

Case Presentation

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Case Presentation

- 50 YO man
- NSTEMI treated with PCI 1 month ago
- Medical History:
 - Obesity: BMI 32, waist circumference 110 cm
 - HTN: well controlled with ACE-I and β -blocker
 - IFG (fasting glucose 108 mg/dL, HbA1c 6.3%)
 - Dyslipidemia treated with simvastatin 20 mg

Case Presentation

- Lipid profile
 - TC 188 mg/dL
 - LDL 90 mg/dL
 - HDL 34 mg/dL
 - TG 320 mg/dL
- CK, GOT, GPT normal. No myalgia.

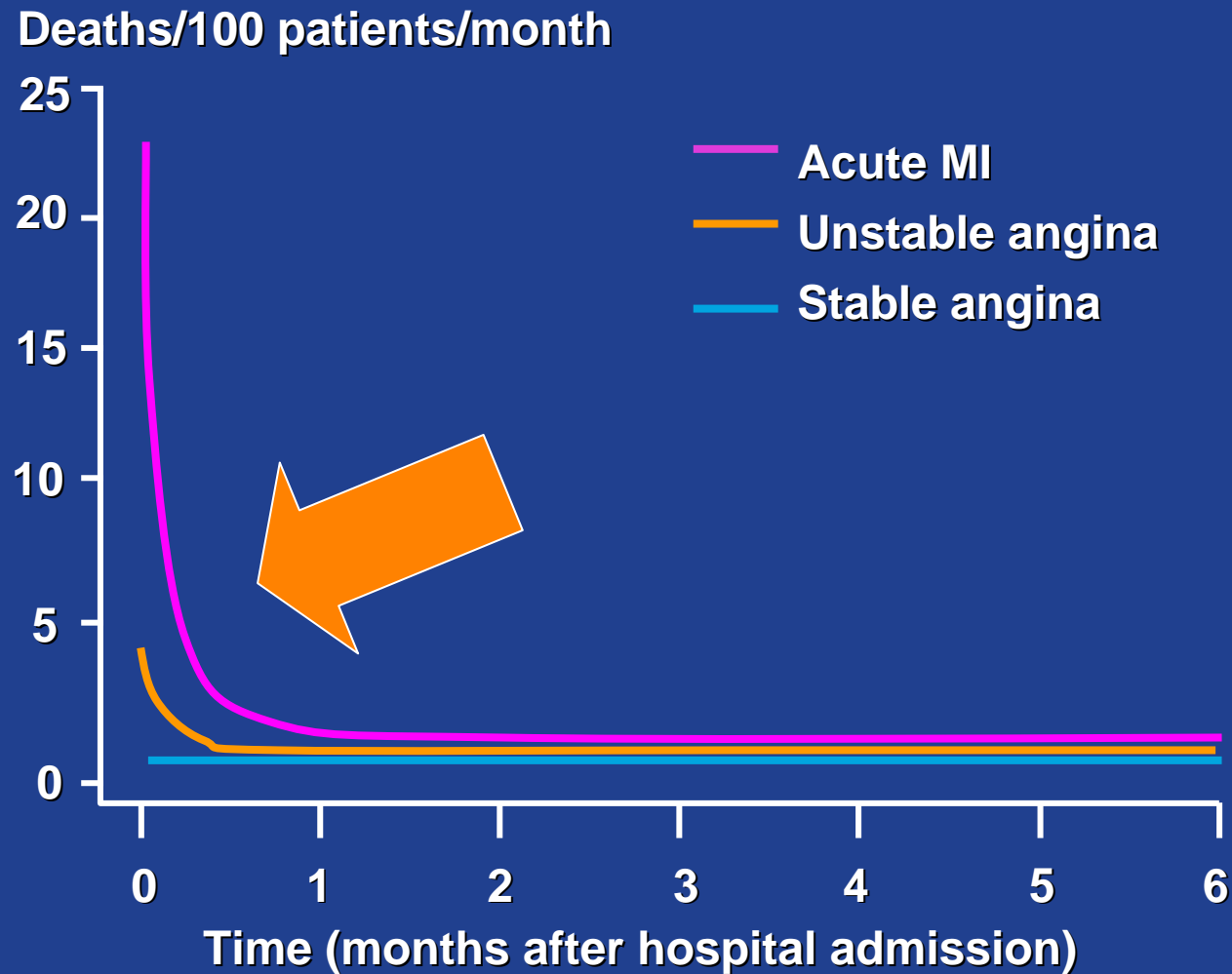
Case Presentation

- Treatment options (+TLC)
 - Atorvastatin 80 mg instead of simva
 - Add fibrate
 - Add niacin ER
 - Add Omega 3

מה תציעו וכן?
תפק?

