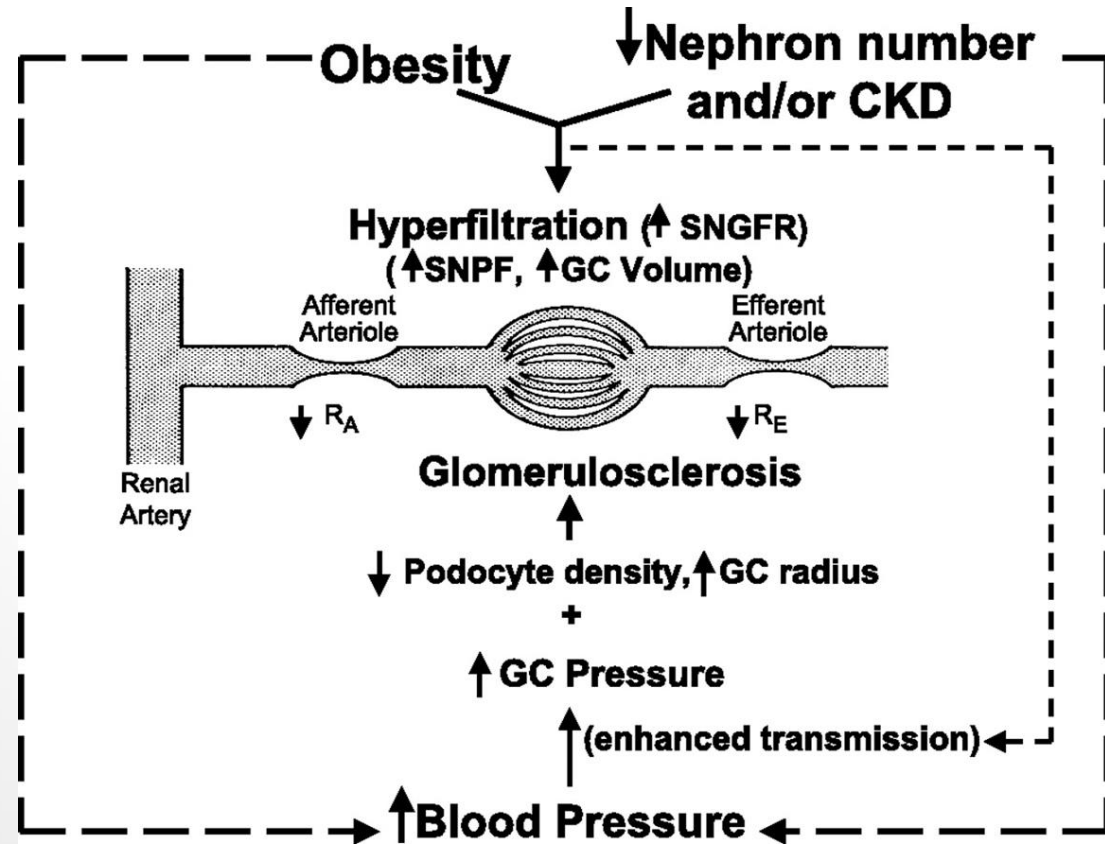
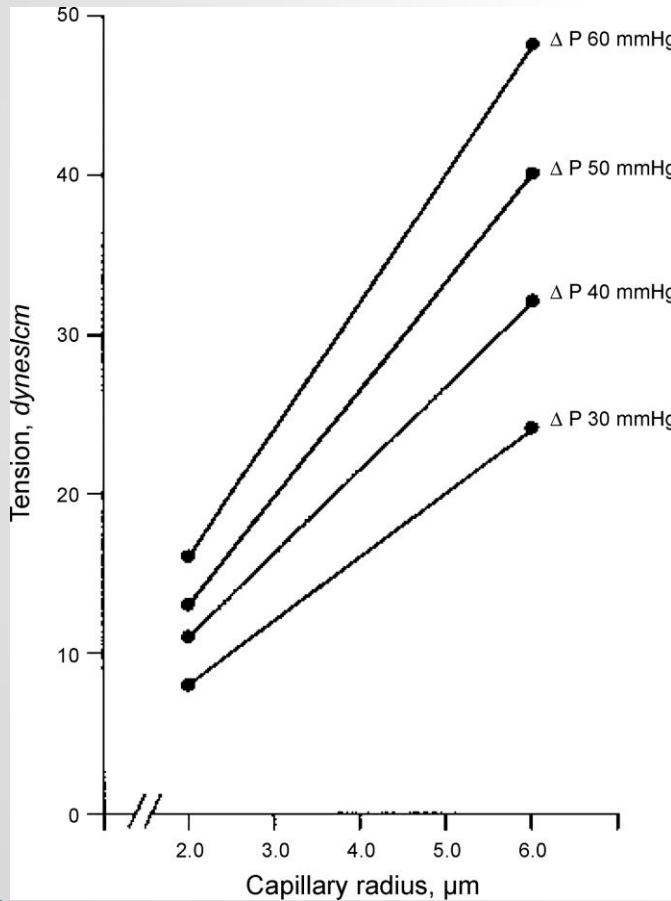
A hypertrophied glomerulus contains two discrete lesions of segmental sclerosis, one in the perihilar region and one in the peripheral tuft, with hyalinosis and adhesion to Bowman's capsule

renal survival (endpoints defined as doubling of serum creatinine or ESRD) over time in ORG, O-FSGS, and control I-FSGS. Analysis by the method of Kaplan and Meier with comparison by the log rank test.

