XXXII Congreso Nacional de la SEMI
XIV Congreso de la Sociedad Canaria de Medicina Interna
26-28 Octubre 2011

C-HDL: ¿Objetivo Primario?

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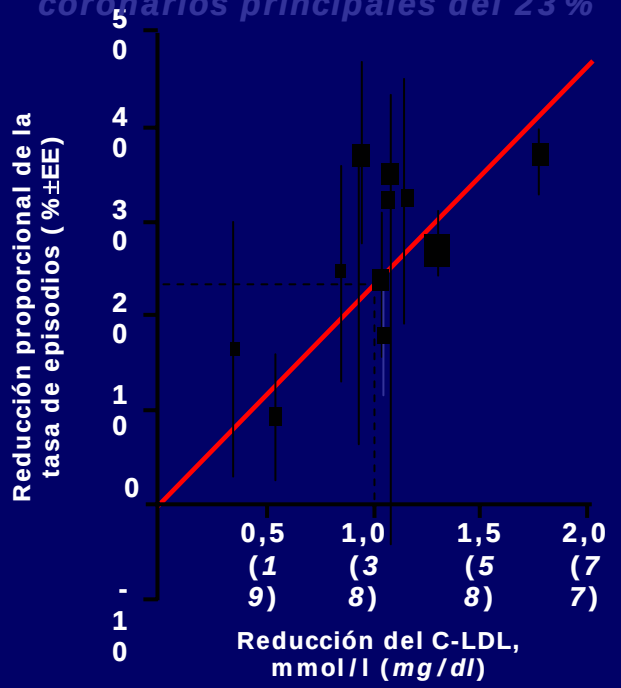
La incidencia de eventos cardiovasculares está relacionada con los niveles de cLDL1

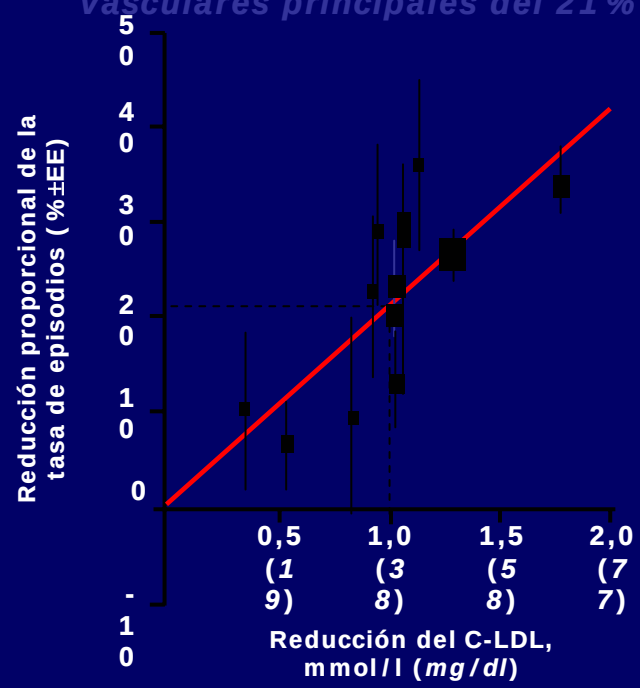
Metanálisis prospectivo de los datos de 90.056 pacientes procedentes de 14 ensayos de estatinas

Una reducción del C-LDL de 1 mmol/l (39 mg/dl) se tradujo en...

... una reducción de los episodios coronarios principales del 23 %



... una reducción de los episodios vasculares principales del 21 %



El descenso del C-LDL en 1 mmol/l (38,7 mg/dl) con estatinas reduce los episodios coronarios mayores en un 23%, dejando un riesgo CV residual sin abordar del 77%.

1 - Baigent C et al. Lancet 2005;366:1267–78.

2. CTT Efficacy or cholesterol-lowering theraphy in 18.686 people with diabetes in 14 randomised trials of statins; a meta-analysis. Lancet 2008;371:117-25.

Estudios prospectivos que ponen de manifiesto el alto riesgo residual CV a pesar de un tratamiento óptimo con estatinas.

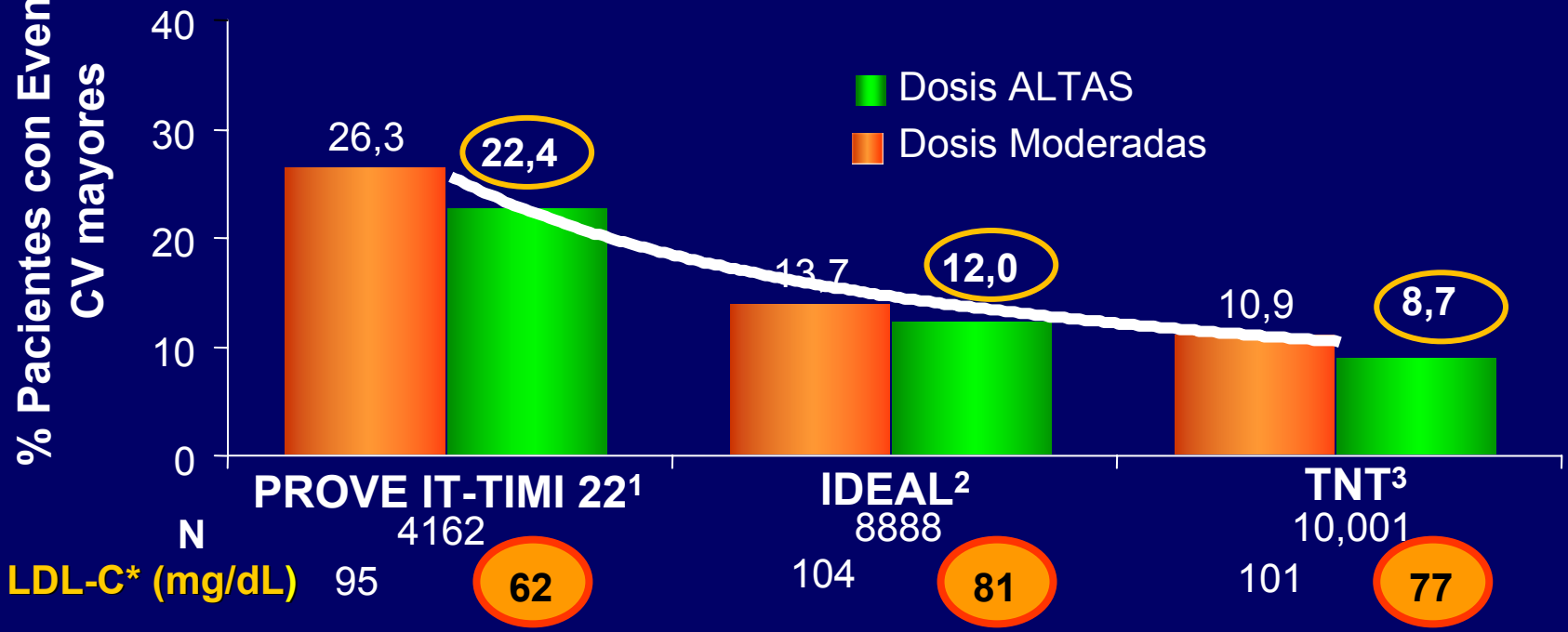
Estudio	N	Objetivo principal	Tasa absoluta de episodios		Reducción del riesgo relativo	Riesgo residual
Prevención secundaria			Control	Estatina		
4S[5]	4.444	IM no mortal y muerte por ECC	28.0	19.0	34	66
CARE[6]	4.159	IM no mortal o muerte por ECC	13.2	10.2	24	76
LIPID[7]	9.014	IM no mortal o muerte por ECC	15.9	12.3	24	76
Prevención primaria y secundaria						
HPS[8]	20.536	IM no mortal o muerte por ECC. Episodios vasculares mayores*	11.8 25.2	8.7 18.8	27 24	73 76
PROSPER[9]	5.804	IM no mortal o muerte por ECC o ictus no mortal. IM no mortal o muerte por ECC.	16.2 12.2	14.1 10.1	15 19	85 81
ASCOT-LLA[10]	10.305	IM no mortal y muerte por ECC.	3.0	1.9	36	64
ALLHAT-LLT[11]	10.355	IM no mortal y muerte por ECC.	8.1	7.4	9	91
ASPEN [c12]	2.410	Episodios mayores de ECV[a]	15.0	13.7	10	90
Prevención primaria						
WOSCOPS[13]	6.595	IM no mortal o muerte por EDD	7.9	5.5	31	69
AFCAPS/ TexCAPS[14]	6.605	Episodios coronarios mayores [b]	5.5	3.5	37	63
CARDS [c15]	2.838	Episodios CV mayores[d]	9.0	5.8	37	63

Millán J et al. Med Clin (Bcn) 2010; 135:165-71

La Reducción Máxima Posible de C-LDL No elimina el Riesgo de ECV

Pese al Beneficio, persiste un Riesgo CV IMPORTANTE:

Riesgo Residual



*Media o mediana de C-LDL tras tratamiento

1. Cannon CP, et al. *N Engl J Med.* 2004;350:1495-1504; 2. Pedersen TR, et al. *JAMA.* 2005;294:2437-2445; 3. LaRosa JC, et al. *N Engl J Med.* 2005;352:1425-1435.

Riesgo residual

Chapman, M. J. et al. Eur Heart J 2009

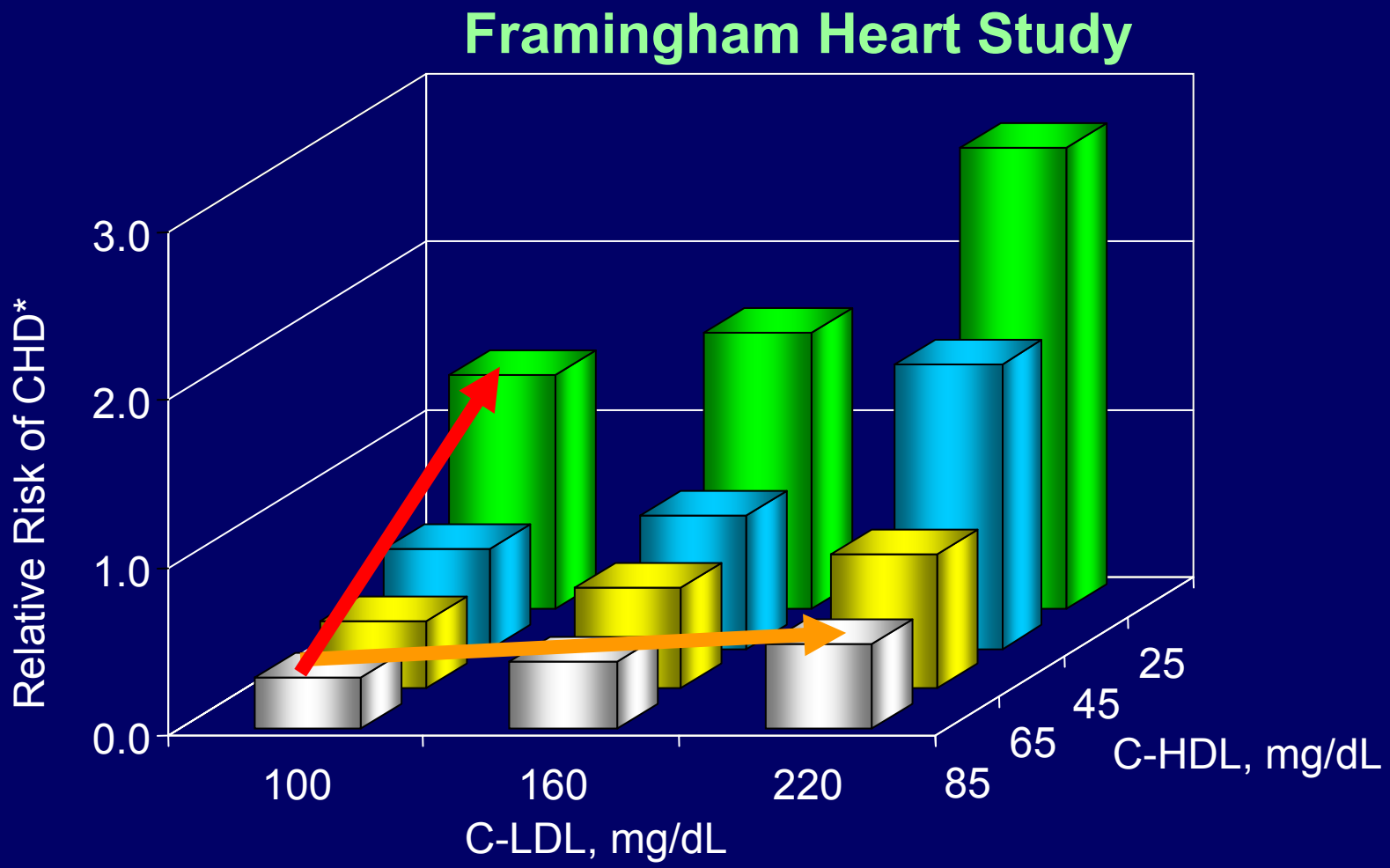
Frecuencia de diferentes FRV en CI prematura

		Casos (n = 321)	
Factores de Riesgo	**Controles (n = 601)**	**Not Ajustado**	**Ajustado**
Consumo Cigarillos	29%	67%*	—
C-HDL<35 mg/dL	**19%**	**63%***	**57%***
Hipertensión (TA >150/90)	21%	41%*	—
C-LDL>160 mg/dL	26%	26%	34%*
Diabetes mellitus	1%	12%*	—

*diferencia significativa con controles (*P* <0.001)

Genest JJ, et al. *Am J Cardiol.* 1991;67:1185–1189

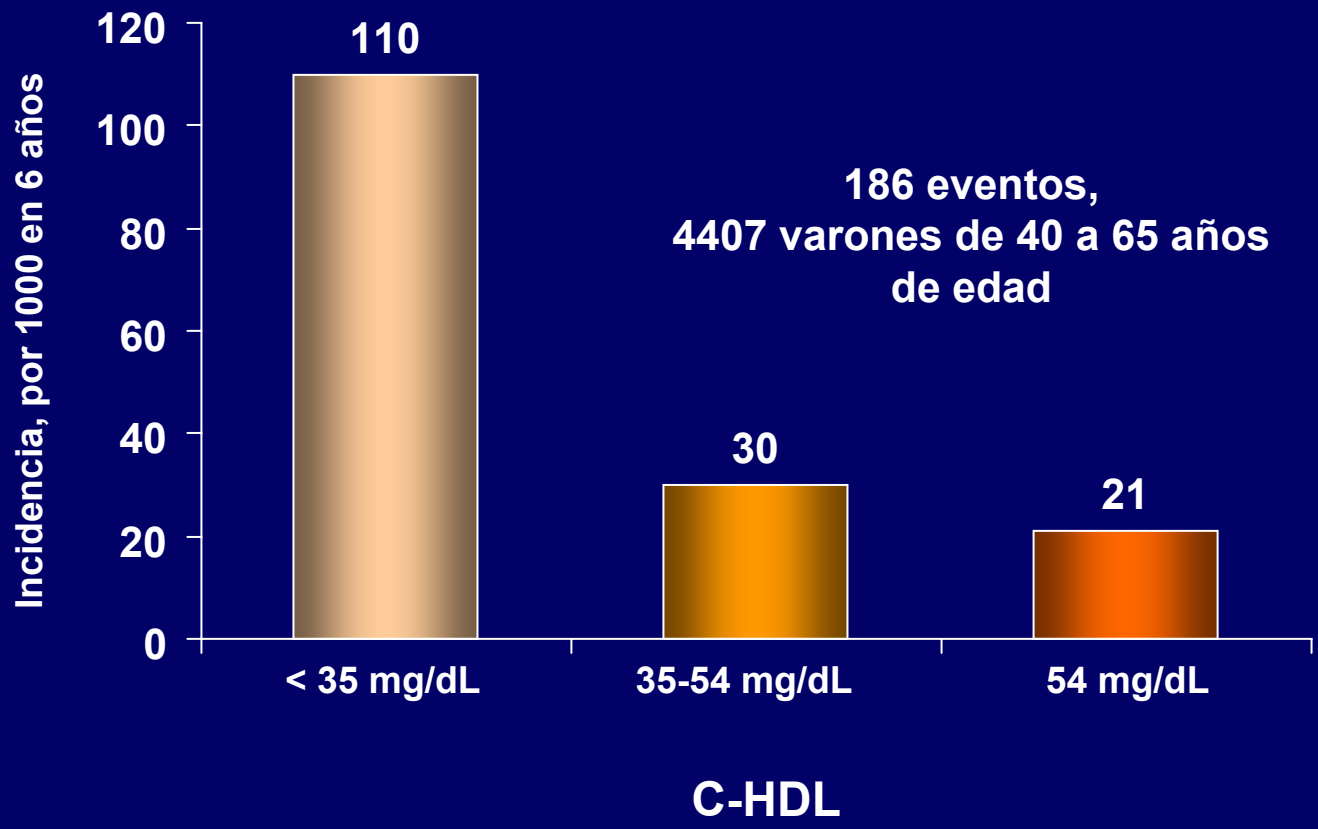
El C-HDL bajo aumenta el riesgo *incluso con C-LDL "normal"*



*Riesgo de EC en hombres de 50 a 70 años, en relación a los niveles de C-HDL-C y C-LDL en 4 años de seguimiento

Castelli WP. *Can J Cardiol*. 1988;4:5A-10A.

C-HDL y riesgo cardiovascular: Estudio PROCAM



Assmann G y cols. En: *Lipid Metabolism Disorders and Coronary Heart Disease: Primary Prevention, Diagnosis and Therapy Guidelines for General Practice*. 2nd ed. Munich: MMV Medizin Verlag; 1993:19–67.

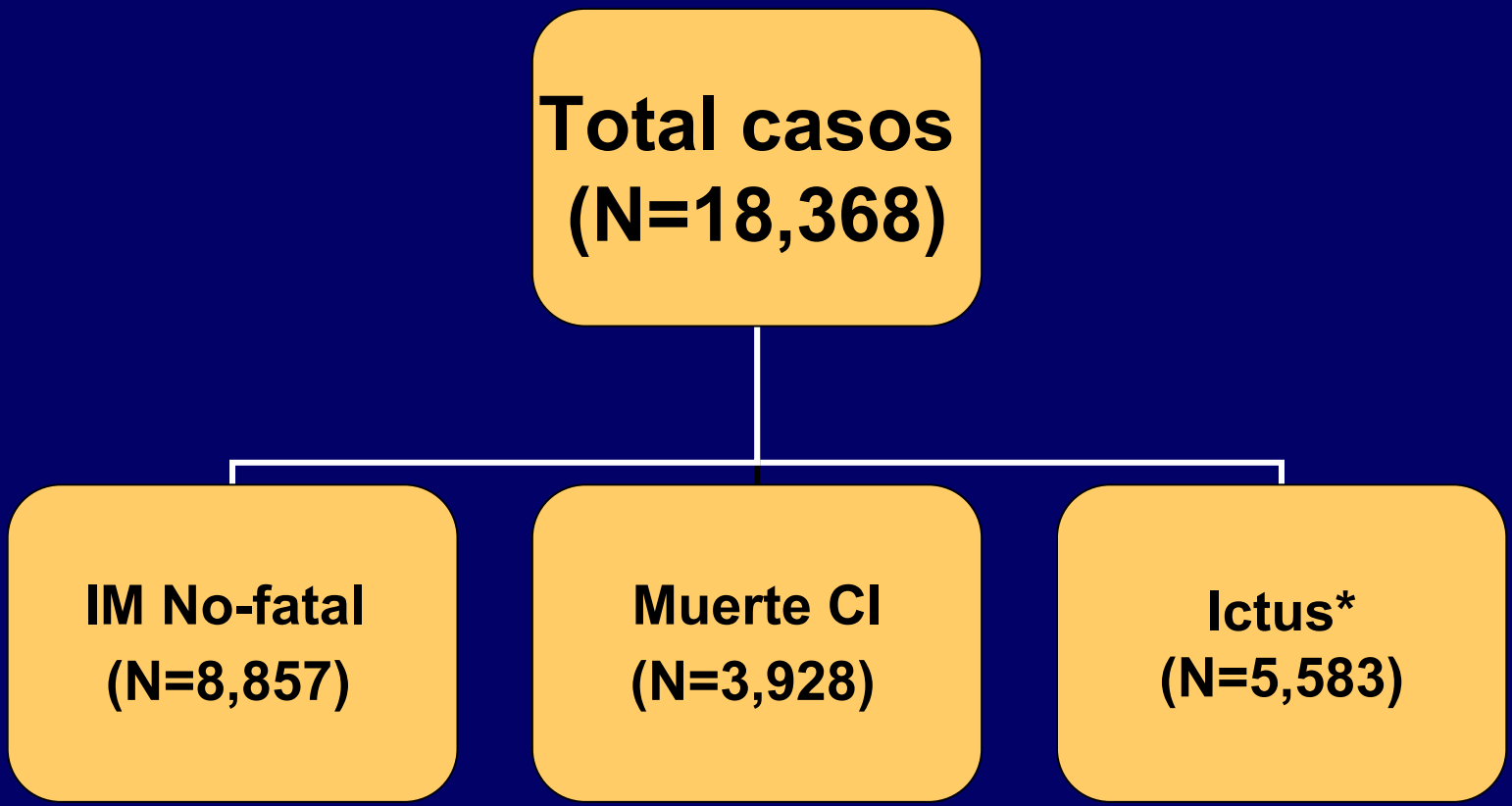
Distribución de C-HDL en hombres con CI: VA-HIT Study

C-HDL (mg/dL)	Blancos (n = 2,891)	Negros (n = 572)	Total (N = 8,578)
<35	42%	20%	38%
35-40	25%	23%	25%
>40	32%	57%	36%

63 %

Rubins HB, et al. *Am J Cardiol.* 1995;75:1196–1201.

