ESTRATIFICACIÓN DEL RIESGO CARDIOVASCULAR: SON SUFICIENTES LAS TABLAS DE RIESGO O DEBE INVESTIGARSE LA ENFERMEDAD ATEROSCLERÓTICA SUBCLÍNICA

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El problema de la prevención primaria

- Varón 44 años
- Colesterol 246 mg/dl
- Triglicéridos 125 mg/dl
- HDLc 53 mg/dl
- LDLc 168 mg/dl
- CT/HDL: 4,6
- TA 136/84 mmHg
- No fumador
- IMC 27,3 kg/m2

- Varón 49 años
- Colesterol 188 mg/dl
- Triglicéridos 156 mg/dl
- HDLc 35 mg/dl
- LDLc 123 mg/dl
- CT/HDL: 5,5
- TA 162/94 mmHg
- No fumador
- IMC 23,7 kg/m2

El problema de la prevención primaria

- Varón 44 años
- Riesgo 10 años
  - Framingham Risk Score: 4%
  - Framingham-REGICOR: 3%
  - SCORE: 0%

- Varón 49 años
- Riesgo 10 años
  - Framingham Risk Score: 7%
  - Framingham-REGICOR: 3%
  - SCORE: 1%

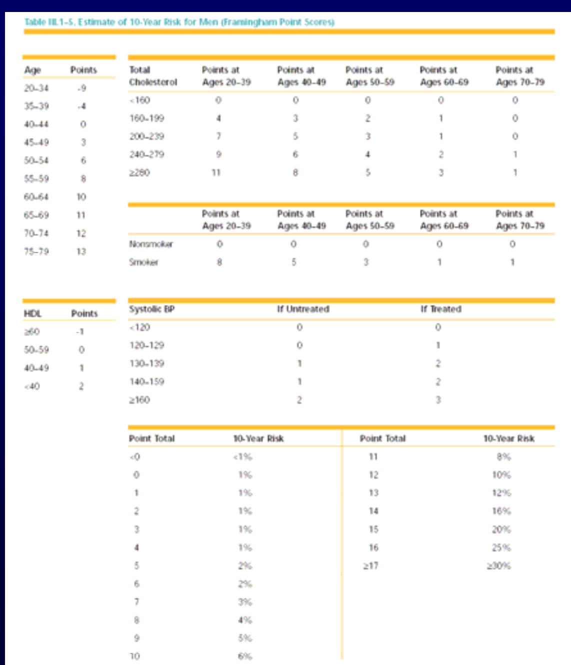


Table III.1-5. Estimate of 10-Year Risk for Men (Framingham Point Scores)

Age	Points
20–34	-9
35–39	-4
40–44	0
45–49	3
50–54	6
55–59	8
60–64	10
65–69	11
70–74	12
75–79	13

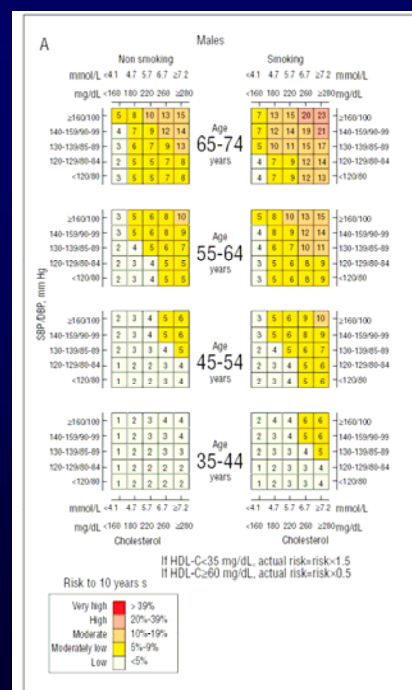
Total Cholesterol	Points at Ages 20–39	Points at Ages 40–49	Points at Ages 50–59	Points at Ages 60–69	Points at Ages 70–79
<160	0	0	0	0	0
160–199	4	3	2	1	0
200–239	7	5	3	1	0
240–279	9	6	4	2	1
≥280	11	8	5	3	1

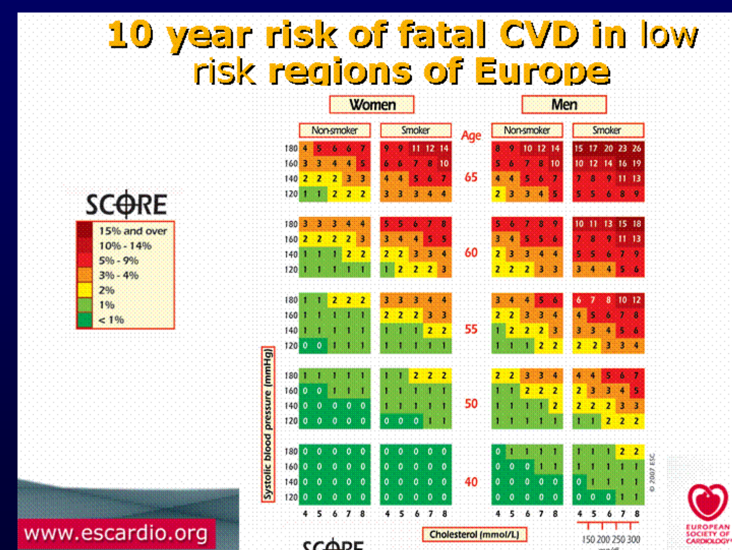
	Points at Ages 20–39	Points at Ages 40–49	Points at Ages 50–59	Points at Ages 60–69	Points at Ages 70–79
Nonsmoker	0	0	0	0	0
Smoker	8	5	3	1	1

HDL	Points
≥60	-1
50–59	0
40–49	1
<40	2

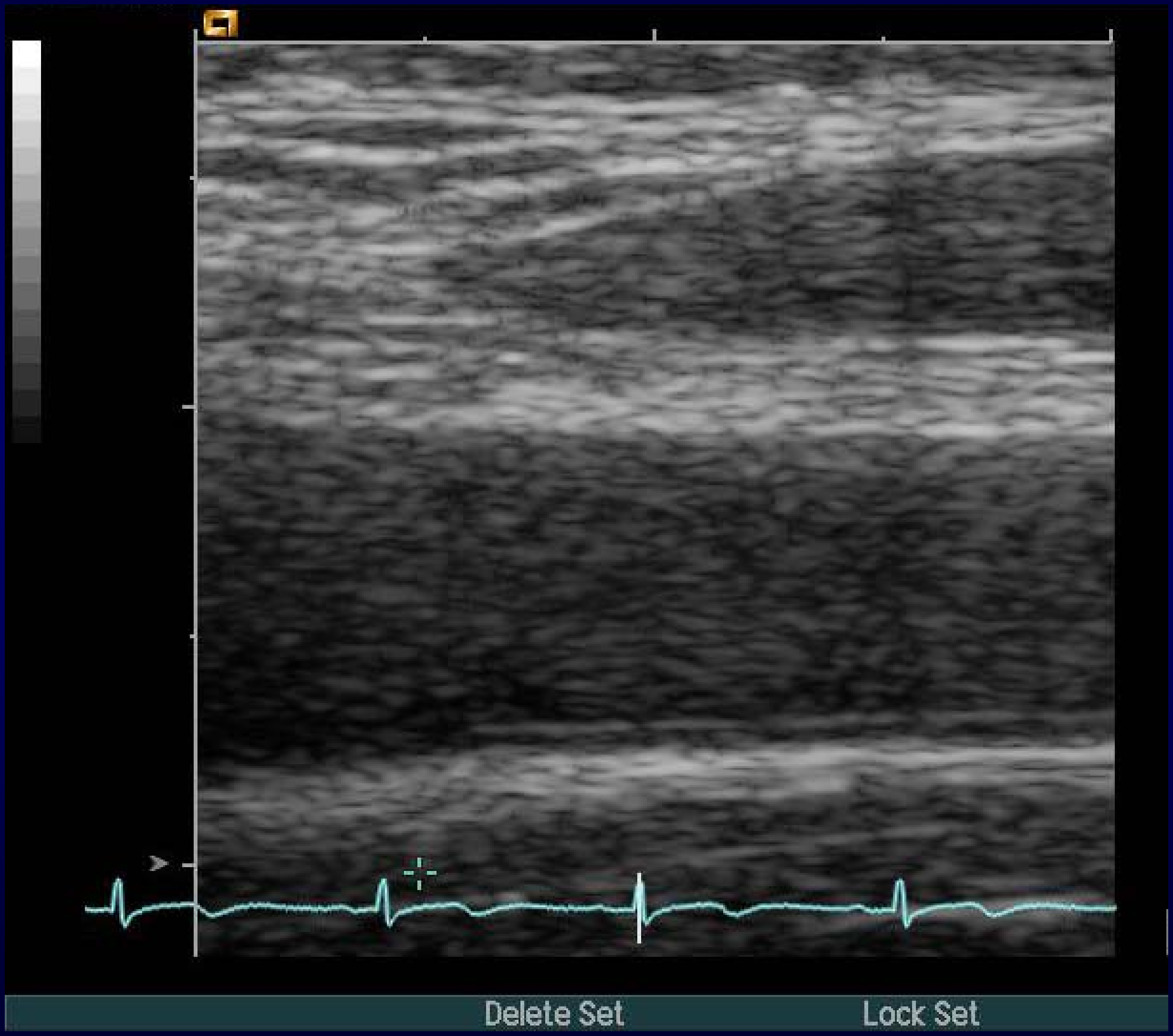
Systolic BP	If Untreated	If Treated
<120	0	0
120–129	0	1
130–139	1	2
140–159	1	2
≥160	2	3

Point Total	10-Year Risk	Point Total	10-Year Risk
<0	<1%	11	8%
0	1%	12	10%
1	1%	13	12%
2	1%	14	16%
3	1%	15	20%
4	1%	16	25%
5	2%	≥17	≥30%
6	2%		
7	3%		
8	4%		
9	5%		
10	6%		





VARÓN DE 44 AÑOS



VARÓN DE 49 AÑOS

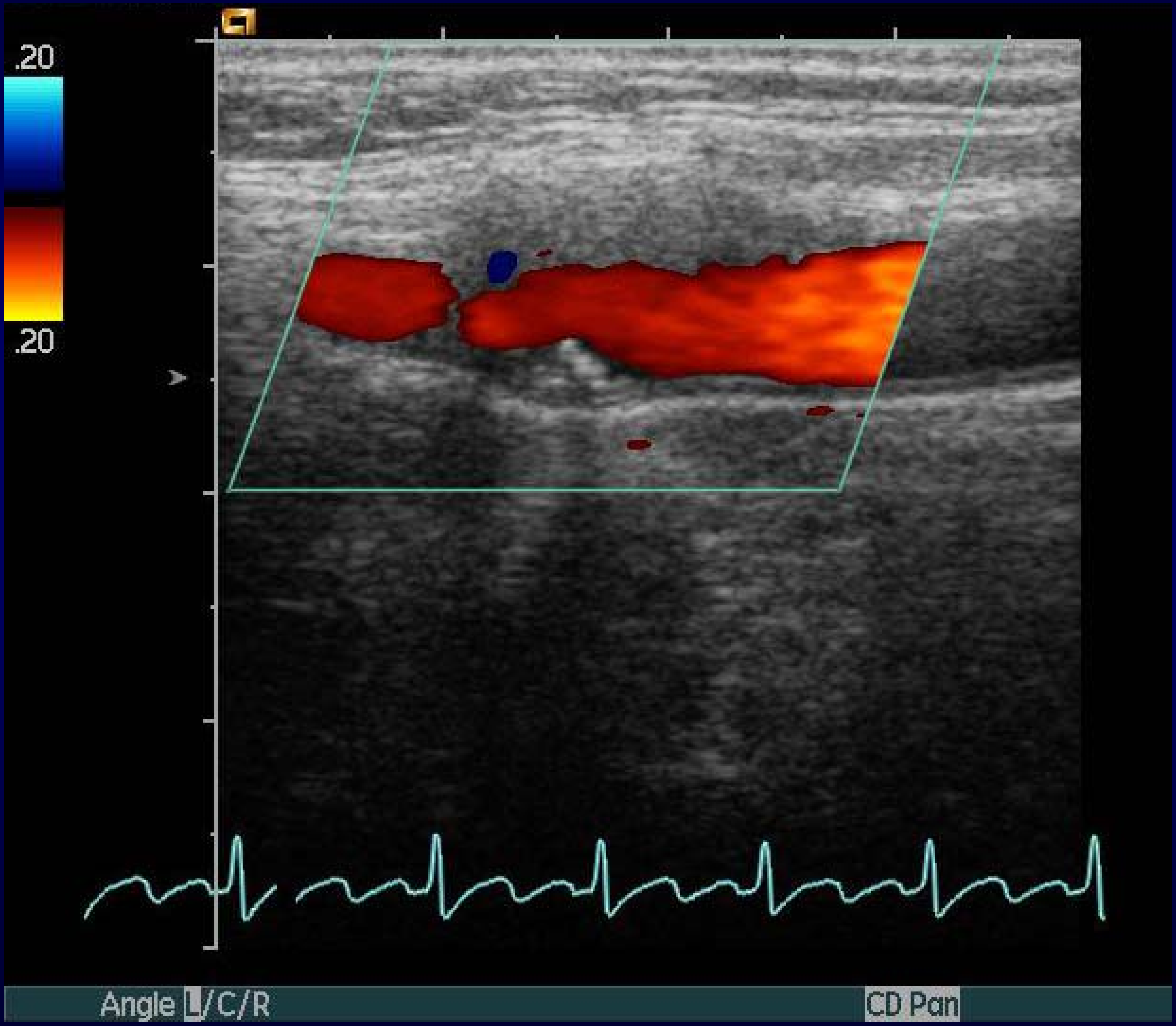


Table II.12–2b. Asymptomatic Carotid Disease

Subjects	Disease severity	CHD events	Estimated 10-yr CHD risk
ACAS trial[504] Entire cohort of 1,662 patients randomized to carotid surgery or medical management; 69% Hx CHD 28% smokers 25% diabetics	Asymptomatic Stenosis ≥60%	2.7 yr follow-up: 84 deaths from MI (n =45) or other cardiac disease	10-yr MI mortality rate 10%; CHD mortality rate 19%
Veterans Affairs Cooperative Study Group[505] Entire cohort of 444 men Mean age 60 27% Hx MI 50% smokers 30% diabetics All received aspirin therapy	Asymptomatic Stenosis ≥50%	4 yr follow-up: 91 deaths from cardiac causes	10-yr CHD mortality rate 51%
Mayo Asymptomatic Carotid Endarterectomy Study[506] 158 patients 40% Hx CAD 15% diabetics	Asymptomatic Stenosis ≥50% Trial stopped due to high event rate in surgical arm secondary to cessation of medical therapy (aspirin)	2.5 yr follow-up: 12 CHD events	10-yr CHD event rate 30%
CASANOVA[507] 410 patients 42% Hx CAD 26% smokers 30% diabetics	Asymptomatic Stenosis ≥50%	3.5 yr follow-up: 50 deaths due to CHD	10-yr CHD mortality rate 35%

ORIGINAL ARTICLE

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.

