SEMI
SOCIEDAD ESPAÑOLA DE MEDICINA INTERNA
LA VISIÓN GLOBAL DE LA PERSONA ENFERMA

FEMI
FUNDACIÓN ESPAÑOLA DE MEDICINA INTERNA

Grupo de Riesgo Vascular

VII Reunión de Riesgo Vascular

Palacio de Congresos. Valencia
5 y 6 de Mayo 2011

VII Reunión de Riesgo Vascular

Palacio de Congresos. Valencia
5 y 6 de Mayo 2011

¿Qué ha habido de nuevo en 2010?
Lípidos

Dr. Carlos Guijarro

Unidad de Medicina Interna

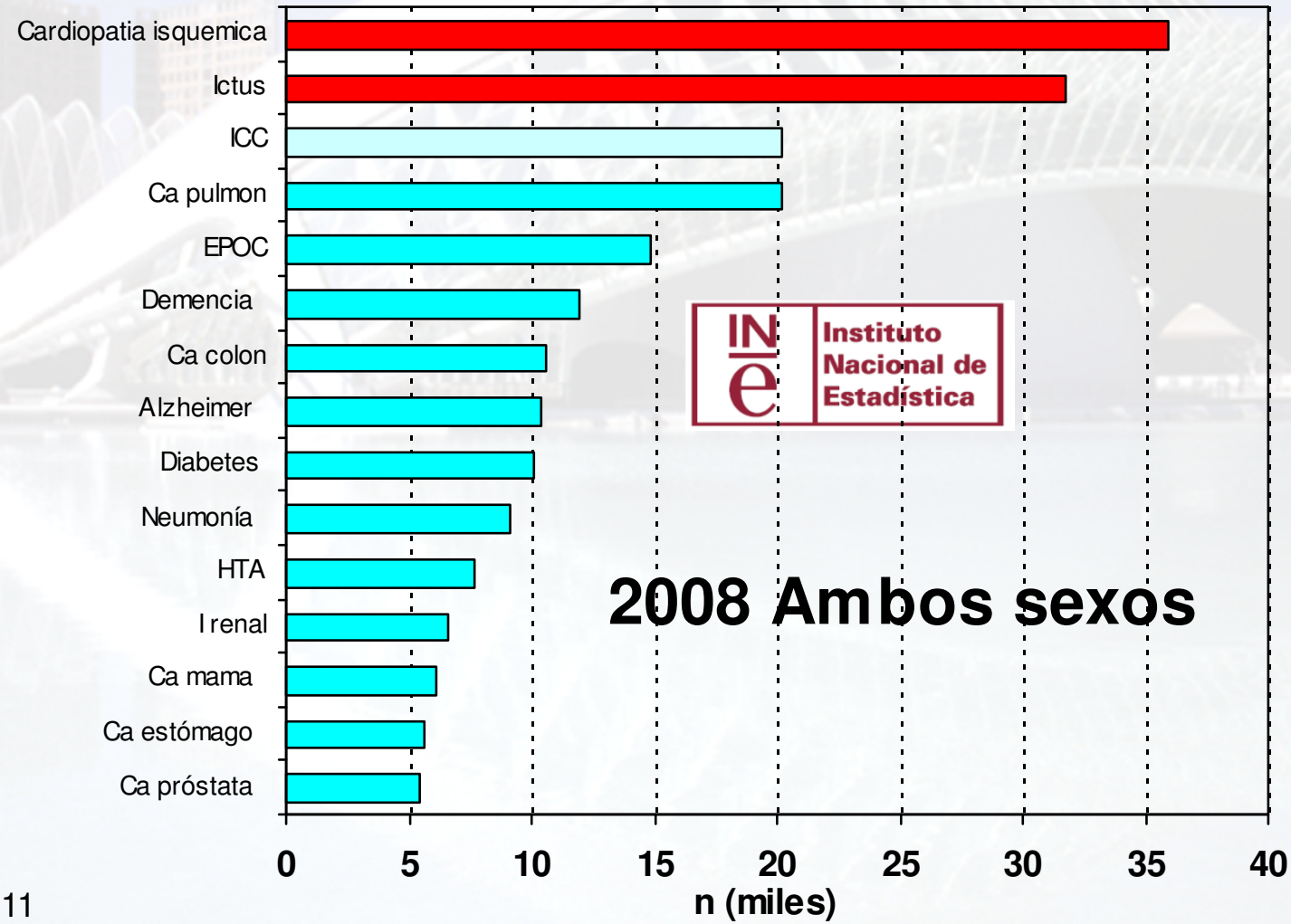
SaludMadrid Hospital Universitario Fundación Alcorcón Comunidad de Madrid

Universidad Rey Juan Carlos

Lipidos

- Evolución mortalidad Cardiovascular
- Consolidación: metaanálisis estatinas
- Más allá de las estatinas: incertidumbres
  - LDL: ezetimiba (SHARP)
  - TG: omega 3
  - HDL
    - Fibratos (Accord)
    - Inhibidores CETP
- Perspectivas

CAUSAS DE MUERTE ESPAÑA

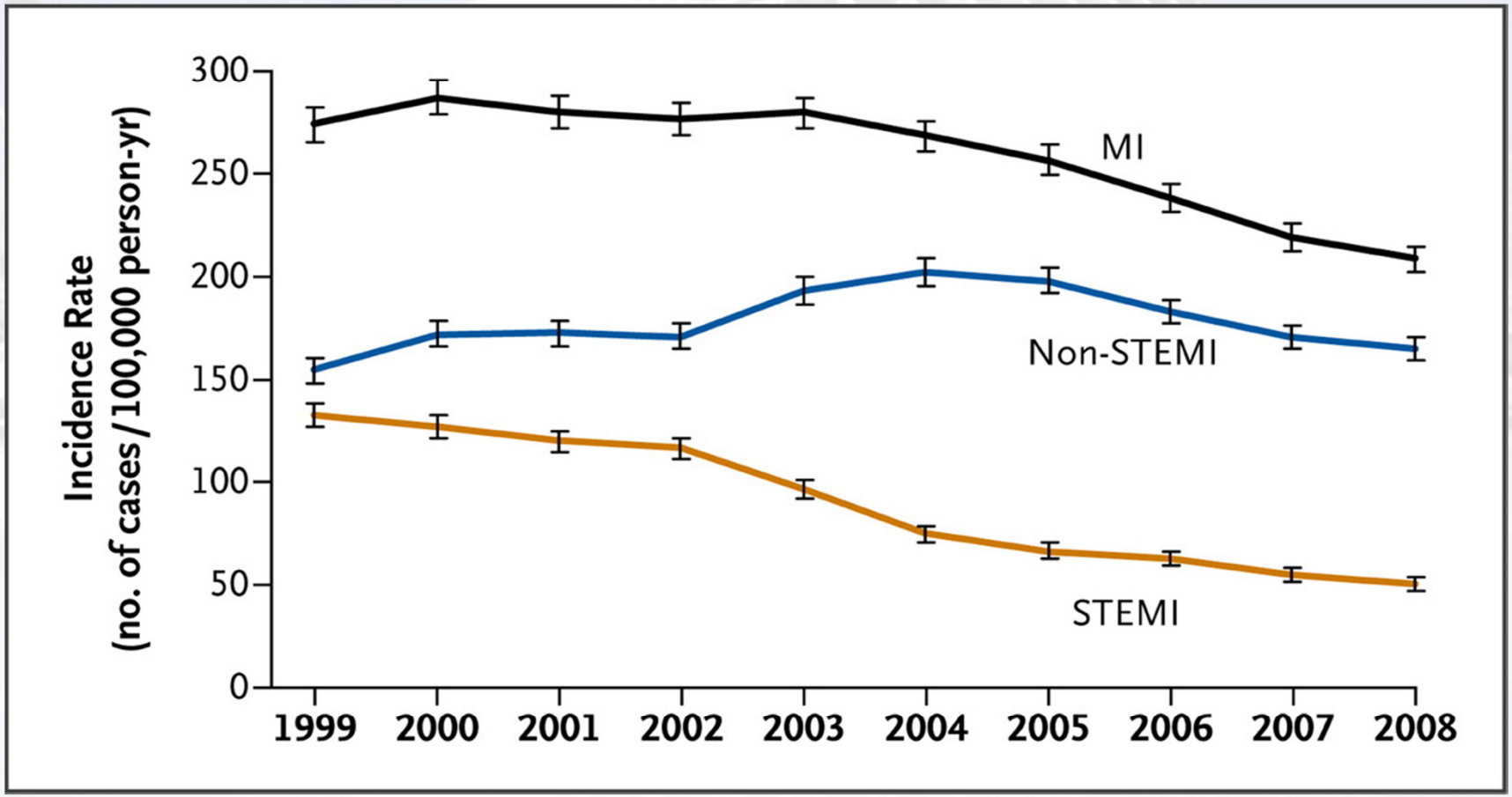


CGH 2011

CGH 2010

INE 2010

Age- and Sex-Adjusted Incidence Rates of Acute Myocardial Infarction USA, 1999 to 2008.

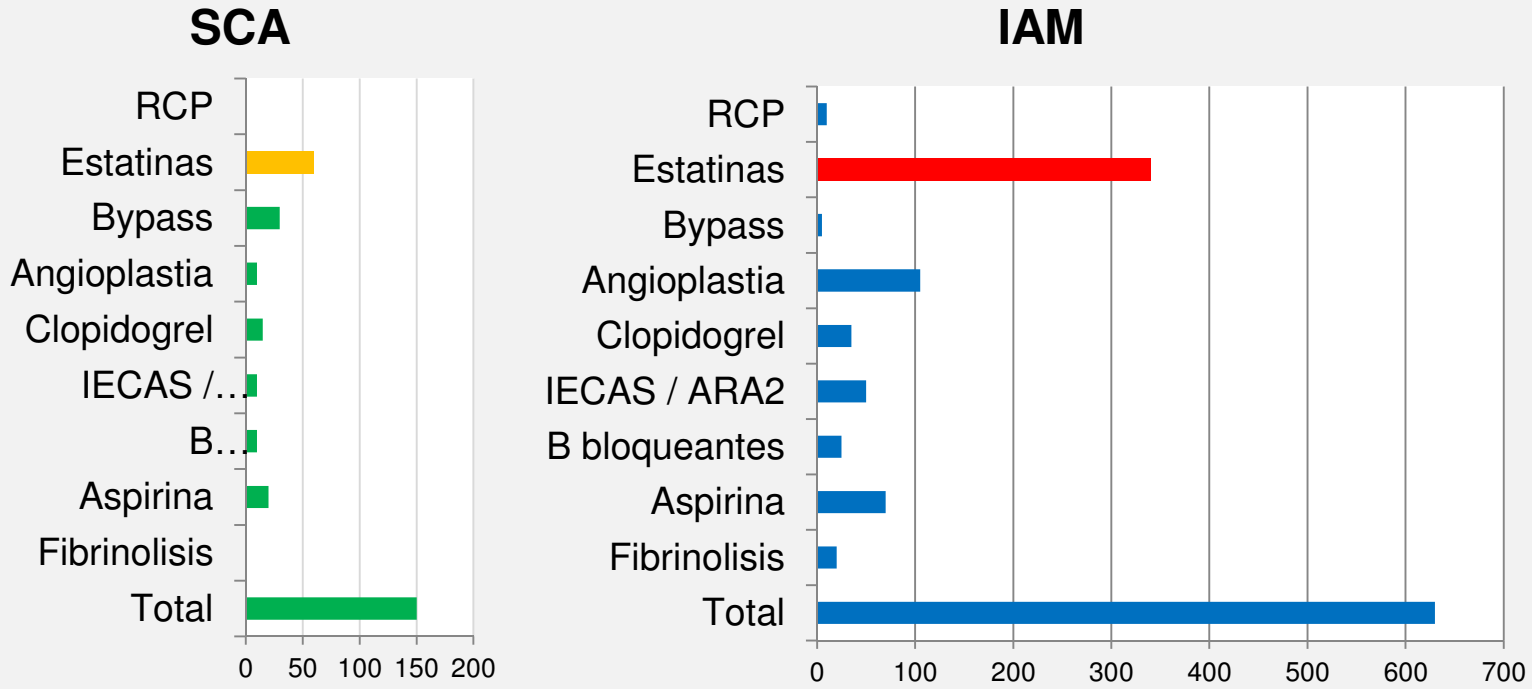


CGH 2011

Yeh RW et al. N Engl J Med 2010;362:2155-2165.

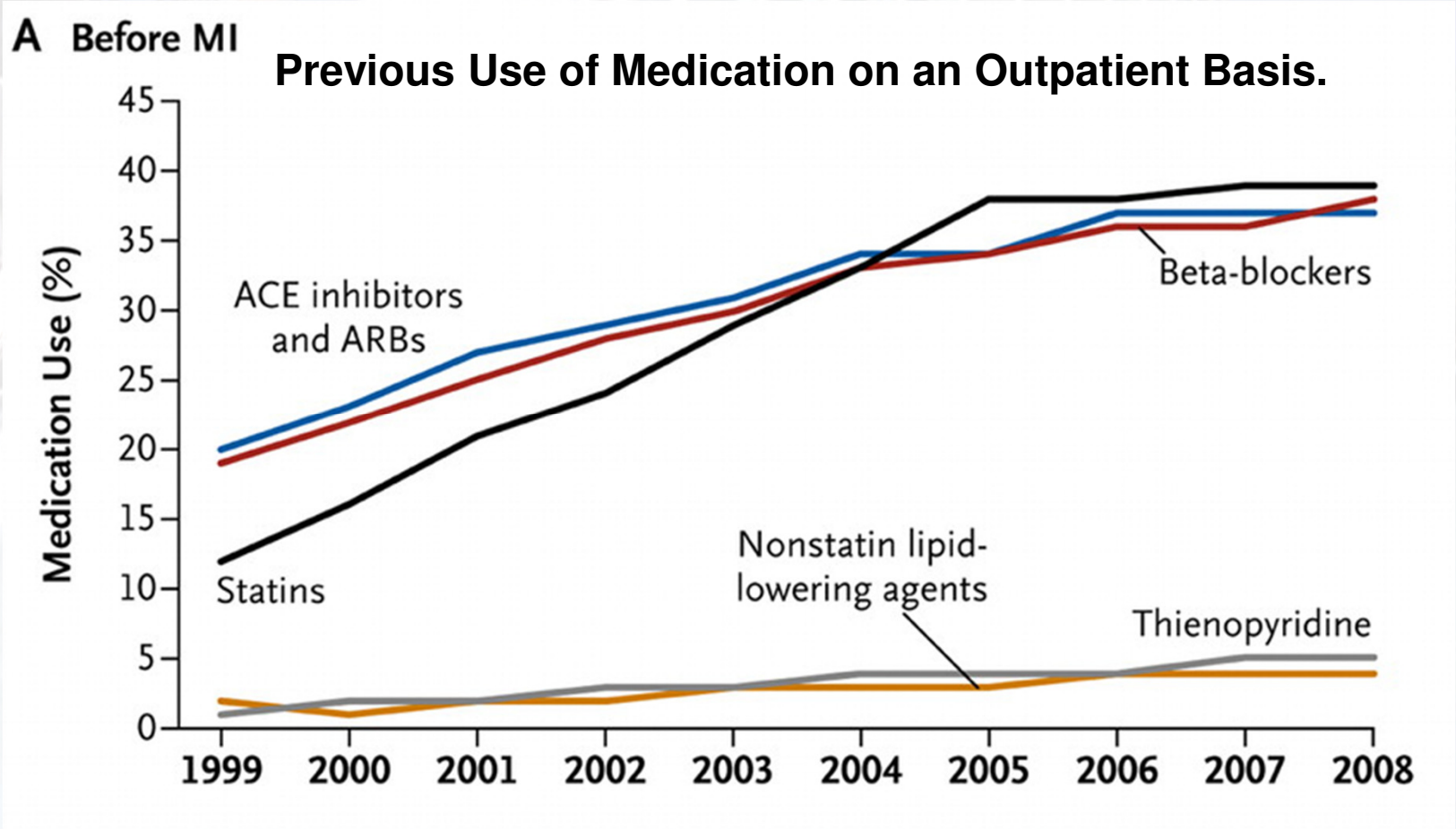
Association of Temporal Trends in Risk Factors and Treatment Uptake With Coronary Heart Disease Mortality, 1994-2005

Factores que explica la reducción en mortalidad (Ontario – Canadá)



JAMA. 2010;303(18):1841-1847

Age- and Sex-Adjusted Incidence Rates of Acute Myocardial Infarction, 1999 to 2008.