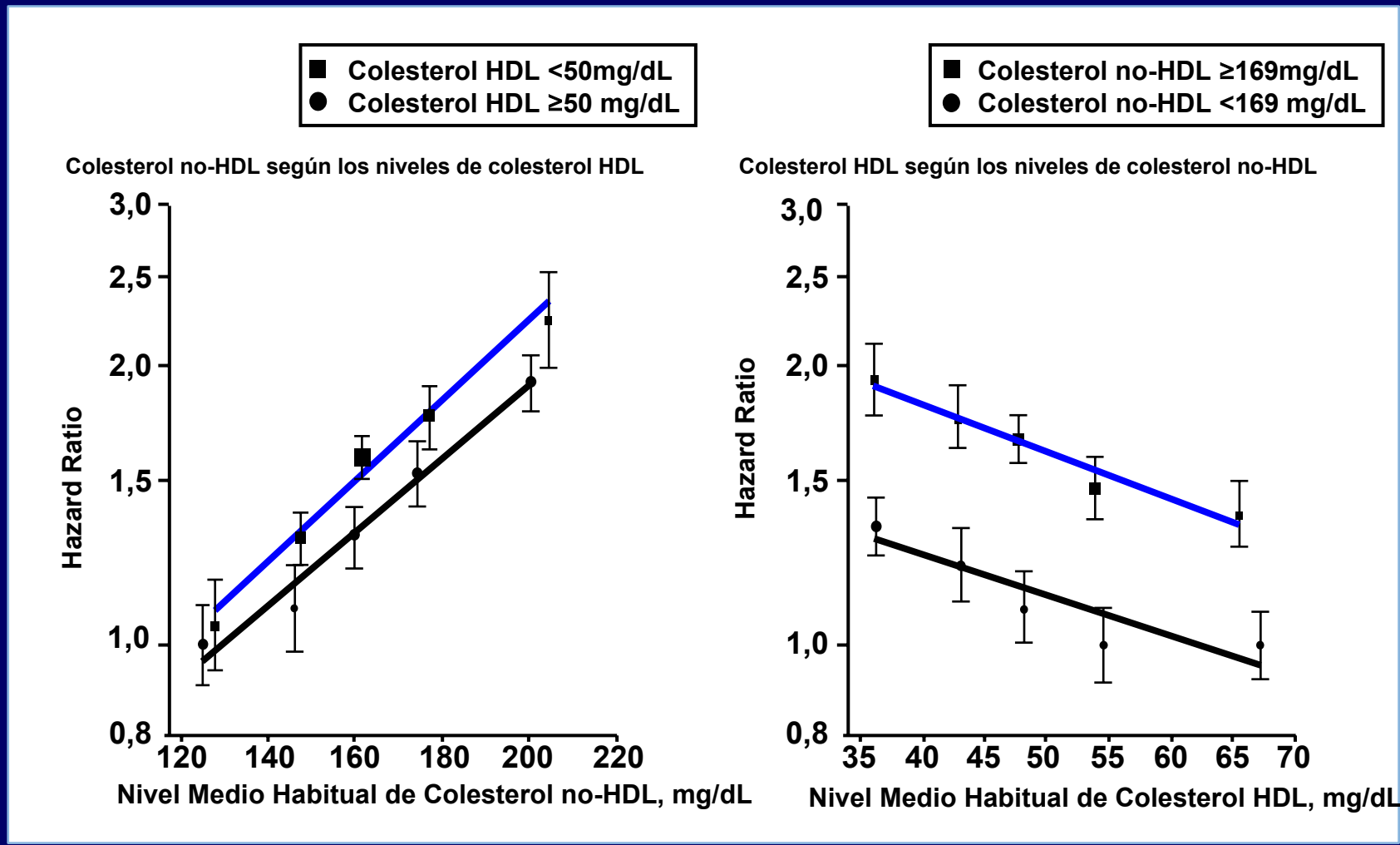
Emerging Risk Factors Collaboration: 2.79 millones/ personas-años



** 2,534 ictus isquémicos, 513 hemorrágicos y 2536 no clasificados*

ERFC. JAMA 2009;302:1993-2000

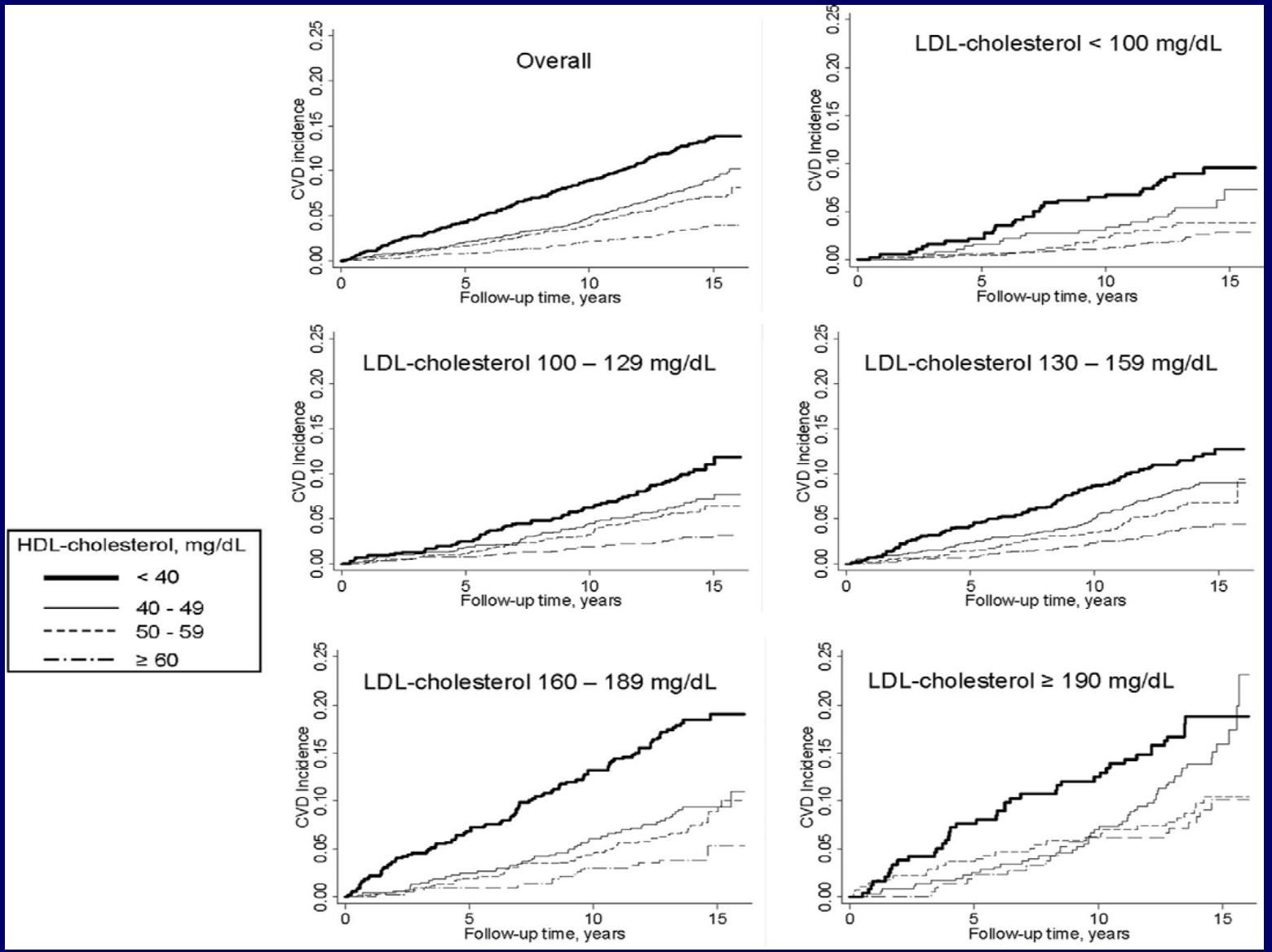
Los niveles de cHDL predicen el riesgo de sufrir cardiopatías coronarias a todos los niveles de colesterol no-HDL. Emerging Risk Factors Collaboration



The Emerging Risk Factors Collaboration (Grupo internacional de colaboración para el estudio de las enfermedades cardiovasculares). *JAMA*. 2009;302:1993–2000.

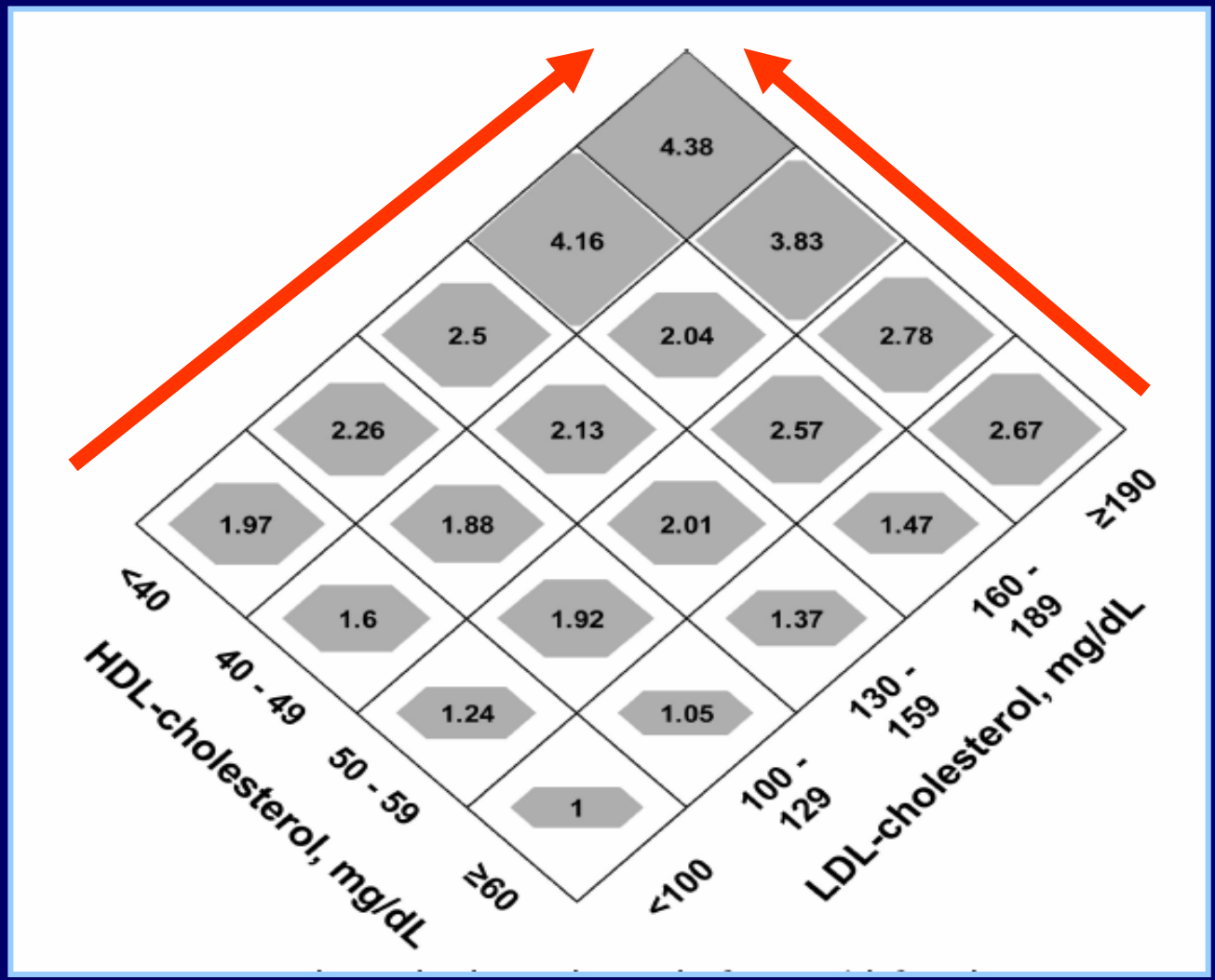
Valor Predictivo de CHDL: ARIC study

Seguimiento: 14 años. Población: 13.615



Muntner P. *Amer J Med Sci 2011;341:173-180*

Riesgo CI según C-LDL y C-HDL



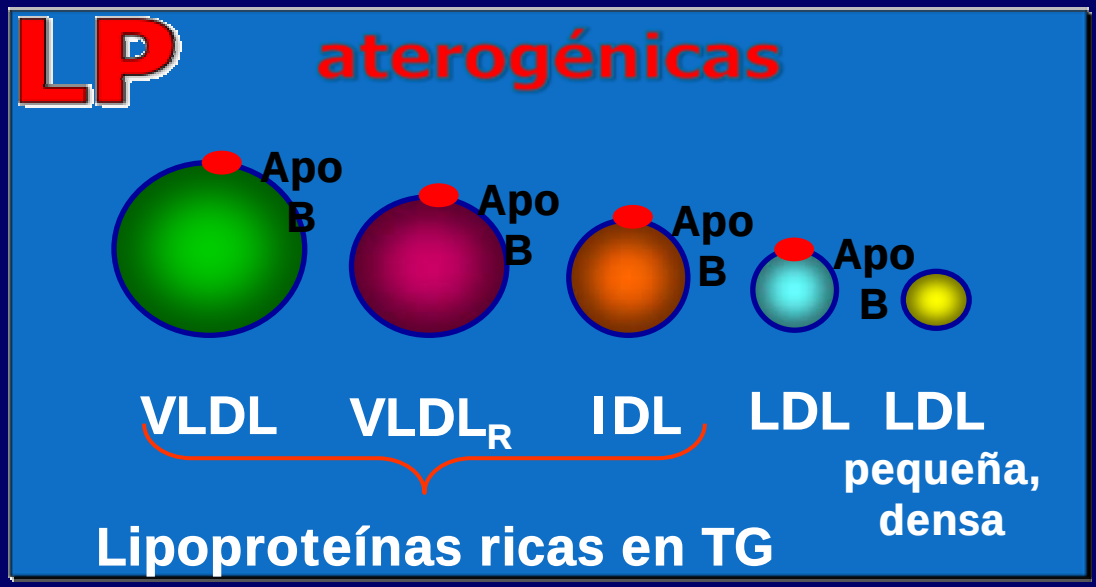
Riesgo de CI (IAM, Muerte coronaria) ajustado por edad, raza, tabaco, alcohol, actividad física, cintura cadera, TAS, DM, IRC

Muntner P. *Amer J Med Sci 2011;341:173-180*

cHDL: un Factor de Riesgo

- 1.- Independiente de cLDL.
- 2.- Frecuentemente relacionado con triglicéridos.
- 3.- Independiente de factores de riesgo no lipídicos.

Relación entre cambios en los niveles de cLDL y cHDL y Riesgo Coronario

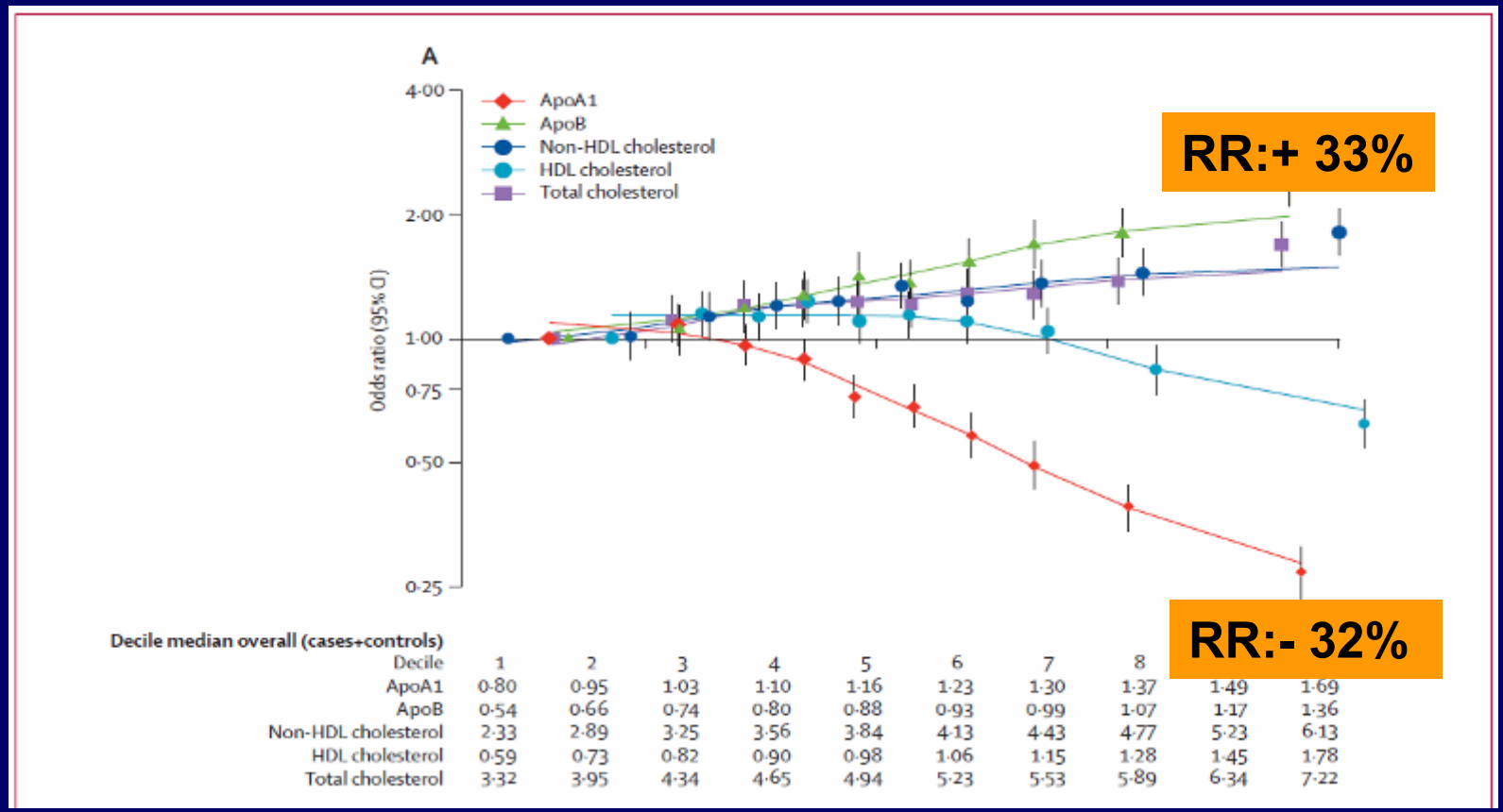


1% disminución en LDL reduce riesgo de EC 1%

1% aumento en HDL reduce riesgo de EC 3%

Third Report of the NCEP Expert Panel. NIH Publication No. 01-3670. 2001
http://hin.nhlbi.nih.gov/ncep_slds/menu.htm

