Tratamiento de la Dislipemia Mixta a la luz de las nuevas guías Europeas y los nuevos ensayos clínicos

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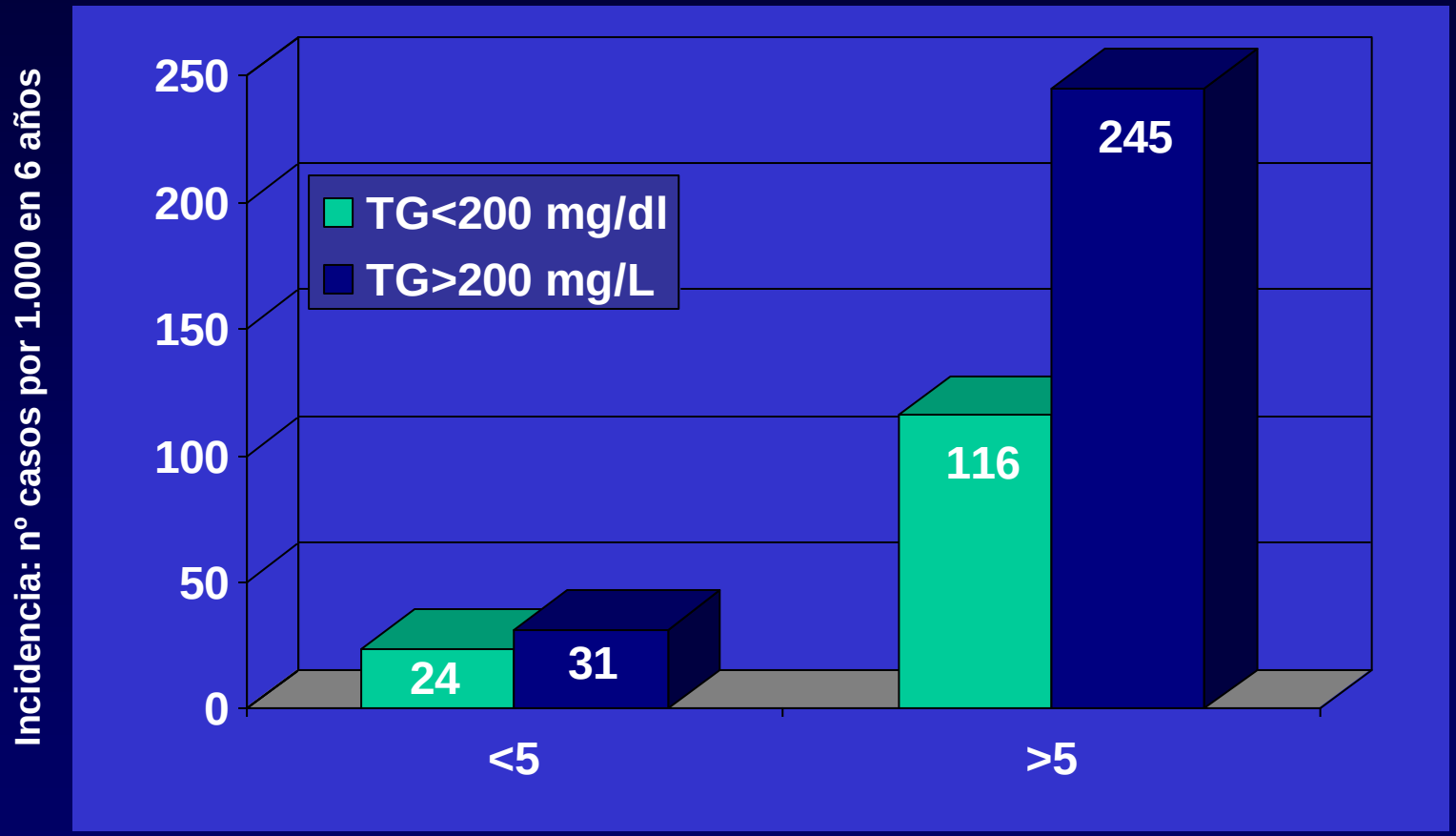
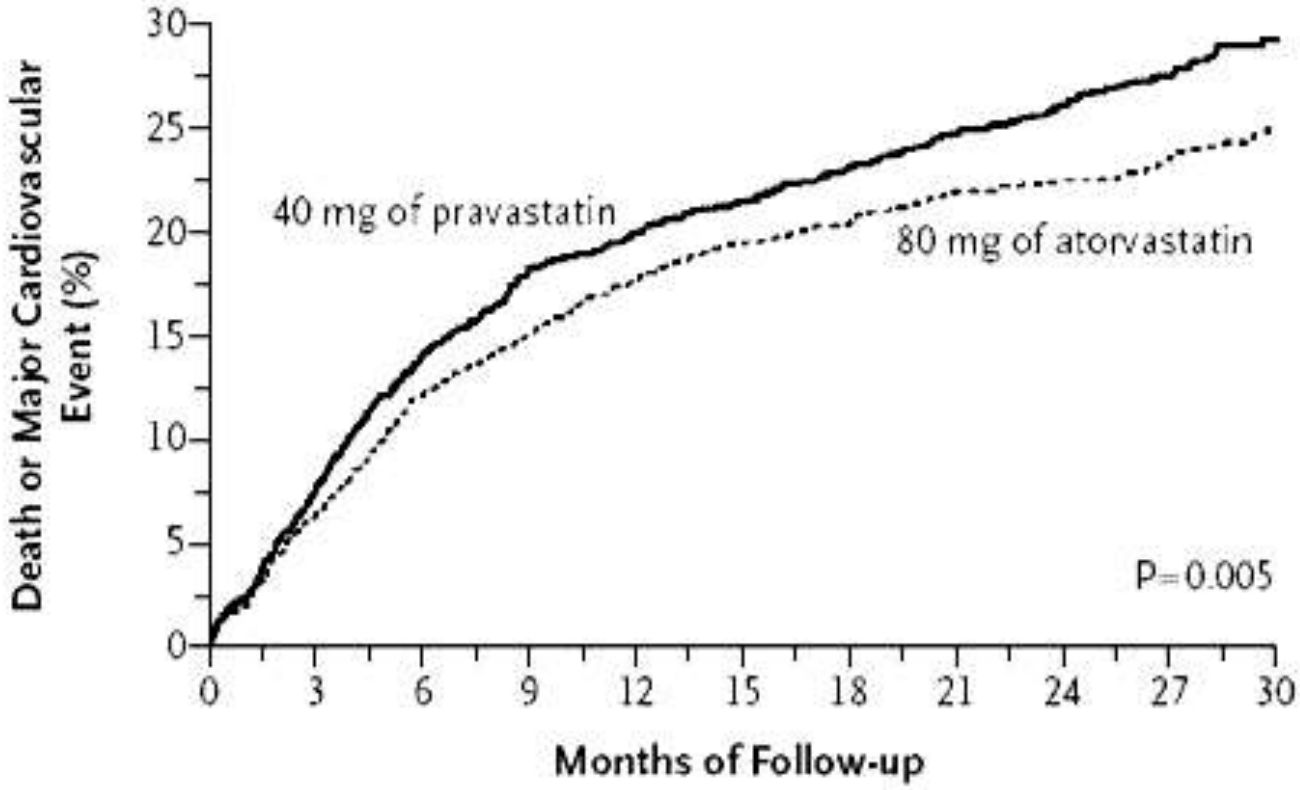
Instituto Aragonès de Ciencias de la Salud

Riesgo coronario según el cociente LDL/HDL y la concentración de TG Estudio PROCAM



Assmann G. MMV Medizin Verlag, Munich, 1993

Estudio PROVE IT



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.

