
¡ AGUAS LOS RECUERDA !

Por una Medicina Integrada de Calidad y a la Vanguardia

Primer Foro Nacional
Medicina Integrada

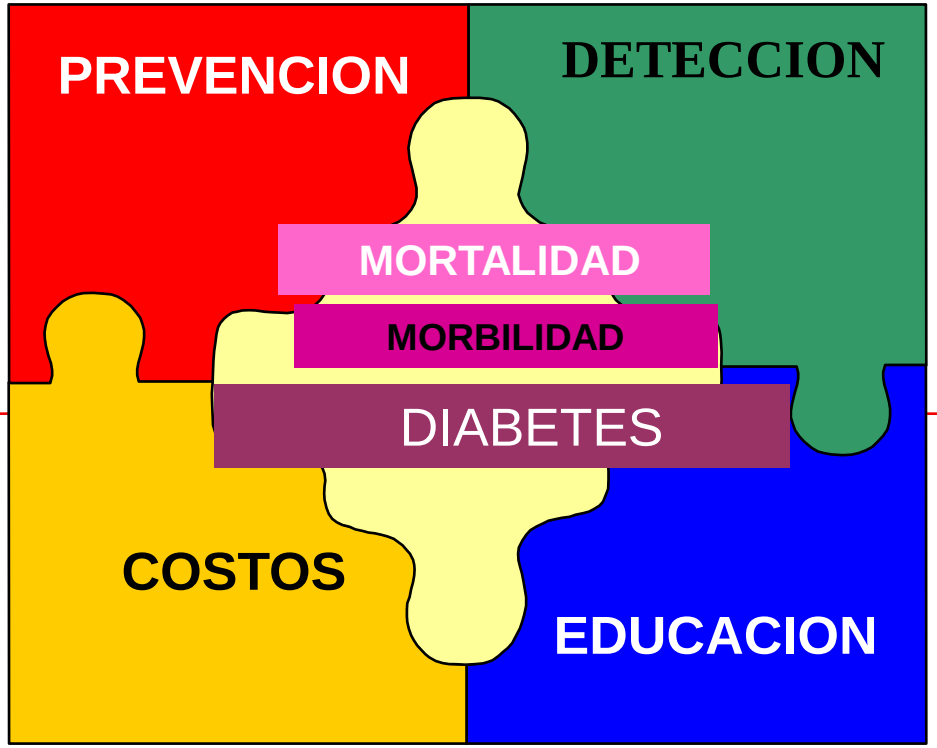
¿ Porquè, para què, y còmo ?

La Diabetes Mellitus desde un punto de vista cardiovascular

La Diabetes Mellitus desde un punto de vista integrado

Diabetes mellitus: su impacto en la salud

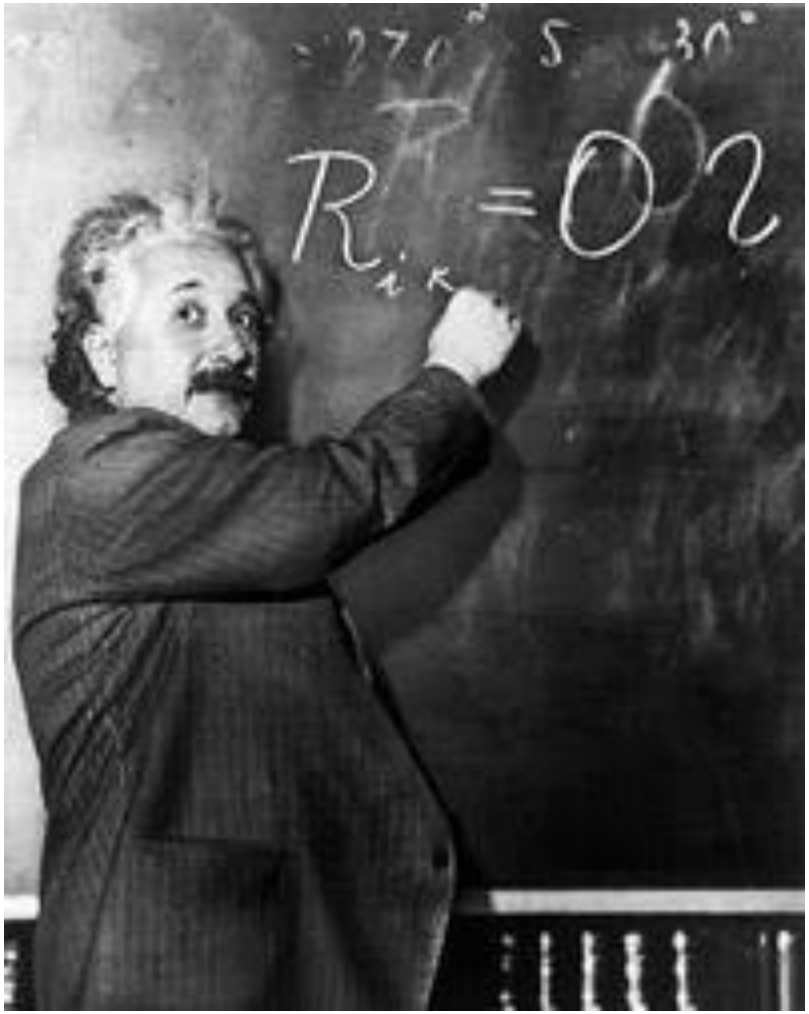
¿Estamos haciendo lo suficiente?



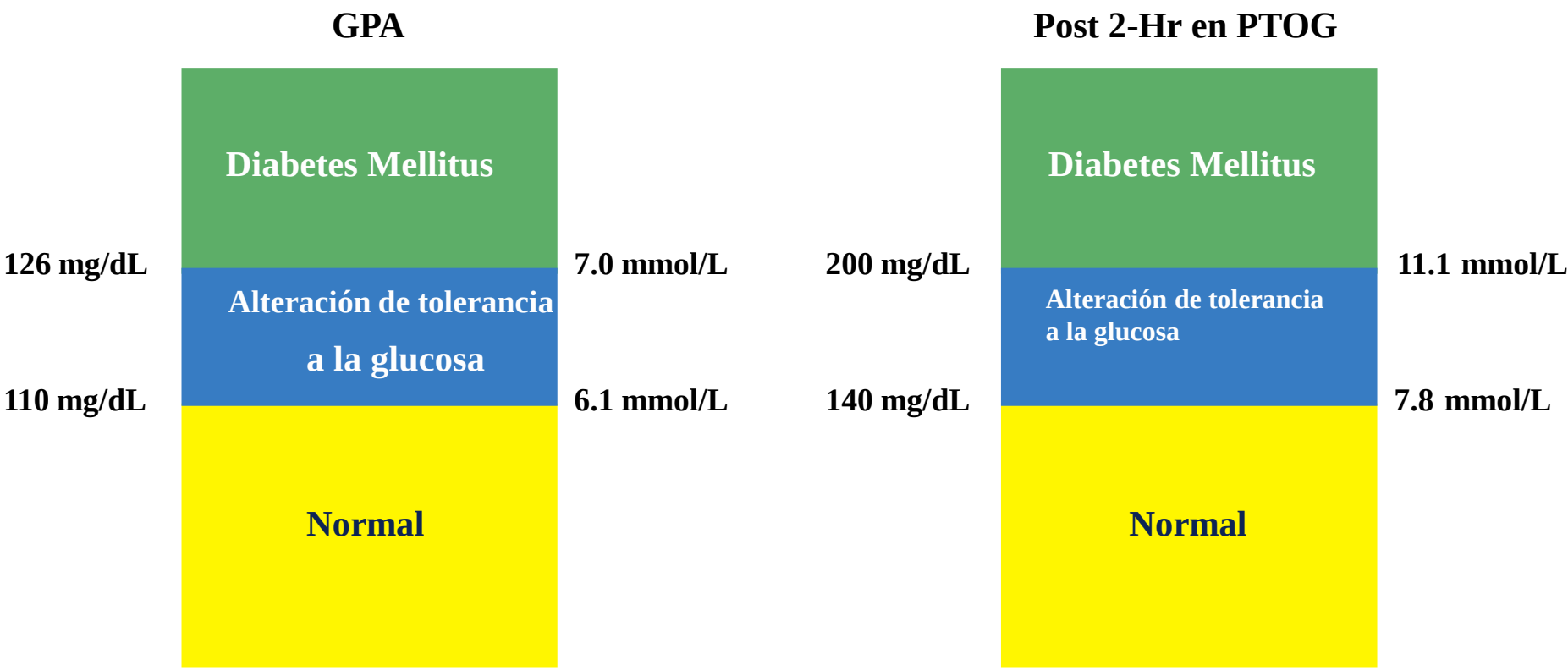
Dr. Carlos A. Domínguez Reyes
Clínica de Diabetes y Metabolismo

Centenario Hospital Miguel Hidalgo, ISEA. Aguascalientes

Planteamiento del problema



Tolerancia a la Glucosa-Categorías



Adapted from The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care.* 1997;20:1183-1197.

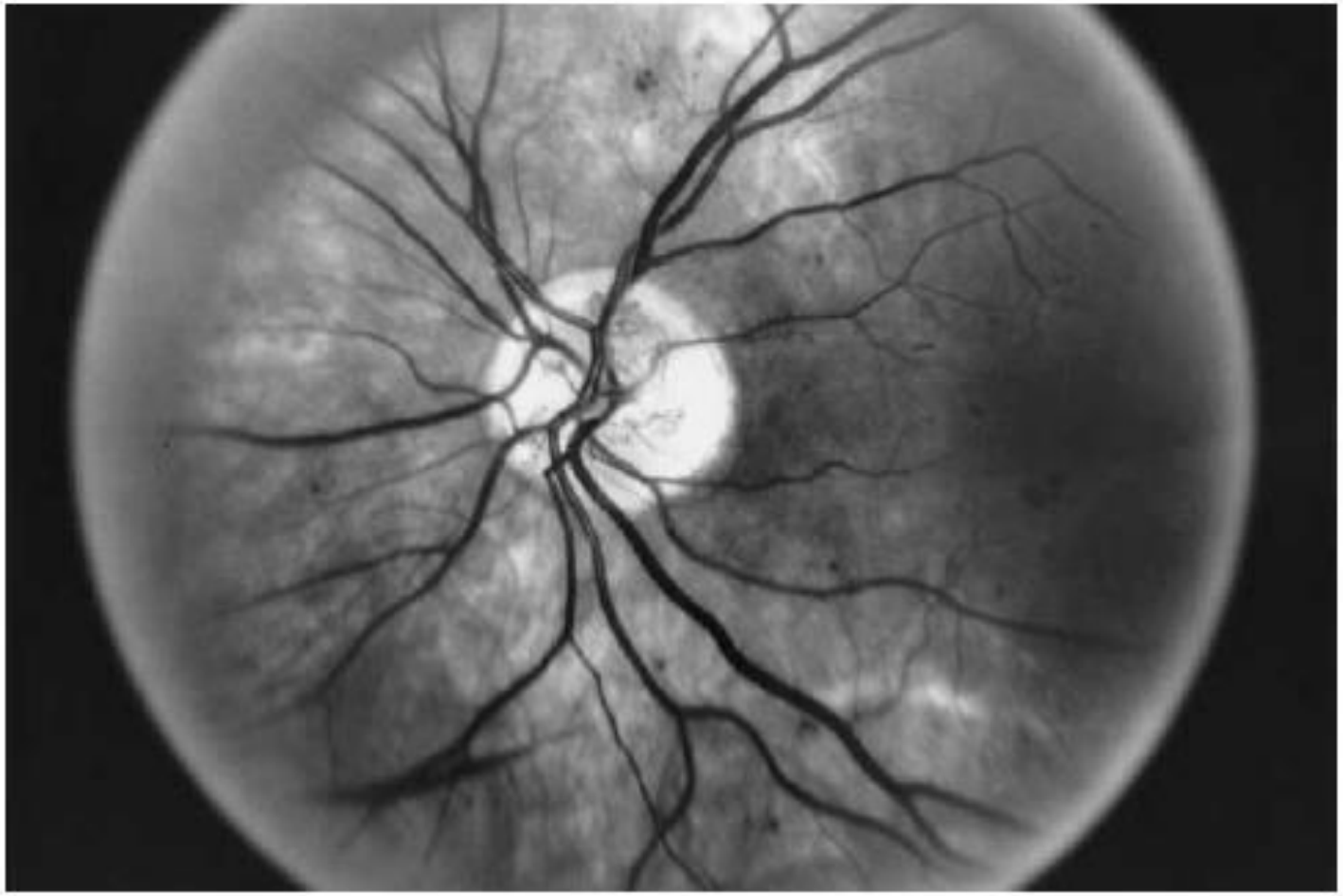


Figure 4. Fundus Photograph of the Eye of a Patient with Neovascularization near the Optic Disk. Patients whose eyes have new vessels of this size or greater on or within 1 disk diameter of the optic disk are at high risk for blindness without treatment.

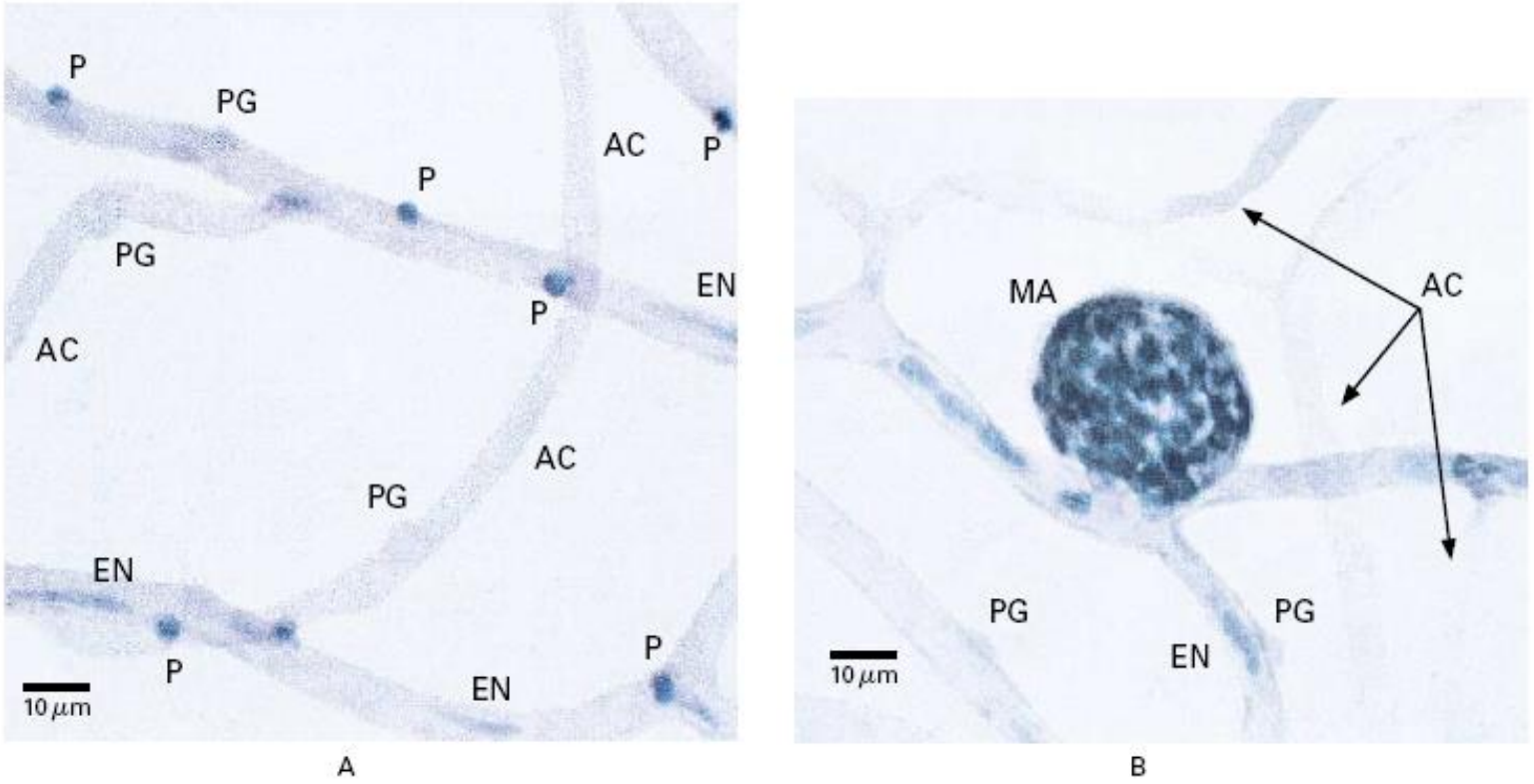


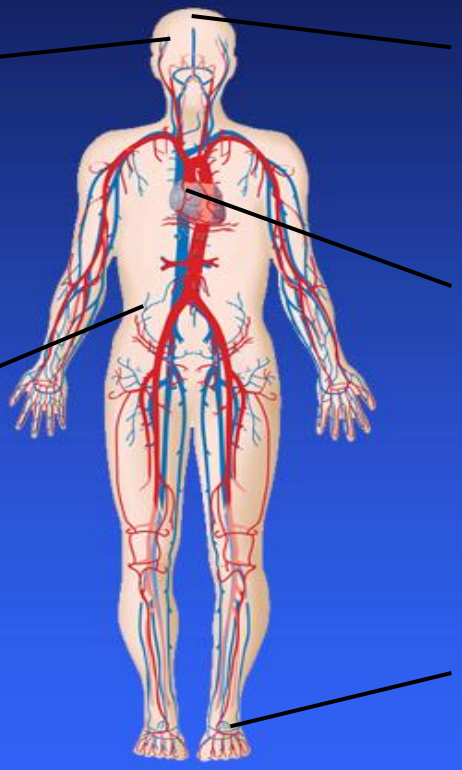
Figure 1. Photomicrographs of Elastase Digest Preparations of the Retinal Vasculature of the Eye of a Patient with Mild, Nonproliferative Diabetic Retinopathy (Periodic Acid–Schiff and Hematoxylin).

Panel A shows normal pericytes (P) and endothelial cells (EN) as well as degenerated pericytes, seen as pericyte "ghosts" (PG), and acellular capillaries (AC). A saccular microaneurysm (MA) is present in Panel B. (Photographs courtesy of W. Gerald Robison, Jr.)

LA DIABETES ES UNA ENFERMEDAD VASCULAR

Retinopatía diabética ~ 50%

Causa principal de ceguera en adultos en edad productiva[1]



Apoplejía

Un aumento de 2 a 3 veces en la mortalidad cardiovascular y apoplejía [3]

Enfermedad cardiovascular ~ 45%

8/10 pacientes diabéticos mueren de eventos CV[4]

Nefropatía diabética ~ 35%

Causa principal de enfermedad renal en etapa terminal[2]

Neuropatía diabética ~ 40%

Causa principal de amputaciones no traumáticas de extremidades inferiores[5]

[1] Fong DS, *et al. Diabetes Care* 2003; 26 (Suppl. 1):S99–S102. [2] Molitch ME, *et al. Diabetes Care* 2003; 26 (Suppl. 1):S94–S98. [3] Kannel WB, *et al. Am Heart J* 1990; 120:672–676. [4] Gray RP & Yudkin JS. In *Textbook of Diabetes* 1997. [5]Mayfield JA, *et al. Diabetes Care* 2003; 26 (Suppl. 1):S78–S79. Decision Resources., Inc.1999.

Características clínicas de pacientes con DM tipo 2
Clínica de Diabetes Hospital Miguel Hidalg 2002 (n=457)

- Edad promedio 51.7 años
- Tiempo de diagnóstico 8.3 años
- Hipertensión arterial 51.2 %
- Microalbuminuria 36.7%
- Retinopatía 49.6%
- Dislipidemia 78.4%
- Neuropatía periférica 69.8%
- Neuropatía autonómica 22.6%
- HbA1c > 8% 45.2%
- Uso insulina 38.7%

Epidemiology/Health Services/Psychosocial Research
ORIGINAL ARTICLE

Characteristics of Patients With Type 2 Diabetes in México

Results from a large population-based nationwide survey

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ANTONIO GONZALEZ CHÁVEZ, MD[3]
AGUSTIN LARA ESQUEDA, PHD[2]
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JUAN A. RULL-RODRIGO, MD[1]
ROBERTO TAPIA CONYER, PHD[2]
FOR THE ENSA (ENCUESTA NACIONAL DE SALUD) 2000 GROUP

OBJECTIVE — To describe the clinical characteristics of the diabetic population that formed part of a population-based survey conducted in México.

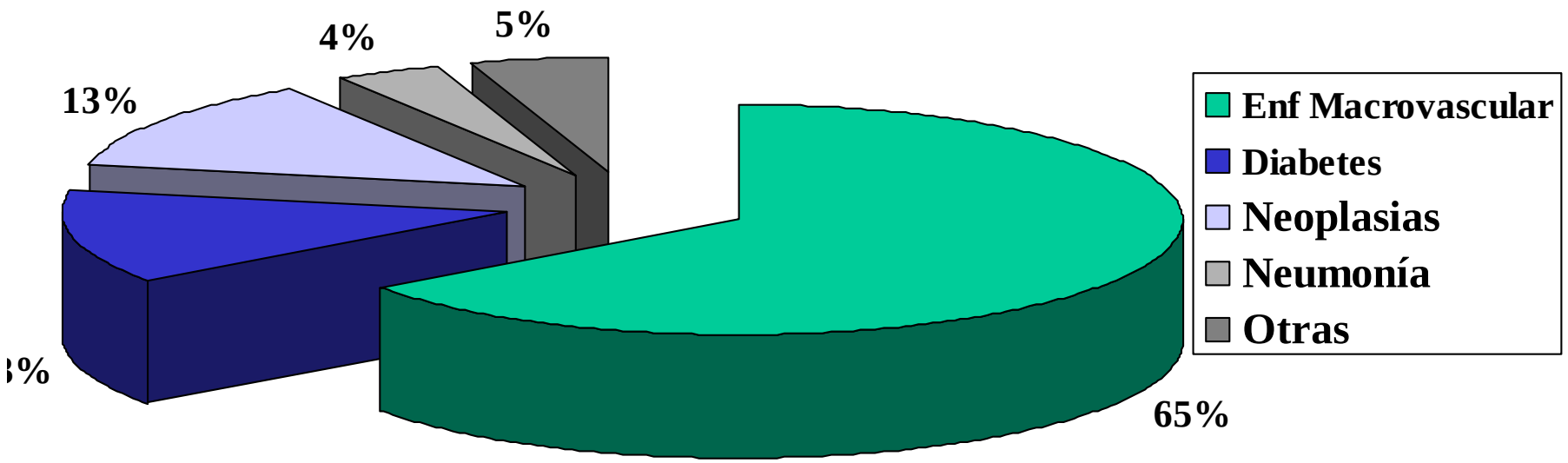
over time (e.g., obesity), influencing treatment choices and the incidence of complications (9). Here, we describe the characteristics of the diabetic population forming part of a nationwide, population-based survey done in México during 2000. Our data demonstrate that Mexican adults with type 2 diabetes have a high prevalence of risk factors that contribute to the occurrence of macro- and micro-

Características de Pacientes con DM tipo 2 en México

- n = 3597
- 55.2 +/- 13.5 años (13% menores de 40 a)
- 9 % con dx de más de 10 años
- IMC 29.2 +/- 5.7
- 50% con hipertensión arterial
- 34% con tabaquismo
- 67.6% con factores de riesgo modificables
- Minoría bajo ejercicio, dieta e insulina

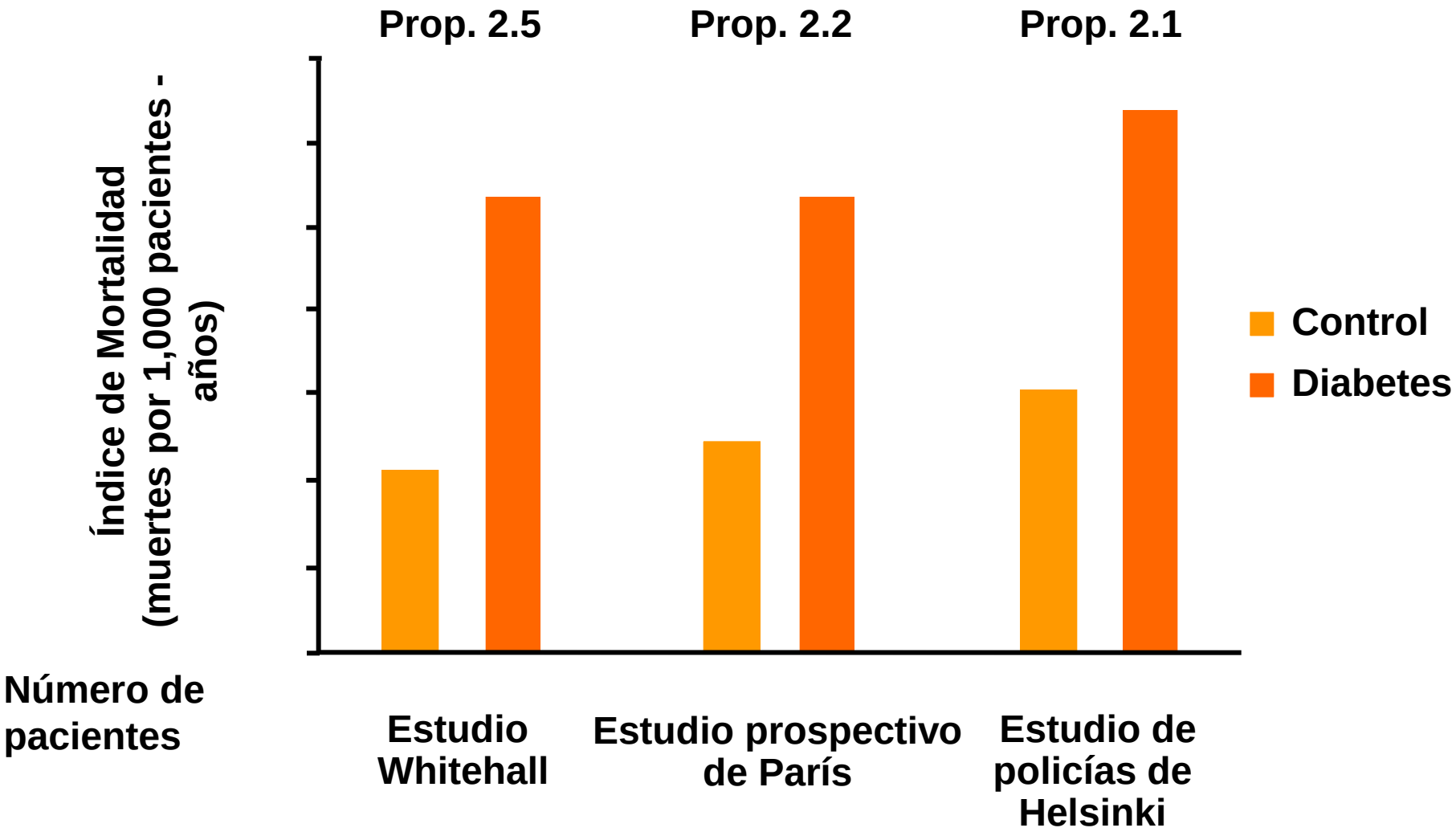
Aguilar-Salinas CA. Diabetes Care; Julio 2003

Principales causas de muerte en diabéticos



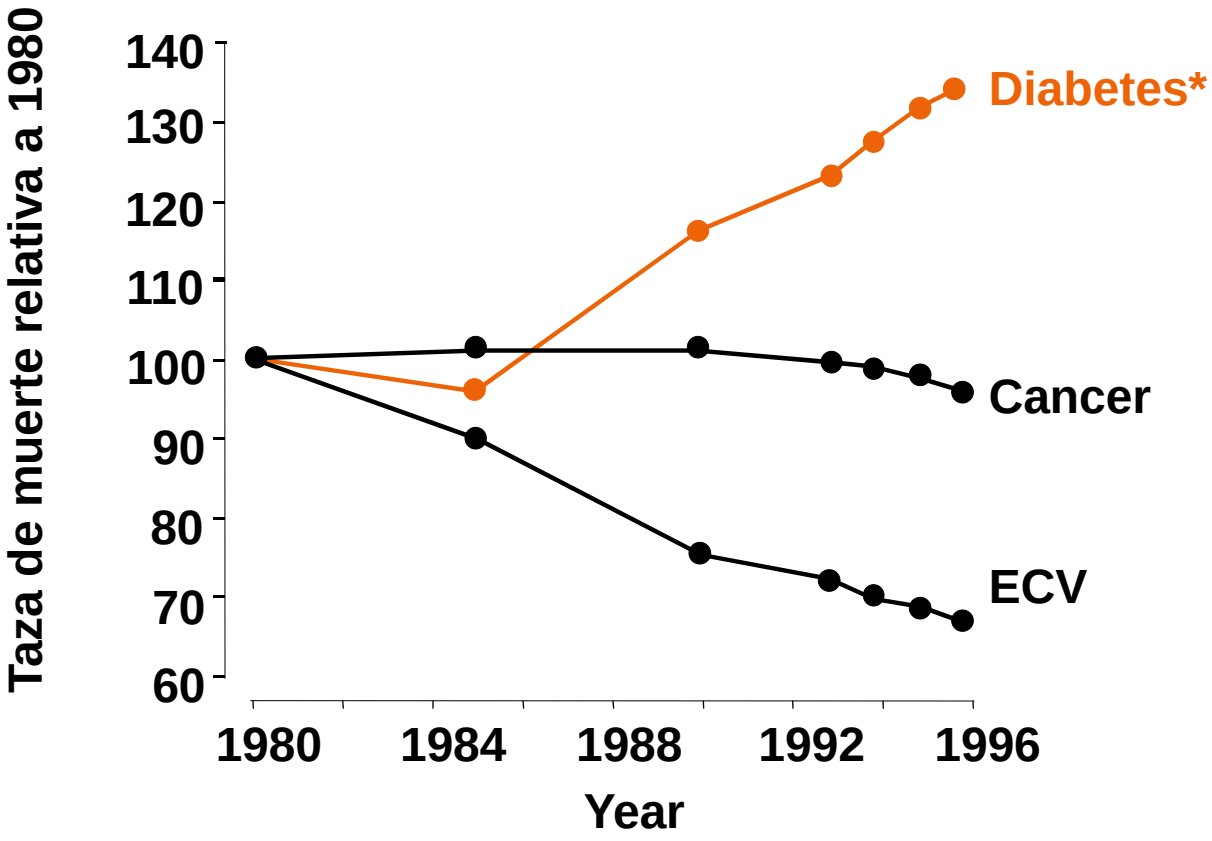
NIH Publication 1995 No. 95: 233-257

El índice de mortalidad es dos veces mayor en pacientes con diabetes



Balkau B, *et al*. *Lancet* 1997; 350:1680.