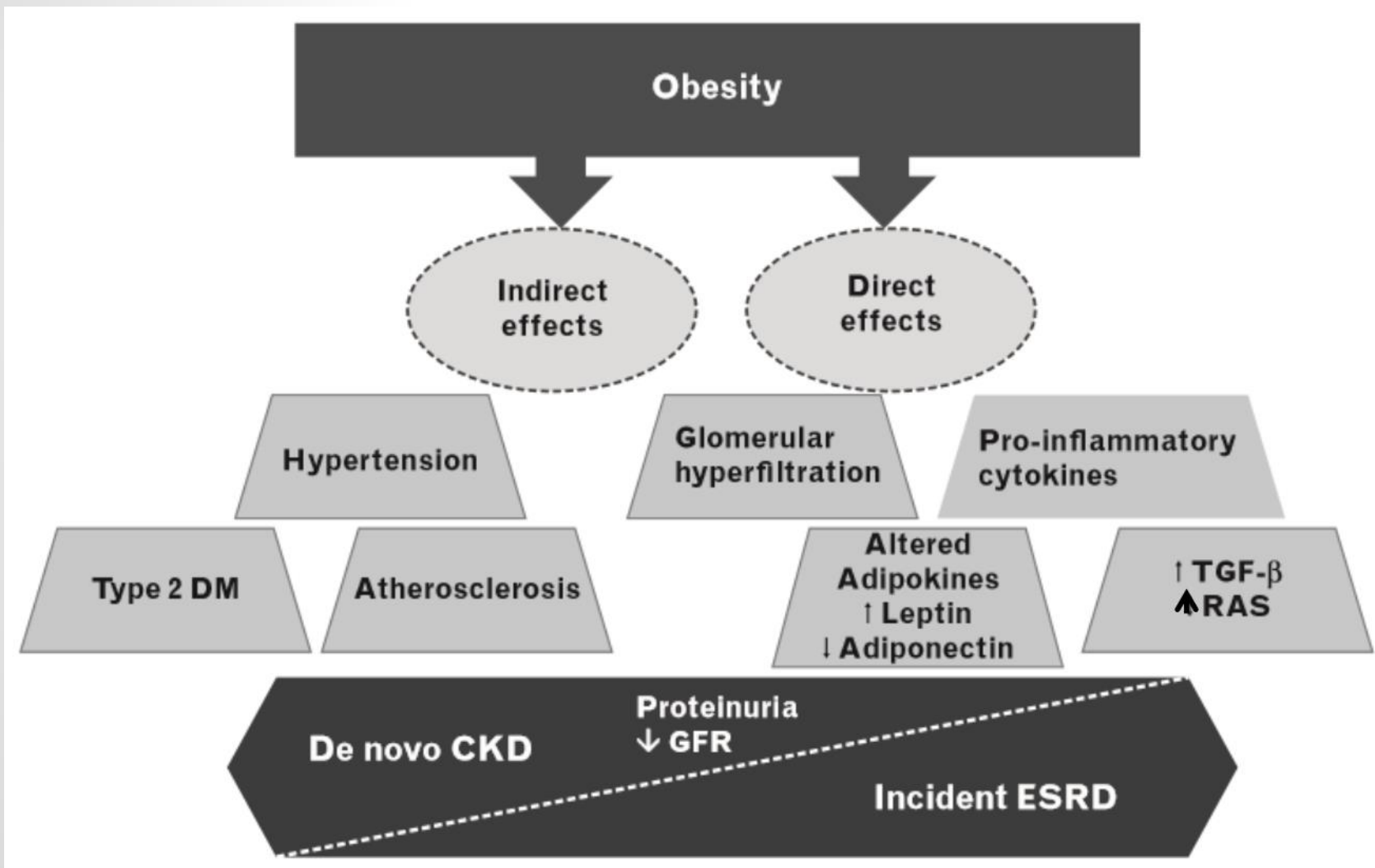


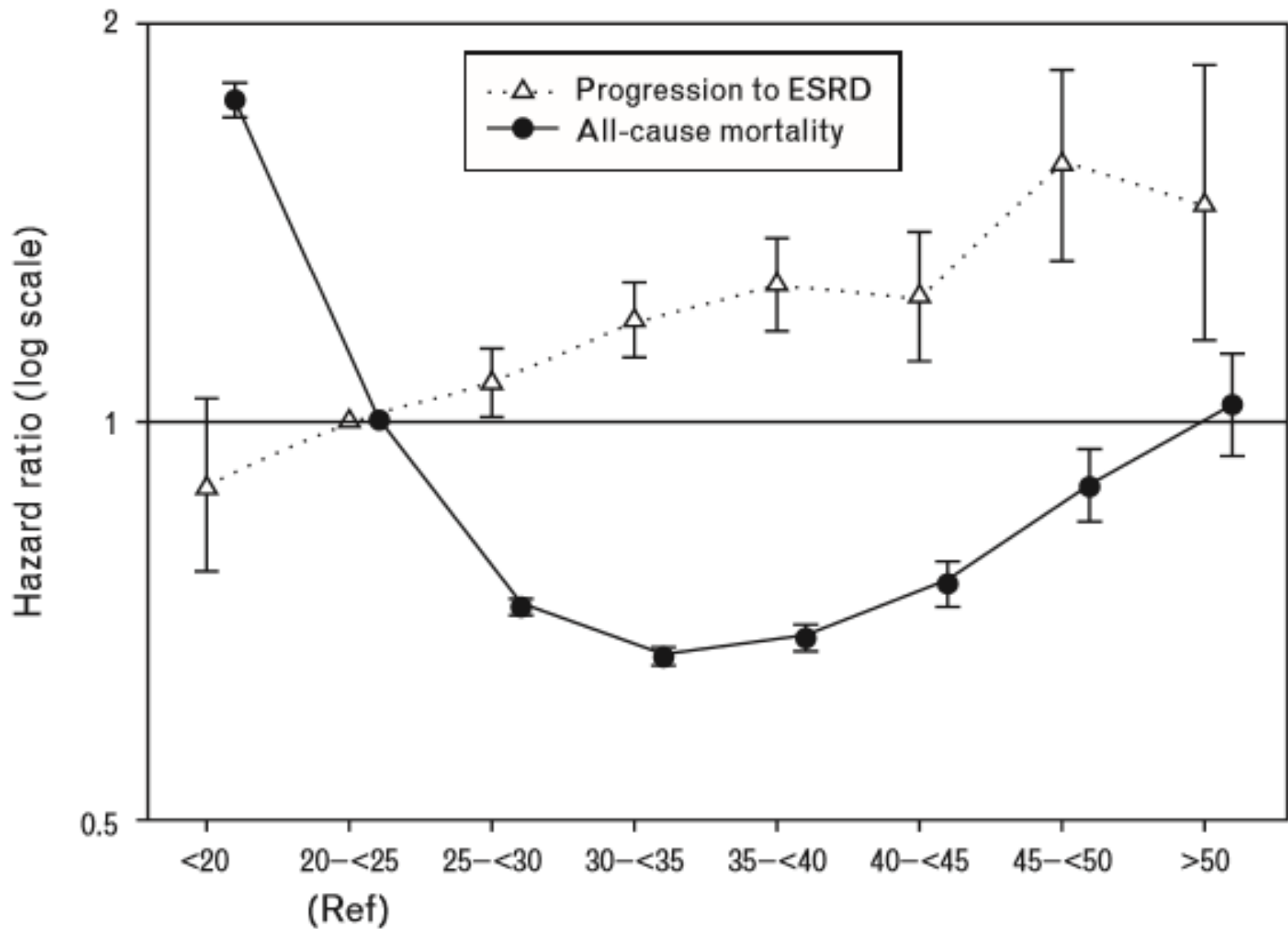
synergistic effects of changes in transcapillary hydrostatic pressure difference (ΔP ; mmHg) and mean glomerular capillary radius (μm) on the calculated capillary wall tension (dynes/cm)

Proposed pathogenesis of glomerulosclerosis in obesity states.

