VI REUNIÓN
RIESGO VASCULAR

SEMI
LA VISIÓN GLOBAL DE LA PERSONA ENFERMA

¿Cuándo y cómo hemos de diagnosticar la placa de ateroma? ¿qué hacemos con ella?: algoritmo de actuación y factores asociados a la progresión y regresión

Dr. Fernando Civeira Murillo

Servicio de Medicina Interna

Hospital Universitario Miguel Servet. Zaragoza

Hospital Universitario Miguel Servet

Guías o recomendaciones de las principales sociedades

- NECP-ATP III. (2002)
  - **“En condiciones adecuadas, la detección de aterosclerosis subclínica puede ser utilizada para identificar a personas con un riesgo mayor del atribuido por los factores de riesgo mayores”**
- *European Guidelines. (2007)*
  - **“Puede ser útil para estratificar mejor el riesgo pero no para tomar decisones de salud-enfermedad”**

“La enfermedad cardiovascular después de los 80 años es designio de Dios y antes de los 80 años un error médico”

S. Yusuf, 2007

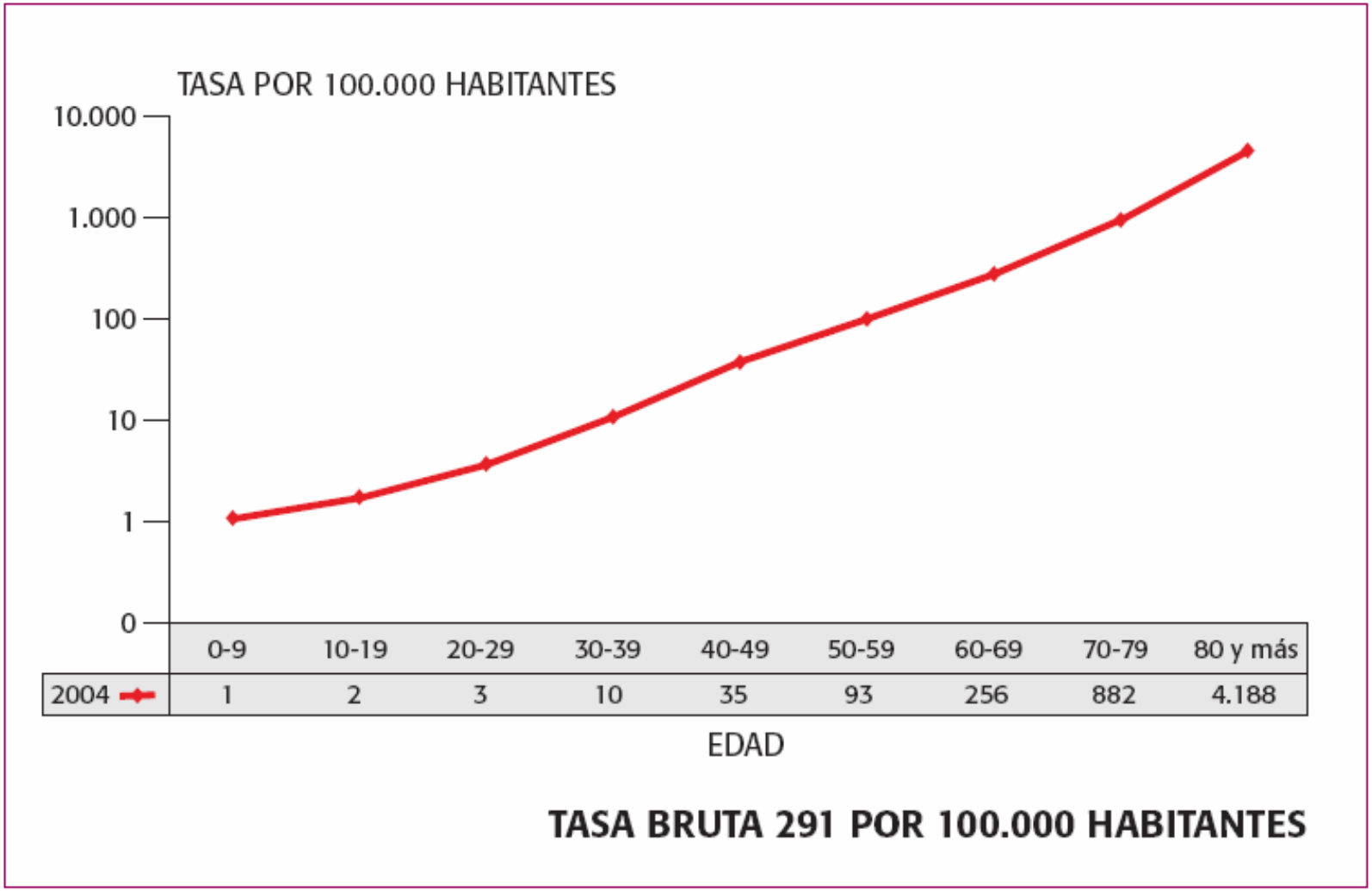


Figura 1.5. Tasa específica por edad de la mortalidad por enfermedades del sistema circulatorio en ambos sexos. España, 2004.

GRUPO DE EDAD (años)	PRIMERA CAUSA DE MUERTE	SEGUNDA CAUSA DE MUERTE
1 - 39	Causas externas	Tumores
40 - 74	Tumores	Enfermedades sistema circulatorio
75 y más	Enfermedades sistema circulatorio	Tumores

Tabla 1.1. Mortalidad proporcional según grupo de edad en España en el año 2004.

Problemas en prevención

1- Estimación individual del riesgo ineficaz

2- Inseguridad de la eficacia del tratamiento

3- Riesgo residual inaceptable

How Good Is NCEP III At Predicting MI?

Akosah et al. JACC 2003:41:1475-9

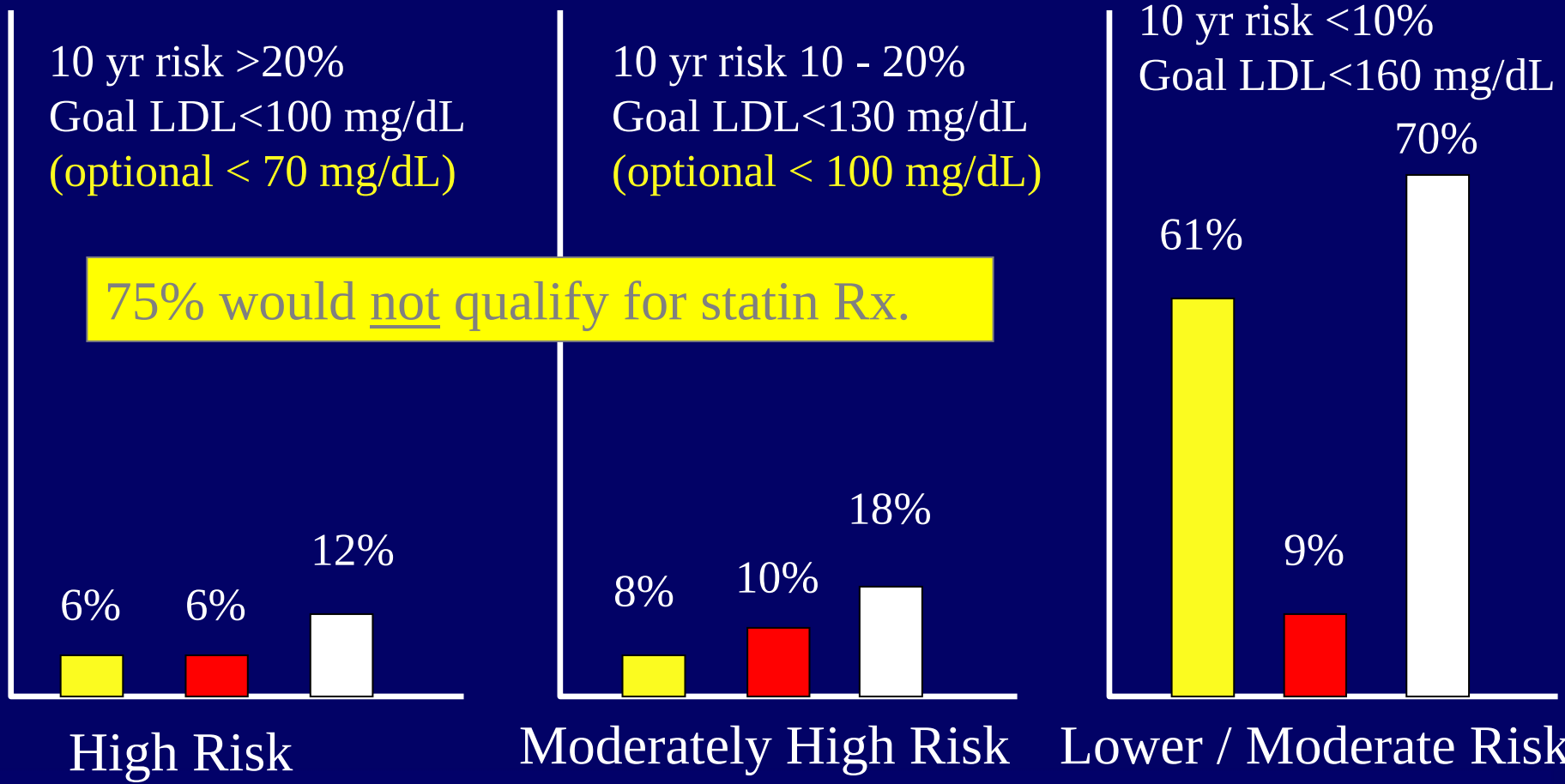
1998 – 2002. 222 patients with 1st acute MI, no prior CAD, no DM. Men <55 y/o (75%), Women <65. 40% hypertensive