RR de IAM y Liproteínas: Estudio INTERHEART



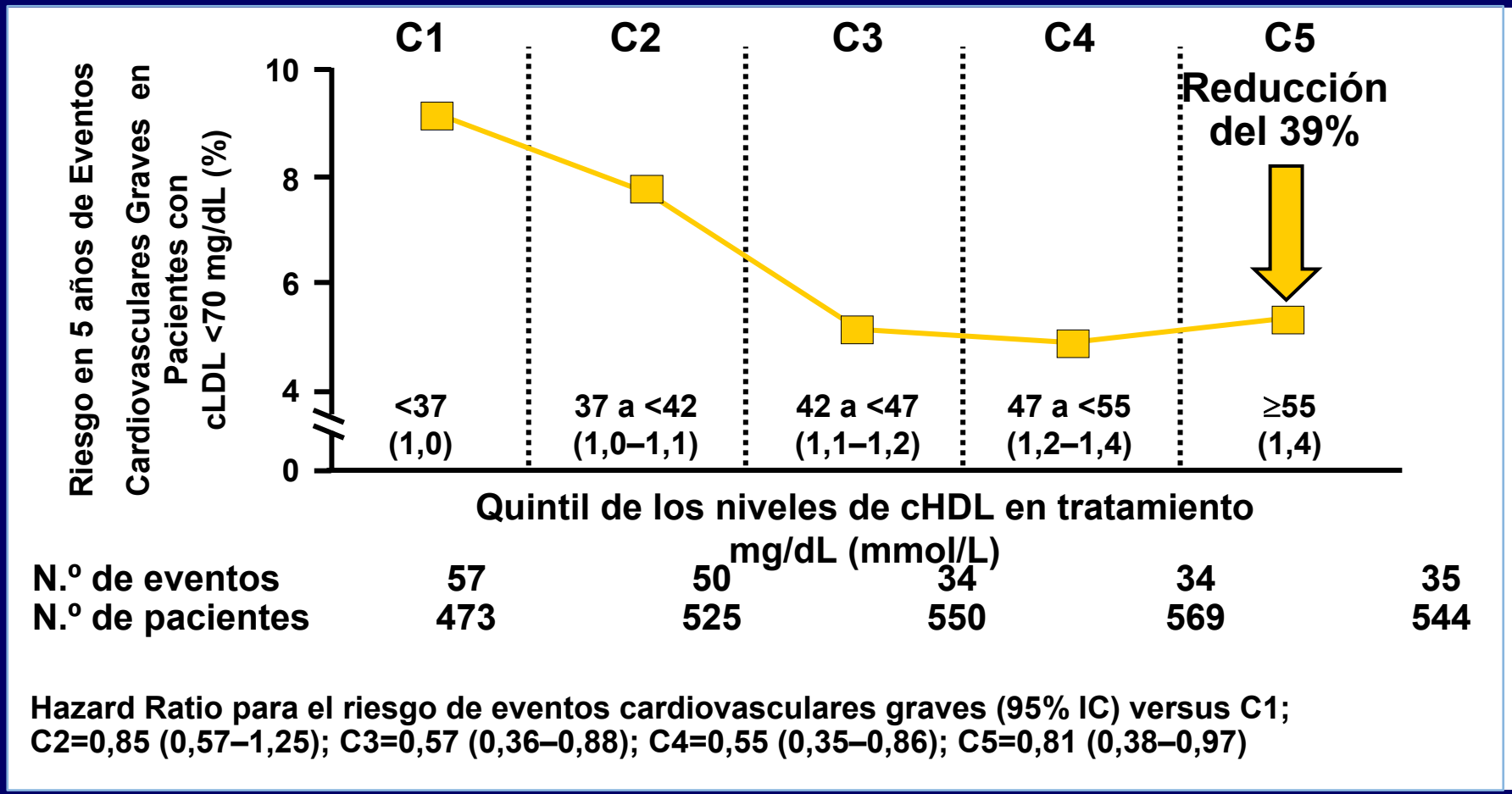
Decile median overall (cases+controls)

Decile	1	2	3	4	5	6	7	8	9	10
ApoA1	0·80	0·95	1·03	1·10	1·16	1·23	1·30	1·37	1·49	1·69
ApoB	0·54	0·66	0·74	0·80	0·88	0·93	0·99	1·07	1·17	1·36
Non-HDL cholesterol	2·33	2·89	3·25	3·56	3·84	4·13	4·43	4·77	5·23	6·13
HDL cholesterol	0·59	0·73	0·82	0·90	0·98	1·06	1·15	1·28	1·45	1·78
Total cholesterol	3·32	3·95	4·34	4·65	4·94	5·23	5·53	5·89	6·34	7·22

McQueen MJ. *Lancet 2008;372:224-33*

¿CONSERVA EL C-HDL SU VALOR PRONÓSTICO EN LOS PACIENTES QUE ALCANZAN VALORES MUY BAJOS DE C-LDL?

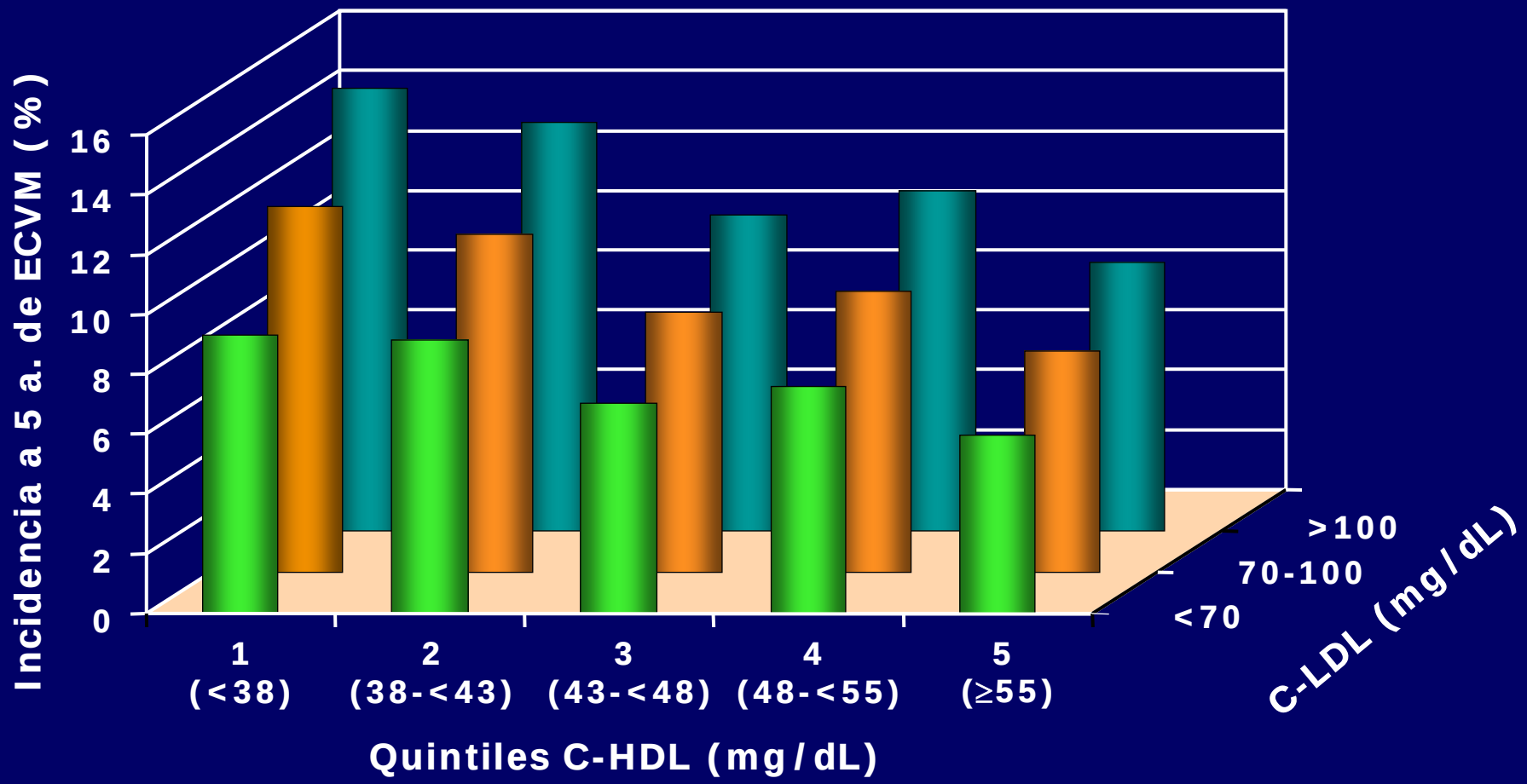
El cHDL es un factor pronóstico de eventos cardiovasculares incluso después de un tratamiento óptimo de reducción del cLDL para los objetivos de referencia: pacientes que alcanzan un cLDL de <70 mg/dL (1,8 mmol/L) Estudio TNT



Hazard Ratio para el riesgo de eventos cardiovasculares graves (95% IC) versus C1; C2=0,85 (0,57–1,25); C3=0,57 (0,36–0,88); C4=0,55 (0,35–0,86); C5=0,81 (0,38–0,97)

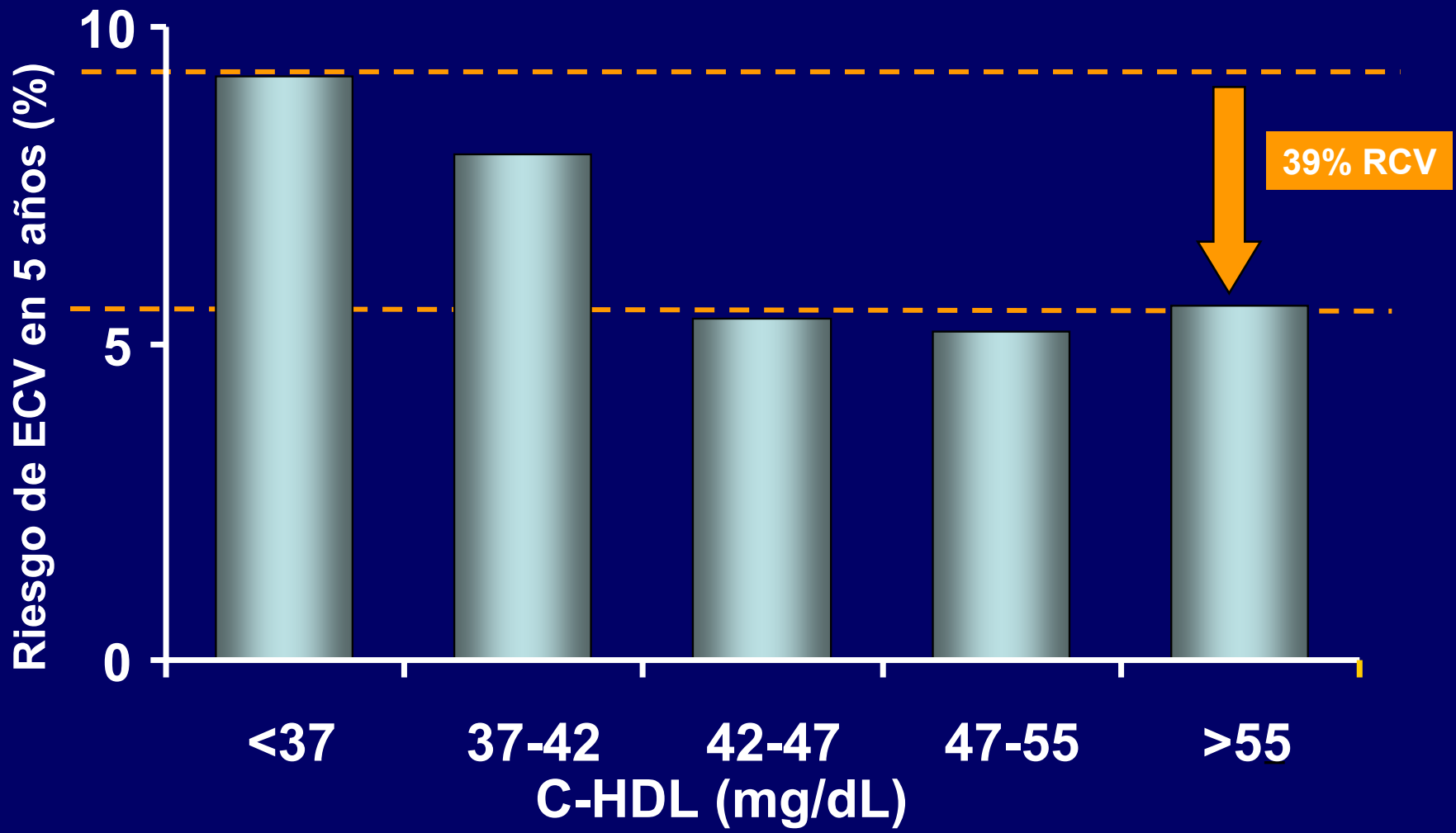
Barter et al. N Engl J Med. 2007;357:1301–1310.

TNT: Eventos según quintiles de C-HDL-C con C-LDL “normal”



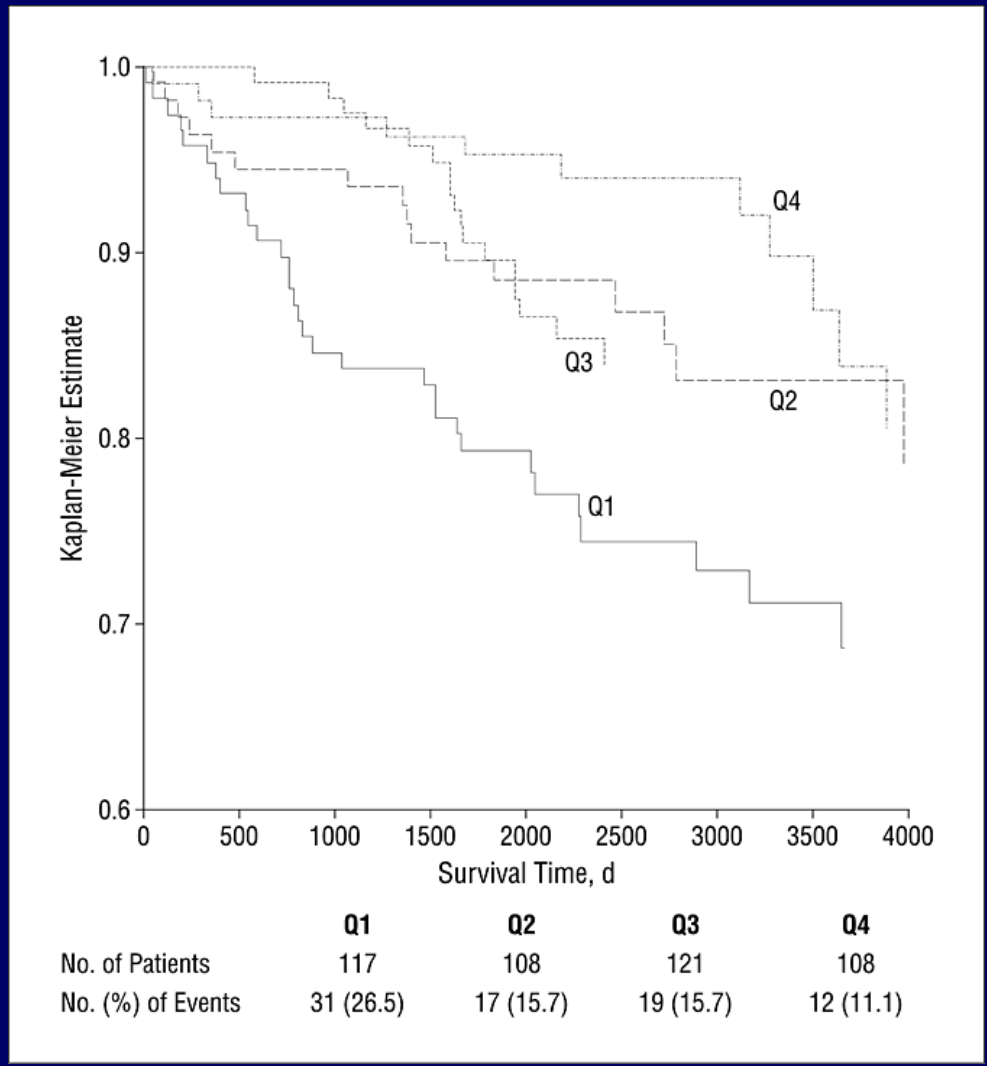
Barter and Kastelein, *NEJM, 2007*

C-HDL elevado Reduce el Riesgo CV aún con C-LDL bajo (<70 mg/dL): TNT study



*Barter P et al. N Engl J Med 2007;**357**:1301-1310*

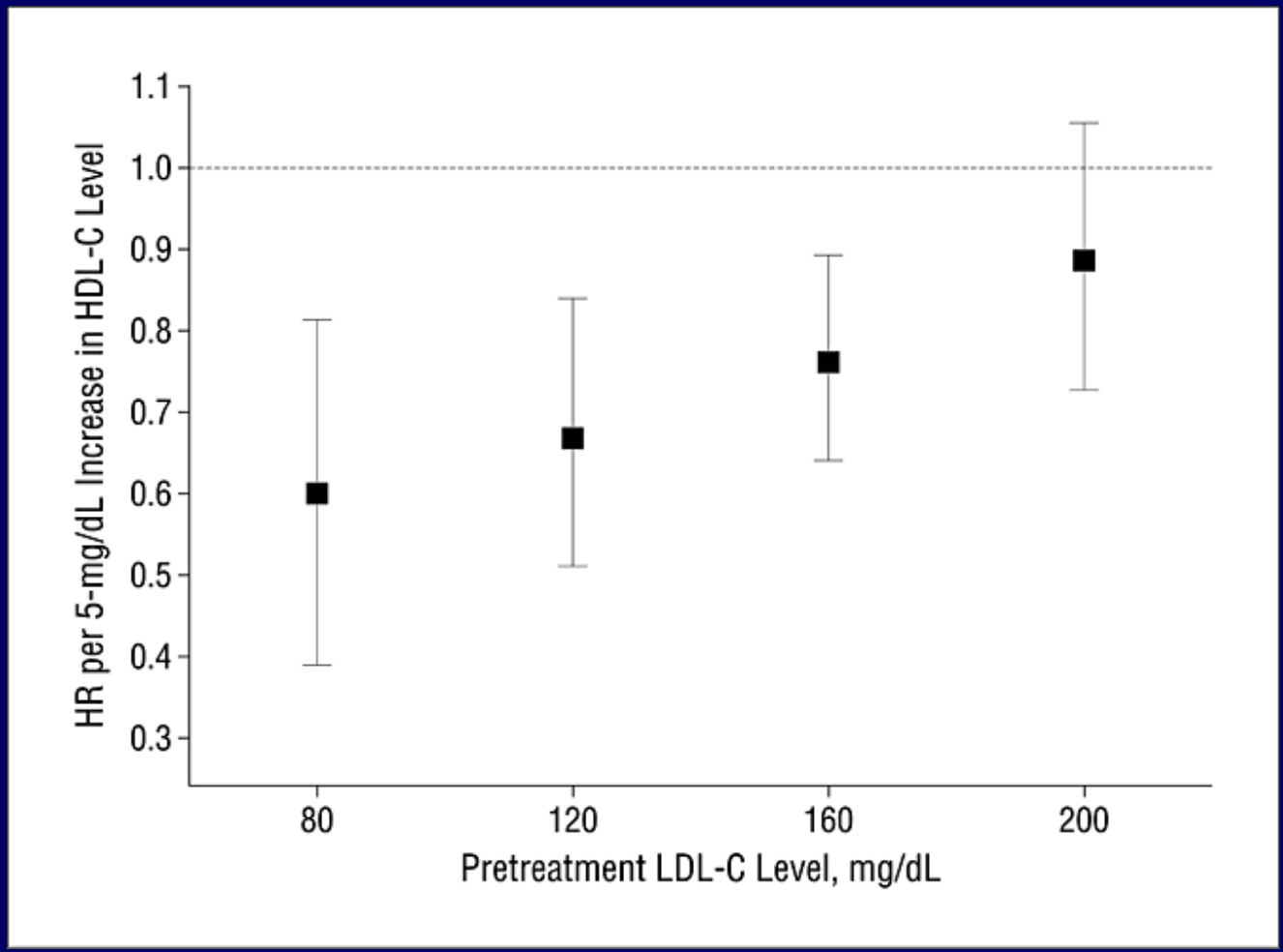
Tiempo de supervivencia libre de eventos CV por cuartiles de variación de HDL-C (Framingham Offprig Study)