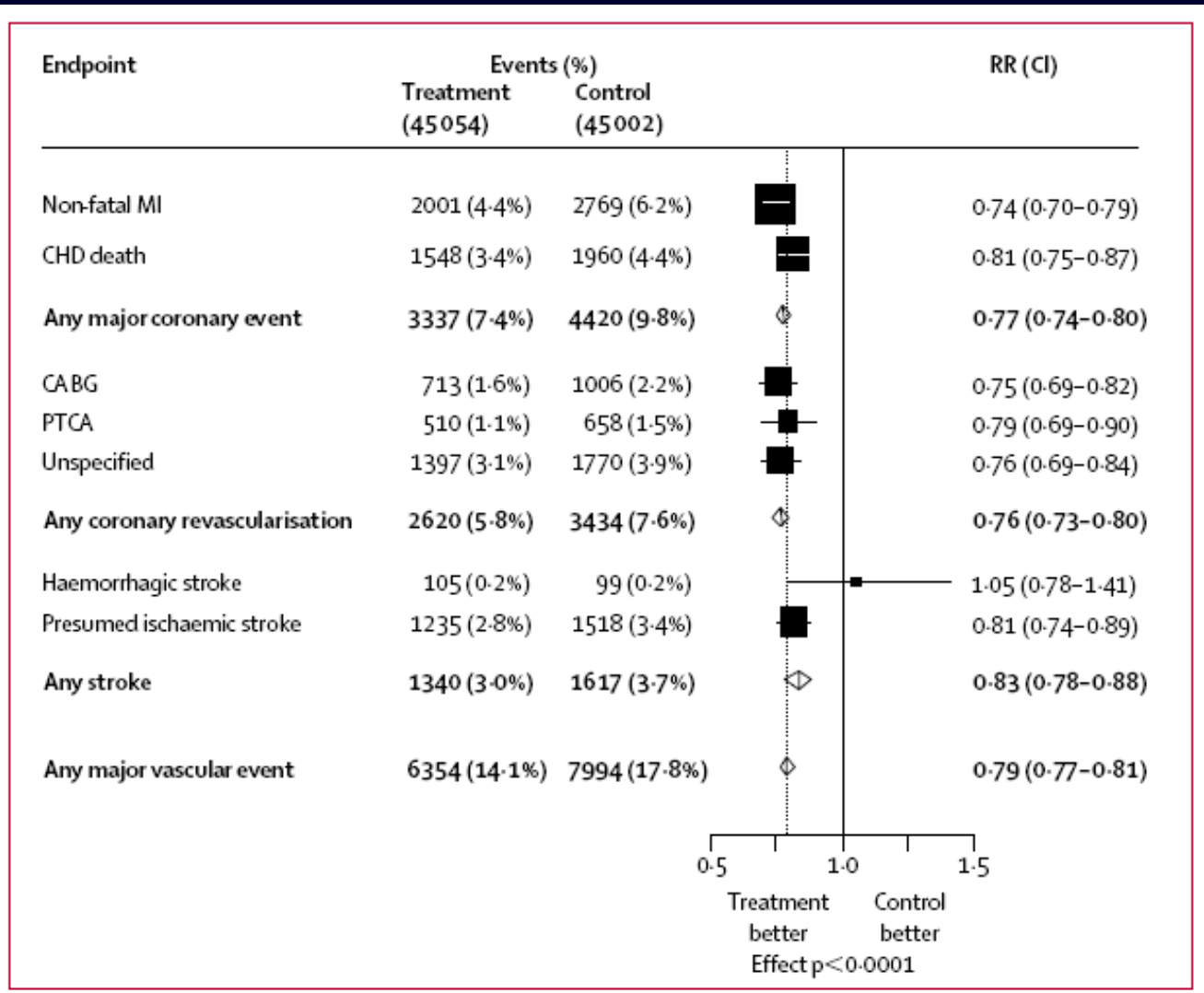
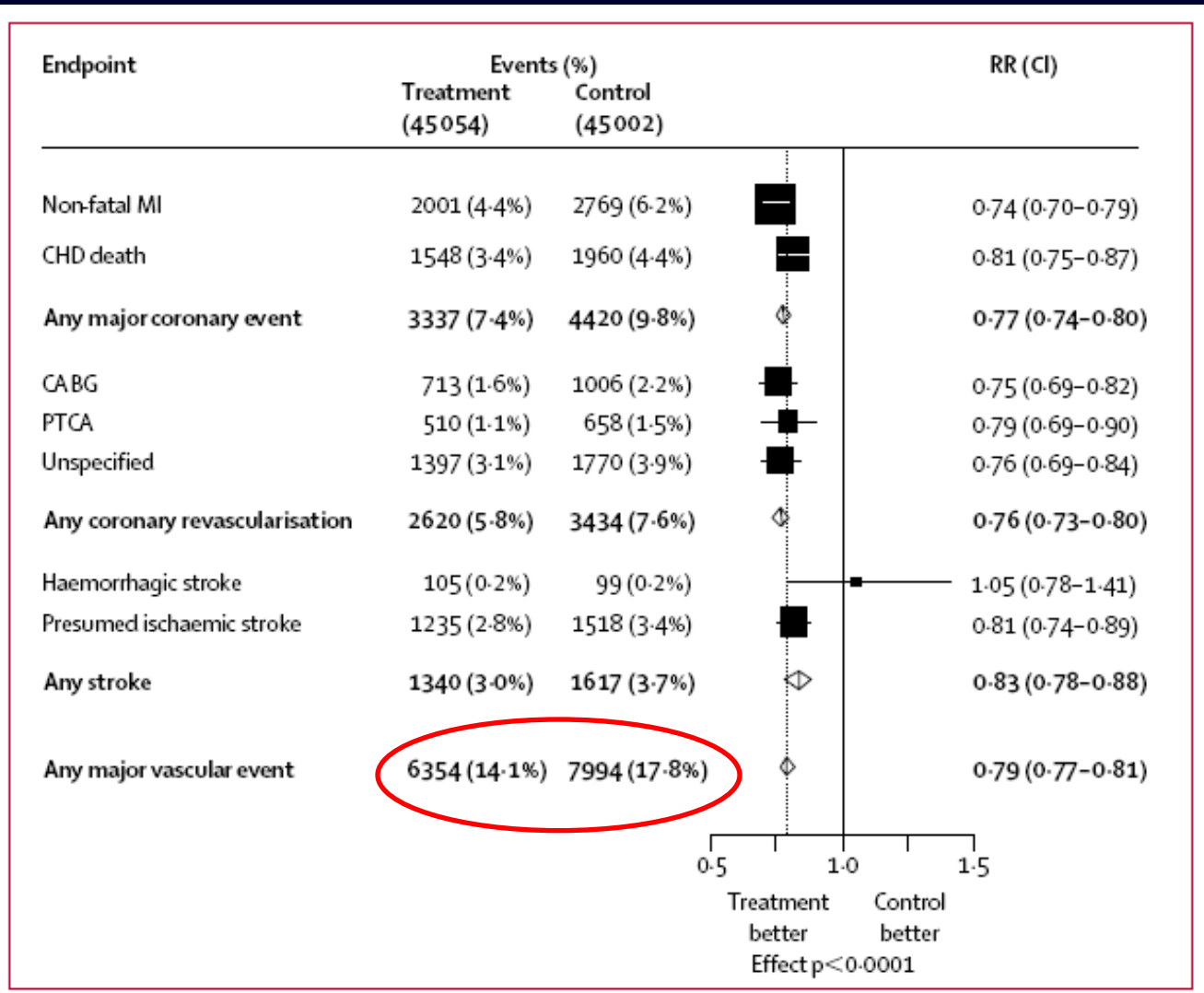