% of total

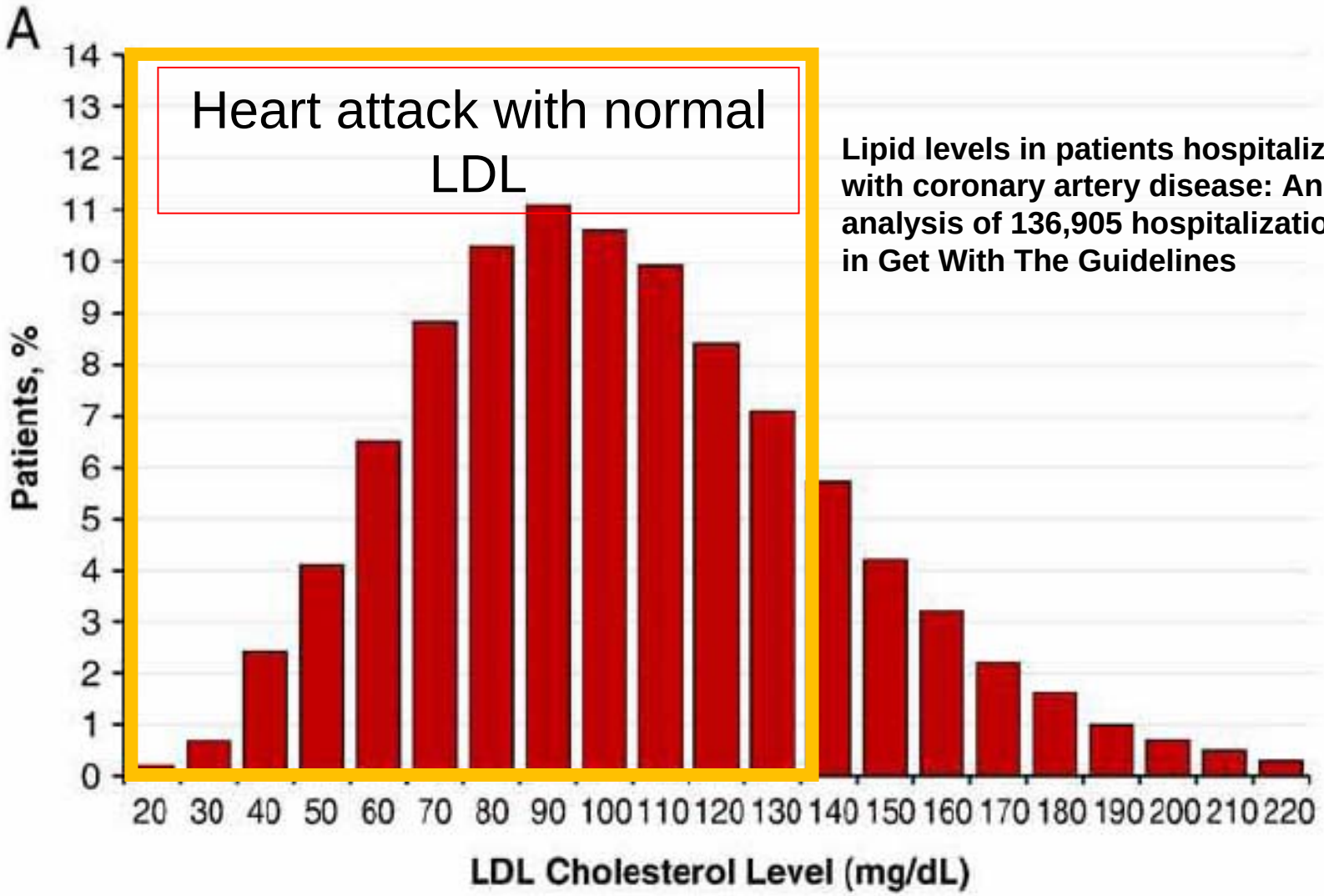
would qualify for statin Rx

would not qualify for statin Rx

What was NCEP risk before the MI?



Of 136,905 patients hospitalized with CAD, more than 75% had LDL levels below 130 mg/dl



Lipid levels in patients hospitalized with coronary artery disease: An analysis of 136,905 hospitalizations in Get With The Guidelines

Sachdeva et al. AHJ, 2009;157:111-117

Estimating Cardiovascular Risk in Spain Using Different Algorithms

Eva Comín,[a] Pascual Solanas,[b,c] Carmen Cabezas,[d] Isaac Subirana,[e] Rafel Ramos,[c,e] Joan Gené-Badia,[f] Ferran Cordón,[b] María Grau,[c,e] Joan J. Cabré-Vila,[g] and Jaume Marrugat[c,e]

TABLE 4. **Sensitivity, Specificity, and Positive Predictive Value of the Different Tables and Risk Limits for Ischemic Heart Disease and Cardiovascular Disease***

	Ischemic Heart Disease (n=180)			Cardiovascular Disease (n=247)			
	Sensitivity, %	Specificity, %	PPV, %	Sensitivity, %	Specificity, %	PPV, %	High-Risk Population, %
				35-74 years			
Framingham 20%	57.3	78.5	6.9	53.4	78.9	10.0	22.4
REGICOR 20%	4.9	98.2	6.9	4.0	98.2	8.8	1.9
REGICOR 15%	16.4	95.4	8.9	15.2	95.5	13.0	4.9
REGICOR 10%	36.8	88.3	8.0	32.8	88.5	11.1	12.4
SCORE 5%				Not applicable			
				35-64 years			
Framingham 20%	59.2	84.2	6.7	53.4	84.5	9.6	16.6
REGICOR 20%	5.7	99.3	13.7	3.6	99.3	13.7	0.8
REGICOR 15%	17.4	97.9	14.0	13.5	98.0	17.1	2.4
REGICOR 10%	33.8	93.0	8.5	29.4	93.2	11.7	7.5
SCORE 5%	33.9	92.1	7.7	32.7	92.4	11.7	8.4
SCORE extrapolated 5%	51.5	84.2	5.9	48.6	84.5	8.8	16.5

*REGICOR indicates REgistre GIroní del COR; SCORE, Systematic COronary Risk Evaluation (not for use with patients aged >64 years); SCORE extrapolated, in patients <60 years with <5% risk at 10 years we also calculated SCORE extrapolated in patients aged 60 years; PPV, positive predictive value.

EDITORIAL

Nuevos instrumentos y los riesgos de siempre

Jaume Marrugat[a] y Joan Sala[b]

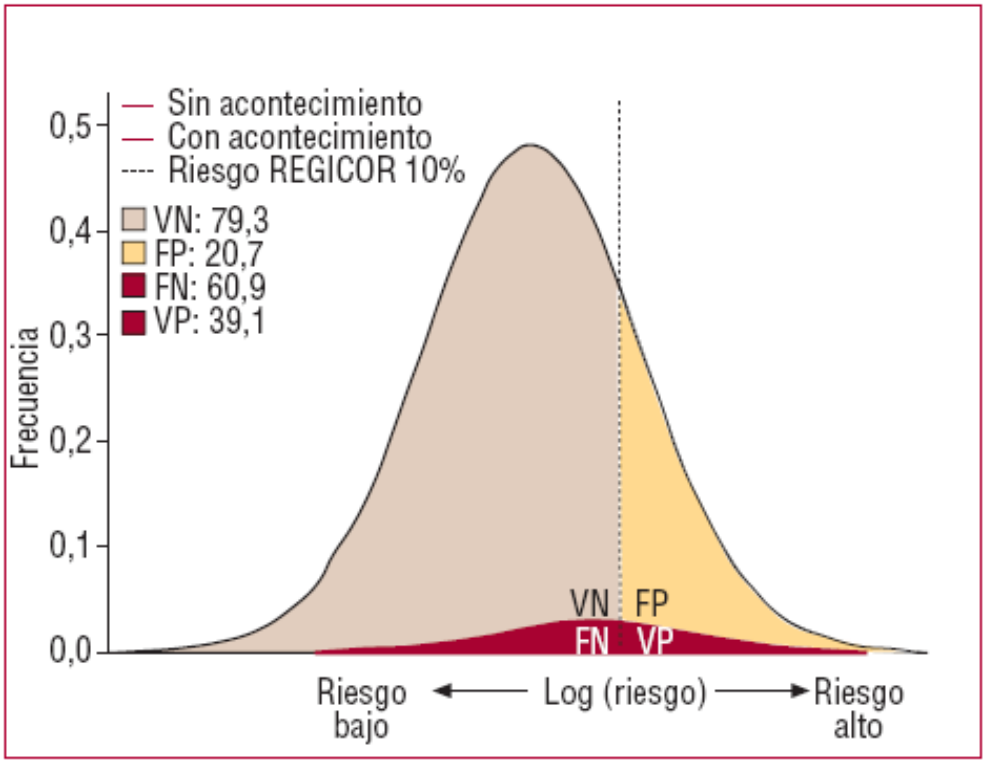


Fig. 2. Distribución de los resultados del logaritmo del riesgo en individuos que han desarrollado y no han desarrollado cardiopatía isquémica en el estudio VERIFICA.
FN: falsos negativos; FP: falsos positivos; VN: verdaderos negativos; VP: verdaderos positivos.

Rev Esp Cardiol. 2007;60(5):464-7

Problemas en prevención

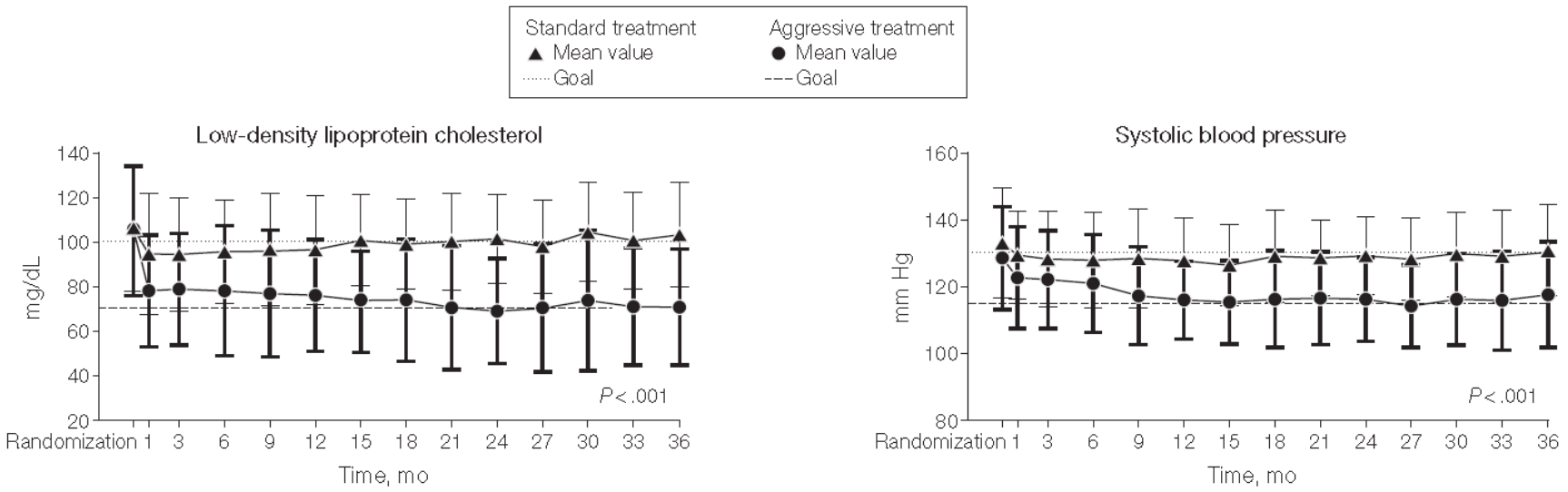
1- Estimación individual del riesgo ineficaz