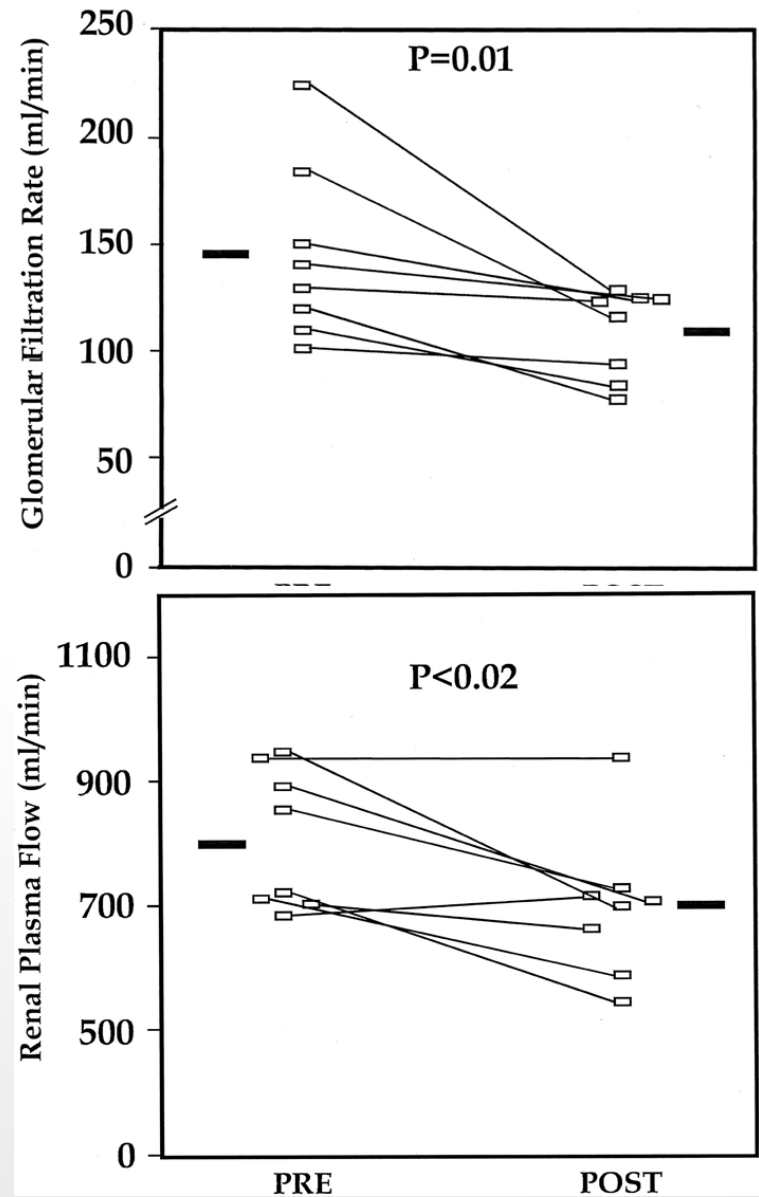
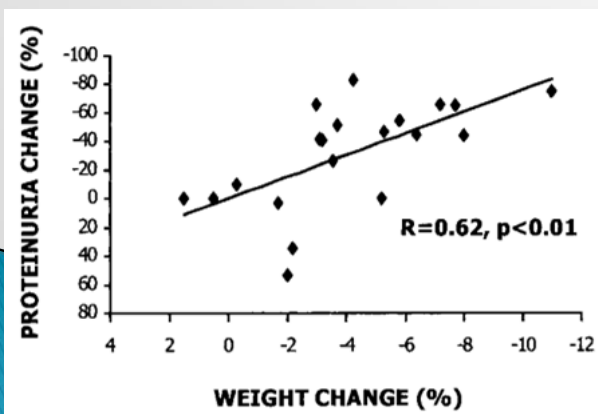
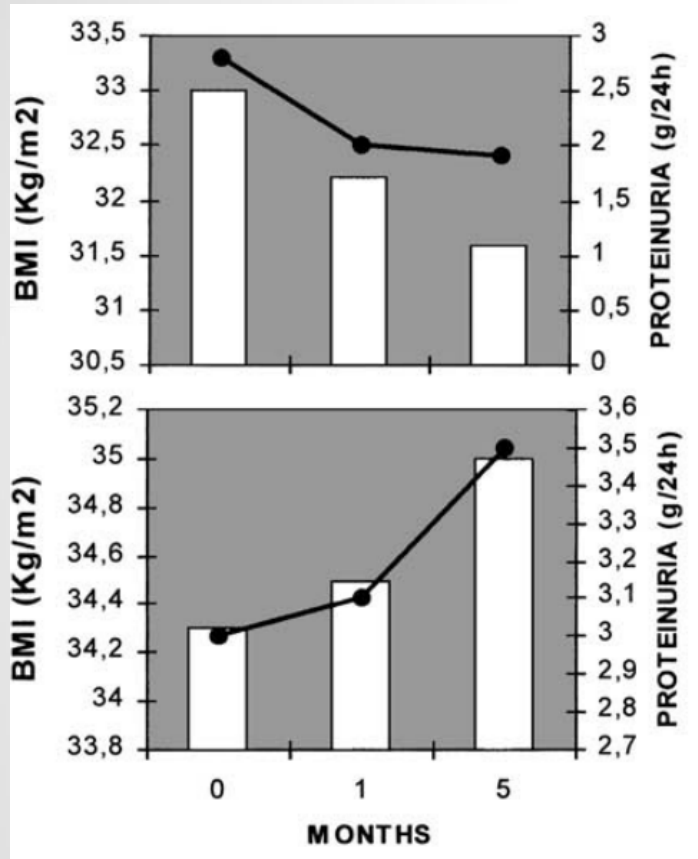


Potential pathways by which obesity leads to the development of chronic kidney disease.



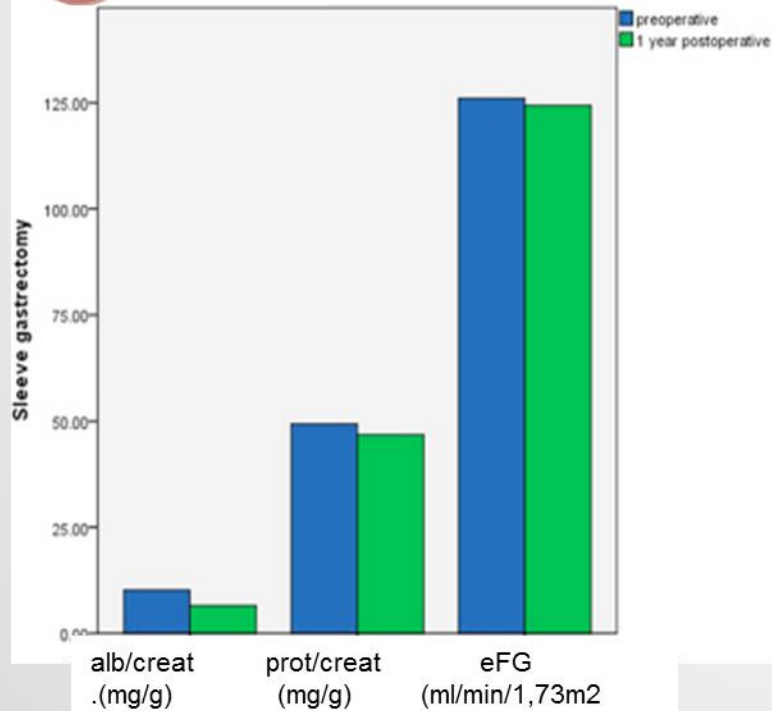
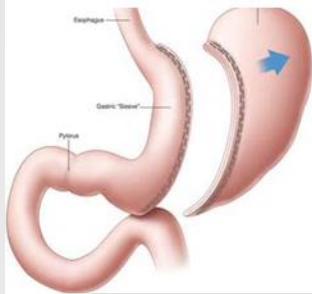