	Q1	Q2	Q3	Q4
No. of Patients	117	108	121	108
No. (%) of Events	31 (26.5)	17 (15.7)	19 (15.7)	12 (11.1)

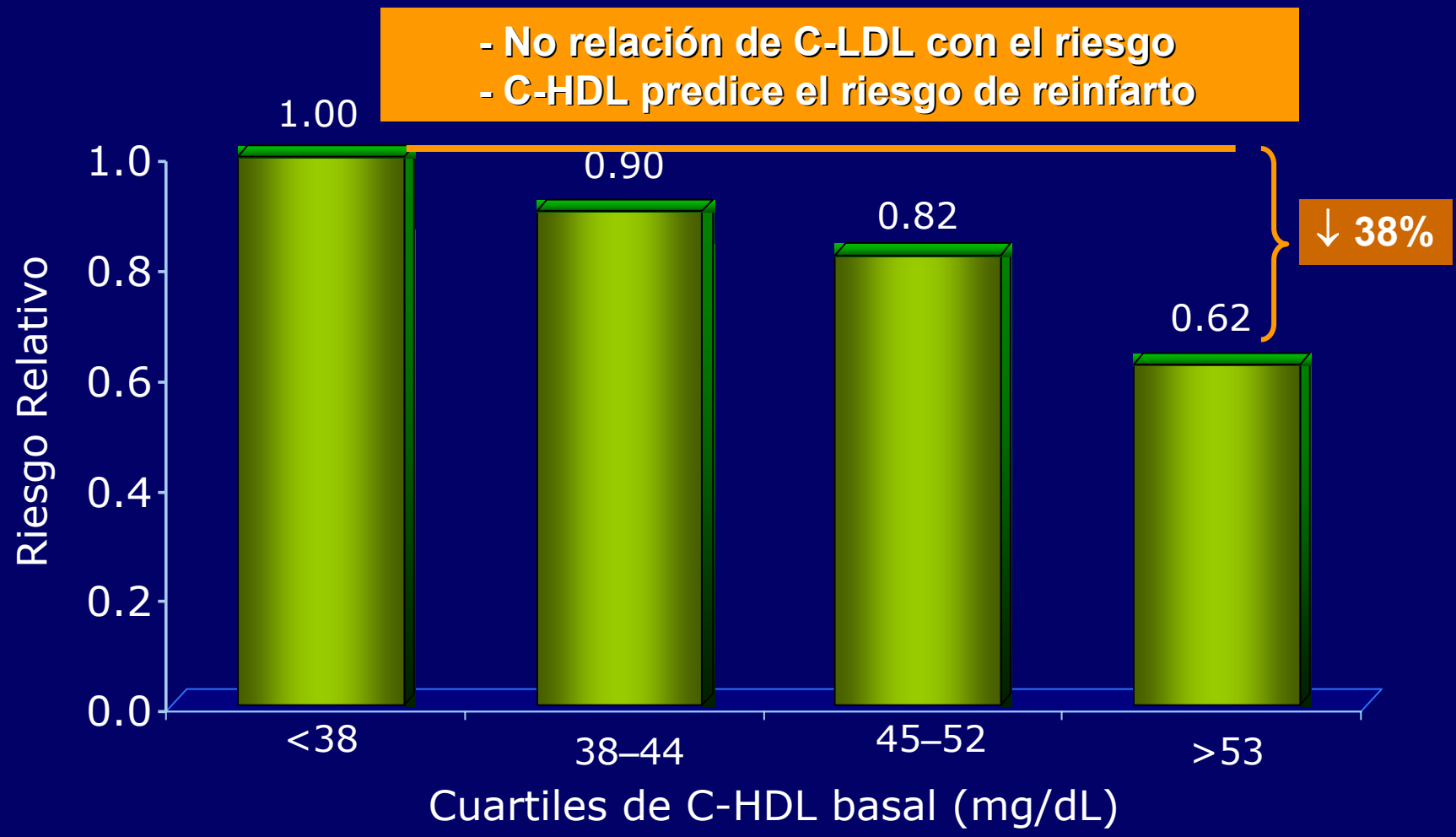
Grover SA et al. Arch Intern Med 2009

Hazard ratios asociados con variaciones de HDL-C. Relación con los niveles de LDL-C al inicio del tratamiento (Framingham Offprig Study)



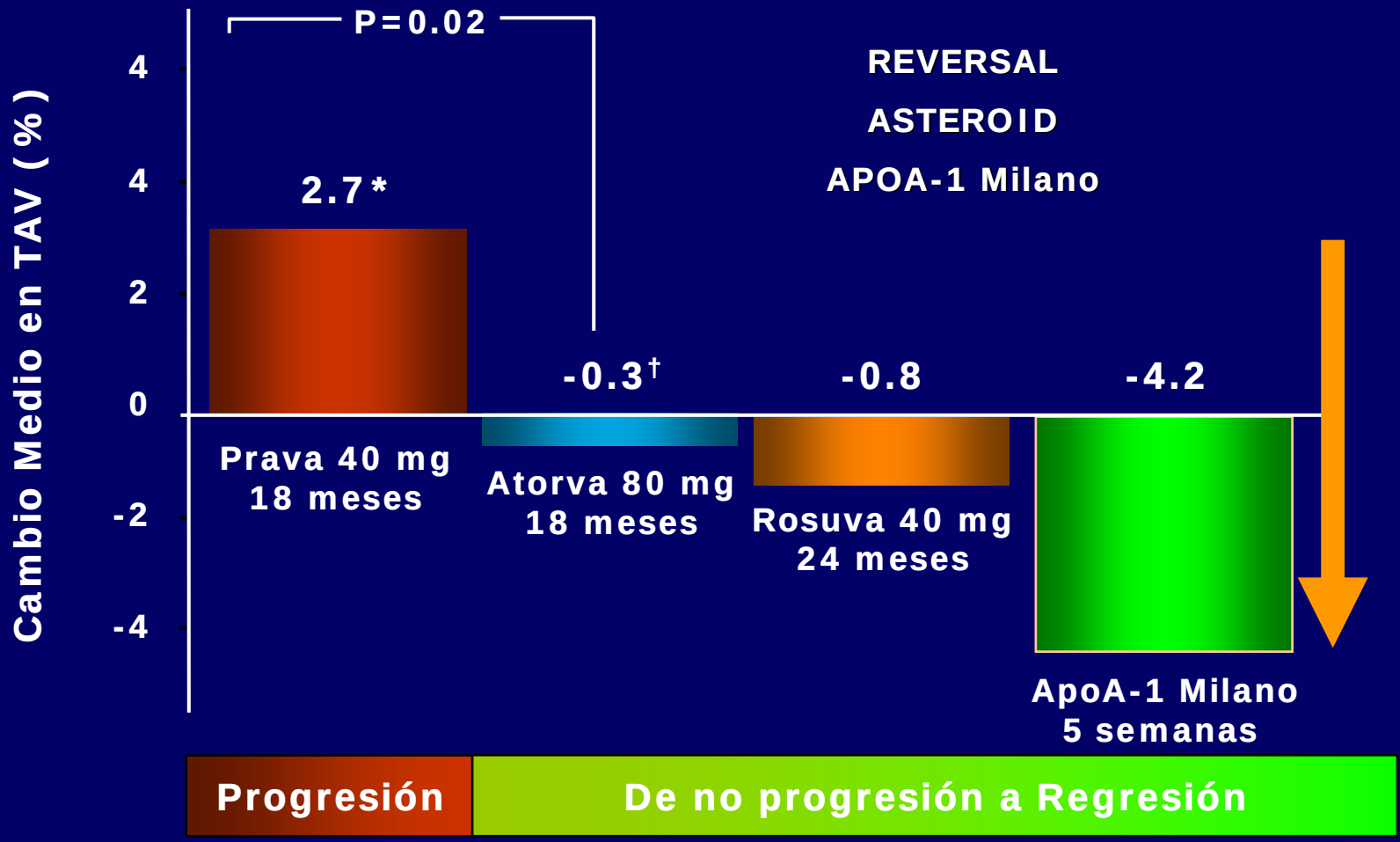
Grover SA et al. Arch Intern Med 2009

Cuartiles de C-HDL basal y y Riesgo de CI: The MIRACL Trial



Olsson AG, et al. *Eur Heart J.* 2005;26:890-896.

% Cambio Volumen ateroma (IVUs) con reducción C-LDL con vs. aumento de C-HDL



Nissen SE et al. *JAMA. 2003 y 2004*

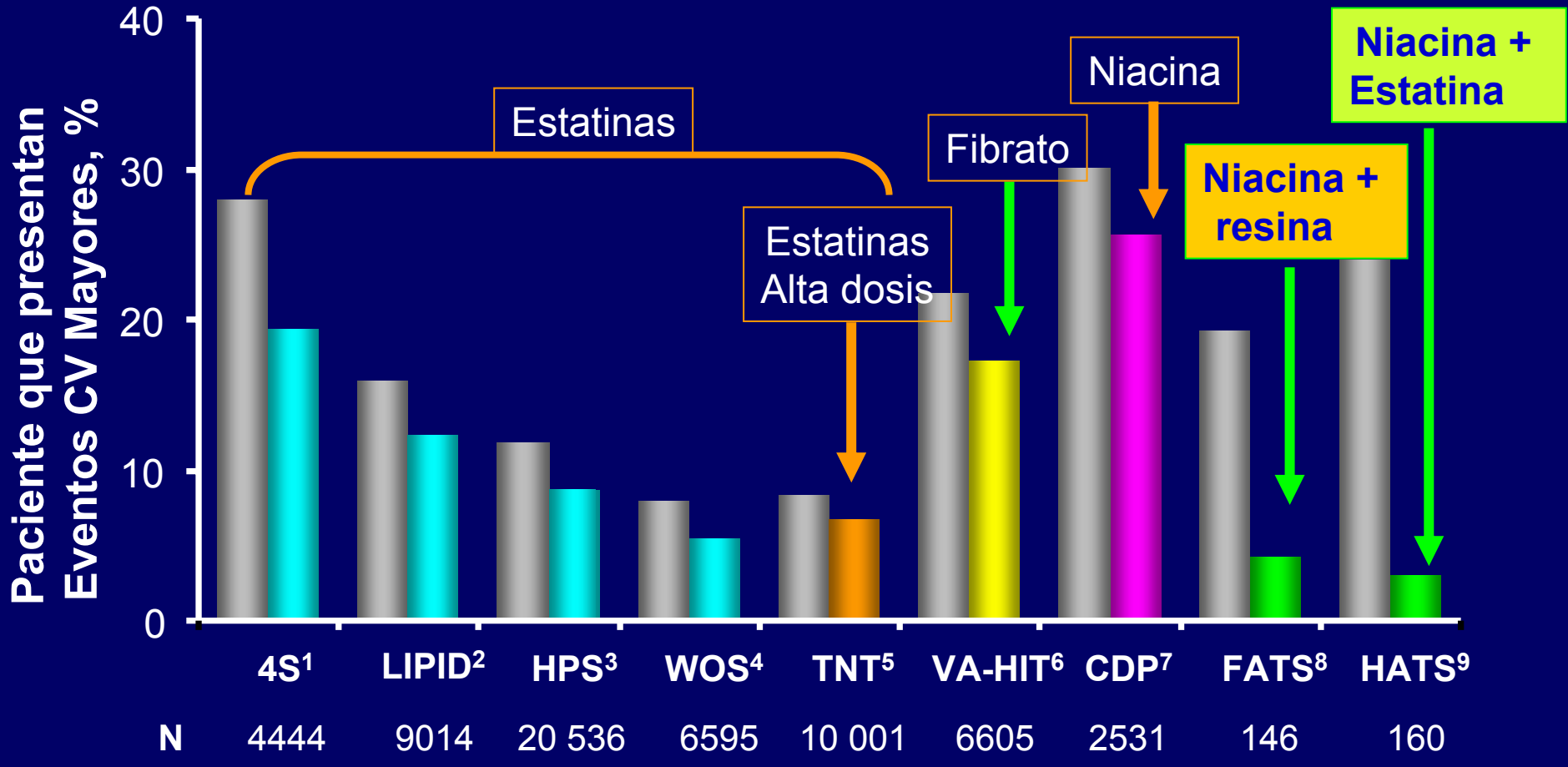
ESTUDIO JUPITER

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	p value
Placebo					
Baseline					
n	2308	2166	2306	2121	
HDL cholesterol in men (mmol/L)	0·88 (0–0·98)	1·09 (0·99–1·17)	1·30 (1·18–1·42)	1·63 (≥1·43)	
HDL cholesterol in women (mmol/L)	1·04 (0–1·17)	1·30 (1·18–1·40)	1·55 (1·41–1·71)	1·92 (≥1·72)	
Incidence (95% CI)*	1·61 (1·33–2·01)	1·36 (1·10–1·74)	1·31 (1·06–1·67)	1·15 (0·91–1·52)	
$HR_{adjusted}$ (95% CI)	1·0	0·78 (0·54–1·13)	0·69 (0·46–1·02)	0·54 (0·35–0·83)	0·0039
On treatment					
n	2074	1995	1908	1888	
HDL cholesterol in men (mmol/L)	0·88 (0–1·01)	1·09 (1·02–1·22)	1·32 (1·23–1·45)	1·68 (≥1·46)	
HDL cholesterol in women (mmol/L)	1·06 (0–1·19)	1·32 (1·20–1·42)	1·58 (1·43–1·74)	1·94 (≥1·75)	
Incidence (95% CI)*	1·47 (1·20–1·86)	1·15 (0·92–1·52)	0·90 (0·69–1·24)	0·88 (0·66–1·22)	
$HR_{adjusted}$ (95% CI)	1·0	0·87 (0·59–1·28)	0·61 (0·39–0·95)	0·55 (0·35–0·87)	0·0047
Rosuvastatin 20 mg					
Baseline					
n	2389	2107	2244	2160	
HDL cholesterol in men (mmol/L)	0·88 (0–0·98)	1·09 (0·99–1·17)	1·30 (1·18–1·42)	1·66 (≥1·43)	
HDL cholesterol in women (mmol/L)	1·04 (0–1·19)	1·30 (1·20–1·40)	1·53 (1·41–1·68)	1·94 (≥1·69)	
Incidence (95% CI)*	0·70 (0·53–0·98)	0·85 (0·65–1·17)	0·86 (0·66–1·17)	0·64 (0·47–0·93)	
$HR_{adjusted}$ (95% CI)	1·0	1·56 (0·95–2·56)	1·53 (0·90–2·61)	1·12 (0·62–2·03)	0·82
On treatment					
n	2128	1997	1920	1872	
HDL cholesterol in men (mmol/L)	0·93 (0–1·06)	1·14 (1·07–1·27)	1·37 (1·28–1·53)	1·76 (≥1·54)	
HDL cholesterol in women (mmol/L)	1·09 (0–1·24)	1·37 (1·25–1·50)	1·63 (1·51–1·81)	2·02 (≥1·82)	
Incidence (95% CI)*	0·64 (0·47–0·91)	0·70 (0·52–1·00)	0·48 (0·33–0·74)	0·62 (0·45–0·92)	
$HR_{adjusted}$ (95% CI)	1·0	1·05 (0·62–1·80)	0·86 (0·47–1·58)	1·03 (0·57–1·87)	0·97

Data are median (range) unless otherwise stated. Hazard ratios (HRs) and 95% CI adjusted as described in the methods. *Incidence per 100 person-years.

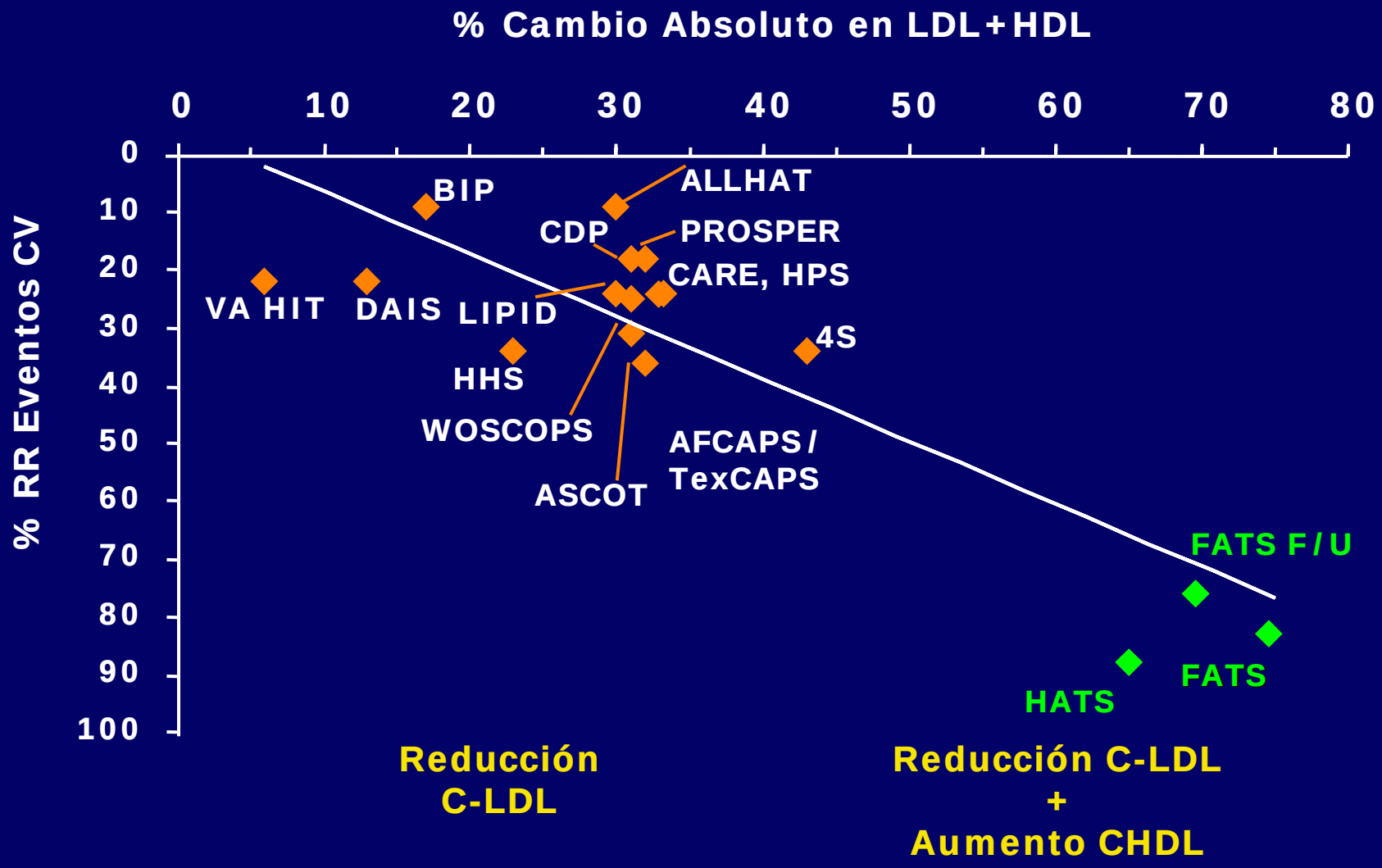
Table 2: **Relation between baseline and on-treatment concentrations of HDL cholesterol and subsequent cardiovascular disease in patients randomly allocated to receive placebo or rosuvastatin 20 mg**

Riesgo CV Residual con Monoterapia Versus Tratamiento Combinado



[1]4S Group. *Lancet.* 1994;344:1383-1389.
[2]LIPID Study Group. *N Engl J Med.* 1998;339:1349-1357.
[3]HPS Collaborative Group. *Lancet*. 2002;360:7-22.
[4]Shepherd J, et al. *N Engl J Med.* 1995;333:1301-1307.
[5]LaRosa JC, et al. *N Engl J Med.* 2005;352:1425-1435.
[6]Rubins HB, et al. *N Engl J Med.* 1999;341:410-418.
[7]CDP Research Group. *JAMA*. 1975;231:360-381.
[8]Brown BG, et al. *N Engl J Med.* 1990;323:1289-1298.
[9]Brown BG, et al. *N Engl J Med.* 2001;345:1583-1592.