Rev Esp Cardiol. 2007;60(7):693-702

EDITORIAL

Nuevos instrumentos y los riesgos de siempre

Jaume Marrugat[a] y Joan Sala[b]

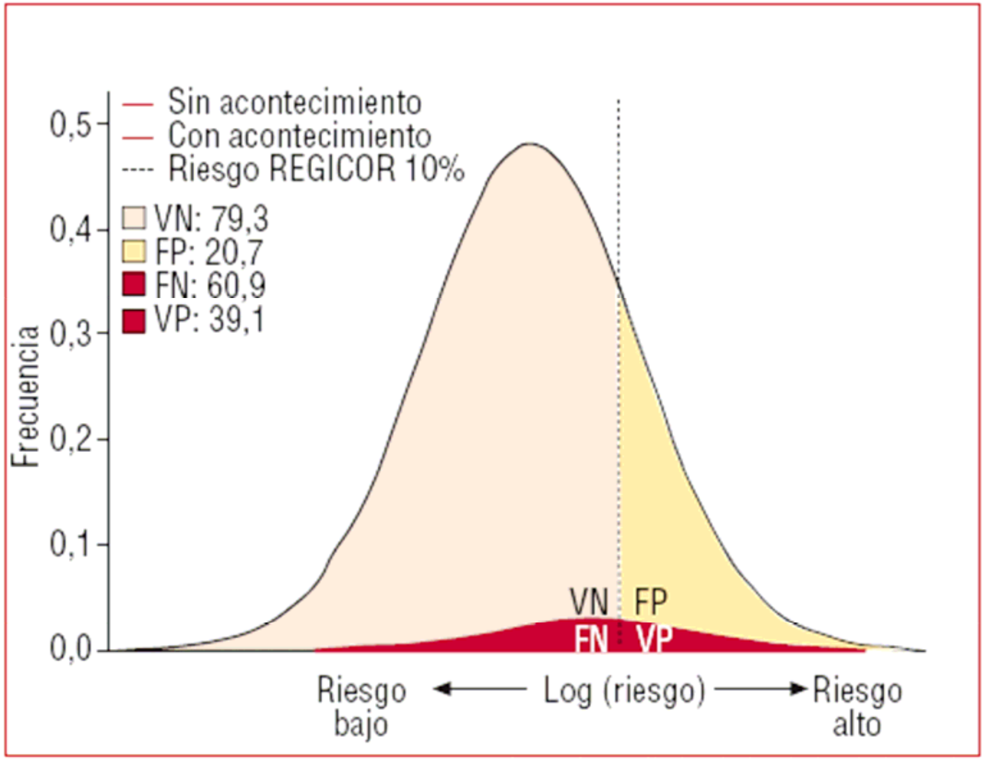
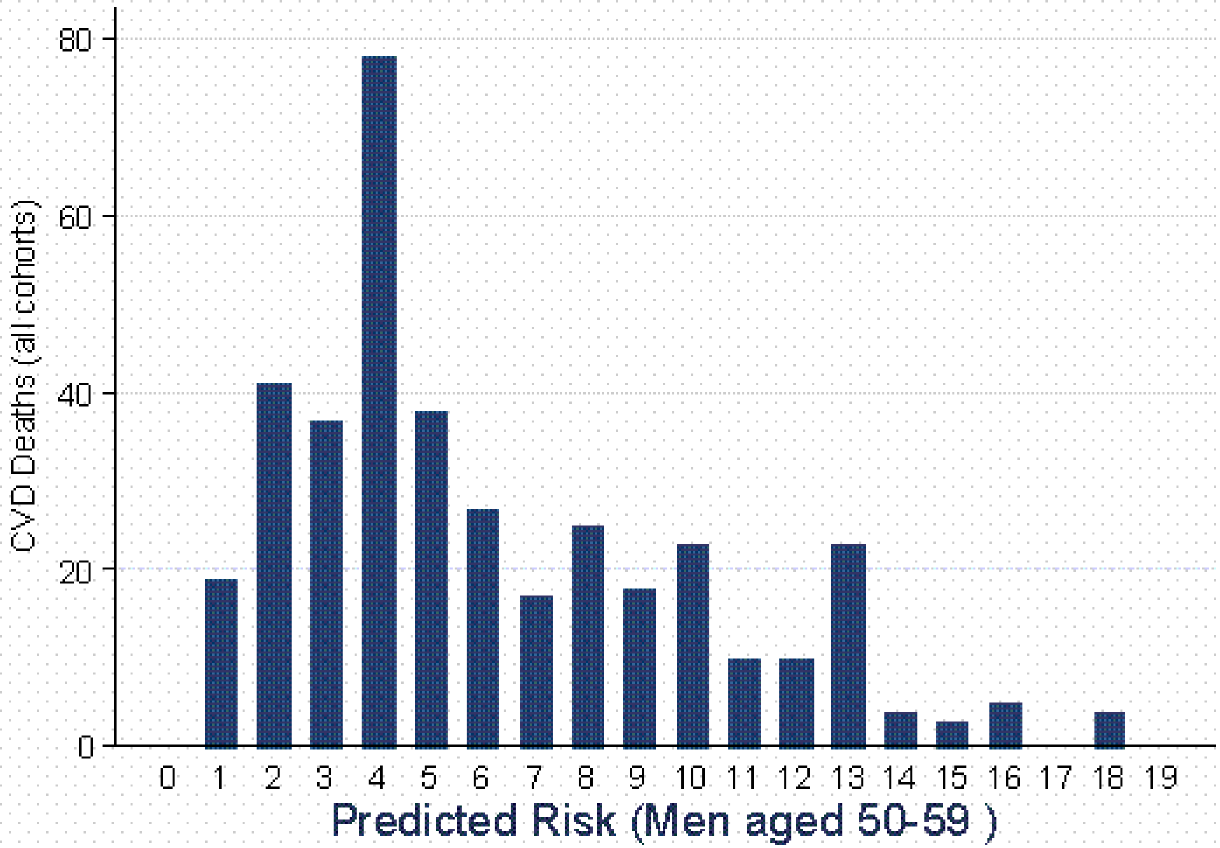


Fig. 2. Distribución de los resultados del logaritmo del riesgo en individuos que han desarrollado y no han desarrollado cardiopatía isquémica en el estudio VERIFICA.
FN: falsos negativos; FP: falsos positivos; VN: verdaderos negativos; VP: verdaderos positivos.

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

Fig. 1 - The expected number of CVD deaths at increasing levels of predicted risk. Illustration of the fact that most events occur in low risk subjects with few deaths among high risk subjects.

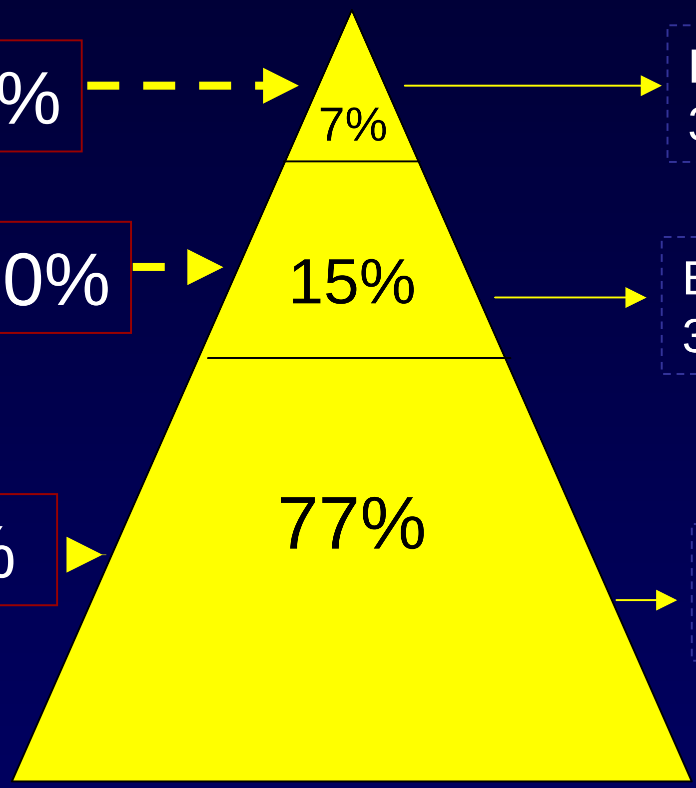


PREDICCIÓN RIESGO. ESTUDIO PROCAM

Riesgo > 20%

Riesgo 10- 20%

Riesgo < 10%



El 33,2% en próximos10 años-> 37% del total de infartos

El 14,3% en próximos10 años-> 31.7% del total de infartos

El 2.7% en próximos10 años-> 31.4% del total de infartos

Assmann G. Congreso Sociedad Española de Arteriosclerosis. Valencia 2007

ESTRATIFICACIÓN DEL RIESGO CARDIOVASCULAR. TABLAS DE RIESGO

- Escasa sensibilidad
- Cierta utilidad para valorar riesgo de poblaciones
- Alta inseguridad a nivel individual, especialmente en personas mayores de 65 años
- Poca utilidad para la prevención a largo plazo
- Sin previsión que la incorporación de nuevos marcadores bioquímicos o genéticos mejoren su poder predictivo
- Herramientas para uso de hipolipemiantes

Managing total CVD risk: Lipids

In ALL cases, look for and manage all risk factors. Those with established CVD, diabetes type 2 or type 1 with microalbuminuria, or with severe hyperlipidaemia are already at high risk. For all other people, the SCORE charts can be used to estimate total risk

Established CVD | **Diabetes as above** | **Markedly raised lipid levels**

- Dietary and exercise advice together with attention to all risk factors comes first.
- Aim to reduce total cholesterol to <4.5 mmol/L (~175 mg/dL) or <4 mmol/L (~155 mg/dL) if feasible, and LDL-cholesterol to <2.5 mmol/L (~100 mg/dL) or <2 mmol/L (~80 mg/dL) if feasible.
- This will require statin treatment in many. Some recommend statins for all CVD and most diabetic patients regardless of baseline levels.

SCORE risk ≥ 5%

Lifestyle advice for 3 months, then reassess SCORE and fasting lipids

SCORE risk still ≥ 5% → (see box on the left)

TC < 5 mmol/l and LDL-C < 3 mmol/l and SCORE now < 5% → (see box on the right)

SCORE risk < 5%

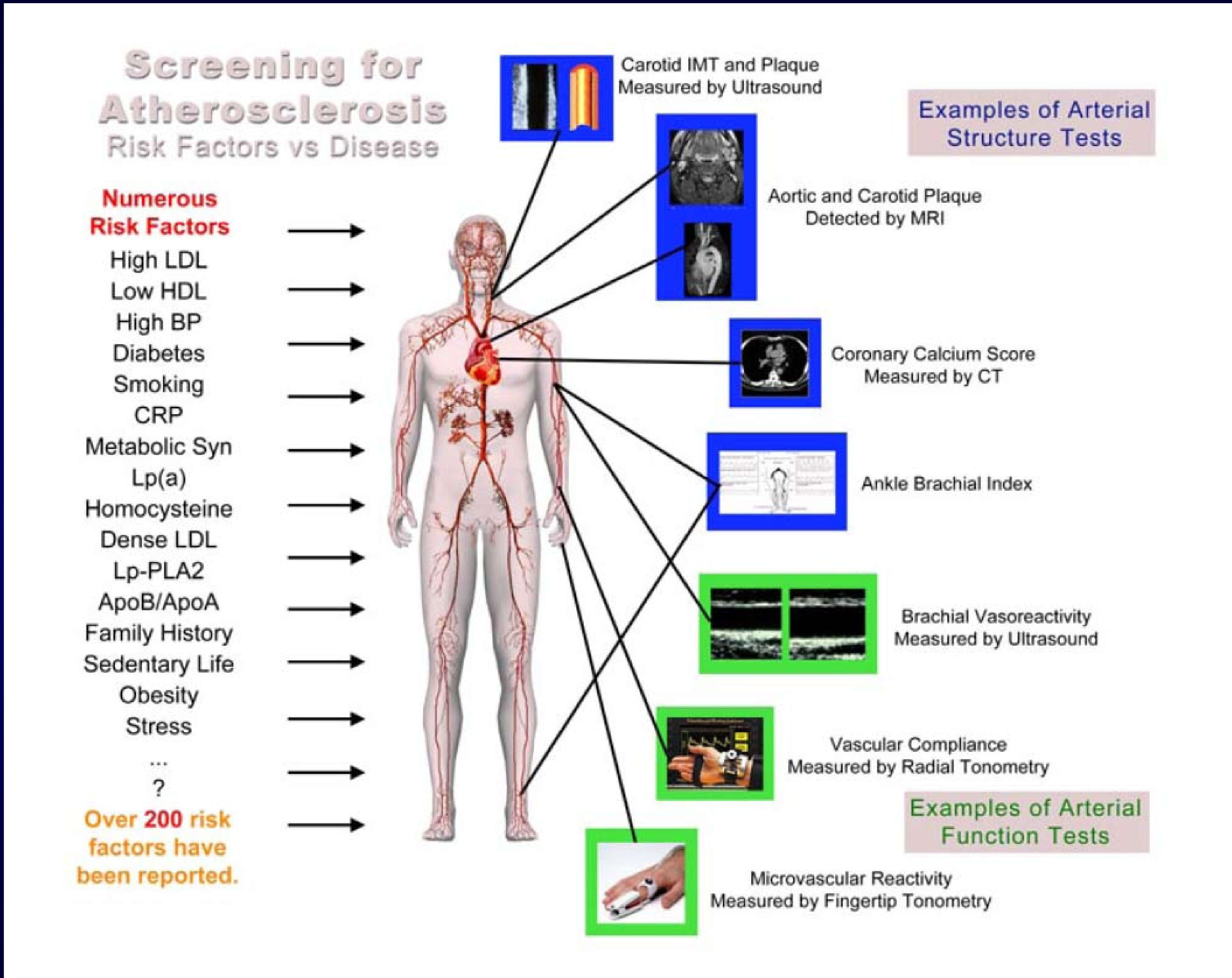
Lifestyle advice to reduce total chol <5 mmol/L (~190 mg/dL) and LDL-C <3 mmol/L (~115 mg/dL)
Regular follow-up

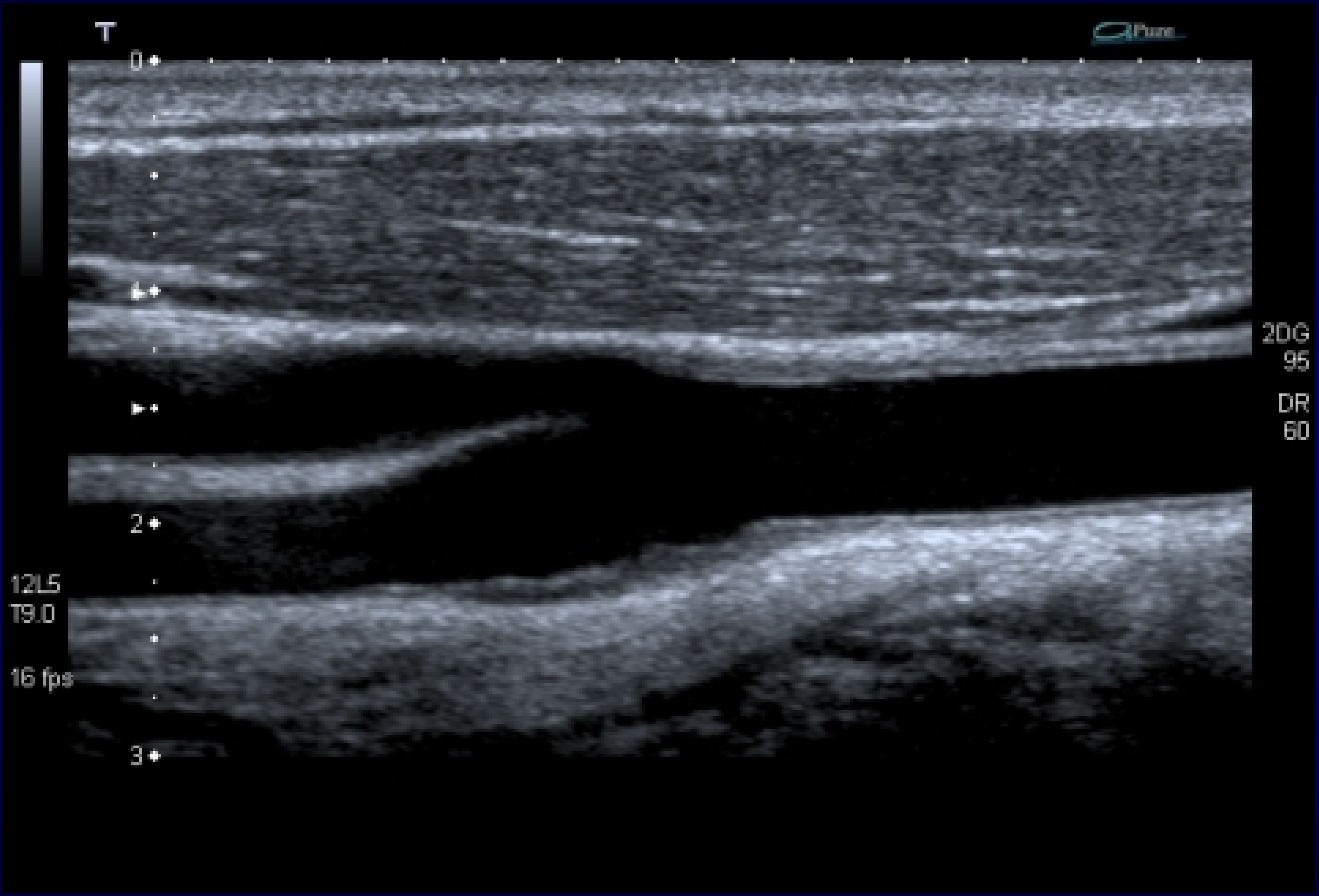
Treatment goals are not defined for HDL cholesterol and triglycerides, but HDL-C <1.0 mmol/L (~40 mg/dL) for men and <1.2 mmol/L (~45 mg/dL) for women and fasting triglycerides of >1.7 mmol/L (~150 mg/dL) are markers of increased cardiovascular risk