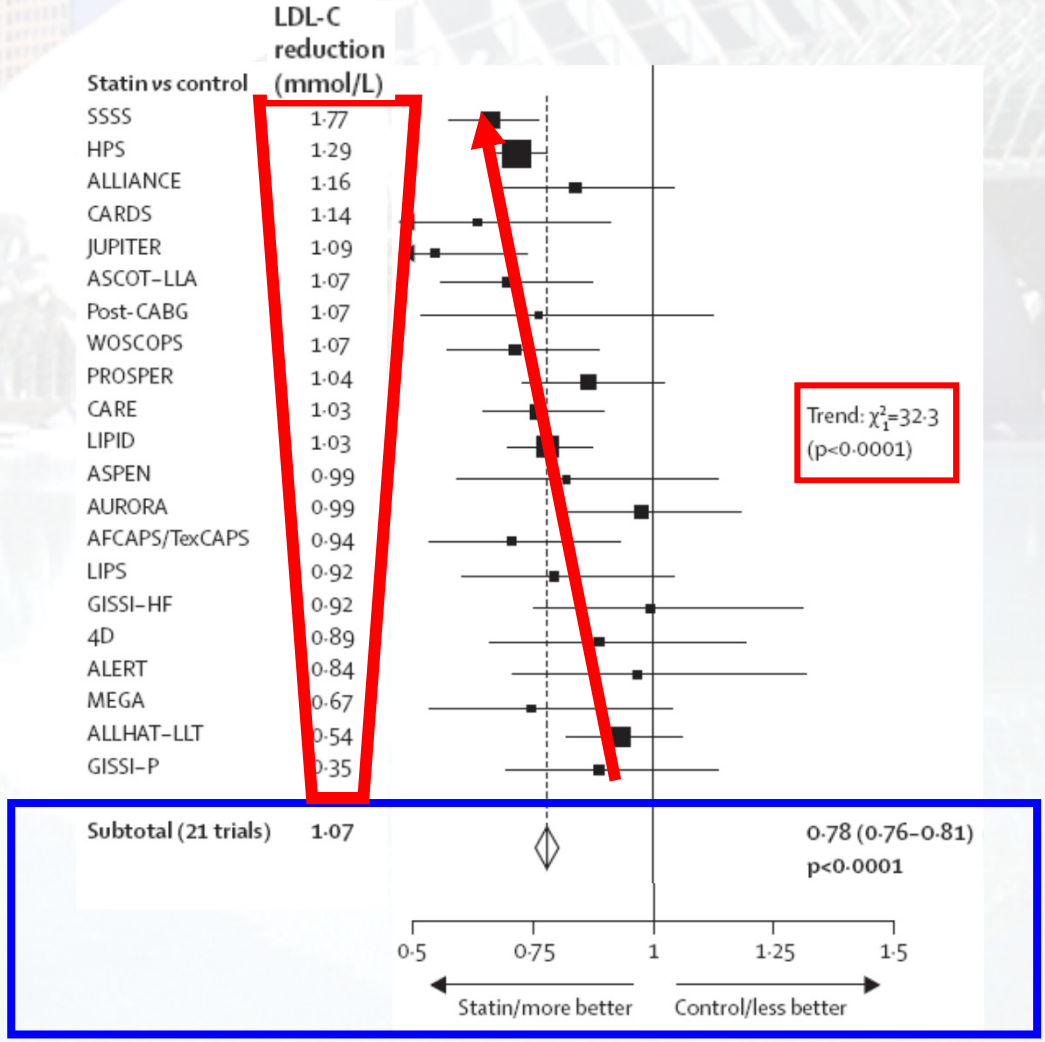


CGH 2011

Yeh RW et al. N Engl J Med 2010;362:2155-2165.

Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials

*Cholesterol Treatment Trialists' (CTT) Collaborators**



CGH 2010
The Lancet 2010 Nov
DOI: 10.1016/S0140-6736(10)61350-5

Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials

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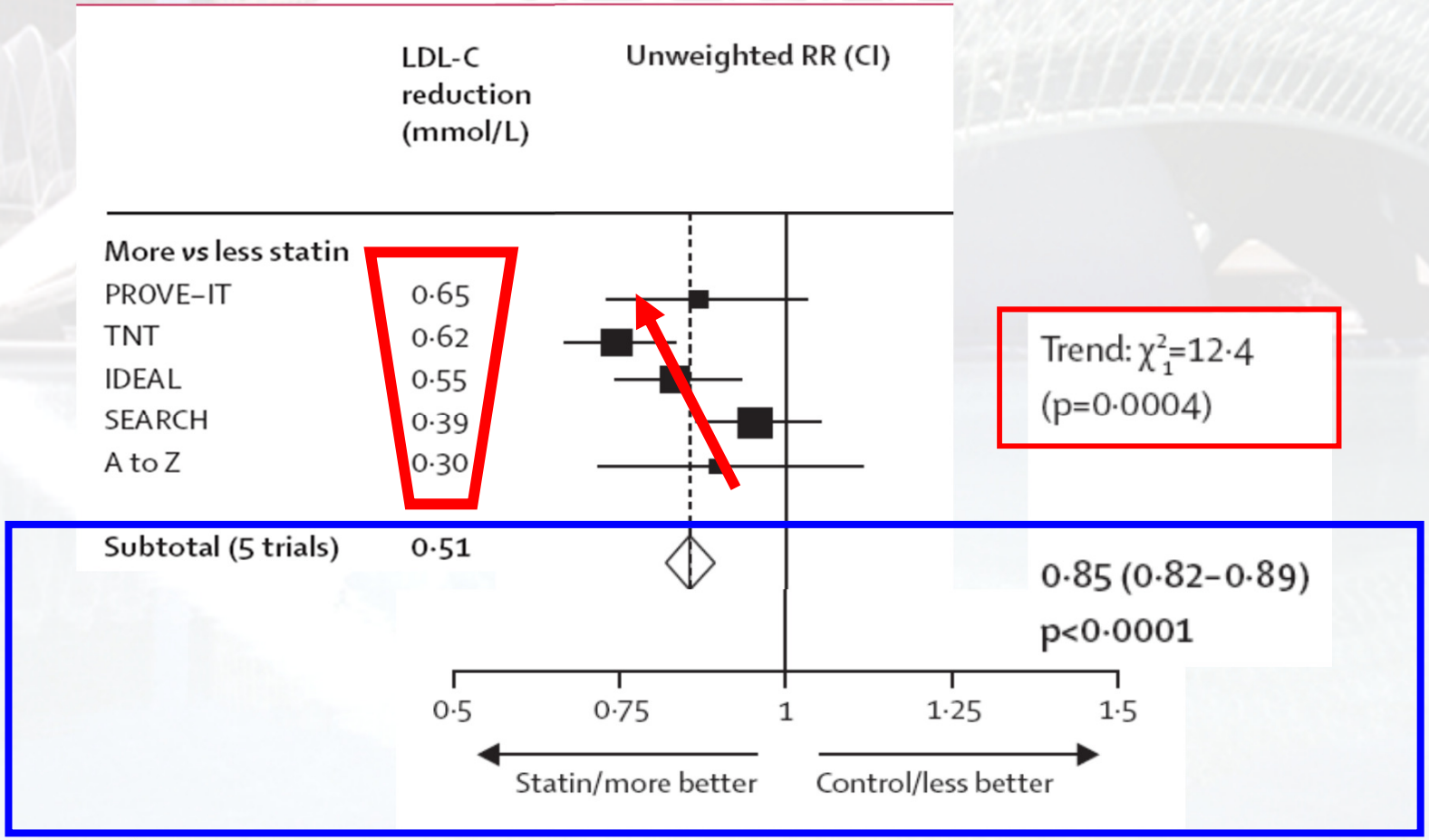

CGH 2010
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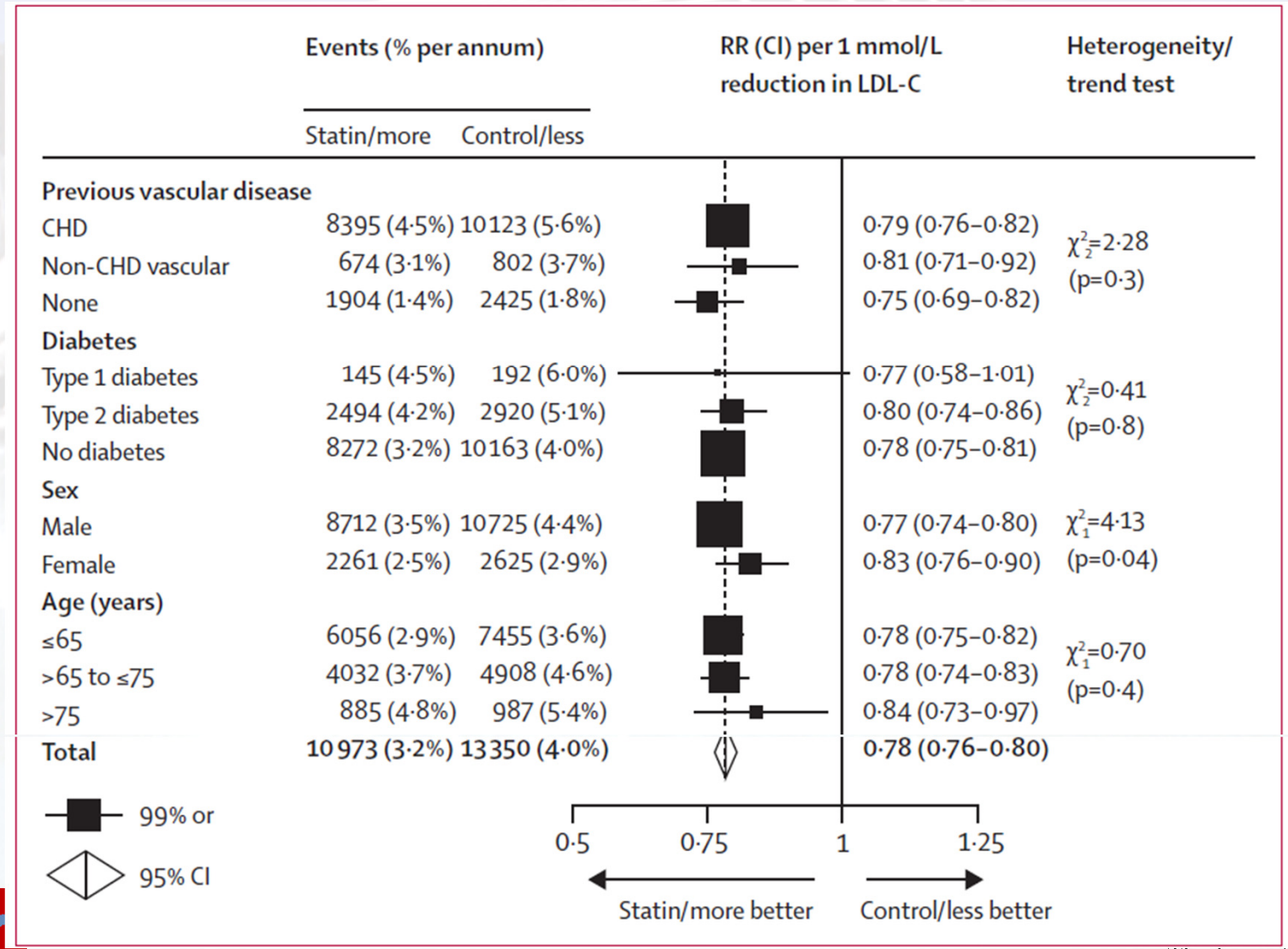

The Lancet 2010 Nov
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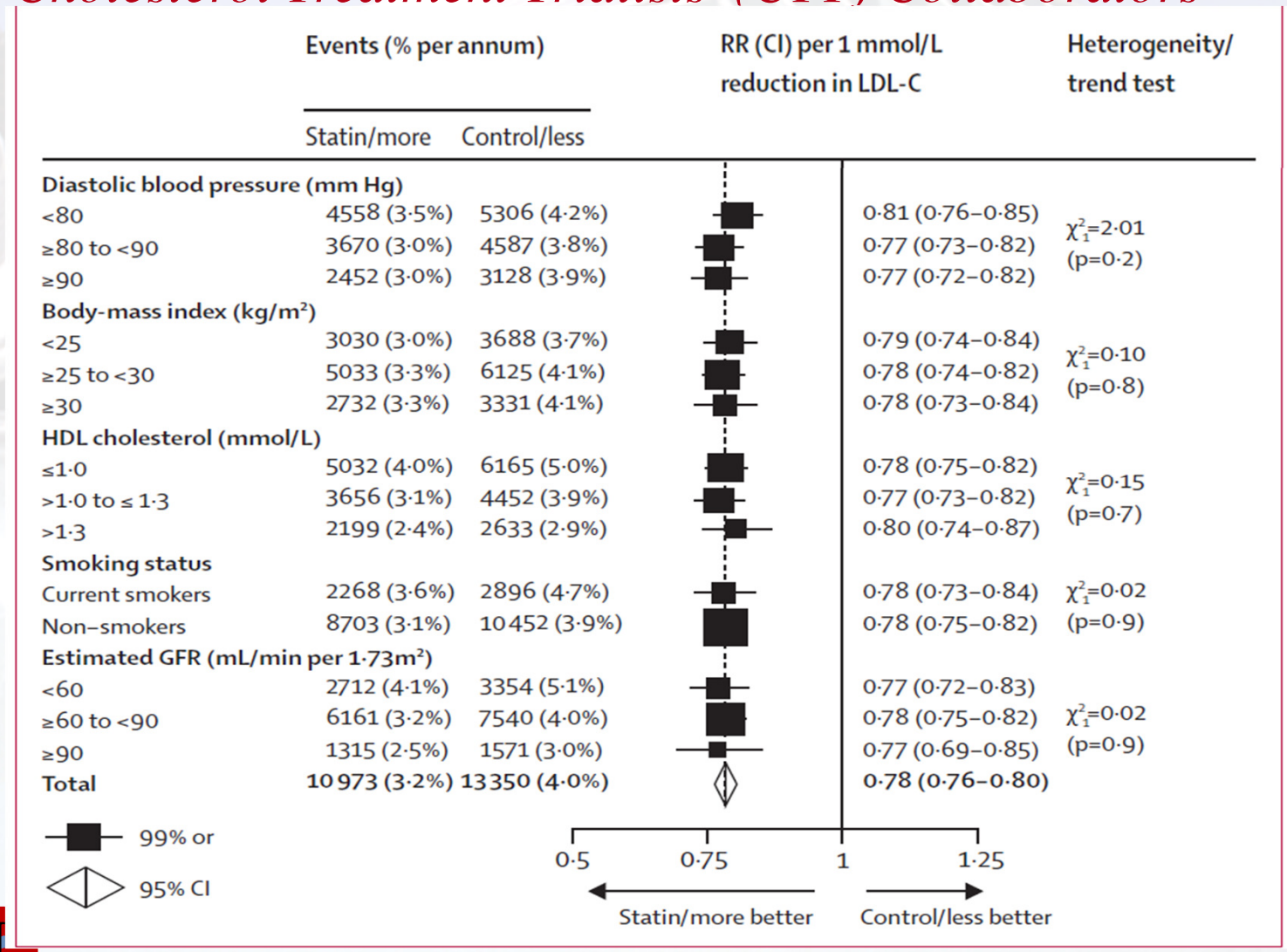

2010

The Lancet 2010 Nov
DOI: 10.1016/S0140-6736(10)61350-5

Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials

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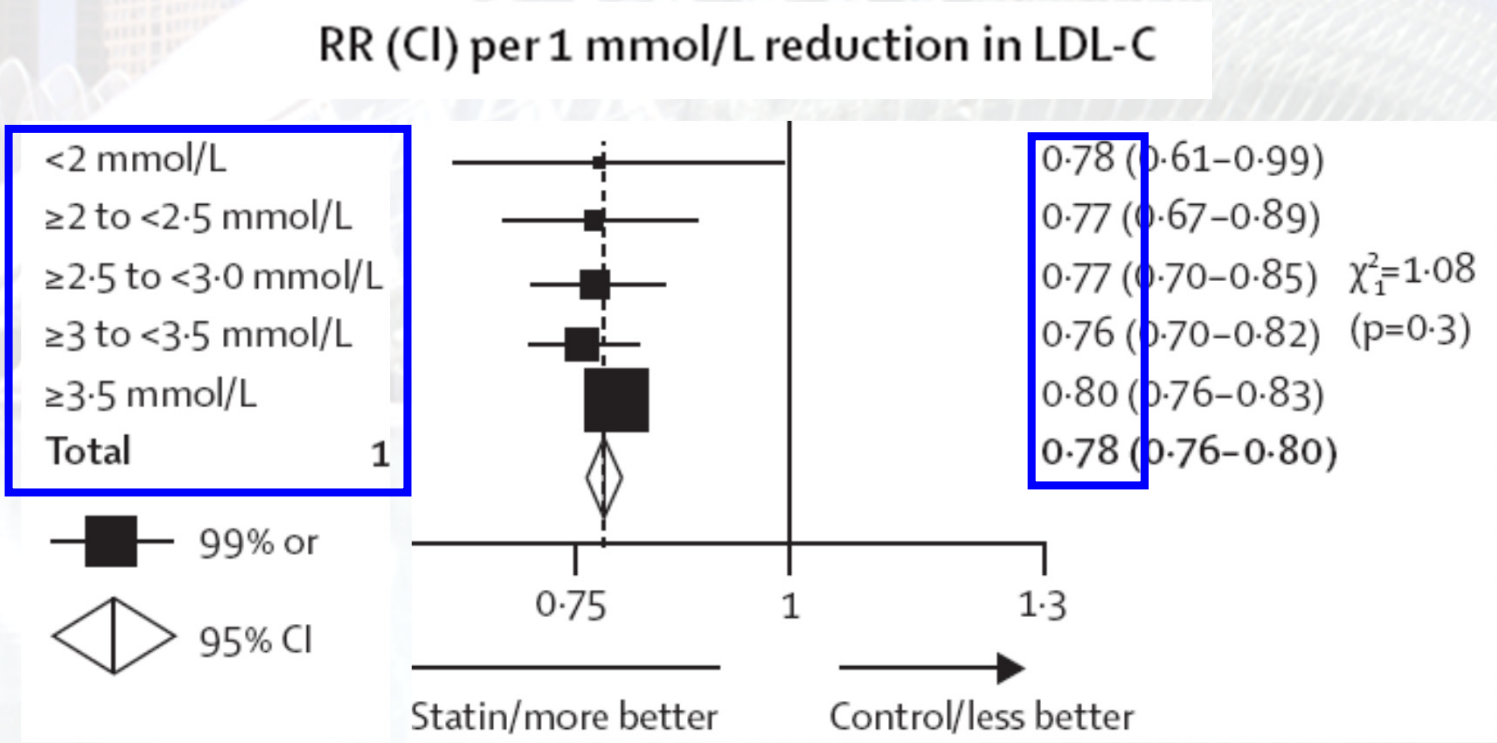