Figure 2: **Proportional effects on major vascular events per mmol/L LDL cholesterol reduction**
Symbols and conventions as in figure 1. Broken vertical line indicates overall RR for any type of major vascular event. CABG=coronary artery bypass graft. PTCA=percutaneous transluminal coronary angioplasty. 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



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Cholesterol Treatment Trialists' (CTT) Collaborators*

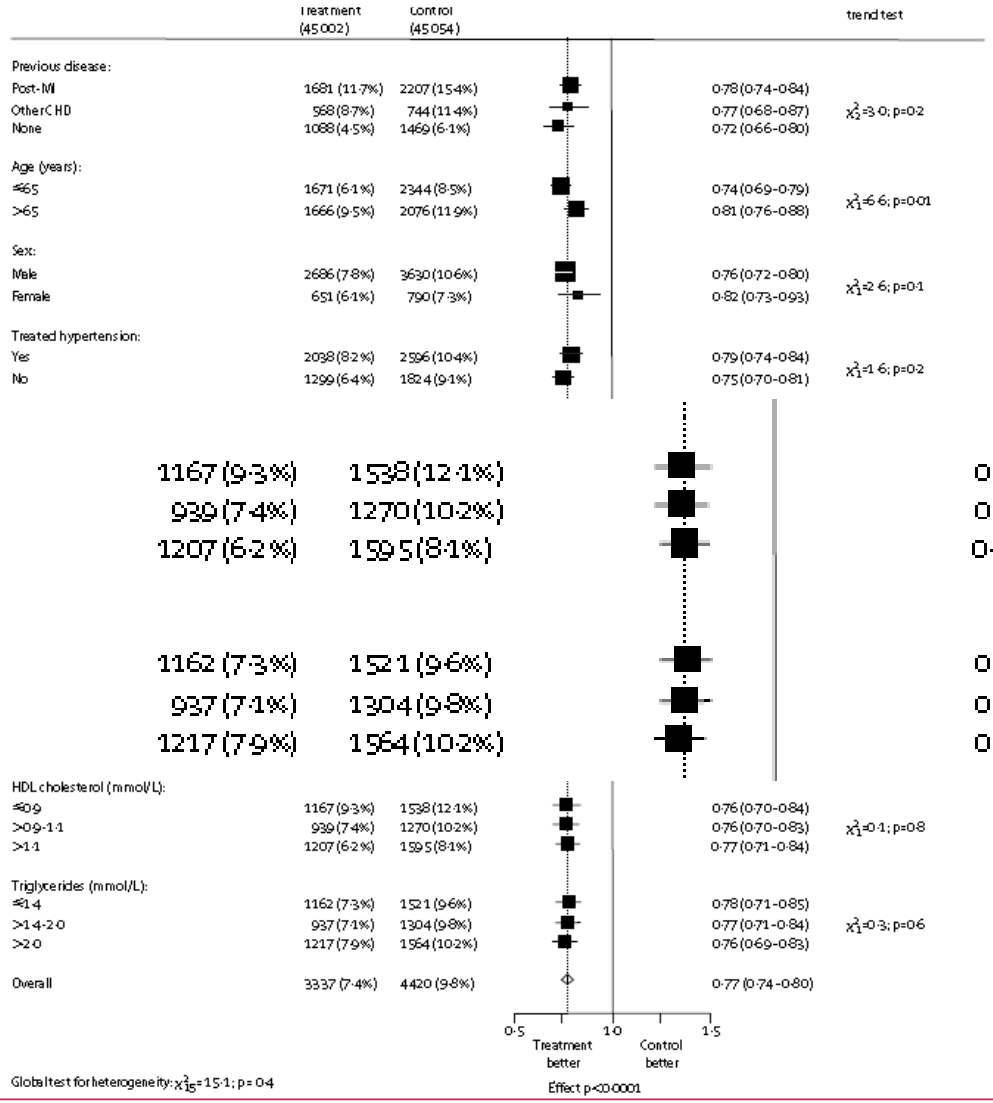
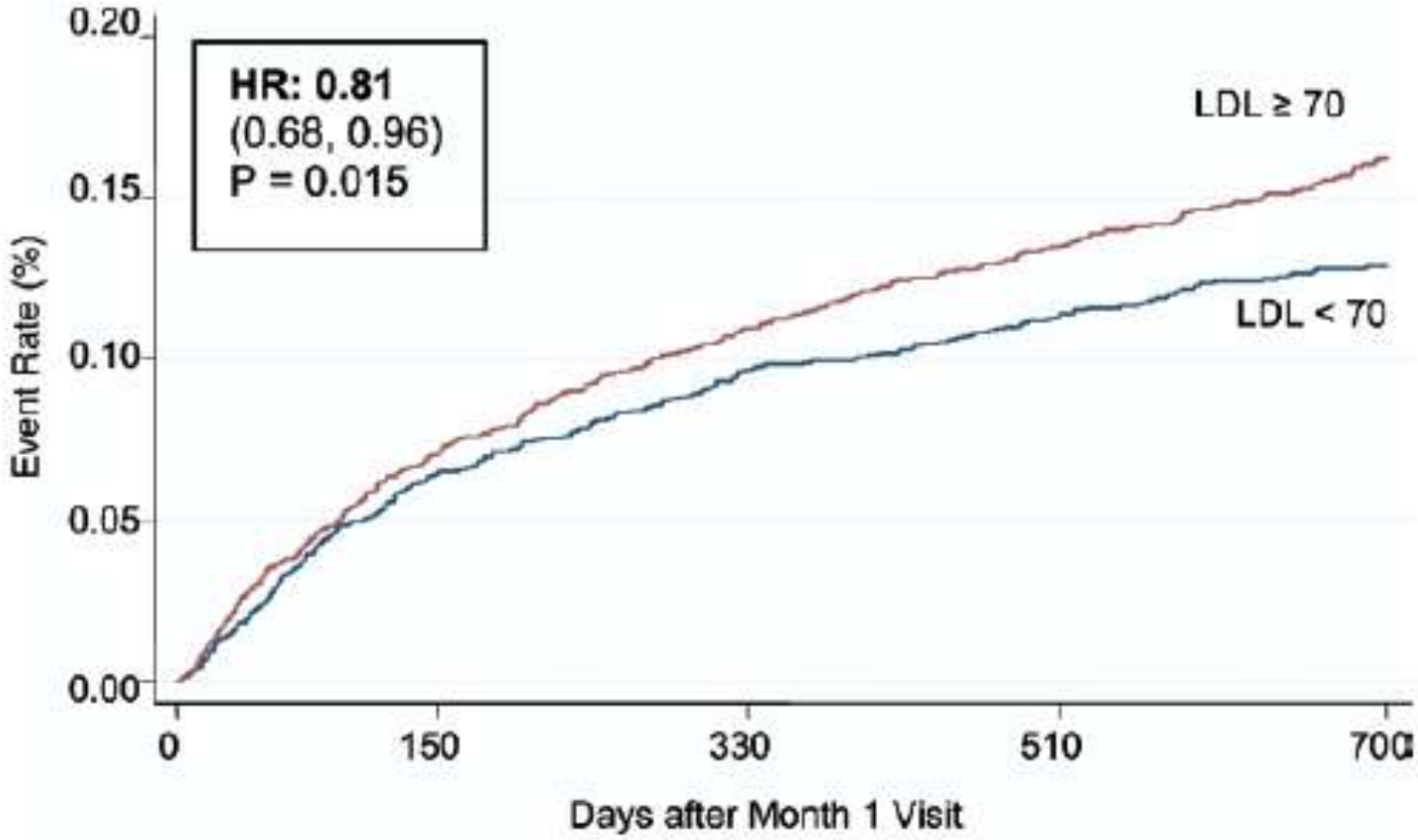