2- Inseguridad de la eficacia del tratamiento

3- Riesgo residual inaceptable

Estudio SANDS

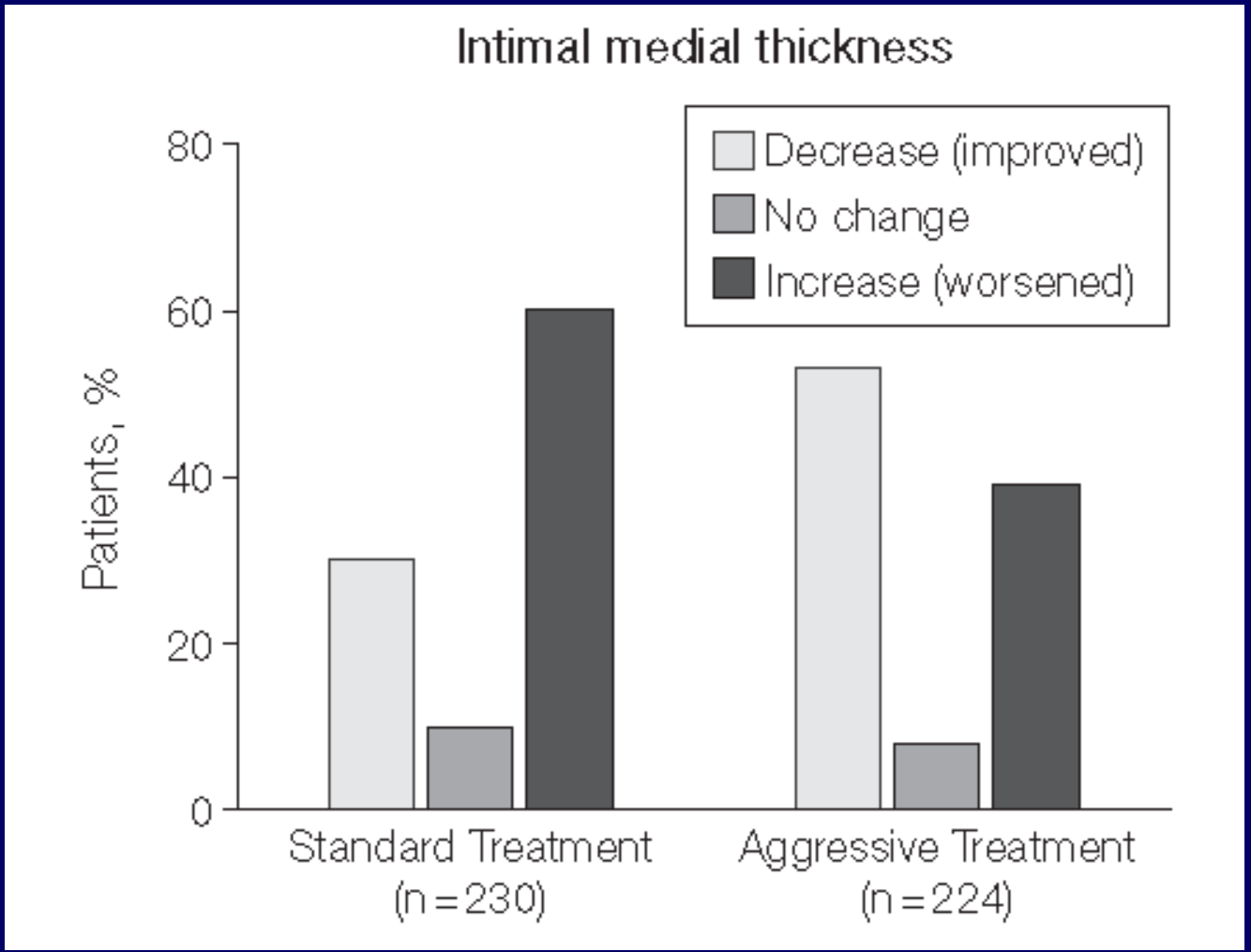
Figure 2. LDL Cholesterol and Systolic Blood Pressure Levels for SANDS Participants



Mean levels for low-density lipoprotein cholesterol (LDL-C) and systolic blood pressure by treatment group at 3-month intervals throughout the study. Error bars denote SD. *P* values denote the significance between treatment groups during months 18 through 36. LDL-C values were obtained from capillary blood. For 2292 samples having both laboratory and capillary measures, mean (SD) values were 89.2 (31.2) and 87.9 (29.1) mg/dL, respectively. To convert cholesterol values to

Howard BV, et al. JAMA 2008;14:1678

Cambios en el GIM carotídeo en el estudio SAND



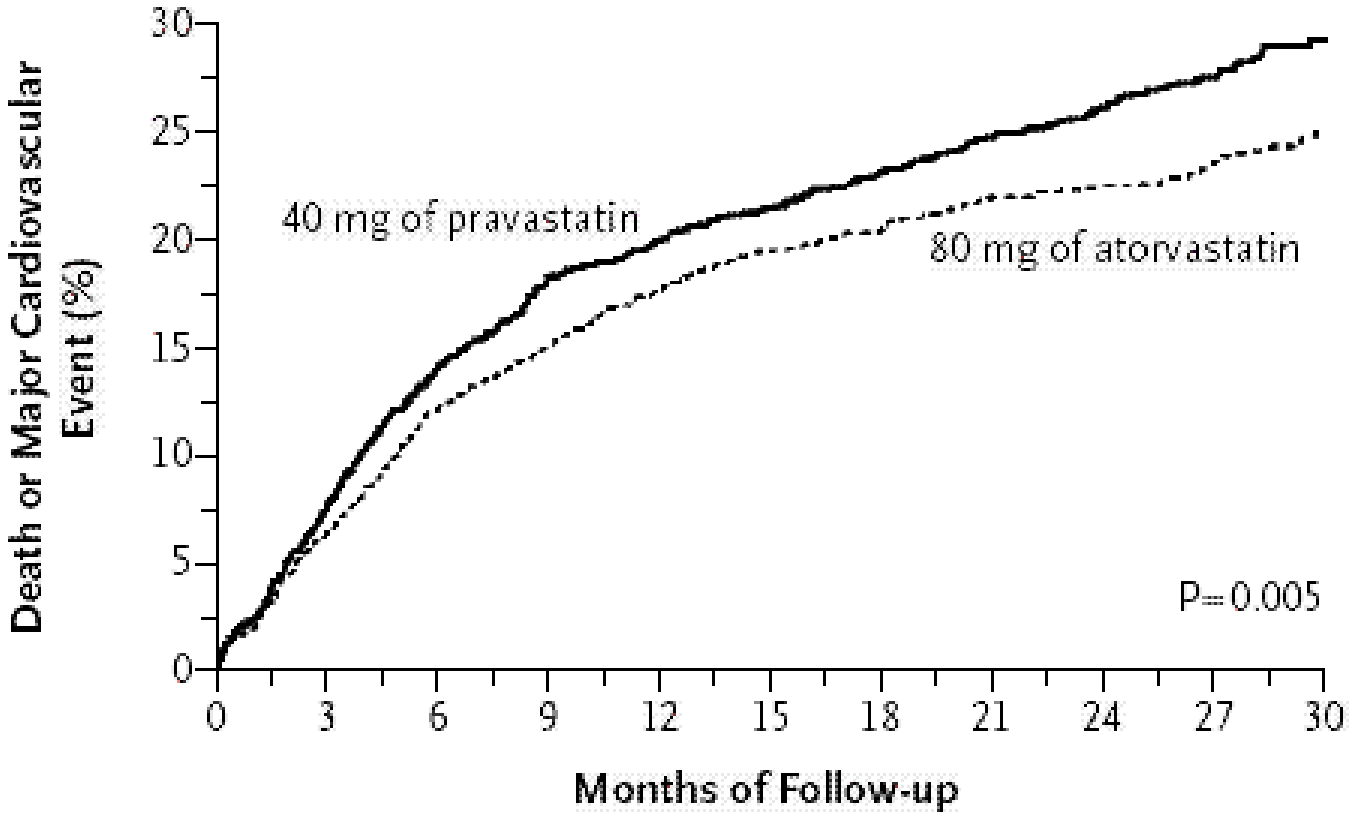
Howard BV, et al. JAMA 2008;14:1678

Problemas en prevención

1- Estimación individual del riesgo ineficaz

2- Inseguridad de la eficacia del tratamiento

3- Riesgo residual inaceptable

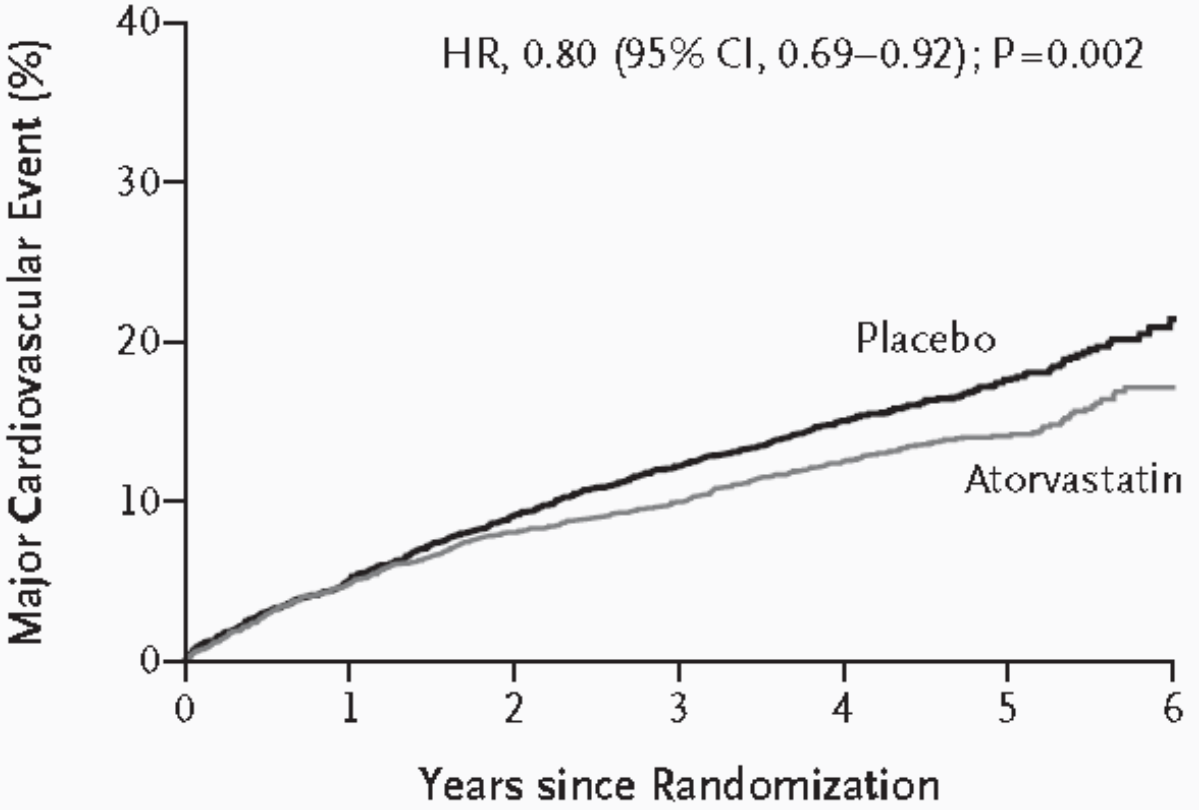


No. at Risk						
Pravastatin	2063	1688	1536	1423	810	138
Atorvastatin	2099	1736	1591	1485	842	133