El aumento de C-HDL tiene efecto ADITIVO a la Reducción de C-LDL

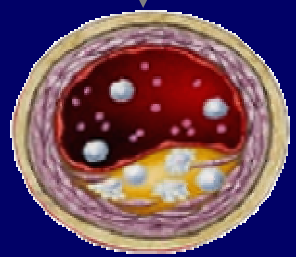


Brown, 2004

TRATAMIENTO COMBINADO: ESTATINAS + FIBRATOS O NIACINA

EFECTOS SOBRE EL METABOLISMO DE LOS LÍPIDOS

- ↓ LDL-C 30-60%
- ↑ HDL-C 10-35%
- ↓ TG 20-50%
- ↓ LDL Pequeñas y densas



Disminución RCV

Estabilidad de la placa

Disminución Riesgo Residual

TABLE 5. **Prevalence of Risk Parameters (Anthropometric and Biochemical Measurements) in the Study Population by Age Group***

	<30 Years (n=67 507)	30-39 Years (n=71 185)	40-49 Years (n=47 548)	50-59 Years (n=25 279)	≥60 Years (n=5392)
SBP ≥140 mm Hg or DBP ≥90 mm Hg	12.0 (11.7-12.2)	16.3 (16.0-16.6)	28.0 (27.6-28.4)	46.9 (46.3-47.5)	59.0 (57.7-60.3)
BMI 25-29.9	28.5 (28.2-28.8)	39.2 (38.8-39.6)	44.7 (44.3-45.2)	48.6 (48.0-49.2)	51.3 (50.0-52.6)
BMI≥30	9.2 (9.0-9.4)	14.4 (14.2-14.7)	19.7 (19.3-20.0)	25.5 (25.0-26.0)	27.0 (25.9-28.2)
Abdominal obesity†	7.6 (7.4-7.8)	12.9 (12.7-13.1)	19.7 (19.3-20.0)	27.2 (26.7-27.8)	34.2 (32.9-35.5)
Blood glucose 110-125 mg/dL	0.90 (0.81-0.95)	2.4 (2.3-2.5)	5.7 (5.5-5.9)	10.5 (10.2-10.9)	12.4 (11.5-13.3)
Blood glucose ≥126 mg/dL	0.40 (0.33-0.42)	0.90 (0.81-0.95)	3.3 (3.2-3.5)	8.2 (7.9-8.6)	11.8 (10.9-12.6)
Cholesterol ≥200 mg/dL	23.7 (23.4-24.0)	46.5 (46.1-46.9)	63.4 (63.0-63.9)	71.7 (71.1-72.3)	70.4 (69.2-71.7)
Cholesterol ≥240 mg/dL	4.3 (4.2-4.5)	13.2 (13.0-13.5)	23.6 (23.3-24.0)	30.5 (30.0-31.1)	28.9 (27.7-30.1)
Low HDL cholesterol‡	26.4 (26.0-26.7)	27.6 (27.2-27.9)	25.0 (24.6-25.4)	20.4 (19.9-20.9)	18.0 (16.9-19.0)
LDL cholesterol ≥160 mg/dL	5.5 (5.3-5.7)	15.6 (15.3-15.9)	25.6 (25.2-26.0)	32.7 (32.2-33.4)	31.0 (29.7-32.2)
Triglycerides ≥200 mg/dL	3.6 (3.4-3.7)	8.5 (8.3-8.8)	12.5 (12.2-12.8)	12.1 (11.7-12.5)	10.0 (9.2-10.8)
Dyslipidemia§	46.6 (46.2-47.0)	65.3 (64.9-65.7)	76.7 (76.3-77.0)	81.6 (81.1-82.1)	80.1 (79.0-81.1)

*HDL indicates high density lipoprotein; LDL, low density lipoprotein; BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure.
†Waist circumference >102 cm (men) or >88 cm (women).
‡HDL cholesterol <40 mg/dL (men) or <50 mg/dL (women).
§Total cholesterol >200 mg/dL or HDL cholesterol <40 mg/dL (men) and <50 mg/dL (women) or LDL cholesterol ≥160 mg/dL or triglycerides ≥200 mg/dL.
All prevalence rates increased significantly with age, except low HDL cholesterol, which decreased significantly with age.
Values are percentages and 95% confidence intervals (in parentheses).

Rev Esp Cardiol 2006

Efecto de las Intervenciones de Estilo de Vida en C-HDL

Intervención	Aumento de C-HDL
Ejercicio Aeróbico	5-10%
Abandono Tabaco	5-10%
Pérdida de Peso	0.35mg/dL/kg peso perdido
Dieta Prudente (rica en ω-3 y monoenoicos)	Hasta 5%
Ingesta moderada de alcohol	5-15%

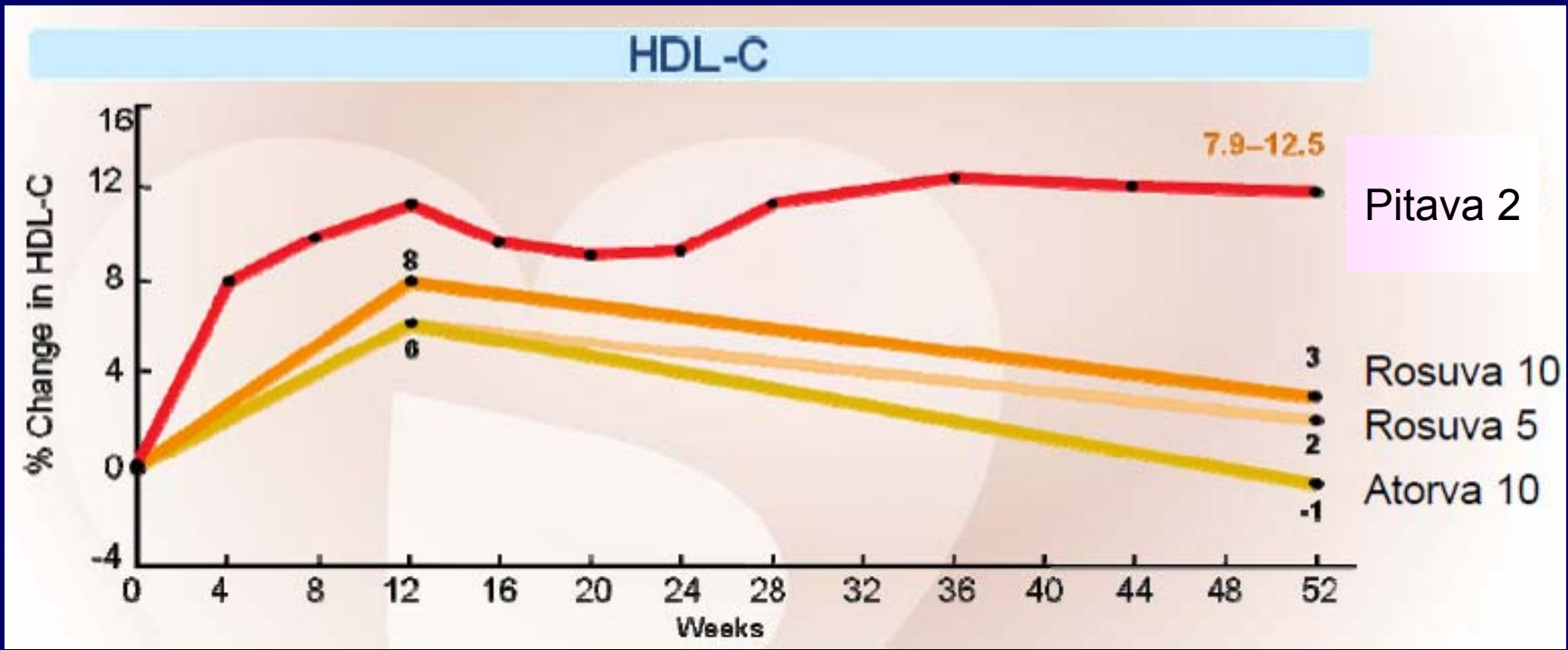
Singh IM et al. JAMA 2007: 298: 786-98.

Increase in HDL-C from baseline across dose ranges of statins: results from the STELLAR study

	HDL-C change, %			
Dose	Rosuvastatin	Atorvastatin	Simvastatin	Pravastatin
10 mg	7.7*	5.7	5.3	3.2
20 mg	9.5*	4.8	6.0	4.4
40 mg	9.6*	4.4	5.2	5.6
80 mg	NA	2.1	6.8	NA

*Significantly different for all dose ranges.
HDL-C=high-density lipoprotein cholesterol; NA=not available.

Fabbri G, Maggioni P. Adv Ther 2009; 26(5): 469-87

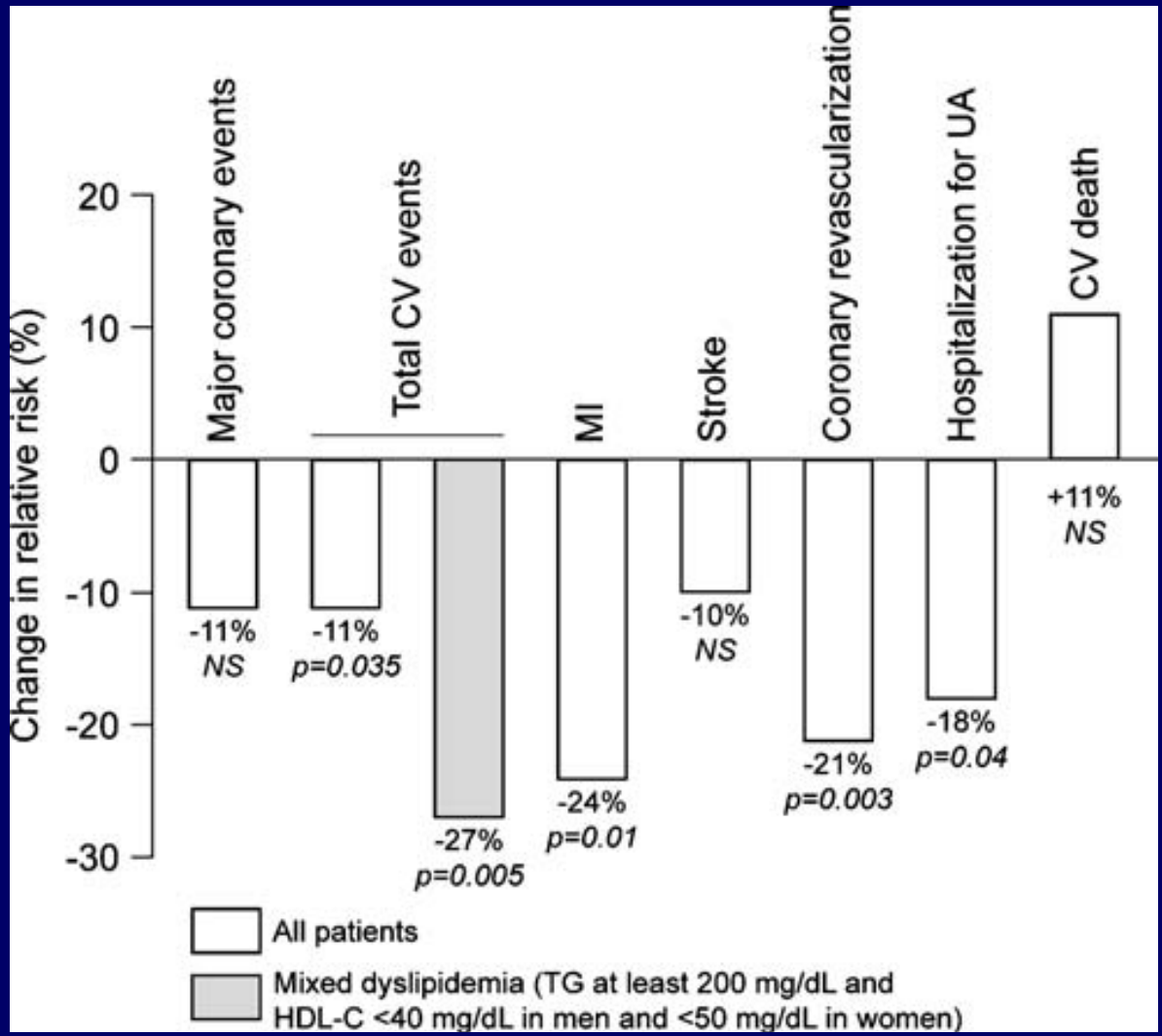


Teramoto T. J Clin Ther Med, 2001; 17:885-914
Olsson AG. Am Hearth J, 2002; 144: 1044-51

	LDL	*HDL*	*TG*
Estatinas	**- 15/55 %**	**+ 5/15 %**	**- 7/30 %**
Resinas	**- 15/30 %**	**+ 3/5 %**	**=**
Fibratos	**- 5/20 %**	**+ 10/20 %**	**- 20/50 %**
Nicotínico	**- 5/25 %**	**+ 15/35 %**	**- 20/50 %**

Circulation 2004; 110:227-239

Effect of fenofibrate on primary and secondary endpoints. Data from the FIELD study



Steiner G. Cardiovasc Drugs Therapy 2009

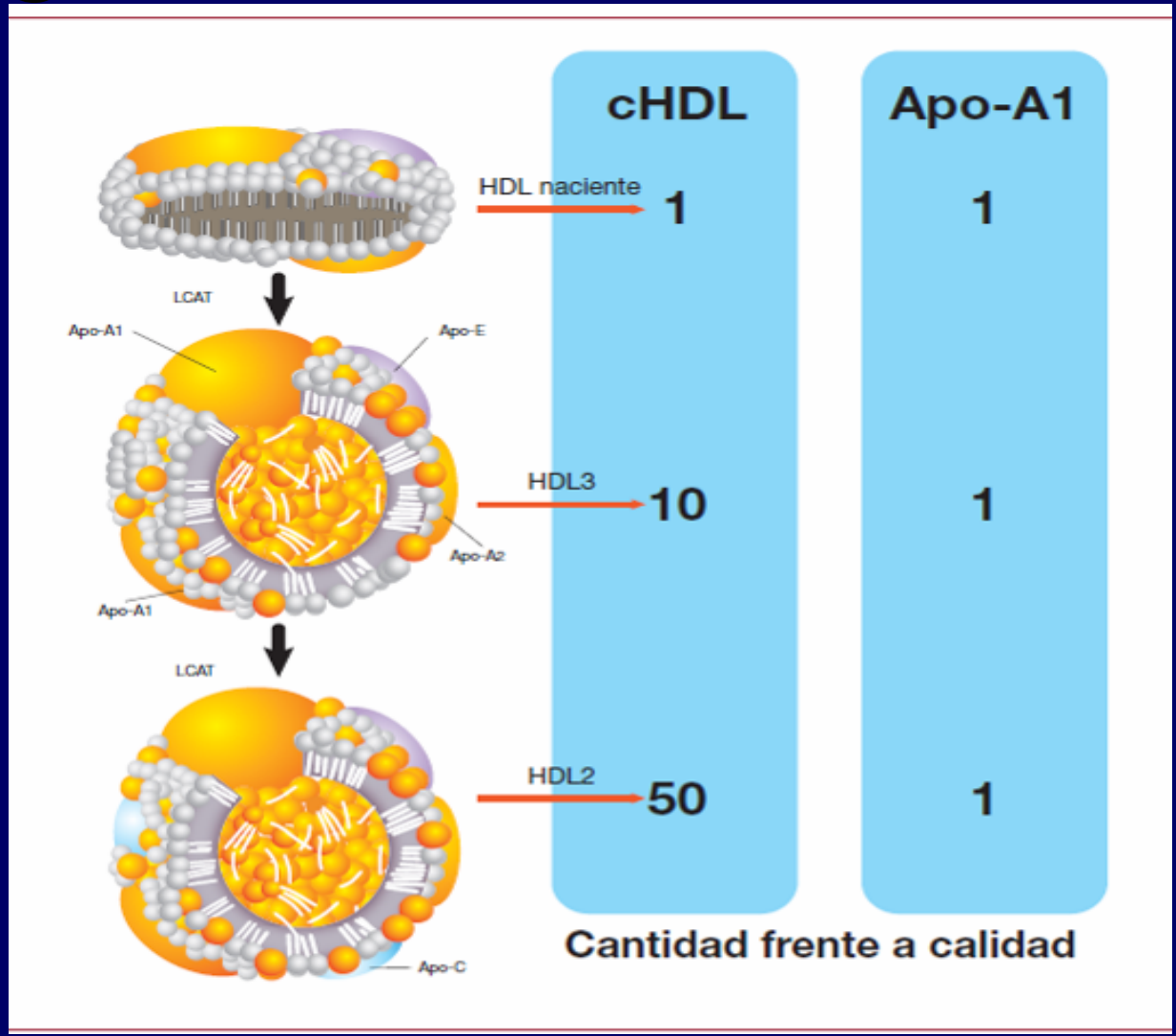
Nuevas terapias

Inhibidores de la CETP

- Dalcetrapib
- Anacetrapib

Bloomfield D, Carlson GL, Sapre A, et al. Efficacy and safety of the cholesteryl ester transfer protein inhibitor anacetrapib as monotherapy and co-administered with atorvastatin in dyslipidemic patients. *Am Heart J* 2009; 157:352-360.

¿Cantidad vs. Calidad?



Badimon JJ. *Rev Esp Cardiol. 2010;63(Supl 2):20-35*

Protein	VLDL	LDL	HDL
Actin	1[b]		
Albumin	1[b]	3[e]	5,6,12
Alpha-1-acid glycoprotein			5,6
Alpha-1-antitrypsin inhibitor	1[b]	4	5,6,7,9,12
Alpha-1B-glycoprotein			6,7
Alpha-1-microglobulin/bikunin			6
Alpha-2-antiplasmin			6
Alpha-2HS-glycoprotein	1[b]		5,6
Alpha-2-macroglobulin		3[d]	5
Alpha-amylase (salivary)			9
Angiotensinogen			6
Apolipoprotein(a)			
ApoA-I	1	3[e],4	5,6,7,8,9,10,12
ApoA-II			5,6,8,9,10,12
ApoA-IV	1	3[c]	6,7,8,9,10,12
ApoB	1	3[d]	6,12
ApoC-I			5,6,9,12
ApoC-II		3[c],4	6,8,9,12
ApoC-III	1	3[c],4	5,6,7,8,9,10,12
ApoC-IV	1		6,12
ApoD			5,6,8,10,12
ApoE	1	3[e],4	5,6,8,9,10,12
ApoF			5,6,12
ApoH			6
ApoJ (Clusterin)		3[c],4	5,6,8,12
ApoL-I	1		6,7,8,9,12
ApoM	1	3[c]	6,8,9,12
C4b binding protein			10
Calgranulin A		3[c]	

Protein	VLDL	LDL	HDL
CETP			6,10
Complement C3			6,8
Complement C4			6
Complement C9			6
Fibrinogen	1[b]	3[d]	6,7,10,12
Fibronectin		3[d]	
Haptoglobin-related protein			5,6,12
Haptopglobin		3[d]	8,10
Hemoglobin			11
Hemopexin	1[b]		6
Immunoglobulin Mu	1[b]	3[d]	
Inter- alpha -trypsin inhibitor chain H4			6,7
Kininogen			6
LCAT			6,10
LPS binding protein			7
Lysozyme C		3[c]	
Paraoxonase 1			5,6,8,12
Paraoxonase 3			6,12
Platelet activating factor-acetyl hydrolase			12
Platelet basic protein			12
PLTP			6,12
Prenylcysteine lyase	1		6
Prothrombin			12
Retinol binding protein			6
SAA1/2			6,9,12
SAA4		3[c],4	5,6,9,12
SerpinF1			6
Transferrin			5,6,8
Transthyreitin			6,7,8,12
Vitamin D binding globulin	1[b]		5,6
Vitronectin			6

a Studies include: 1. Mancone, 2007 (37); 2. Bondarenko, 1999 (40); 3. Karlsson, 2005 (34); 4. Stahlman, 2008 (39); 5. Heller, 2005 (44); 6. Vaisar, 2007 (15); 7. Hortin, 2006 (69); 8. Rezaee, 2006 (38); 9. Karlsson, 2005 (33); 10. Kunitake, 1994 (36); 11. Watanabe, 2007 (46); 12. Davidson, 2009 (64).
b Proteins detected in ultracentrifuge-purified VLDL and described by the authors as contaminants.
c Proteins detected in ultracentrifuge-purified LDL and not in LDL prepared by size exclusion chromatography.
d Proteins detected in LDL prepared by size exclusion chromatography and not in ultracentrifuge-purified LDL.
e Proteins detected in LDL prepared by size exclusion chromatography and ultracentrifugation