Irrespective of baseline LDL cholesterol levels

CGH 2010
The Lancet 2010 Nov
DOI: 10.1016/S0140-6736(10)61350-5

Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials

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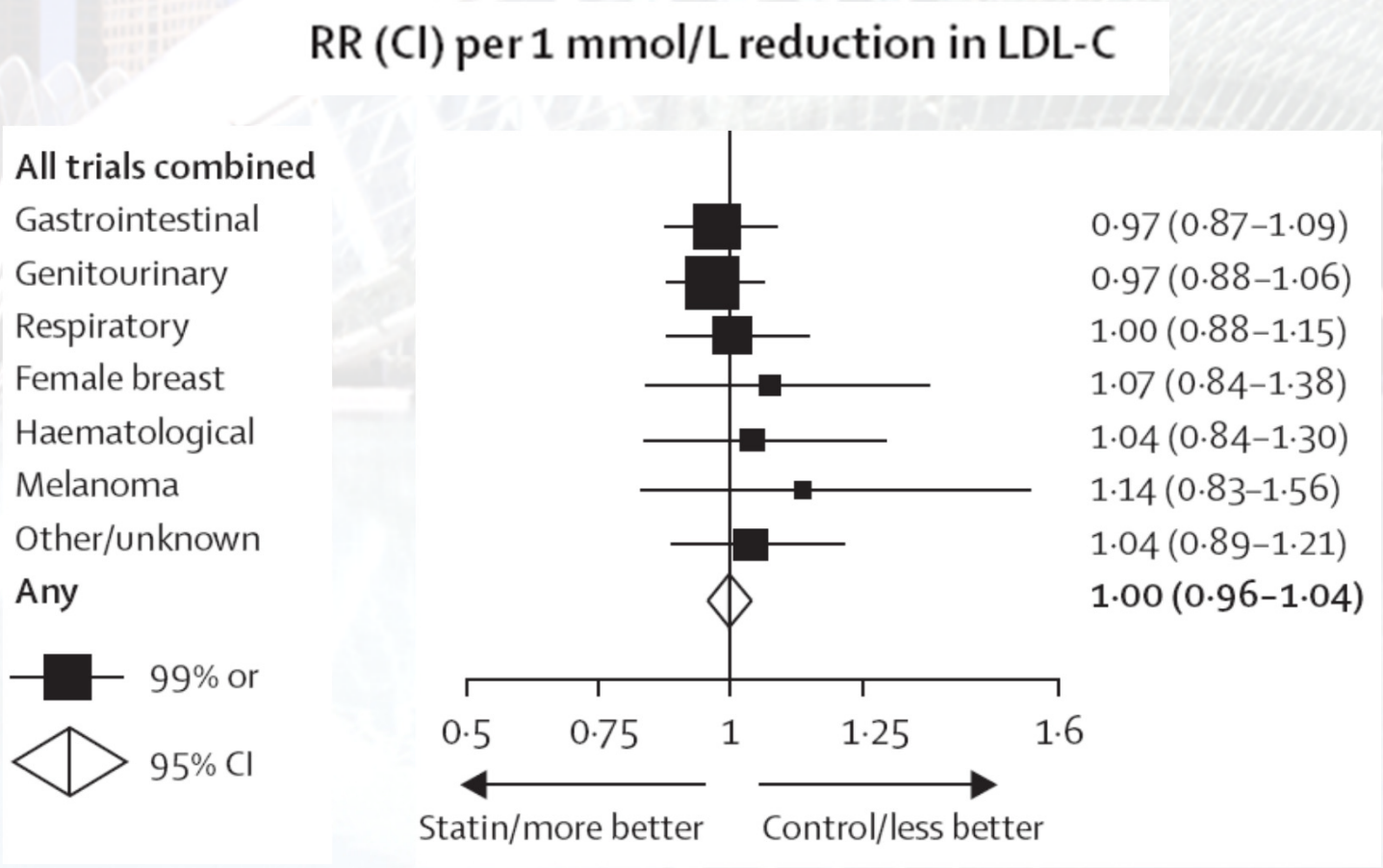
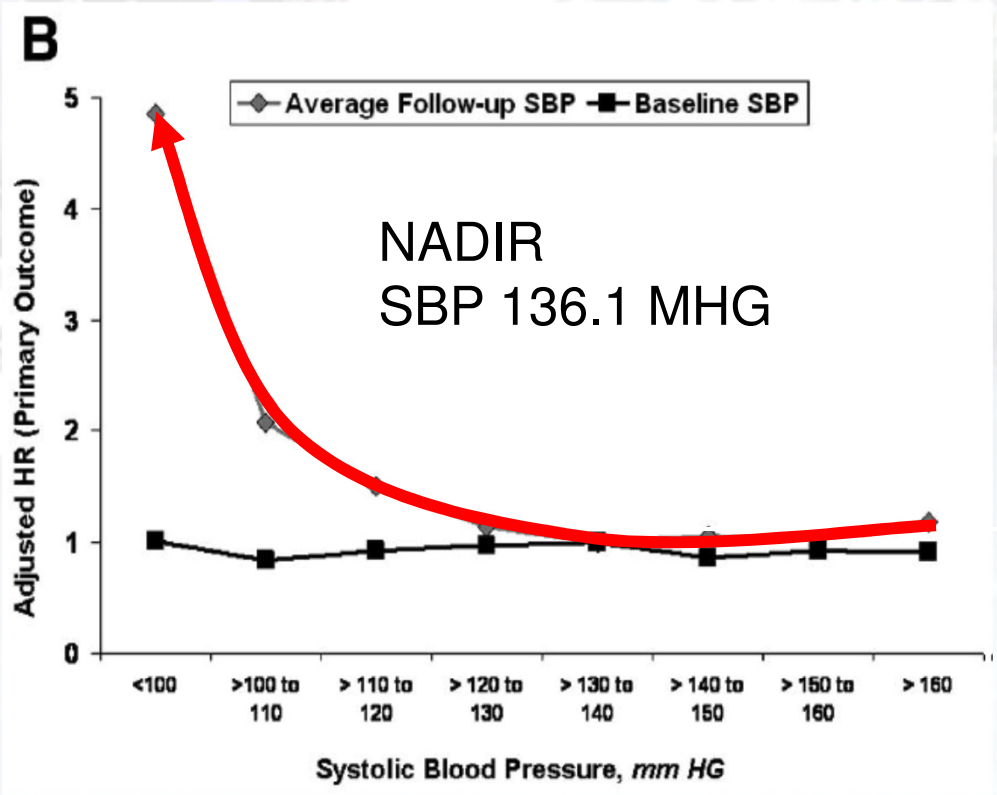
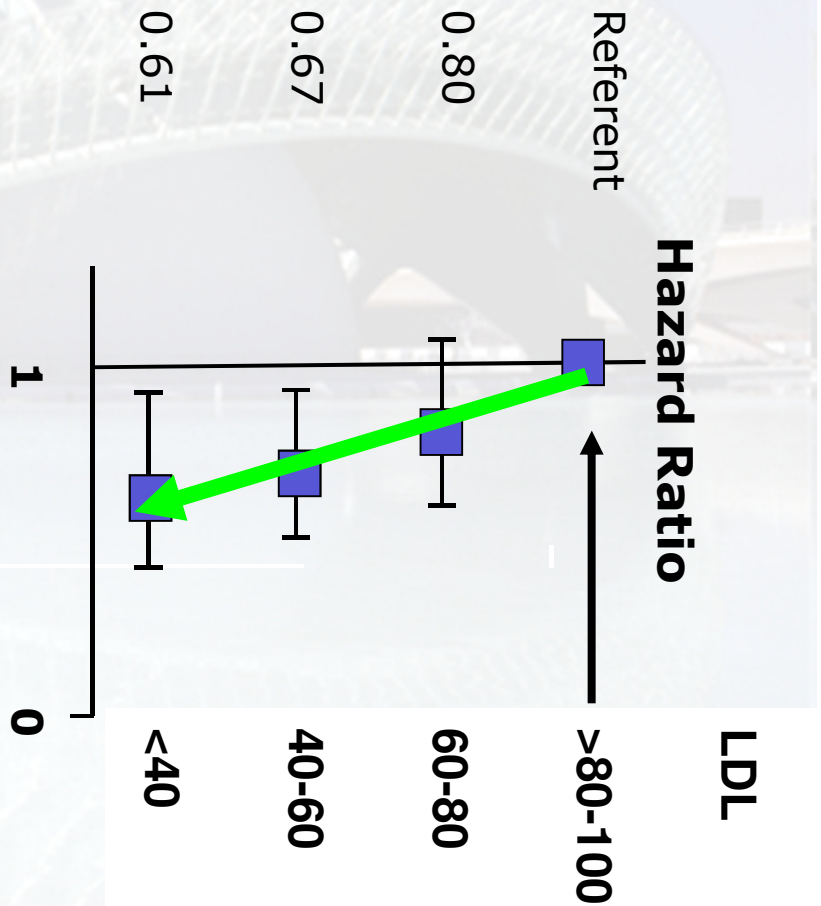


Cancer

CGH 2010
The Lancet 2010 Nov
DOI: 10.1016/S0140-6736(10)61350-5

PROVE-IT: J curve ?
Blood pressure vs LDL levels





CGH 2011

Bangalore et al.*Circulation*. 2010;122:2142

Wiviott SD et al. *JACC*. 2005;46:1411.

Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials

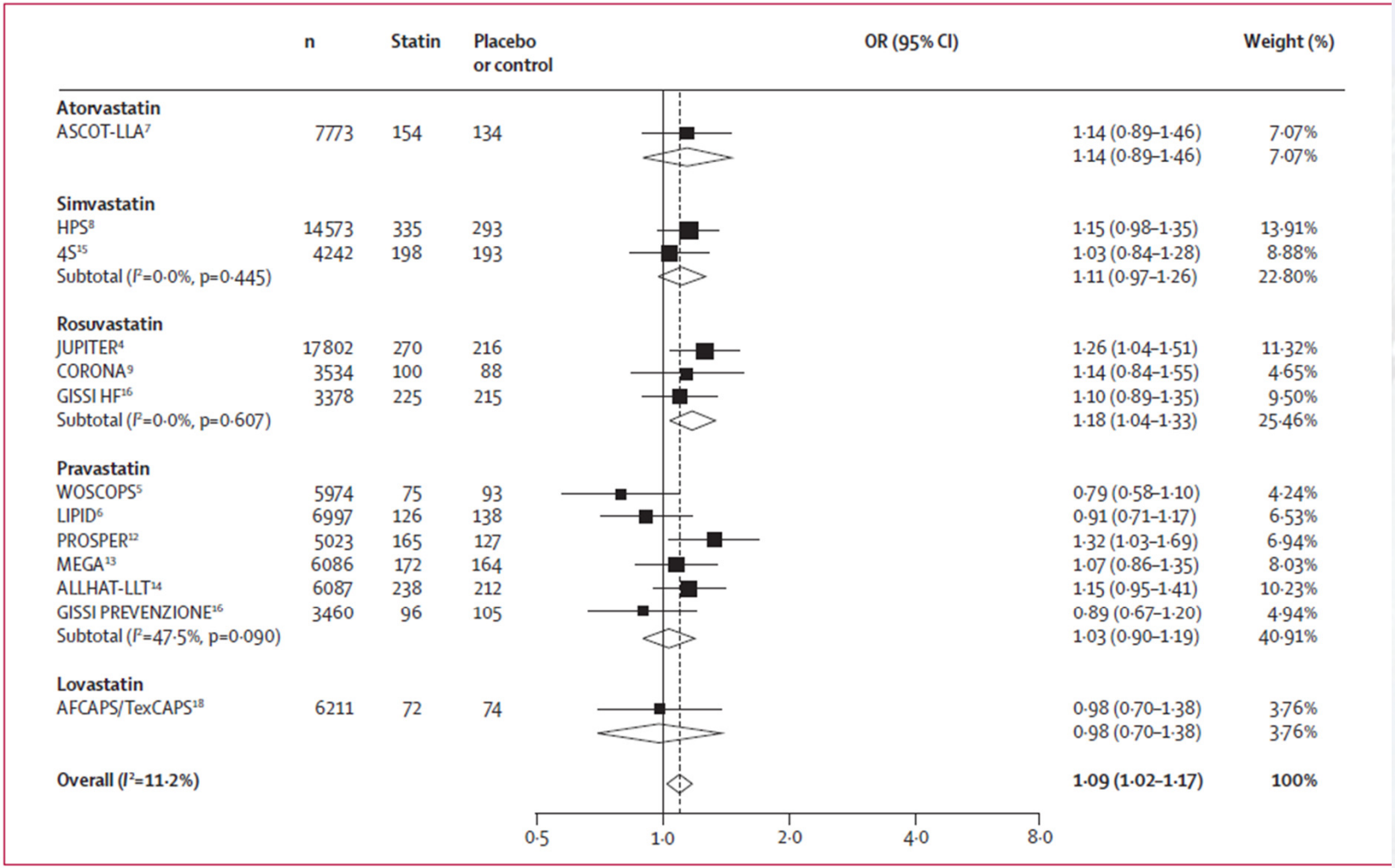
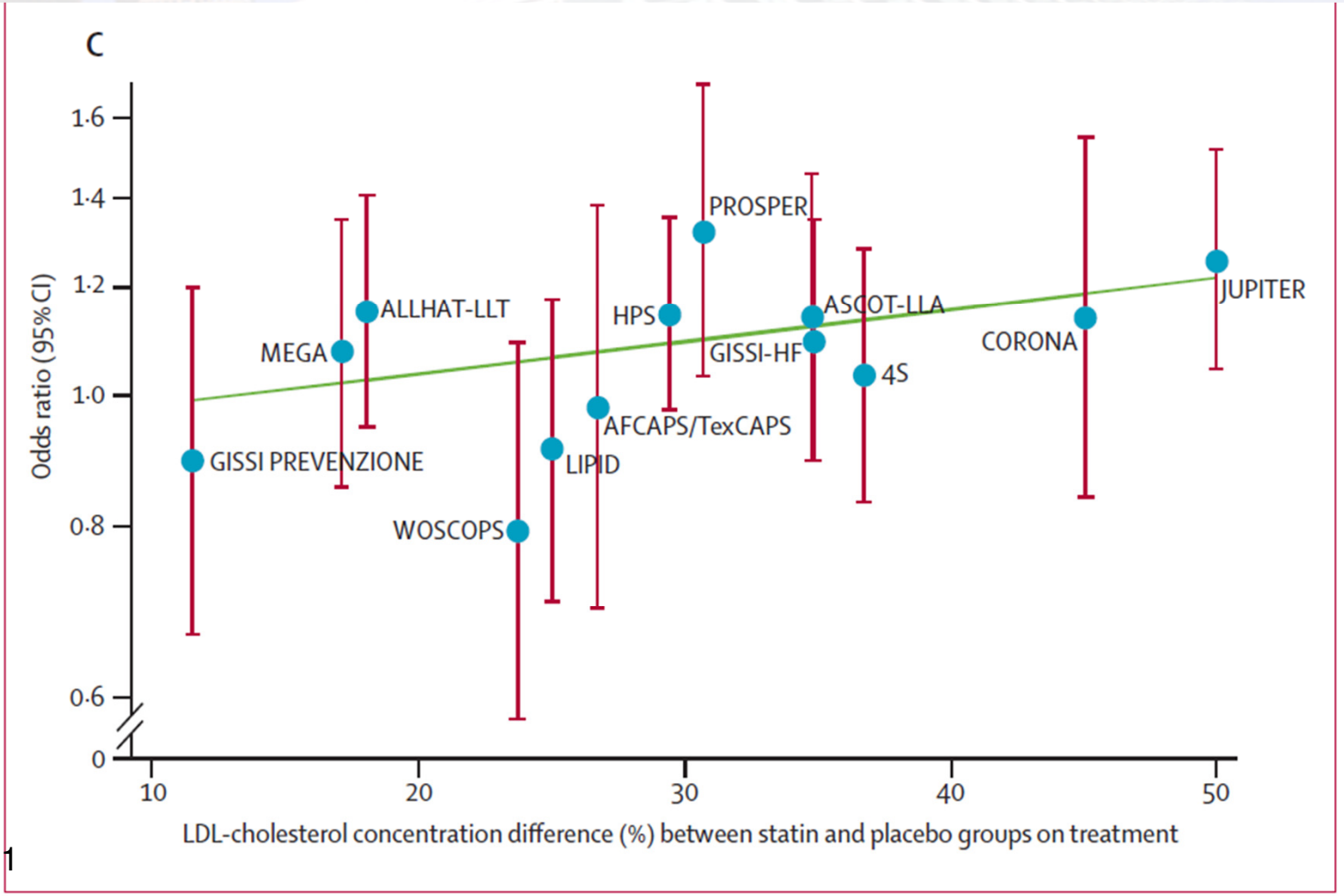


Figure 3: Association between different statins and development of diabetes

Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials



CGH 2011

Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials

- 13 statin trials with 91 140 participants,
- 4278 developed diabetes during a mean of 4 years.
- Statin therapy was associated with a 9% increased risk for incident diabetes (odds ratio [OR] 1·09; 95% CI 1·02–1·17),
- **NNH 255** (95% CI 150–852) for 4 years = **one extra case of diabetes, but would avoid 5.4 CHD events**

- Statin therapy is associated with a slightly increased risk of development of diabetes, **but the risk is low both in absolute terms and when compared with the reduction in coronary events**.

- **Clinical practice** in patients with moderate or high cardiovascular risk or existing cardiovascular disease **should not change**.

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Statins and risk of incident diabetes
Jupiter: not so sweet

Table 4. Monitored Adverse Events, Measured Laboratory Values, and Other Reported Events of Interest during the Follow-up Period.*

Event	Rosuvastatin (N=8901)	Placebo (N=8901)	P Value
Glycated hemoglobin at 24 mo — %			0.001
Median	5.9	5.8	
Interquartile range	5.7–6.1	5.6–6.1	
Fasting glucose at 24 mo — mg/dl			0.12
Median	98	98	
Interquartile range	91–107	90–106	
>Trace of glucose in urine at 12 mo — no. (%)	36 (0.5)	32 (0.4)	0.64
Other events			
Newly diagnosed diabetes (physician-reported) — no. (%)	270 (3.0)	216 (2.4)	0.01

CGH 2011

N Engl J Med 2008;359:2195207.