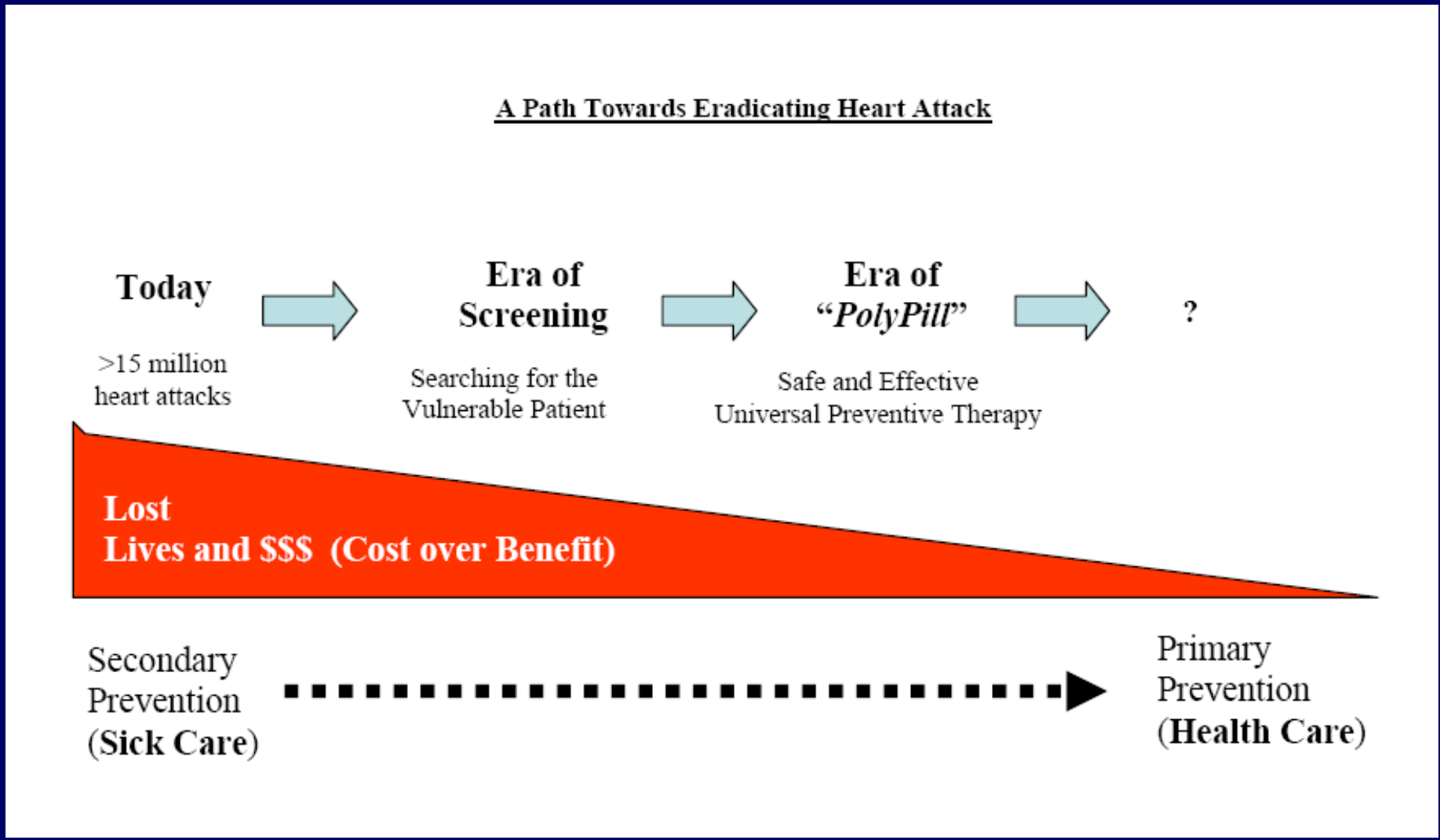
Figure 2. Kaplan–Meier Estimates of the Incidence of the Primary End Point of Death from Any Cause or a Major Cardiovascular Event.

The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Investigators*

C



No. at Risk							
Atorvastatin	2365	2198	2092	2015	1913	910	121
Placebo	2366	2200	2082	1969	1874	858	134


A Path Towards Eradicating Heart Attack
Today
>15 million heart attacks
Era of Screening
Searching for the Vulnerable Patient
Era of "PolyPill"
Safe and Effective Universal Preventive Therapy
?
Lost Lives and $$$ (Cost over Benefit)
Secondary Prevention (Sick Care)
Primary Prevention (Health Care)

¿Qué técnica?

Screening for Atherosclerosis

Risk Factors vs Disease

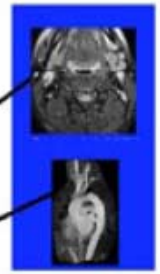
Numerous Risk Factors

- High LDL
- Low HDL
- High BP
- Diabetes
- Smoking
- CRP
- Metabolic Syn
- Lp(a)
- Homocysteine
- Dense LDL
- Lp-PLA2
- ApoB/ApoA
- Family History
- Sedentary Life
- Obesity
- Stress
- ...
- ?

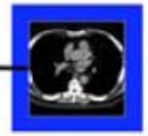
Over 200 risk factors have been reported.

Carotid IMT and Plaque Measured by Ultrasound

Examples of Arterial Structure Tests

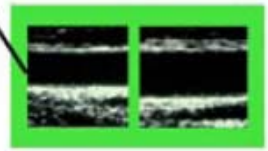


Aortic and Carotid Plaque Detected by MRI



Coronary Calcium Score Measured by CT

Ankle Brachial Index



Brachial Vasoreactivity Measured by Ultrasound

Vascular Compliance Measured by Radial Tonometry

Examples of Arterial Function Tests

Microvascular Reactivity Measured by Fingertip Tonometry

Coronary Artery Calcification Compared With Carotid Intima-Media Thickness in the Prediction of Cardiovascular Disease Incidence

The Multi-Ethnic Study of Atherosclerosis (MESA)

Aaron R. Folsom, MD; Richard A. Kronmal, PhD; Robert C. Detrano, MD, PhD; Daniel H. O'Leary, MD; Diane E. Bild, MD; David A. Bluemke, MD, PhD; Matthew J. Budoff, MD; Kiang Liu, PhD; Steven Shea, MD; Moyses Szklo, MD, DrPH; Russell P. Tracy, PhD; Karol E. Watson, MD, PhD; Gregory L. Burke, MD

Table 3. Hazard Ratios (HRs) for an Incident CVD, CHD, or Stroke Event in Relation to Quartiles of Maximal Carotid IMT or CAC Score (MESA, 2000-2004)

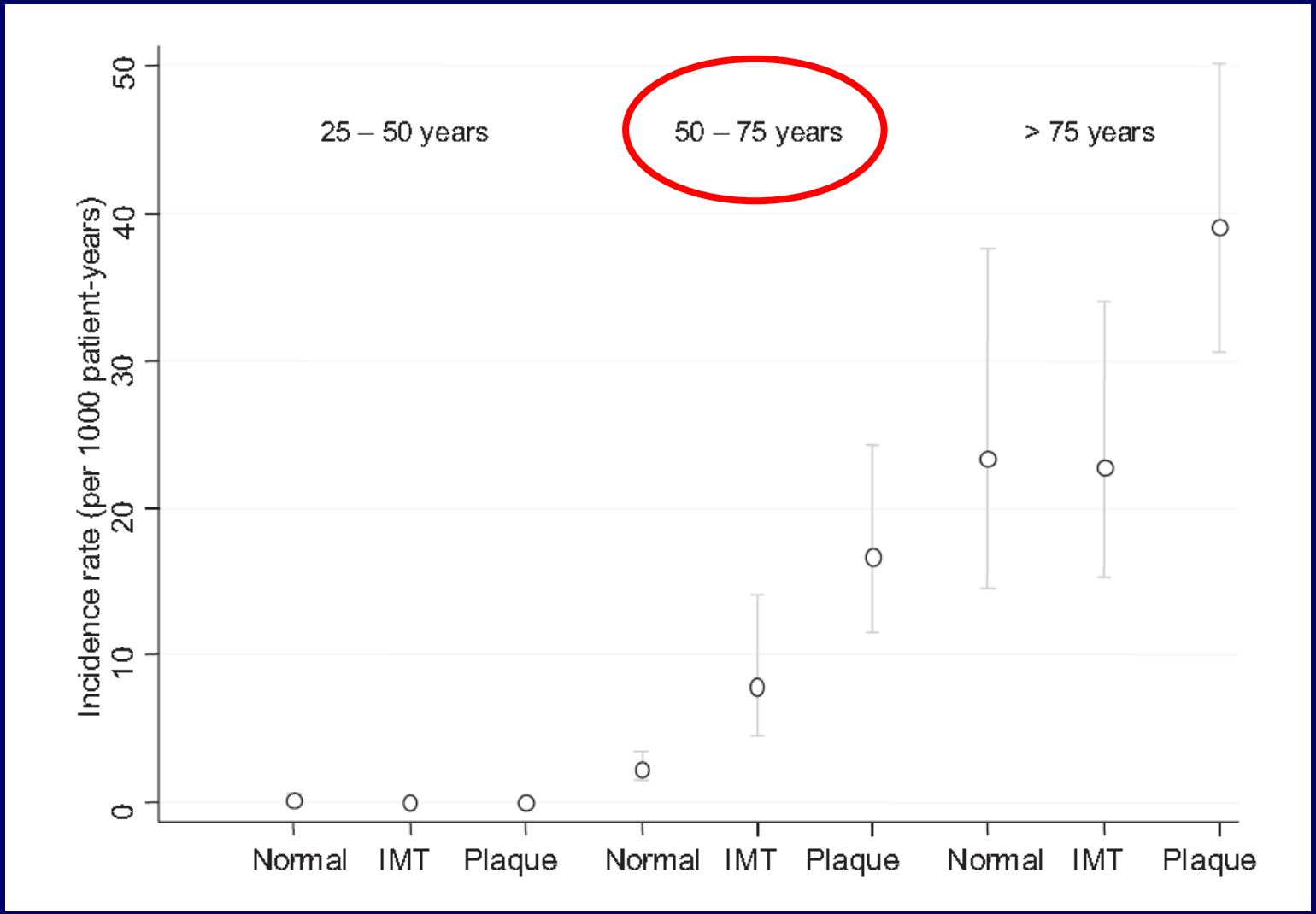
Measure[a]	HR (95% CI)			χ^2 Statistic	*P* Value
	<50th Percentile	Quartile 3	Quartile 4		
CVD (n = 222)					
Age-, race-, and sex-adjusted					
z Score max IMT	1 [Reference]	1.4 (0.9-2.0)	2.2 (1.5-3.2)	20.1	<.001
CAC score	1 [Reference]	2.6 (1.6-4.1)	5.3 (3.4-8.2)	58.4	<.001
Multivariable-adjusted[b]					
z Score max IMT	1 [Reference]	1.3 (0.9-2.0)	1.7 (1.2-2.5)	8.7	.01
CAC score	1 [Reference]	2.3 (1.5-3.7)	4.4 (2.8-6.8)	44.7	<.001
CHD (n = 159)					
Age-, race-, and sex-adjusted					
z Score max IMT	1 [Reference]	1.5 (1.0-2.4)	2.1 (1.4-3.3)	11.5	<.01
CAC score	1 [Reference]	4.1 (2.2-7.7)	10.3 (5.6-18.9)	63.8	<.001
Multivariable-adjusted[b]					
z Score max IMT	1 [Reference]	1.5 (0.9-2.3)	1.7 (1.1-2.7)	5.4	.07
CAC score	1 [Reference]	3.5 (1.9-6.6)	8.2 (4.5-15.1)	51.5	<.001
Stroke (n = 59)					
Age-, race-, and sex-adjusted					
z Score max IMT	1 [Reference]	0.9 (0.4-2.0)	2.4 (1.2-4.7)	9.9	<.01
CAC score	1 [Reference]	1.4 (0.8-2.7)	1.2 (0.6-2.4)	0.7	.70