Changes in BMI and proteinuria in the diet group and control group.

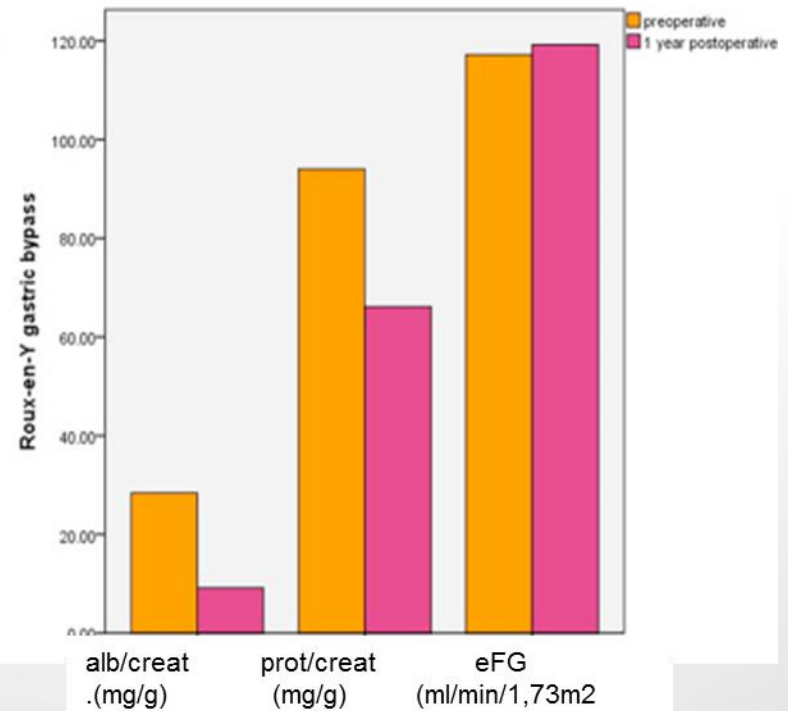
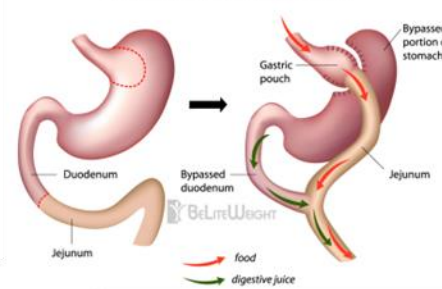


Cirugía bariátrica y función renal

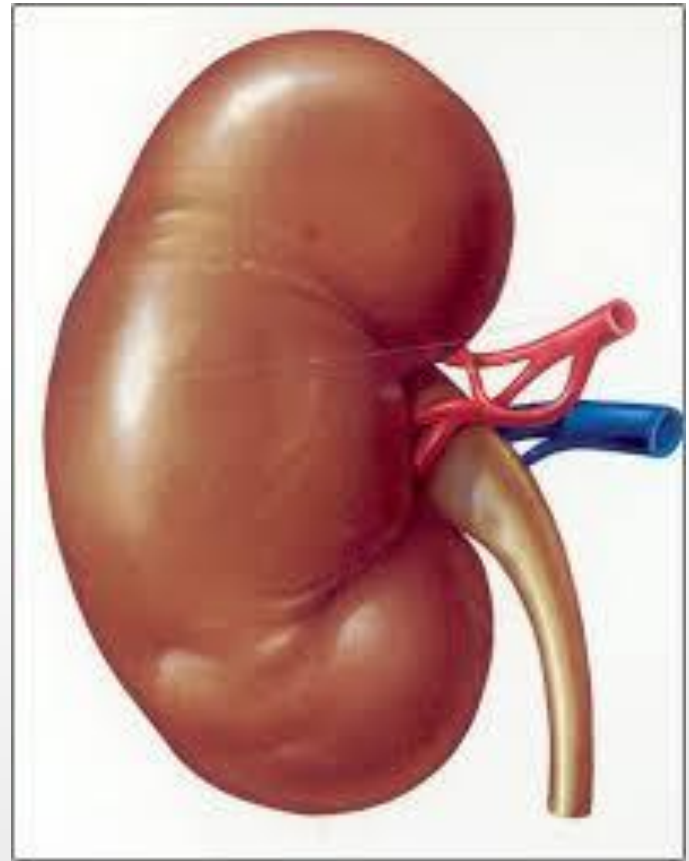
Sleeve gastrectomy



Roux-en-Y Gastric Bypass (RNY)