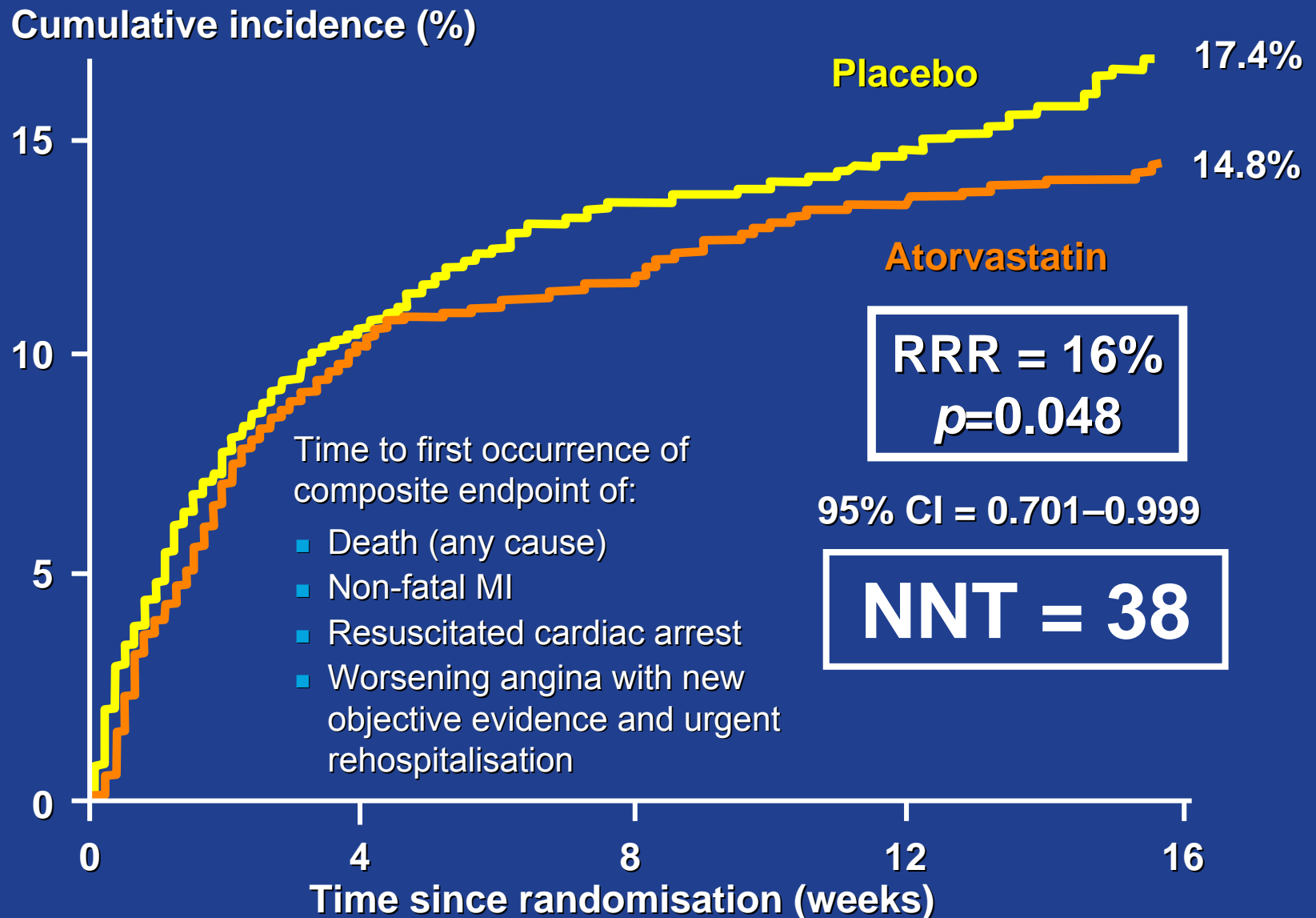


Risk of death in patients with CHD is greatest *early* after an ACS



Braunwald (1996)