Safety and efficacy of long-term statin treatment for cardiovascular events in patients with coronary heart disease and abnormal liver tests in the Greek Atorvastatin and Coronary Heart Disease Evaluation (GREACE) Study: a post-hoc analysis

*Vasilios G Athyros, et al for the GREACE Study Collaborative Group**

- Prospective, randomised intention-to-treat study
- 1600 patients with coronary heart disease
- Atorvastatin (10-80 mg) vs usual care
- 437 with abnormal liver test (NAFLD)
- CV events
- Liver function tests

CGH 2011

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THE LANCET

Lancet 2010; 376: 1916–22

GREACE Study: a post-hoc analysis

*Vasilios G Athyros, et al for the GREACE Study Collaborative Group**

ESTATINA

CONTROL

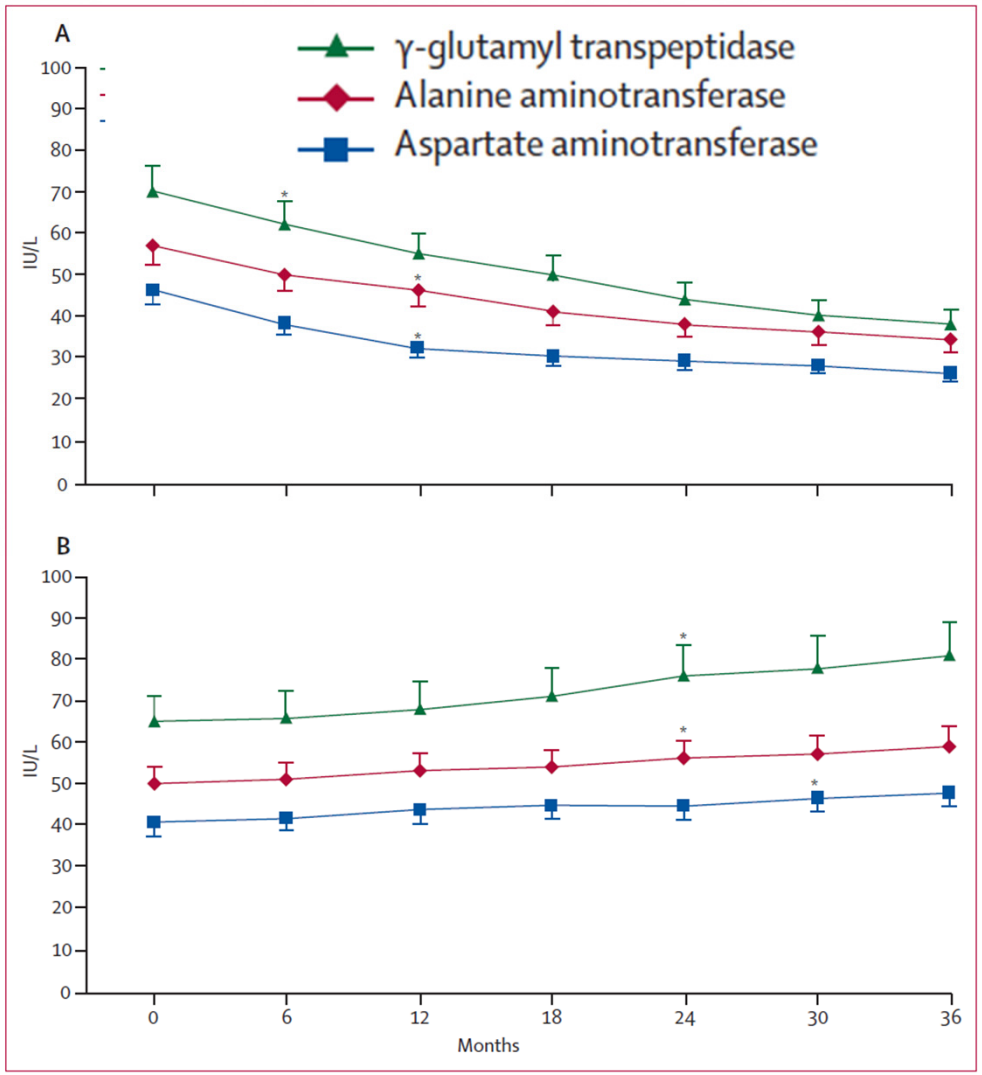
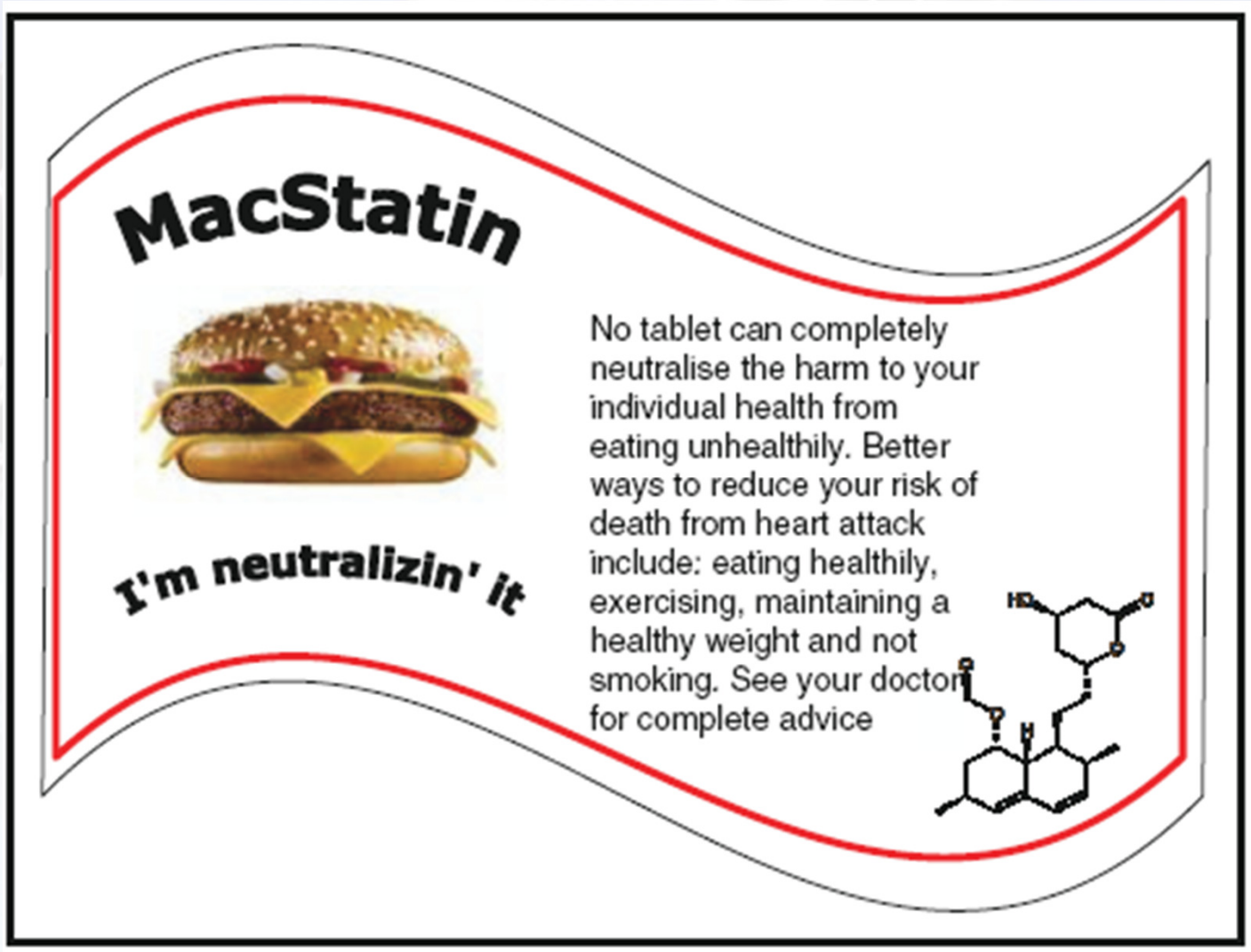


Figure 2: Enzyme activity during 3-year follow-up in patients with raised liver enzymes

CGH 2011

***Lancet* 2010; 376: 1916–22**

¿Cuál es la realidad?



CGH 2011

Am J Cardiol 2010

Métodos (I)

Estudio epidemiológico, internacional multicéntrico, transversal,

Criterios de inclusión

- En tratamiento actual con estatinas ≥3 meses
- Edad ≥ 45 años
- Perfil lipídico
- Consentimiento informado

	GLOBAL	ESPAÑA
Pacientes (n)	**22063**	**3710**
Centros	**2987**	**477**
Atención primaria	**73,8%**	**68,8%**
Especialistas	**26,2%**	**31,2%**

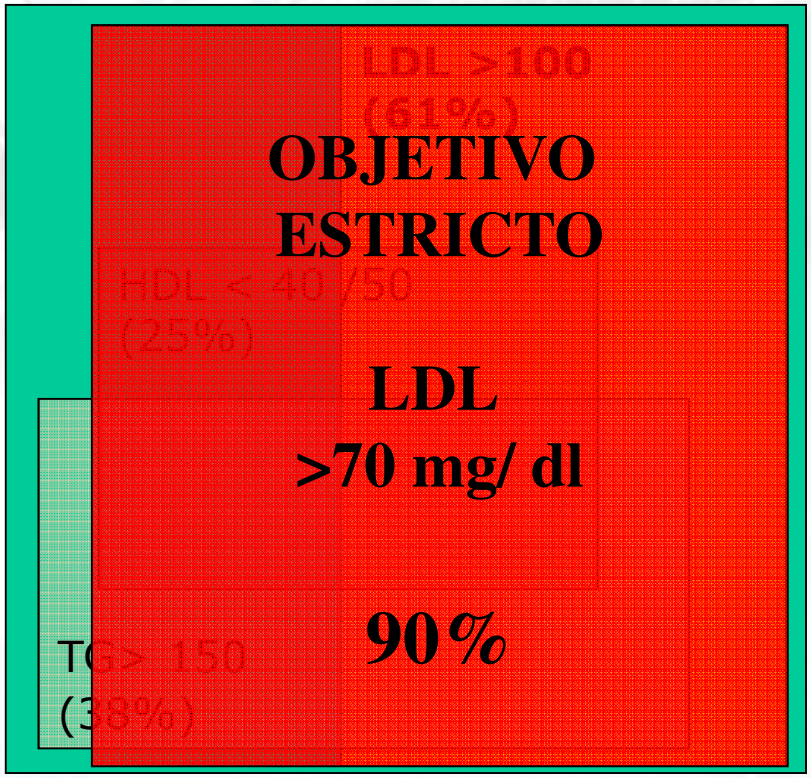
CGH 2011

G Juanatey Rev Esp Cardiol. 2011;64(4):286-294.

Control de colesterol LDL en pacientes de alto riesgo en tto con estatinas

Alteraciones lipídicas en pacientes de Alto Riesgo*
(ECV, Diabetes y/o ESC-Score ≥5%)

ESPAÑA n = 1794



CGH 2011

G Juanatey Rev Esp Cardiol. 2011;64(4):286-294.

¿hay vida más allá de las estatinas?

- Colesterol LDL:
  - **ezetimibe (SHARP)**
- Colesterol HDL / TG
  - Fibratos (Accord)
  - Omega 3
  - Inhibidores CETP
  - Otros

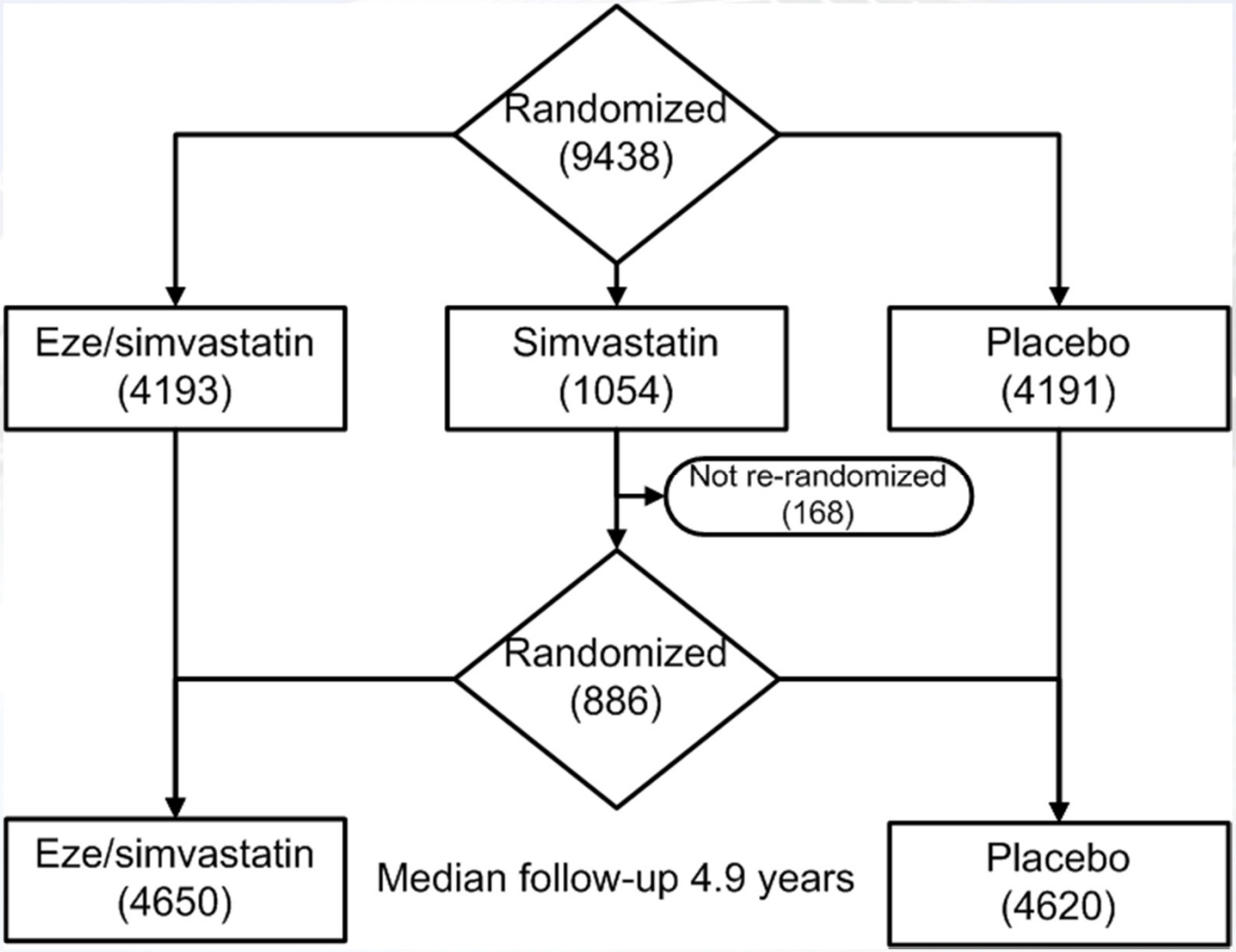
SHARP: Criterios de Inclusión

- Pacientes con historia de enfermedad renal crónica
  - No dializados: creatinina elevada en 2 ocasiones
    - Hombres: ≥1.7 mg/dL (150 µmol/L)
    - Mujeres: ≥1.5 mg/dL (130 µmol/L)
  - En diálisis: hemodiálisis o diálisis peritoneal.
- Edad ≥40 años
- Sin historia de infarto de miocardio o revascularización coronaria.