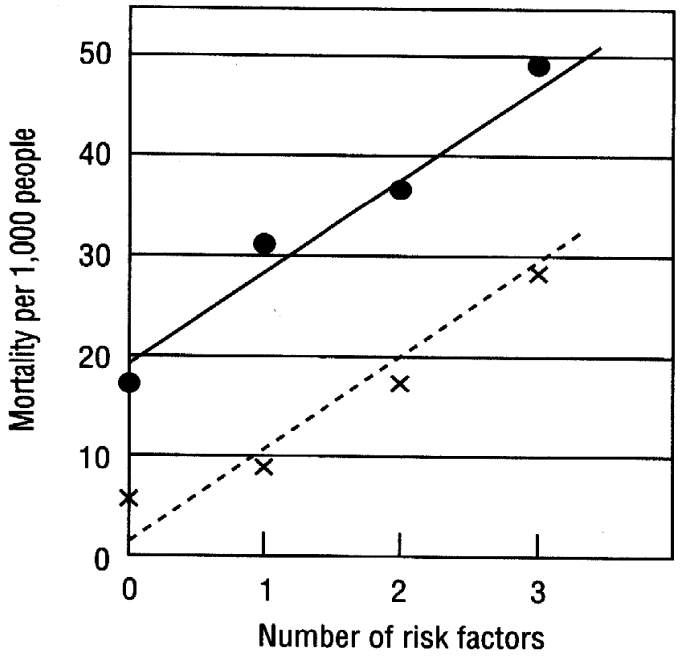
Tendencia secular



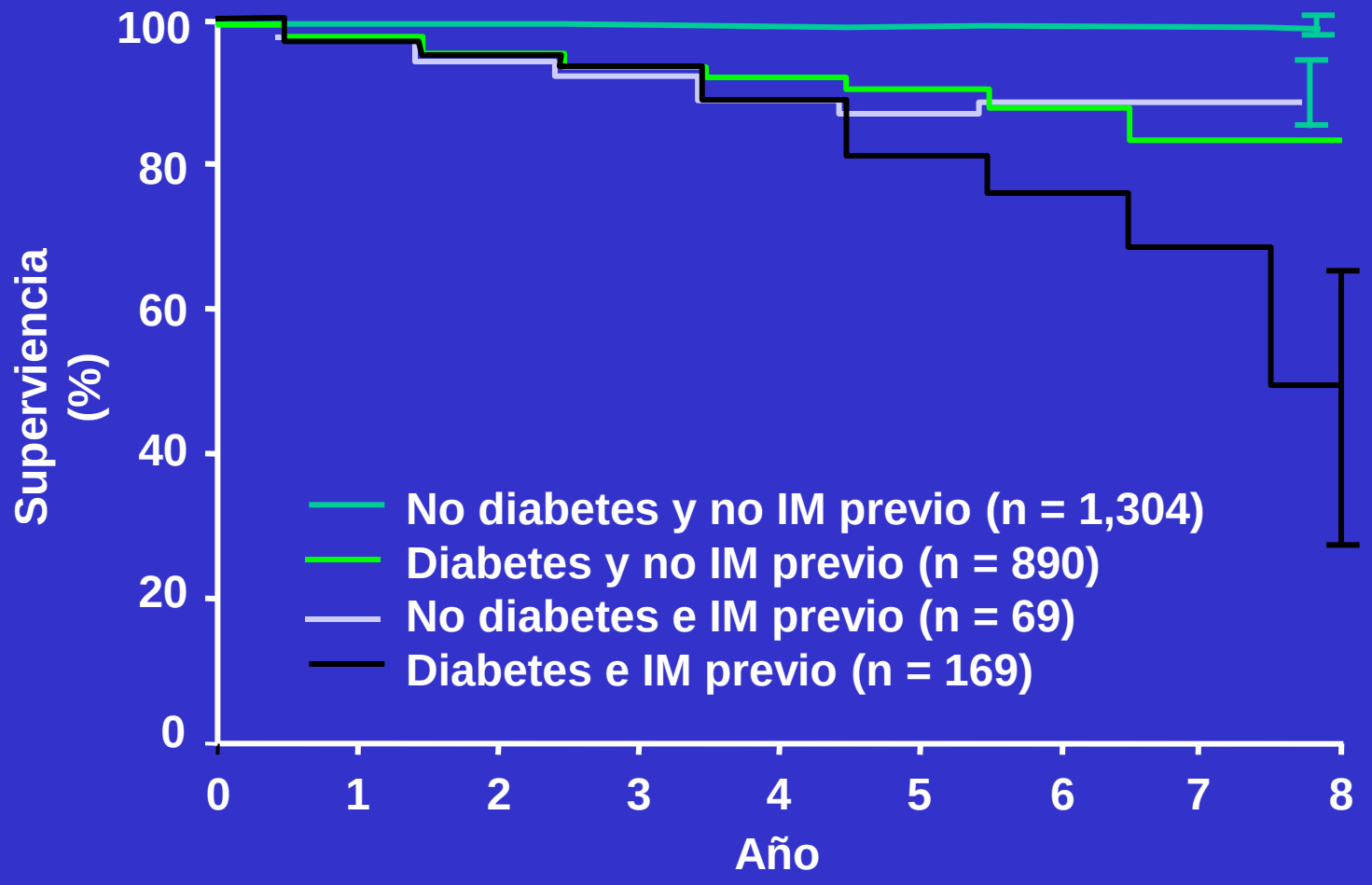
*Many diabetes deaths are due to cardiovasular causes.
†Deaths due to cardiovascular causes in persons withhout diabetes.
Source: National Center of Health Statistics, 1998.

La población con DM tiene un riesgo mayor y diferenciado (equivalente de CI)

Figure 17. Effects of three major risk factors (hypercholesterolemia, smoking, and diastolic hypertension) on age-standardized cardiovascular disease mortality in 5,245 subjects with diabetes (*solid line*) and 350,977 nondiabetic subjects (*dashed line*) between ages 35 and 57 and free of myocardial infarction at baseline. Follow-up was 6 years



La mortalidad por ECV es alta en la diabetes de tipo 2

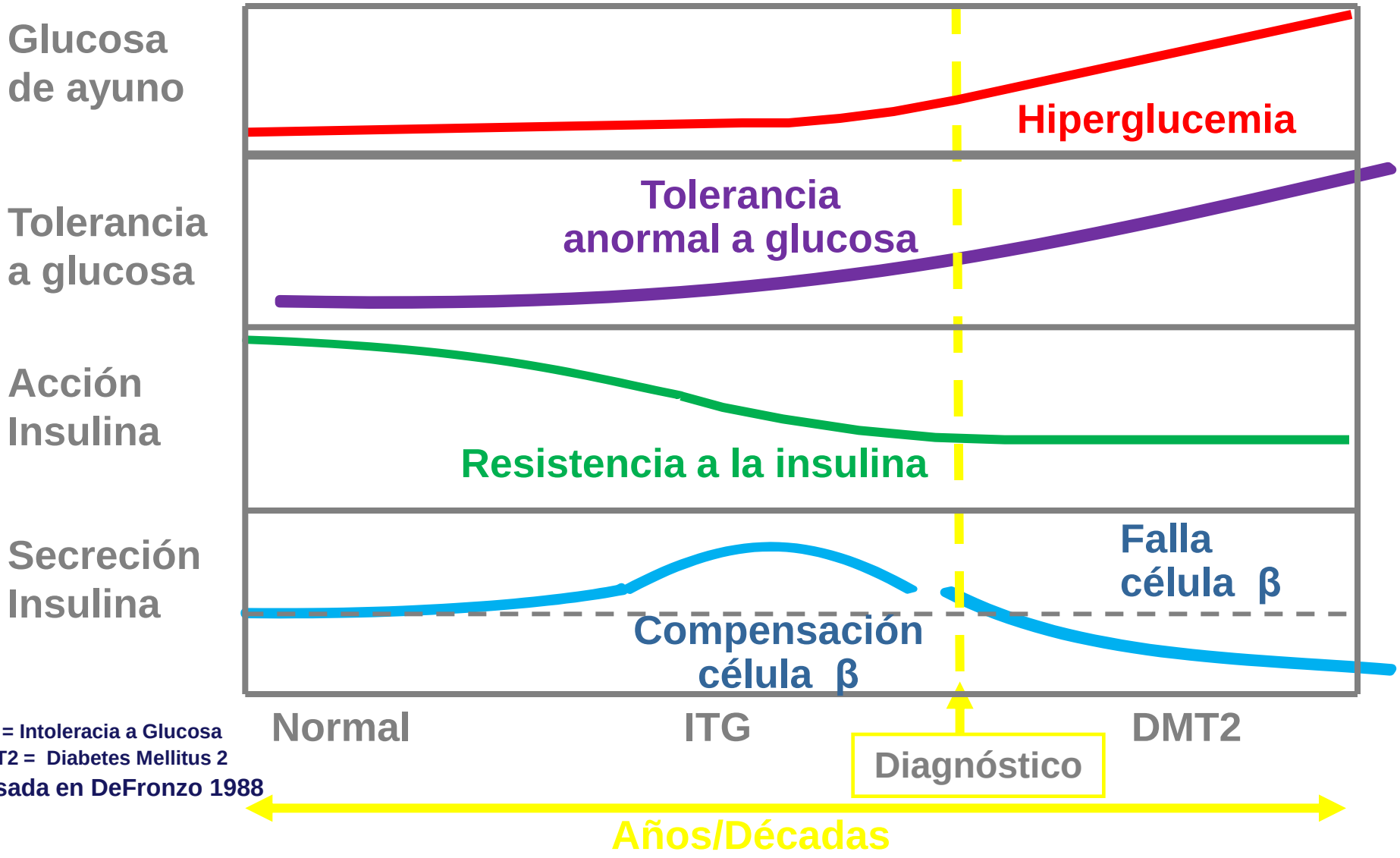


IM: infarto del miocardio
Las barras de error indican IC del 95%

Haffner SM, *et al*. *N Engl J Med* 1998; 339:229–234.

Diabetes tipo 2

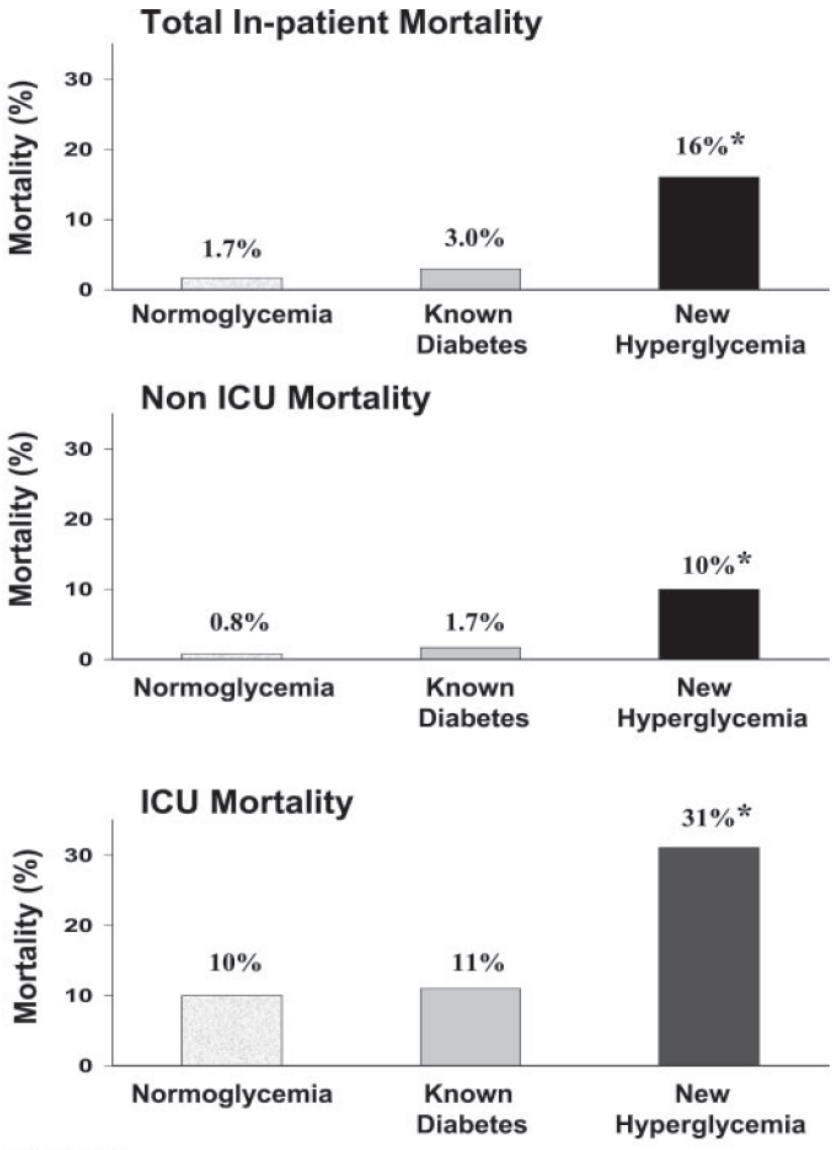
Resistencia Insulina + disfunción célula β= Diabetes tipo 2



ITG = Intoleracia a Glucosa
DMT2 = Diabetes Mellitus 2
Basada en DeFronzo 1988

Hiperglucemia como indicador independiente de morbilidad y mortalidad intrahospitalaria

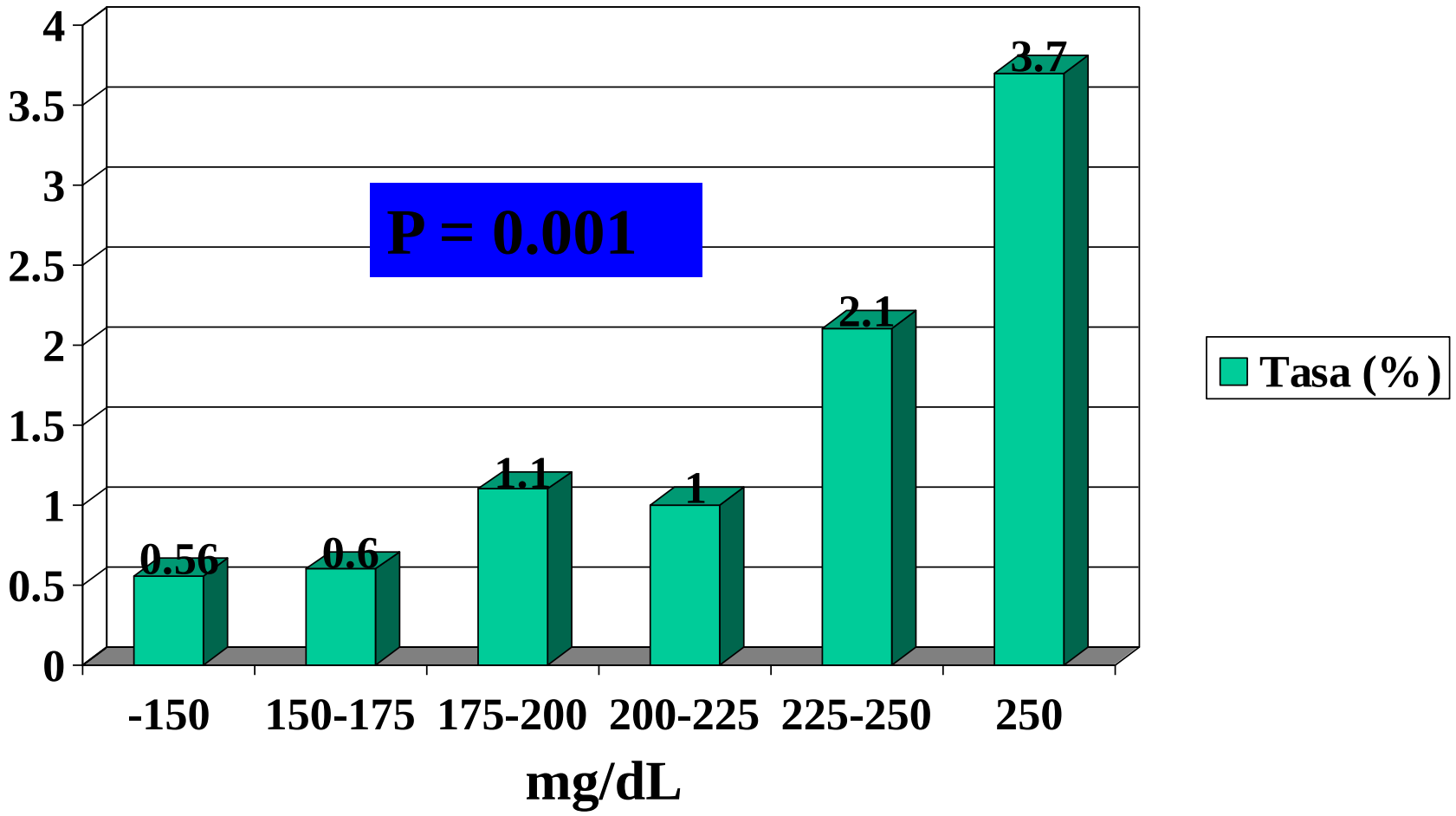
- El nivel de glucemia incrementa la morbilidad - mortalidad en unidades de cuidados intensivos y áreas generales de hospitalización
- Enfermedad isquémica cardíaca y cerebral
- Pacientes en estado crítico
- Condiciones obstétricas



Umpierrez GE, et al.

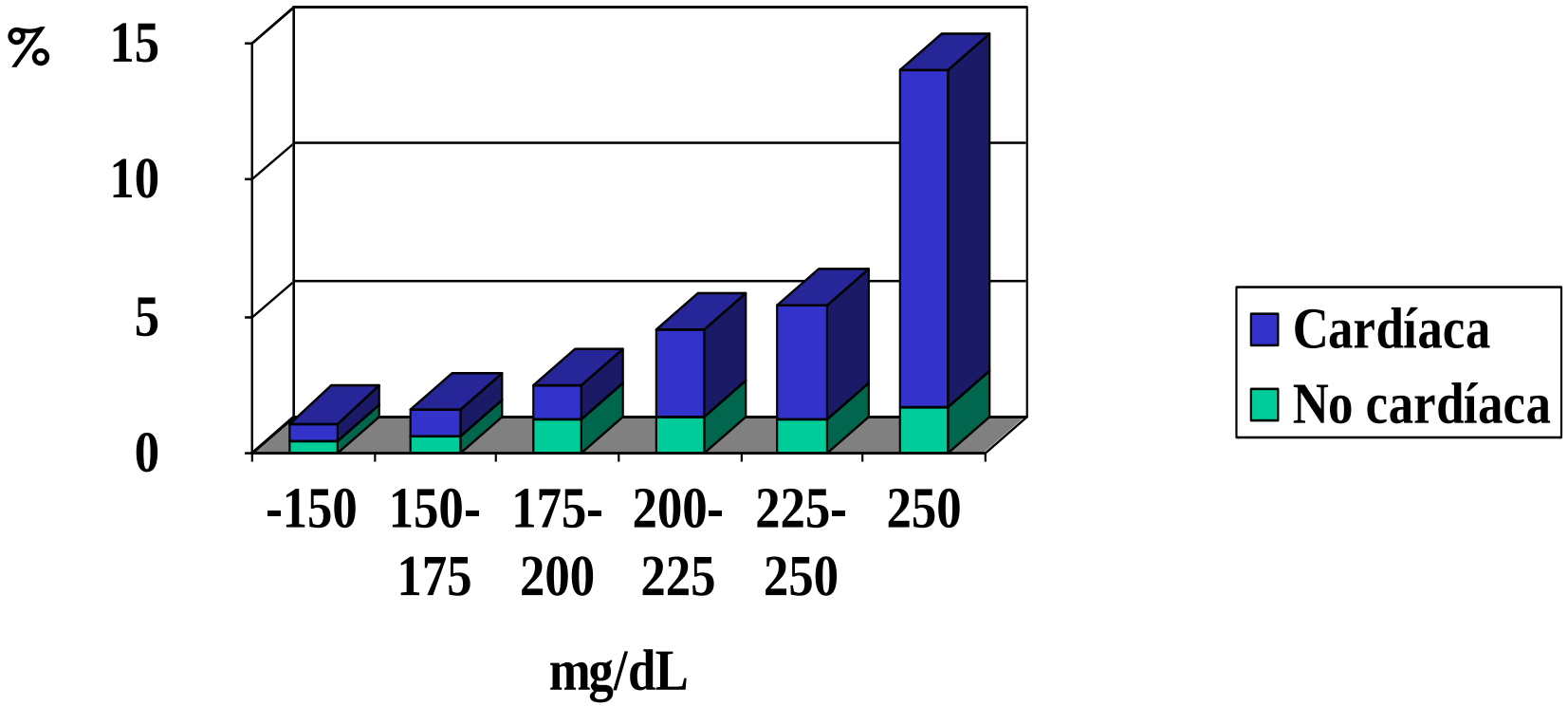
J Clin Endocrinol Metab 87:978-82, 2002

Tasa de heridas esternales profundas infectadas en 4,864 pacientes con DM sometidos a cirugía cardíaca abierta: media de [glucosa] 3 días postoperatorios



Adaptado de Zerr KJ et al. Ann Thorac Surg 1997; 63: 356 - 361

Mortalidad cardíaca y no cardíaca en 3,554 personas con DM sometidas a cirugía coronaria

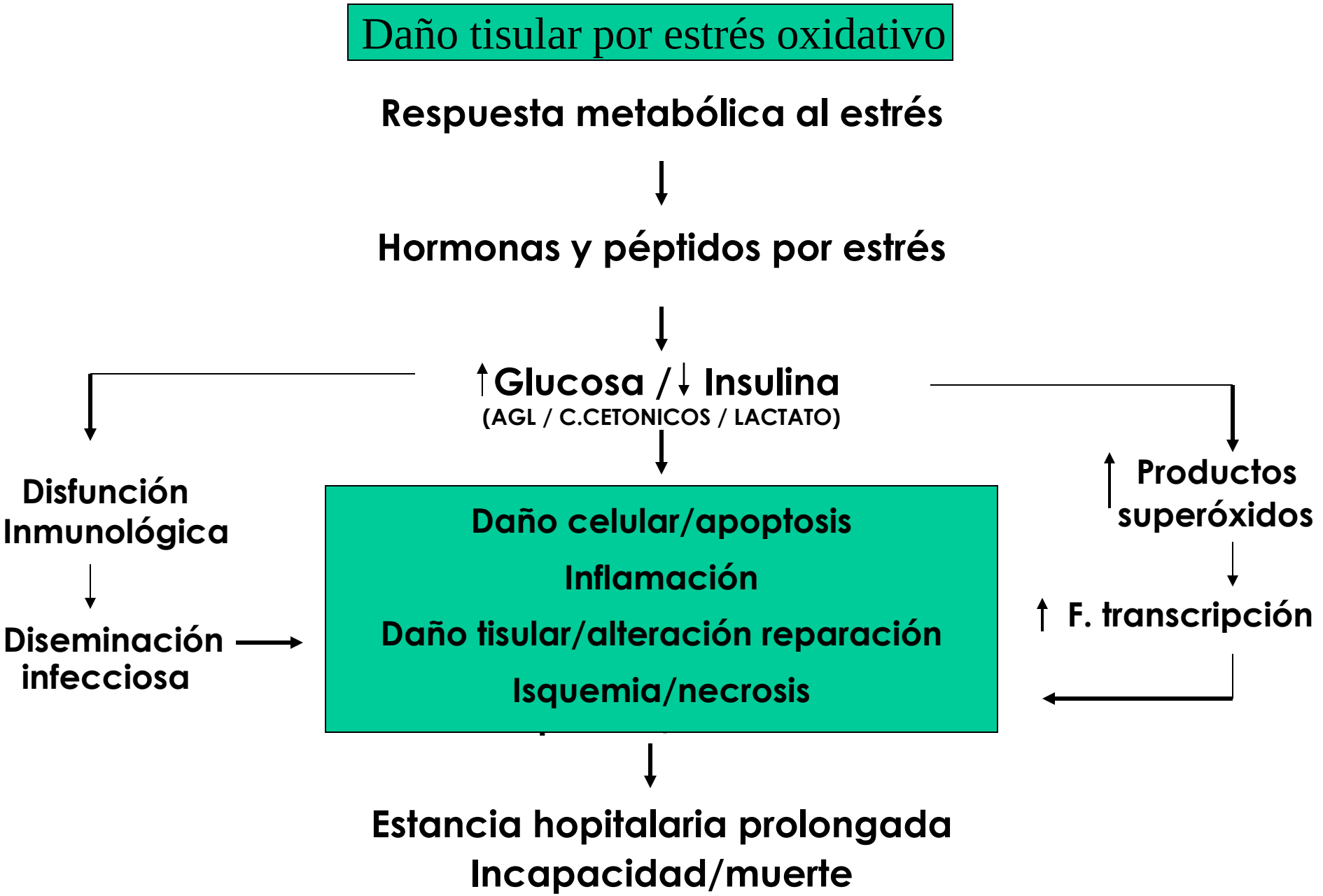


Modificado de Furnary AP, et al. Circulation 1999; 100(18):I-591

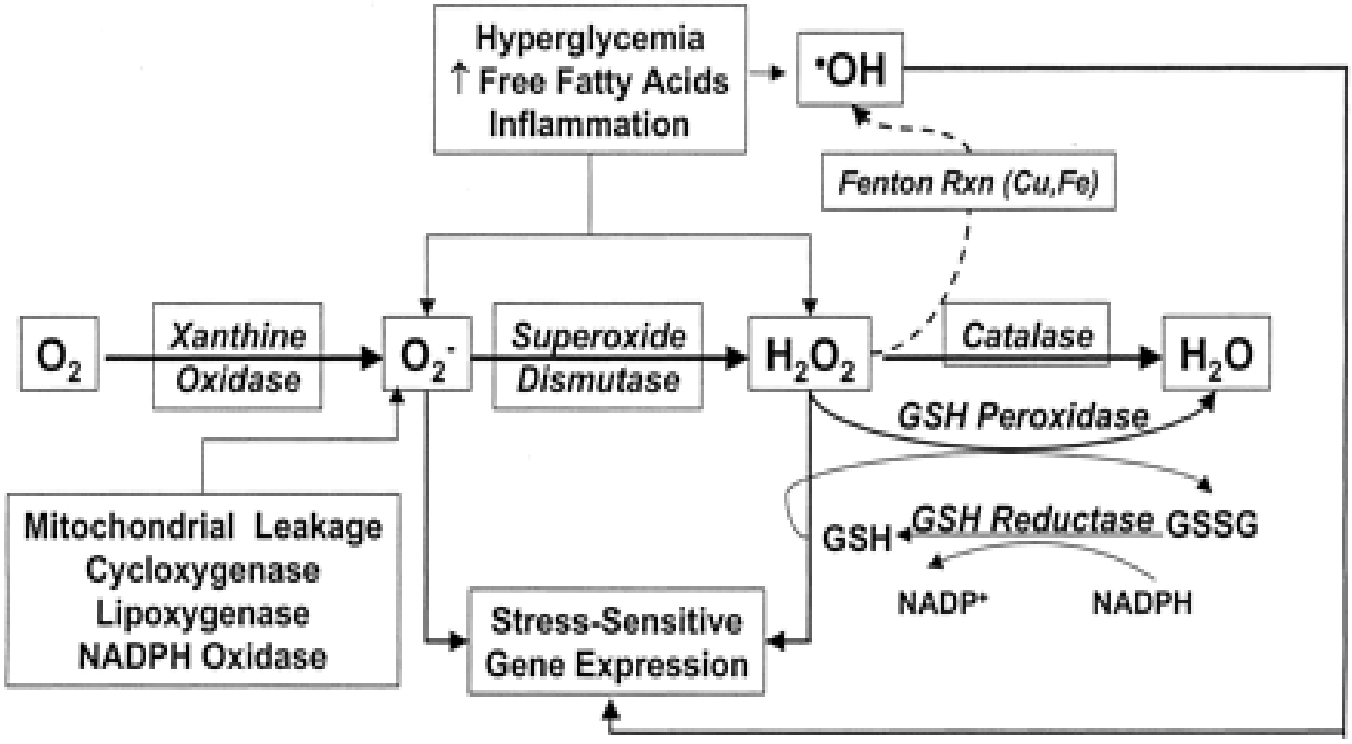
Hiperglucemia y morbi-mortalidad

Van den Berghe UCI (2001)[1]	mortalidad 4.6% vs 8.0% (Int vs Conv) p = 0.04 ↓46% sepsis; ↓41% diálisis o hemodiálisis
Pulsinelli et al. EVC (1983)[2]	>120 mg/dL predictor incapacidad DM y no DM
Weir et al EVC (1997)[3]	>148 mg/dL duplicó riesgo de mortalidad
Jorgenson et al. EVC (1994)[4]	>104 mg/dL correlación linear con gravedad EVC
Kalin et al. Qx bypass (1998)[5]	Insulina pre-bypass reduce mortalidad 50%
Pomposelli et al.[6]	>220 mg/dL 1d postoperatorio > infección 6X