Managing total CVD risk: Blood Pressure

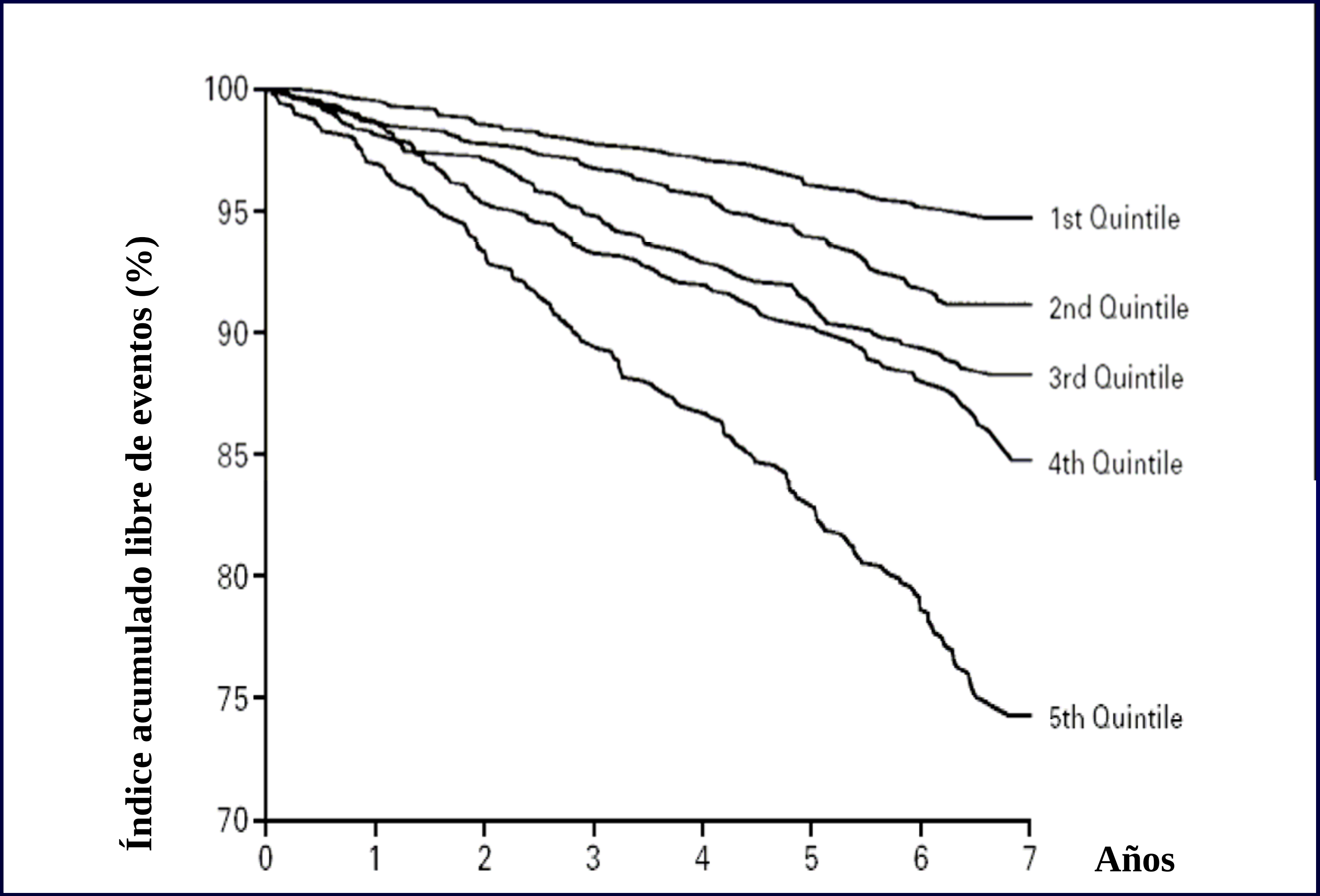
In ALL cases, look for and manage all risk factors. Those with established CVD, diabetes or renal disease are at markedly increased risk, and a BP of <130/80 is desirable if feasible. For all other people, check SCORE risk. Those with target organ damage are managed as 'increased risk'.

SCORE CVD risk	Normal <130/85	High Normal 130–139/ 85–89	Grade 1 140–159/ 90–99	Grade 2 160–179/ 100–109	Grade 3 ≥180/110
Low <1%	Lifestyle advice	Lifestyle advice	Lifestyle advice	Drug Rx if persists	Drug Rx
Moderate 1–4%	Lifestyle advice	Lifestyle advice	+consider drug Rx	Drug Rx if persists	Drug Rx
Increased 5-9%	Lifestyle advice	+consider drug Rx	Drug Rx	Drug Rx	Drug Rx
Markedly increased ≥10%	Lifestyle advice	+consider drug Rx	Drug Rx	Drug Rx	Drug Rx


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


T
0
2
3
2DG
95
DR
60
12L5
T9.0
16 fps

Índice acumulado del tiempo libre de eventos (ictus e infarto de miocardio) de acuerdo al quintil basal de GIM en el estudio de Salud Cardiovascular (Cardiovascular Health Study)



O'Leary DH, et al. N Engl J Med. 1999;340:14-22

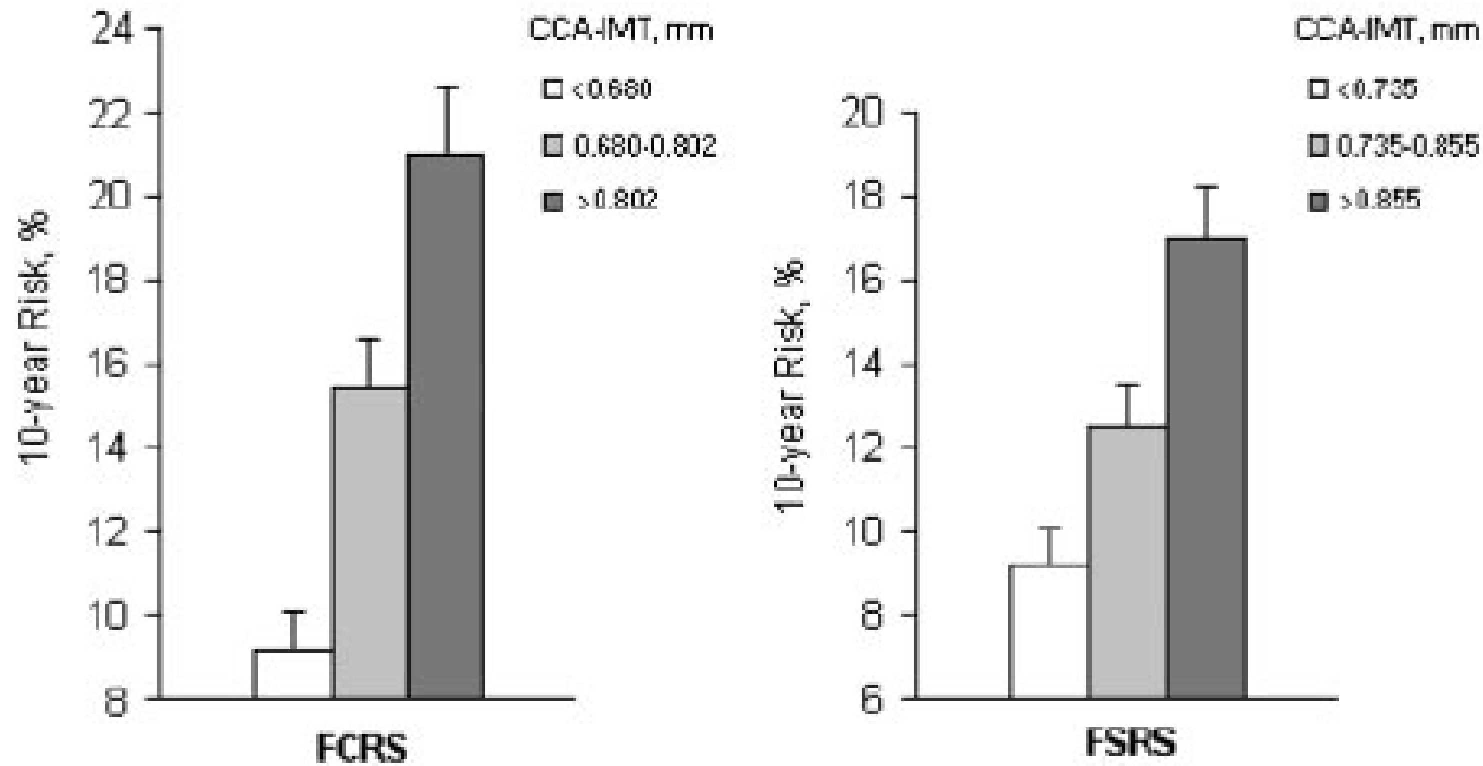


Figure 1. Geometric means of FCRS (left panel) and FSRS (right panel) by tertiles of CCA-IMT. Upper bounds of 95% CI are indicated.

Touboul P-J, et al. Stroke 2005;36:1741-45

Riesgo de IAM e ictus por cada 0,1 mm de GIM. Ajustado por edad y sexo

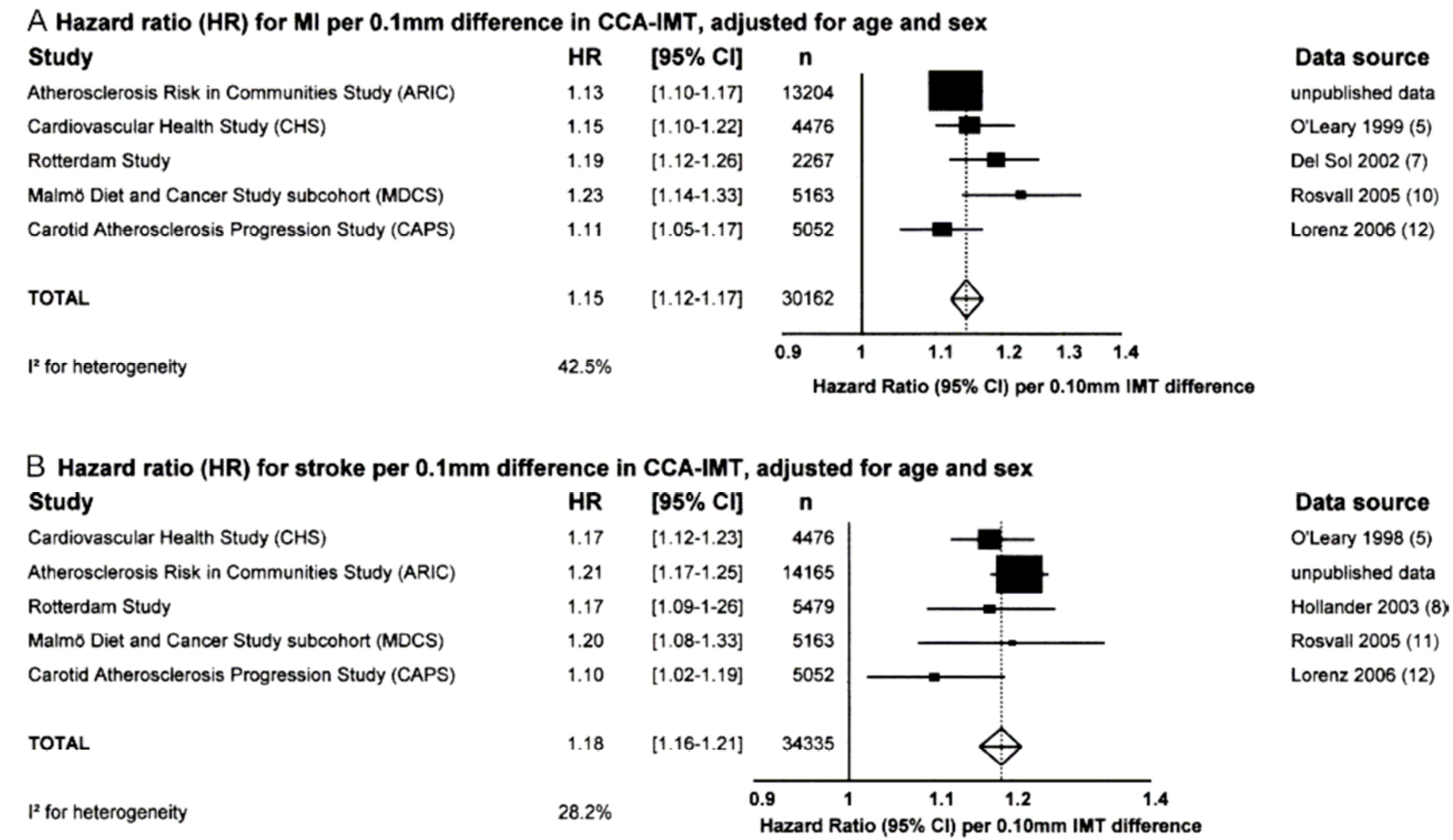


Figure 4. Forest plots of the HRs per 0.10-mm difference in the CCA-IMT, adjusted for age and sex.

Lorenz MW, et al. Circulation 2007;115:459-467

Riesgo de IAM e ictus por cada 0,1 mm de GIM. Ajustado por edad, sexo y factores de riesgo