CGH 2011

CGH 2010

SHARP: Diseño



CGH 2011

SHARP: Resultados

- **Principal**
  - Principales eventos isquémicos (muerte coronaria, Infarto de miocardio, Ictus no-hemorrágico, o revascularización)
- **Secundarios**
  - Principales eventos cardiovasculares (muerte de origen cardíaco, IM, ictus, o revascularización)
  - Causas de los principales eventos isquémicos
- **Sobre parámetros renales**
  - Necesidad de diálisis o transplante al final del estudio

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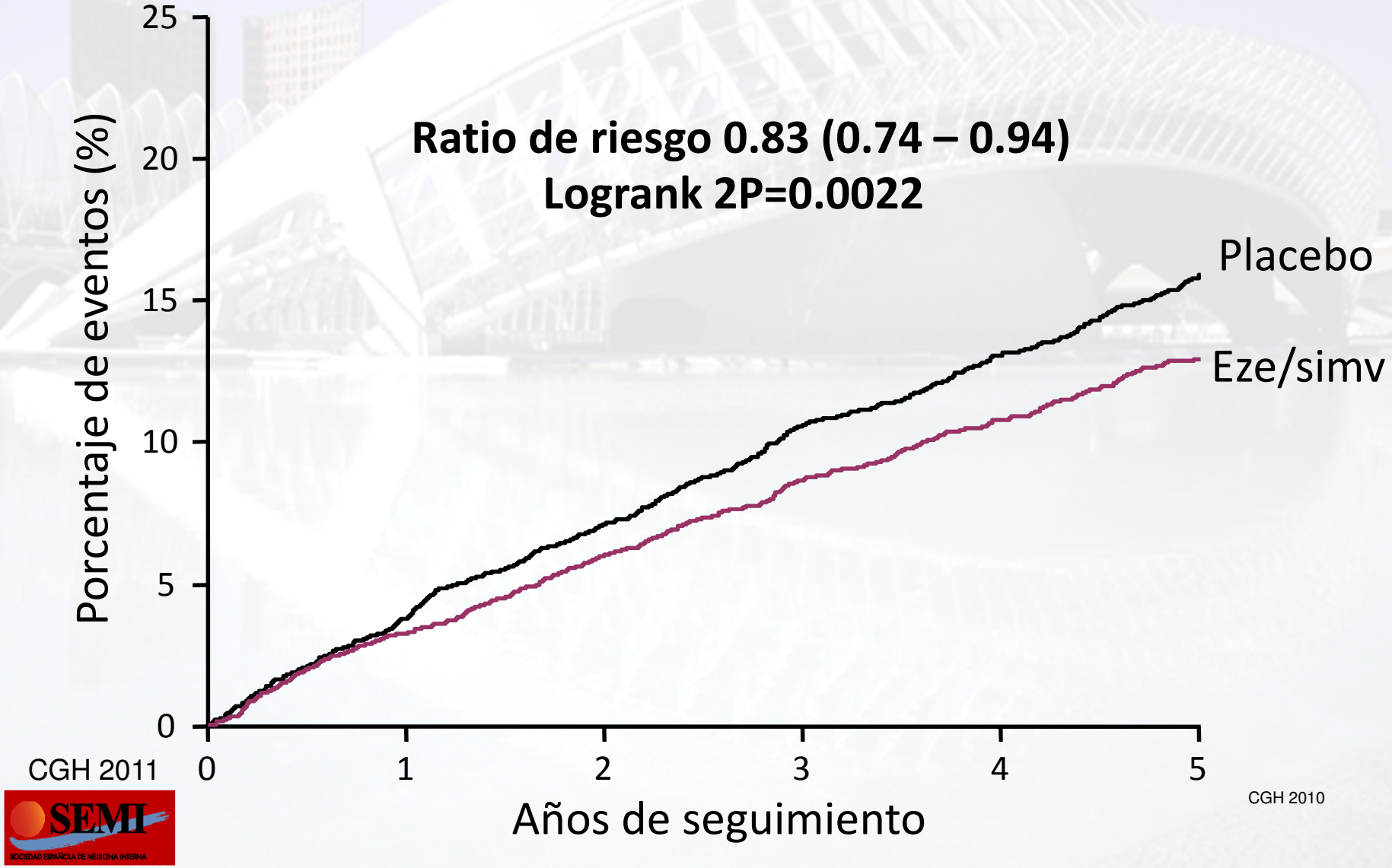
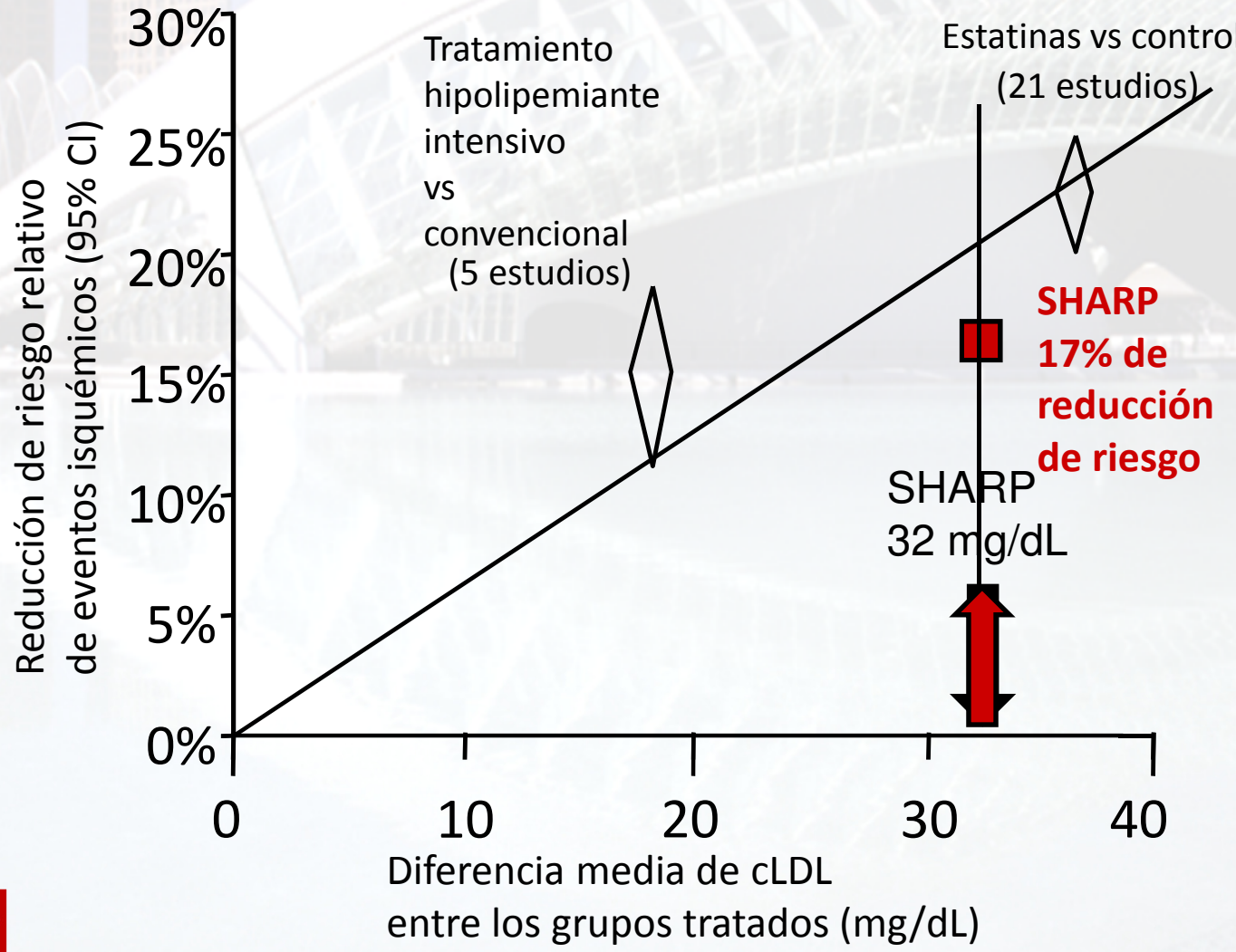
SHARP: Principales eventos isquémicos



CGH 2011

CGH 2010

CTT: Efectos sobre los eventos isquémicos



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¿hay vida más allá de las estatinas?

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  - **Fibratos (Accord)**
  - Omega 3
  - Inhibidores CETP
  - Otros

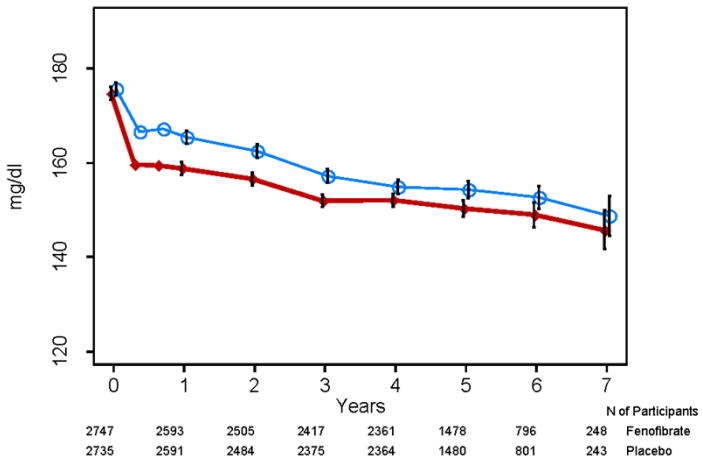
Tratamiento hipolipemiante combinado

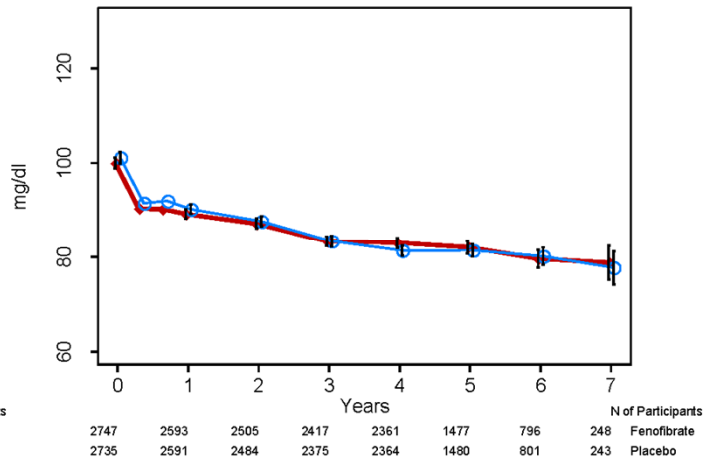
- ¿Es útil el tratamiento con fibratos en pacientes diabéticos ya en tto con estatinas?
- 5518 pacientes con diabetes
- Todos tratamiento con simvastatina
- Aleatorizacion
  - Simvastatina + placebo
  - Simvastatina + fenofibrato (160 mg/día)
- Seguimiento 4,7 años
- Variable valoración: IAM, ictus, muerte CV

N Engl J Med. 2010;362:1563-74.

Plasma Lipid Levels During Trial

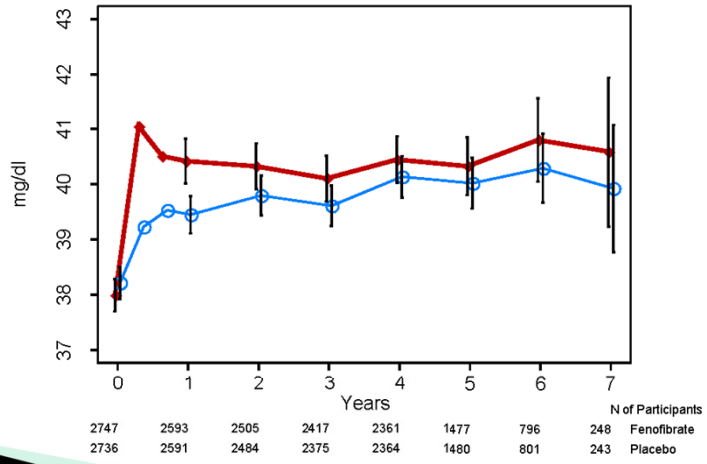
C total

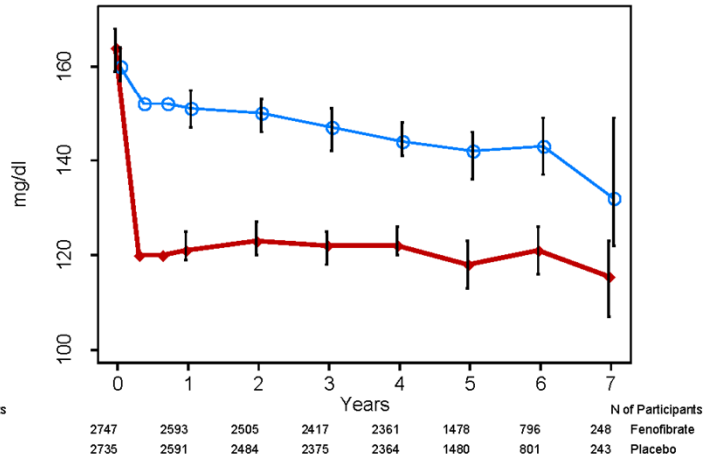




LDL

HDL





TG

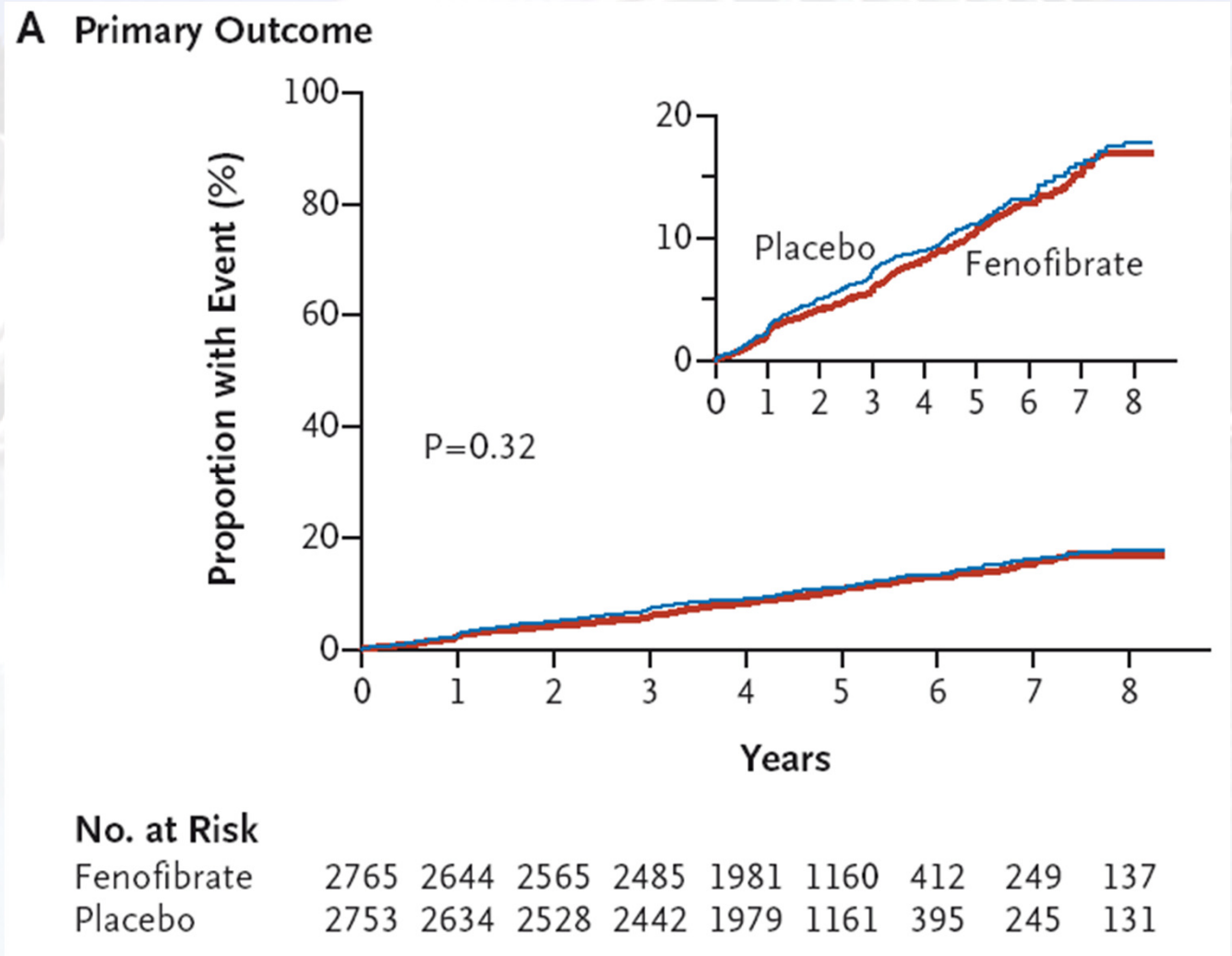
010

N Engl J Med. 2010;362:1563-74.

Action to Control Cardiovascular Risk in Diabetes
ACCORD

Action to Control Cardiovascular Risk in Diabetes

ACCORD



CGH 2011

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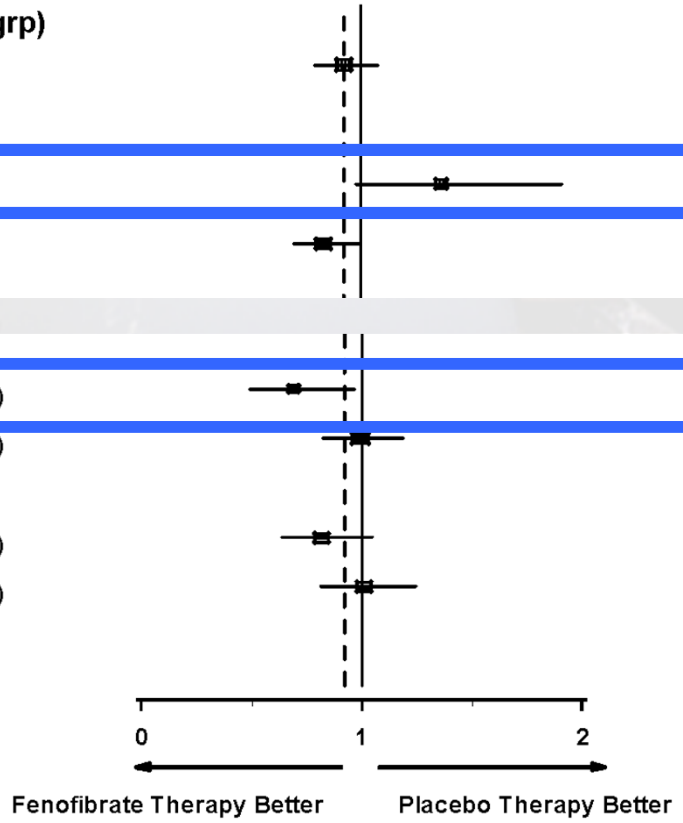
N Engl J Med. 2010;362:1563-74.

Action to Control Cardiovascular Risk in Diabetes

ACCORD

Subgroup	Fenofibrate % Events (# in grp)	Placebo % Events (# in grp)	Interaction P-Value
Overall	10.5% (2765)	11.3% (2753)	
Sex			
Women	9.1% (851)	6.6% (843)	
Men	11.2% (1914)	13.3% (1910)	0.0106
Trig/HDL combination			
TG204+ /HDL<=34	12.4% (485)	17.3% (456)	0.0567
All Others	10.1% (2264)	10.1% (2284)	
A1c Median			
A1c <= 8.0	8.7% (1324)	10.6% (1335)	0.2045
A1c 8.1+	12.2% (1435)	11.9% (1415)	



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N Engl J Med. 2010;362:1563-74.

¿hay vida más allá de las estatinas?

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  - **Omega 3**
  - Inhibidores CETP
  - Otros

Original Article

n–3 Fatty Acids and Cardiovascular Events after Myocardial Infarction

Daan Kromhout, M.P.H., Ph.D., Erik J. Giltay, M.D., Ph.D., Johanna M. Geleijnse, Ph.D., for the Alpha Omega Trial Group

Study Overview

- In this clinical trial involving patients who had had an MI, supplementation with low doses of n–3 fatty acids in margarine did not have a significant effect on the risk of subsequent cardiovascular events.