Figure 5: Proportional effects on major coronary events per mmol/L LDL cholesterol reduction subdivided by baseline prognostic factors
Symbols and conventions as in figure 1.

Lancet 2005; 366: 1267–78

Estudio PROVE IT

Eventos coronarios de acuerdo a cLDL durante el ensayo

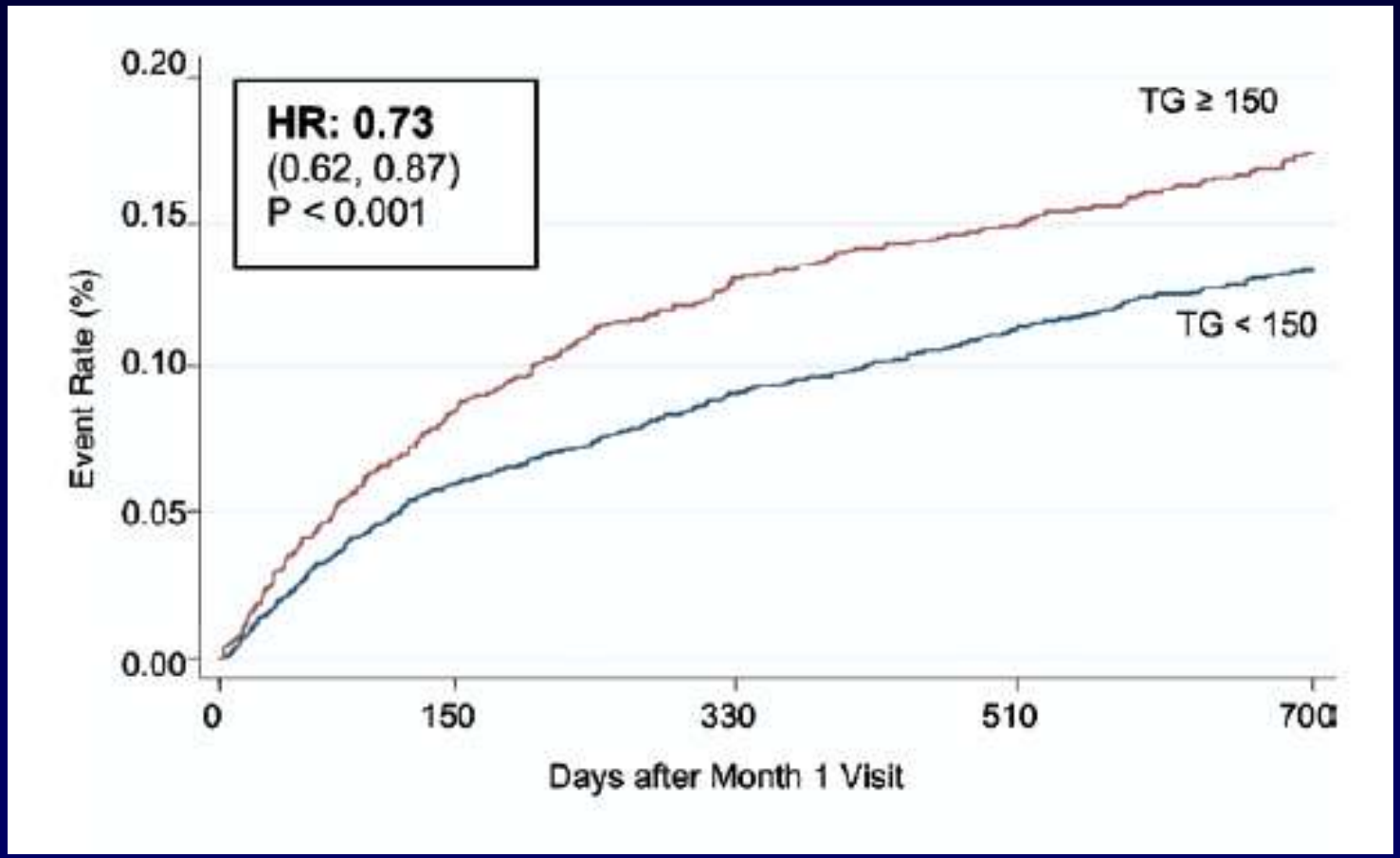


JACC Vol. 51, No. 7, 2008
February 19, 2008:724–30

Miller *et al.*
Impact of Triglycerides After ACS

Estudio PROVE IT

Eventos coronarios de acuerdo a triglicéridos durante el ensayo



JACC Vol. 51, No. 7, 2008
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Miller *et al.*
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Estudio PROVE IT