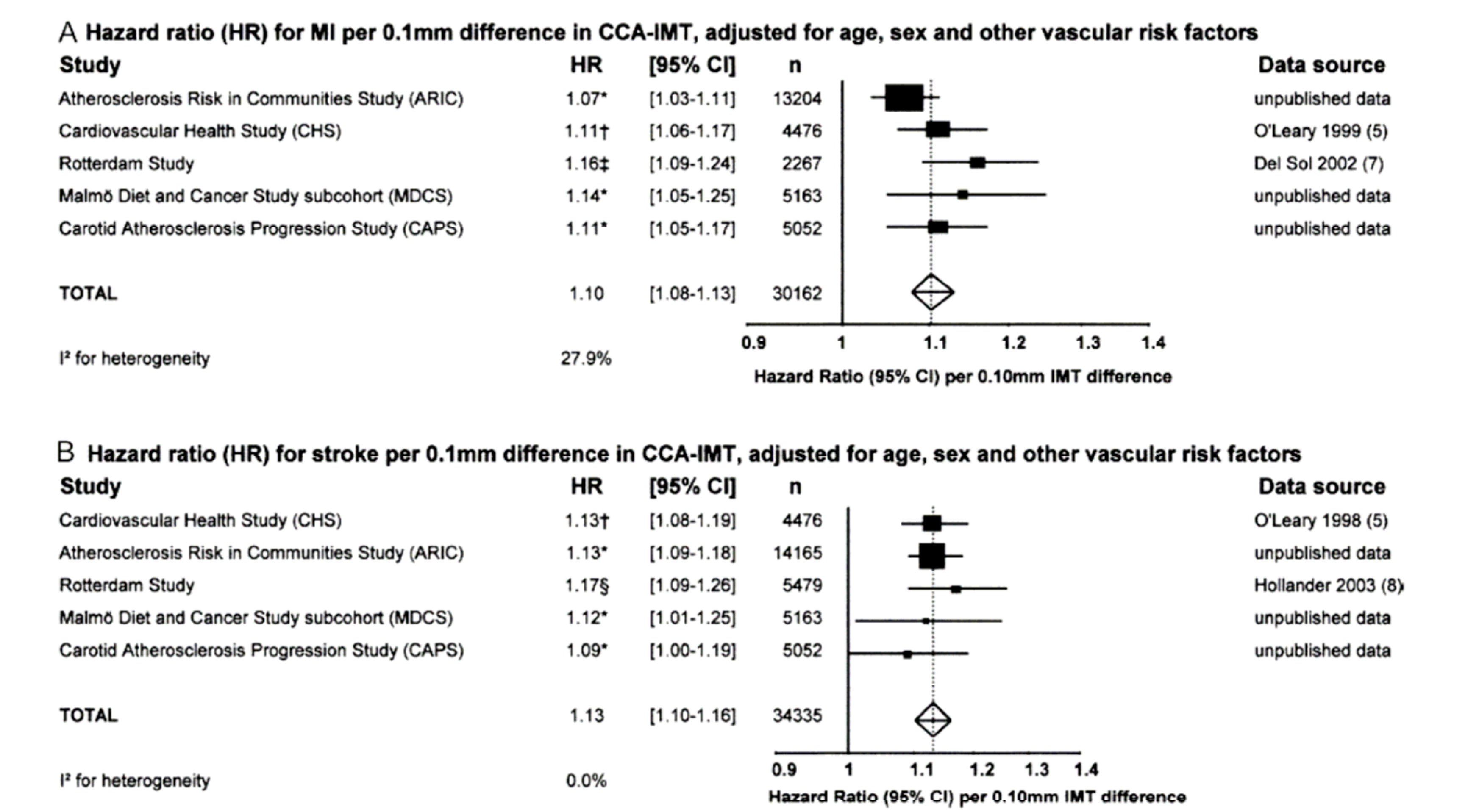
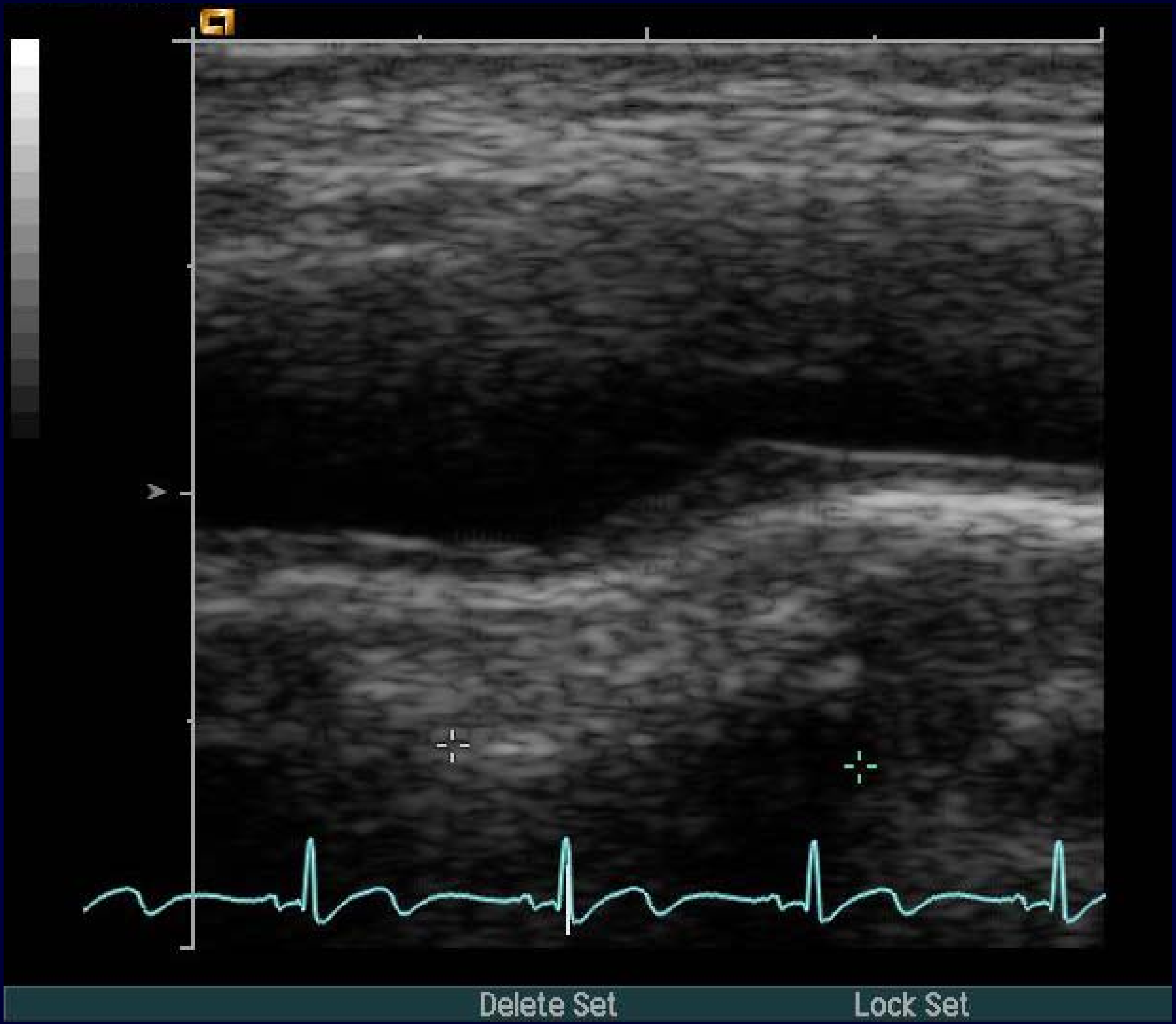


Figure 6. Forest plots of the HRs per 0.10-mm difference in the CCA-IMT, adjusted for age and sex and other vascular risk factors. *Adjusted for age, sex, body mass index, systolic and diastolic blood pressure, LDL cholesterol, smoking and diabetes. †Adjusted for age, sex, systolic and diastolic blood pressure, smoking, and diabetes. ‡Adjusted for age, sex, BMI, systolic and diastolic blood pressure, total and HDL cholesterol, smoking, and diabetes. §Adjusted for age, sex, systolic and diastolic blood pressure, total and HDL cholesterol, smoking, diabetes, and cardiovascular disease.

Lorenz MW, et al. Circulation 2007;115:459-467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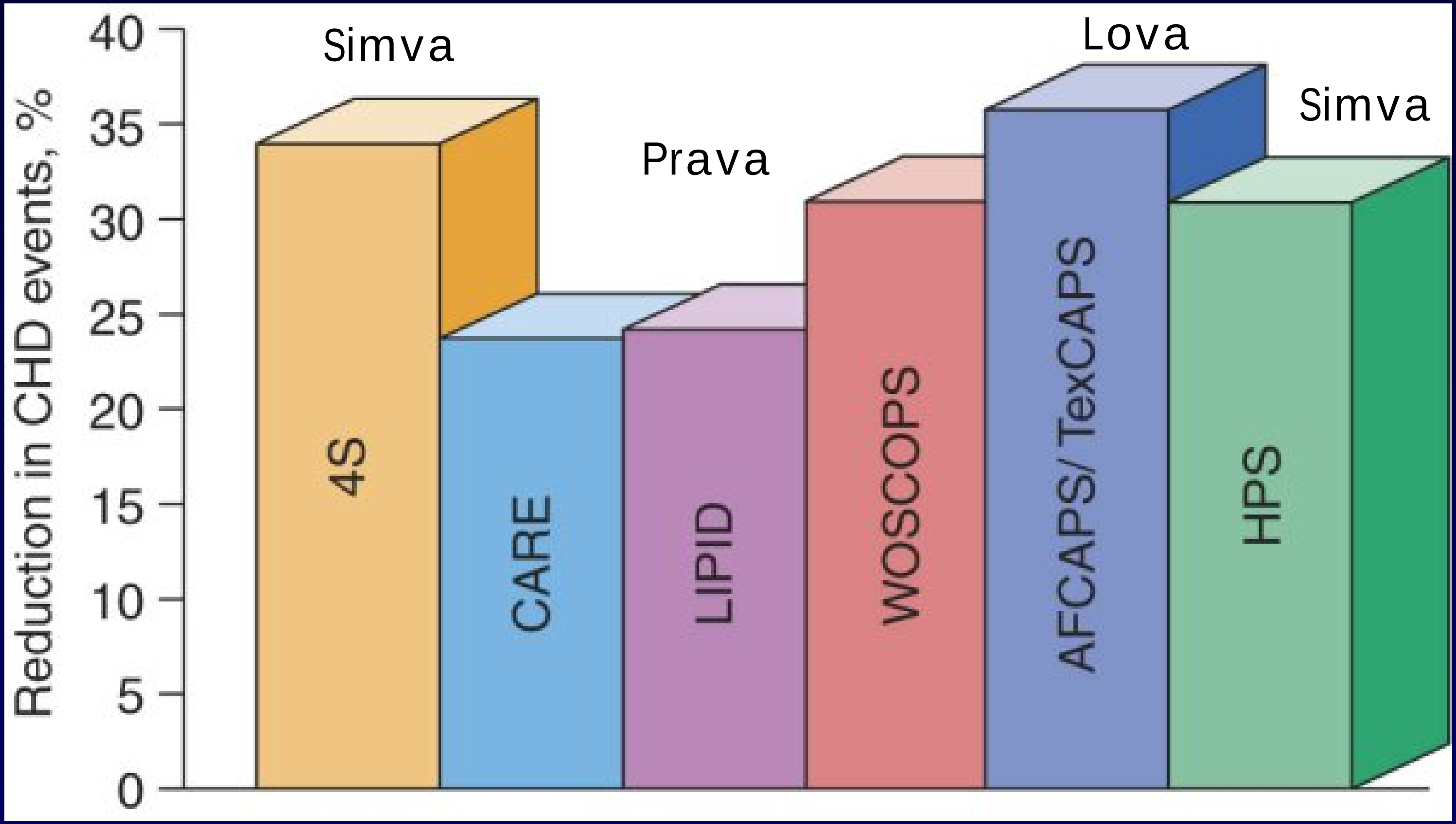
Guías o recomendaciones de las principales sociedades

- **NECP-ATP III. (2002)**
  - **GIM dentro de los procedimientos para detectar la extensión de las placas de aterosclerosis.**
  - **Considera que su precio, disponibilidad, y las dificultades para su estandarización lo hacen poco recomendable a la hora de modificar la intensidad del tratamiento hipolipemiante.**
  - **Concluyen: "si la exploración del GIM se hace en condiciones adecuadas, el GIM puede ser utilizado 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 decisiones de salud-enfermedad"**



Harrison's, 2004. Edición 16

Eventos coronarios en estudios con estatinas

	Without Diabetes		With Diabetes	
Trial	On Statin	On Placebo	On Statin	On Placebo
HPS (CAD patients)*[4]	19.8%	25.7%	33.4%	37.8%
CARE†[7]	19.6%	24.6%	28.7%	36.8%
LIPID*[8]	11.7%	15.2%	19.7%	22.8%
PROSPER*[9]	13.1%	16%	23.1%	18.4%
ASCOT*[10]	4.9%	8.7%	9.6%	11.4%
	High HDL-C on Statin	**High HDL-C on Placebo**	**Low HDL-C on Statin**	**Low HDL-C on Placebo**
HPS*[4]	17%	20.9%	22.0%	29.9%
CARE/LIPID*†[7,8]	18.5%	22.4%	25%	30.8%
PROSPER*[9]	12.8%	11.6%	13%	19.3%

ASCOT = Anglo-Scandinavian Cardiac Outcomes Trial; CARE = Cholesterol and Recurrent Events; HDL-C = high-density lipoprotein cholesterol; HPS = Heart Protection Study; LIPID = Long-Term Prevention with Pravastatin in Ischaemic Disease; PROSPER = Prospective Study of Pravastatin in the Elderly at Risk.

* Coronary artery disease (CAD) death, nonfatal myocardial infarction, coronary or noncoronary revascularization, stroke.

† CAD death and nonfatal myocardial infarction.

Davidson MH. Am J Cardiol 2005;96[suppl]:3K–13K

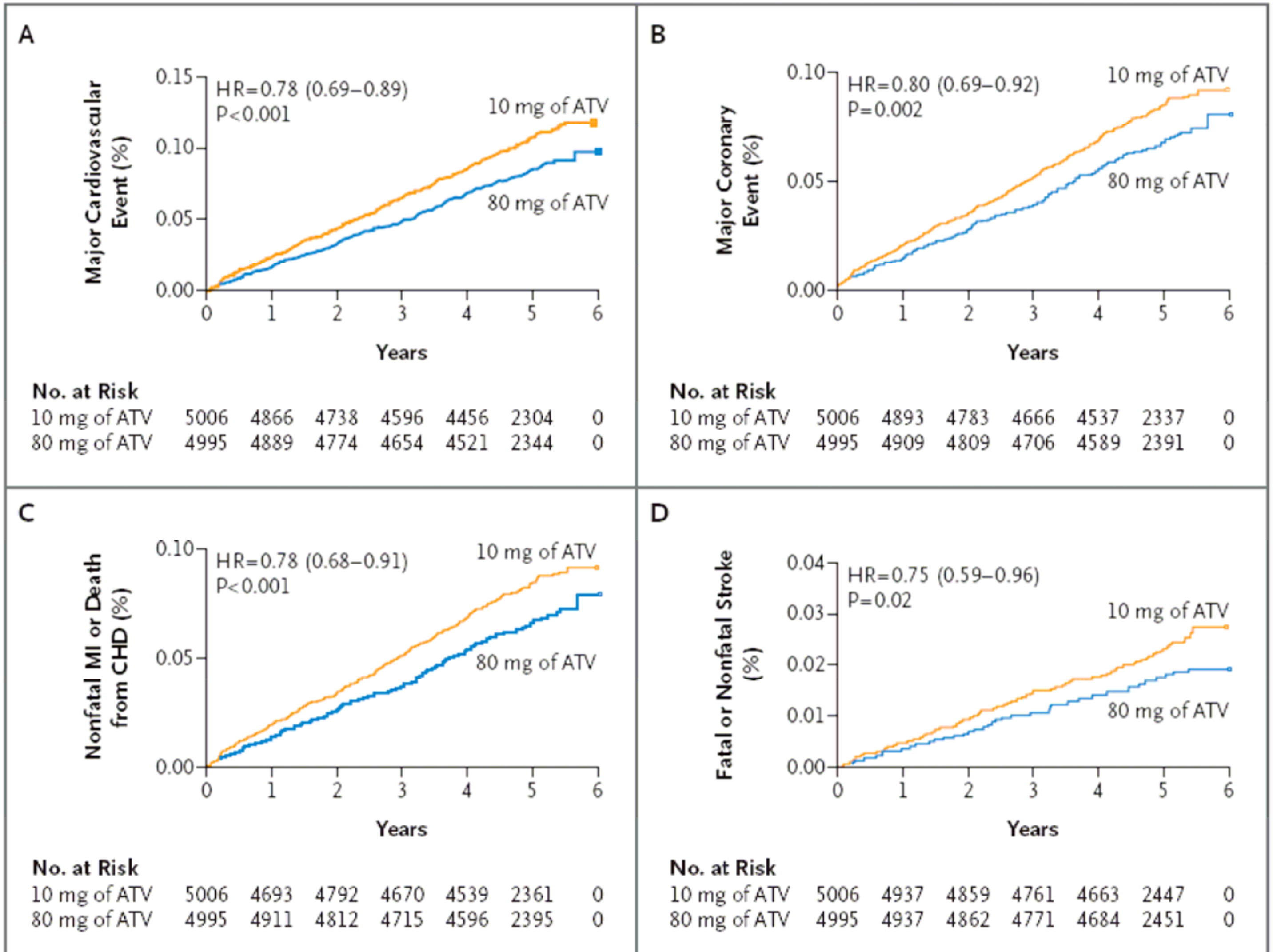


Figure 3. Cumulative Incidence of a First Major Cardiovascular Event (Panel A), a First Major Coronary Event (Panel B), Nonfatal Myocardial Infarction (MI) or Death from CHD (Panel C), and a First Fatal or Nonfatal Stroke (Panel D).

The NEW ENGLAND JOURNAL of MEDICINE

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Optimal Medical Therapy with or without PCI for Stable Coronary Disease

William E. Boden, M.D., Robert A. O'Rourke, M.D., Koon K. Teo, M.B., B.Ch., Ph.D., Pamela M. Hartigan, Ph.D., David J. Maron, M.D., William J. Kostuk, M.D., Merril Knudtson, M.D., Marcin Dada, M.D., Paul Casperson, Ph.D., Crystal L. Harris, Pharm.D., Bernard R. Chaitman, M.D., Leslee Shaw, Ph.D., Gilbert Gosselin, M.D., Shah Nawaz, M.D., Lawrence M. Title, M.D., Gerald Gau, M.D., Alvin S. Blaustein, M.D., David C. Booth, M.D., Eric R. Bates, M.D., John A. Spertus, M.D., M.P.H., Daniel S. Berman, M.D., G.B. John Mancini, M.D., and William S. Weintraub, M.D., for the COURAGE Trial Research Group*

METHODS

We conducted a randomized trial involving 2287 patients who had objective evidence of myocardial ischemia and significant coronary artery disease at 50 U.S. and Canadian centers. Between 1999 and 2004, we assigned 1149 patients to undergo PCI with optimal medical therapy (PCI group) and 1138 to receive optimal medical therapy alone (medical-therapy group). The primary outcome was death from any cause and nonfatal myocardial infarction during a follow-up period of 2.5 to 7.0 years (median, 4.6).