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med
Volume 363(21):2015-2026
November 18, 2010

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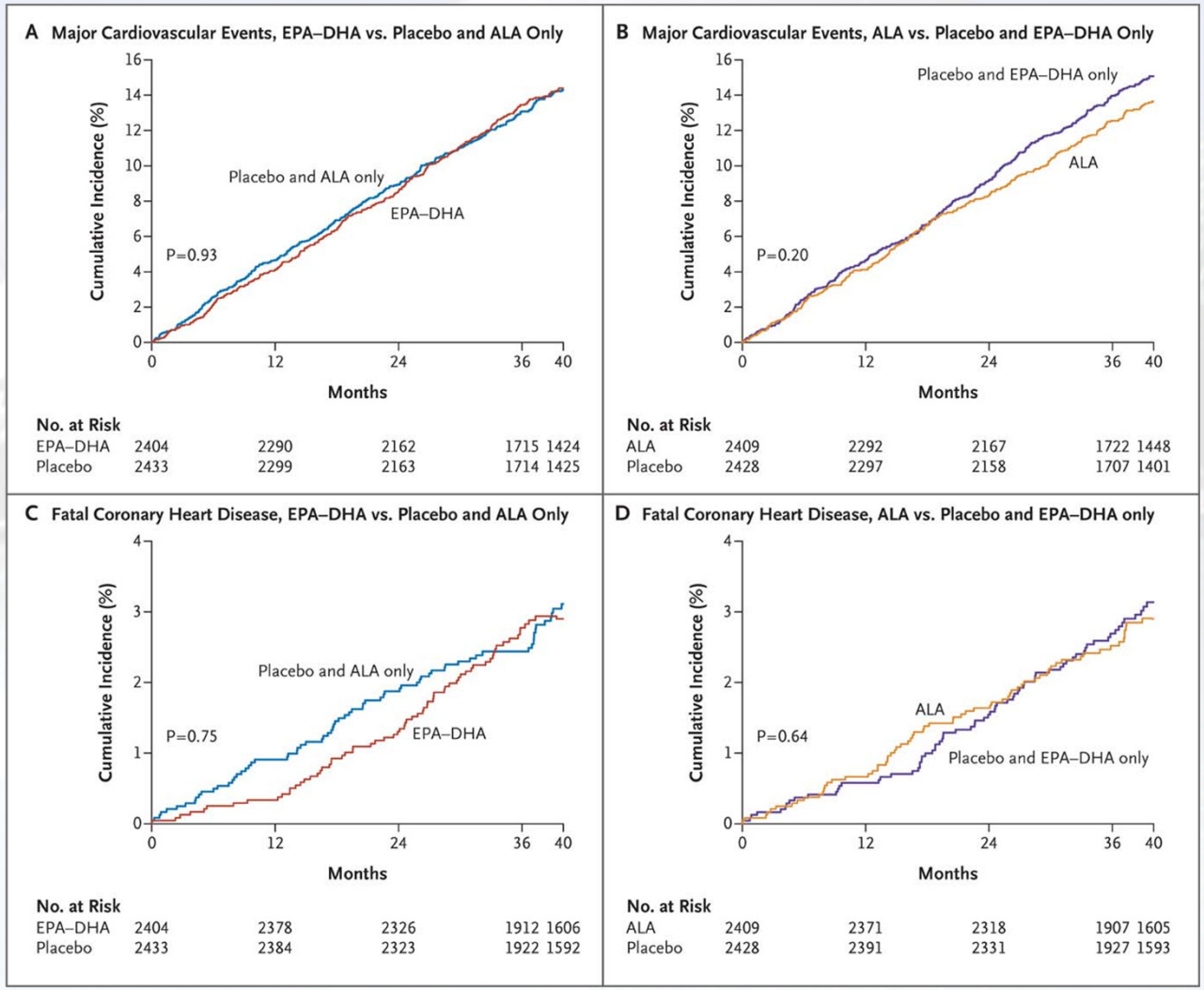
Kaplan–Meier Curves for Primary and Secondary End Points



Kromhout D et al. N Engl J Med 2010;363:2015-2026

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The NEW ENGLAND JOURNAL of MEDICINE

OMEGA, a Randomized, Placebo-Controlled Trial to Test the Effect of Highly Purified Omega-3 Fatty Acids on Top of Modern Guideline-Adjusted Therapy After Myocardial Infarction.

Rauch, Bernhard; Schiele, Rudolf; Schneider, Steffen; Diller, Frank; Victor, Norbert; Gohlke, Helmut; Gottwik, Martin; Steinbeck, Gerhard; Del Castillo, Ulrike; Sack, Rudolf; Worth, Heinrich; Katus, Hugo; Spitzer, Wilhelm; Sabin, Georg; Senges, Jochen

Circulation. 122(21):2152-2159, November 23, 2010.
DOI: 10.1161/CIRCULATIONAHA.110.948562

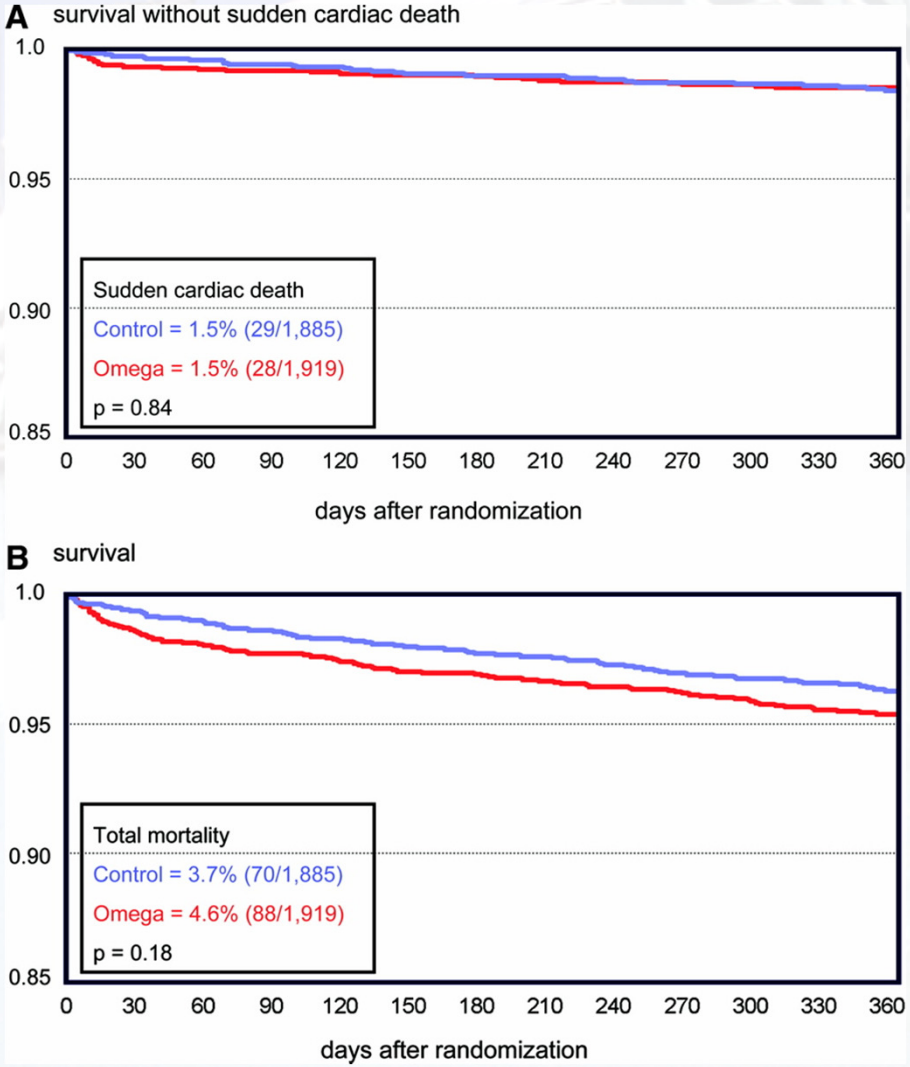

Figure 2. Kaplan-Meier diagrams (P values are those of the univariate analysis; see Table 4).

A, Survival without SCD during the 1-year follow-up (red line, omega group; blue line, control group).

B, Total survival during the 1-year follow-up (red line, omega group; blue line, control group).

¿hay vida más allá de las estatinas?

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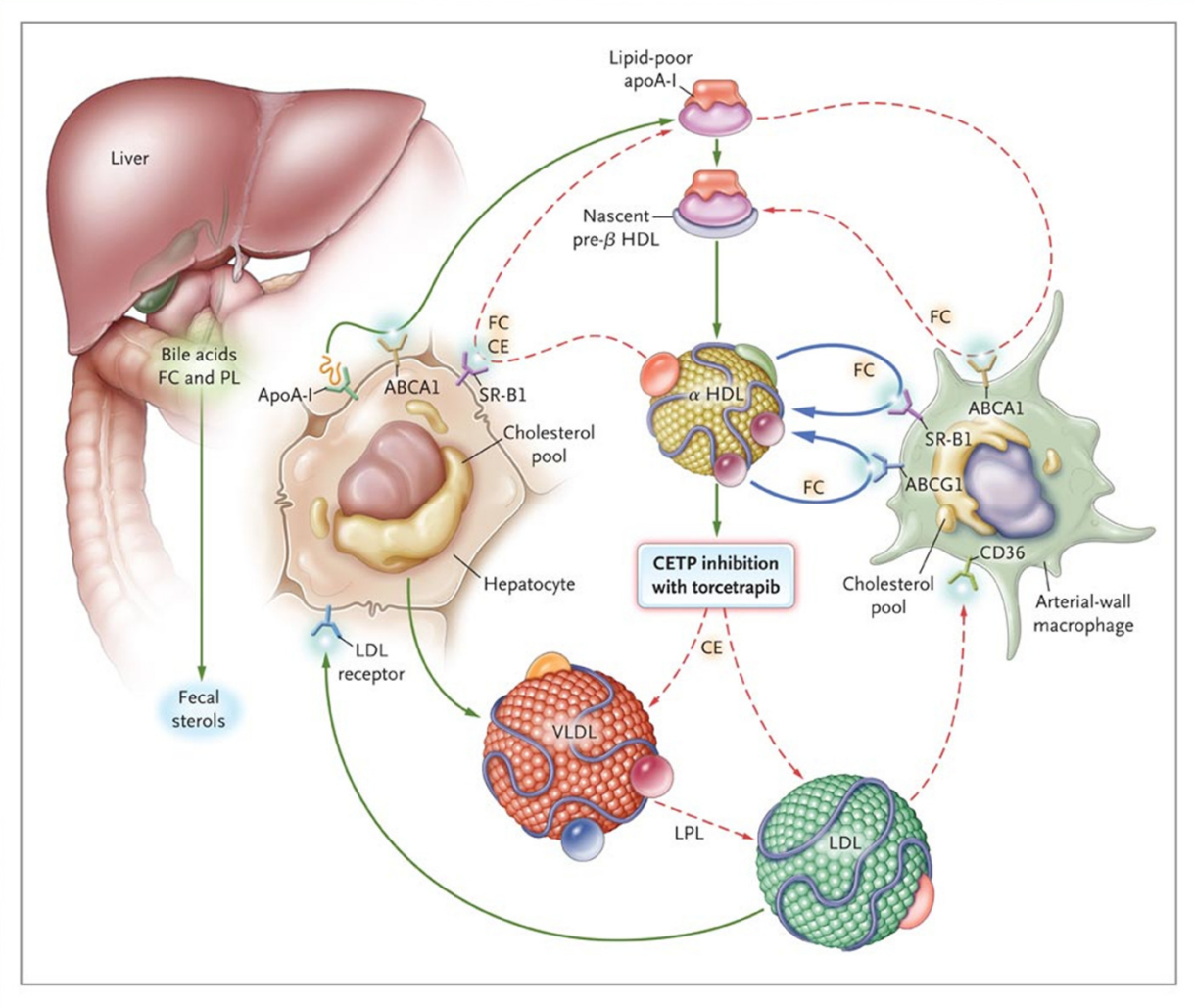
  - Omega 3
  - **Inhibidores CETP**
  - Otros

Schematic Representation of the Metabolism of HDL Cholesterol



Nissen SE et al. N Engl J Med 2007;356:1304-1316

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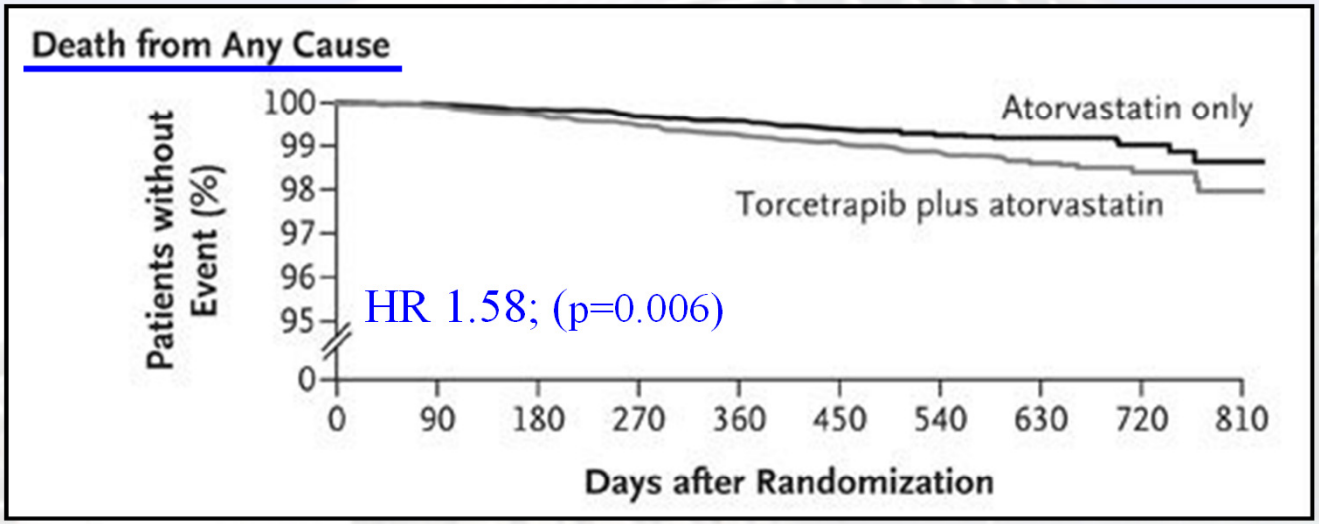
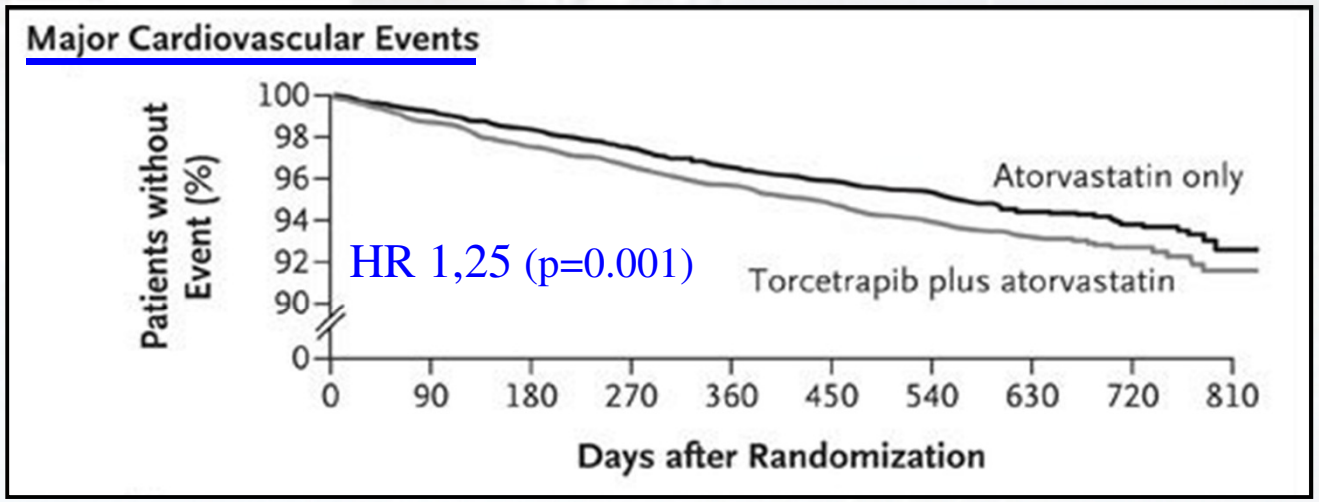
ILLUMINATE

Kaplan-Meier Curves for Death from Any Cause and for the Primary Composite Outcome

Kaplan-Meier Curves for Death from Any Cause and for the Primary Composite Outcome