>75

Arch Intern Med. 2008;168(12):1333-1339

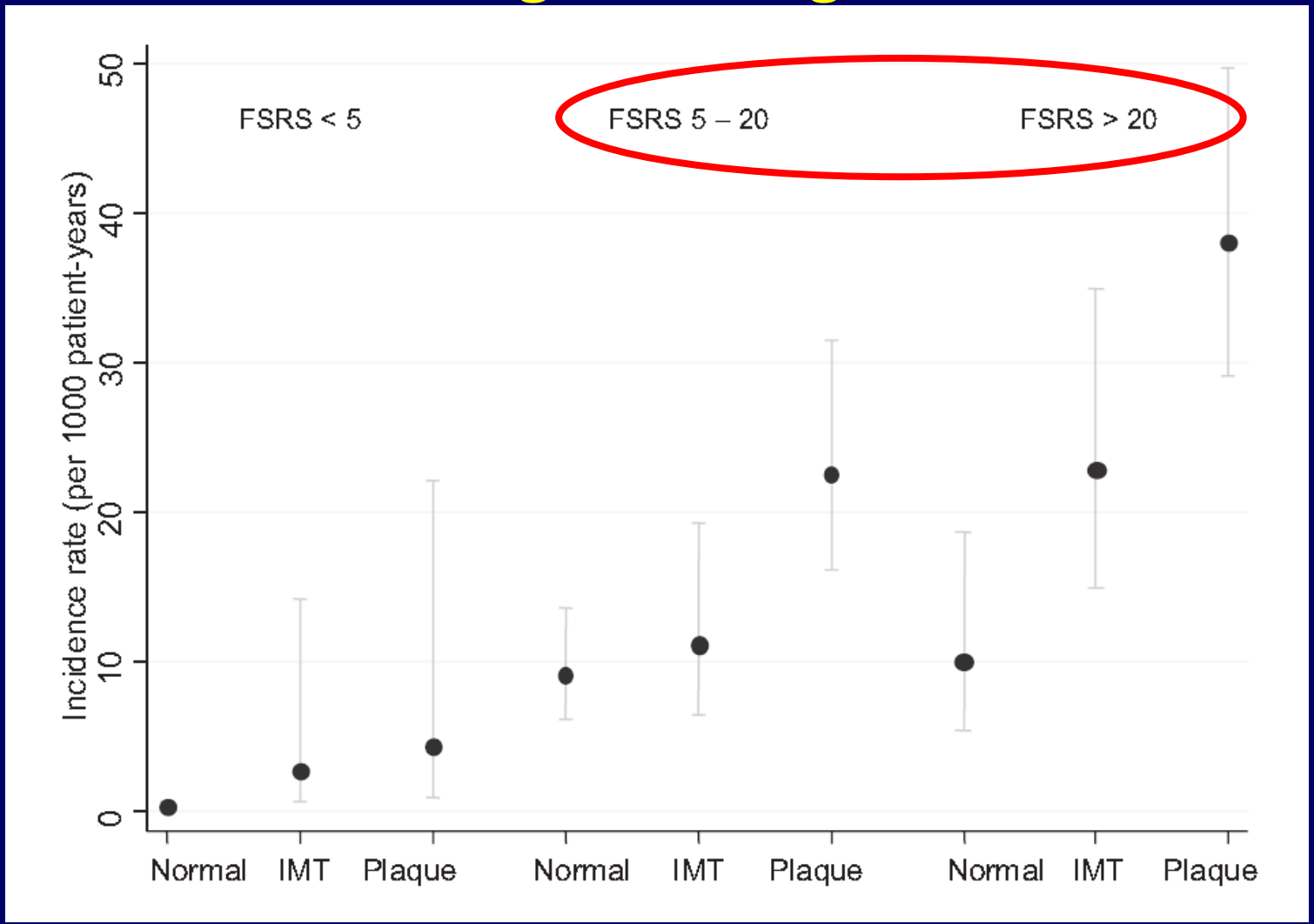
¿A quién?

Eventos cerebrovasculares o muerte cardiovascular de acuerdo a GIM de carótida y edad



Prati P, et al. Stroke 2008;39:2470

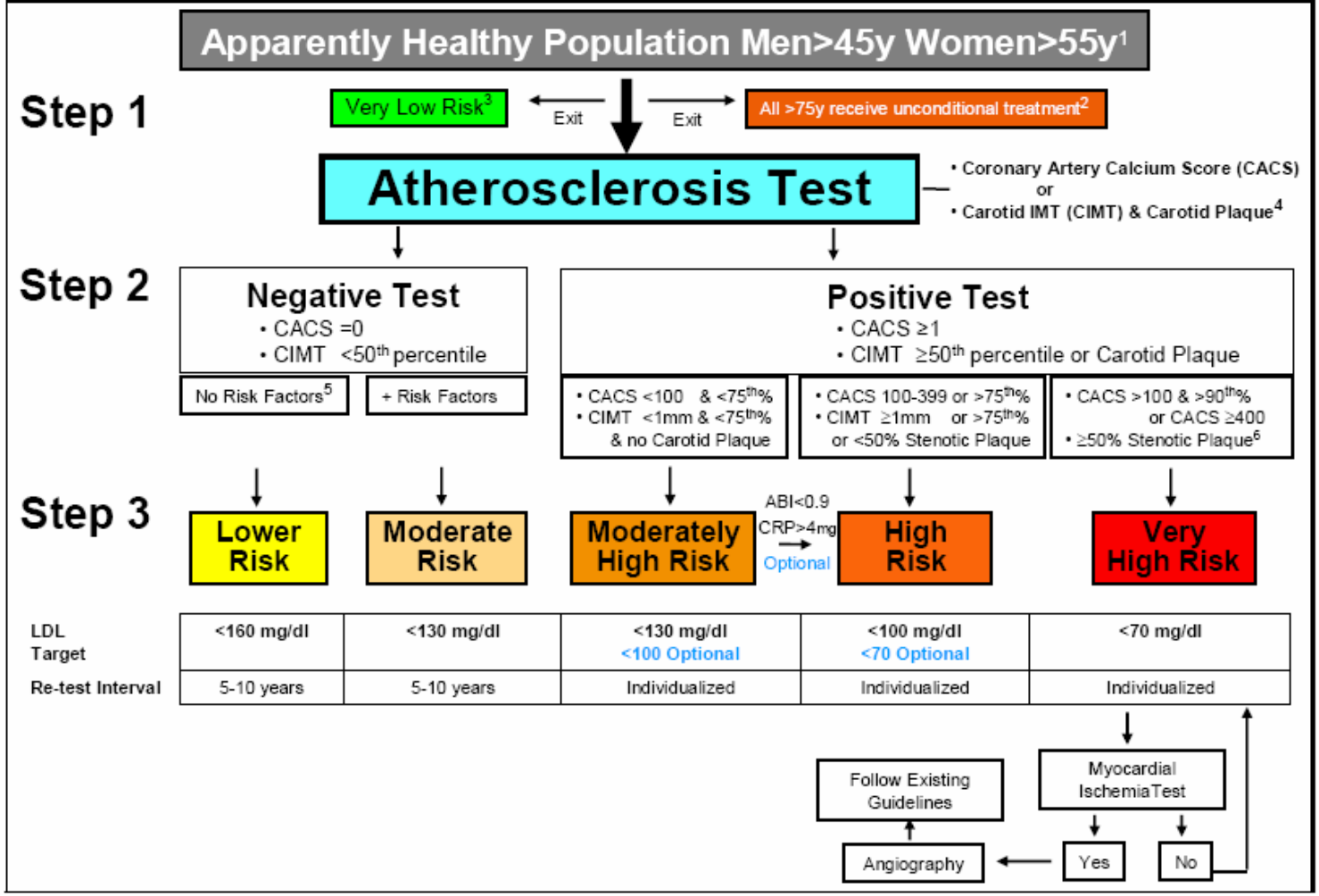
Eventos cerebrovasculares o muerte cardiovascular de acuerdo a GIM de carótida y riesgo Framingham



Prati P, et al. Stroke 2008;39:2470

The 1st S.H.A.P.E. Guideline

Towards the National Screening for Heart Attack Prevention and Education (SHAPE) Program



1: No history of angina, heart attack, stroke, or peripheral arterial disease.

2: Population over age 75y is considered high risk and must receive therapy without testing for atherosclerosis.

3: Must not have any of the following: Chol>200 mg/dl, blood pressure >120/80 mmHg, diabetes, smoking, family history, metabolic syndrome.

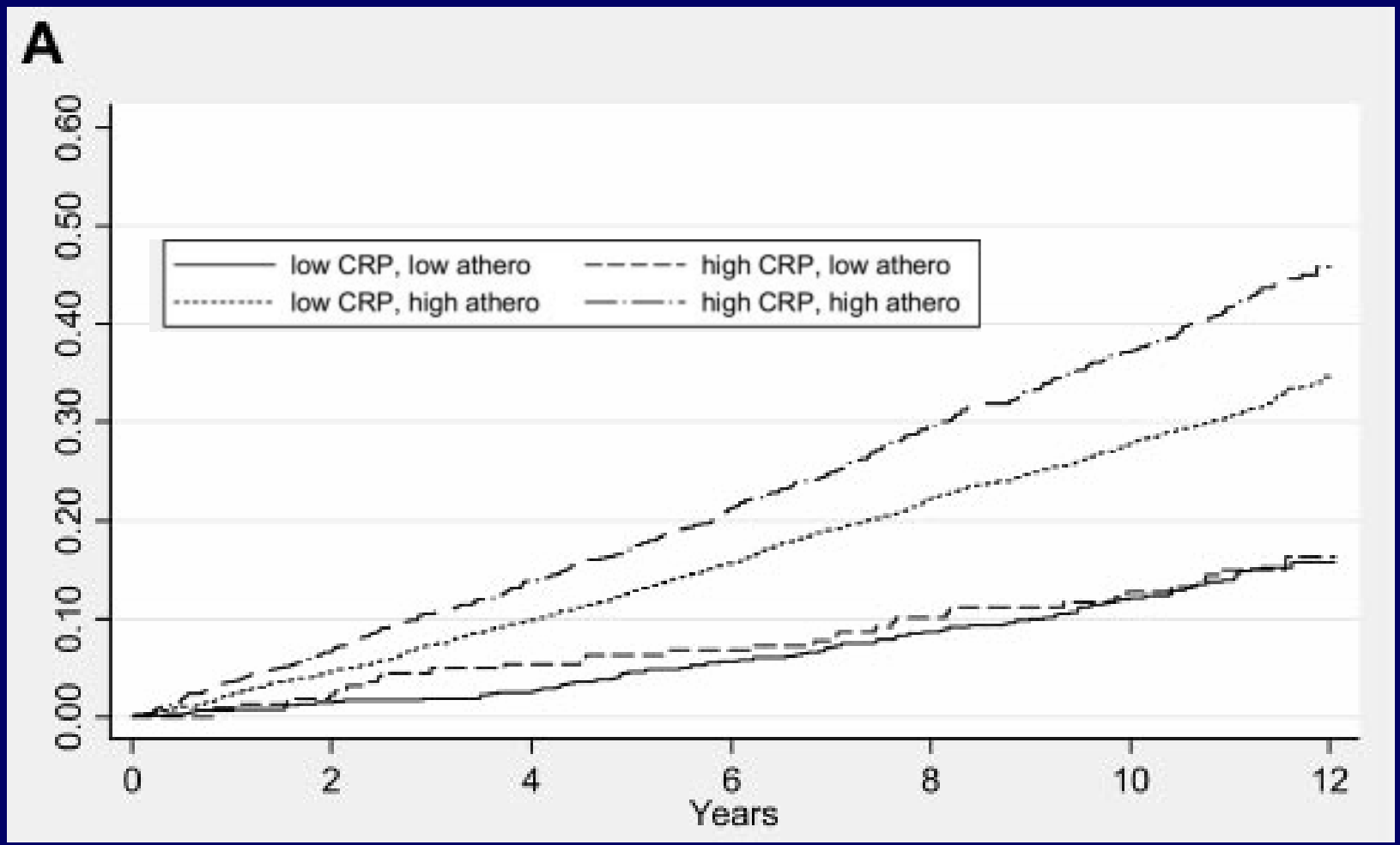
4: Pending the development of standard practice guidelines.