HTA Y RIÑÓN

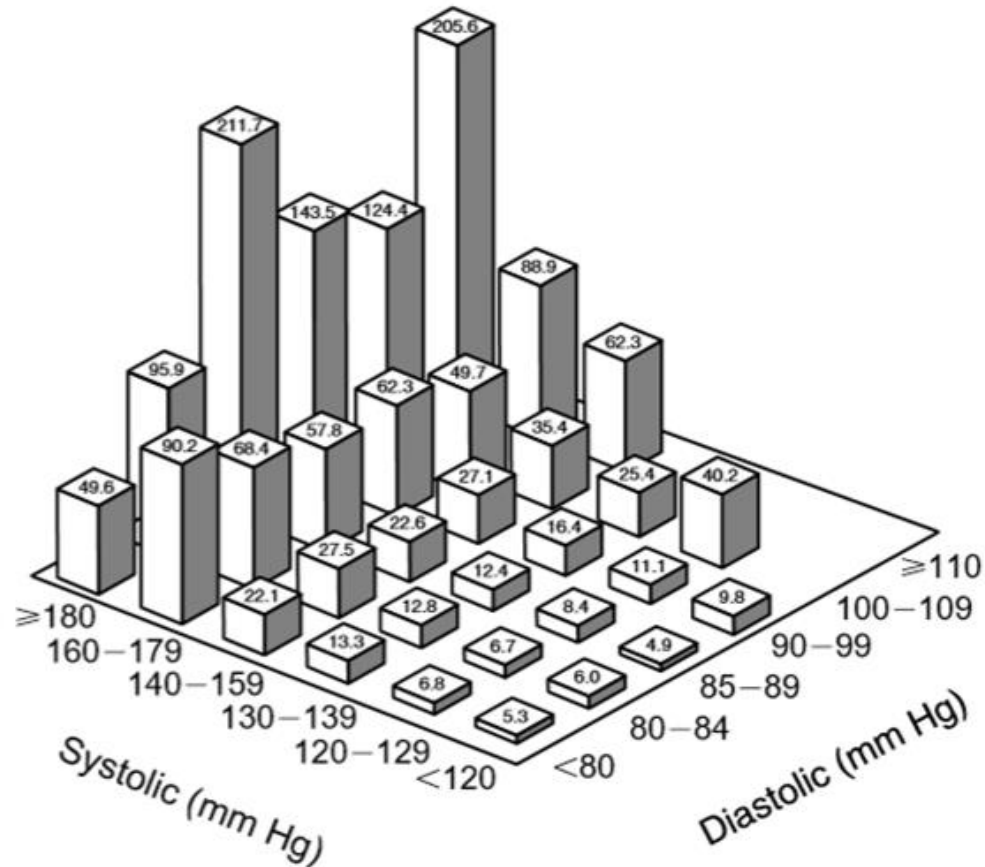


Age-adjusted rate of end-stage renal disease

due to any cause / 100.000 person-years

Multiple Risk Factor Intervention Trial (MRFIT).

N:332,544
Seg 16 años



Fenotipos de HTA en ERC

Prevalencia MUCH (n:333,propectivo)

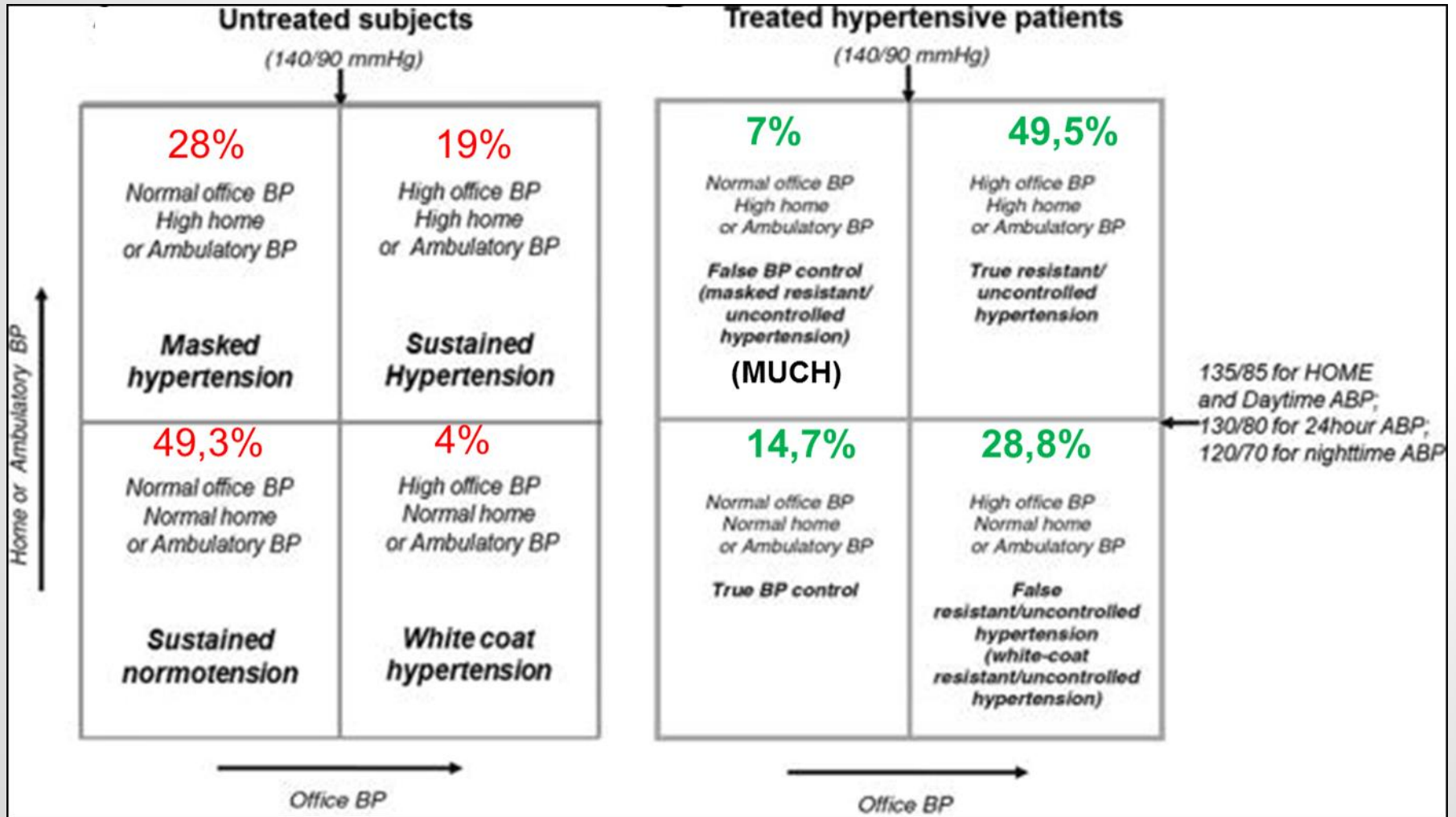
(Agarwal et al JASN 2016)

-MAPA dia.....26,7%.

-MAPA 24 h.....32,8%

-MAPA día ó noche.....56,1%

-AMPA.....50,85



Definición de HTA en ERC en base a MAPA ó AMPA

-Parati et al Hypertension. 2016.