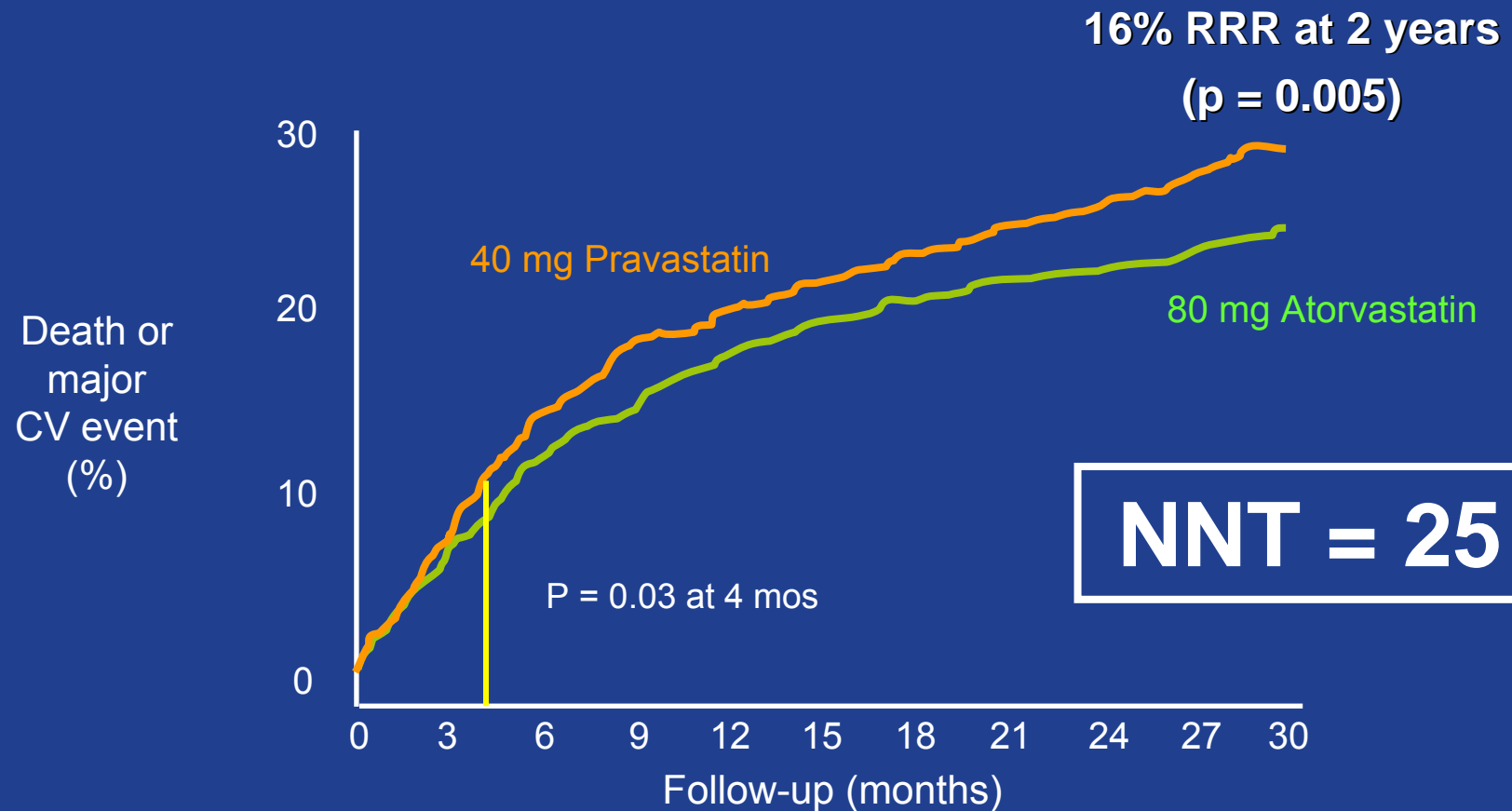
MIRACL: Primary efficacy measure



JAMA. 2001;285:1711

PROVE IT-TIMI 22: Early benefit with intensive lipid lowering

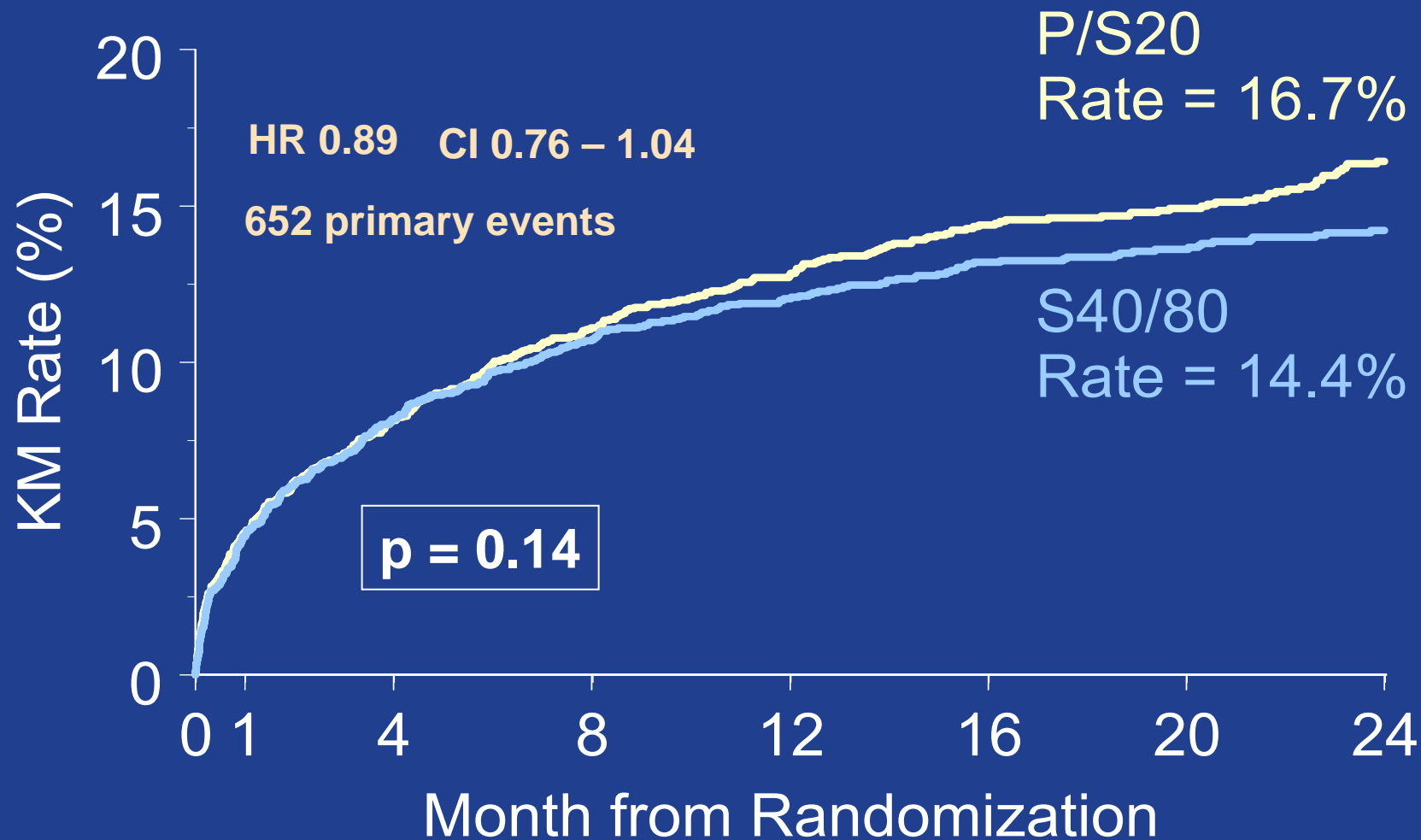
N = 4162 with ACS



Ray KK and Cannon CP *Am J Cardiol.* 2005;96(suppl):54F-60F.
Adapted from Cannon CP et al. *N Engl J Med.* 2004;350:1495-504.

A to Z: Primary Endpoint

Composite CV Death, MI, ACS or Stroke



JAMA. 2004;292:1307

CRP - EFFECT ONLY IN ACS?