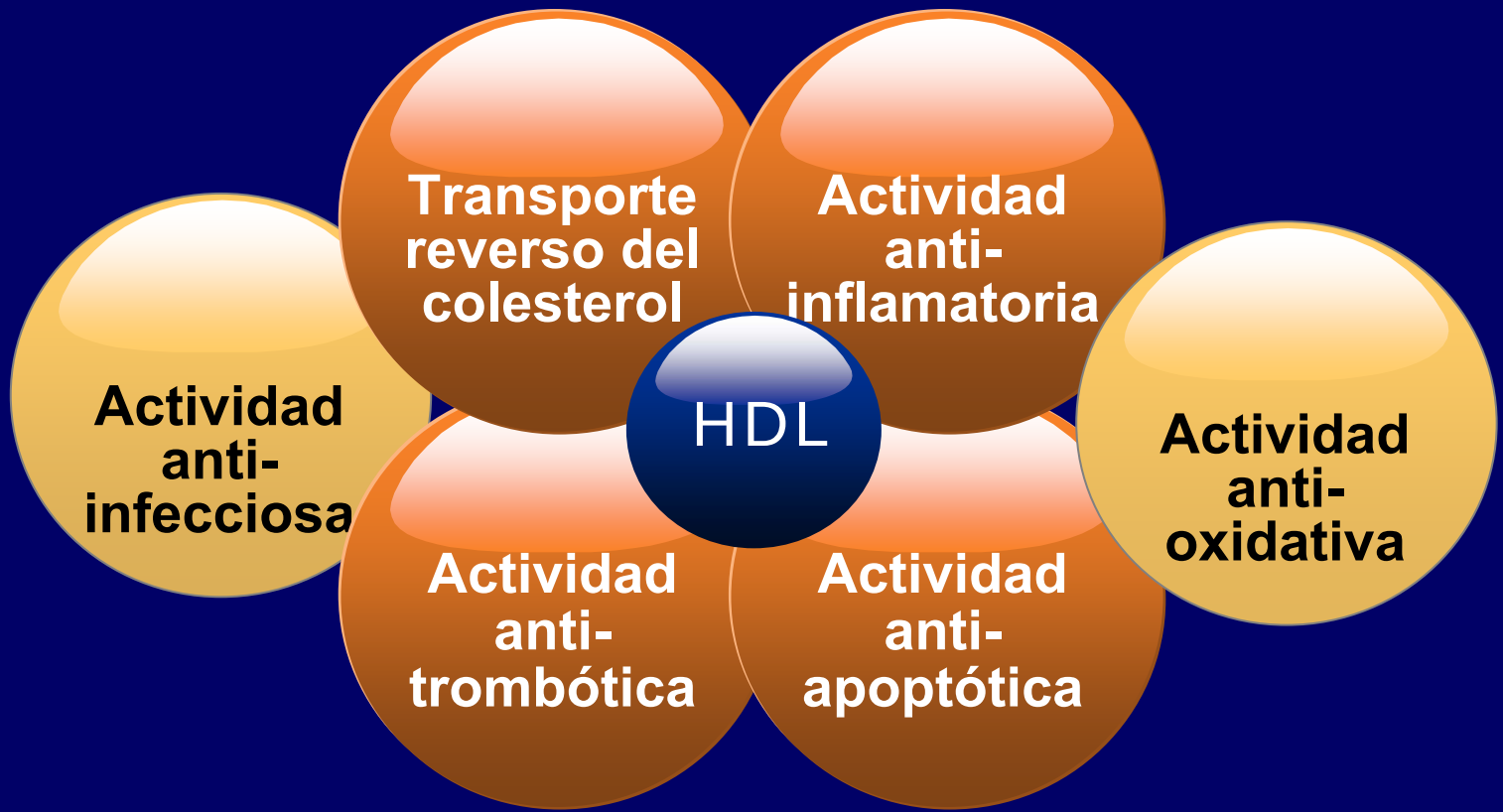
Hoofnagle AN, Heinecke JW. J Lipid Res 2009; 50(10): 1967-75

Heterogeneidad HDL: Hasta 10 subpoblaciones

Más de 100 proteínas no estructurales y cambiantes en subpoblaciones y estado funcional

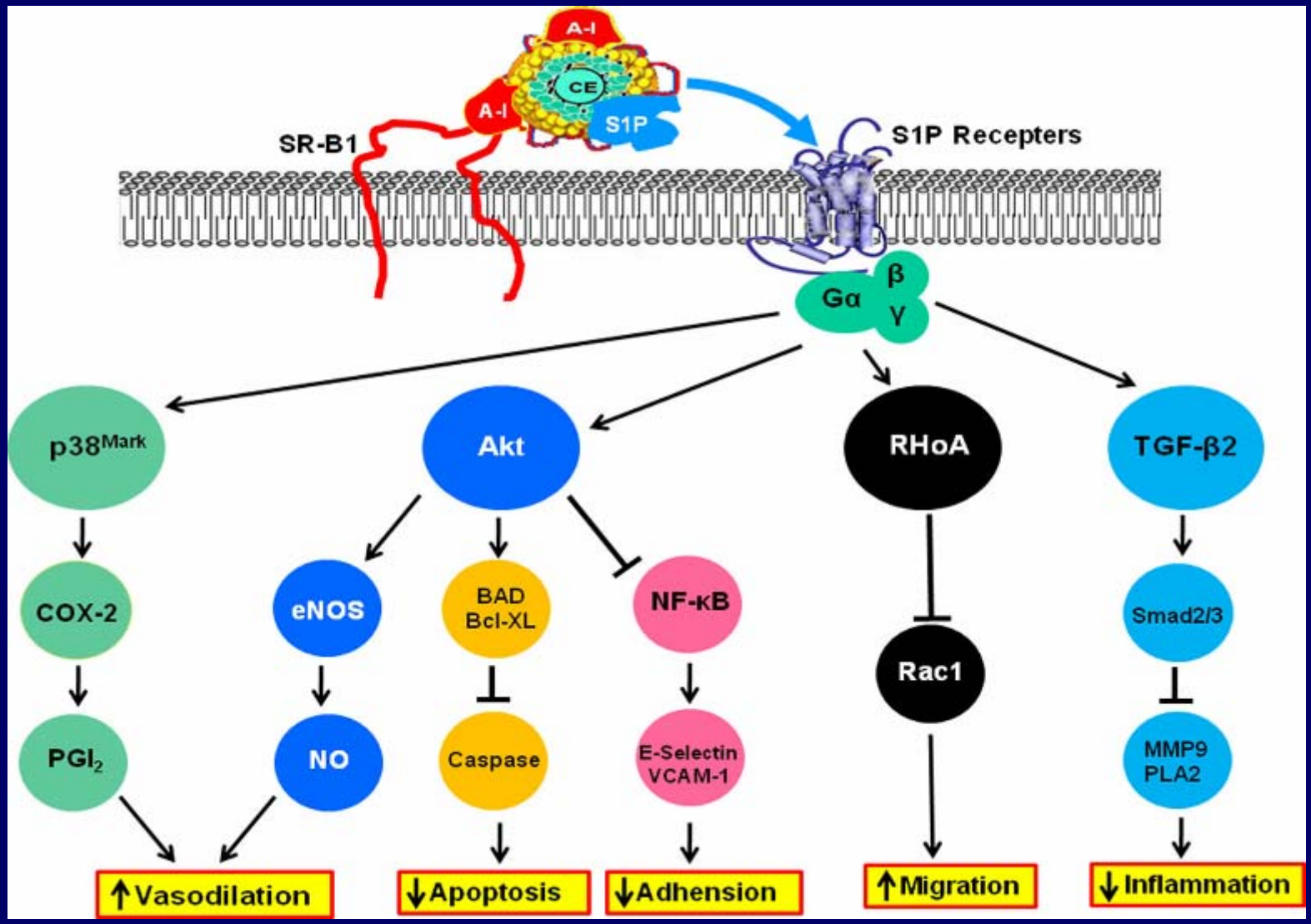
- Forma: ¿discoidal o esférica?
- Densidad: ¿HDL_2 vs HDL_3?
- Tamaño: ¿pequeñas o grandes?
- Composición protéica: ¿apo A1 vs apo A1+apoA2?
- Carga de superficie

Principales mecanismos de la acción antiaterogénica de HDL



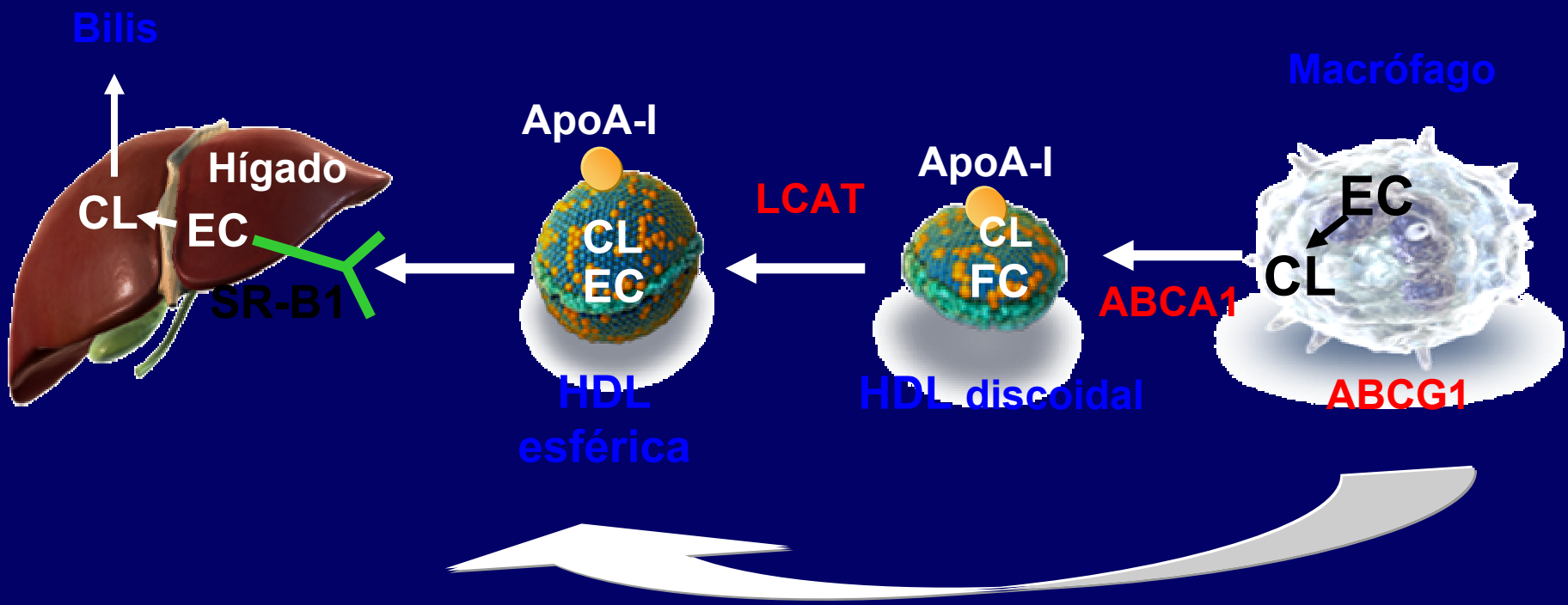
Chapman MJ et al. Current Medical Research and Opinion 2004; 20(8): 1253-68

Mecanimos de Acción de HDL



Brewer HB. J Clin Endocrinol Metabo 2011;96:1246-57

El transporte reverso de colesterol desde los macrófagos hasta su excreción



Adaptado de: Duffy D, Rader DJ. Circulation 2006;113:1140–1150.

Eflujo de Colesterol y GIM

Linear-Regression Covariates*	Beta Coefficient per 1-SD Increase in Efflux Capacity (95% CI)	P Value
Age and sex	−0.02 (−0.04 to −0.003)	0.02
Age, sex, and cardiovascular risk factors	−0.02 (−0.04 to −0.004)	0.02
Age, sex, cardiovascular risk factors, and high-density lipoprotein cholesterol	−0.03 (−0.06 to −0.01)	0.003
Age, sex, cardiovascular risk factors, and apolipoprotein A-I	−0.04 (−0.06 to −0.01)	0.005

* Cardiovascular risk factors were systolic blood pressure, glycated hemoglobin, and low-density lipoprotein cholesterol.

EC según capacidad eflujo, por cuartiles

Variable	No. of Patients	Odds Ratio for Coronary Artery Disease (95% CI)*		
		Adjusted for Cardiovascular Risk Factors	Adjusted for Cardiovascular Risk Factors and HDL Cholesterol	Adjusted for Cardiovascular Risk Factors and Apolipoprotein A-I
Quartile 1	198	1.00	1.00	1.00
Quartile 2	198	0.75 (0.48–1.16)	0.79 (0.51–1.24)	0.77 (0.49–1.21)
Quartile 3	198	0.58 (0.37–0.89)	0.64 (0.41–1.00)	0.63 (0.40–0.99)
Quartile 4	199	0.40 (0.25–0.63)	0.48 (0.30–0.78)	0.46 (0.28–0.75)
P value for trend		<0.001	0.002	0.002

* Cardiovascular risk factors included in the logistic-regression model were age, sex, smoking status, presence or absence of diabetes, presence or absence of hypertension, and low-density lipoprotein cholesterol. HDL denotes high-density lipoprotein.

Khera AV. *NEJM 2011;364:127-35*

OR de EC según capacidad de Eflujo y otros RFCV

Risk Factor	Odds Ratio (95% CI)	P Value

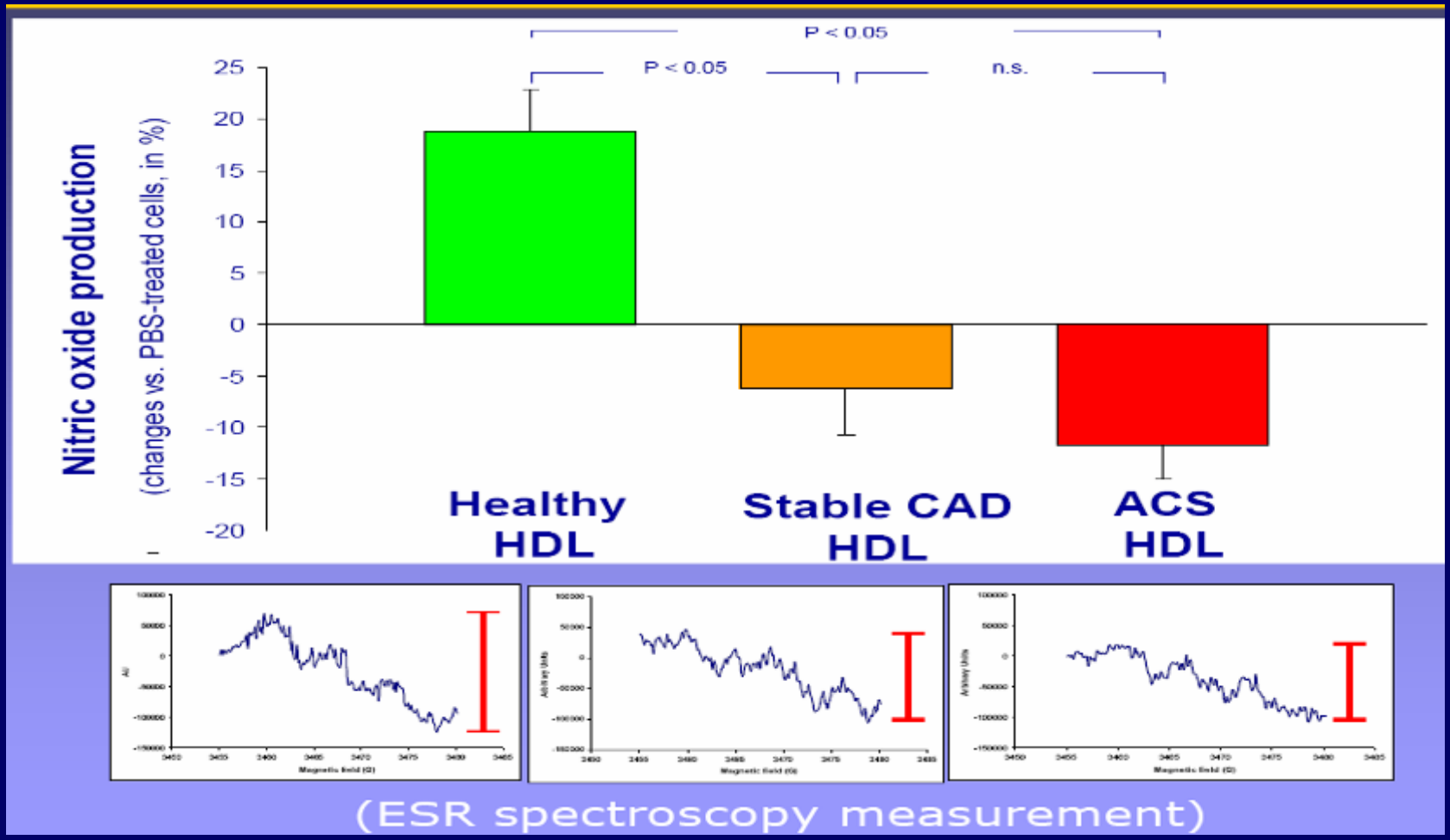
Modificacion capacidad Eflujo por Fármacos

Pharmacologic Intervention	No. of Patients	Percent Change in Cholesterol Efflux Capacity (95% CI)	P Value vs. Baseline	P Value vs. Placebo
Thiazolidinedione				
Pioglitazone	16	11.3 (1.8 to 20.8)	0.02	0.04
Placebo	23	0.0 (−6.2 to 6.1)	0.99	
Statin				
Pravastatin, 40 mg	23	−0.4 (−6.5 to 5.6)	0.88	0.71
Atorvastatin, 10 mg	26	2.7 (−4.8 to 10.2)	0.47	0.81
Atorvastatin, 80 mg	25	−2.5 (−9.1 to 4.1)	0.45	0.38
Placebo	25	−1.1 (−6.5 to 4.2)	0.66	

* Patients treated with pioglitazone received 30 mg per day for 6 weeks, followed by 45 mg per day for an additional 6 weeks. Patients treated with statins received continuous therapy at a fixed dose for 16 weeks.