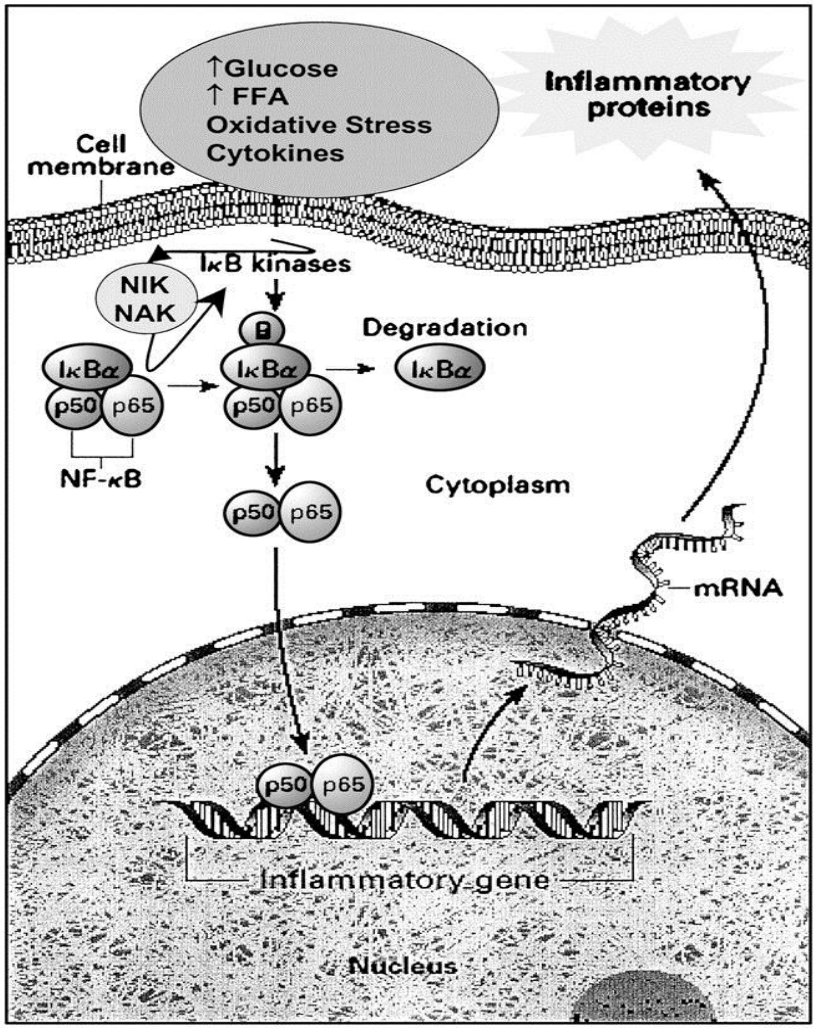
1.NEJM 345:1359-67; 2. Am J Med 74:540-3; 3. BMJ 314:1303-06; 4. Stroke 25:1977-84
5. Diabetes 47(suppl 1) : A87 6. J Paraenteral Enteral Nutr 22: 77-81


Daño tisular por estrés oxidativo
Respuesta metabólica al estrés
Hormonas y péptidos por estrés
↑Glucosa / ↓ Insulina
(AGL / C.CETONICOS / LACTATO)
Disfunción Inmunológica
Diseminación infecciosa
Daño celular/apoptosis
Inflamación
Daño tisular/alteración reparación
Isquemia/necrosis
↑ Productos superóxidos
↑ F. transcripción
Estancia hopitalaria prolongada
Incapacidad/muerte

Estrés oxidativo y endotelio



Estrés oxidativo e inflamación



Diabetologia (2002) 45:924–930

Diabetologia

For Debate

The anti-inflammatory and potential anti-atherogenic effect of insulin: a new paradigm

P. Dandona, A. Aljada, P. Mohanty

Division of Endocrinology, Diabetes and Metabolism, State University of New York at Buffalo, and Kaleida Health, Buffalo, New York, USA

0021-972X/01/$03.00/0
The Journal of Clinical Endocrinology & Metabolism

Vol. 86, No. 7
Printed in U.S.A.

Insulin Inhibits Intranuclear Nuclear Factor κB and Stimulates IκB in Mononuclear Cells in Obese Subjects: Evidence for an Anti-inflammatory Effect?

PARESH DANDONA, AHMAD ALJADA, PRIYA MOHANTY, HUSAM GHANIM, WAEL HAMOUDA, EZZAT ASSIAN, AND SHAKEEL AHMAD

Division of Endocrinology, Diabetes & Metabolism, State University of New York at Buffalo and Kaleida Health, Buffalo, New York 14209

ABSTRACT

In view of the fact that insulin resistance is associated with atherogenesis and that troglitazone, an insulin sensitizer, has anti-inflammatory effects, we examined the effect of insulin on the key protein of nicotinamide adenine dinucleotide phosphate oxidase also fell at 2 h and 4 h, reverting toward the baseline at 6 h ($P <$ 0.05). In addition, soluble intercellular adhesion molecule-1 (sICAM-

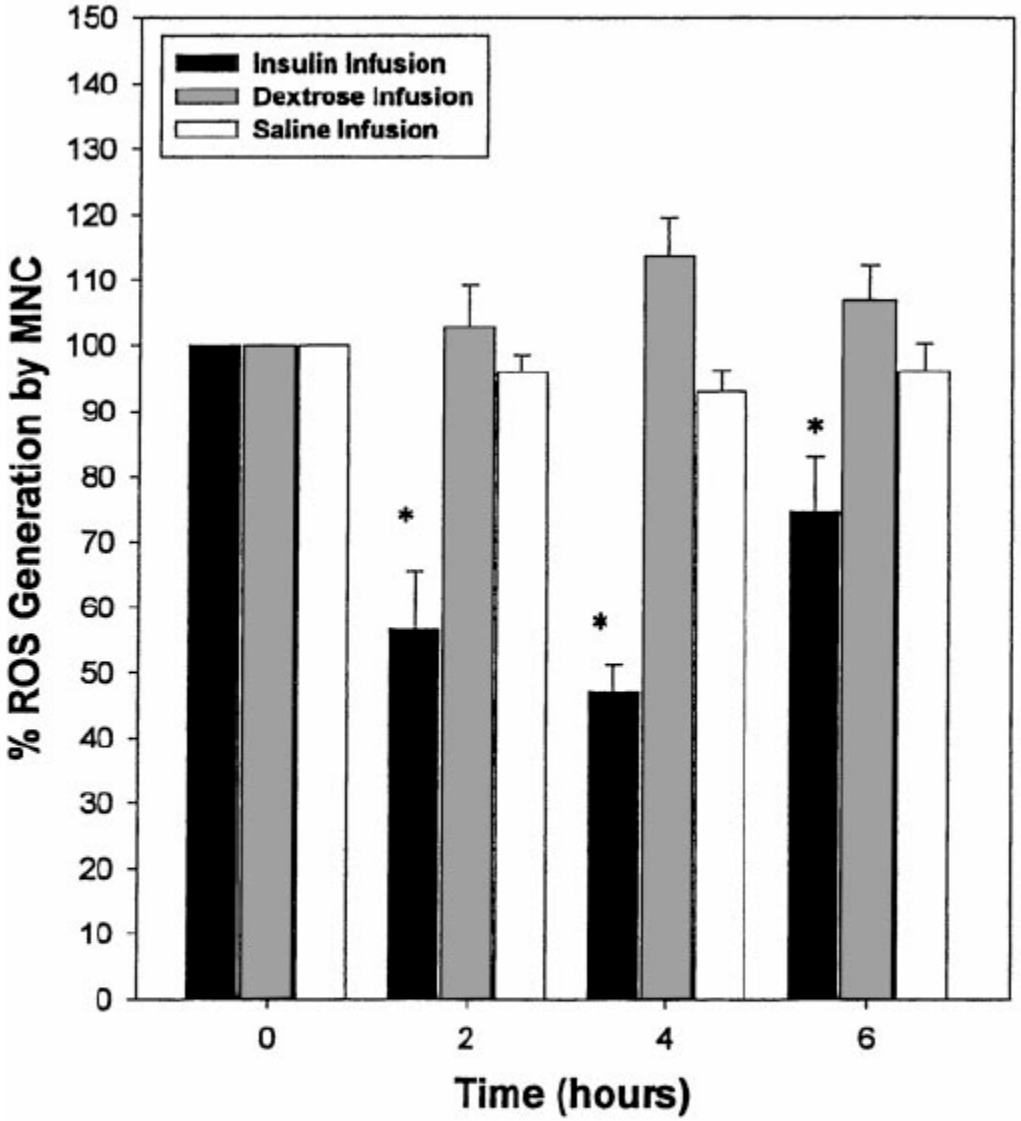


FIG. 5. ROS generation by MNC in obese subjects following insulin or dextrose or saline infusions. Note that ROS generation decreased significantly at 2 h and continued to be inhibited and reached a nadir at 4 h ($P < 0.005$). ROS generation started to increase thereafter after insulin infusion was stopped. Dextrose or saline infusions did not cause any significant change in ROS generation (*, $P < 0.05$).

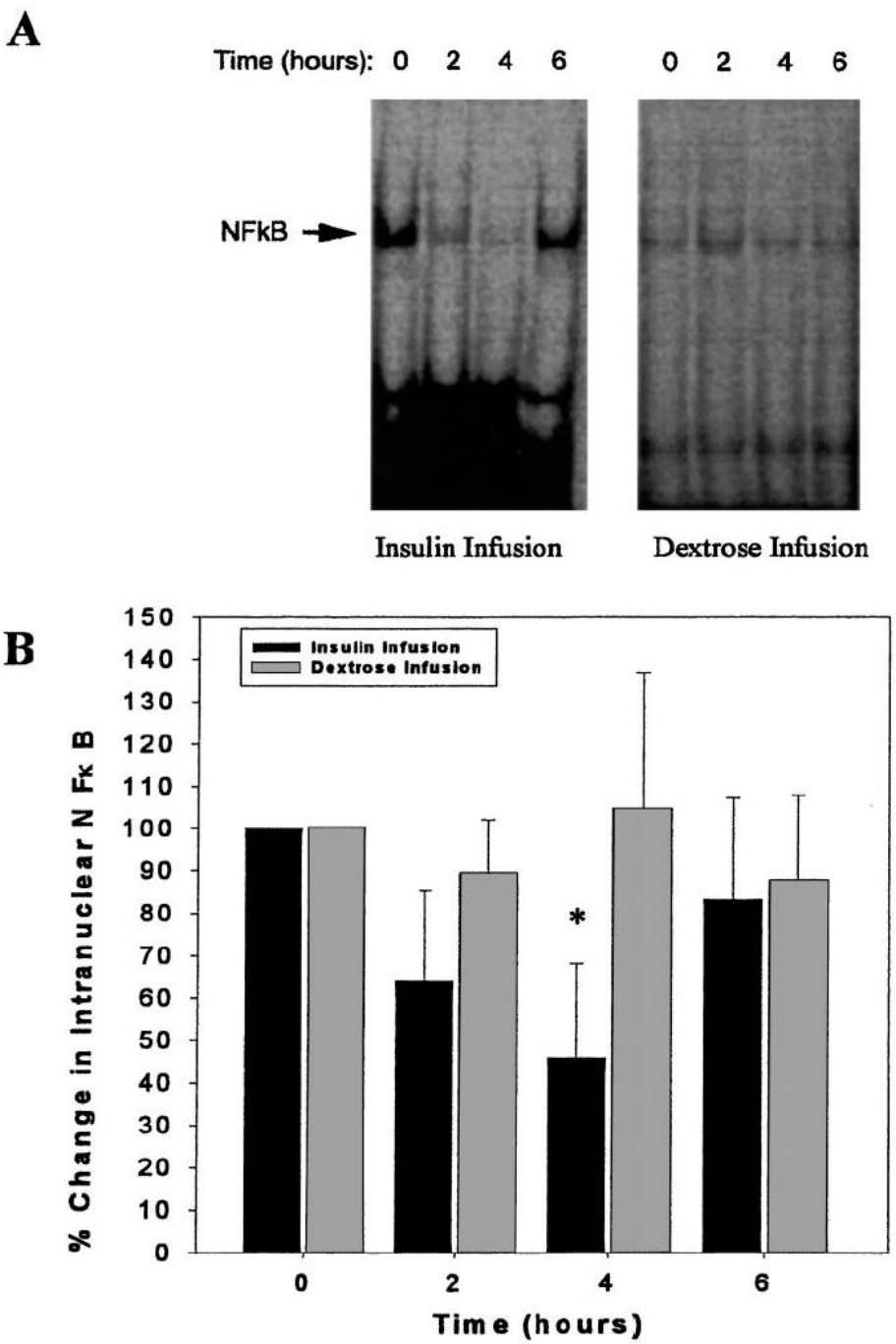
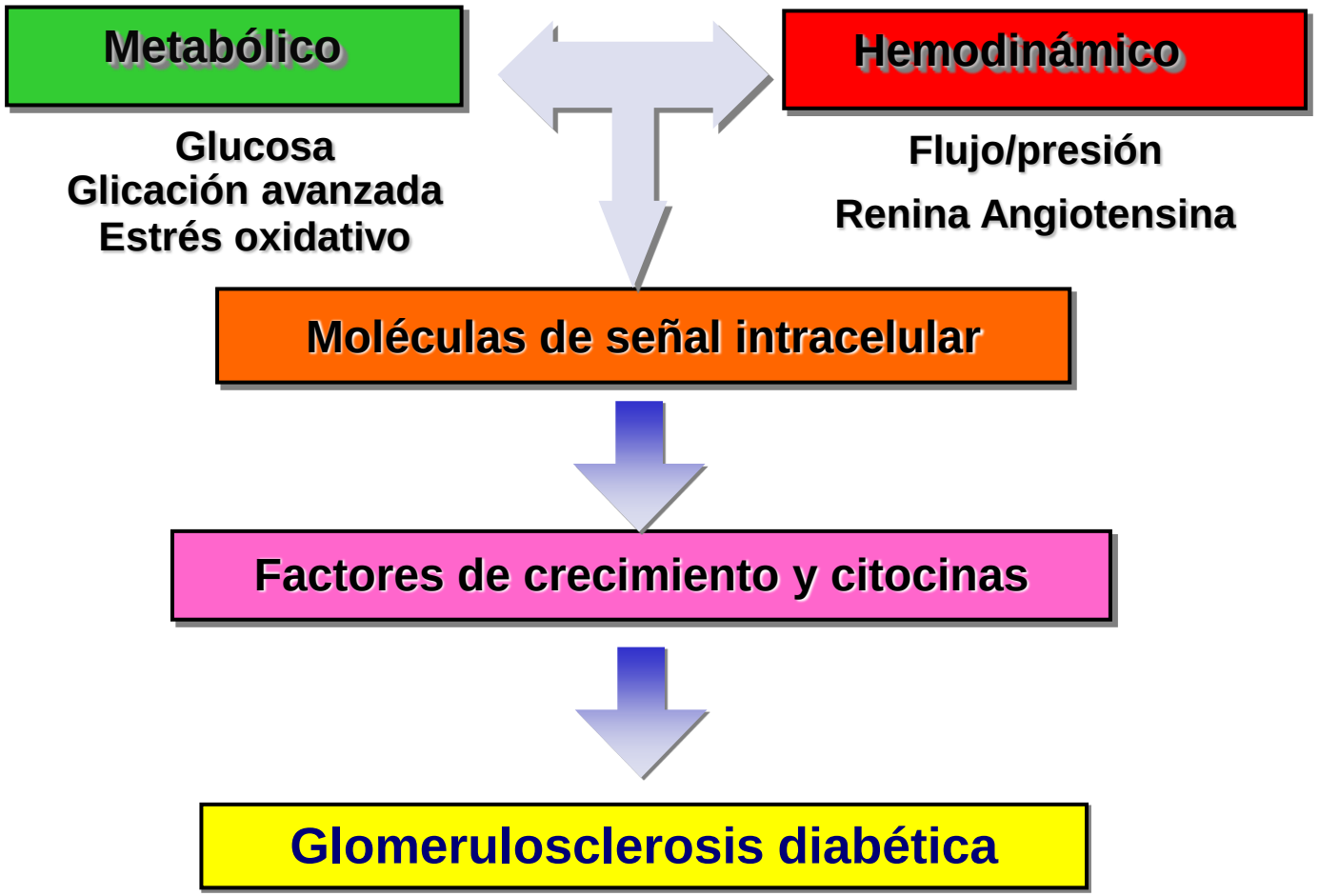
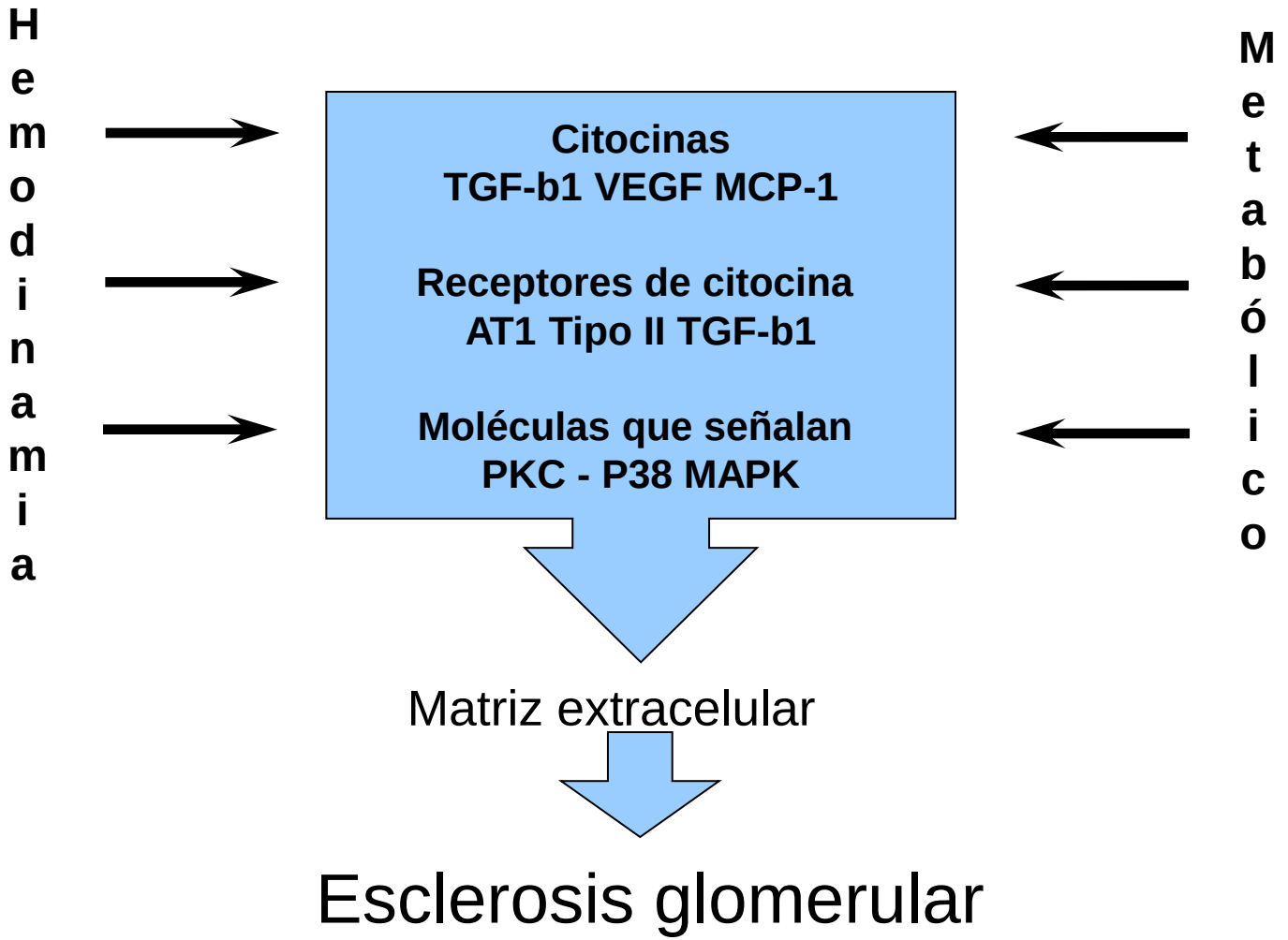


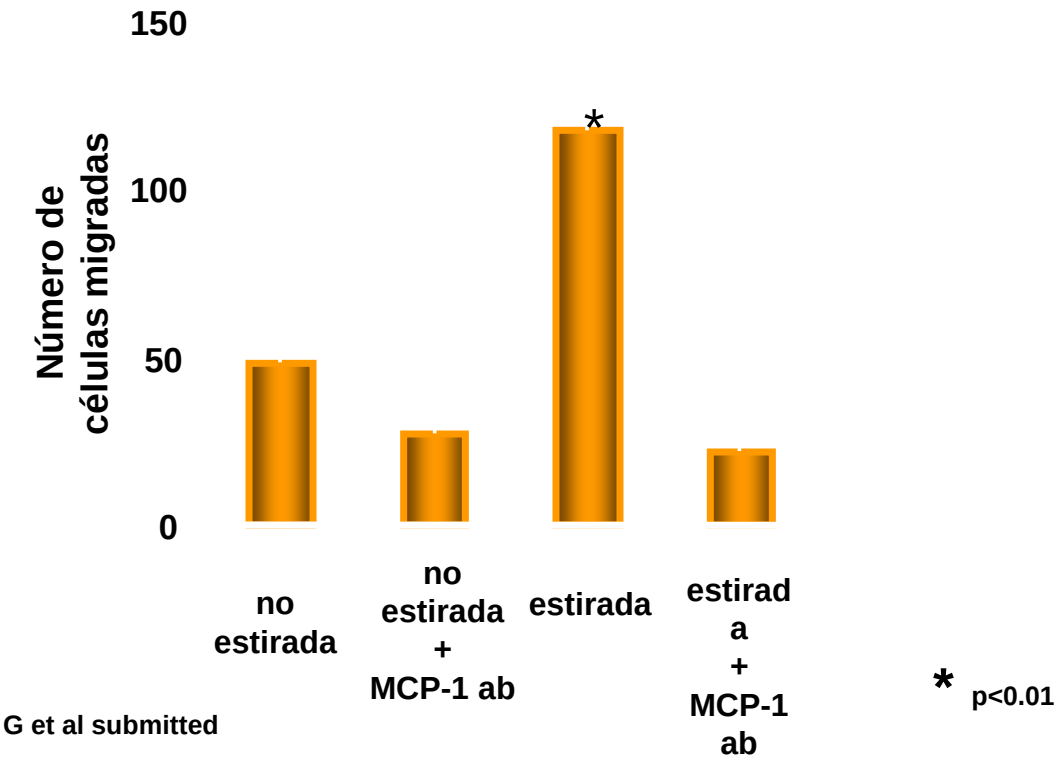
FIG. 3. A, Gel shift assay showing the relative NFκB binding to the double-stranded oligonucleotide containing NFκB DNA binding site following insulin or dextrose infusion. Band-shift assays were performed using 5 μg MNC nuclear extract for each time point. B, Relative NFκB binding to double-stranded oligonucleotide containing NFκB DNA binding site. All values were normalized to 100% for baseline levels and the following values were expressed as percent of basal. The results are presented as mean ± SE; *, $P < 0.05$.