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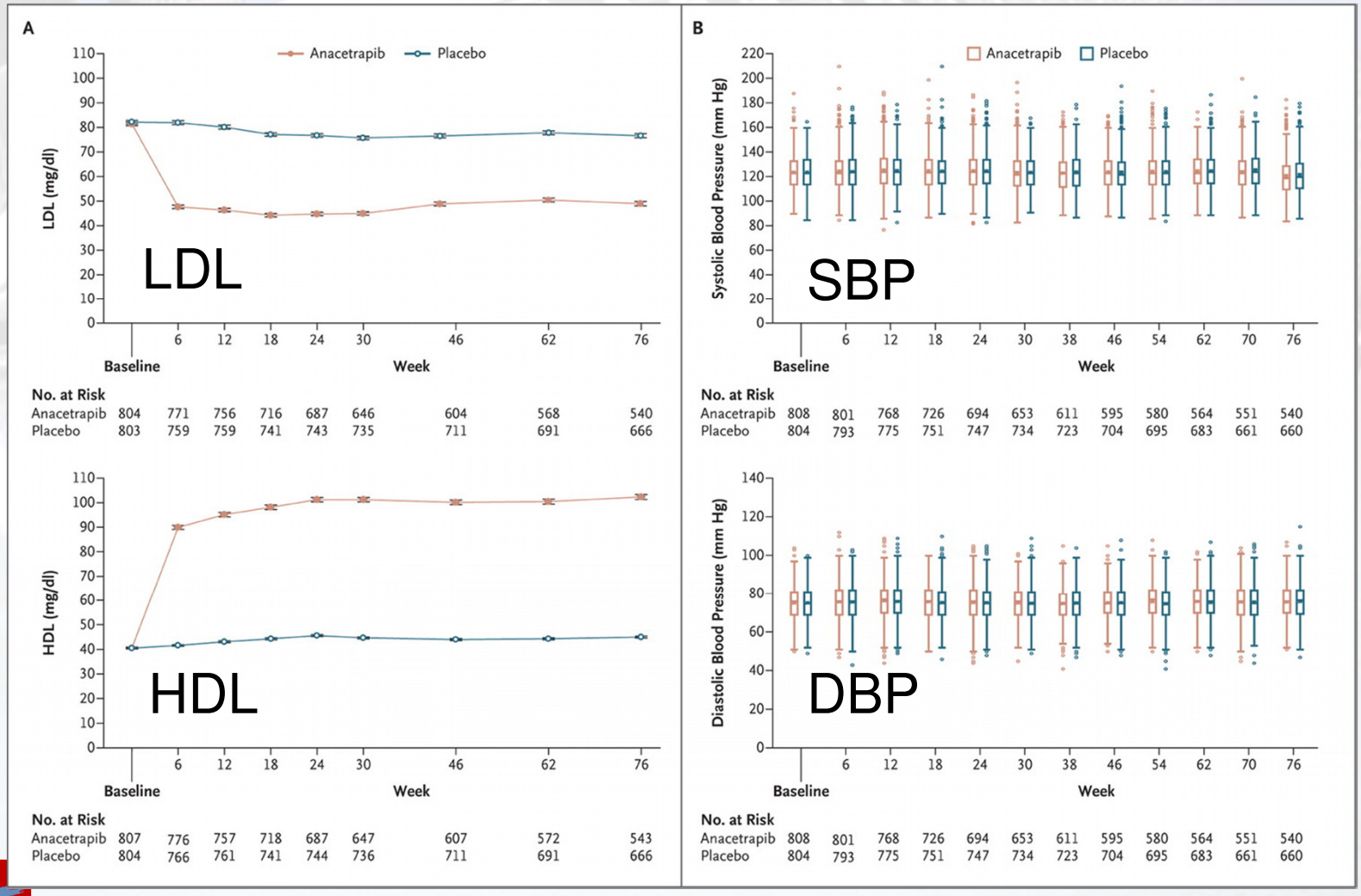
The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2007;357:2109-2122

CGH 2010

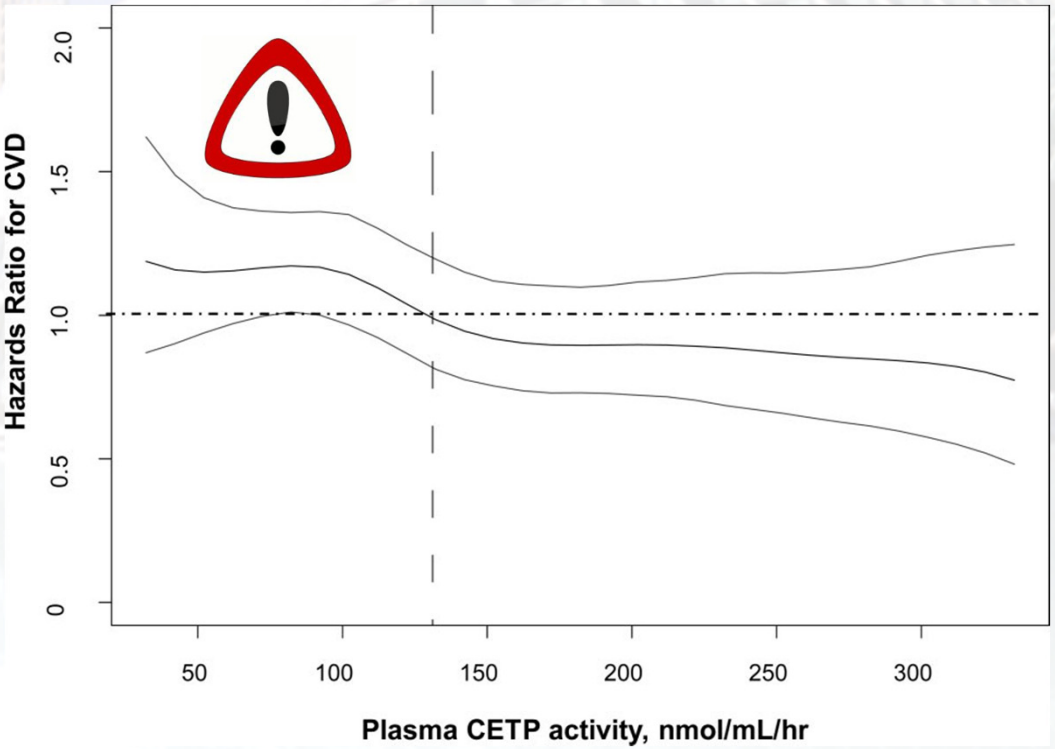
Original Article

Safety of Anacetrapib in Patients with or at High Risk for Coronary Heart Disease



N Engl J Med 2010; 363:2406-2415

Association of Circulating CETP Activity With Incidence of Cardiovascular Disease



Conclusions—

[…] **lower plasma CETP** activity was associated with **greater CVD risk**.

These observations, challenge the concept that CETP inhibition may lower CVD risk.

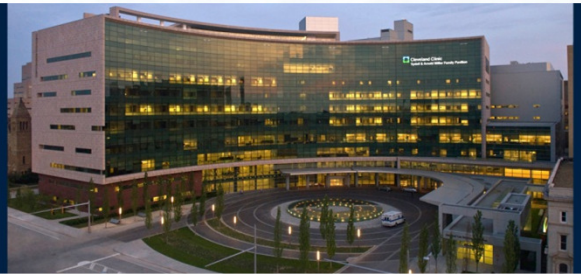
Circulation. 120(24):2414-2420, December 15, 2009.
DOI: 10.1161/CIRCULATIONAHA.109.87270

Results of the First Major Clinical Trial of An Oral Agent Inducing ApoA-I Synthesis: A New Approach to Raising HDL and CV Risk Modification

The ASSERT Study

SJ Nicholls, CM Ballantyne, JJP Kastelein, A Taylor, A Gordon, J Johansson, K Wolski, M Borgman and SE Nissen

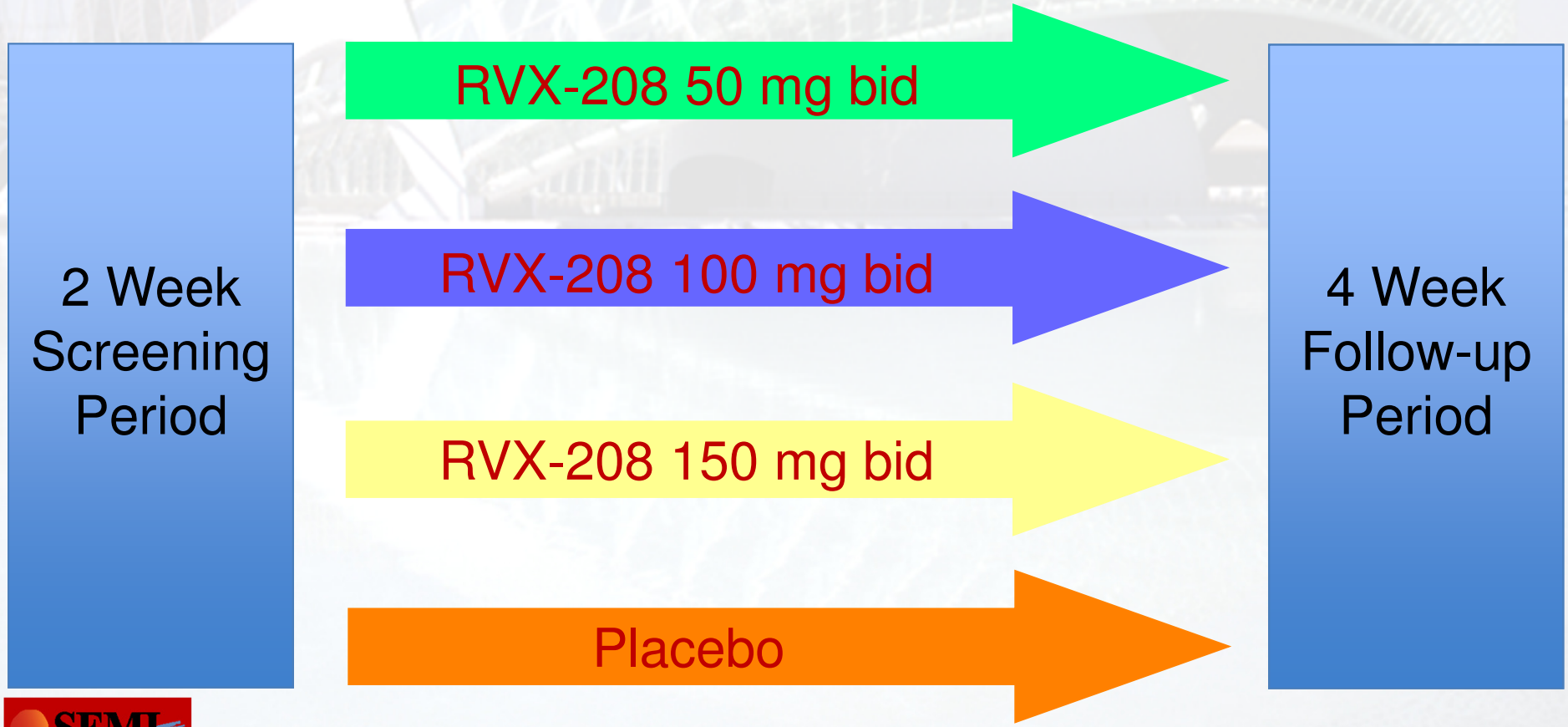
Cleveland Clinic
Heart & Vascular Institute



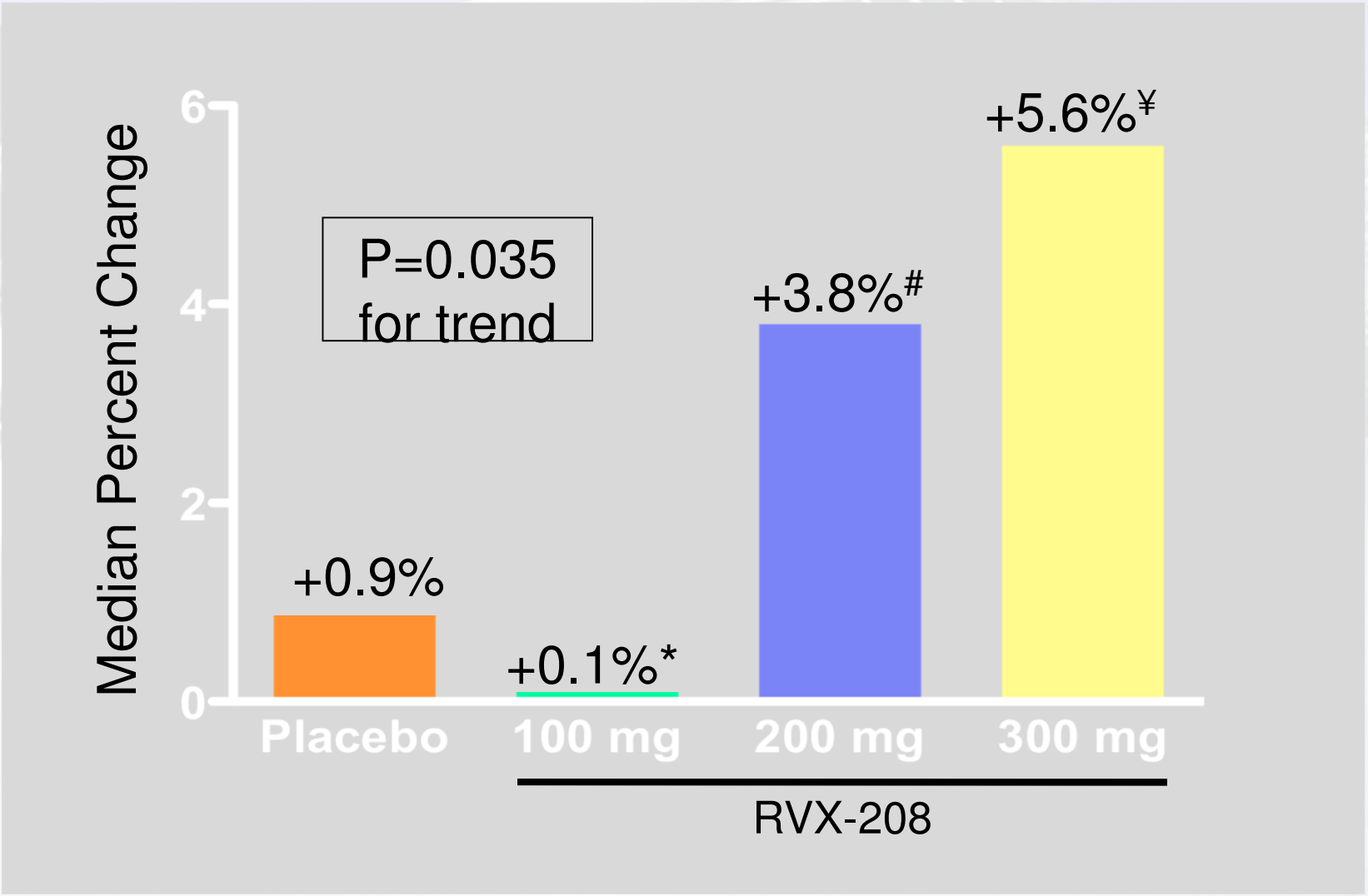
C5Research
Cleveland Clinic Coordinating Center for Clinical Research

ASSERT Study Design

299 Statin-Treated Patients with Stable Coronary Artery Disease at 35 sites in the US



Median Change in ApoA-I from Baseline

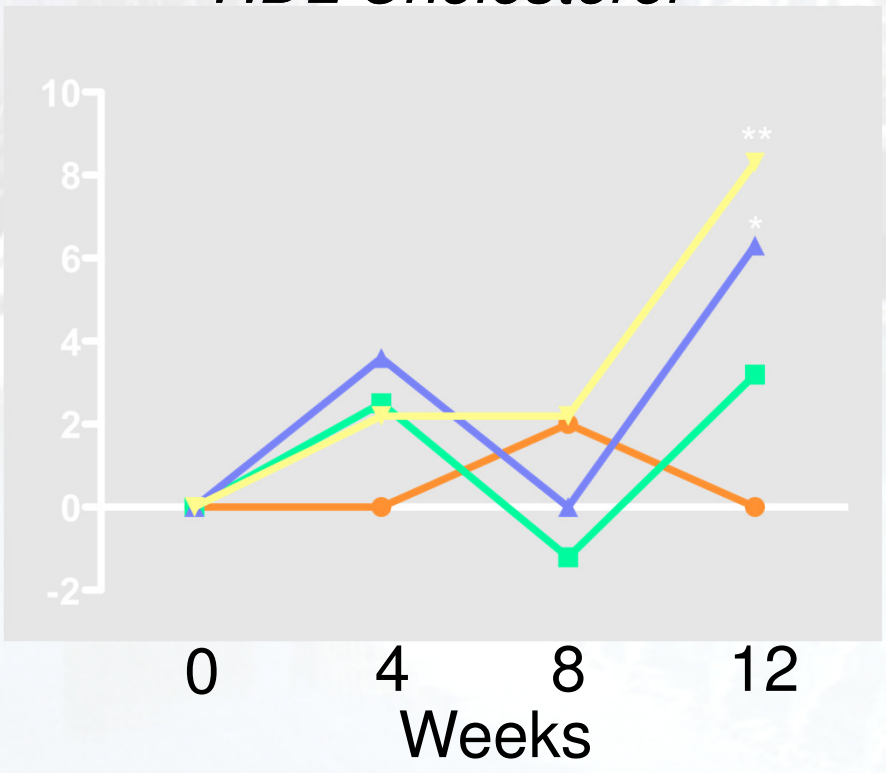


*P=0.09, #P=0.10 and ¥P=0.06 compared with placebo

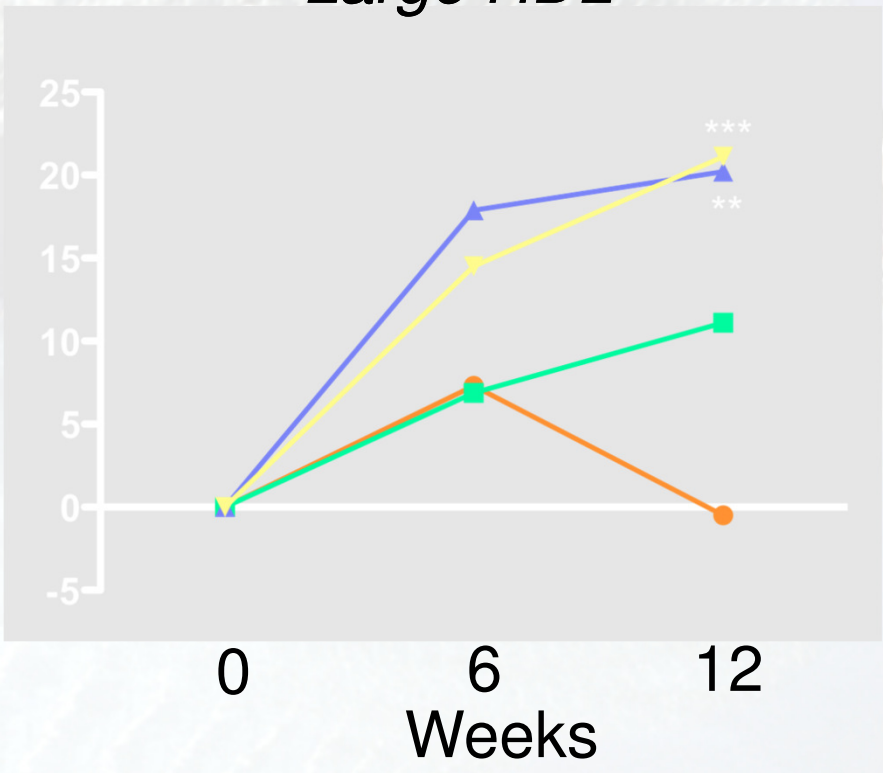
Timing of Increase in HDL Measures

Median Percentage Change from Baseline

HDL Cholesterol



Large HDL



Placebo RVX 100 mg RVX 200 mg RVX 300 mg

* P<0.05, ** P<0.01 and *** P<0.001 compared with placebo

Mipomersen, an apolipoprotein B synthesis inhibitor, for lowering of LDL cholesterol concentrations in patients with homozygous familial hypercholesterolaemia: a randomised, double-blind, placebo-controlled trial