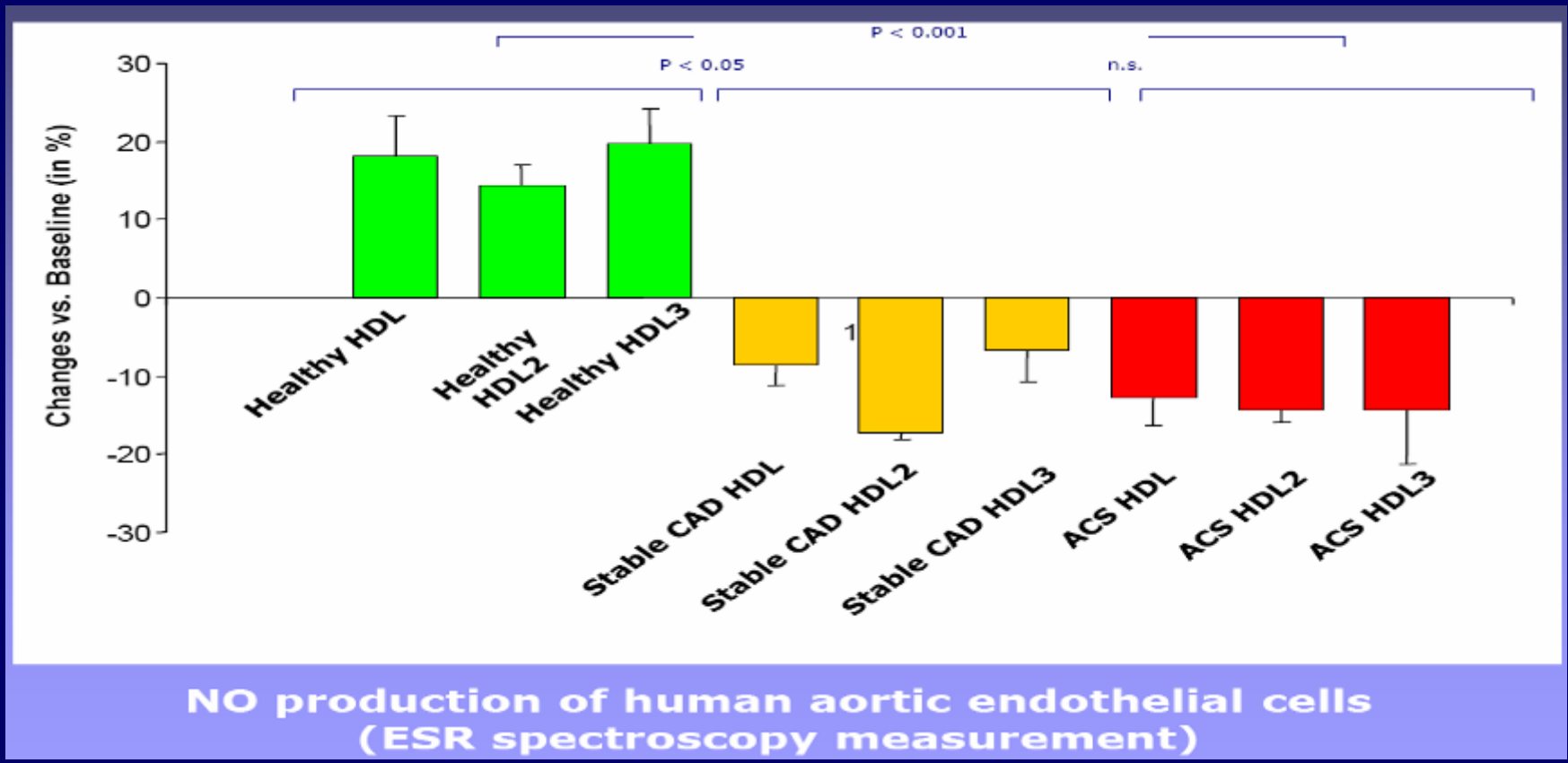
Khera AV. *NEJM 2011;364:127-35*

Efectos de HDL y Producción de NO por Endotelio en pacientes con CC



Besler C. J Clin Invest. 2011;121(7):2693–2708

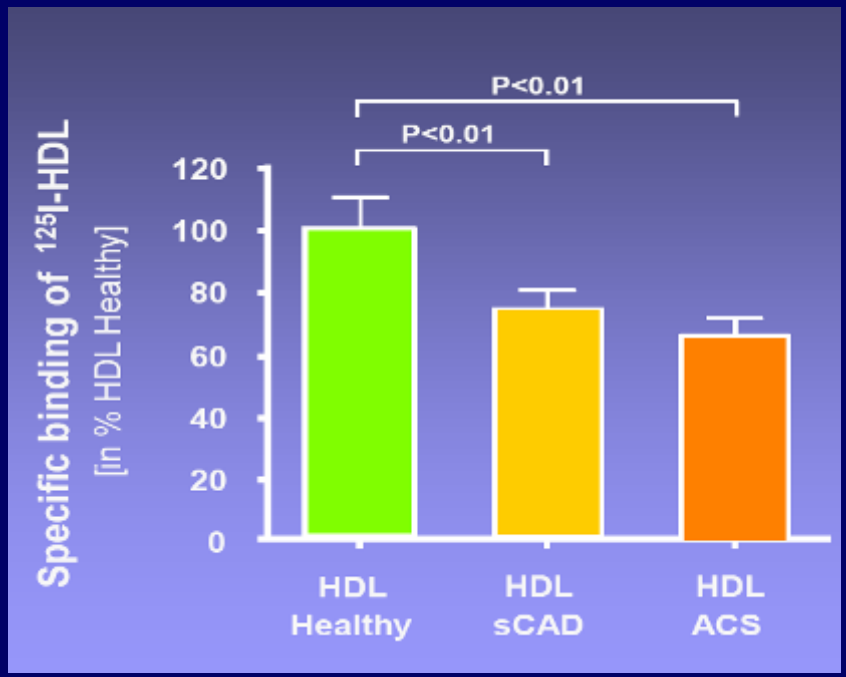
HDL: Efecto en la producción de NO Endotelial



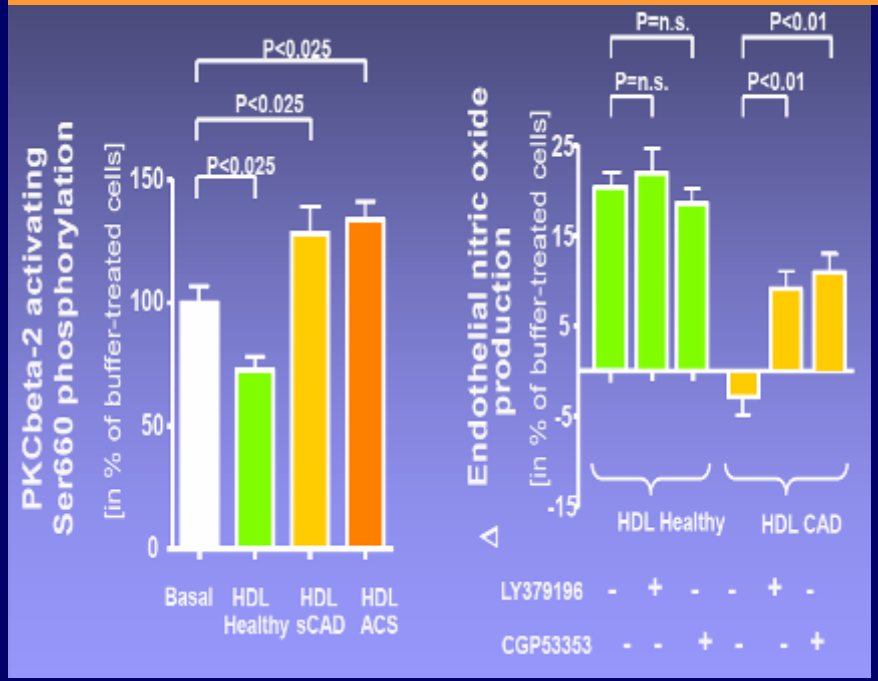
Besler C. J Clin Invest. 2011;121(7):2693–2708

Interacción HDL-Endotelio en EC

Adhesión HDL-Endotelio

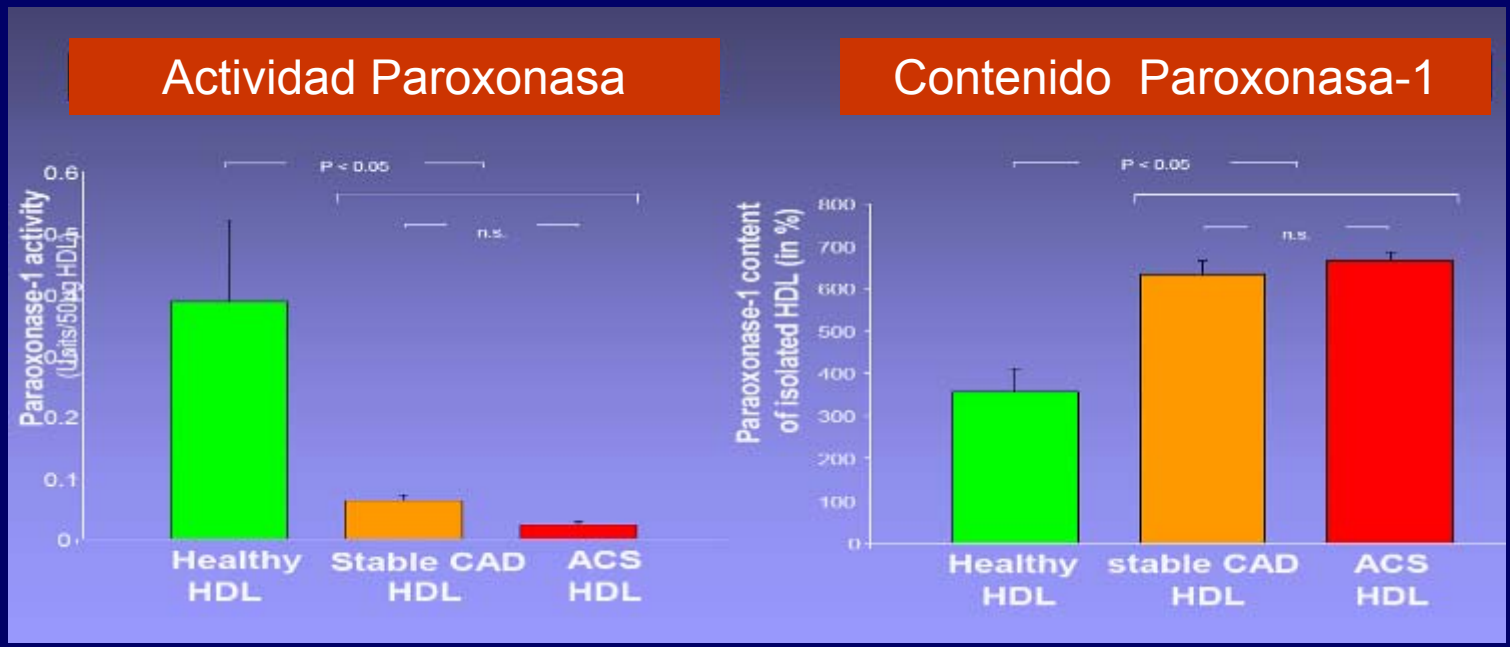


Activación PKbeta2 Endotelial por HDL



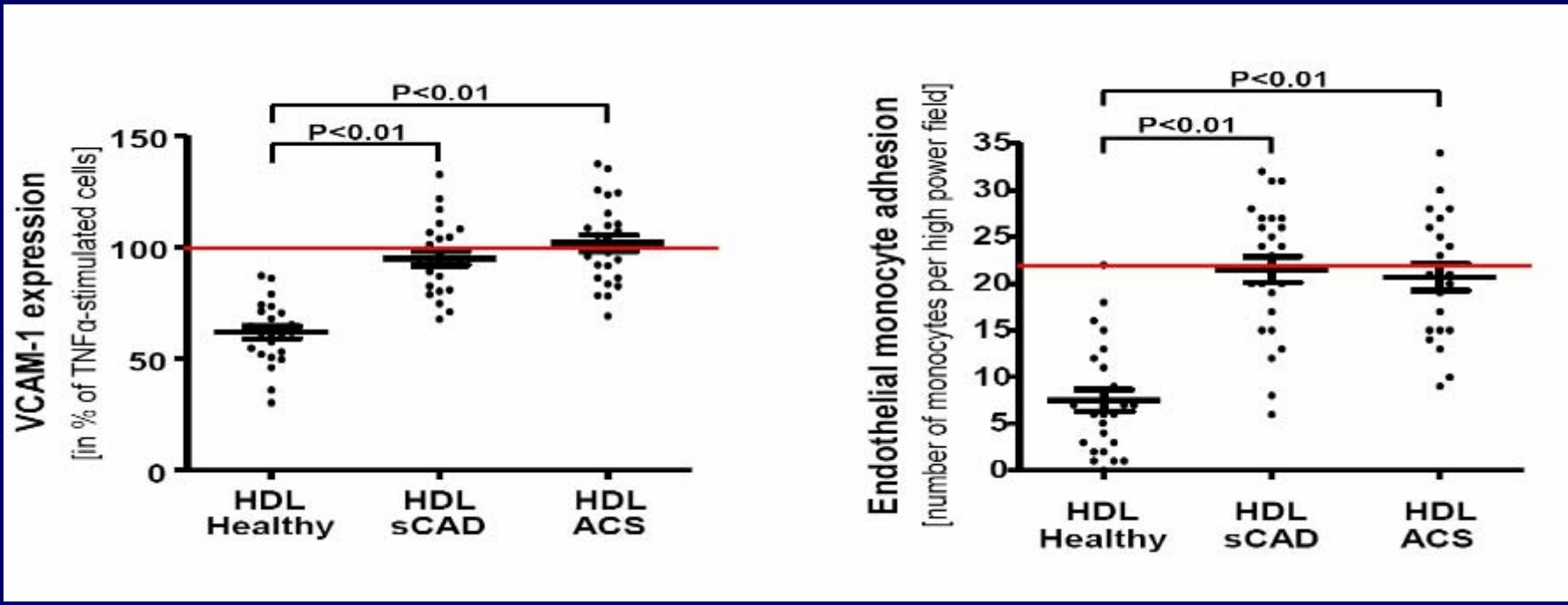
Besler C. J Clin Invest. 2011;121(7):2693–2708

Actividad Paroxonasa de HDL



Besler C. J Clin Invest. 2011;121(7):2693–2708

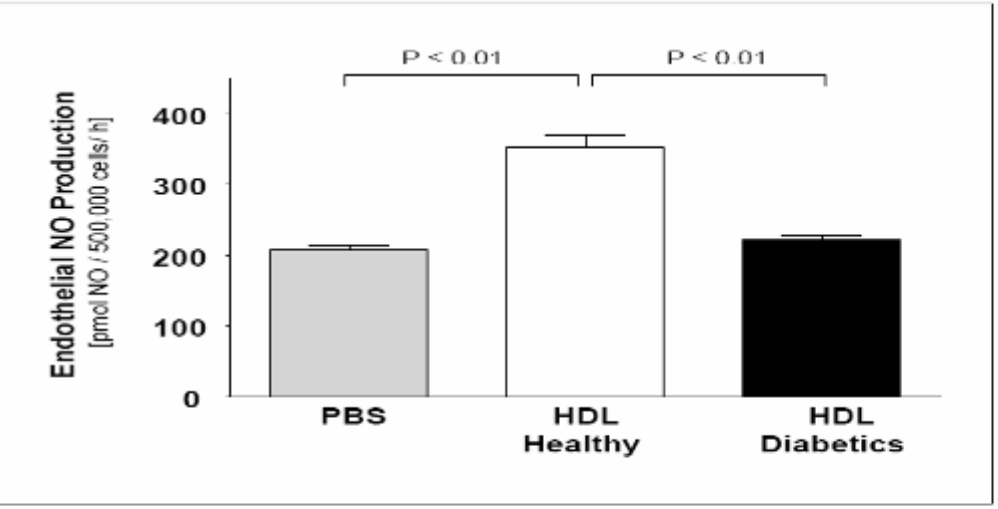
Efectos d HDL en adhesión de monocitos a endotelio mediada por TNFα: Papel de NO sintetasa

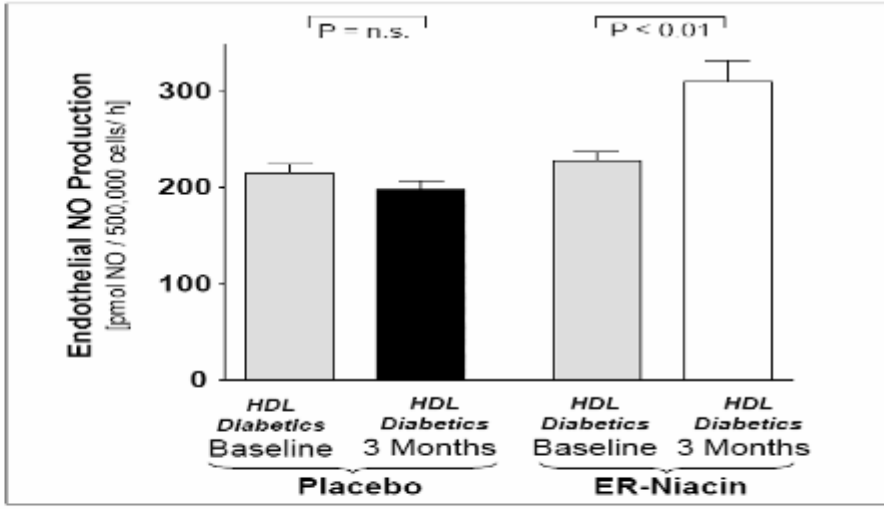


Besler C. J Clin Invest. 2011;121(7):2693–2708

Propiedades Vasoprotectoras de HDL en DM

Endothelial-Vasoprotective Effects of High-Density Lipoprotein Are Impaired in Patients With Type 2 Diabetes Mellitus but Are Improved After Extended-Release Niacin Therapy





Sorrentino SA*, Besler C* et al.; Circulation 2010; 121(1):110-22

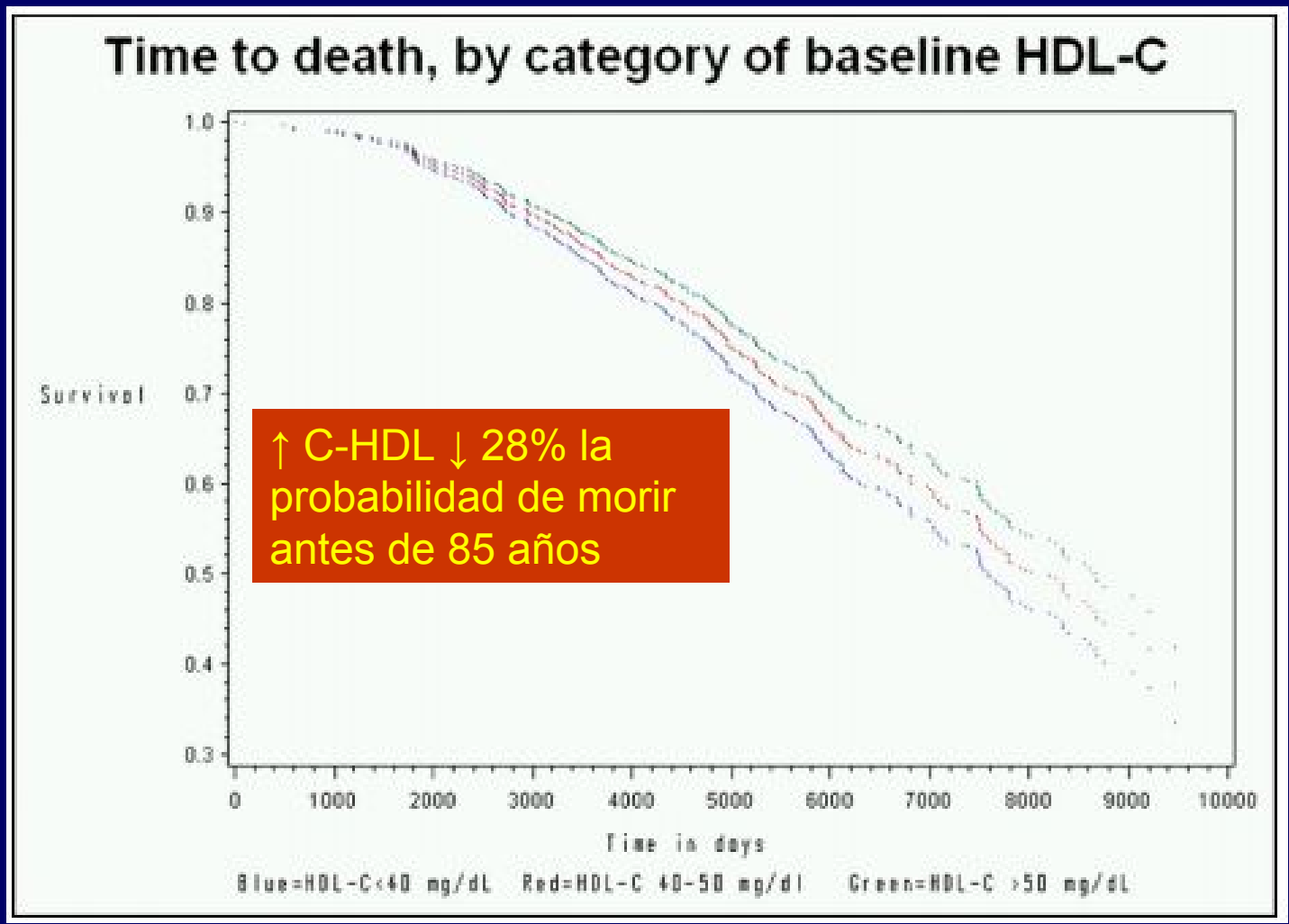
CONCLUSIONES

- Tras la reducción del C-LDL con estatinas, persiste un riesgo residual importante, incluso con valores muy bajos de C-LDL.
- El C-HDL bajo suele ser un componente importante del riesgo residual.
- El valor pronóstico del C-HDL bajo es independiente de los niveles de C-LDL.
- En prevención CV, la elevación del C-HDL tiene un efecto aditivo a la disminución de C-LDL.
- El disponer de fármacos de accíón más potente sobre el C-HDL nos permitirá evaluar mejor su valor en prevención CV.
- La introducción de métodos de estudio de la capacidad funcional de HDL abre un interesante camino de investigación en relación con su acción patogénica y posibles modificaciones terapéuticas