Metabólico
Hemodinámico
Glucosa
Glicación avanzada
Estrés oxidativo
Flujo/presión
Renina Angiotensina
Moléculas de señal intracelular
Factores de crecimiento y citocinas
Glomerulosclerosis diabética

Mecanismos de nefropatía diabética

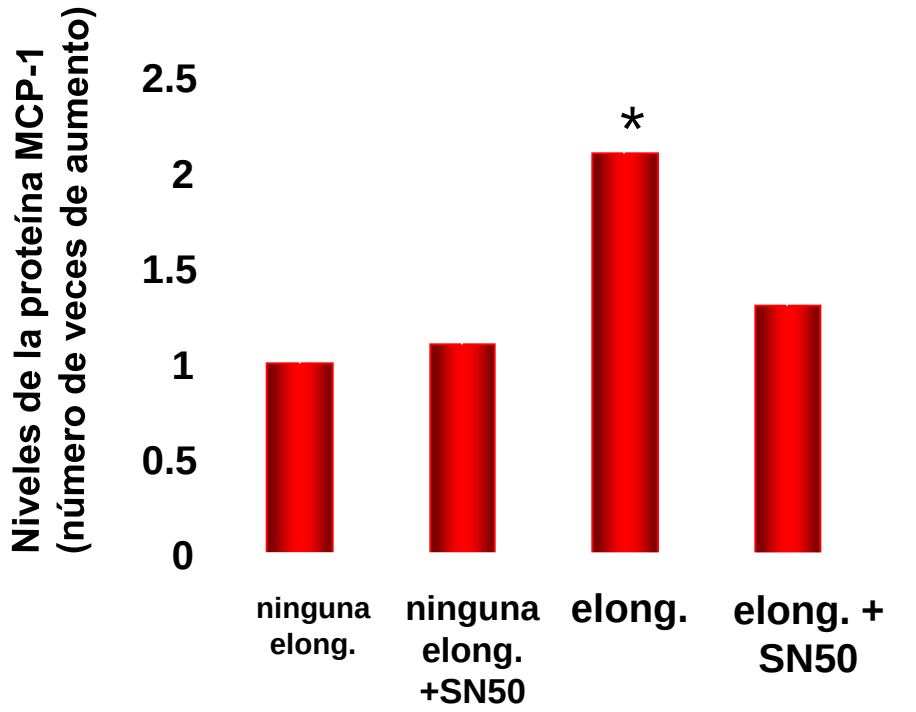


La elongación induce la quimiotaxis de los monocitos en las células mesangiales humanas a través de MCP-1



Gruden G et al submitted

La inhibición de NFκB impide la producción de MCP-1 inducida por la elongación en las células mesangiales humanas



* $p<0.05$

Gruden G et al submitted

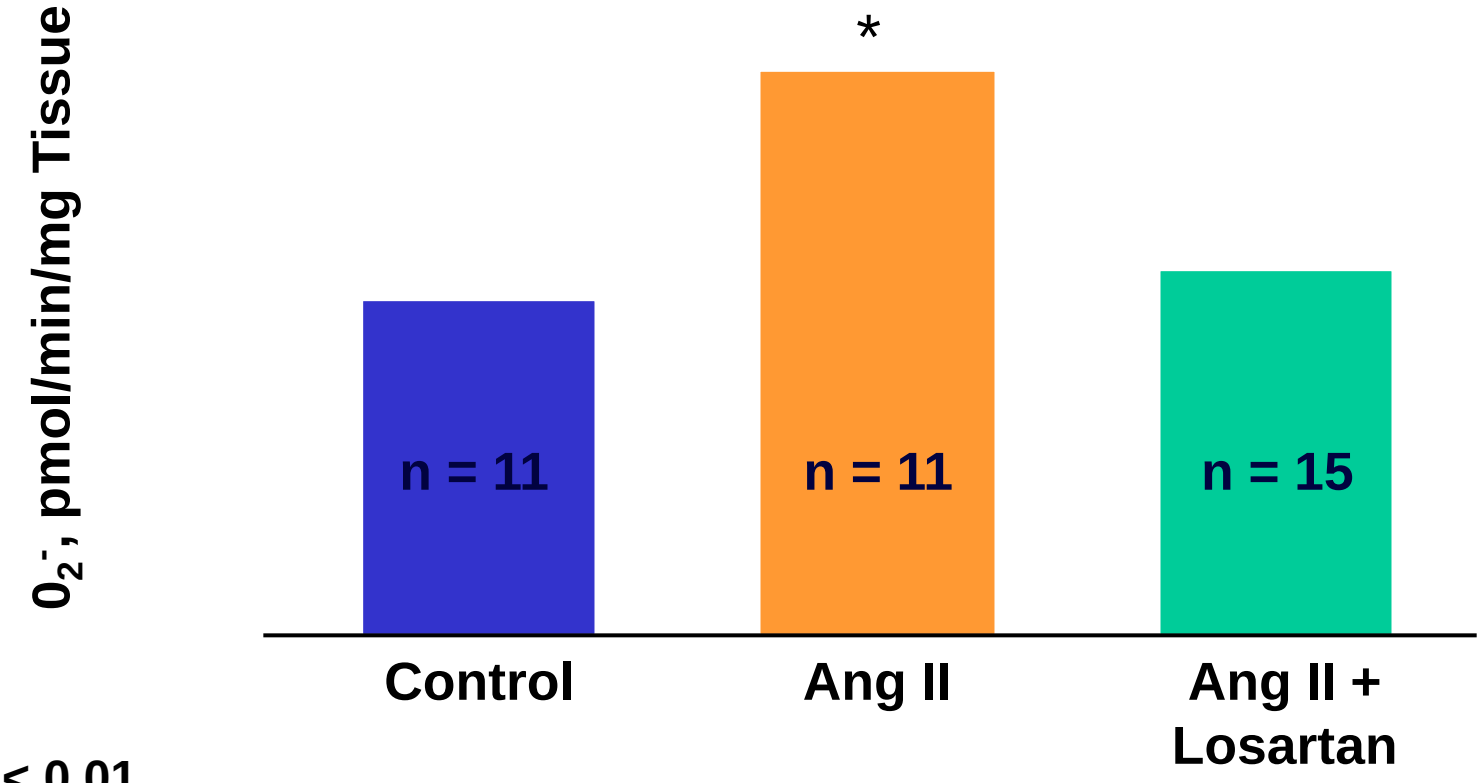
SN50: inhibidor muy específico de NFκB (1μM)

Oxidative Stress: Multiple Sources and Mechanisms

Normal	→	**ROS**
Diabetes	→	**ROS**
Obesity	→	**ROS**
Hypertension	→	**ROS**
Cigarette Smoking	→	**ROS**
High LDL (or low HDL) Cholesterol	→	**ROS**
Estrogen Withdrawal	→	**ROS**
Increased Angiotensin II	→	**ROS**

Angiotensin II Induces Superoxide Production In Human Vascular Tissue

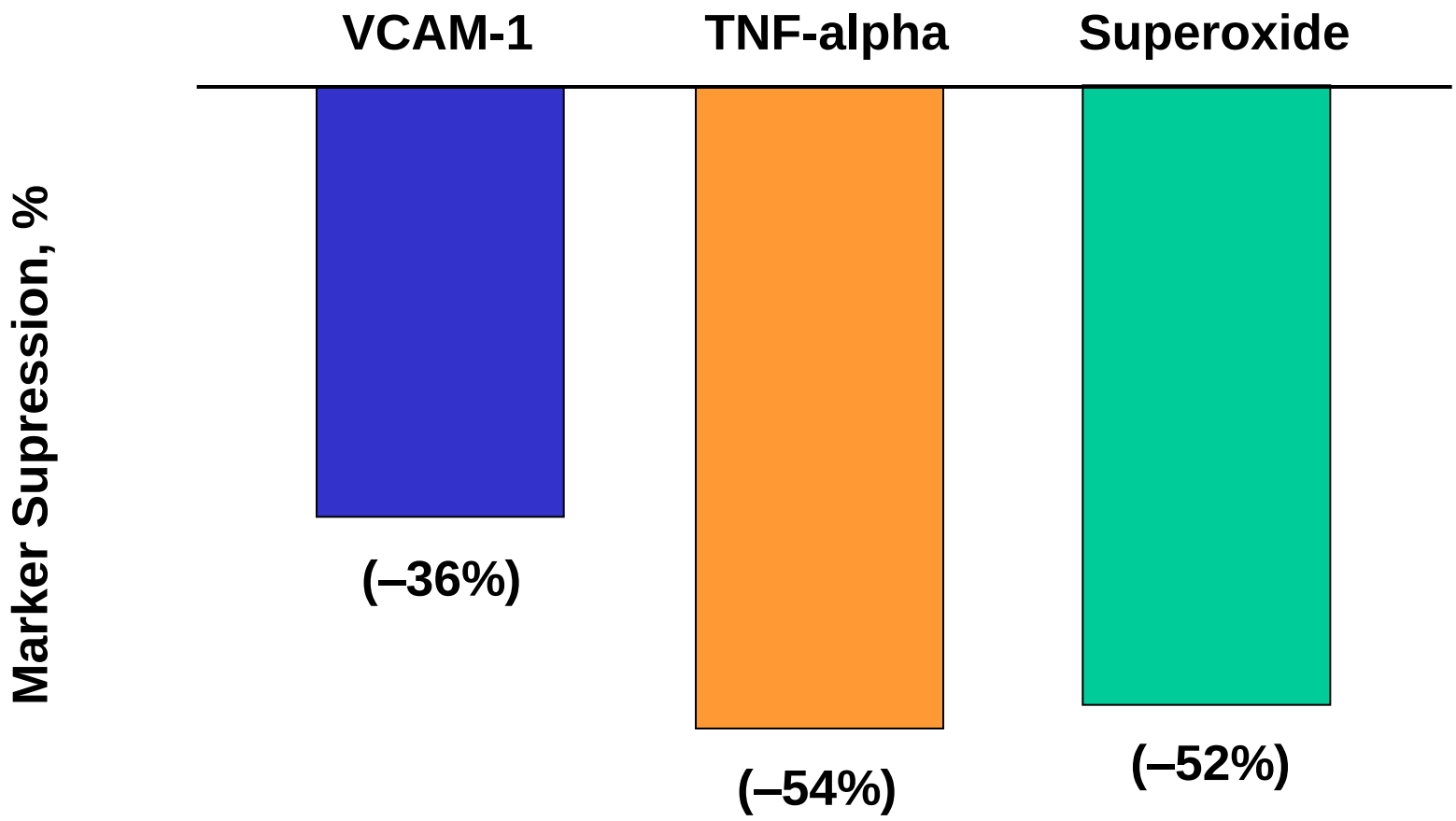
Human Internal Mammary Arteries Incubated With 1 μM Angiotensin II



***P* < 0.01.**

Reprinted with permission from Berry C et al. *Circulation*. 2000;101:2206–2212.

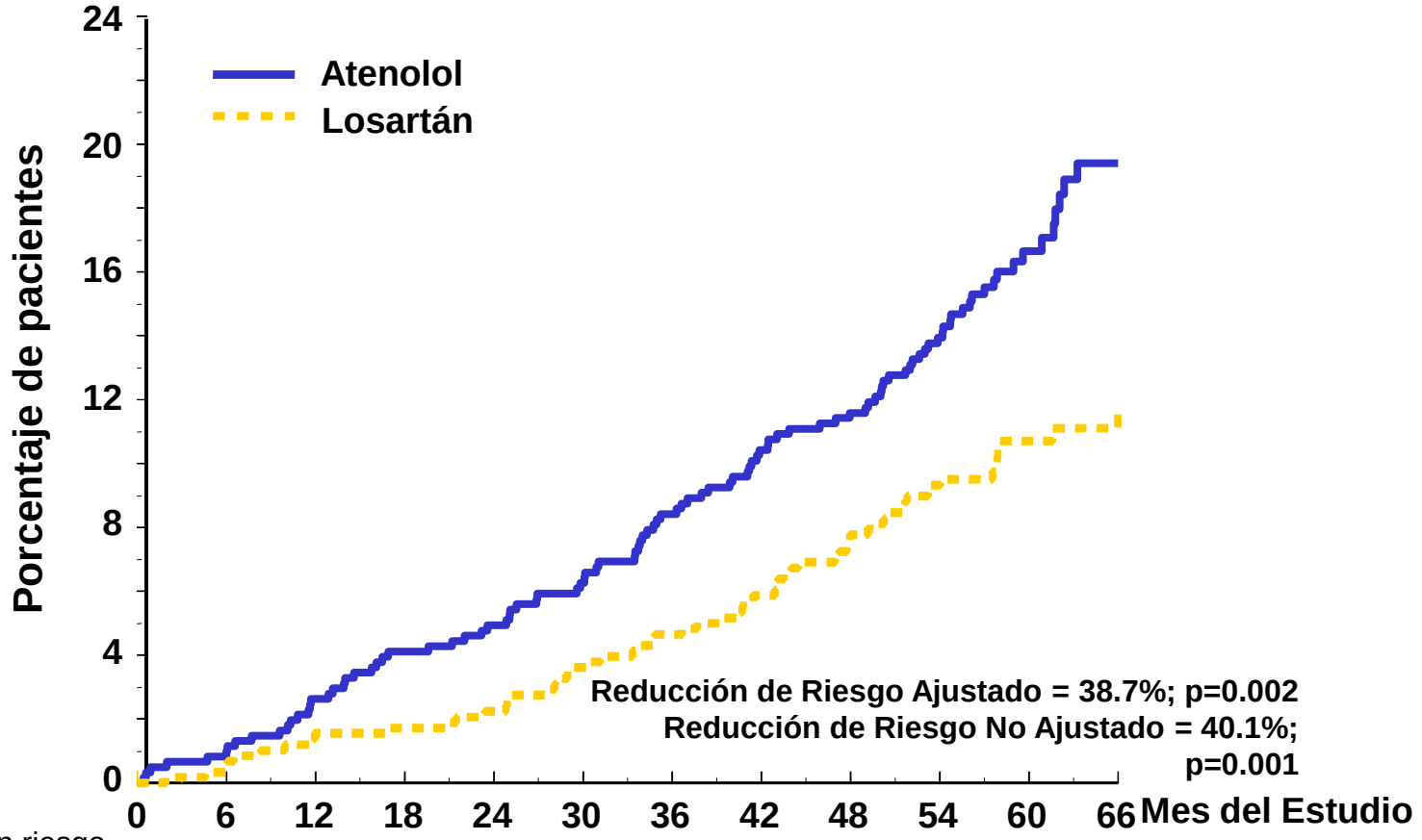
Effecto of Irbesartan sobre marcadores de inflamación



N = 33 normotensive CAD patients (Irbesartan 75 mg–150 mg for 24 weeks).

Reprinted with permission from Navalkar S et al. *J Am Coll Cardiol*. 2001; 37:440–444.

Pacientes Diabéticos – Mortalidad Total

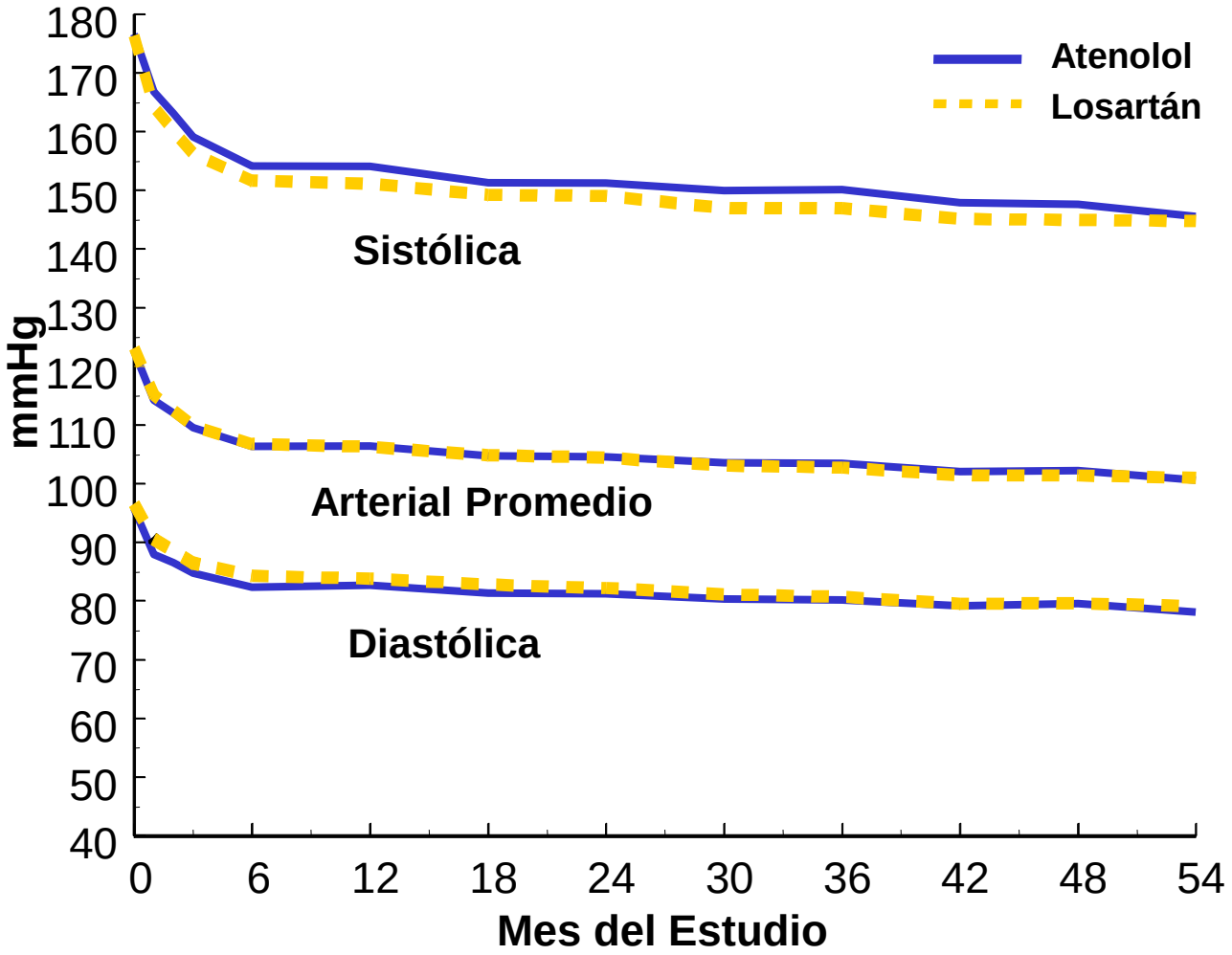


Número en riesgo												
Losartán	586	579	573	572	566	558	552	543	533	513	265	136
Atenolol	609	604	592	582	576	566	552	537	529	495	232	113

Lindholm LH y cols. *Lancet* 2002; 359:1004-1010.

Pacientes Diabéticos

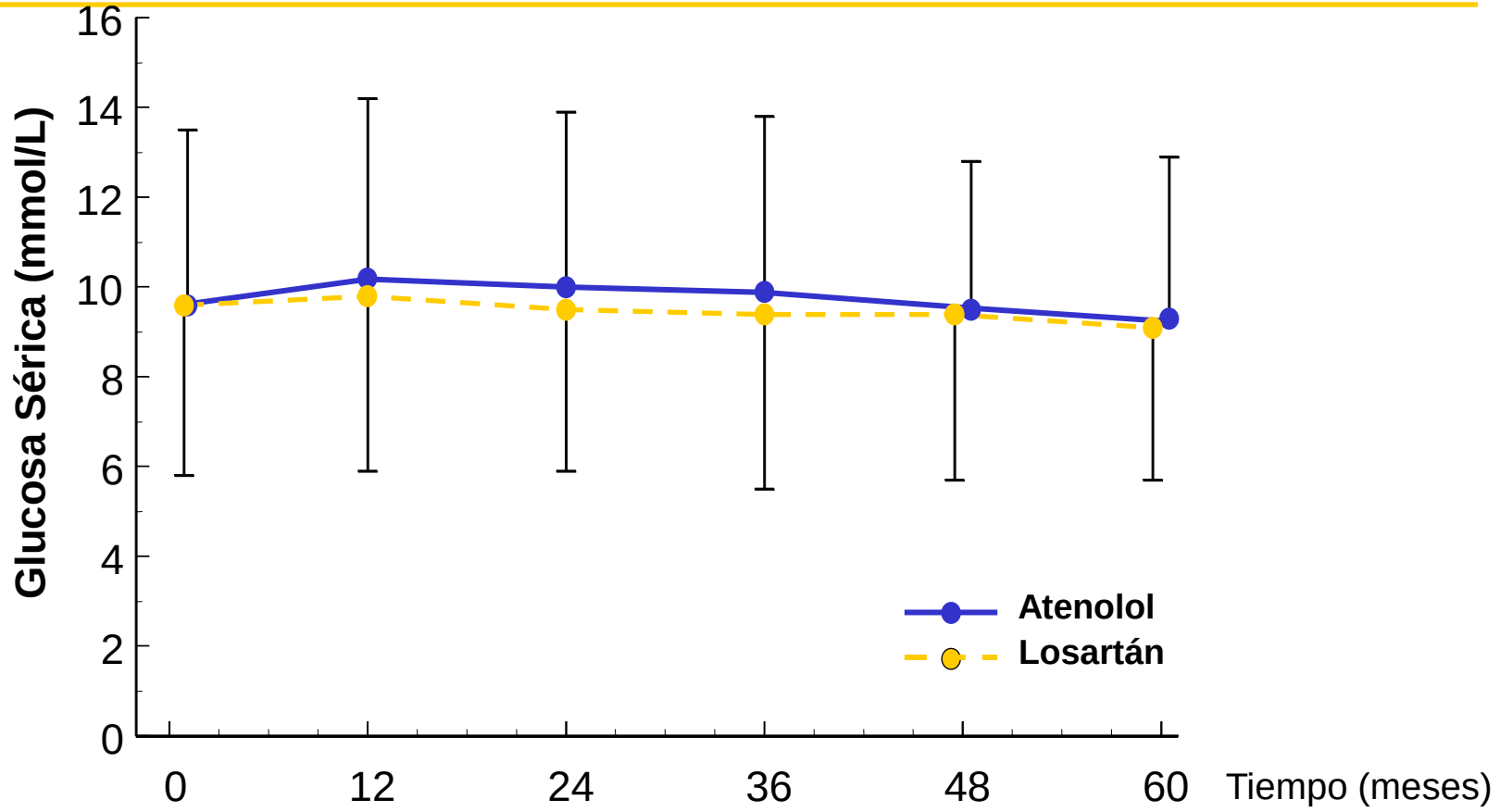
Presión Arterial Durante el Seguimiento



Lindholm LH y cols. *Lancet* 2002; 359:1004-1010.

Pacientes Diabéticos

Concentraciones de Glucosa Sérica no en Ayuno

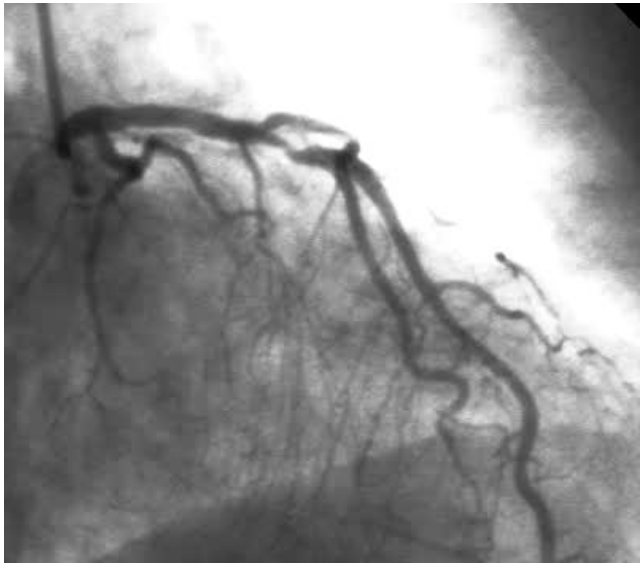


Losartán (n)	563	521	503	494	471	345
Atenolol (n)	580	548	514	473	461	306

Lindholm LH y cols. *Lancet* 2002; 359:1004-1010.

Introducción

- La enfermedad vascular ateroesclerosa está asociada a marcadores de riesgo bien identificados
- Una proporción significativa no presenta marcadores clínicos clásicos de riesgo vascular
- La hiperglucemia y la albuminuria han sido identificados como marcadores asociados a disfunción endotelial y ateroesclerosis



Relación directa de diferentes grados de albuminuria con hiperlipidemia e hipertensión arterial en pacientes con diabetes mellitus tipo 2

Domínguez-Reyes CA.*
Bravo-Ornelas Nubia*
Paredes-Ureña Enriqueta*

BIOMÉDICA Número cero, oct-dic. del 2005

CARACTERISTICAS GENERALES

VARIABLE	GPO A 1 VASO	GPO B 2 VASOS	GPO C 3 VASOS
N (%)	14 (25)	16 (28)	26 (47)
Género M (%)	(55)	(69)	(78)
Edad (DE)	50.8 (10)	61.2 (9)	60.4 (8)
Tabaquismo (%)	45	52	56
DM	65	71	75
HbA1c (DE)	6.0 (0.9)	6.8 (1.2)	7.3 (1.8)

DISTRIBUCION DE VARIABLES CLINICAS

VARIABLE	GPO A 1 VASO	GPO B 2 VASOS	GPO C 3 VASOS	P* (A vs C)
TA SIST (mmHg)	121 +/- 12	131 +/- 18	137 +/- 21	0.03
TA DIAS (mmHg)	76 +/- 10	87 +/- 13	88 +/- 14	0.02
C – LDL (mg/dl)	95 +/- 45	93 +/- 38	107 +/- 35	NS
C noHDL (mg/dl)	112 +/- 56	107 +/- 38	121 +/- 45	NS
GA(mg/dl)	118 +/- 21	107 +/- 31	137 +/- 44	NS
G PP-2hr (mg/dl)	125 +/- 26	161 +/- 30	201+/- 53	0.001

* Prueba t de Student no pareada

DISTRIBUCION DE VARIABLES CLINICAS

VARIABLE	GPO A 1 VASO	GPO B 2 VASOS	GPO C 3 VASOS	P* (A vs C)
Albuminuria (mg/dl)	14.2 +/- 6	91 +/- 85	163 +/- 102	0.013
Rel Alb/Cr (mg/g)	19.7 +/- 9	128 +/- 78	245 +/- 56	0.006

* Prueba t de Student no pareada

ANALISIS DE VARIANZA DE LOS 3 GRUPOS

Test Statistics[a,b]

	GP2H	HbA1c	Albúmna Ur#	Rel# Alb/Cr#	TAS	TAD	Glucosa	CT	NHDL	HDL	LDL
Chi-Square	15.863	3.248	5.581	6.838	4.182	5.039	2.399	.756	1.458	.356	1.150
df	2	2	2	2	2	2	2	2	2	2	2
Asymp. Sig.	.000	.197	.061	.033	.124	.081	.301	.685	.482	.837	.563

a. Kruskal Wallis Test

b. Grouping Variable: EAC

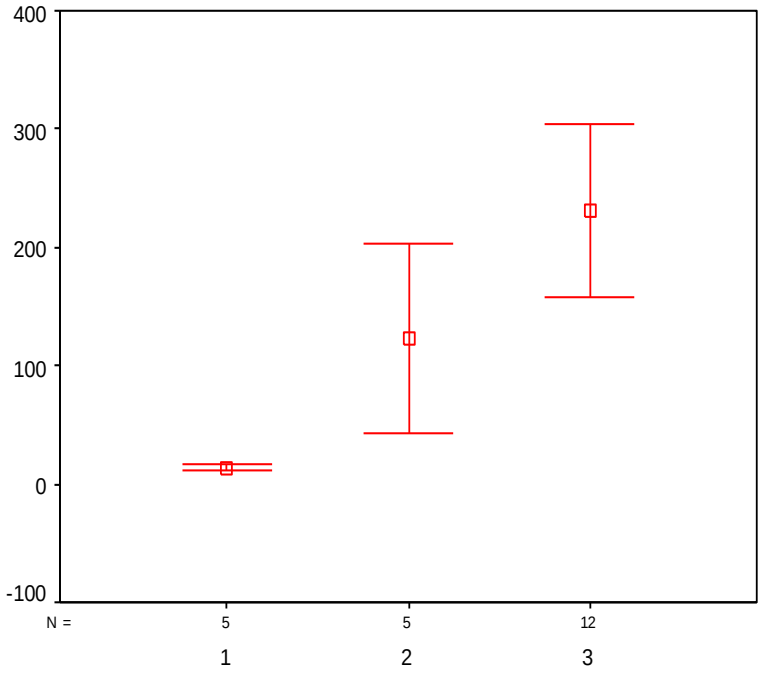
Análisis de regresión multivariado

Coefficients[a]