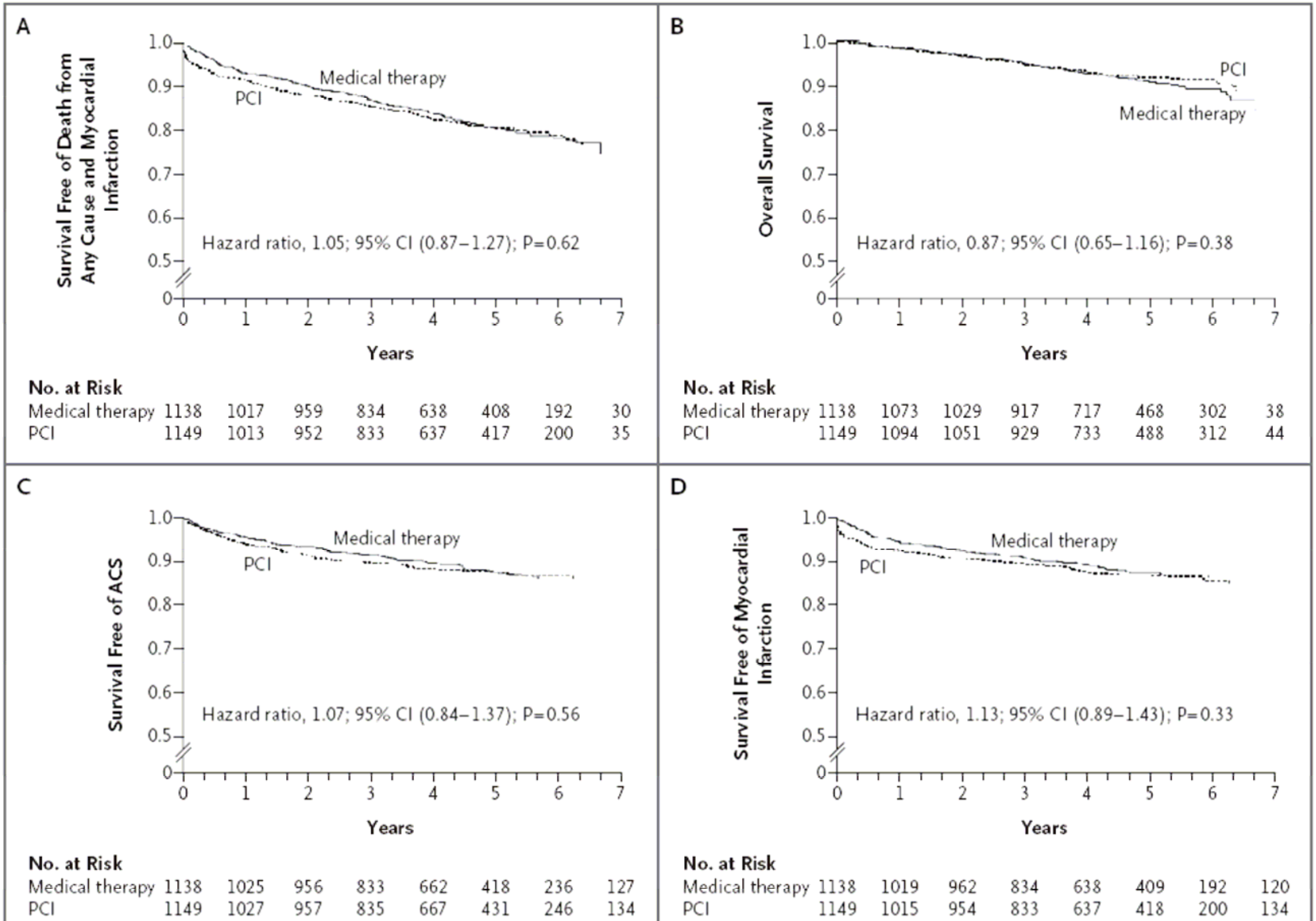


Figure 2. Kaplan–Meier Survival Curves.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Sequence Variations in *PCSK9*, Low LDL, and Protection against Coronary Heart Disease

Jonathan C. Cohen, Ph.D., Eric Boerwinkle, Ph.D., Thomas H. Mosley, Jr., Ph.D., and Helen H. Hobbs, M.D.

N ENGL J MED 354;12 WWW.NEJM.ORG MARCH 23, 2006

Table 1. Nonsense Mutations in *PCSK9* and Cardiovascular Risk Factors among 3363 Black Participants in the Study.*

Variable	Noncarriers	Carriers			P Value†
		PCSK9^{142X}	*PCSK9*^{679X}	*PCSK9*^{142X} or *PCSK9*^{679X}	
Mutation status — no. of subjects (%)	3278 (97.4)	26 (0.8)	60 (1.8)	85 (2.6)‡	
Age — yr§	53±6	54±6	53±6	54±6	0.61
Male sex — %	37	42	27	31	0.22
Body-mass index	29.6±6.1	28.7±4.4	29.7±5.5	29.5±5.2	0.88
Total cholesterol — mg/dl	215±44	177±44	172±45	173±44	<0.001
Triglycerides — mg/dl	113±81	97±38	94±39	94±38	0.04
LDL cholesterol — mg/dl	138±42	103±39	100±45	100±43	<0.001
HDL cholesterol — mg/dl	55±17	55±14	54±17	55±16	0.72
Hypertension — %¶	55	42	36	37	0.001
Diabetes — %‖	18	12	13	13	0.26
Smoking — %**	30	38	23	27	0.62
Carotid-artery intima–media thickness — mm	0.73±0.16	0.72±0.17	0.69±0.11	0.70±0.13	0.04
Coronary heart disease — no. of subjects	319	0	1	1	0.008
Stroke — no. of subjects (%)	217 (6.6)	3 (11.5)	3 (5.0)	6 (7.1)	0.87
Death — no. of subjects (%)	580 (17.7)	4 (15.4)	8 (13.3)	12 (14.1)	0.39

N ENGL J MED 354;12 WWW.NEJM.ORG MARCH 23, 2006

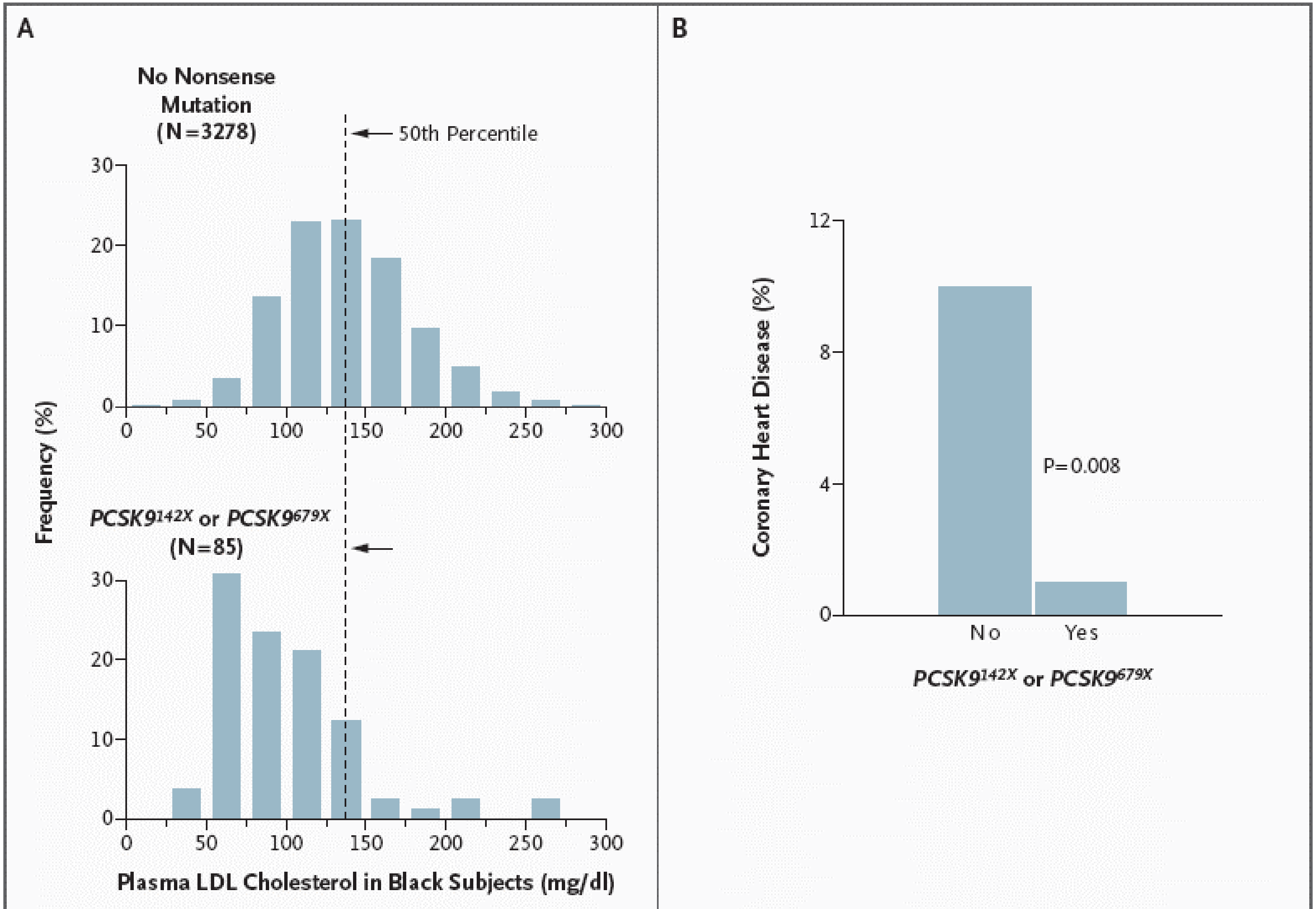


Figure 1. Distribution of Plasma LDL Cholesterol Levels (Panel A) and Incidence of Coronary Heart Disease (Panel B) among Black Subjects, According to the Presence or Absence of a *PCSK9*^{142X} or *PCSK9*^{679X} Allele.

N ENGL J MED 354;12 WWW.NEJM.ORG MARCH 23, 2006

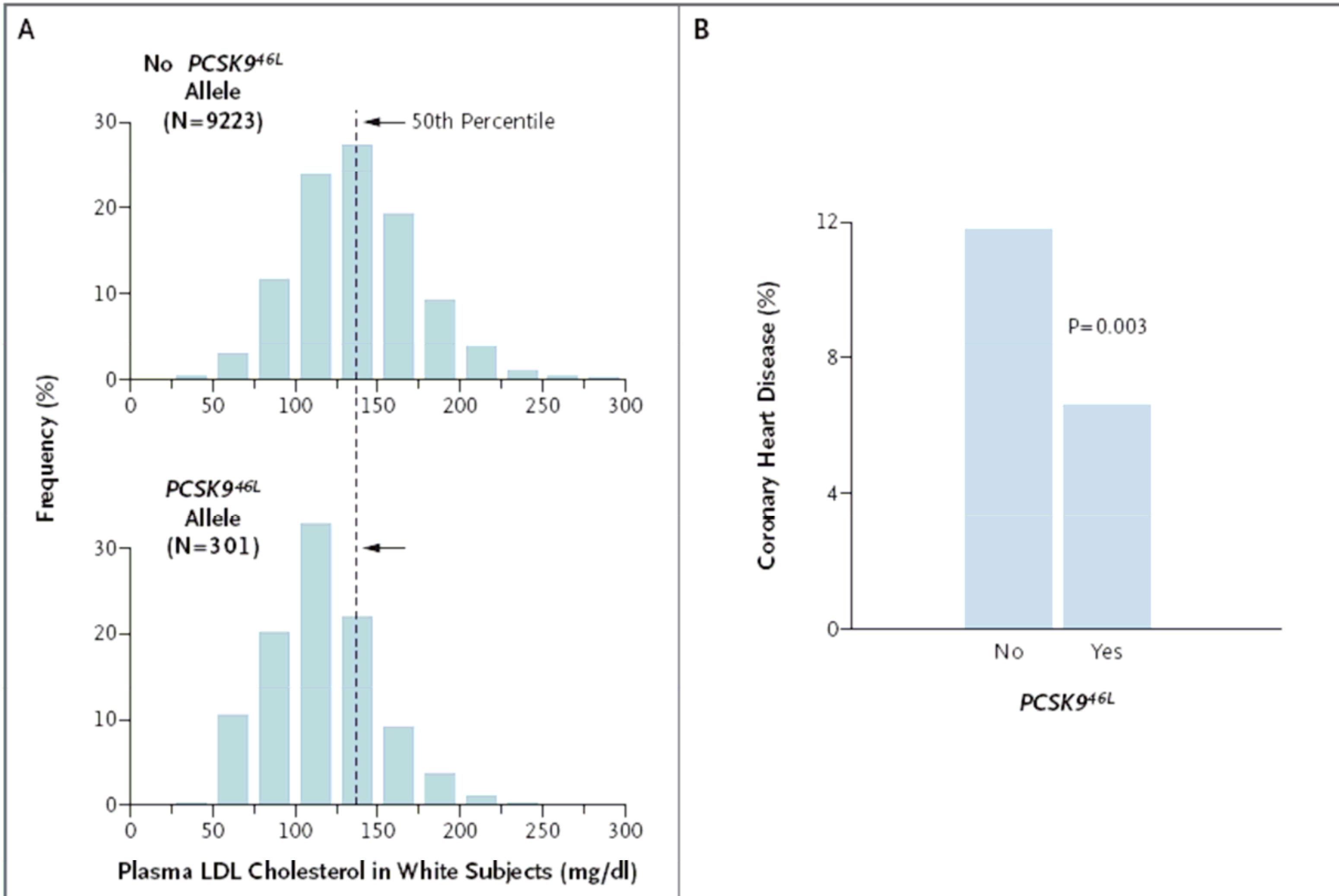


Figure 2. Distribution of Plasma LDL Cholesterol Levels (Panel A) and Incidence of Coronary Events (Panel B) among White Subjects, According to the Presence or Absence of a $PCSK9^{46L}$ Allele.