- 51 Pacientes con HF homozigota
- Dosis máxima de estatinas
- Asignación aleatoria a mipopersen SC vs placebo
  - Oligonucleótido antisentido
  - Degradación de ARNm Apo B
  - Inhibidor de síntesis de ApoB

Lancet 2010; 375: 998–1006

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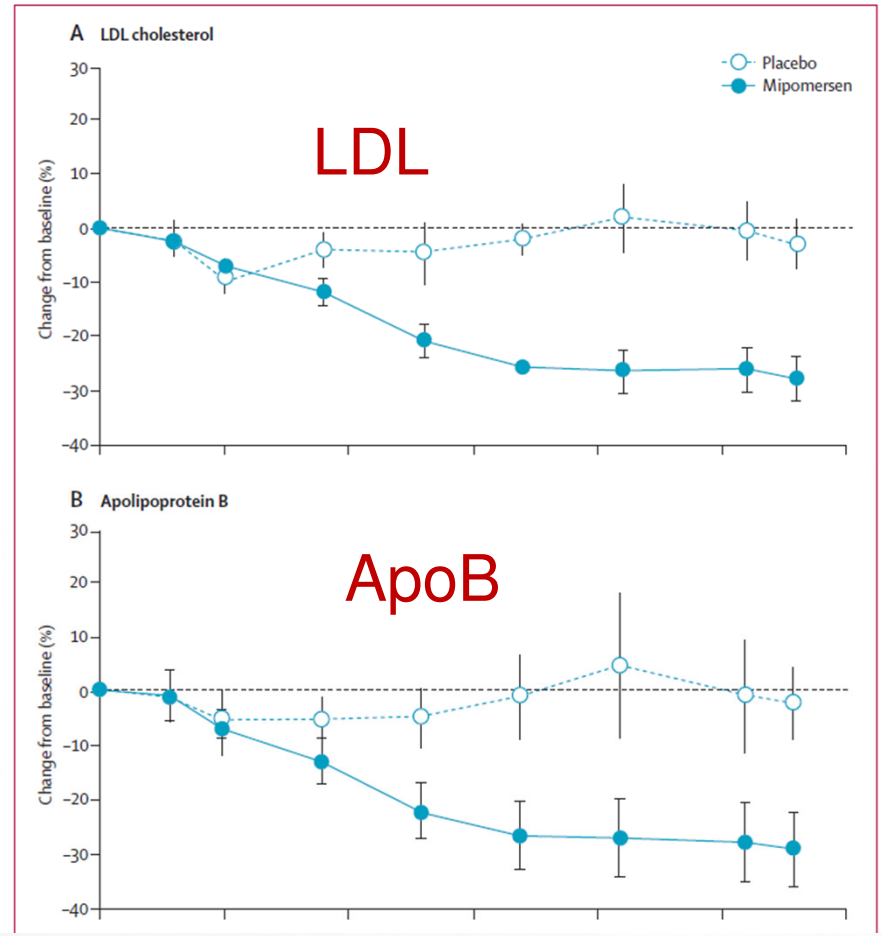

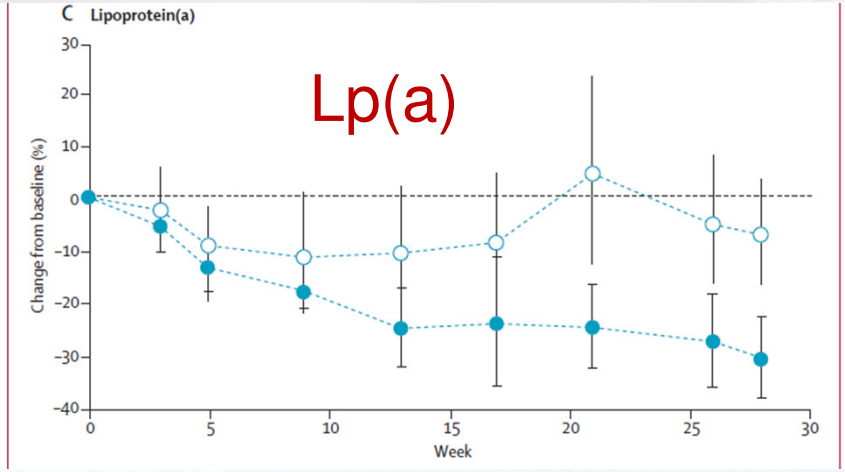

Lancet 2010; 375: 998–1006

Original Article

Use of the Thyroid Hormone Analogue Eprotirome in Statin-Treated Dyslipidemia

Paul W. Ladenson, M.D., Jens D. Kristensen, M.D., Ph.D., E. Chester Ridgway, M.D., Anders G. Olsson, M.D., Ph.D., Bo Carlsson, M.Sc., Irwin Klein, M.D., John D. Baxter, M.D., and Bo Angelin, M.D., Ph.D.

- Randomized, placebo-controlled, double-blind, multicenter trial
- Eprotirome (thyromimetic)
  - safety and efficacy
  - lowering LDL (on statin therapy)
- Eprotirome was associated with decreased LDL levels in patients treated with statins

N Engl J Med
Volume 362(10):906-916
March 11, 2010

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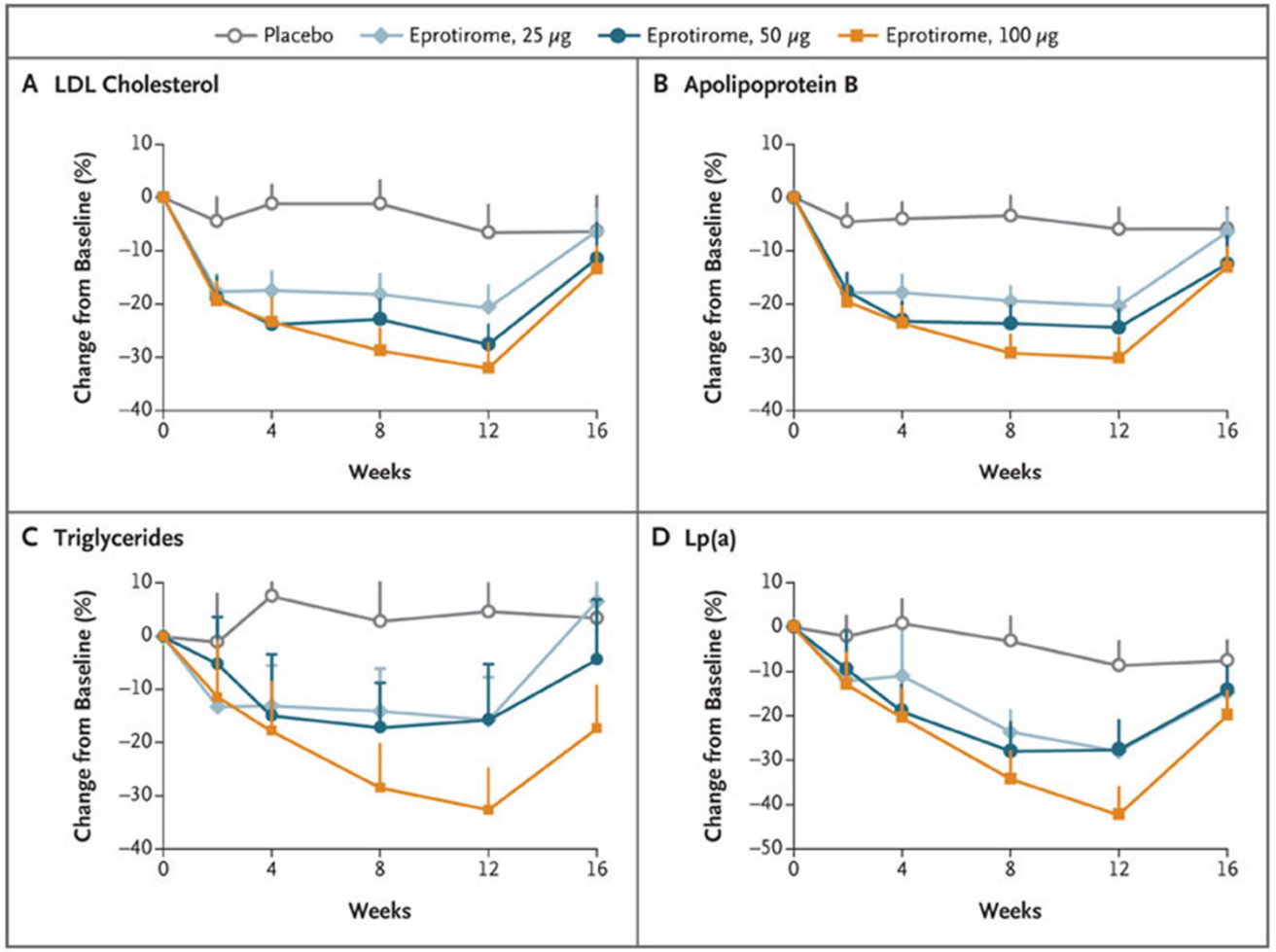
The NEW ENGLAND JOURNAL of MEDICINE

Effects of Eprotirome on Serum Levels of Cholesterol, Lipoproteins, and Triglycerides

LDL

ApoB



TG

Lp(a)

Ladenson PW et al. N Engl J Med 2010;362:906-916

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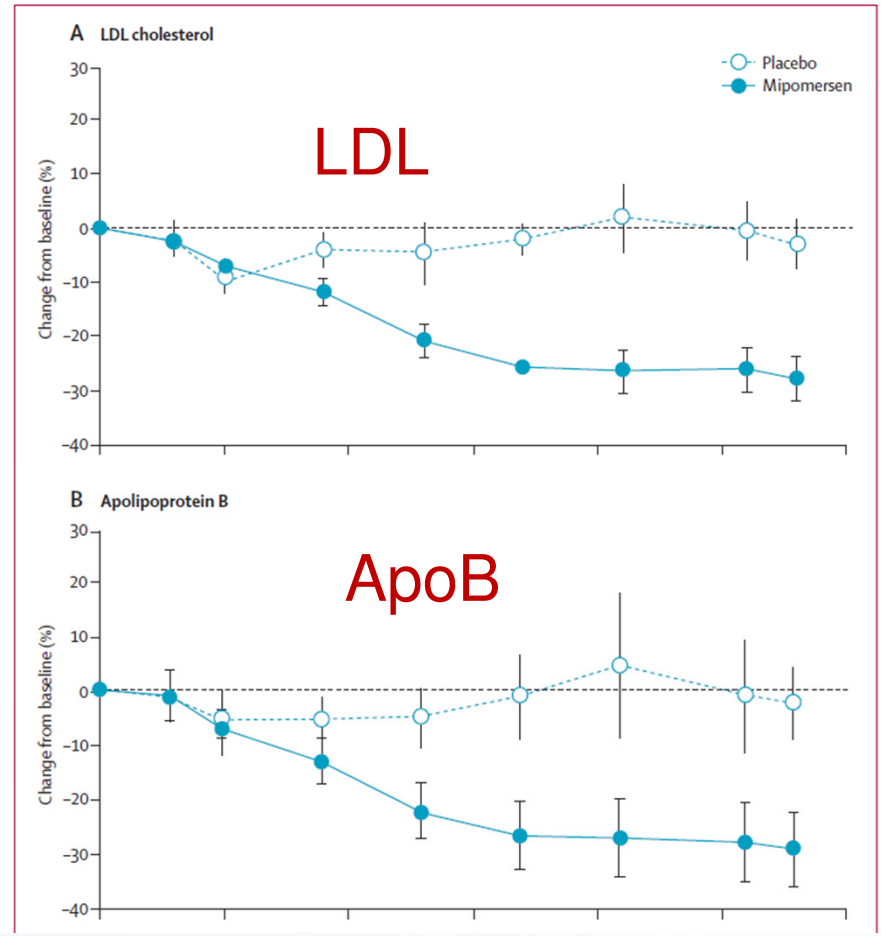

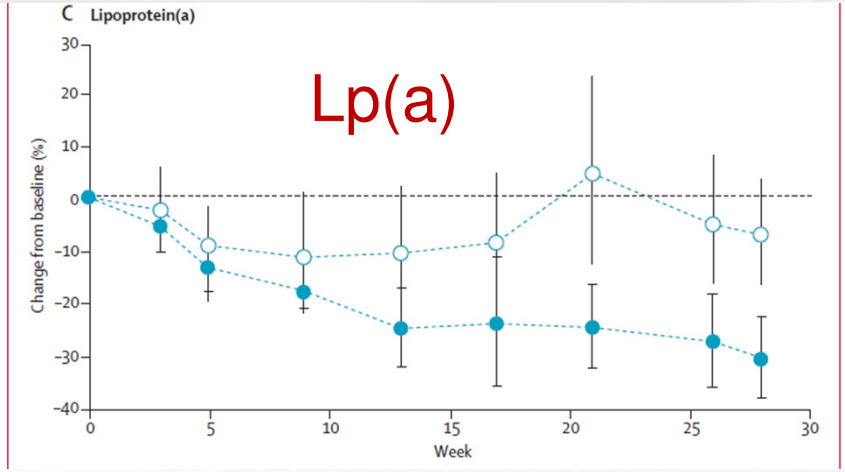

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Gracias

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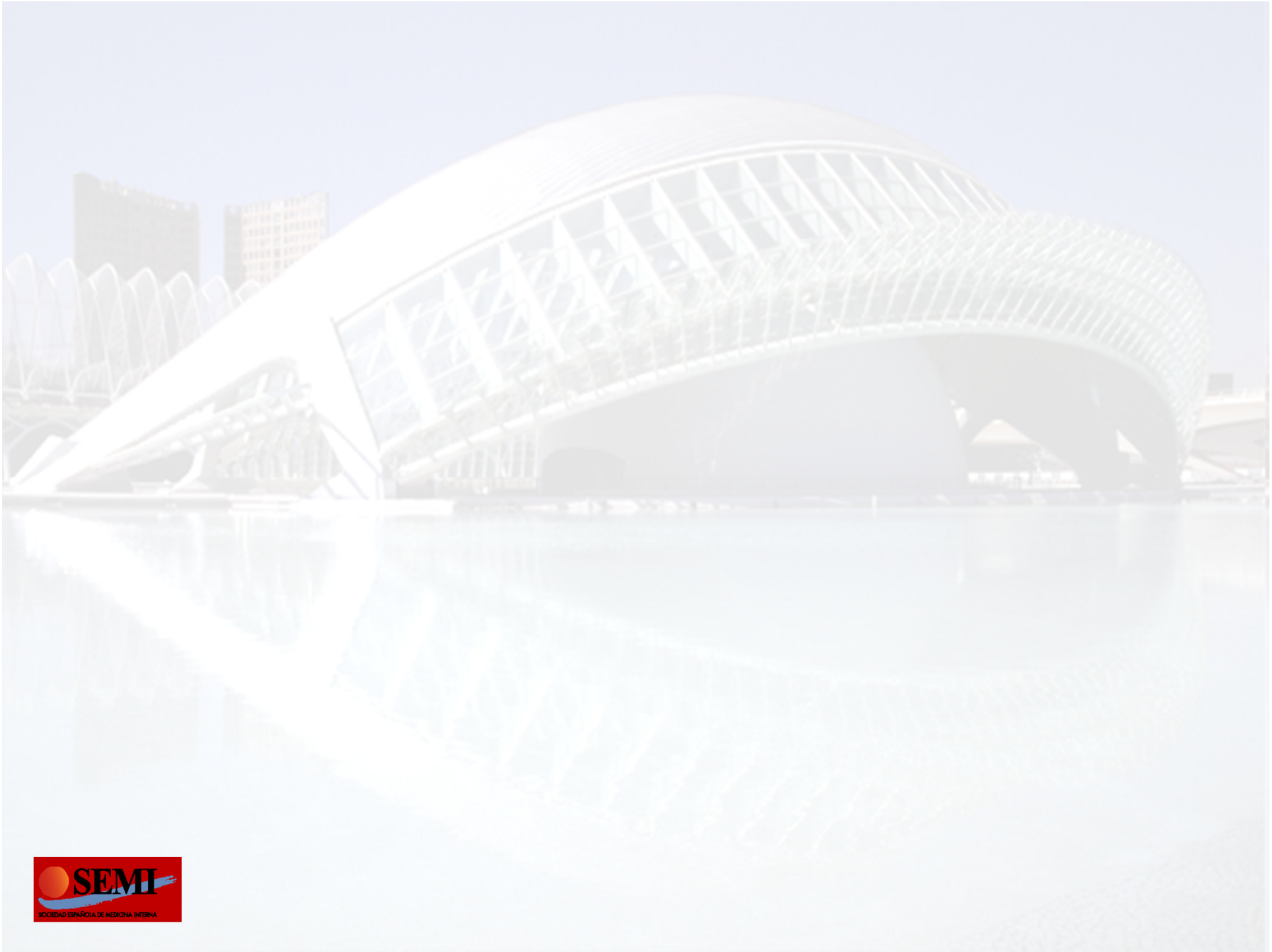

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