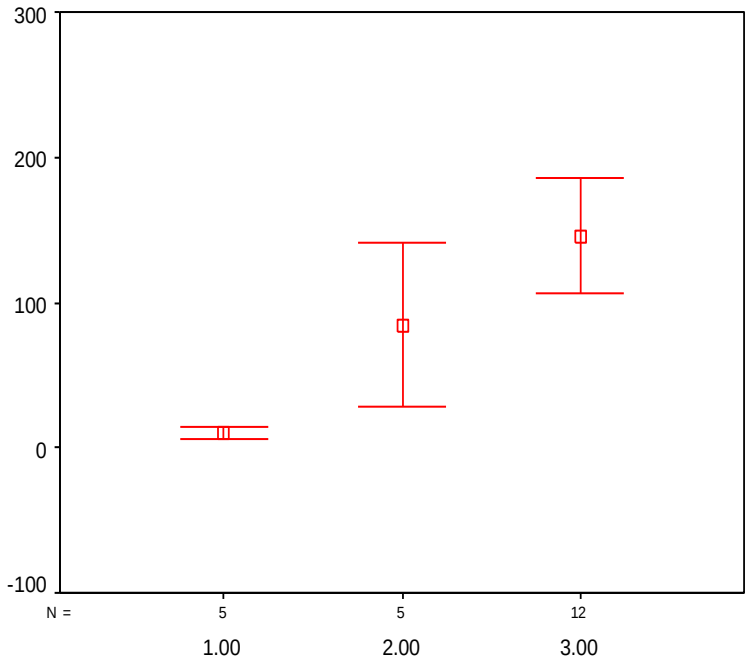
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	.174	1.171		.148	.884
	GP2H	1.508E-02	.004	.653	3.598	.002
	HbA1c	-.069	.083	-.176	-.842	.412
	Albúmna Ur#	1.863E-03	.001	.283	1.272	.222
	Rel# Alb/Cr#	1.011E-03	.001	.263	1.202	.247
	DM-2	-.201	.331	-.123	-.607	.552

a. Dependent Variable: EAC

Marcadores de gravedad no clásicos



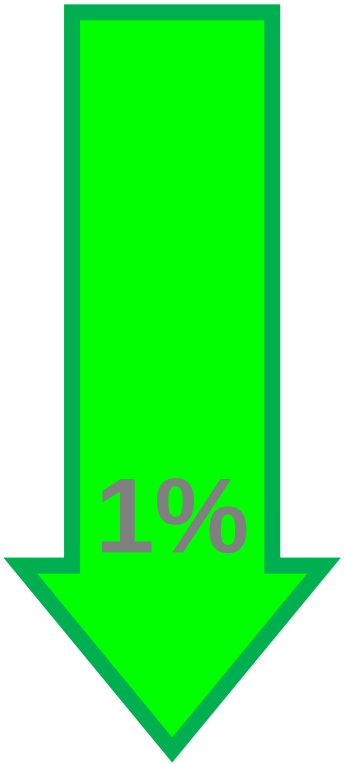
Relación Alb/Cr Ur P= 0.006



Albuminuria p= 0.013

Mejor control:
Significa menos complicaciones

Cada 1%
de reducción en HbA_{1C}



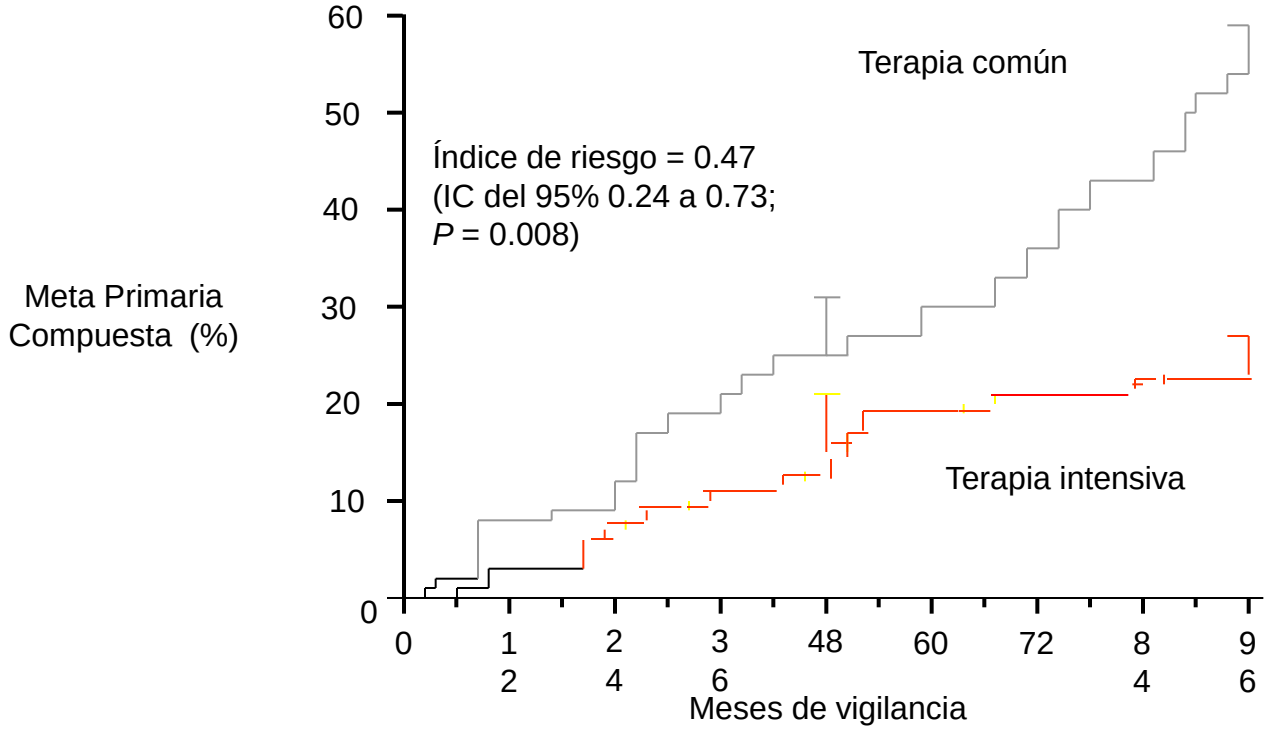
Reducción de riesgo*

Muertes por diabetes	-21%
Ataques cardiacos	-14%
Complicaciones microvasculares	-37%
Enfermedad arterial periférica	-43%

*p<0.0001

UKPDS 35. BMJ 2000; 321: 405-12

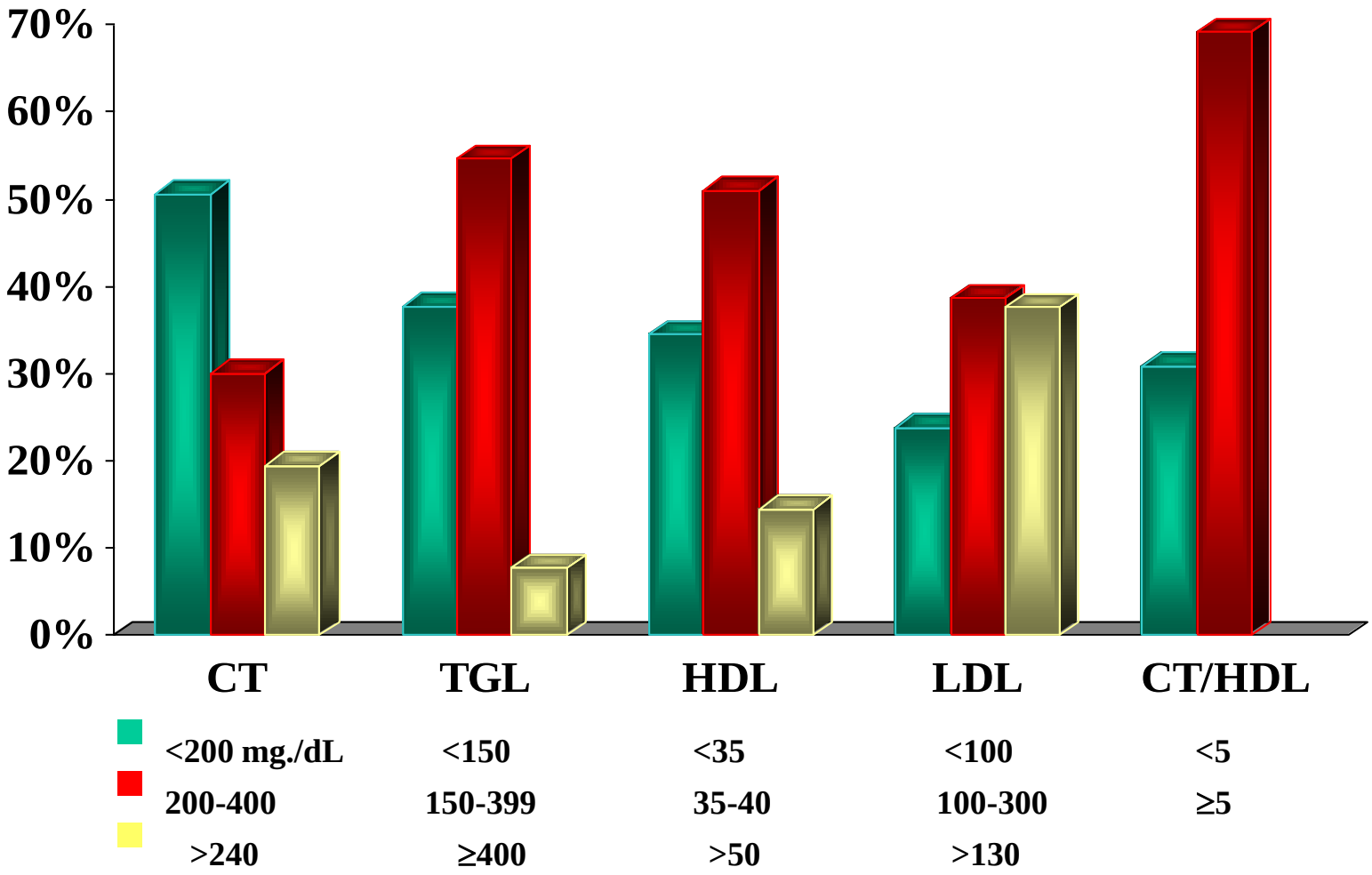
STENO 2: La terapia intensiva reduce la morbilidad y mortalidad por ECV



Meta compuesta = Muerte por causas CV, IM no fatal, injerto de derivación de las arterias coronarias, Intervención percutánea coronaria, apoplejía no fatal, amputación, o cirugía en una enfermedad de arterias ateroscleróticas periféricas.

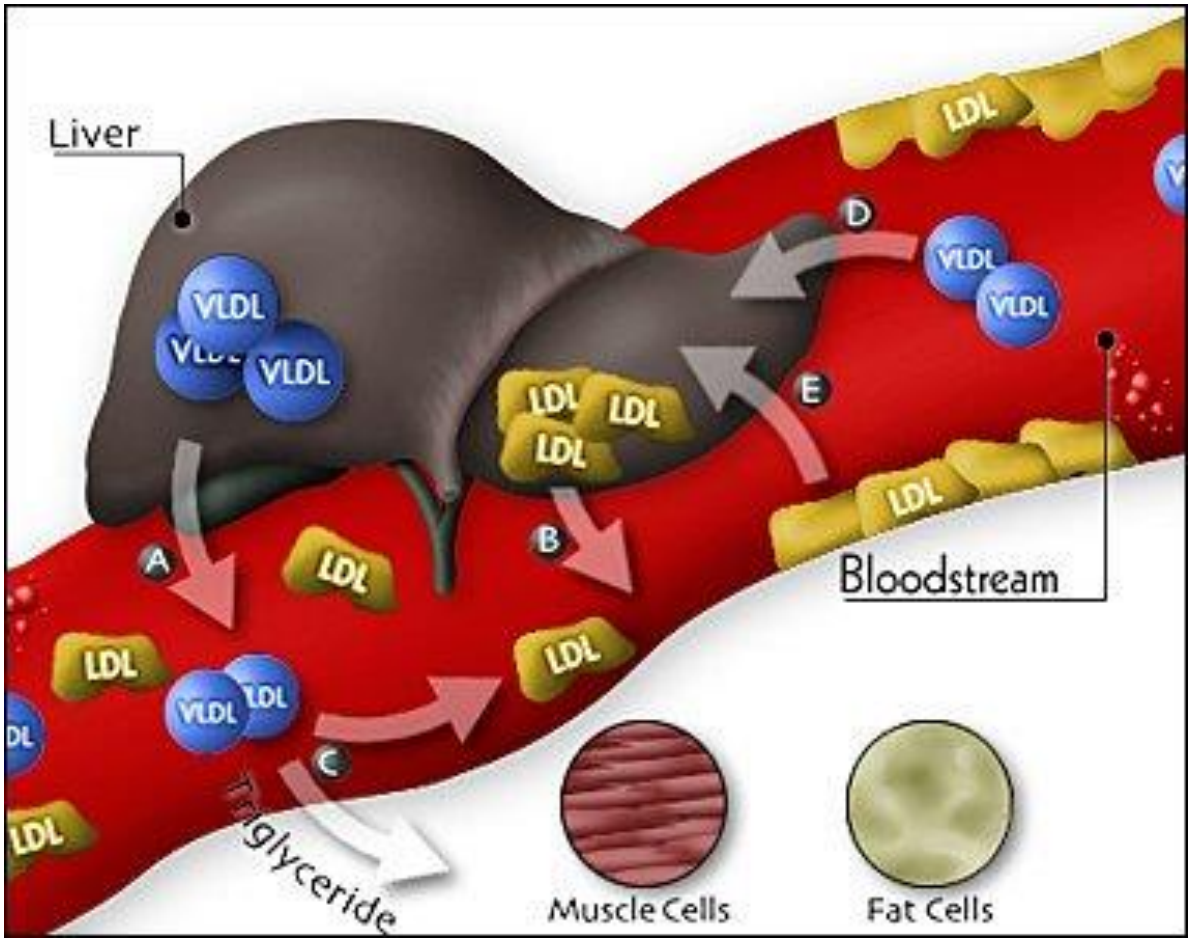
Gaede P et al. *N Engl J Med.* 2003;348:383-393.

Qué tan frecuente es la hiperlipidemia en la población con DM tipo 2 ?

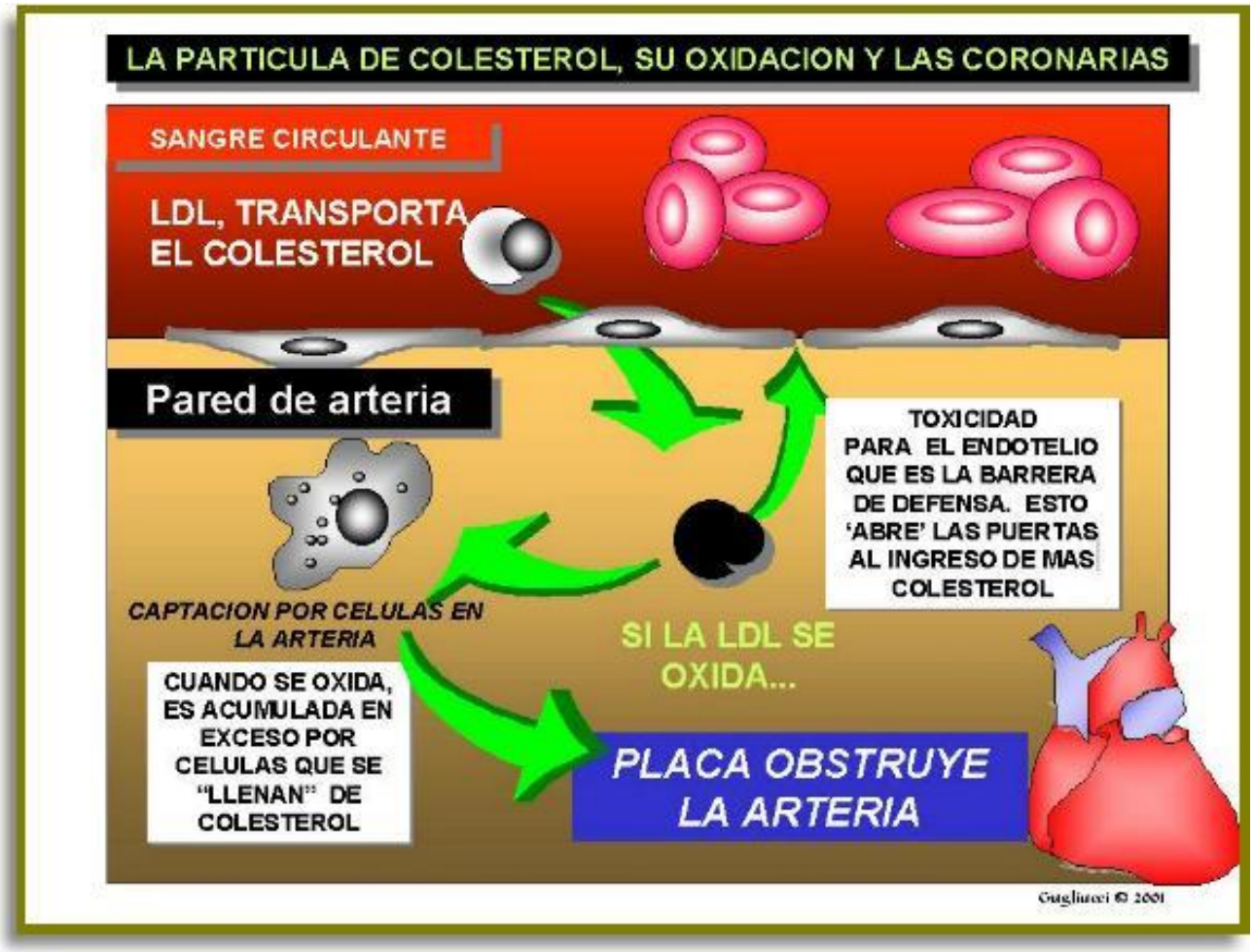


terol, 3.06 mmol/l. The most prevalent abnormality was HDL cholesterol below 0.9 mmol/l (46.2% for men and 28.7% for women). Hypertriglyceridemia (>2.26 mmol/l) was the second most prevalent abnormality (24.3%). Severe hypertriglyceridemia (>11.2 mmol/l) was observed in 0.42% of the population. Increased LDL cholesterol (≥4.21 mmol/l) was observed in 11.2% of the sample. Half of the hypertriglyceridemic subjects had a mixed dyslipidemia or low HDL cholesterol. More

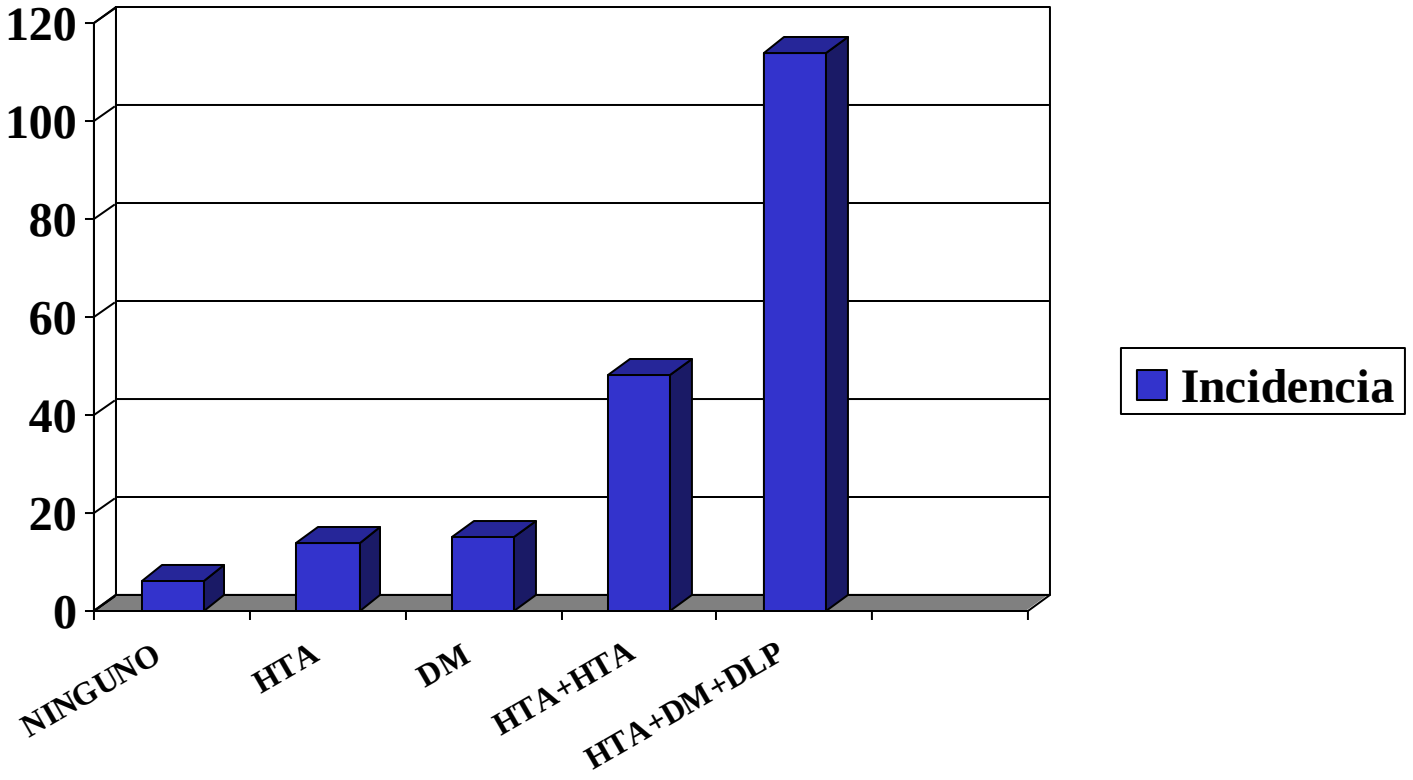
Metabolismo de lípidos y lipoproteínas (VLDL y LDL)



Anormalidades funcionales de lípidos en DM



Estudio PROCAM
Interacción de factores de riesgo
(n = 2574)



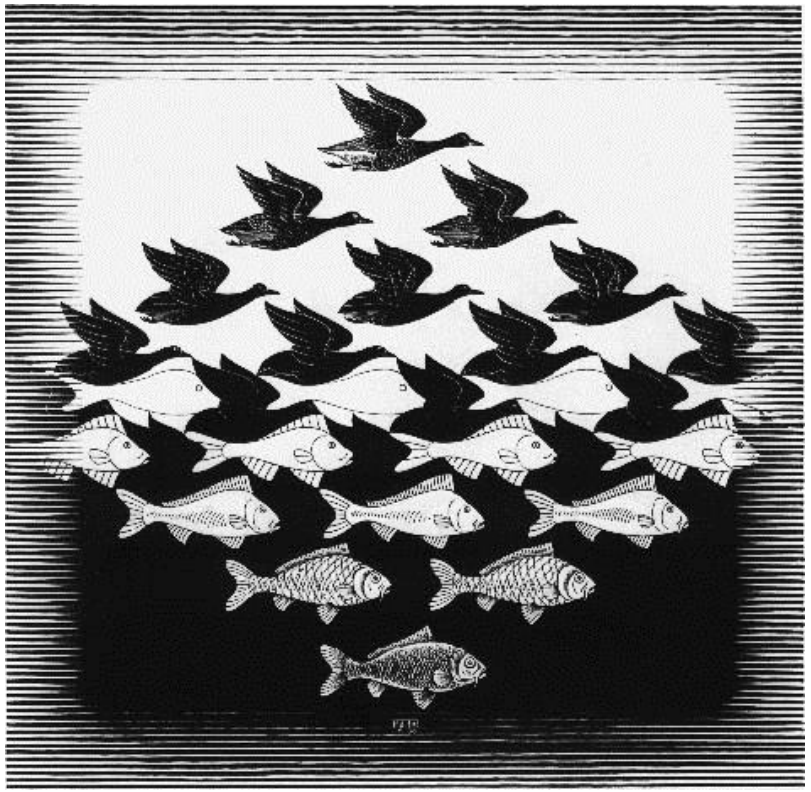
Adaptado de Assman G. Am Heart J 1998; 116:1713-24

Hipertrigliceridemia: un factor de riesgo cardiovascular?

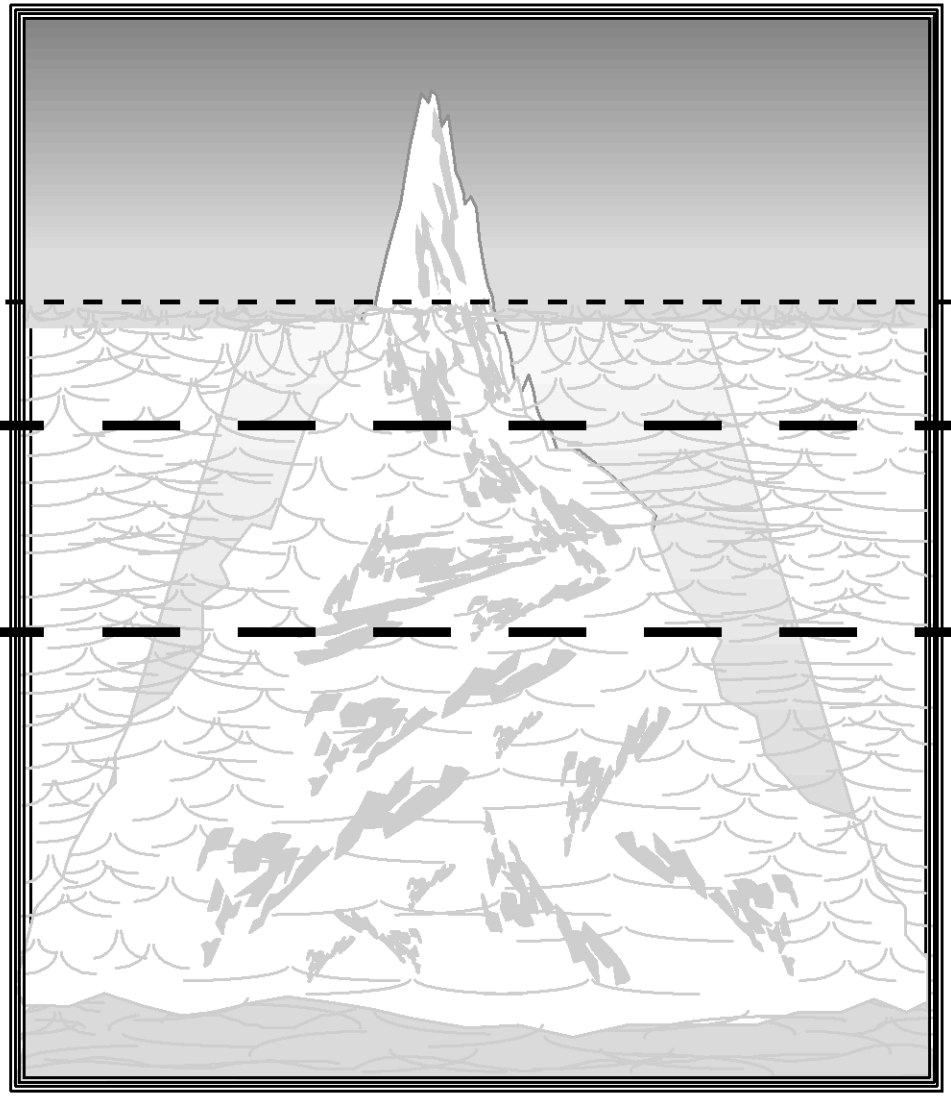
- No se deposita en el endotelio vascular
- El efecto proaterogéncio se relaciona con el incremento de moléculas saturadas con TGL
- Se eleva la actividad tranferasa de esteres de colestrol y resulta en aumento de IDL y disminución de HDL

Dislipidemia: Factor de riesgo ó marcador metabólico?