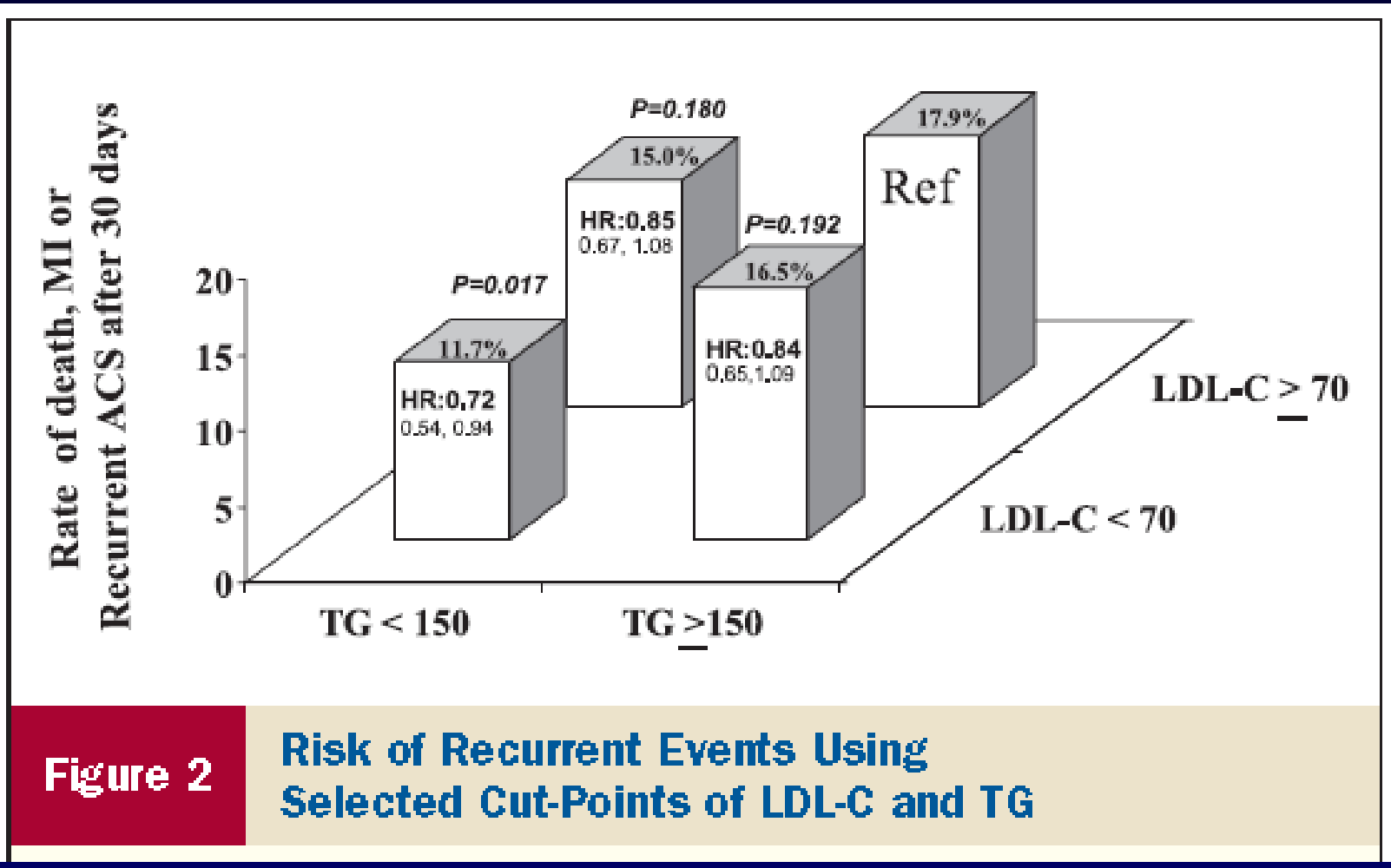


Figure 2 **Risk of Recurrent Events Using Selected Cut-Points of LDL-C and TG**

JACC Vol. 51, No. 7, 2008
February 19, 2008:724–30

Estudios IDEAL y TNT

Table 1. On-Treatment Values of Lipids, Apolipoproteins, and Their Ratios in Both Treatment Groups of TNT and IDEAL

	TNT		IDEAL	
	Atorvastatin 10 mg (n=4665)	Atorvastatin 80 mg (n=4654)	Simvastatin 20–40 mg (n=4369)	Atorvastatin 80 mg (n=4330)
Total cholesterol, mg/dL*	178.1 (28.5)	147.5 (29.5)	176.1 (29.9)	147.9 (34.1)
LDL cholesterol, mg/dL	101.0 (22.3)	75.3 (22.6)	102.2 (25.2)	79.5 (28.0)
HDL cholesterol, mg/dL	46.2 (10.9)	46.1 (11.2)	47.1 (12.7)	45.7 (12.5)
Non-HDL cholesterol, mg/dL†	131.9 (27.9)	101.4 (28.0)	129.0 (29.5)	102.2 (32.2)
Triglycerides, mg/dL	156.0 (86.5)	131.3 (76.8)	139.4 (83.8)	116.6 (66.3)
Apolipoprotein B, mg/dL	113 (22)	91 (21)	107 (27)	84 (28)
Total/HDL cholesterol	4.0 (1.0)	3.3 (0.9)	4.0 (1.2)	3.4 (1.1)
LDL/HDL cholesterol	2.3 (0.7)	1.7 (0.6)	2.3 (0.8)	1.9 (0.8)
Apolipoprotein B/A-I	0.8 (0.2)	0.7 (0.2)	0.8 (0.2)	0.6 (0.2)