LDL-C, CRP, and Early Clinical Benefit in A to Z, MIRACL, and PROVE IT-TIMI 22

	A-to-Z	MIRACL	PROVE IT
Number of patients randomized	4497	3086	4162
Early* LDL achieved on treatment, mg/dL	62	72	62
Early* LDL cholesterol differential, mg/dL	62	63	33
CRP differential, %	0/17	34	38
Early event reduction, %	0*	16*	18†

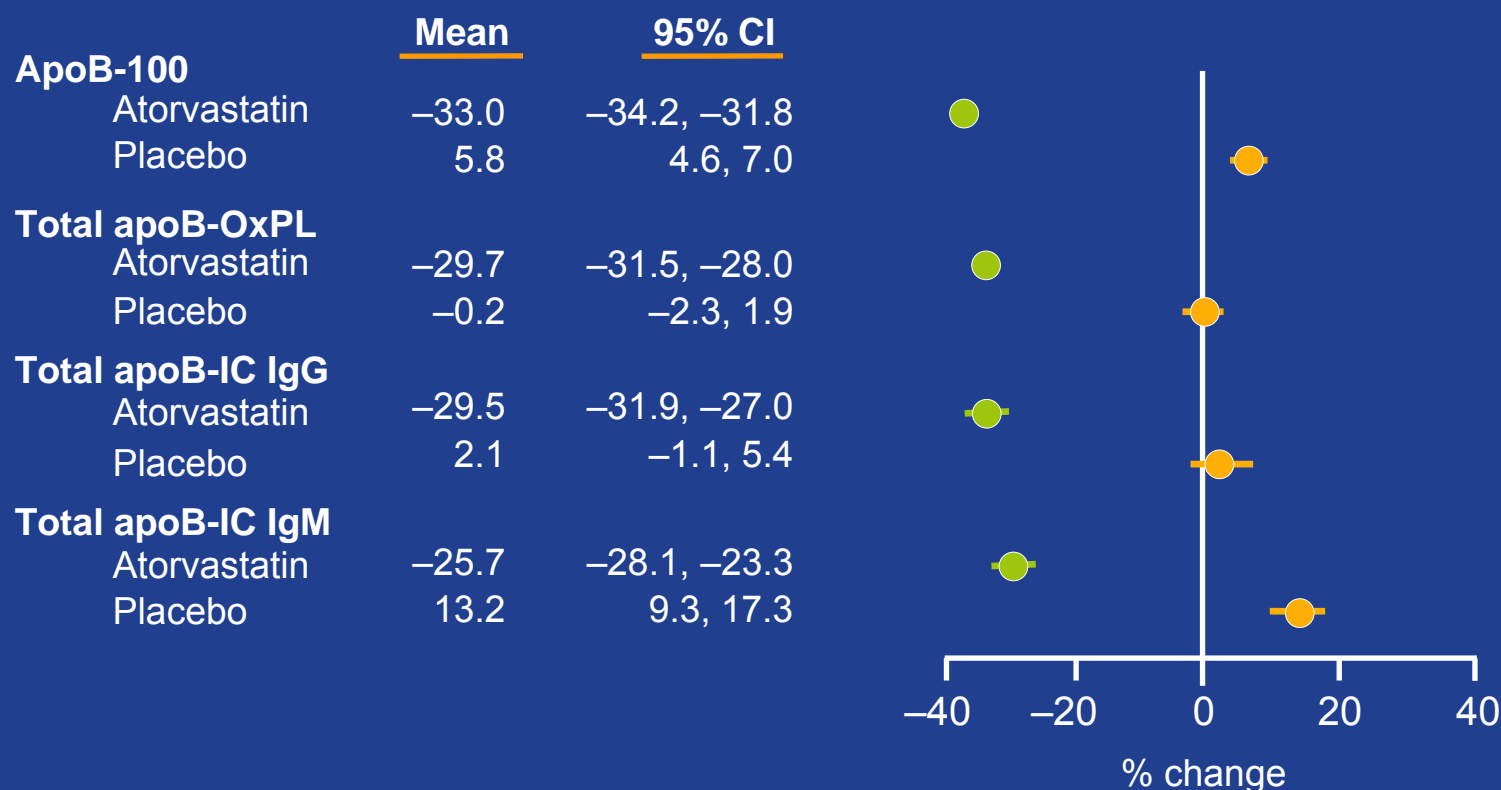
* Measured 120 days after randomization.

† Measured 90 days after randomization.

Adapted from Nissen. *JAMA*. 2004;292:1365, with permission.