Multiple Risk Factor Intervention Trial (MRFIT). Mortalidad tras 16 años de seguimiento de acuerdo a la concentración basal de colesterol (69.205 varones)

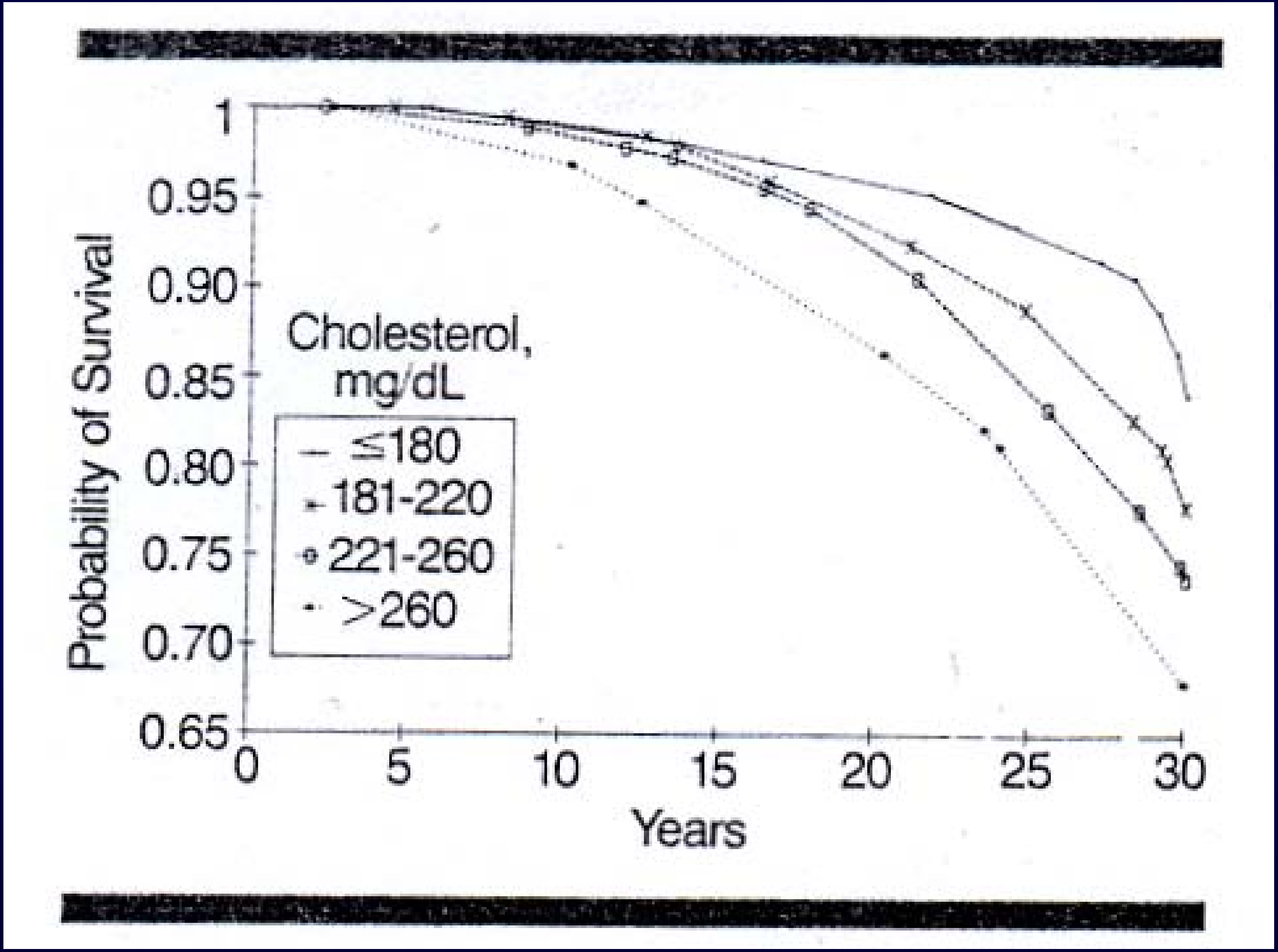
Table 4. Baseline Serum Cholesterol Level and 16-Year Coronary Heart Disease, Cardiovascular Disease, and All-Cause Mortality, MRFIT Cohort, Aged 35 Through 39 Years at Baseline*

Baseline Serum Cholesterol Level (Stratum Mean), mg/dL	No. of Men	All CHD Deaths, No. (Rate)†	All CHD RR (95% CI)‡	MI Deaths, No. (Rate)†	MI RR (95% CI)‡	All CVD Deaths, No. (Rate)†	All CVD RR (95% CI)‡	All Causes Deaths, No. (Rate)†	All Causes RR (95% CI)‡
5-Strata Analyses									
<160 (145.4)	6582	24 (2.3)	1.00	16 (1.6)	1.00	43 (4.2)	1.00	208 (20.1)	1.00
160-199 (181.3)	25 569	146 (3.6)	1.46 (0.95-2.24)	82 (2.0)	1.23 (0.72-2.11)	225 (5.6)	1.26 (0.91-1.74)	775 (19.2)	0.93 (0.79-1.08)
200-239 (217.5)	25 033	257 (6.5)	2.39 (1.57-3.64)	149 (3.8)	2.10 (1.25-3.53)	365 (9.3)	1.89 (1.37-2.59)	952 (24.2)	1.09 (0.94-1.27)
240-279 (255.3)	9541	186 (12.4)	4.12 (2.69-6.32)	100 (6.7)	3.37 (1.98-5.74)	233 (15.6)	2.89 (2.08-4.00)	443 (29.6)	1.24 (1.05-1.47)
≥280 (307.1)	2480	104 (27.3)	8.09 (5.17-12.67)	57 (15.1)	6.86 (3.92-12.01)	130 (33.8)	5.53 (3.90-7.83)	197 (51.3)	1.97 (1.62-2.40)
3-Strata Analysis									
<200 (173.9)	32 151	170 (3.4)	1.00	98 (1.9)	1.00	268 (5.3)	1.00	983 (19.4)	1.00
200-239 (217.5)	25 033	257 (6.5)	1.74 (1.43-2.11)	149 (3.8)	1.76 (1.36-2.28)	365 (9.3)	1.56 (1.33-1.82)	952 (24.2)	1.16 (1.06-1.27)
≥240 (266.0)	12 021	291 (15.5)	3.63 (3.00-4.41)	158 (8.4)	3.47 (2.68-4.48)	363 (19.3)	2.87 (2.44-3.36)	640 (34.0)	1.49 (1.34-1.65)
Total	**69 205**	**718** (6.6)		**405** (3.7)		**996** (9.2)		**2575** (23.7)	

*MRFIT indicates Multiple Risk Factor Intervention Trial; CHD, coronary heart disease; MI, myocardial infarction; CVD, cardiovascular disease; RR, relative risk; and CI, confidence interval. To convert mg/dL to mmol/L, multiply by 0.0259. Cox multivariate coefficient for serum cholesterol level (adjusted for age, systolic blood pressure, No. of cigarettes smoked per day, race, and education) for all CHD, 0.0099 ($P<.001$); MI, 0.0098 ($P<.001$); all CVD, 0.0087 ($P<.001$); and all-cause mortality, 0.0043 ($P<.001$).
†Age-adjusted rate per 1000 men.
‡Relative risk is adjusted for age, systolic blood pressure, No. of cigarettes smoked per day, race, and education.

Stamler J, et al. JAMA 2000;284:311-318

MORTALIDAD TOTAL FRAMINGHAM
Varones 31-39 años al inicio



The Johns Hopkins Precursors Study

Table 2. Cumulative Incidence of Cardiovascular Disease and Total Mortality in 1017 White Men after 40 Years of Follow-up, According to the Base-Line Serum Cholesterol Level.

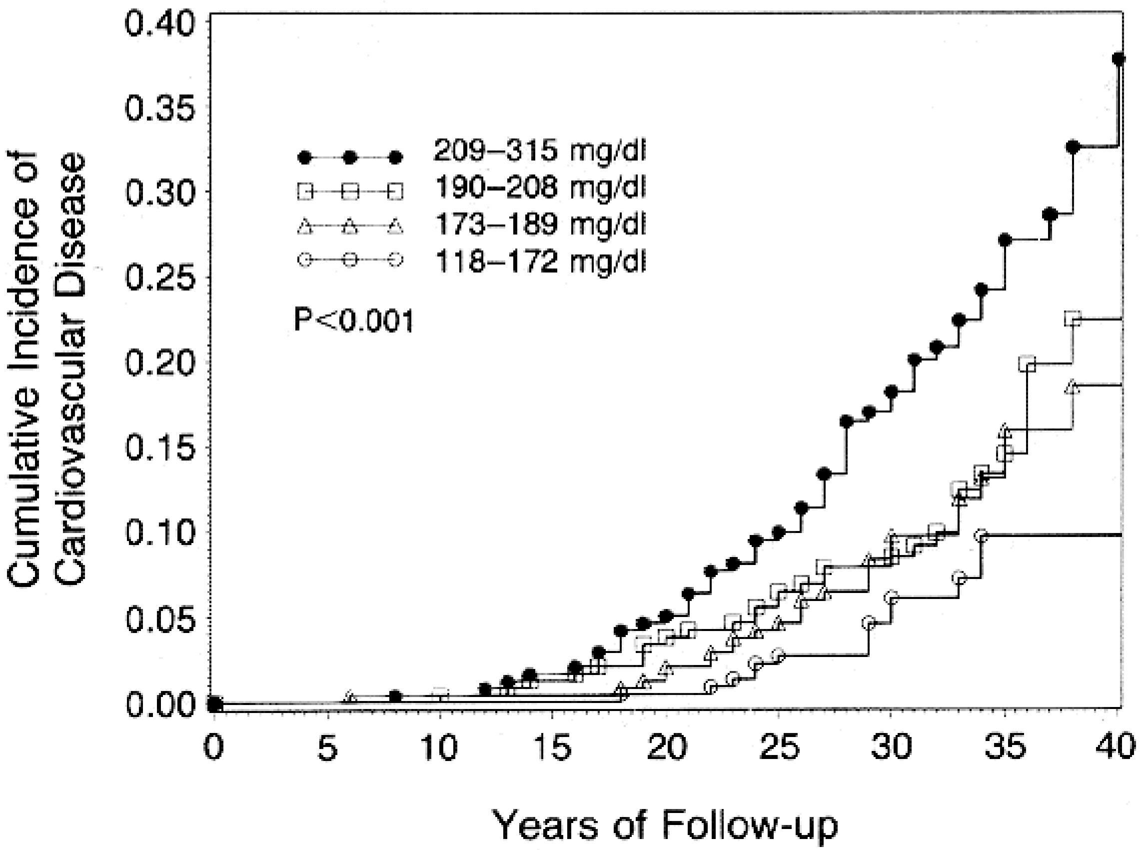
Variable	No. of Events*	Quartile of Cholesterol Level†				P Value‡
		118–172 mg/dl	173–189 mg/dl	190–208 mg/dl	209–315 mg/dl	
Cardiovascular disease	125	9.7	18.5	22.4	37.7	<0.001
Coronary heart disease	97	6.9	11.5	17.5	35.2	<0.001
Myocardial infarction	62	3.4	5.1	7.2	29.2	<0.001
Angina pectoris	49	5.7	4.2	13.4	9.2	<0.08
Cardiovascular-disease mortality	21	1.2	5.0	2.7	14.0	<0.001
Total mortality	95	10.8	14.9	16.8	29.2	0.01

*For men who had more than one type of event, the first event to occur was used for analysis.

†To convert values for cholesterol to millimoles per liter, multiply by 0.02586.

‡By the log-rank test.

Klag MJ, et al. N Engl J Med 1993;328:313-318



QUARTILE (mg/dl)									
118–172	250	248	245	240	234	217	128	61	7
173–189	258	256	254	250	243	216	131	62	15
190–208	254	251	248	240	228	208	155	75	12
209–315	255	251	243	235	222	196	140	78	13
Total	1017	1006	990	965	927	837	554	276	47

Klag MJ, et al. N Engl J Med 1993;328:313-318

Chicago Heart Association Project. Mortalidad tras 22 años de seguimiento de acuerdo a la concentración basal de colesterol

Table 2. Baseline Serum Cholesterol Level and 22-Year Coronary Heart Disease, Cardiovascular Disease, and All-Cause Mortality, CHA Cohort, Aged 18 Through 39 Years at Baseline*

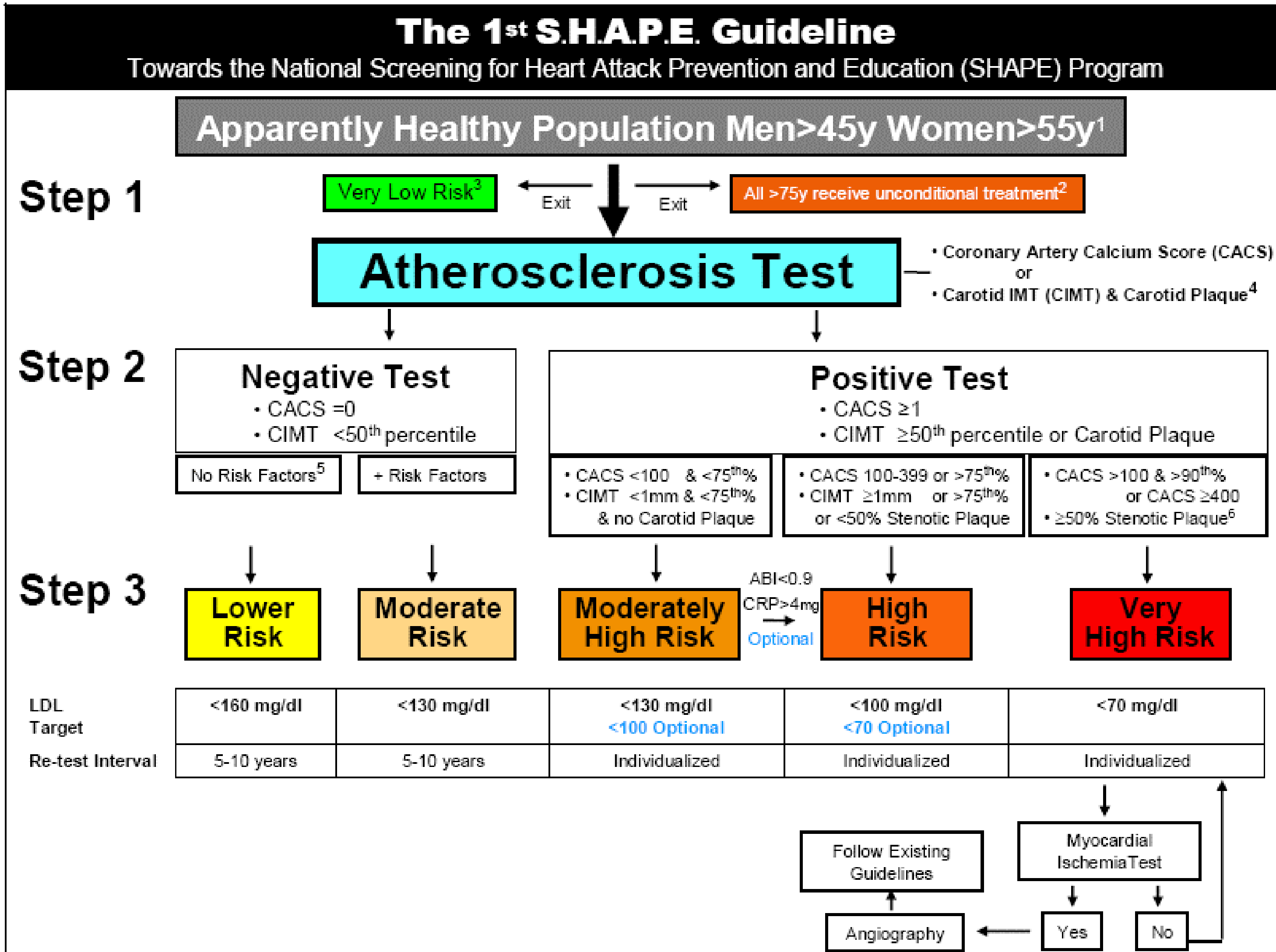
		Mortality							
		All CHD		MI		All CVD		All Cause	
Baseline Serum Cholesterol Level (Stratum Mean), mg/dL	No. of Men	Deaths, No. (Rate)†	RR (95% CI)‡	Deaths, No. (Rate)†	RR (95% CI)‡	Deaths, No. (Rate)†	RR (95% CI)‡	Deaths, No. (Rate)†	RR (95% CI)‡
5-Strata Analyses									
<160 (142.5)	2115	8 (5.5)	1.00	5 (2.8)	1.00	14 (10.1)	1.00	92 (54.4)	1.00
160-199 (179.0)	4773	57 (12.4)	2.52 (1.20-5.31)	31 (6.7)	2.30 (0.90-5.94)	84 (18.4)	2.12 (1.20-3.74)	304 (65.8)	1.27 (1.01-1.60)
200-239 (215.7)	3155	84 (24.0)	4.57 (2.19-9.55)	45 (12.7)	4.19 (1.64-10.75)	103 (29.5)	3.18 (1.80-5.61)	261 (74.8)	1.44 (1.12-1.84)
240-279 (253.8)	806	39 (47.8)	6.57 (3.01-14.32)	24 (31.8)	7.21 (2.68-19.45)	47 (58.8)	4.47 (2.42-8.26)	90 (111.4)	1.57 (1.16-2.13)
≥280 (301.9)	168	15 (84.0)	11.93 (4.96-28.72)	8 (50.9)	11.28 (3.59-35.51)	19 (98.8)	8.53 (4.20-17.32)	32 (169.7)	2.76 (1.82-4.17)
3-Strata Analysis									
<200 (167.8)	6888	65 (10.6)	1.00	36 (5.7)	1.00	98 (16.1)	1.00	396 (62.3)	1.00
200-239 (215.7)	3155	84 (24.0)	2.12 (1.52-2.96)	45 (12.7)	2.13 (1.36-3.33)	103 (29.5)	1.72 (1.29-2.28)	261 (74.8)	1.20 (1.02-1.41)
≥240 (262.1)	974	54 (54.2)	3.46 (2.37-5.05)	32 (35.3)	3.99 (2.41-6.60)	66 (65.9)	2.18 (2.01-3.86)	122 (120.9)	1.47 (1.19-1.82)
Total	**11 017**	**203** (18.4)		**113** (10.3)		**267** (24.2)		**779** (70.7)	

*CHA indicates Chicago Heart Association Detection Project in Industry; CHD, coronary heart disease; MI, myocardial infarction; CVD, cardiovascular disease; RR, relative risk; and CI, confidence interval. To convert mg/dL to mmol/L, multiply by 0.0259. Cox multivariate coefficient for serum cholesterol level (adjusted for age [coefficient for all cause mortality, 0.0718], systolic blood pressure, No. of cigarettes smoked per day, body mass index, body mass index squared, electrocardiogram abnormalities, race, and education) for all CHD, 0.0147 ($P<.001$); MI, 0.0157 ($P<.001$); all CVD, 0.0125 ($P<.001$); and all-cause mortality, 0.0051 ($P<.001$).