Predicción del Riesgo por edad y 1SD de cada parámetro lipidico: INTERHEART

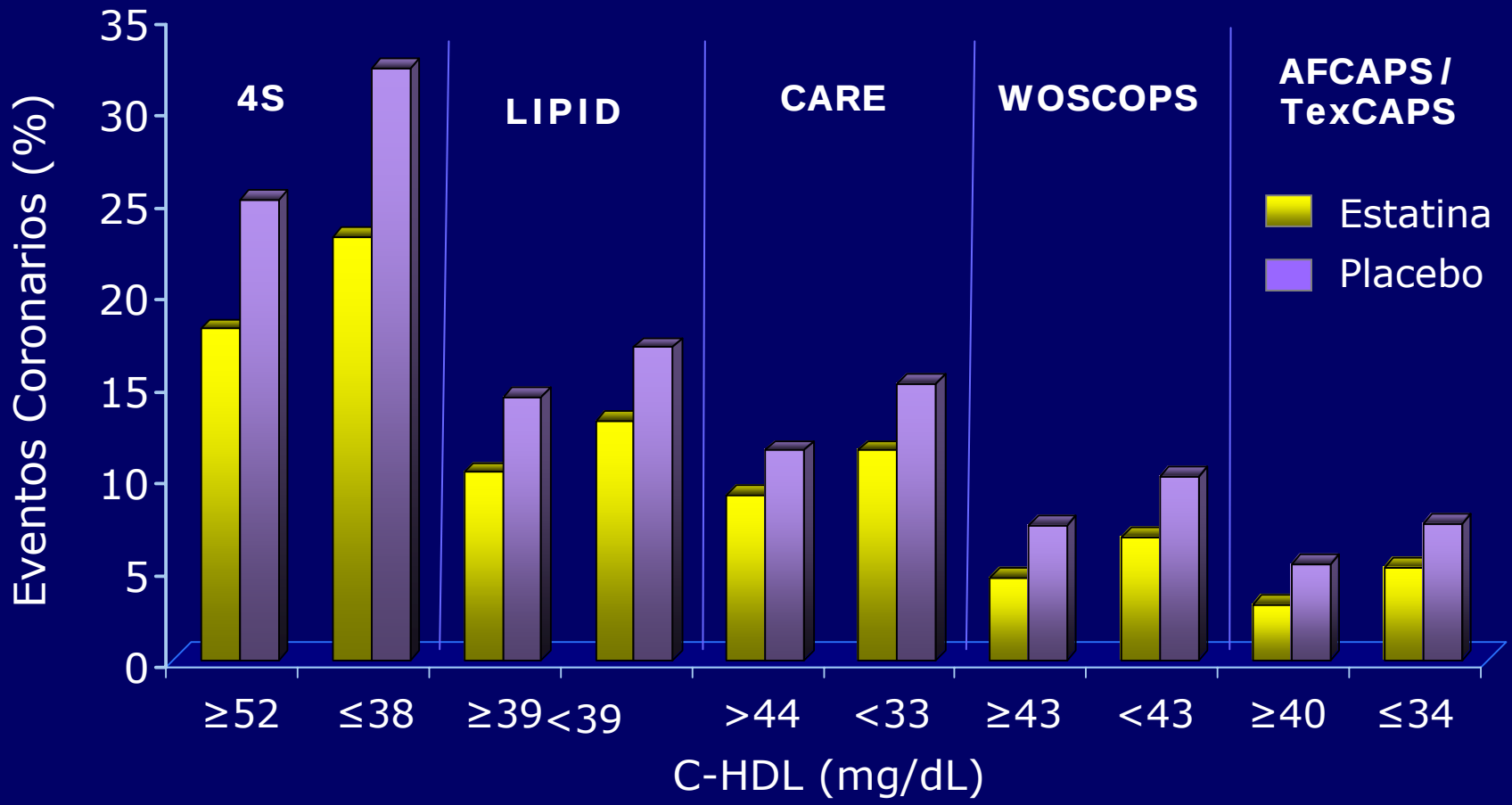
	Apo A_1	Apo B	ApoB/ApoA_1	CT/C-HDL
± 1SD	0,27	0,26	0,32	2,53
Edad				
< 45	0,62 (0,57-0,67)	1.49 (1,39-1,59)	1,76 (1,63-1,89)	1,18 (1.23-1.25)
45-55	0,67 (0,63-0,71)	1,46 (1,38-1,54)	1,70 (1,59-1,81)	1,23 (1,16-1,30)
56-65	0,68 (0,69-0,72)	1,32 (1,24-1,34)	1,59 (1,49-1,70)	1,22 (1,14-1,30)
66-70	0,63 (0,57-0,68)	1,10 (1,01-1,94)	1,52 (1,37-1,69)	**1,08 (0,9-1,107)**
>70	0,77 (0,72-0,83)	**1,06 (0,98-1,14)**	1,24 (1,13-1,35)	**0,98 (0,9-1,07)**

C-HDL y Longevidad



Amer J Cardiol, 2011

Riesgo Coronario y HDL: Estudios con Estatinas

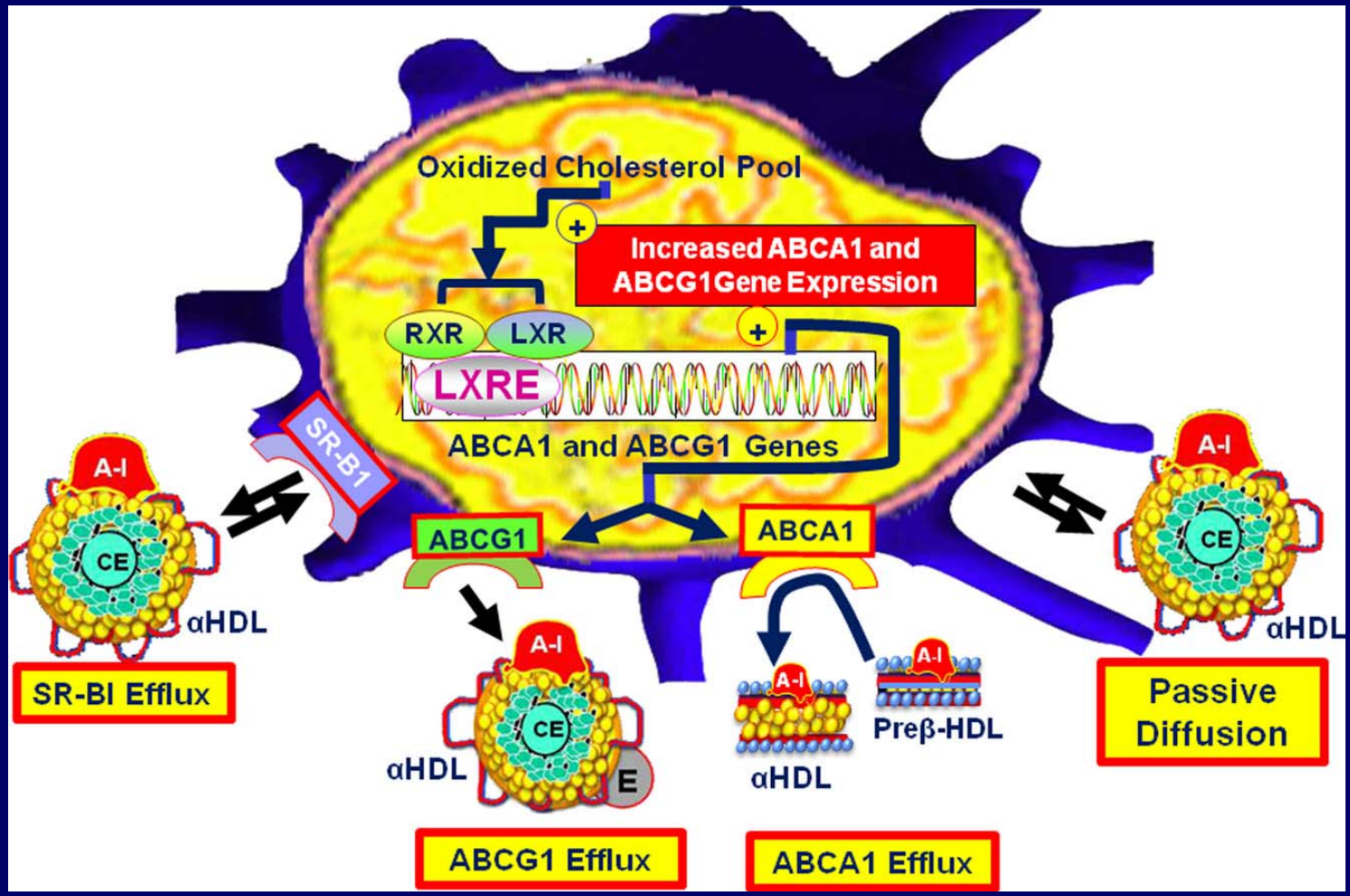


Ballantyne CM. et al. *Prev Cardiol.* 2001;4:65–72

HDL y Aterosclerosis

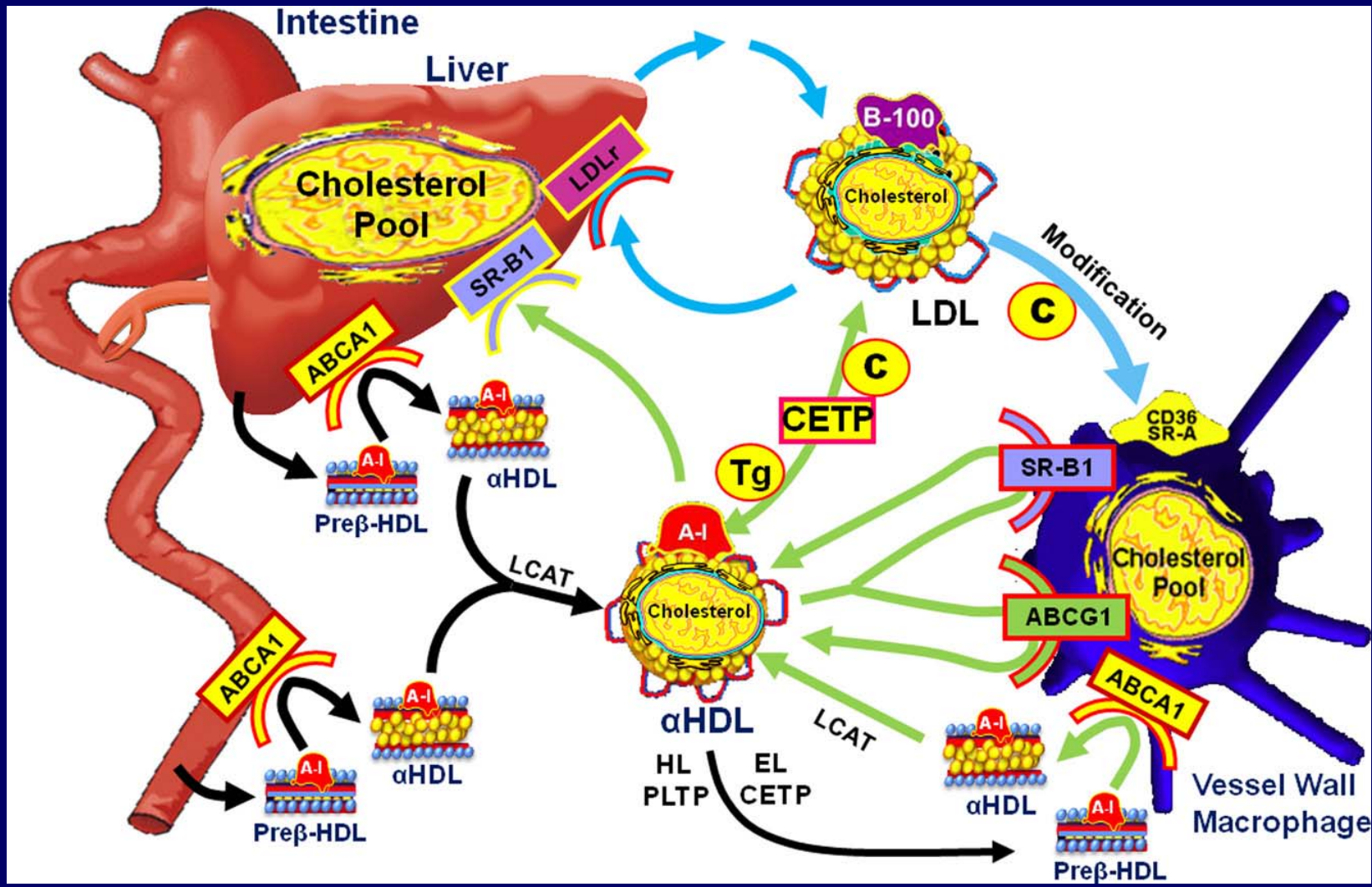
- Transporte Reverso colesterol
- Anti-oxidante
- Anti-inflamatoria
- Anti-trombótica
  - ↑ prostaciclina
- Promueve reactividad vascular
  - ↑ NOS

Eflujo de Colesterol desde Macrófago



Brewer HB. J Clin Endocrinol Metabo 2011;96:1246-57

Transporte Centípetro del Colesterol



Brewer HB. J Clin Endocrinol Metabo 2011;96:1246-57

Objetivo C-HDL en las Guías Clínicas

Guia (año)

Objetivo Recomendado

Table 6 Recommendations for lipid analyses for characterization of dyslipidaemias before treatment

Recommendations	Class[a]	Level[b]
LDL-C is recommended to be used as the primary lipid analysis.	I	C
TG adds information to risk and is indicated for diagnosis and choice of treatment.	I	C
HDL-C is recommended to be analysed before initiation of treatment.	I	C
Non-HDL-C should be recommended for further characterization of combined hyperlipidaemias and dyslipidaemia in diabetes, the MetS or CKD.	IIa	C
Apo B should be recommended for further characterization of combined hyperlipidaemias and dyslipidaemia in diabetes, the MetS or CKD.	IIa	C
Lp(a) should be recommended in selected cases at high risk and in subjects with a family history of premature CVD.	IIa	C
TC may be considered but is usually not enough for the characterization of dyslipidaemia before initiation of treatment.	IIb	C

[a]Class of recommendation.
[b]Level of evidence.
Apo = apolipoprotein; CKD = chronic kidney disease; CVD = cardiovascular

Table 7 Recommendations for lipid analyses as treatment target in the prevention of CVD

Recommendations	Class[a]	Level[b]	Ref[c]
LDL-C is recommended as target for treatment.	I	A	15, 16, 17
TC should be considered as treatment target if other analyses are not available.	IIa	A	5, 15
TG should be analysed during the treatment of dyslipidaemias with high TG levels.	IIa	B	52
Non-HDL-C should be considered as a secondary target in combined hyperlipidaemias, diabetes, the MetS or CKD.	IIa	B	48
Apo B should be considered as a secondary treatment target.	IIa	B	48, 53
HDL-C is not recommended as a target for treatment.	III	C	-
The ratios apo B/apo A1 and non-HDL-C/HDL-C are not recommended as targets for treatment.	III	C	-

Eur Heart J 2011;32:1769-1818

Reduction in the 5-year incidence of cardiovascular events per 1.0 mmol/L reduction in LDL-C: a meta-analysis of 14 randomized trials of statins

Endpoint	Events		RR (95% CI)
	Treatment (n=45,054)	Control (n=45,002)	
Any death, %	8.5	9.7	0.88 (0.84, 0.91)
Coronary heart disease death, %	3.4	4.4	0.81 (0.76, 0.85)
Nonfatal myocardial infarction, %	4.4	6.2	0.74 (0.70, 0.79)
Coronary revascularization, %	5.8	7.6	0.76 (0.73, 0.80)
Any stroke, %	3.0	3.7	0.83 (0.78, 0.88)

CI=confidence intervals; LDL-C=low-density lipoprotein cholesterol; RR=rate ratio.

Fabbri G, Maggioni P. Adv Ther 2009; 26(5): 469-87

cHDL y ECV en el anciano

- **cHDL bajo es un factor de riesgo para mortalidad por ECC y ECV en ancianos.**
  Arch Intern Med 2003;163:1549-54.

- **cHDL como factor de riesgo independiente para ECC y ECV.**
  Stroke 2003;34:863-8.

- **cHDL factor de riesgo independiente para cualquier subtipo de ECV.**
  Arch Gerontol Geriatr 2003;37:51-62.

- **La elevación del cHDL se relaciona con longevidad.**
  Clin Wochenschr 1991;31:780-5.

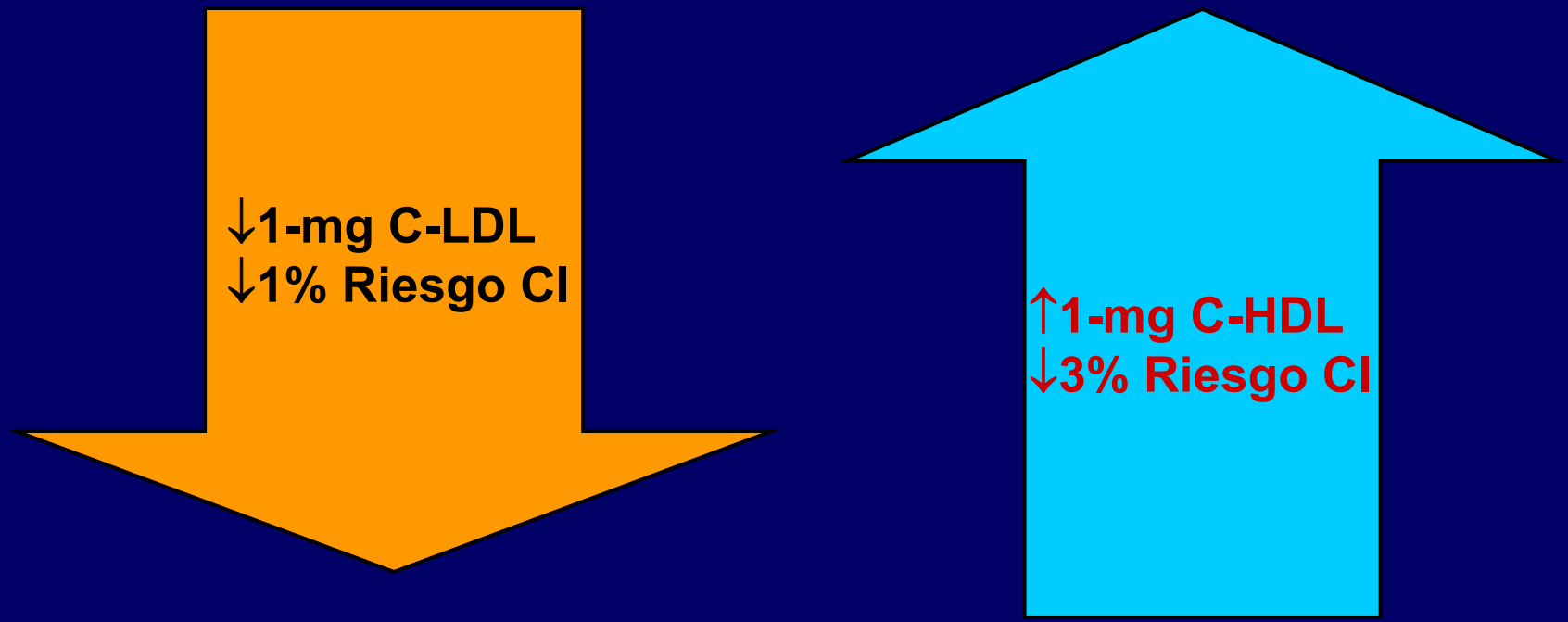
LDL pequeñas y densas en pacientes con DM tipo 2. Comparación entre normo- e hipertrigliceridémicos

	TOTAL (n = 122)	TG < 150 mg/dl (n = 74)	TG > 150 mg/dl (n = 48)
C-sLDL	8.59 ± 10.34	4.34 ± 4.98	16.02 ± 12.89 *
% C-sLDL	9.99 ± 10.59	5.64 ± 6.89	17.62 ± 11.66 *

* p < 0.000 vs TG < 150 mg/dl

T. González Alegre et al. Atherosclerosis Sup 2004; 5(1): 121

Relación entre C-LDL y C-HDL y Riesgo CI



Third Report of the NCEP Expert Panel. NIH Publication No. 01-3670. 2001.
http://hin.nhlbi.nih.gov/ncep_slds/menu.htm