5: High cholesterol, high blood pressure, diabetes, smoking, family history, metabolic syndrome.

6: For stroke prevention, follow existing guidelines.

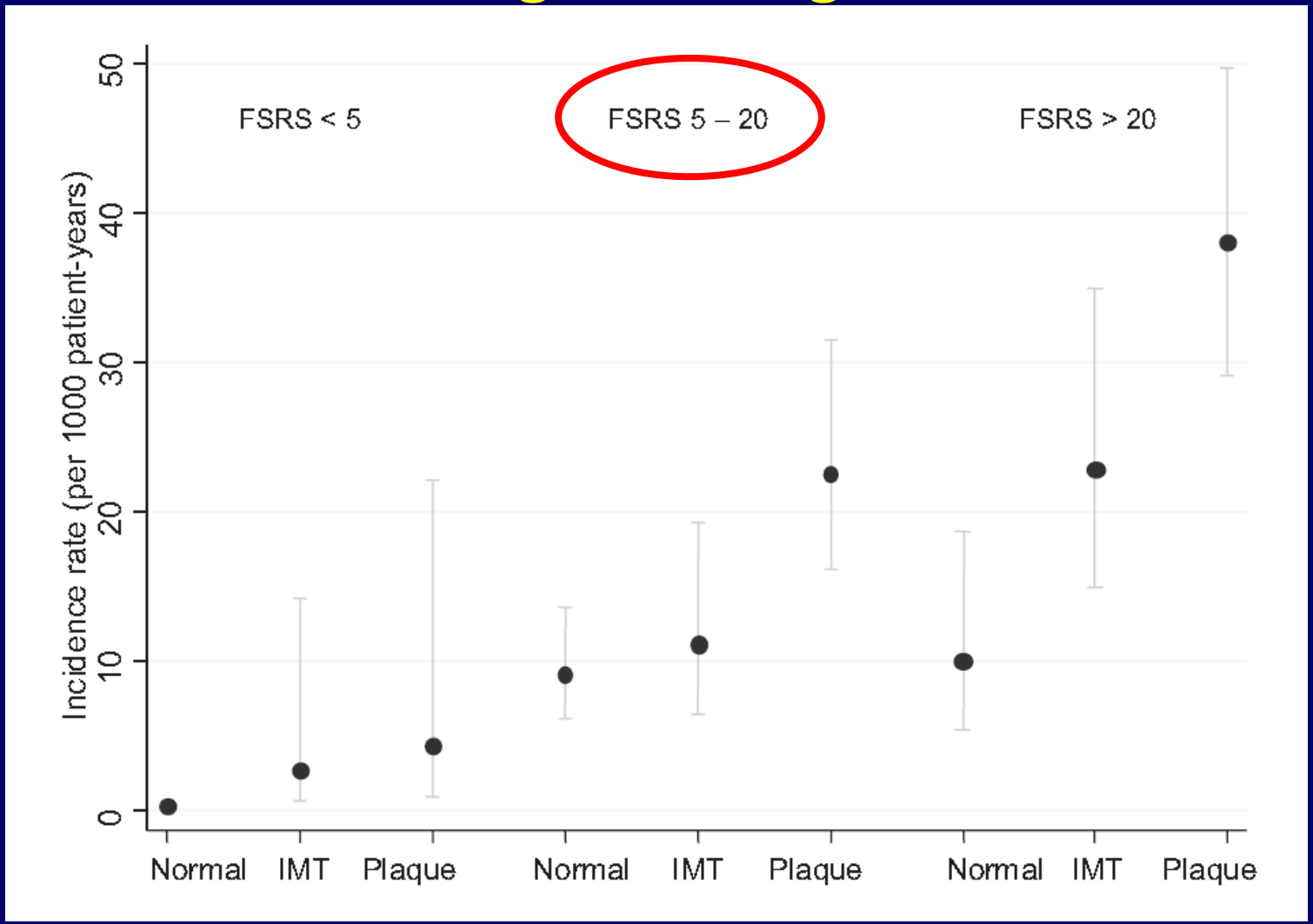
¿Qué hacemos con ella?

Eventos cardiovasculares de acuerdo a GIM de carótida y PCR. The Cardiovascular Health Study



Cao et al, Circulation 2007;116:32

Eventos cerebrovasculares o muerte cardiovascular de acuerdo a GIM de carótida y riesgo Framingham



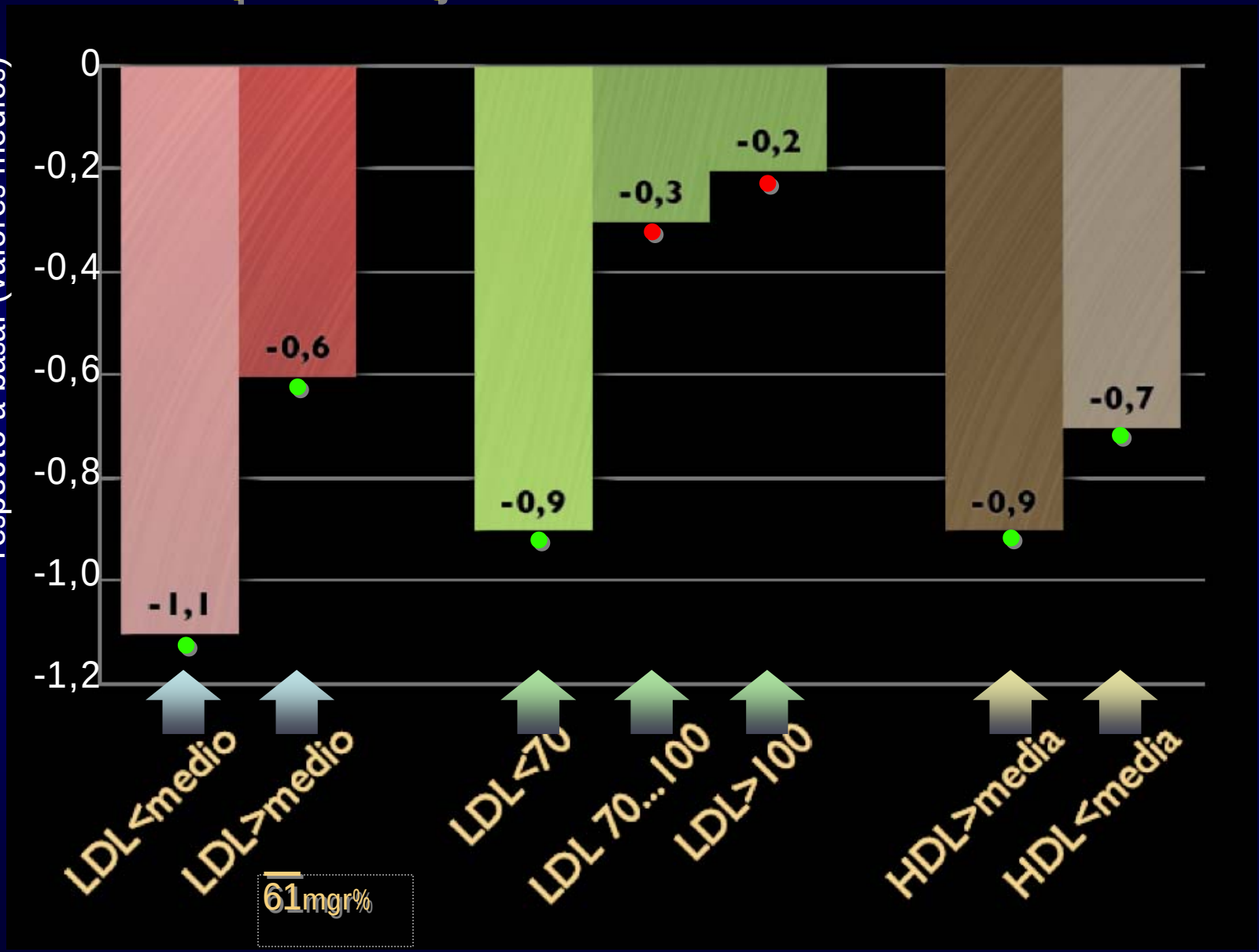
Prati P, et al. Stroke 2008;39:2470

¿Qué hacemos con ella?