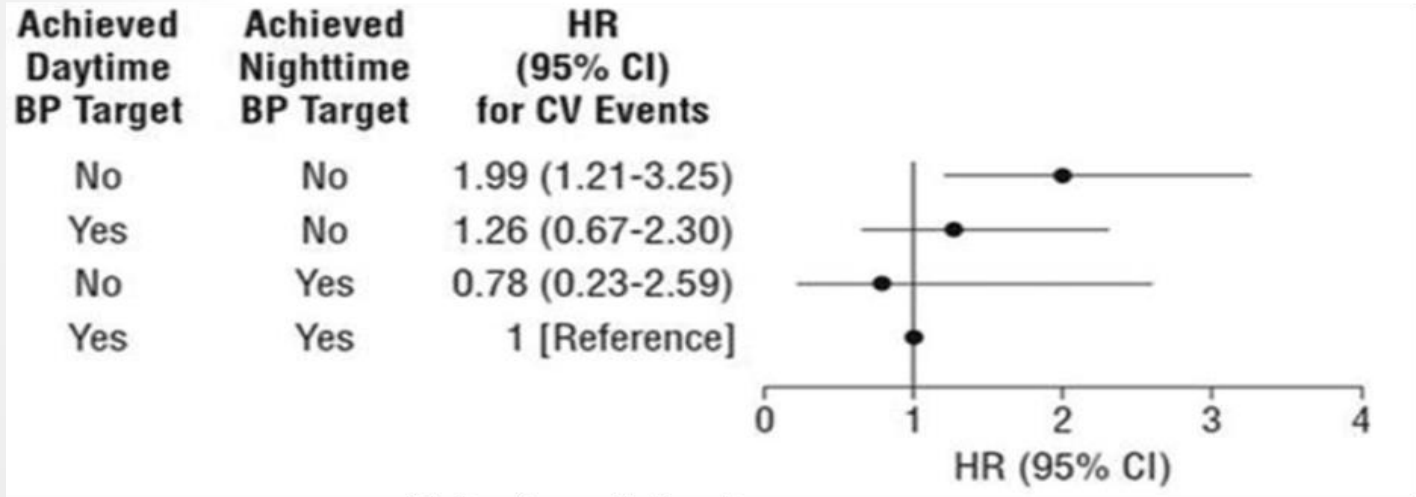
-Drawz et al (CRIC,n:1492)CJASN 2016

-Gorostidi n:5.693)Am J Kidney Dise.2013

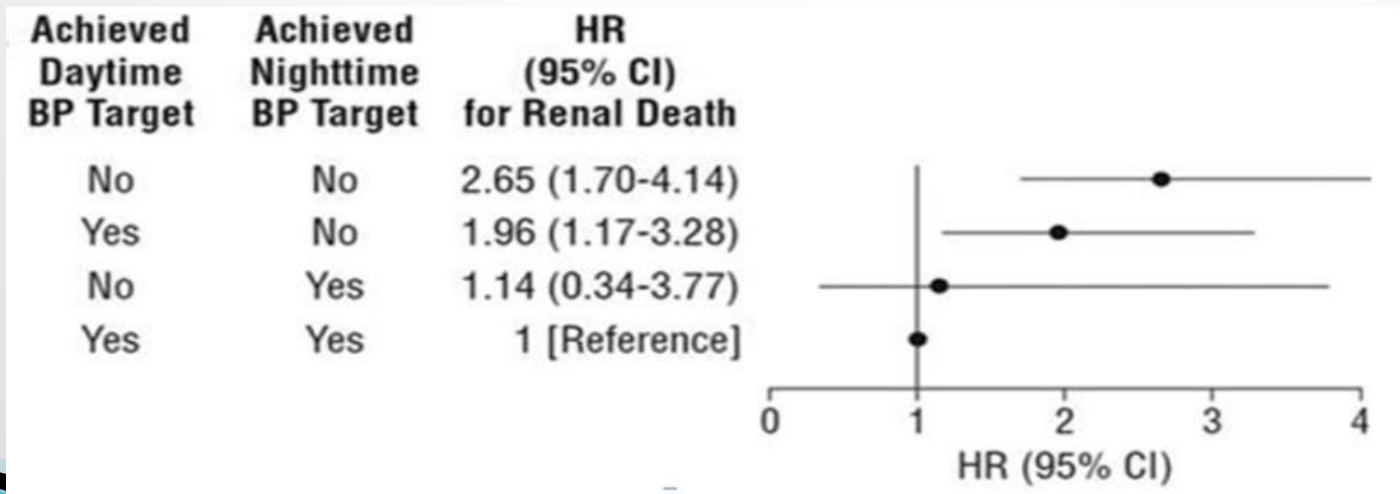
Superior prognostic power of ABP over office BP