- No es solo FR cardiovascular
- Manifestación concomitante frecuente de enfermedades sistémicas o alteraciones metabólicas
- Indicador de tamizaje para otros trastornos



El "ICEBERG" de la Diabetes



Personas con
Diabetes: 4-5 millones

Horizonte clínico

30% desconocen su enfermedad

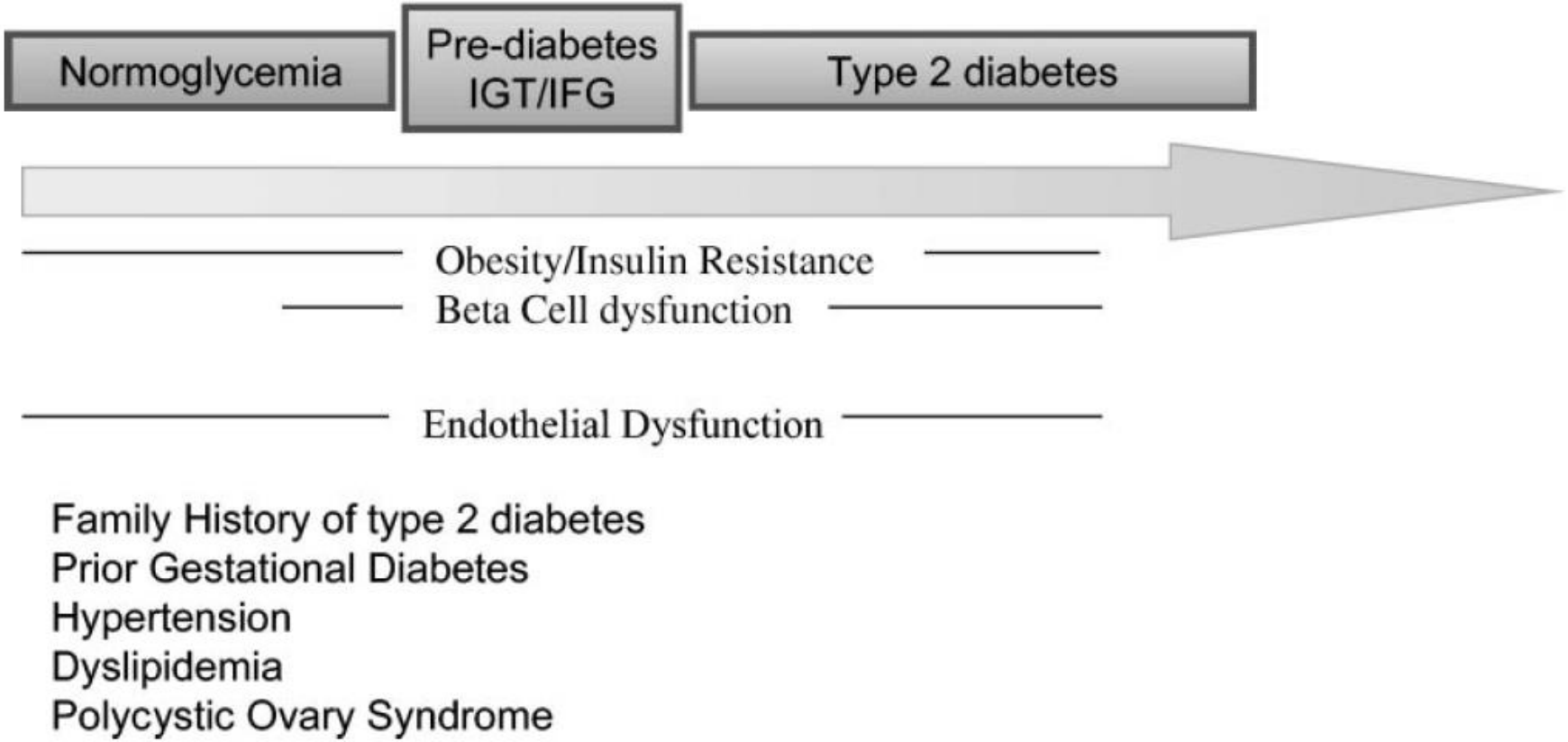
(cambio irreversible)

Personas con intolerancia a la glucosa (8-9 millones)

(cambio reversible)

Población sin diabetes, (expuesta a factores de riesgo) (35-37 millones)

White M. F. y Gutiérrez H., Seminario Internacional: La Diabetes, un Reto para la Salud Pública y los Servicios de Salud. Nov. 4-5 de noviembre de 1996.



OBESITY RESEARCH Vol. 11 No. 11 November 2003

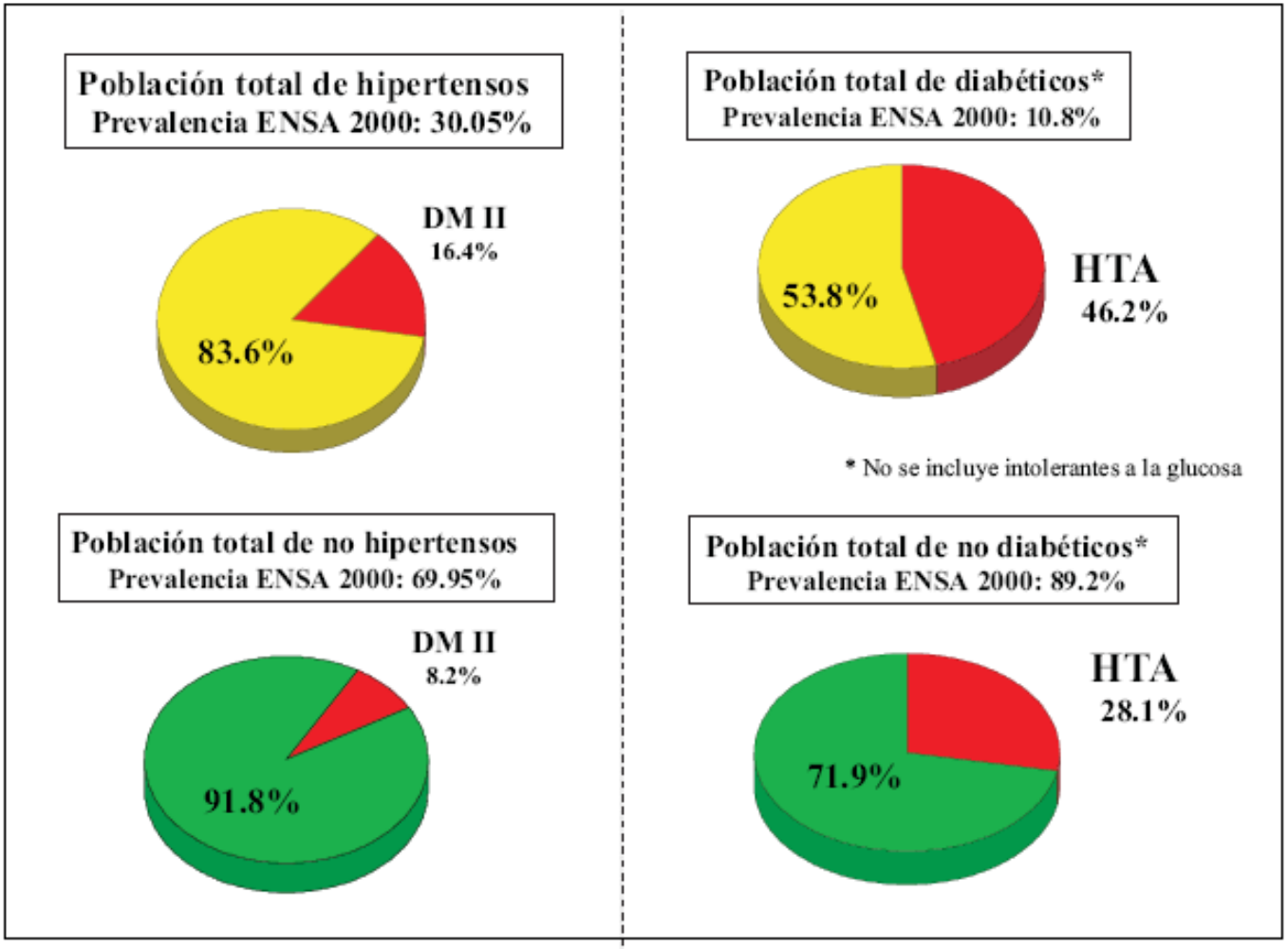
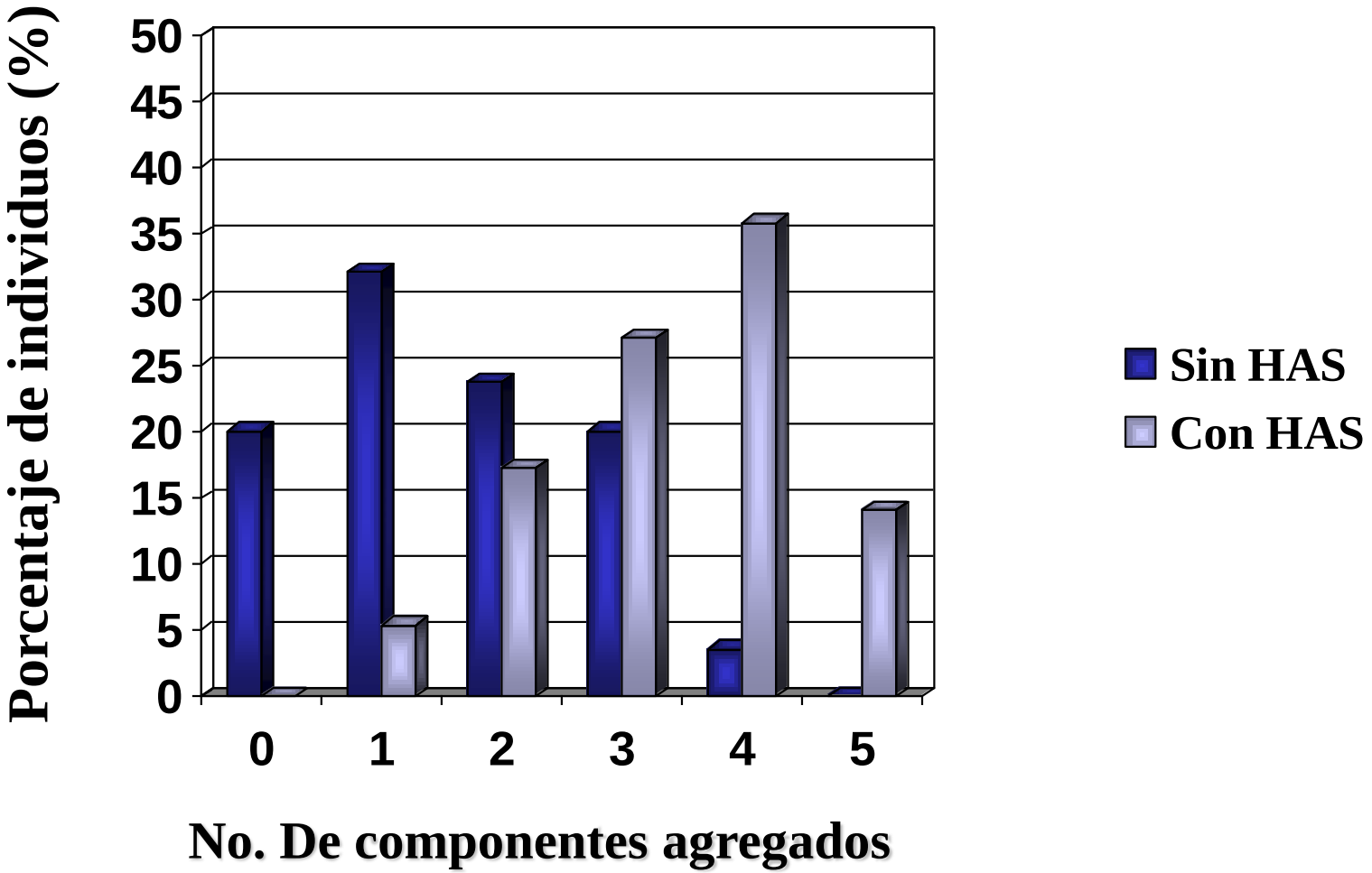


Fig. 8. Relación bidireccional en la prevalencia de HTAS y DM-2. Note que la presencia de una duplica el riesgo de la prevalencia de la otra.

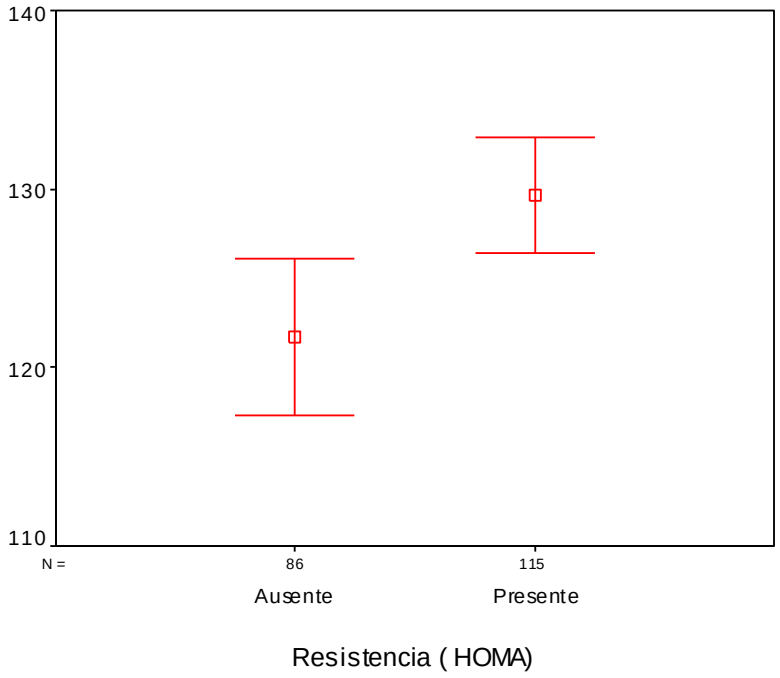
Distribución porcentual de agregación de los componentes del síndrome metabólico en los grupos con y sin hipertensión

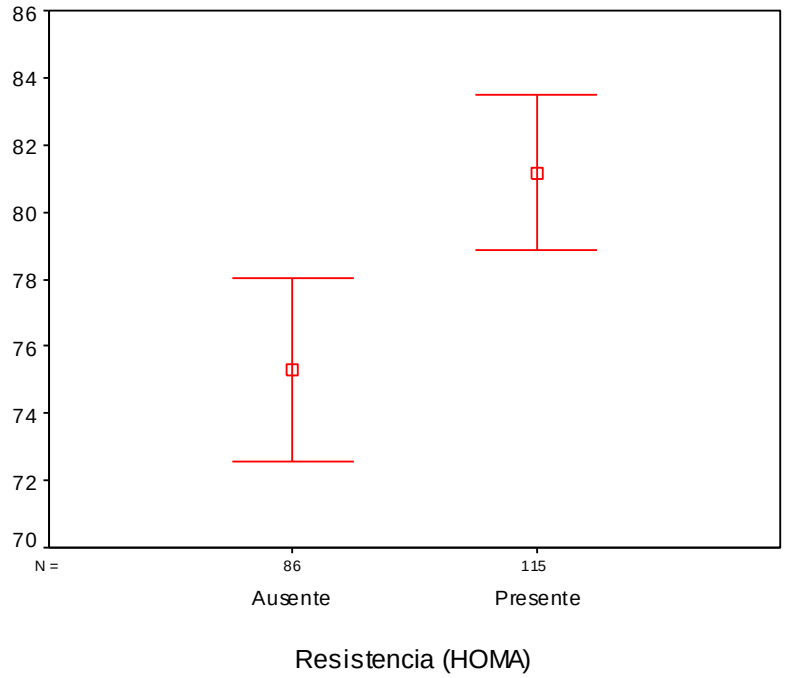


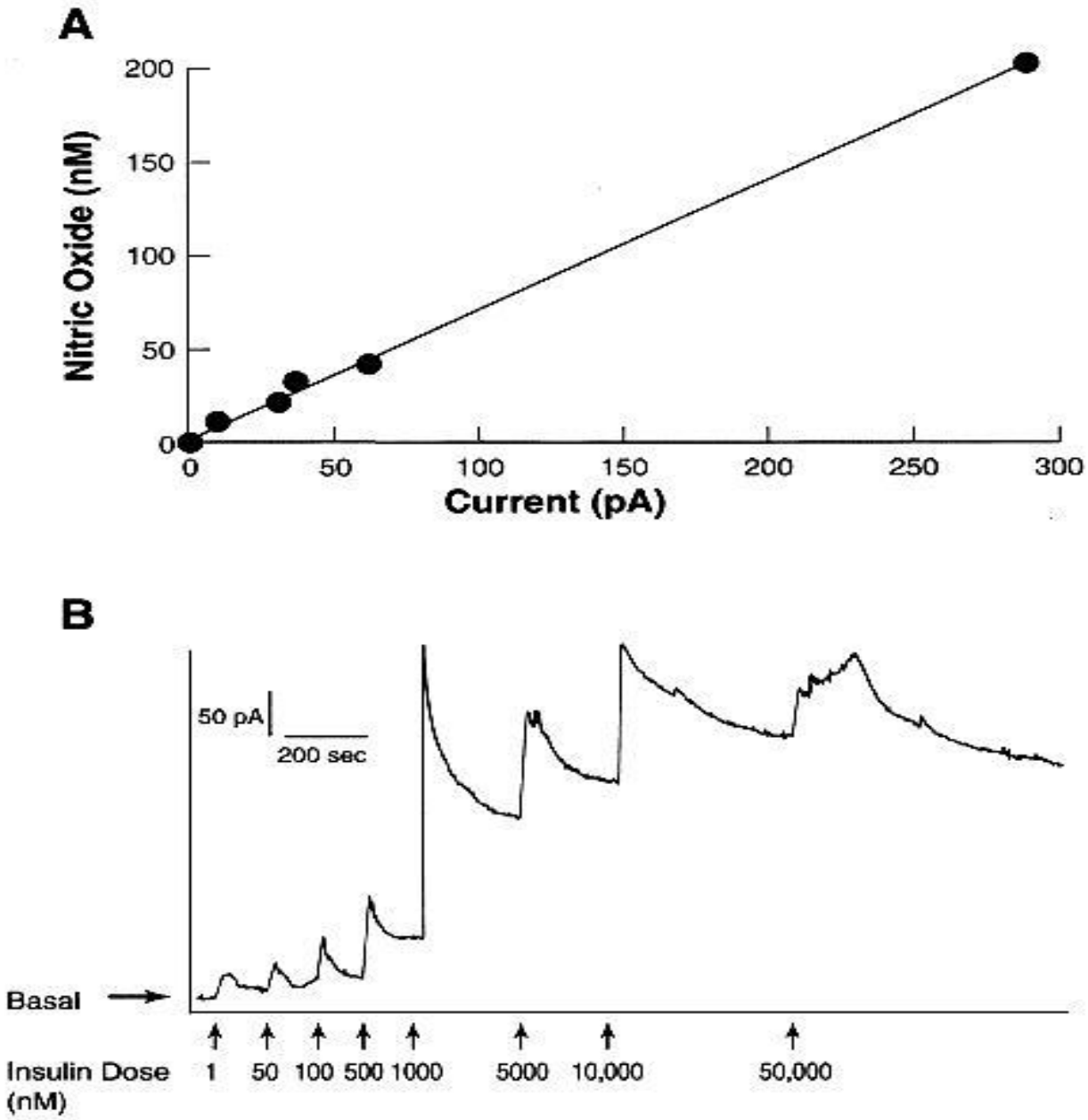
	Personas con Hipertensión (n=92)		
	Sin RI (n=33)	Con RI (n=59)	
Variables	**Media (DE)**	**Media (DE)**	**(*P*)**
Edad (años):	**55.4±14.3**	**45.4±14.4**	**<0.002**
IMC (Kg/m^2)	**28.7±3.7**	**36.1±7.3**	**<0.001**
Glucosa en ayuno(mg/dL)	**99.0±13.0**	**117±55.7**	**0.006**
Glucosa a 2 hr (mg/dL)	**121 ±48.9**	**165.5±88.4**	**0.105**
Colesterol total (mg/dL)	**215.7±43.3**	**212.7±47.2**	**0.775**
Trigliceridos (mg/dL)	**158.9±1109**	**221.8±116**	**0.011**
Colesterol HDL (mg/dL)	**41.8±9.3**	**41.6±12.7**	**0.946**
Colesterol LDL (mg/dL)	**131.8±41.4**	**131.8±41.9**	**<0.340**
No de componentes	**2.6±1.1**	**3.7±8.6**	**<0.001**

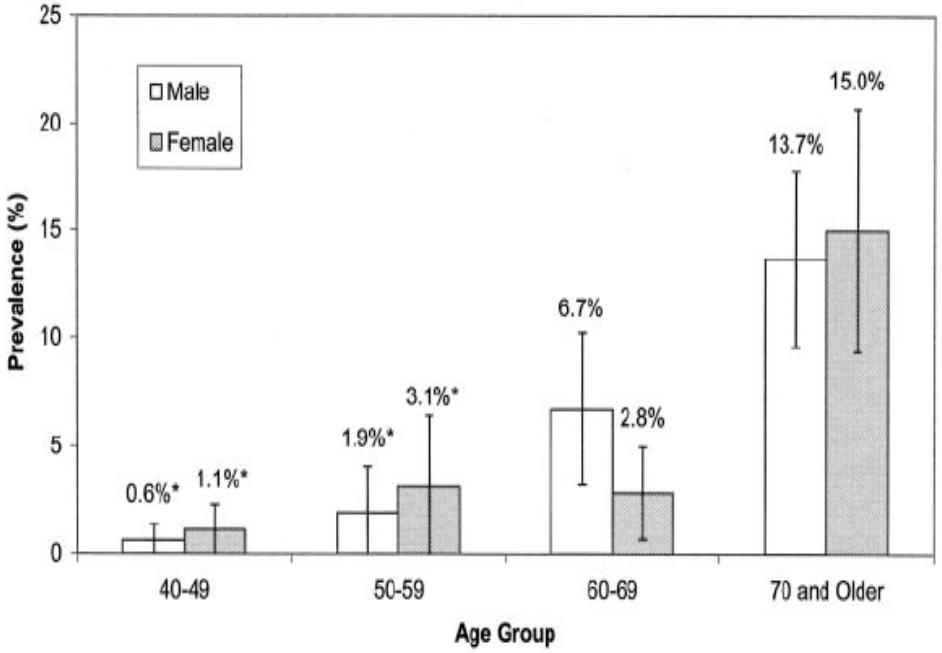
	Personas Sin Obesidad (n=104)		
	Con HAS (n=33)	Sin HAS (n=71)	
Variables	**Media (DE)**	**Media (DE)**	**(*P*)**
Edad (años):	**58.7 ±12.9**	**33.5±10.0**	**<0.001**
Glucosa en ayuno(mg/dL)	**115.0 ±67**	**84.3 ±10.8**	**0.013**
Glucosa a 2 hr (mg/dL)	**159.8 ±130**	**101 ±29.3**	**0.086**
Colesterol total (mg/dL)	**212.0 ±40.3**	**181 ±32.9**	**0.001**
Triglicéridos (mg/dL)	**172.8 ±98.9**	**126.8 ±65.4**	**0.019**
Colesterol HDL (mg/dL)	**40.7 ± 9.9**	**45.0 ±13.0**	**0.064**
Colesterol LDL (mg/dL)	**139.6 ±38.7**	**109.1 ±30.6**	**<0.001**
Factores	**2.6 ±1.0**	**1.0 ±0.85**	**<0.001**
HOMA	**4.2 ±3.5**	**2.4 ±1.3**	**0.134**

Efecto de la resistencia a la insulina sobre la presión arterial






A
Nitric Oxide (nM)
200
150
100
50
0
0
50
100
150
200
250
300
Current (pA)
B
50 pA
200 sec
Basal
Insulin Dose (nM)
1
50
100
500
1000
5000
10,000
50,000



Prevalence of PAD by age and gender, adults 40 years and older, United States, 1999–2000 (n=2174). Error bars are 95% CIs. *Estimate has relative standard error >30%.

TABLE 2. Cardiovascular Disease Risk Factors Among Persons With and Without Prevalent PAD, Adults Aged 40 Years and Older, United States, 1999–2000 (n=2174)

	Prevalent PAD (n=141), % (SE)	No PAD (n=2033), % (SE)
Mean age, y	68.7 (1.5)	55.7 (0.4)
Male, %	46.2 (5.8)	48.2 (0.8)
Hypertension, %	73.6 (4.7)	45.4 (1.7)
Hypercholesterolemia, %	60.6 (4.5)	44.9 (1.5)
Diabetes, %	26.4 (8.4)	10.1 (1.5)
Current smoking, %	32.8 (5.5)	20.3 (1.4)
Hypertension, hypercholesterolemia, diabetes, or current smoking, %	95.2 (2.7)	75.7 (1.4)

Diabetic Patients Detected by Population-Based Stepwise Screening Already Have a Diabetic Cardiovascular Risk Profile

ANNEMIEKE M.W. SPIJKERMAN, MSC[1]
MARCEL C. ADRIAANSE, MSC[1]
JACQUELINE M. DEKKER, PHD[1]
GIEL NIJPELS, MD, PHD[1]
COEN D.A. STEHOUWER, MD, PHD[1,2]
LEX M. BOUTER, PHD[1]
ROBERT J. HEINE, MD, PHD[1,3]

based or universal screening attempts to screen every person in the entire population or in an entire age-group. Selective or targeted screening is directed at individuals with a high prevalence of risk factors.

RESULTS — A total of 11,679 inhabitants of the West-Friesland region of the Netherlands, aged 50–75 years, were invited. Of the inhabitants, 9,169 (78%) responded, and, of those, 417 had previously diagnosed diabetes. The SRQ score was calculated for 7,736 participants, and 3,301 of those had a score of >6. A total of 2,885 subjects (87.3%) attended for capillary glucose measurement. Diagnostic testing was carried out in 509 participants, and we identified 217 diabetic patients. In these patients detected by screening, mean HbA_{1c} was 6.7% (±1.4). Hypertension and high total cholesterol levels (>5.0 mmol/l) were present in 70%, 33% had high triglyceride (>3.0 mmol/l) or low HDL cholesterol levels (<1.0 mmol/l in men and <1.1 mmol/l in women), and 40% were obese (BMI ≥30 kg/m^2).

CONCLUSIONS — The high response rate was the main feature of the screening by means of the Symptom Risk Questionnaire and fasting capillary glucose measurement followed by diagnostic testing. The 217 diabetic patients detected by the screening were characterized by relatively low HbA_{1c} levels and by a cardiovascular risk profile typical of diabetic patients.

Diabetes Care 25:1784–1789, 2002

Table 3—*Clinical characteristics of screening-detected diabetic patients*

	All SDM	Non–OGTT-SDM	OGTT-SDM	
			2-h SDM	Mixed OGTT-SDM
n	195	33	29	133
HbA_{1c} (%)	6.7 ± 1.4	8.8 ± 1.5*	5.8 ± 0.5†	6.4 ± 0.9
Cholesterol (mmol/l)	5.7 ± 1.1	5.7 ± 1.2	5.5 ± 1.0	5.8 ± 1.1
High cholesterol (%)	73.1	66.7	69.0	75.6
HDL cholesterol (mmol/l)	1.3 ± 0.4	1.2 ± 0.3	1.3 ± 0.4	1.3 ± 0.4
Low HDL				
Women (%)	27.7	43.8	0†	28.8
Men (%)	35.4	11.8*	16.7	41.5
Cholesterol/HDL ratio	4.84 ± 1.45	5.00 ± 1.77	4.46 ± 1.29	4.88 ± 1.39
High cholesterol/HDL ratio (%)	35.9	36.4	27.6	44.3
LDL cholesterol (mmol/l)	3.57 ± 0.96	3.59 ± 0.96	3.46 ± 0.81	3.59 ± 0.99
High LDL (%)	77.2	74.2	71.4	79.2
Triglycerides (mmol/l)	1.7 (1.2–2.4)	1.6 (1.2–2.4)	1.4 (1.0–1.9)†	1.8 (1.3–2.4)
High triglycerides (%)	34.2	33.3	17.2†	38.2
Lipid-lowering therapy (%)	20.4	13.9	25.0	20.8
BMI (kg/m^2)	29.8 ± 5.3	29.9 ± 6.4	28.4 ± 4.1	30.1 ± 5.3
Obesity (%)	40.0	36.4	31.0	42.9
Systolic blood pressure (mmHg)	141 ± 18	141 ± 19	148 ± 15†	140 ± 19
Diastolic blood pressure (mmHg)	86 ± 10	88 ± 11	88 ± 8	85 ± 9
Antihypertensive medication (%)	45.2	38.9	44.4	47.2
Hypertension (%)	69.6	69.4	75.0	68.3

Data are means ± SD for continuous variables and median (interquartile range) for triglycerides. High total cholesterol: cholesterol >5.0 mmol/l; low HDL cholesterol: HDL cholesterol <1.0 mmol/l for men and HDL cholesterol <1.1 for women; high LDL cholesterol: LDL cholesterol ≥3.0 mmol/l; high triglycerides: triglycerides >2.0 mmol/l; high cholesterol/HDL cholesterol ratio >5. Obesity: BMI ≥30 kg/m^2. Hypertension: diastolic blood pressure ≥90 mmHg, systolic blood pressure ≥140 mmHg, and/or use of antihypertensive medication. 2-h SDM group, 2-h value of the OGTT decisive for diagnosis, with none or only one elevated fasting value; mixed SDM group, two elevated fasting values or two elevated fasting and elevated 2-h values; non–OGTT SDM, patients with fasting capillary glucose >8.5 mmol/l, diagnosed on two fasting values, with no OGTT performed; OGTT-SDM, patients diagnosed on OGTT. *High fasting SDM significantly different from OGTT-SDM; †2-h SDM significantly different from mixed SDM.