Tratamiento de alto riesgo

Factores asociados a progresión y regresión

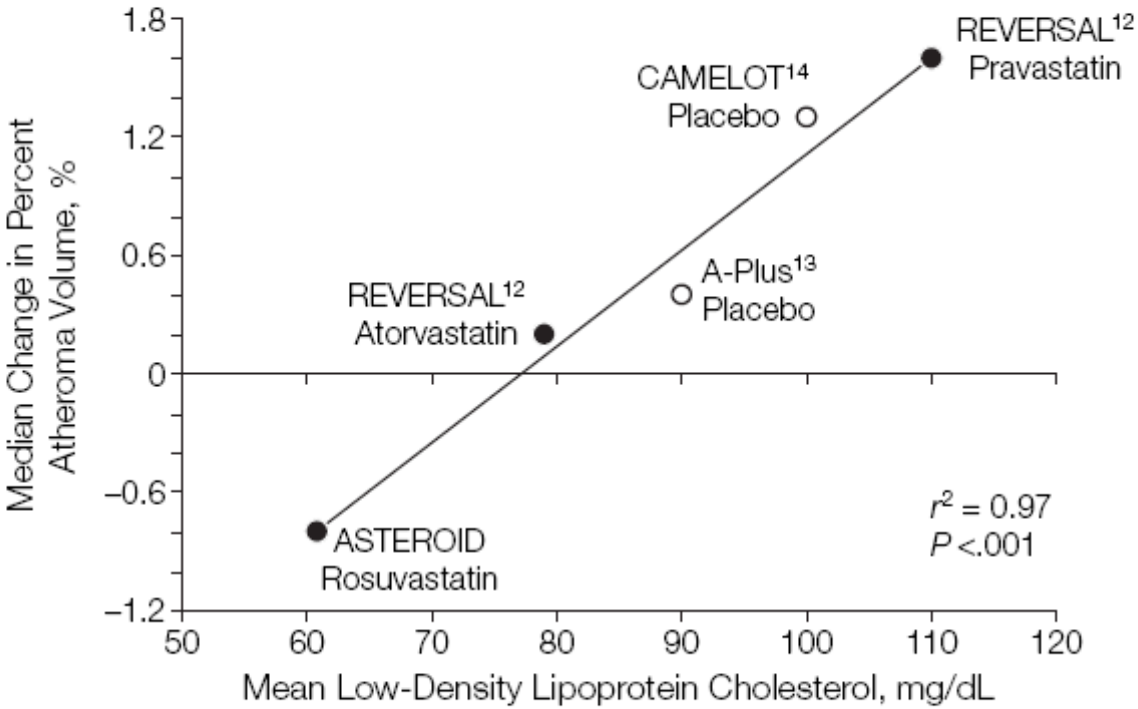
ASTEROID… en quienes mejora el ateroma



● p<0.001, ● p:NS, basal *vs* ROSU40

Nissen SE, Nichols SJ, Sipahi I, Raichlen JS, Ballantyne CM, Davignon J, et al. Effect of Very High-Intensity Statin Therapy on Regression of Coronary Atherosclerosis. The ASTEROID Trial. JAMA. 2006;295:642-51

Figure 3. Relationship Between Mean Low-Density Lipoprotein Cholesterol Levels and Median Change in Percent Atheroma Volume for Several Intravascular Ultrasound Trials



There is a close correlation between these 2 variables (r^2=0.97). REVERSAL indicates Reversal of Atherosclerosis With Aggressive Lipid-Lowering[12]; CAMELOT, Comparison of Amlodipine vs Enalapril to Limit Occurrences of Thrombosis[14]; A-Plus, Avasimibe and Progression of Lesions on Ultrasound[13]; and ASTEROID, A Study to Evaluate the Effect of Rosuvastatin on Intravascular Ultrasound-Derived Coronary Atheroma Burden.

Table 1. Baseline Characteristics of the 208 Study Patients Who Completed the 14-Month Assessment of Carotid Intima–Media Thickness, According to Treatment Group.*

Characteristic	Ezetimibe (N=111)	Niacin (N=97)	P Value
Male sex — no. (%)	91 (82)	76 (78)	0.51
Age — yr	65±11	64±11	0.49
Diabetes mellitus — no. (%)	44 (40)	31 (32)	0.25
Hypertension — no. (%)	96 (86)	82 (85)	0.69
Tobacco use — no. (%)	5 (5)	6 (6)	0.86
Family history of coronary heart disease — no. (%)	42 (38)	48 (49)	0.09
History of coronary heart disease — no. (%)			
Angina with documented ischemia	41 (37)	34 (35)	0.78
Angiographic coronary disease	70 (63)	63 (65)	0.78
Myocardial infarction	37 (33)	27 (28)	0.32
Percutaneous coronary revascularization	49 (44)	29 (30)	0.05
Coronary bypass surgery	26 (23)	25 (26)	0.69
Cholesterol — mg/dl			
Total cholesterol	146.6±23.3	145.6±24.0	0.74
LDL	83.7±19.9	80.5±17.2	0.22
HDL	43.3±8.5	42.5±8.6	0.48
Triglycerides — mg/dl			0.56
Median	122	126	
Interquartile range	87–162	94–163	

N Engl J Med 2009;361.

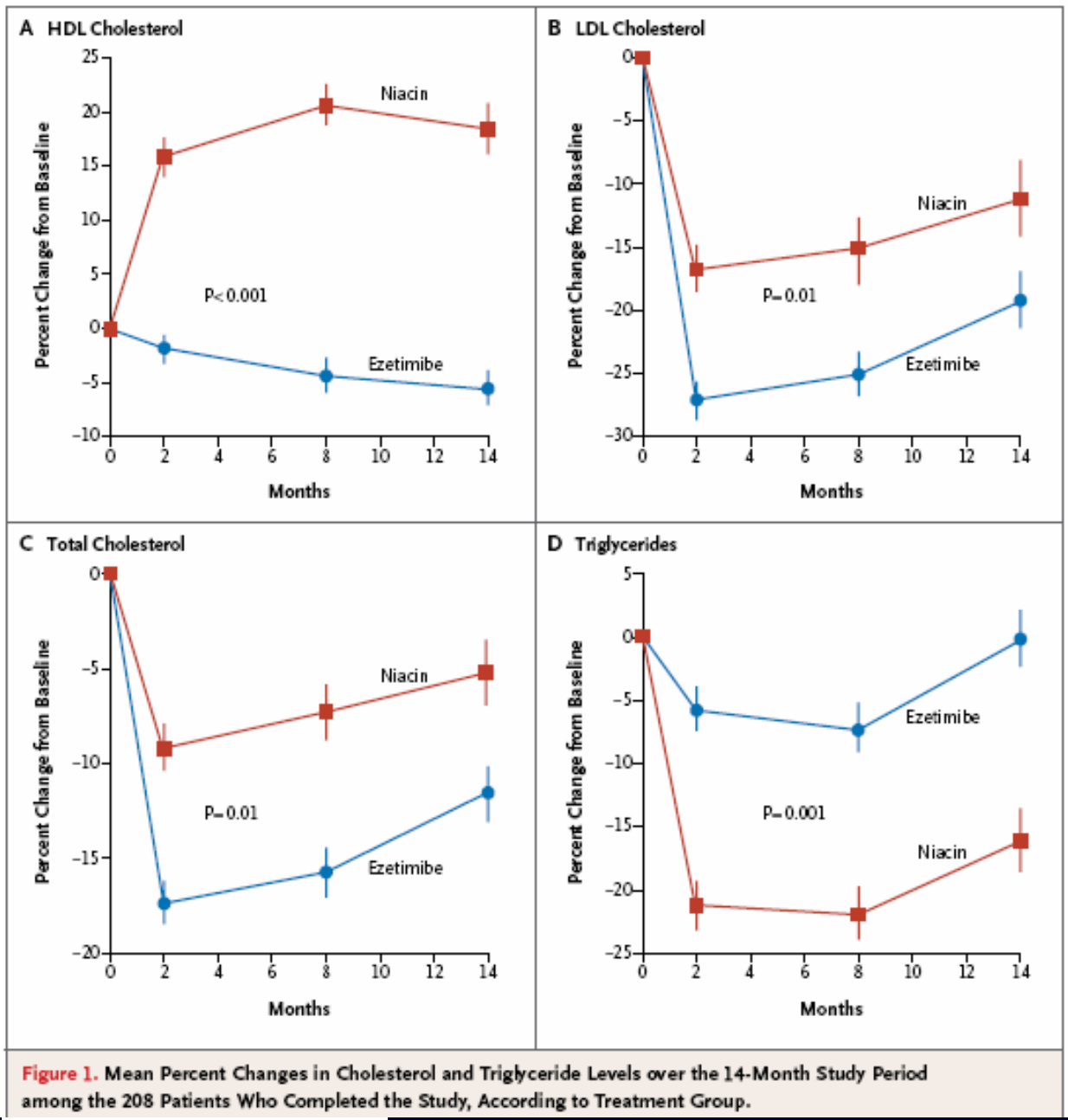


Figure 1. Mean Percent Changes in Cholesterol and Triglyceride Levels over the 14-Month Study Period among the 208 Patients Who Completed the Study, According to Treatment Group.

N Engl J Med 2009;361.

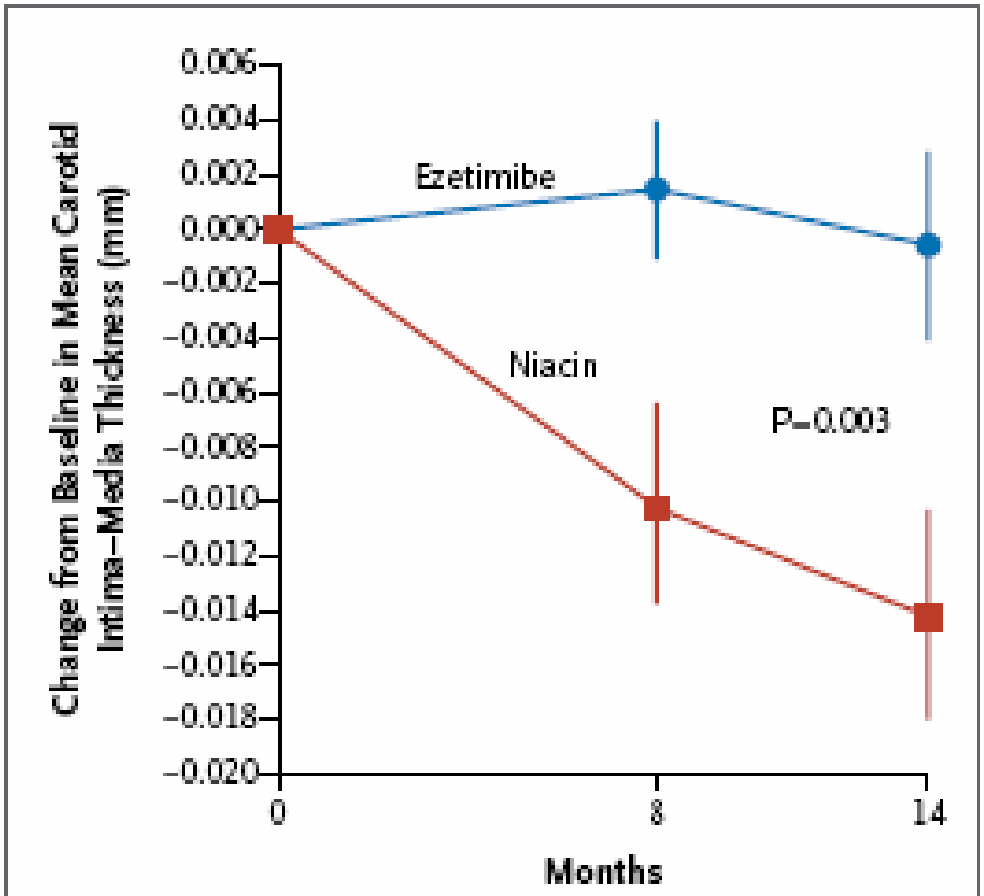
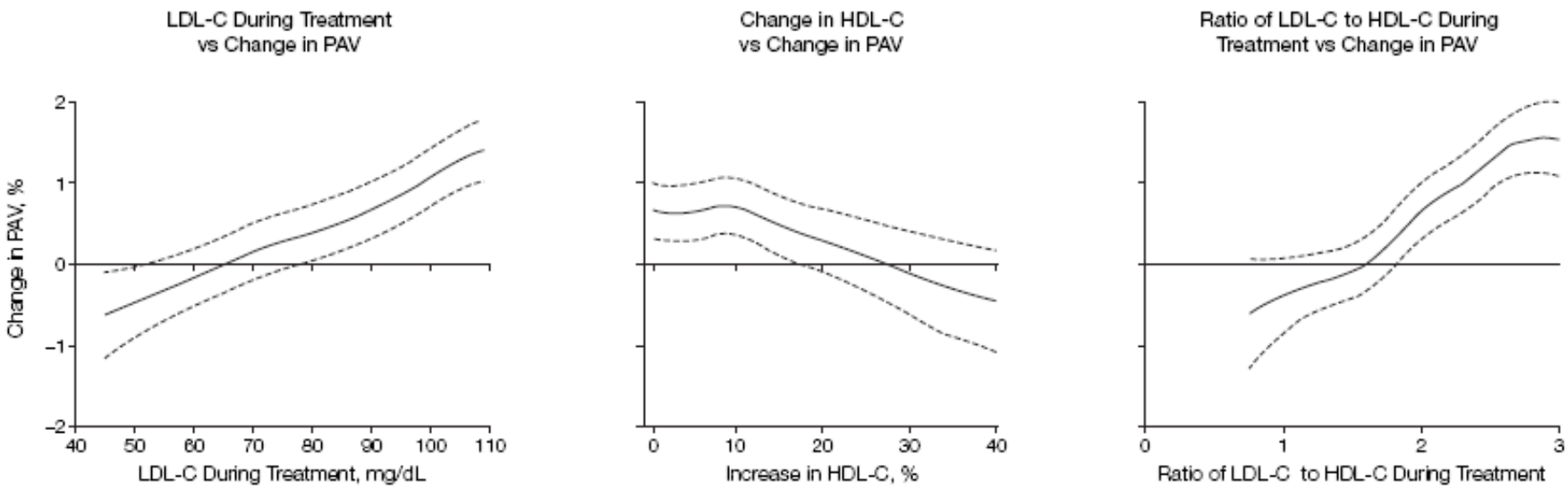