N:436
Seg 4,2 y

Risk of fatal and nonfatal cardiovascular (CV) events

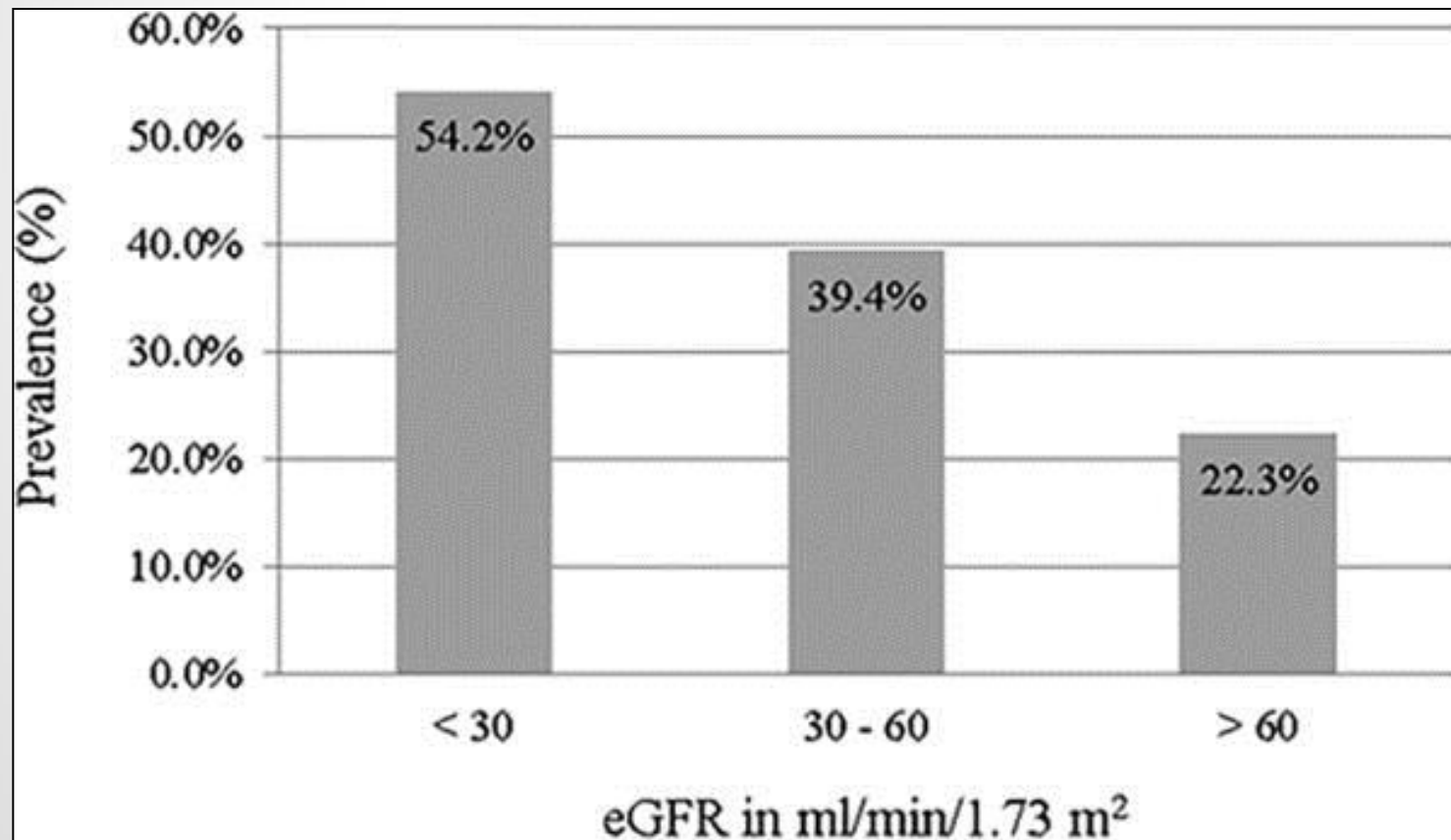


Risk of renal death



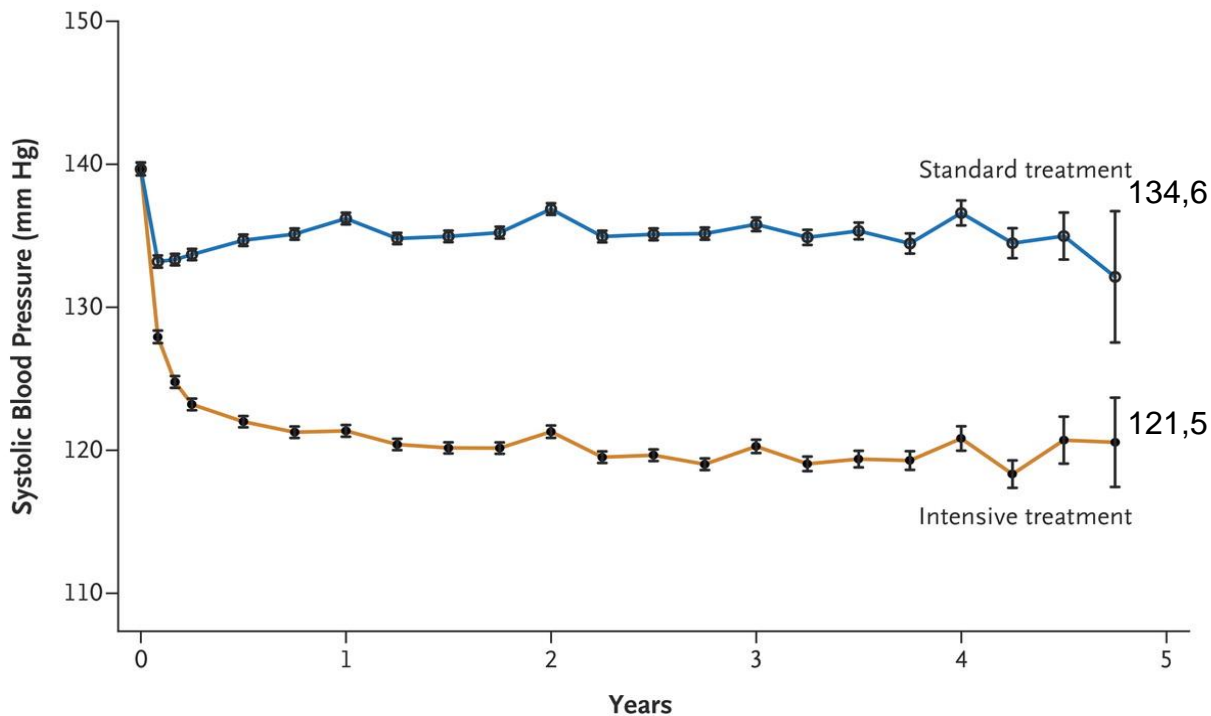
Prevalence of apparent treatment resistant hypertension by estimated glomerular filtration rate (eGFR) status.

3367 hypertensive participants in the Chronic Renal Insufficiency Cohort (CRIC)



Guía	General	Ancianos	DM	ERC proteinuria	
				No	Sí
ISHB (2010)	Bajo riesgo <140/90 Riesgo elevado: <130/80				
NICE (2011)(2014)	<140/90	>80 años <150/90	<140/80	ERC<140/90 ERC+DM <130/80	<130/80
KDIGO(2012)				<140/90	<130/80
CHEP(2013)	<140/90	<80 años :<140/90 ≥80 años :<150/90	<130/80	<140/90	
ESH/ESC (2013)	<140/90	<80 años:150-140/90 - No frágil: Considerar <140 - Frágil: Según tolerancia ≥80 años :150-140 si buenas condiciones físicas y mentales	<140/85	<140/90	<130
ASH/ISH(2014)	<140/90	≥80 años: <150/90	<140/90	<140/90	<130/80
ACC/AHA/ASH (2015) HTA + Enf.Coronaria	<140/90 (prevención 2ª) <130/80 puede ser adecuado en algunos casos (postIM, ICTUS, AIT, enf carót. ,arteriop ,AAA) En HTA diastólica ↓paulatina de PA y evitar <60 mmHg	≥80 años :<150/90	<140/90 <130/80 en algunos casos	No recomendaciones	
JNC8 (2014)	<140/90	≥ 60 años (sin ERC,DM, ECV): <150/90	<140/90	<140/90 Sujetos ≥70 años: individualizar según fragilidad, proteinuria ,comorbilidad.	
ADA (2015)		≥65 años :<140/90 Ancianos frágiles: <150/90	<140/90 <130/80 (jóvenes)	<140/90	

Systolic Blood Pressure in the Two Treatment Groups over the Course of the Trial.