Diabetes Mellitus

Subclinical Cardiovascular Disease and Risk of Incident Cardiovascular Disease and All-Cause Mortality

Lewis H. Kuller, Priscilla Velentgas, Joshua Barzilay, Norman J. Beauchamp, Daniel H. O'Leary, Peter J. Savage

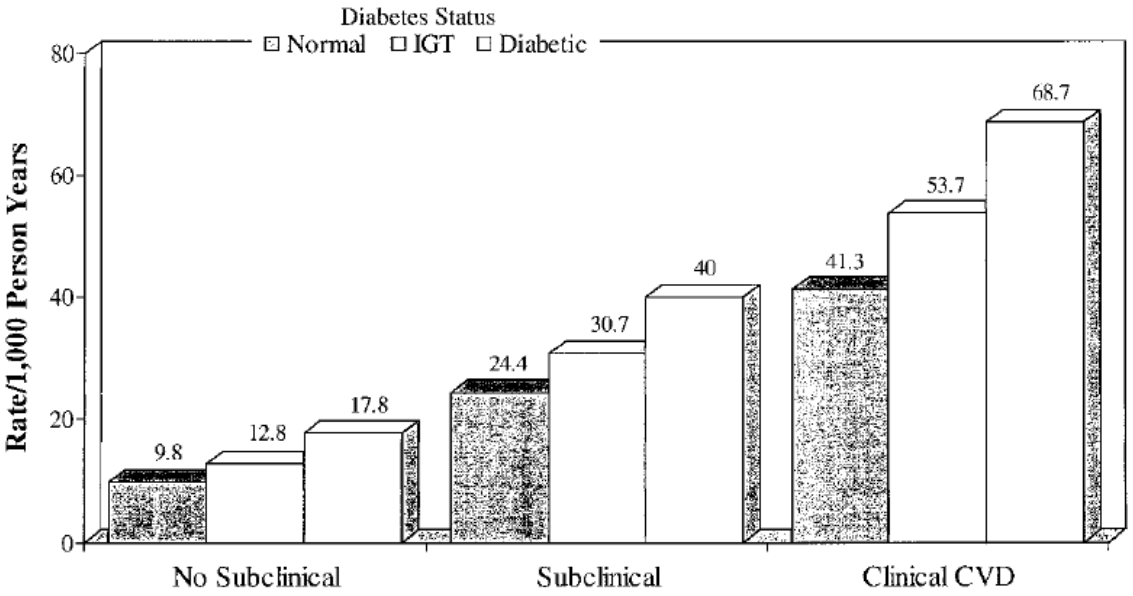
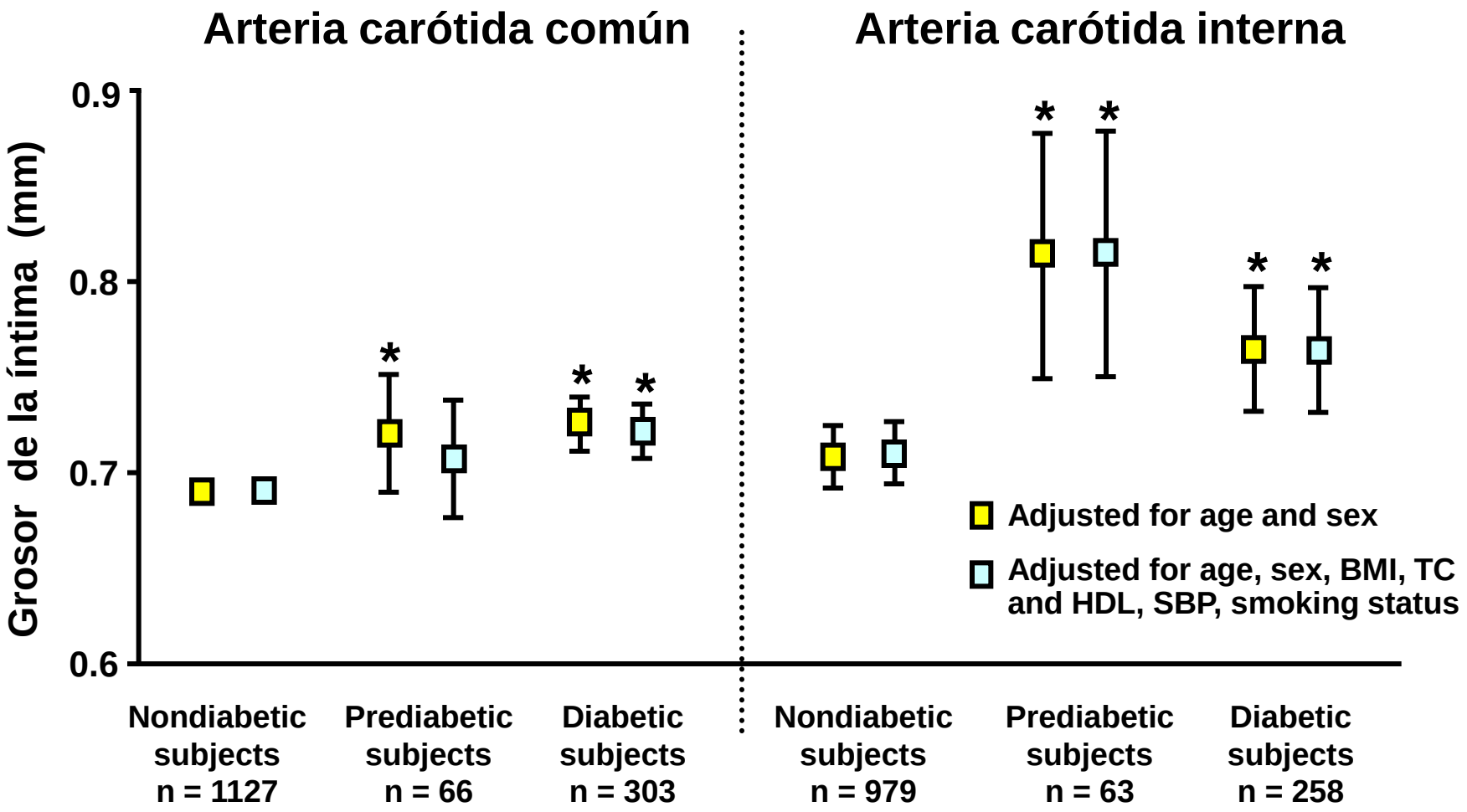


Figure 1. Diabetes status and presence of subclinical/clinical CVD at baseline and incidence of specific events among men and women in the CHS (outcome: death).

Mexico City Diabetes Study: La aterogénesis temprana se presenta antes del inicio de la diabetes



Hunt KJ, *et al. Arterioscler Thromb Vasc Biol* 2003; 23:1845–1850.

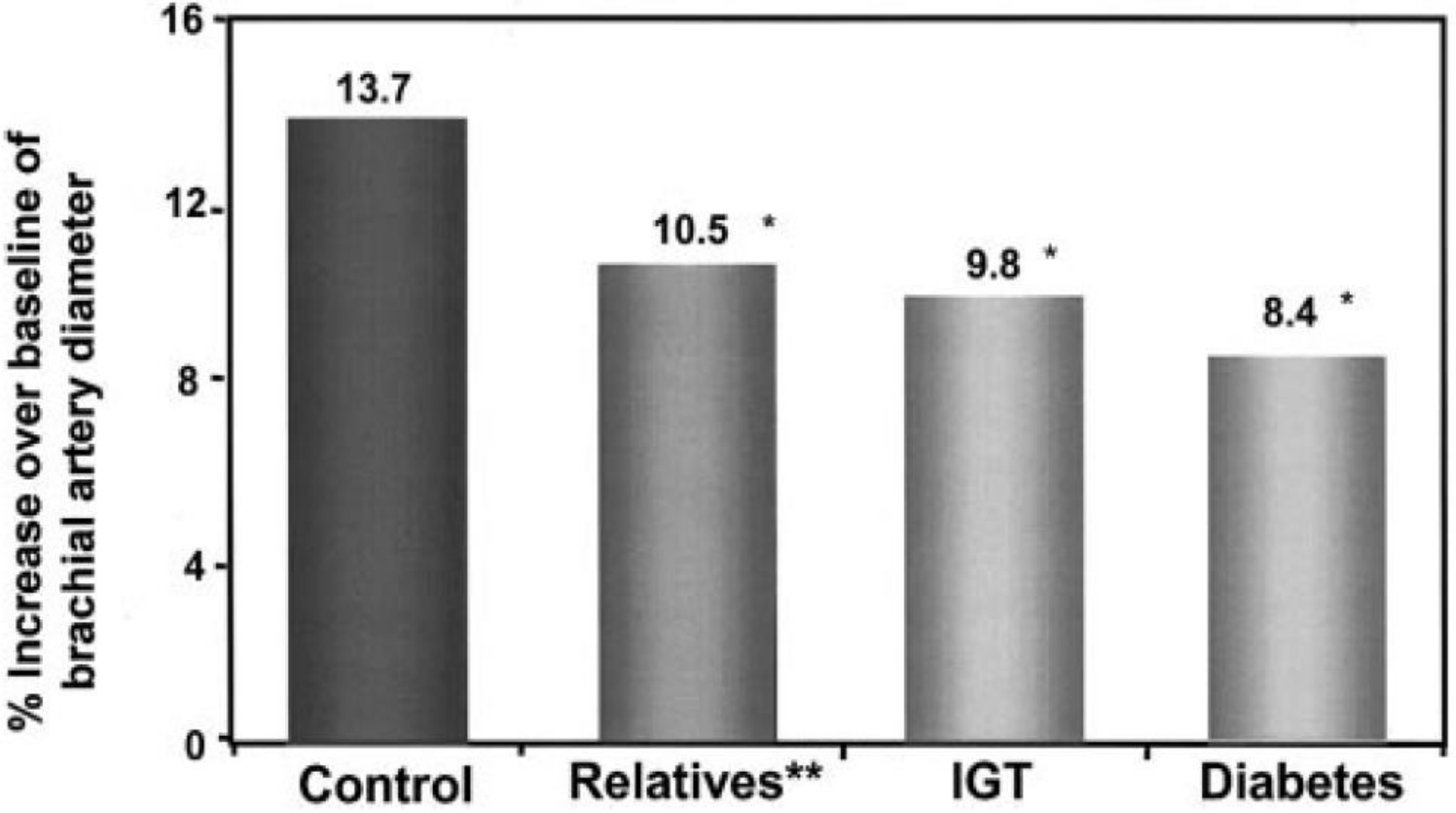

% Increase over baseline of brachial artery diameter
16
12
8
4
0
13.7
10.5 *
9.8 *
8.4 *
Control
Relatives**
IGT
Diabetes

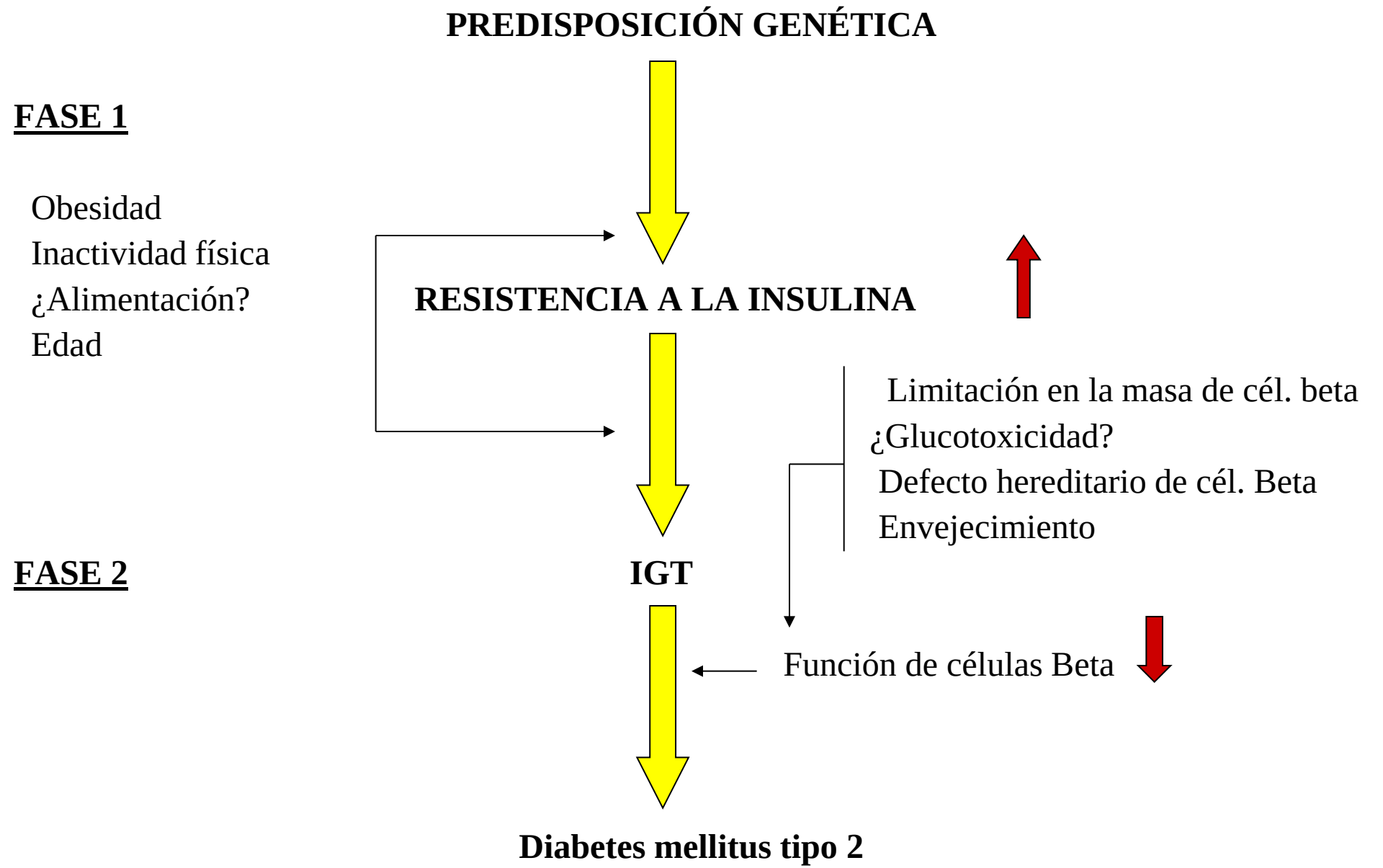
Table 1. Clinical characteristics and markers of endothelial activation in studied groups

	Controls	Relatives	IGT	Diabetes
No.	30	39	32	42
Age (years)	48 ± 9	49 ± 10	50 ± 10	53 ± 9
Sex (M/F)	14/16	19/20	15/17	21/21
High-density lipoproteins (mg/dL)	54 ± 15	49 ± 17	48 ± 13	42 ± 10*
Low-density lipoproteins (mg/dL)	120 ± 31	128 ± 36	143 ± 33	134 ± 36
vWF (%)	110 ± 49	103 ± 41	121 ± 45	135 ± 51*
ET-1 (pg/mL)	3.8 (1.4 to 12.3)	5.3 (1.2 to 33.4)*	6.8 (1.3 to 43.1)*	5.4 (1.5 to 39.1)*
sICAM (ng/mL)	222 ± 57	251 ± 89	264 ± 56*	301 ± 106*
sVCAM (ng/mL)	661 ± 176	747 ± 171*	759 ± 254	831 ± 257*

Mean ± SD unless stipulated otherwise.
* $p = <0.05$ vs. controls.

sICAM (ng/mL)	222 ± 57	251 ± 89	264 ± 56*	301 ± 106*
sVCAM (ng/mL)	661 ± 176	747 ± 171*	759 ± 254	831 ± 257*

Mean ± SD unless stipulated otherwise.
* $p = <0.05$ vs. controls.
OGTT, oral glucose-tolerance test.



Fases principales en la génesis de DM2

The New England
Journal of Medicine

VOLUME 346 FEBRUARY 7, 2002 NUMBER 6

REDUCTION IN THE INCIDENCE OF TYPE 2 DIABETES WITH LIFESTYLE INTERVENTION OR METFORMIN

DIABETES PREVENTION PROGRAM RESEARCH GROUP*

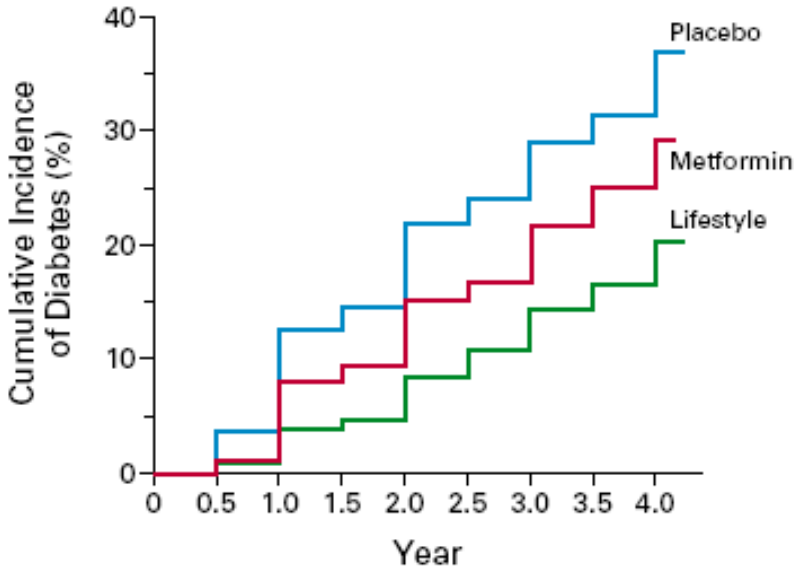
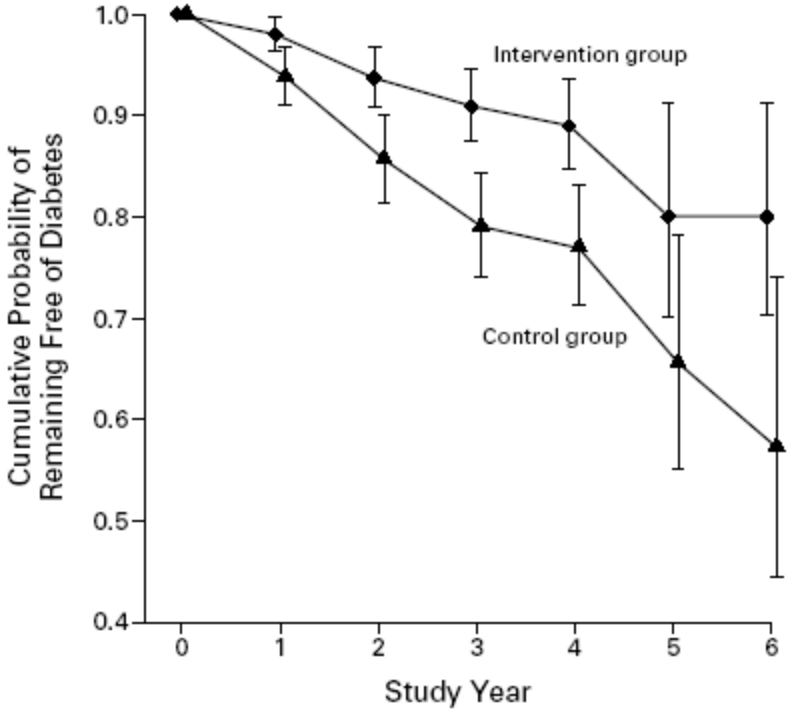


Figure 2. Cumulative Incidence of Diabetes According to Study Group.

The New England
Journal of Medicine

VOLUME 344 MAY 3, 2001 NUMBER 18

PREVENTION OF TYPE 2 DIABETES MELLITUS BY CHANGES IN LIFESTYLE AMONG SUBJECTS WITH IMPAIRED GLUCOSE TOLERANCE



Estudios clínicos de prevención con Tiazolidinedionas

Preservation of Pancreatic β-Cell Function and Prevention of Type 2 Diabetes by Pharmacological Treatment of Insulin Resistance in High-Risk Hispanic Women

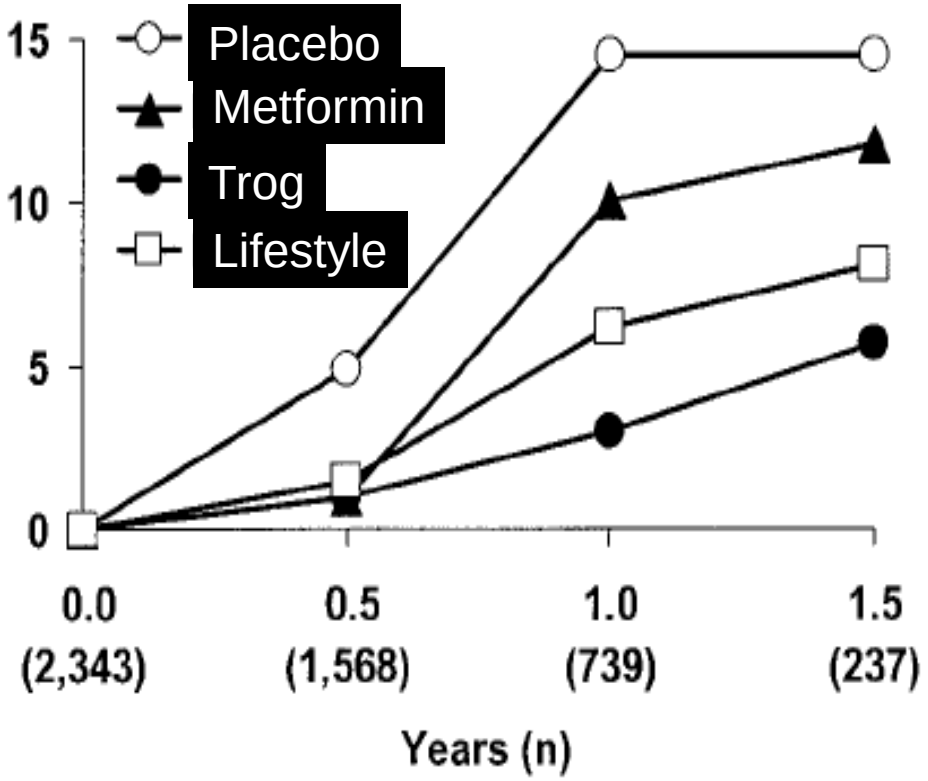
Thomas A. Buchanan,[1,2,3] Anny H. Xiang,[3,4] Ruth K. Peters,[3,4] Siri L. Kjos,[2,3] Aura Marroquin,[1] Jose Goico,[1] Cesar Ochoa,[1] Sylvia Tan,[1] Kathleen Berkowitz,[2] Howard N. Hodis,[1,3,4] and Stanley P. Azen[3,4]

Type 2 diabetes frequently results from progressive failure of pancreatic β-cell function in the presence of chronic insulin resistance. We tested whether chronic amelioration of insulin resistance would preserve pancreatic β-cell function and delay or prevent the onset of type 2 diabetes in high-risk Hispanic women. Women with previous gestational diabetes were randomized to

with the preservation of pancreatic β-cell function and appeared to be mediated by a reduction in the secretory demands placed on β-cells by chronic insulin resistance

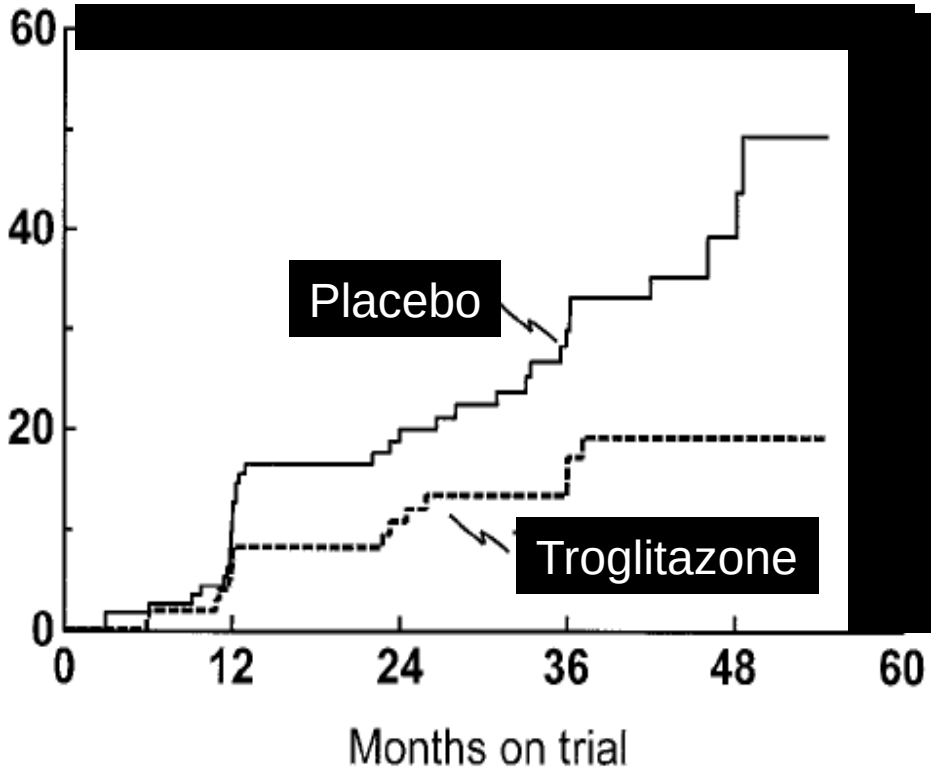
Diabetes 51:2796–2803, 2002

Troglitazone y Diabetes de novo



Mediana=0.9 años; (Trog)=585

HR = 0.25 (95%CI 0.14-0.43)



Mediana=30 mes; (Trog)=133

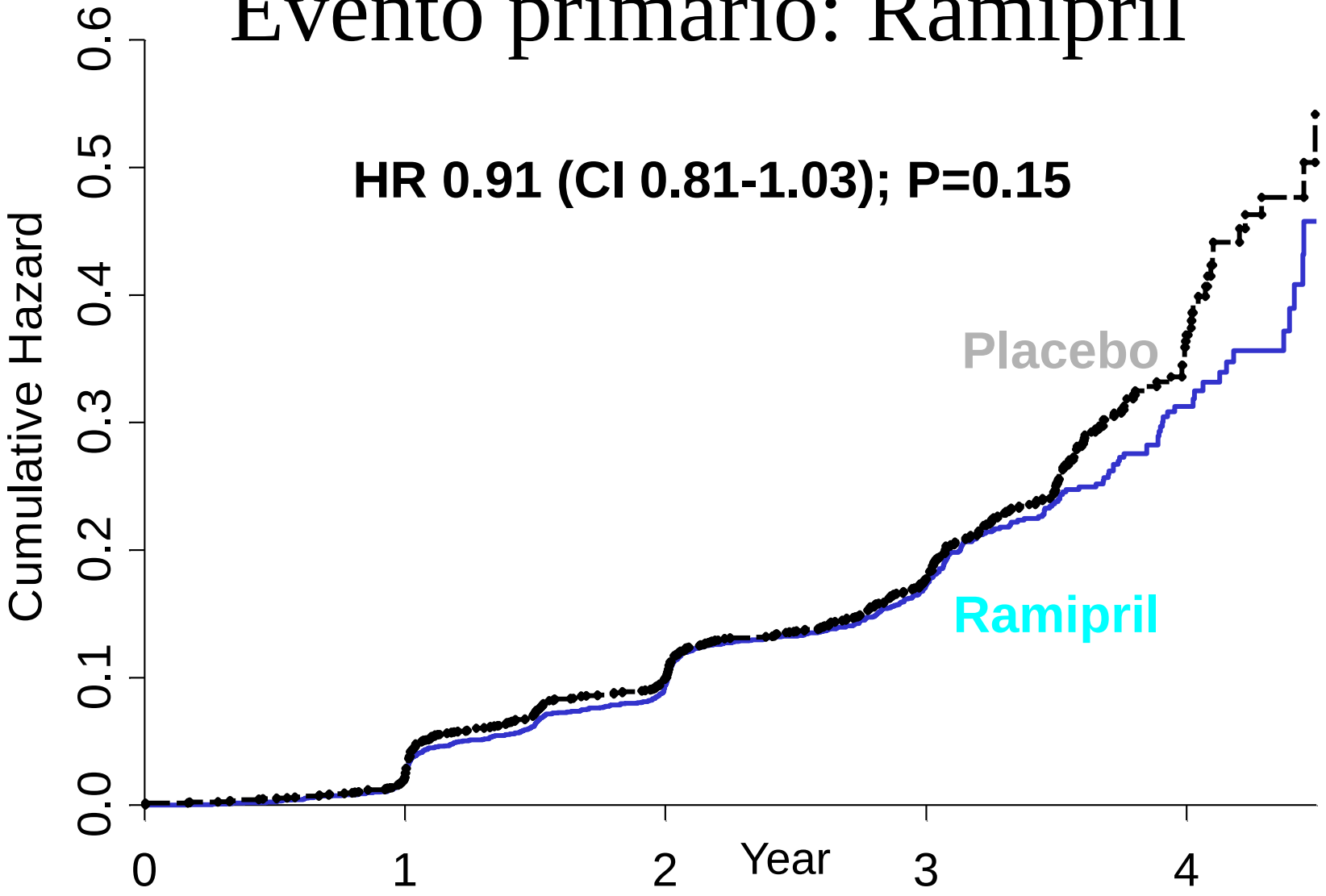
HR = 0.45 (95%CI 0.25-0.83)