Figure 2. Changes in the Mean Carotid Intima–Media Thickness over the 14-Month Study Period, According to Treatment Group.

N Engl J Med 2009;361.

Volumen de ateroma coronario y cambios lipídicos. Metaanálisis de 4 estudios con IVUS

Figure. Relationships Between Change in Percent Atheroma Volume and Low-Density Lipoprotein Cholesterol, High-Density Lipoprotein Cholesterol, and Ratio of Low-Density Lipoprotein Cholesterol to High-Density Lipoprotein Cholesterol in Patients Receiving Statins



HDL-C indicates high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PAV, percent atheroma volume.

JAMA. 2007;297:499-508

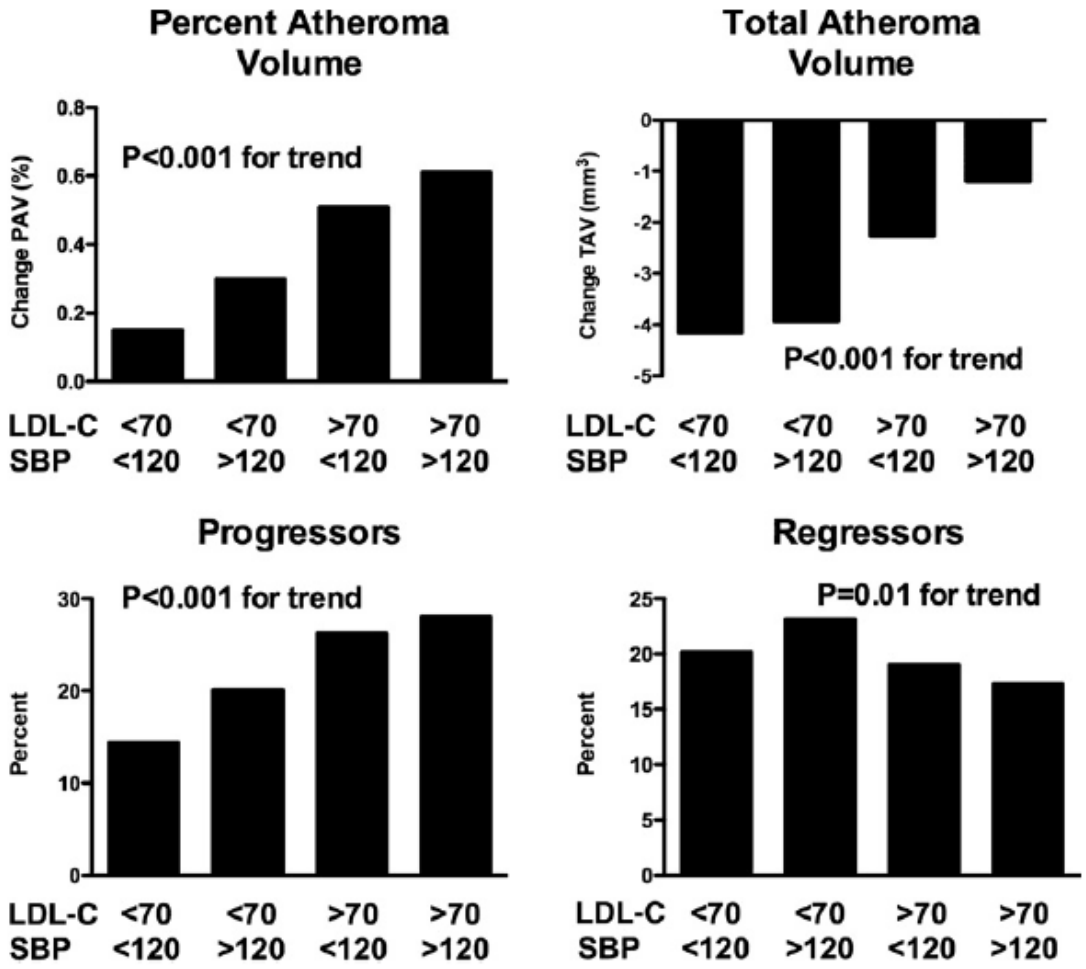
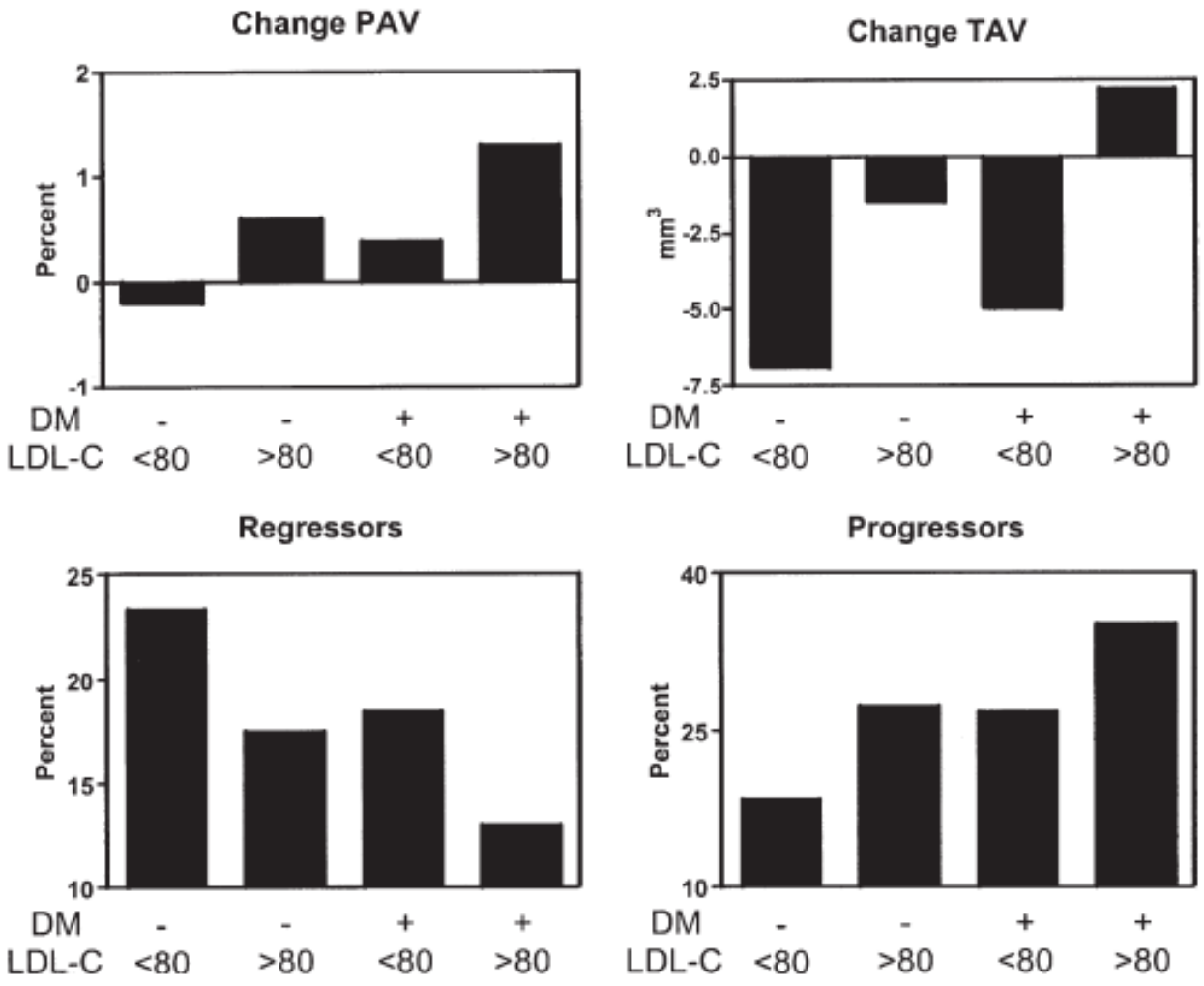


Figure 1 Serial Changes in Atheroma Burden

Change in percent atheroma volume (PAV) and total atheroma volume (TAV) and percentage of subjects undergoing substantial atheroma progression and regression, stratified according to on-treatment low-density lipoprotein cholesterol (LDL-C) and systolic blood pressure (SBP).

Effect of Diabetes on Progression of Coronary Atherosclerosis and Arterial Remodeling

A Pooled Analysis of 5 Intravascular Ultrasound Trials



(J Am Coll Cardiol 2008;52:255–62)

Resumen

- La detección de la aterosclerosis puede
  - Mejorar la predicción cardiovascular individual
  - Establecer objetivos terapéuticos
  - Monitorizar la eficacia del tratamiento
- La regresión del componente lipídico de la aterosclerosis es posible con intervenciones agresivas sobre los factores de riesgo que deben incluir en la mayor parte de sujetos descensos de LDLc < 70 mg/dL
- El ascenso de HDLc >20% asociado a la reducción de LDLc parece una herramienta muy útil para obtener regresión en pacientes de alto riesgo