†Age-adjusted rate per 1000 men.

‡Relative risk is adjusted for age, systolic blood pressure, No. of cigarettes smoked per day, body mass index, body mass index squared, electrocardiogram abnormalities, race, and education.

Stamler J, et al. JAMA 2000;284:311-318



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

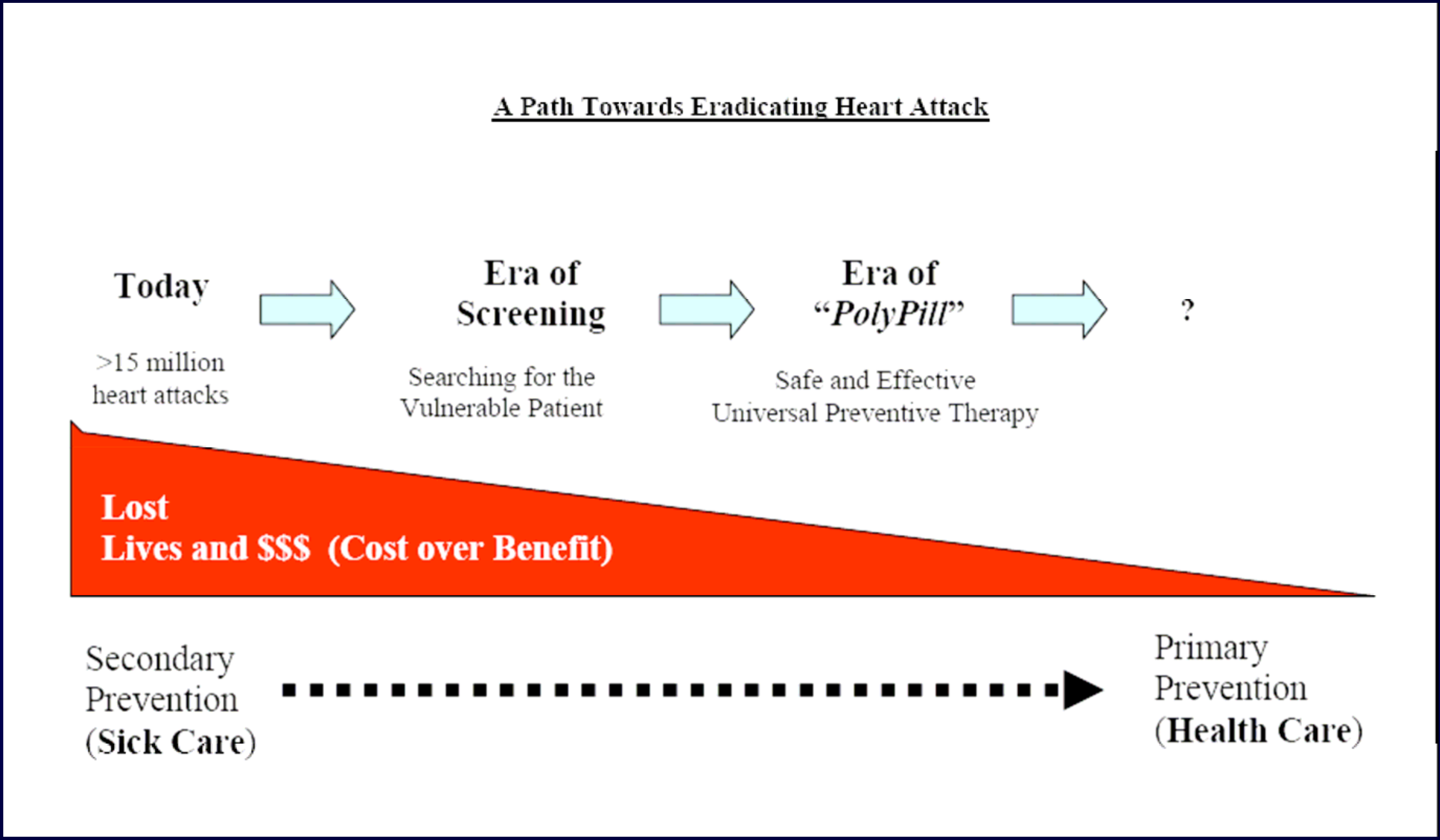
2: Population over age 75y is considered high risk and must receive therapy without testing for atherosclerosis.

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.


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)

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

S. Yusuf, 2007

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 12, 2007 VOL. 356 NO. 15

Optimal Medical Therapy with or without PCI for Stable Coronary Disease

William E. Boden, M.D., Robert A. O'Rourke, M.D., Koon K. Teo, M.B., B.Ch., Ph.D., Pamela M. Hartigan, Ph.D., David J. Maron, M.D., William J. Kostuk, M.D., Merril Knudtson, M.D., Marcin Dada, M.D., Paul Casperson, Ph.D., Crystal L. Harris, Pharm.D., Bernard R. Chaitman, M.D., Leslee Shaw, Ph.D., Gilbert Gosselin, M.D., Shah Nawaz, M.D., Lawrence M. Title, M.D., Gerald Gau, M.D., Alvin S. Blaustein, M.D., David C. Booth, M.D., Eric R. Bates, M.D., John A. Spertus, M.D., M.P.H., Daniel S. Berman, M.D., G.B. John Mancini, M.D., and William S. Weintraub, M.D., for the COURAGE Trial Research Group*

ary prevention. All patients received aggressive therapy to lower low-density lipoprotein (LDL) cholesterol levels (simvastatin alone or in combination with ezetimibe) with a target level of 60 to 85 mg per deciliter (1.55 to 2.20 mmol per liter). After the LDL cholesterol target was achieved, an attempt was made to raise the level of high-density lipoprotein (HDL) cholesterol to a level above 40 mg per deciliter (1.03 mmol per liter) and lower triglyceride to a level below 150 mg per deciliter (1.69 mmol per liter) with exercise, extended-release niacin, or fibrates, alone or in combination.

Table 1. (Continued.)

Characteristic	PCI Group (N=1149)	Medical-Therapy Group (N=1138)	P Value
Angiographic			
Vessels with disease — no. (%)			0.72
1	361 (31)	343 (30)	
2	446 (39)	439 (39)	
3	341 (30)	355 (31)	
Disease in graft¶	77 (62)	85 (69)	0.36
Proximal LAD disease	360 (31)	417 (37)	0.01
Ejection fraction	60.8±11.2	60.9±10.3	0.86

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Table 2. Clinical Status, Risk and Lifestyle Factors, and Use of Medication.*

Variable	PCI Group (N=1149)				Medical-Therapy Group (N=1138)			
	Baseline	1 Yr	3 Yr	5 Yr	Baseline	1 Yr	3 Yr	5 Yr
	median ±SE							
Clinical status								
No. evaluated	1148	1031	820	423	1137	1010	824	406
Medication								
No. evaluated	1147	1044	837	428	1138	1028	838	417
ACE inhibitor — no. (%)	669 (58)	668 (64)	536 (64)	284 (66)	680 (60)	633 (62)	522 (62)	260 (62)
ARB — no. (%)	48 (4)	93 (9)	104 (12)	49 (11)	54 (5)	99 (10)	108 (13)	67 (16)
Statin — no. (%)	992 (86)	972 (93)	780 (93)	398 (93)	1014 (89)	972 (95)	769 (92)	386 (93)
Other antilipid — no. (%)	89 (8)	236 (23)	324 (39)	211 (49)	94 (8)	253 (25)	321 (38)	224 (54)
Aspirin — no. (%)	1097 (96)	995 (95)	792 (95)	408 (95)	1077 (95)	977 (95)	796 (95)	391 (94)
Beta-blocker — no. (%)	975 (85)	887 (85)	705 (84)	363 (85)	1008 (89)	916 (89)	724 (86)	357 (86)
Calcium-channel blocker — no. (%)§	459 (40)	415 (40)	360 (43)	180 (42)	488 (43)	501 (49)	418 (50)	217 (52)
Nitrates — no. (%)¶	714 (62)	553 (53)	396 (47)	173 (40)	825 (72)	690 (67)	511 (61)	237 (57)

Por cada 40 mg/dl de descenso del c-LDL obtenemos una reducción de eventos cardiovasculares del 21%

Endpoint	Events (%) Treatment (45054)	Control (45002)	RR (CI)
Non-fatal MI	2001 (4·4%)	2769 (6·2%)	0·74 (0·70–0·79)
CHD death	1548 (3·4%)	1960 (4·4%)	0·81 (0·75–0·87)
Any major coronary event	**3337 (7·4%)**	**4420 (9·8%)**	**0·77 (0·74–0·80)**
CABG	713 (1·6%)	1006 (2·2%)	0·75 (0·69–0·82)
PTCA	510 (1·1%)	658 (1·5%)	0·79 (0·69–0·90)
Unspecified	1397 (3·1%)	1770 (3·9%)	0·76 (0·69–0·84)
Any coronary revascularisation	**2620 (5·8%)**	**3434 (7·6%)**	**0·76 (0·73–0·80)**
Haemorrhagic stroke	105 (0·2%)	99 (0·2%)	1·05 (0·78–1·41)
Presumed ischaemic stroke	1235 (2·8%)	1518 (3·4%)	0·81 (0·74–0·89)
Any stroke	**1340 (3·0%)**	**1617 (3·7%)**	**0·83 (0·78–0·88)**
Any major vascular event	**6354 (14·1%)**	**7994 (17·8%)**	**0·79 (0·77–0·81)**

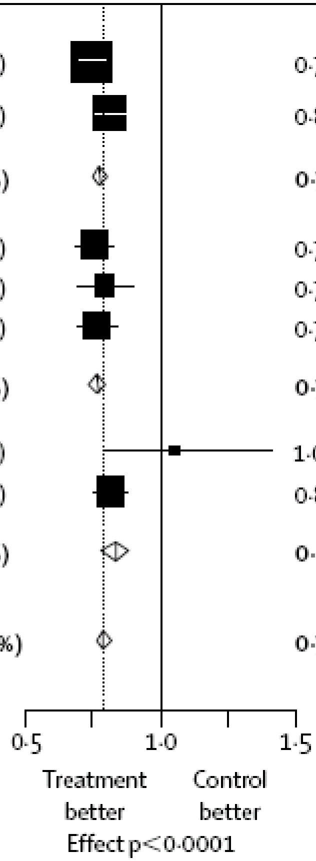
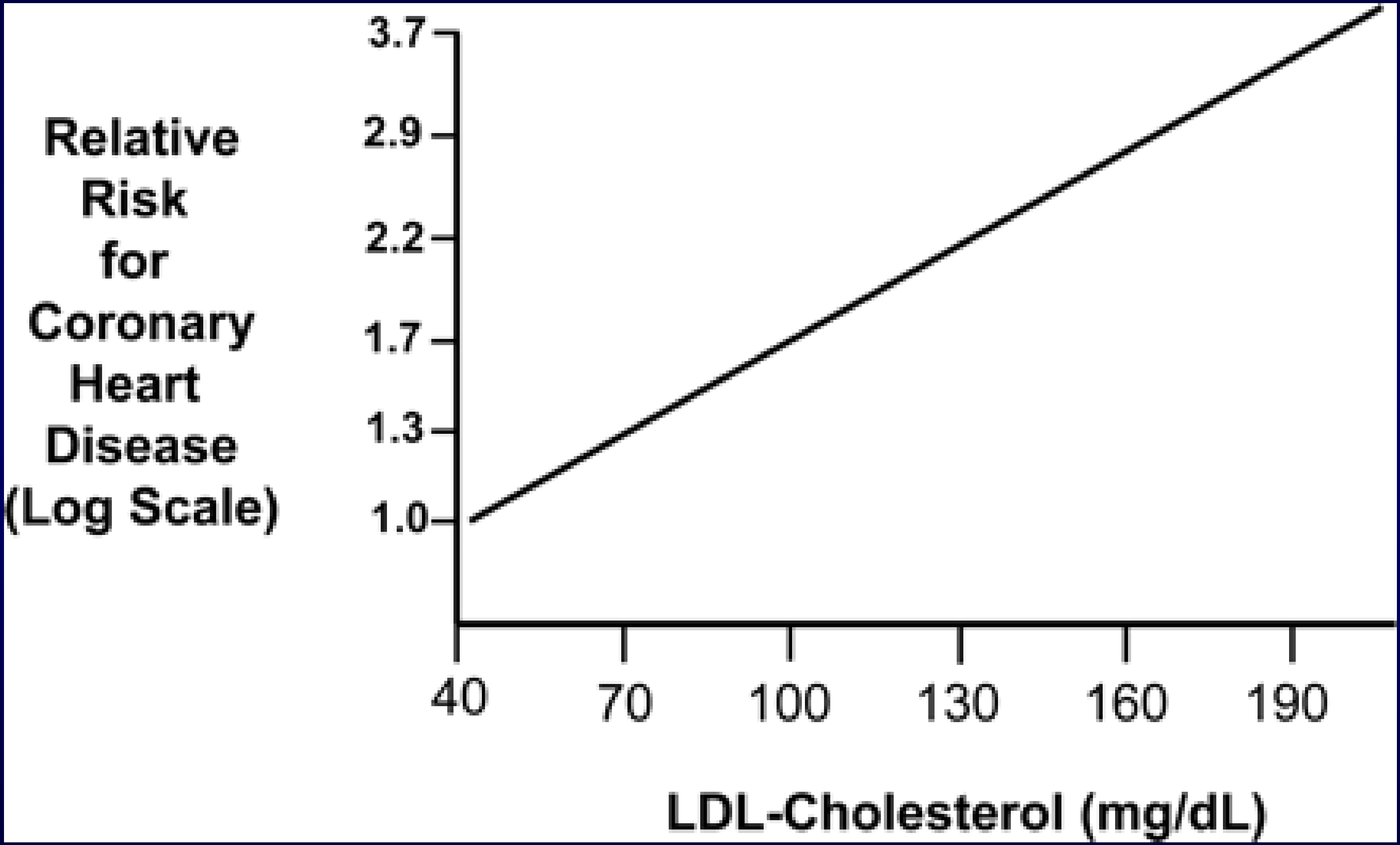


Figure 2: **Proportional effects on major vascular events per mmol/L LDL cholesterol reduction**
Symbols and conventions as in figure 1. Broken vertical line indicates overall RR for any type of major vascular event. CABG=coronary artery bypass graft. PTCA=percutaneous transluminal coronary angioplasty. LIPS only provided data on fatal strokes[20] and so does not contribute to the stroke analyses.

Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90 056 participants in 14 randomised trials of statins Cholesterol Treatment Trialists' (CTT) Collaborators. Lancet 2005;366:1267

RELACION ENTRE LDL-COLESTEROL Y RIESGO DE ENFERMEDAD CORONARIA



Circulation July 13, 2004

Eventos coronarios en estudios con estatinas

Trial	Without Diabetes: On Statin	Without Diabetes: On Placebo	With Diabetes: On Statin	With Diabetes: On Placebo
HPS (CAD patients)*[4]	19.8%	25.7%	33.4%	37.8%
CARE†[7]	19.6%	24.6%	28.7%	36.8%
LIPID*[8]	11.7%	15.2%	19.7%	22.8%
PROSPER*[9]	13.1%	16%	23.1%	18.4%
ASCOT*[10]	4.9%	8.7%	9.6%	11.4%
	High HDL-C on Statin	**High HDL-C on Placebo**	**Low HDL-C on Statin**	**Low HDL-C on Placebo**
HPS*[4]	17%	20.9%	22.0%	29.9%
CARE/LIPID*†[7,8]	18.5%	22.4%	25%	30.8%
PROSPER*[9]	12.8%	11.6%	13%	19.3%

ASCOT = Anglo-Scandinavian Cardiac Outcomes Trial; CARE = Cholesterol and Recurrent Events; HDL-C = high-density lipoprotein cholesterol; HPS = Heart Protection Study; LIPID = Long-Term Prevention with Pravastatin in Ischaemic Disease; PROSPER = Prospective Study of Pravastatin in the Elderly at Risk.

* Coronary artery disease (CAD) death, nonfatal myocardial infarction, coronary or noncoronary revascularization, stroke.

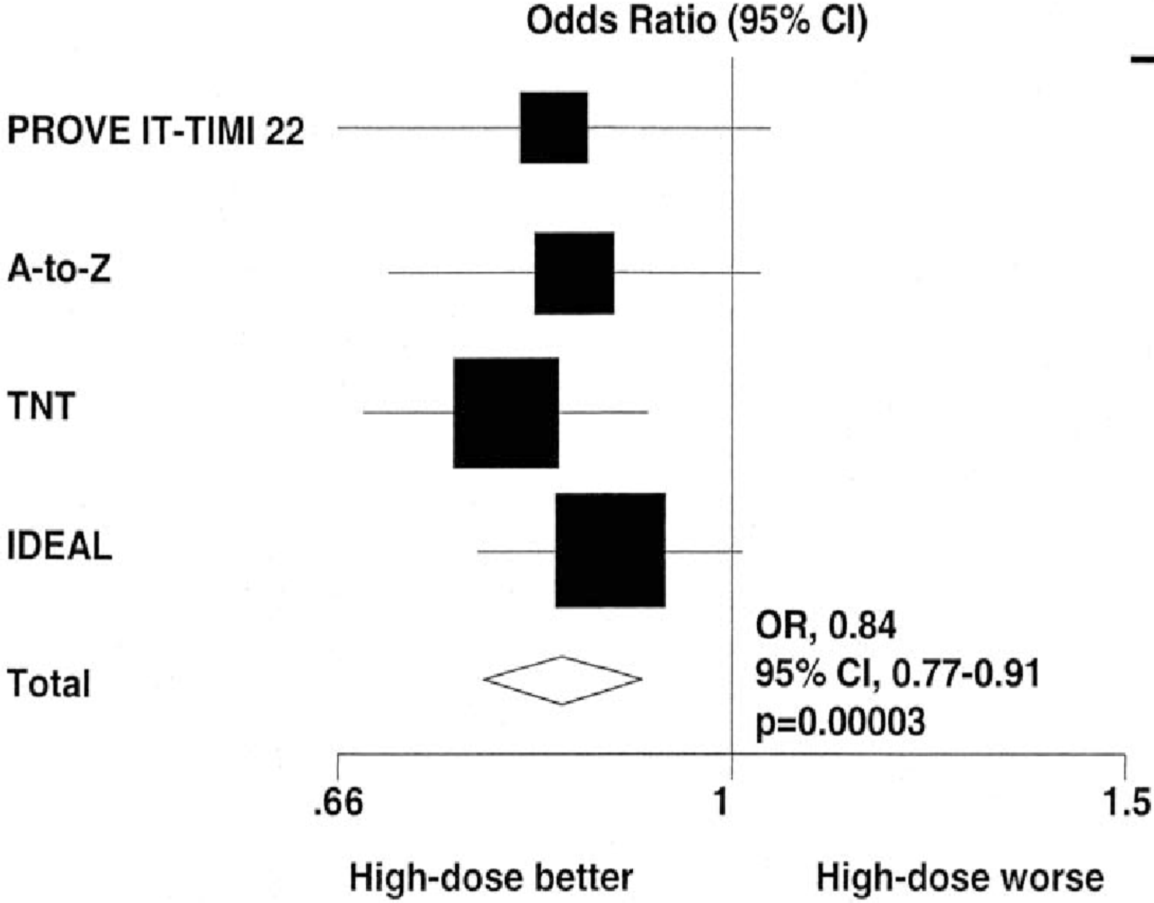
† CAD death and nonfatal myocardial infarction.

Davidson MH. Am J Cardiol 2005;96[suppl]:3K–13K

Meta-Análisis de estudios (con eventos cardiovasculares como objetivo) comparando tratº LDL-c intensivo vs moderado

Cannon C et al. J Am Coll Cardiol 2006.

Muerte coronaria o IAM



	Odds Reduction	Event Rates No./Total (%) High Dose	Event Rates No./Total (%) Std Dose
PROVE IT-TIMI 22	-17%	147/2099 (7.0)	172/2063 (8.3)
A-to-Z	-15%	205/2265 (9.1)	235/2232 (10.5)
TNT	-21%	334/4995 (6.7)	418/5006 (8.3)
IDEAL	-12%	411/4439 (9.3)	463/4449 (10.4)
Total	-16%	1097/13798 (8.0)	1288/13750 (9.4)

		Women										Men									
		Non-smoker					Smoker					Non-smoker					Smoker				
Age	Systolic blood pressure (mmHg)	4	5	6	7	8	4	5	6	7	8	4	5	6	7	8	4	5	6	7	8
65	180	4	5	6	6	7	9	9	11	12	14	8	9	10	12	14	15	17	20	23	26
	160	3	3	4	4	5	6	6	7	8	10	5	6	7	8	10	10	12	14	16	19
	140	2	2	2	3	3	4	4	5	6	7	4	4	5	6	7	7	8	9	11	13
	120	1	1	2	2	2	3	3	3	4	4	2	3	3	4	5	5	5	6	8	9
60	180	3	3	3	4	4	5	5	6	7	8	5	6	7	8	9	10	11	13	15	18
	160	2	2	2	2	3	3	4	4	5	5	3	4	5	5	6	7	8	9	11	13
	140	1	1	1	2	2	2	2	3	3	4	2	3	3	4	4	5	5	6	7	9
	120	1	1	1	1	1	1	2	2	2	3	2	2	2	3	3	3	4	4	5	6
55	180	1	1	2	2	2	3	3	3	4	4	3	4	4	5	6	6	7	8	10	12
	160	1	1	1	1	1	2	2	2	3	3	2	2	3	3	4	4	5	6	7	8
	140	1	1	1	1	1	1	1	1	2	2	1	2	2	2	3	3	3	4	5	6
	120	0	0	1	1	1	1	1	1	1	1	1	1	1	2	2	2	2	3	3	4
50	180	1	1	1	1	1	1	1	2	2	2	2	2	3	3	4	4	4	5	6	7
	160	0	0	1	1	1	1	1	1	1	1	1	1	2	2	2	2	3	3	4	5
	140	0	0	0	0	0	1	1	1	1	1	1	1	1	1	2	2	2	2	3	3
	120	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	2	2	2
40	180	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	2	2
	160	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1
	140	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1
	120	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1

Cholesterol (mmol/l)

150 200 250 300 mg/dl

SCORE

- 15% and over
- 10–14%
- 5–9%
- 3–4%
- 2%
- 1%
- < 1%

10-year risk of fatal CVD in populations at **low CVD risk**

Age	Systolic blood pressure (mmHg)	Women Non-smoker 3	4	5	6	7	Women Smoker 3	4	5	6	7	Men Non-smoker 3	4	5	6	7	Men Smoker 3	4	5	6	7
65	180	4	5	6	7	8	8	9	11	13	15	7	8	10	12	15	13	16	19	23	28
	160	3	3	4	5	6	6	6	8	9	11	5	6	7	9	11	9	11	13	16	20
	140	2	2	3	3	4	4	5	5	6	8	4	4	5	6	8	7	8	10	12	14
	120	1	2	2	2	3	3	3	4	5	6	2	3	4	4	6	5	6	7	8	10
60	180	2	3	3	4	5	4	5	6	7	9	5	5	7	8	10	9	10	12	15	19
	160	2	2	2	3	3	3	4	4	5	6	3	4	5	6	7	6	7	9	11	13
	140	1	1	2	2	2	2	2	3	4	4	2	3	3	4	5	4	5	6	8	10
	120	1	1	1	1	2	1	2	2	3	3	2	2	2	3	4	3	4	4	5	7
55	180	1	1	2	2	2	2	3	3	4	5	3	3	4	5	6	5	6	8	10	12
	160	1	1	1	1	2	2	2	2	3	3	2	2	3	4	5	4	5	6	7	9
	140	1	1	1	1	1	1	1	2	2	2	1	2	2	3	3	3	3	4	5	6
	120	0	0	1	1	1	1	1	1	1	2	1	1	1	2	2	2	2	3	3	4
50	180	1	1	1	1	1	1	1	1	2	2	2	2	2	3	4	3	4	5	6	7
	160	0	0	1	1	1	1	1	1	1	2	1	1	2	2	3	2	3	3	4	5
	140	0	0	0	0	1	0	1	1	1	1	1	1	1	2	2	2	2	2	3	4
	120	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	2	2	3
40	180	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	2	2
	160	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1
	140	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1	1
	120	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1

Total cholesterol: HDL-cholesterol ratio

SCORE

15% and over
10–14%
5–9%
3–4%
2%
1%
< 1%

10-year risk of fatal CVD in populations at **low CVD risk**

Figure 5 SCORE chart: 10-year risk of fatal CVD in populations at low CVD risk based on the following risk factors: age, gender, smoking, systolic blood pressure, and total cholesterol:HDL cholesterol ratio. © The European Society of Cardiology.

Relative Risk Chart

This chart may used to show younger people at low absolute risk that, relative to others in their age group, their risk may be many times higher than necessary. This may help to motivate decisions about avoidance of smoking, healthy nutrition and exercise, as well as flagging those who may become candidates for medication

Systolic Blood Pressure (mmHg)	Non-Smoker					Smoker				
180	3	3	4	5	6	6	7	8	10	12
160	2	3	3	4	4	4	5	6	7	8
140	1	2	2	2	3	3	3	4	5	6
120	1	1	1	2	2	2	2	3	3	4
Cholesterol (mmol/L)	4	5	6	7	8	4	5	6	7	8

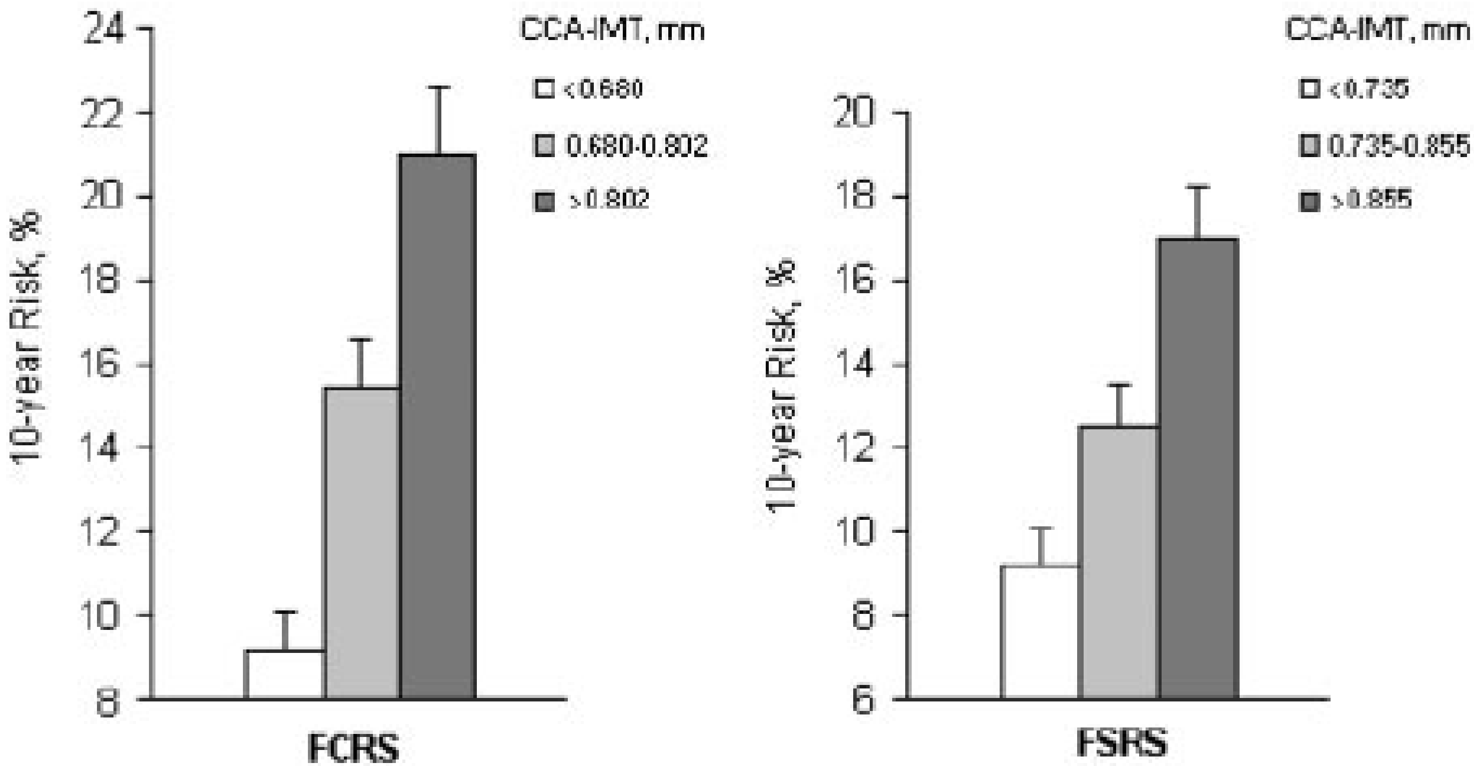


Figure 1. Geometric means of FCRS (left panel) and FSRS (right panel) by tertiles of CCA-IMT. Upper bounds of 95% CI are indicated.

Touboul P-J, et al. Stroke 2005;36:1741-45

10 year risk of fatal CVD in low risk regions of Europe

SCORE

- 15% and over
- 10% - 14%
- 5% - 9%
- 3% - 4%
- 2%
- 1%
- < 1%

Age	Systolic blood pressure (mmHg)	Women Non-smoker					Women Smoker					Men Non-smoker					Men Smoker				
	Cholesterol (mmol/L)	4	5	6	7	8	4	5	6	7	8	4	5	6	7	8	4	5	6	7	8
65	180	4	5	6	6	7	9	9	11	12	14	8	9	10	12	14	15	17	20	23	26
	160	3	3	4	4	5	6	6	7	8	10	5	6	7	8	10	10	12	14	16	19
	140	2	2	2	3	3	4	4	5	6	7	4	4	5	6	7	7	8	9	11	13
	120	1	1	2	2	2	3	3	3	4	4	2	3	3	4	5	5	5	6	8	9
60	180	3	3	3	4	4	5	5	6	7	8	5	6	7	8	9	10	11	13	15	18
	160	2	2	2	2	3	3	4	4	5	5	3	4	5	5	6	7	8	9	11	13
	140	1	1	1	2	2	2	2	3	3	4	2	3	3	4	4	5	5	6	7	9
	120	1	1	1	1	1	1	2	2	2	3	2	2	2	3	3	3	4	4	5	6
55	180	1	1	2	2	2	3	3	3	4	4	3	4	4	5	6	6	7	8	10	12
	160	1	1	1	1	1	2	2	2	3	3	2	2	3	3	4	4	5	6	7	8
	140	1	1	1	1	1	1	1	1	2	2	1	2	2	2	3	3	3	4	5	6
	120	0	0	1	1	1	1	1	1	1	1	1	1	1	2	2	2	2	3	3	4
50	180	1	1	1	1	1	1	1	2	2	2	2	2	3	3	4	4	4	5	6	7
	160	0	0	1	1	1	1	1	1	1	1	1	1	2	2	2	2	3	3	4	5
	140	0	0	0	0	0	1	1	1	1	1	1	1	1	1	2	2	2	2	3	3
	120	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	2	2	2
40	180	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	2	2
	160	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1
	140	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1
	120	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1

150 200 250 300
mg/dl

SCORE

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