DPP. Diabetes 2005; 1150

DREAM

Diabetes REduction Assessment with ramipril and rosiglitazone Medication

Evento primario: Ramipril

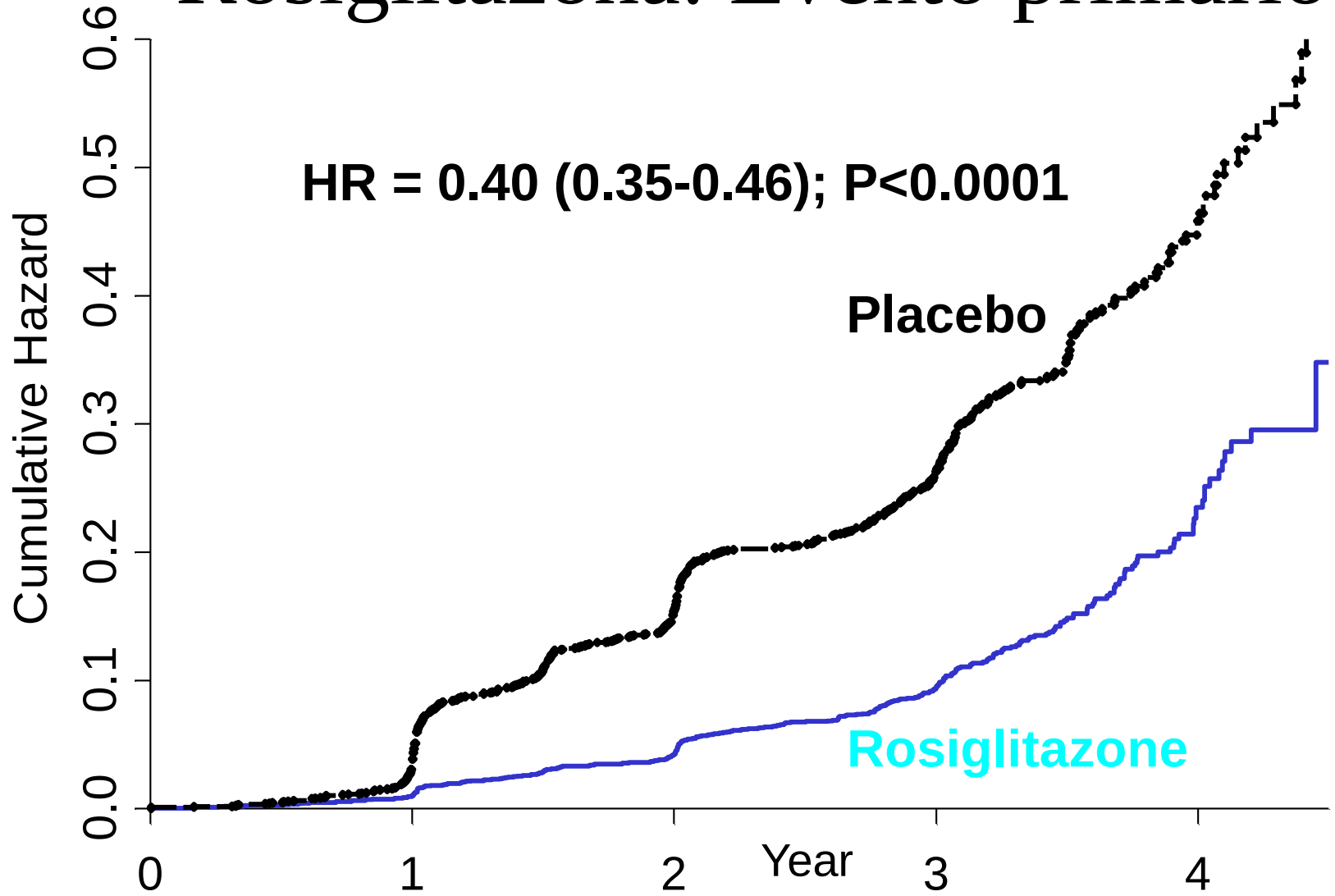


No. at Risk

Placebo	2646	2510	2277	1240	200
Ramipril	2623	2498	2287	1218	194

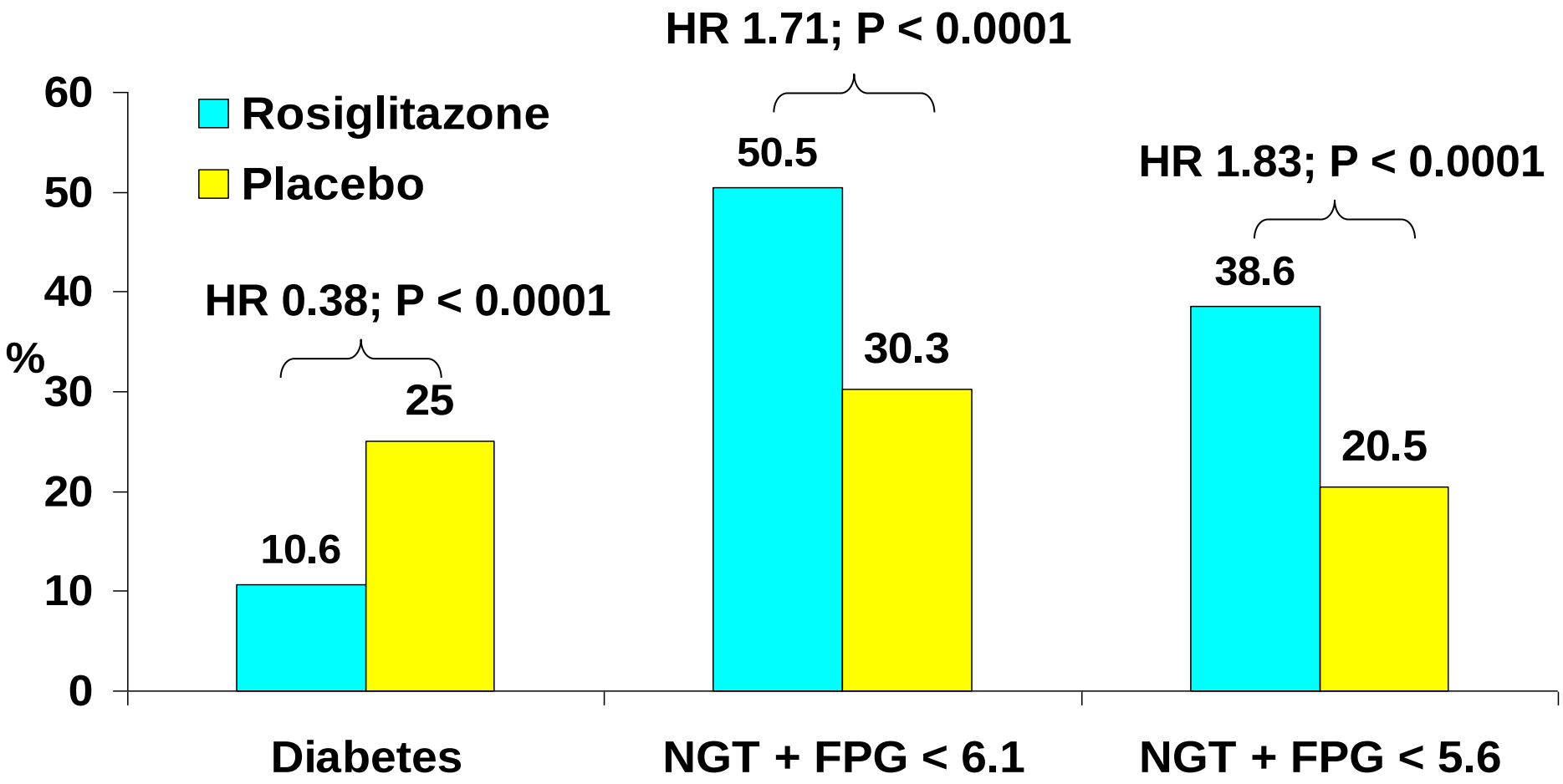
Placebo 2646 2510 2277 1240 200
Ramipril 2623 2498 2287 1218 194

Rosiglitazona: Evento primario

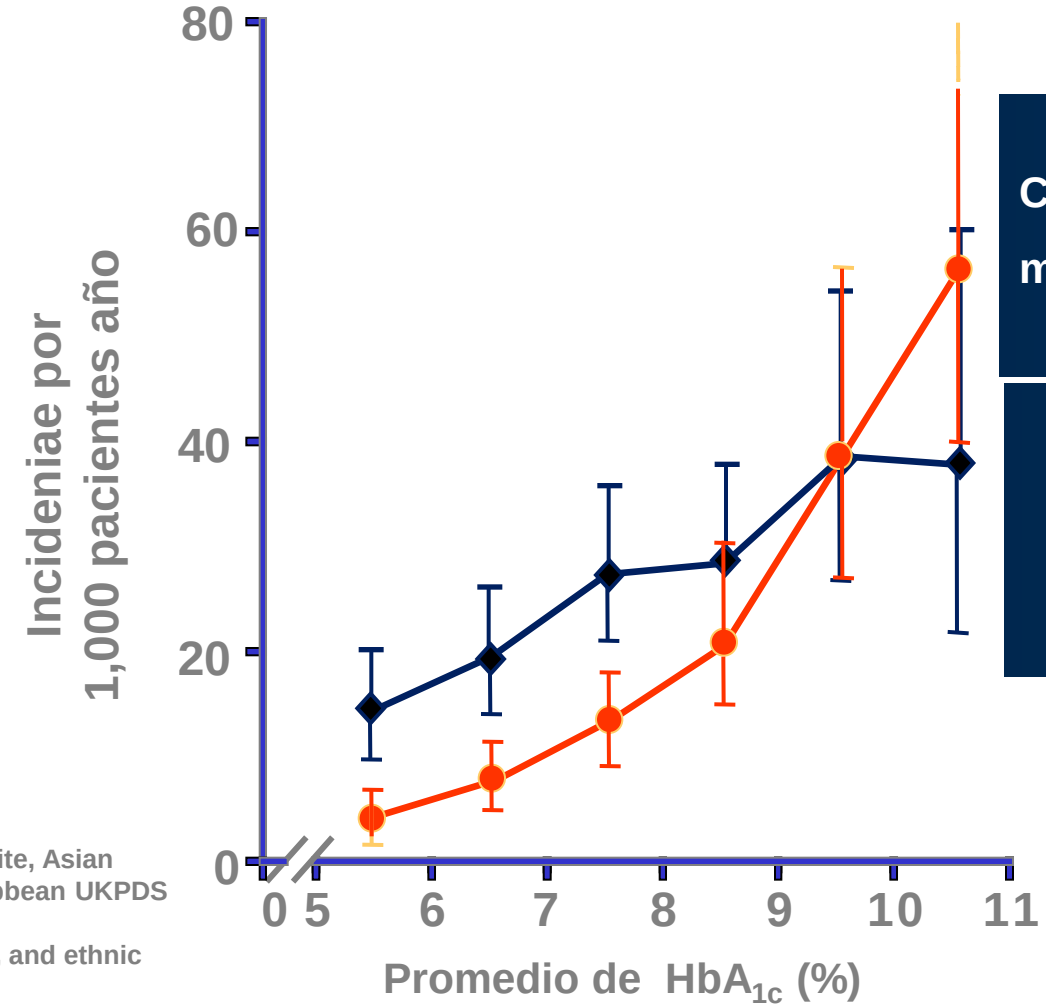


No. at Risk					
Placebo	2634	2470	2150	1148	177
Rosiglitazone	2635	2538	2414	1310	217

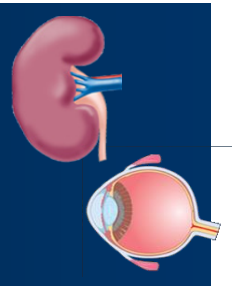
Efecto en categorías de glucosa: Rosiglitazona



Beneficios del control glucémico: no hay un umbral inferior



Complicaciones microvasculares



Infarto del miocardio

Error bars = 95% CI

Study population: white, Asian Indian, and Afro-Caribbean UKPDS patients (n = 4,585)
Adjusted for age, sex, and ethnic group

Adapatdo de Stratton IM, *et al.* *Br Med J* 2000; 321:405–412.

Contribución de la inflamación y el estrés oxidativo en la ateroesclerosis

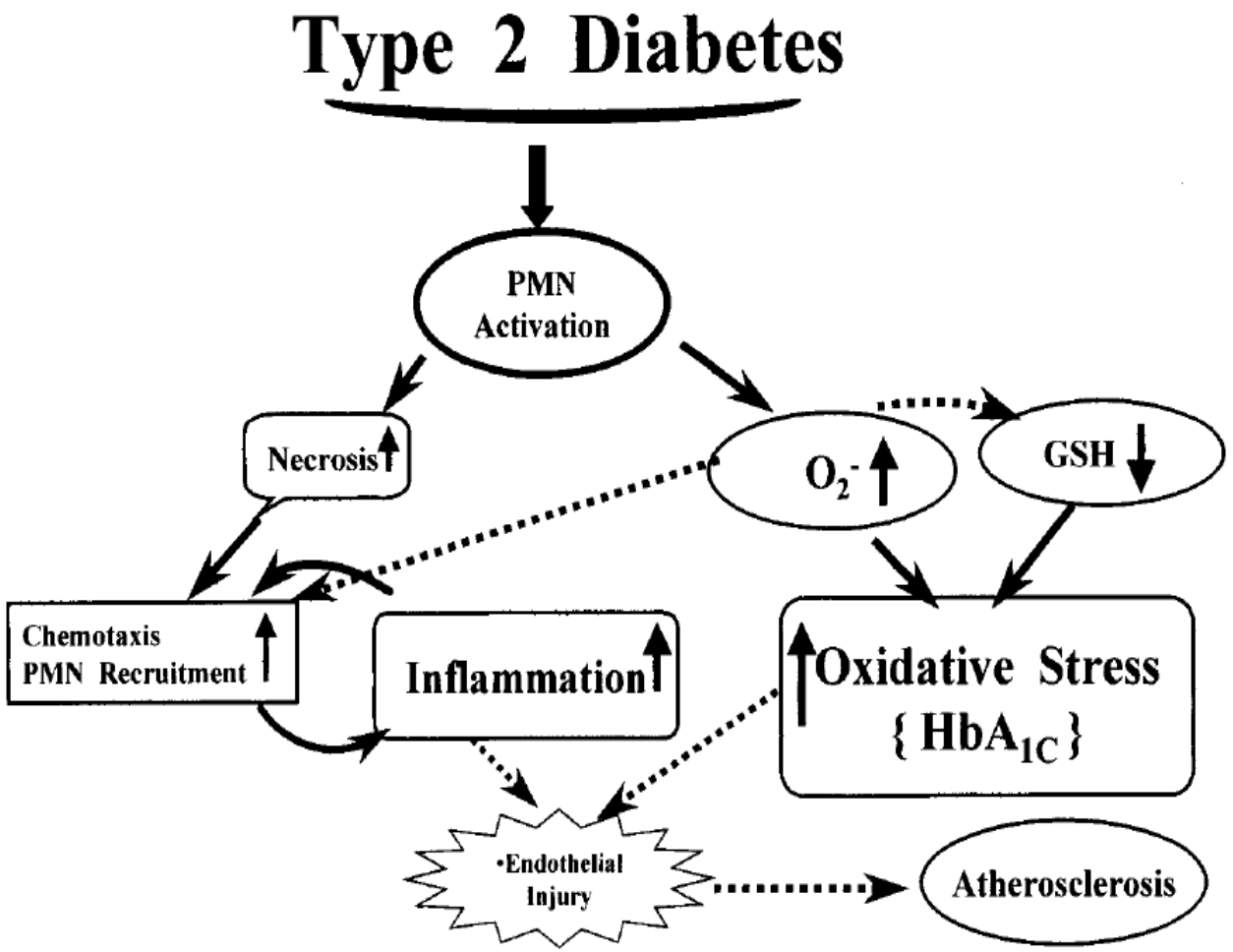
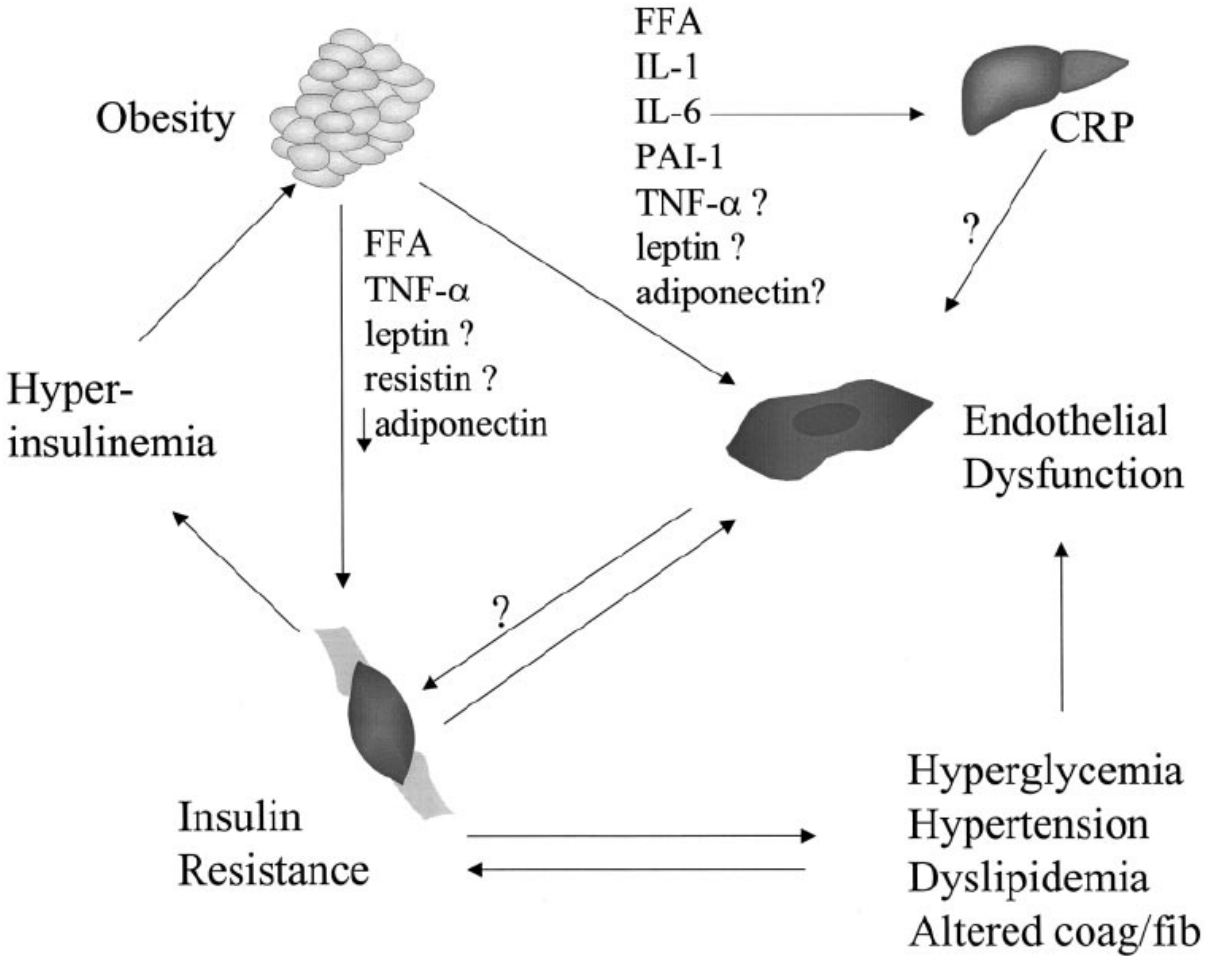
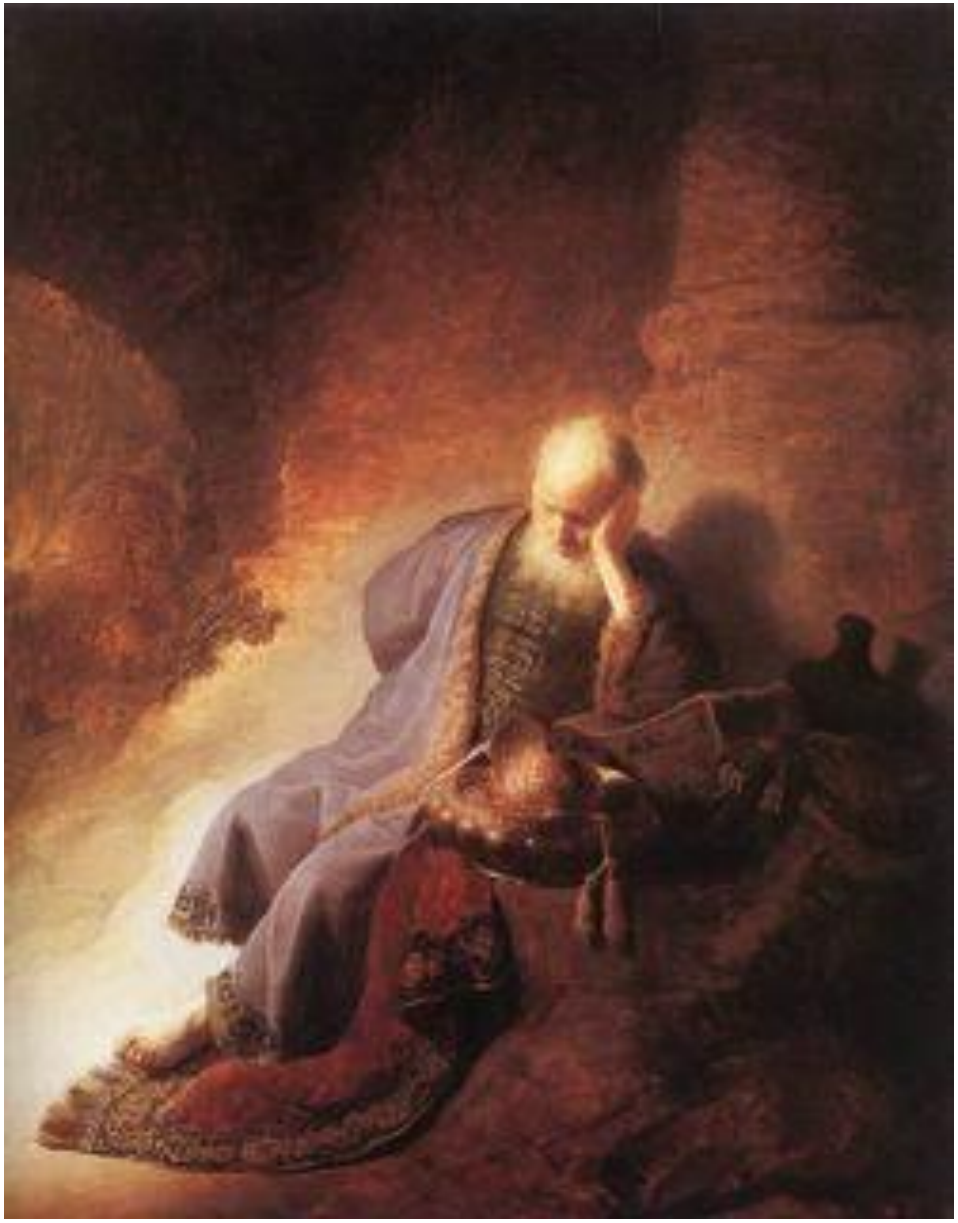
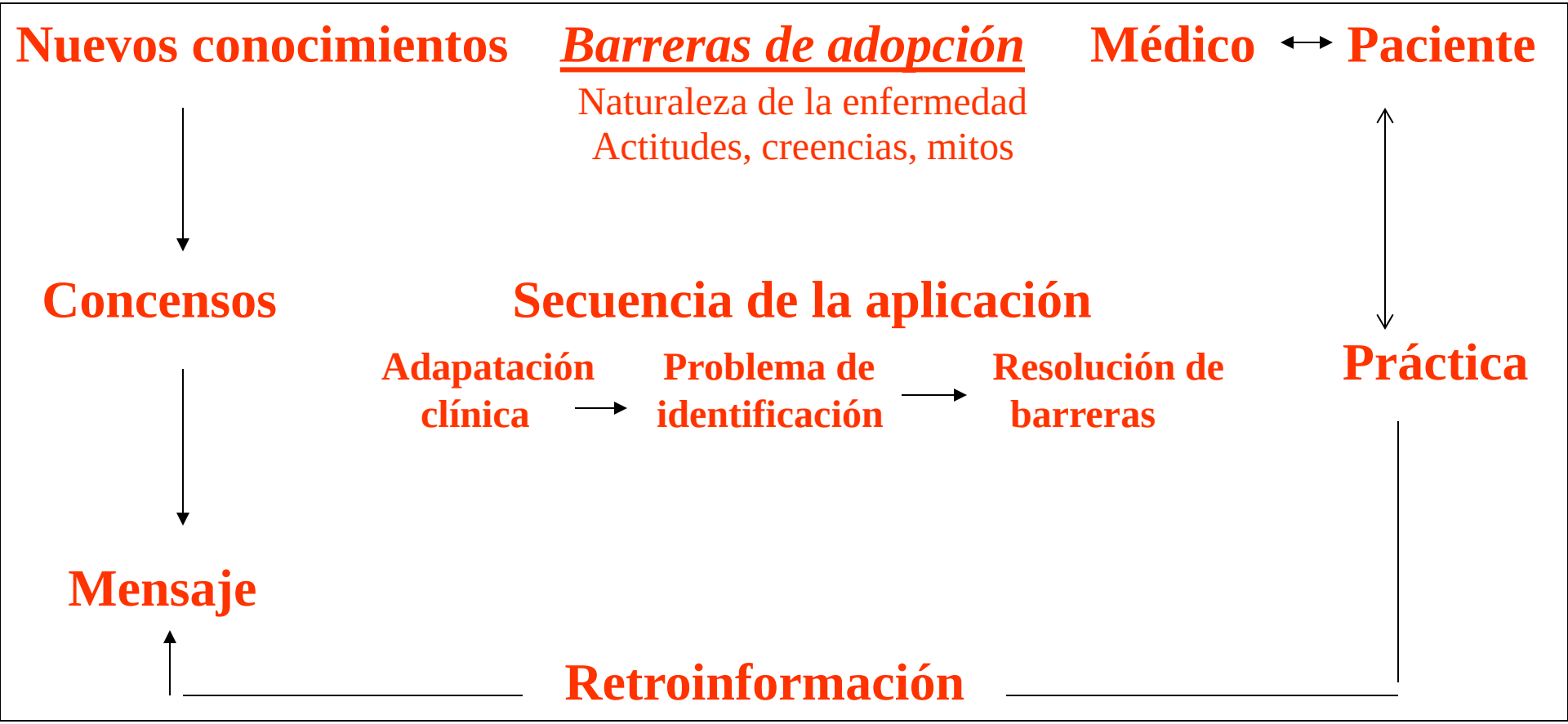


Figure 5—*Schematic diagram showing the concomitant contribution of PMNs to OS and inflammation in type 2 diabetes.*


Obesity
FFA
IL-1
IL-6
PAI-1
TNF-α ?
leptin ?
adiponectin?
CRP
?
FFA
TNF-α
leptin ?
resistin ?
↓adiponectin
Hyper-
insulinemia
Endothelial
Dysfunction
?
Insulin
Resistance
Hyperglycemia
Hypertension
Dyslipidemia
Altered coag/fib



Colocar el conocimiento en acción



La atenciòn mèdica efectiva

NUEVA	ANTERIOR
Atencion basada en relaciones curativas ctte	Atencion basada principalmente en visitas
Atencion diseñada a las necesidades del paciente	Autonomia del prestador dirige la variabilidad
Paciente fuente de control	Mèdico controla la atencion
El conocimiento se comparte	La informaciòn es un dato en el expediente
Las decisiones se basan en evidencias	Decisiones basadas en experiencia adquirida
Las necesidades se anticipan	El sistema reacciona a las necesidades

Gracias