On-Statin Prediction of Cardiovascular Events

Circulation **June 10, 2008**

Estudios IDEAL y TNT

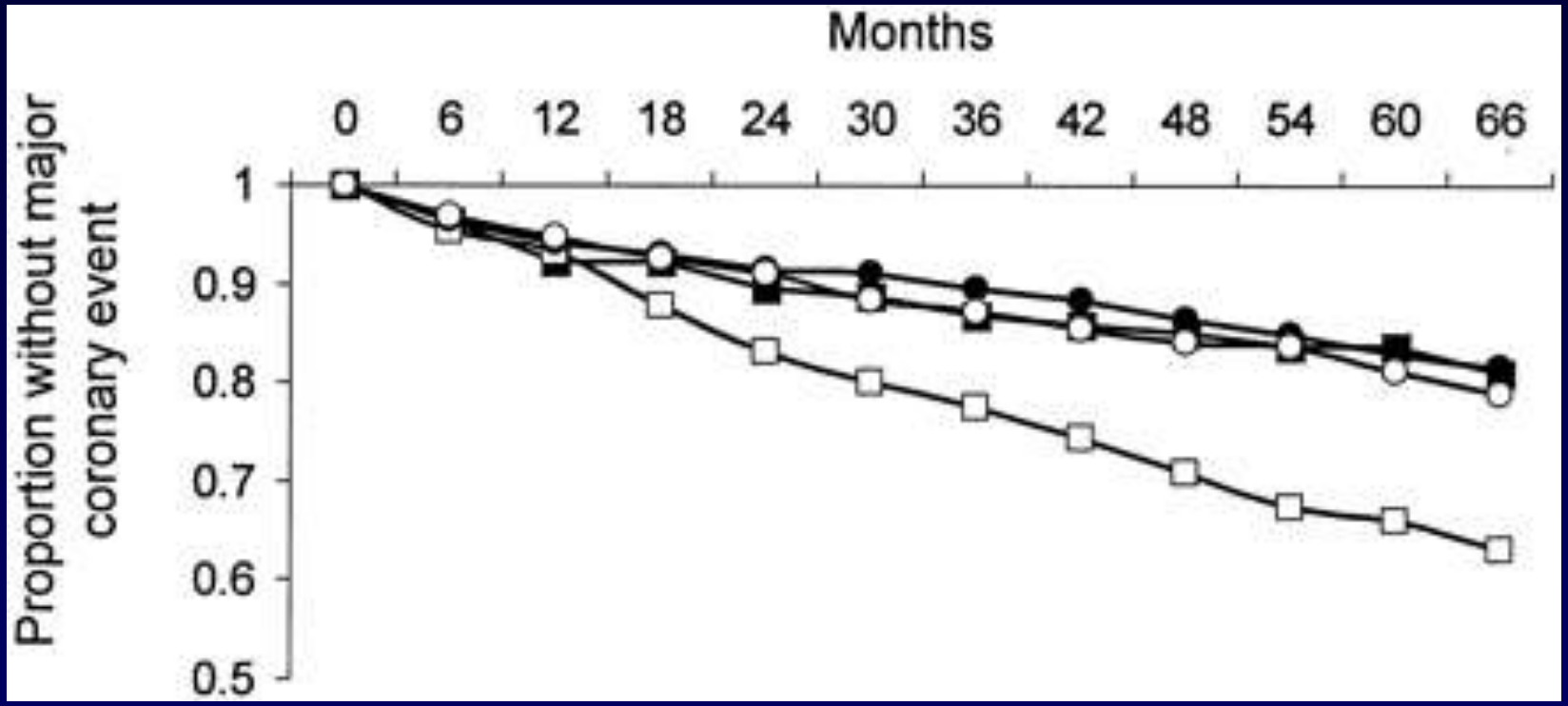
Table 3. Direct Pairwise Comparisons of the Relationships With MCVEs for On-Treatment Levels of LDL Cholesterol, Non-HDL Cholesterol, Apolipoprotein B, or Their Ratios in TNT and IDEAL

	Hazard Ratio*	95% CI	*P*
Comparisons of single measures			
LDL cholesterol	0.90	0.82–0.99	0.04
Non-HDL cholesterol†	1.31	1.19–1.44	<0.001
LDL cholesterol	0.95	0.87–1.05	0.33
Apolipoprotein B	1.24	1.13–1.36	<0.001
Non-HDL cholesterol†	1.14	1.00–1.30	0.06
Apolipoprotein B	1.05	0.92–1.20	0.47

On-Statin Prediction of Cardiovascular Events

Circulation **June 10, 2008**

Supervivencia en el estudio 4S de acuerdo a la cifra basal de HDL-c y triglicéridos



Blanco: placebo. Negro: simvastatina.
Cuadrado: cuartil bajo de c-HDL (<39 mg/dl) y alto de TG (> 159 mg/dl
Círculo: cuartil alto de c-HDL (>52 mg/dl) y bajo de TG (<98 mg/dl)

Ballantyne CM, et al. Circulation 2001;104:3046-3051

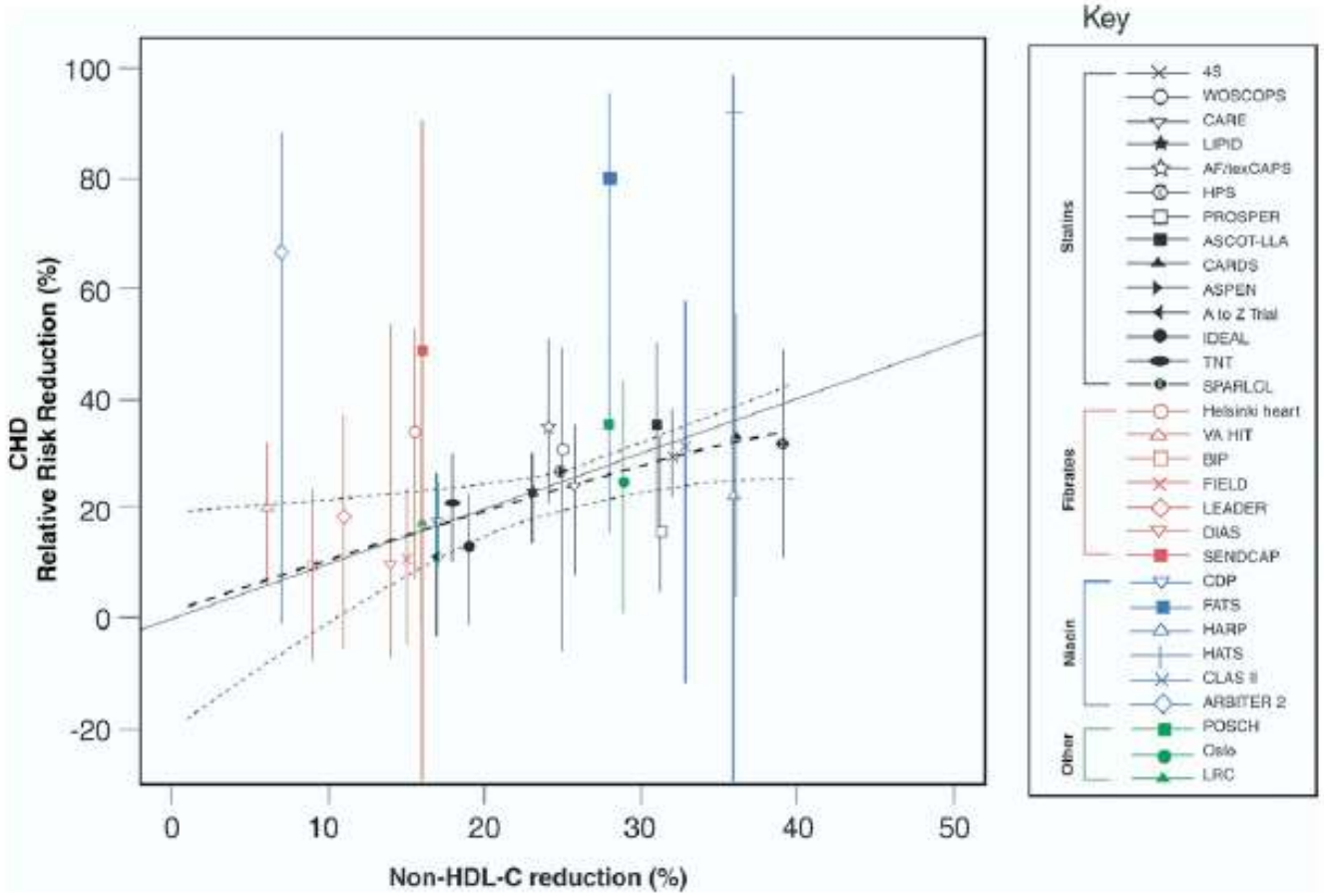


Figure 1 Change in Relative Risk of CHD Event

Robinson *et al.*
Non–HDL-C Meta-Analysis

JACC Vol. 53, No. 4, 2009
January 27, 2009:316–22

Atherosclerosis 2175 (2011) S1–S44

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Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

Review

ESC/EAS Guidelines for the management of dyslipidaemias

The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS)☆,☆☆

European Heart Journal Advance Access published May 3, 2012

European Heart Journal
doi:10.1093/eurheartj/ehs092

JOINT ESC GUIDELINES

European Guidelines on cardiovascular disease prevention in clinical practice (version 2012)

The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts)

Recommendations for treatment targets for LDL-C.