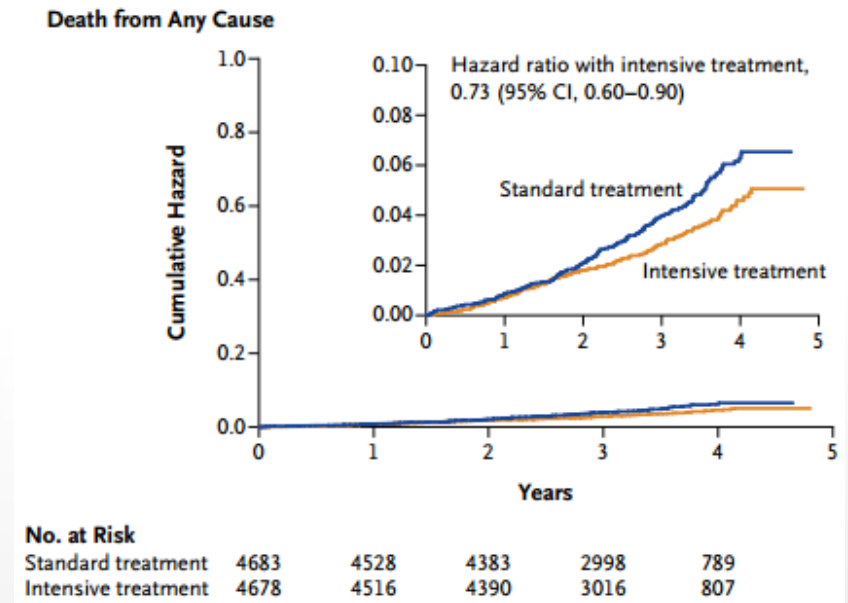
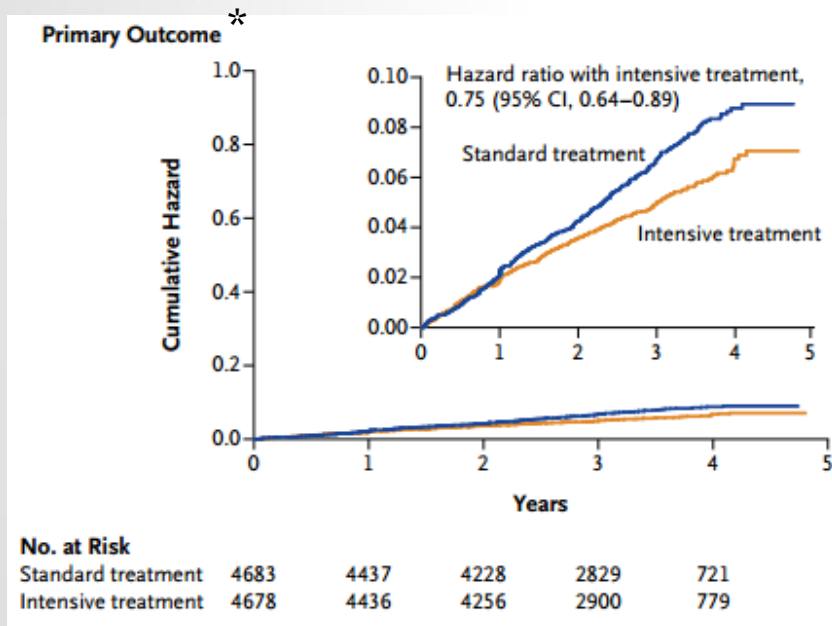
No. with Data

Standard treatment	4683	4345	4222	4092	3997	3904	3115	1974	1000	274
Intensive treatment	4678	4375	4231	4091	4029	3920	3204	2035	1048	286

Mean No. of Medications

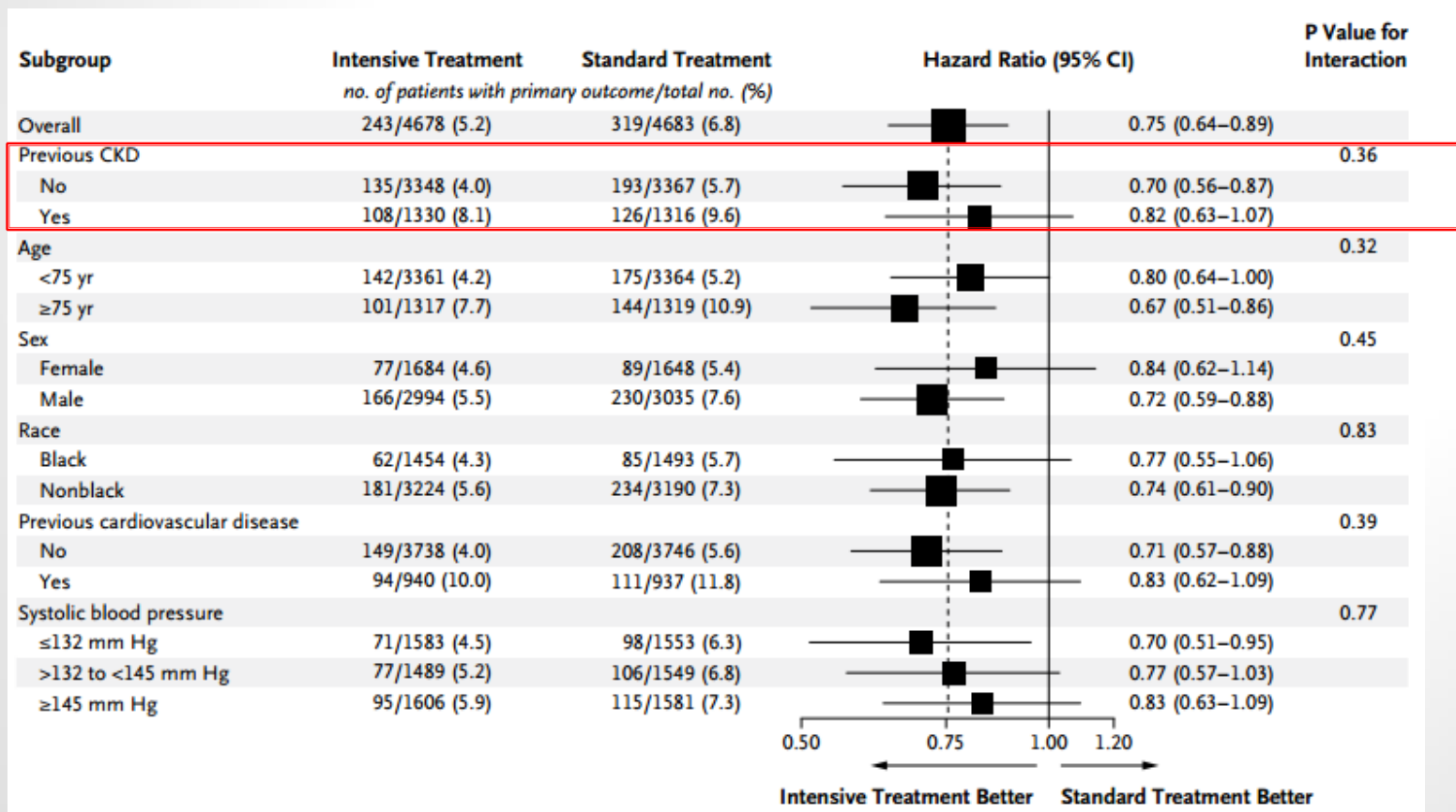
Standard treatment	1.9	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.9
Intensive treatment	2.3	2.7	2.8	2.8	2.8	2.8	2.8	2.8	2.8	3.0

Primary Outcome and Death from Any Cause.



* myocardial infarction, acute coronary syndrome, stroke, heart failure, or death from cardiovascular causes.

Forest Plot of Primary Outcome According to Subgroups



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