Recommendations	Class[a]	Level[b]	Ref[c]
In patients at VERY HIGH CV risk (established CVD, type 2 diabetes, type 1 diabetes with target organ damage, moderate to severe CKD or a SCORE level ≥10%) the LDL-C goal is <1.8 mmol/L (less than ~70 mg/dL) and/or ≥50% LDL-C reduction when target level cannot be reached.	I	A	15, 32, 33
In patients at HIGH CV risk (markedly elevated single risk factors, a SCORE level ≥5 to <10%) an LDL-C goal <2.5 mmol/L (less than ~100 mg/dL) should be considered.	IIa	A	15, 16, 17
In subjects at MODERATE risk (SCORE level >1 to ≤5%) an LDL-C goal <3.0 mmol/L (less than ~115 mg/dL) should be considered.	IIa	C	-

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

Atherosclerosis 217S (2011) S1–S44

Table 7
Recommendations for lipid analyses as treatment target in the prevention of CVD [53].

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	-

ESC/EAS Guidelines for the management of dyslipidaemias

The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS)☆,☆☆

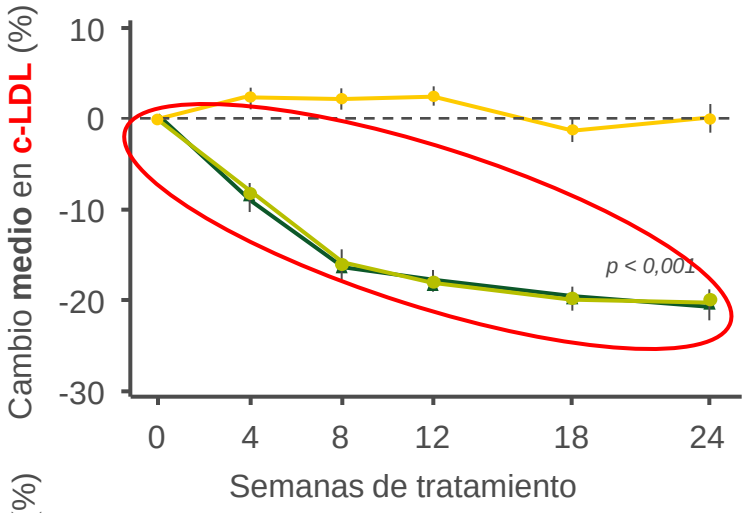
Summary of the efficacy of drug combinations for the management of mixed dyslipidaemias.

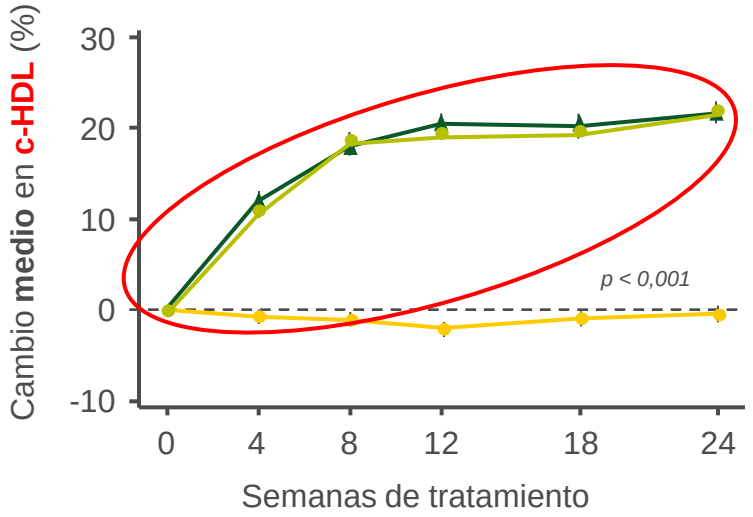
• In combined dyslipidaemia an increase of HDL-C and a decrease of TG, on top of the LDL-C reduction that can be achieved with a statin, may be considered. Therefore a combination of statin with nicotinic acid can be considered, but the adverse effect of flushing may affect compliance.
• A combination of statins with fibrates can also be considered while monitoring for myopathy, but the combination with gemfibrozil should be avoided.
• If TG are not controlled by statins or fibrates, prescription of *n*-3 fatty acids may be considered to decrease TG further, and these combinations are safe and well tolerated.

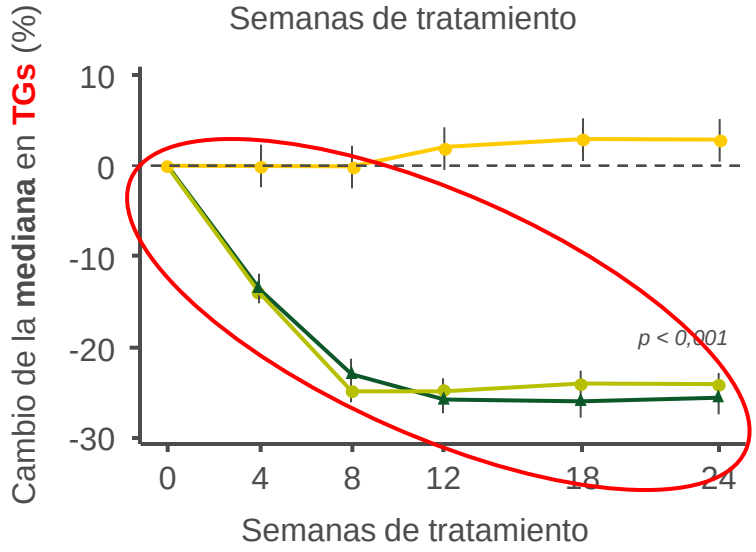
HDL-C: high-density lipoprotein-cholesterol; LDL-C: low-density lipoprotein-cholesterol; TG: triglyceride.

Atherosclerosis 217S (2011) S1–S44

Laropiprant no altera el efecto del Ac. Nicotínico sobre los lípidos







Placebo (n = 257)
Niacina LP (n = 434)
NLP/LRPT (n = 696)

PN: 020

*Diferencia porcentual entre grupos de tratamientos desde nivel basal Maccubbin DL et al. *Int J Clin Pract*. 2008;62:1959–1970.

Estudio lípidos/rubefacción: Eficacia sobre el resto de los parámetros lipídicos (Semanas 12–24)

Parámetro	Placebo	Niacina LP	Niacina LP /Laropiprant*
C Total	–0,6% (n = 257)	–9 % (n = 434)	–9,2% (n = 696)
C no HDL	0,8% (n = 257)	–18,6% (n = 434)	–19 % (n = 696)
Apo B	2,5% (n = 252)	–15,5% (n = 425)	–16,4% (n = 676)
Apo AI	4,3% (n = 252)	11,5% (n = 425)	11,2% (n = 676)
c-LDL: c-HDL	2,3% (n = 257)	–29,2% (n = 434)	–28,9% (n = 696)
CT: c-HDL	1,9% (n = 257)	–22,0% (n = 434)	–21,2% (n = 696)
Lp (a) (mediana)	1,1% (n = 252)	–21,4% (n = 426)	–17,6% (n = 678)

*Significativo frente a placebo en todos los parámetros ($p < 0,001$).

PN: 020

European Agency for the Evaluation of Medical Products (EMEA). CHMP Assessment Report for Tredaptive. EMEA Document: EMEA/348364/2008.
http://www.emea.europa.eu/humandocs/PDFs/EPAR/tredaptive/H-889-en6.pdf.
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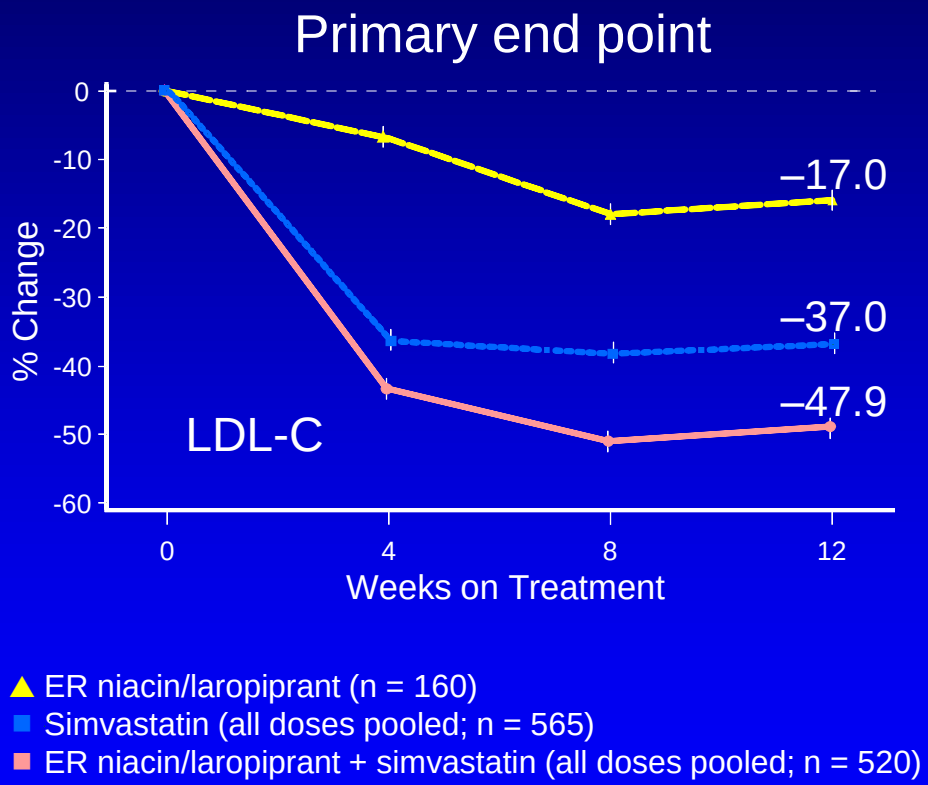
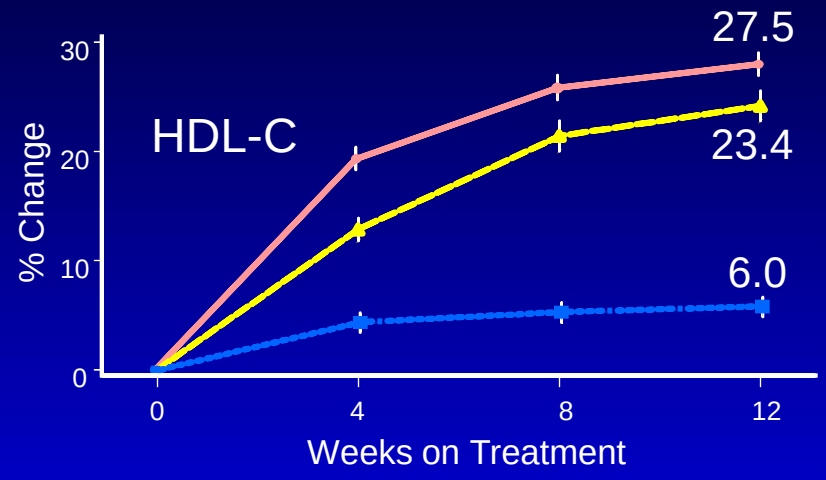
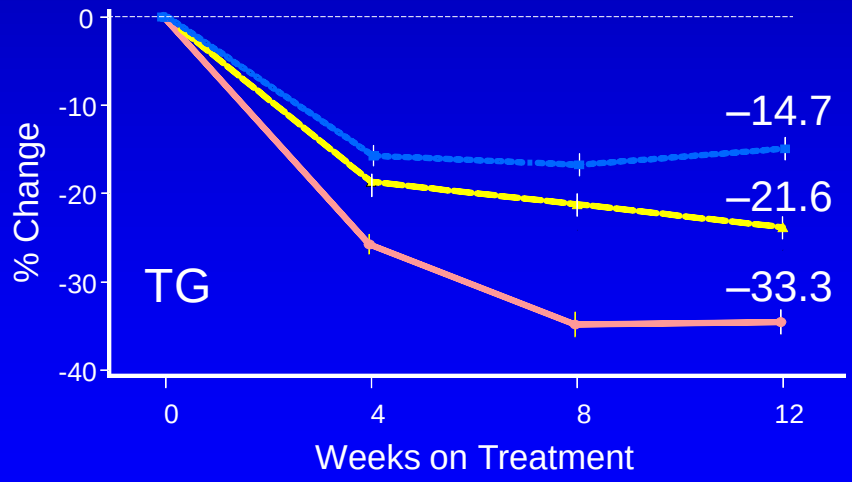
Factorial Study: Lipid Efficacy







▲ ER niacin/laropiprant (n = 160)
■ Simvastatin (all doses pooled; n = 565)
■ ER niacin/laropiprant + simvastatin (all doses pooled; n = 520)

Conclusiones

- La hiperlipemia mixta es la dislipemia más frecuente en sujetos con enfermedad coronaria prematura
- Es típica de la HFC, diabetes tipo 2, y síndrome metabólico
- En sujetos con hiperlipemia mixta el objetivo del tratamiento debe ser el cLDL y el c-noHDL
- En muchas ocasiones el tratamiento combinado con estatinas y otro hipolipemiante será necesario para lograr objetivos lipídicos
- En sujetos con hiperlipemias mixtas sin control con estatinas, la combinación con la niacina/laropiprant es una buena opción terapéutica