High-Dose Statin Treatment Reduces Ox-LDL Markers

MIRACL study subgroup analysis, N = 2341 with ACS, atorvastatin 80 mg for 16 weeks



OxPL = oxidized phospholipids

IC-IgG, -IgM = immune complexes with IgG and IgM, respectively

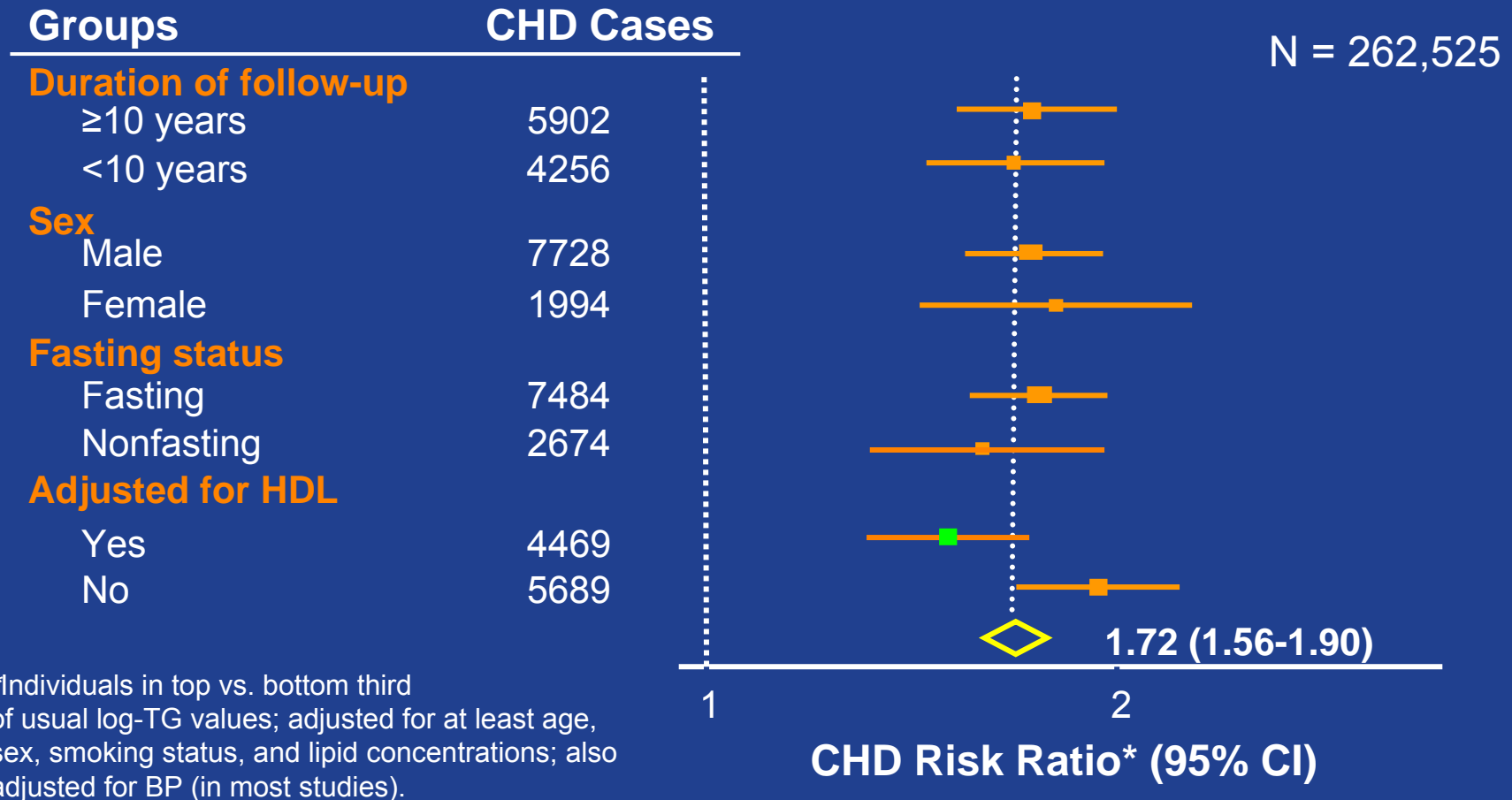
Myocardal Ischemia Reduction with Aggressive Cholesterol Lowering

Tsimikas S et al.
Circulation. 2004;110:1406-12.

Case Presentation

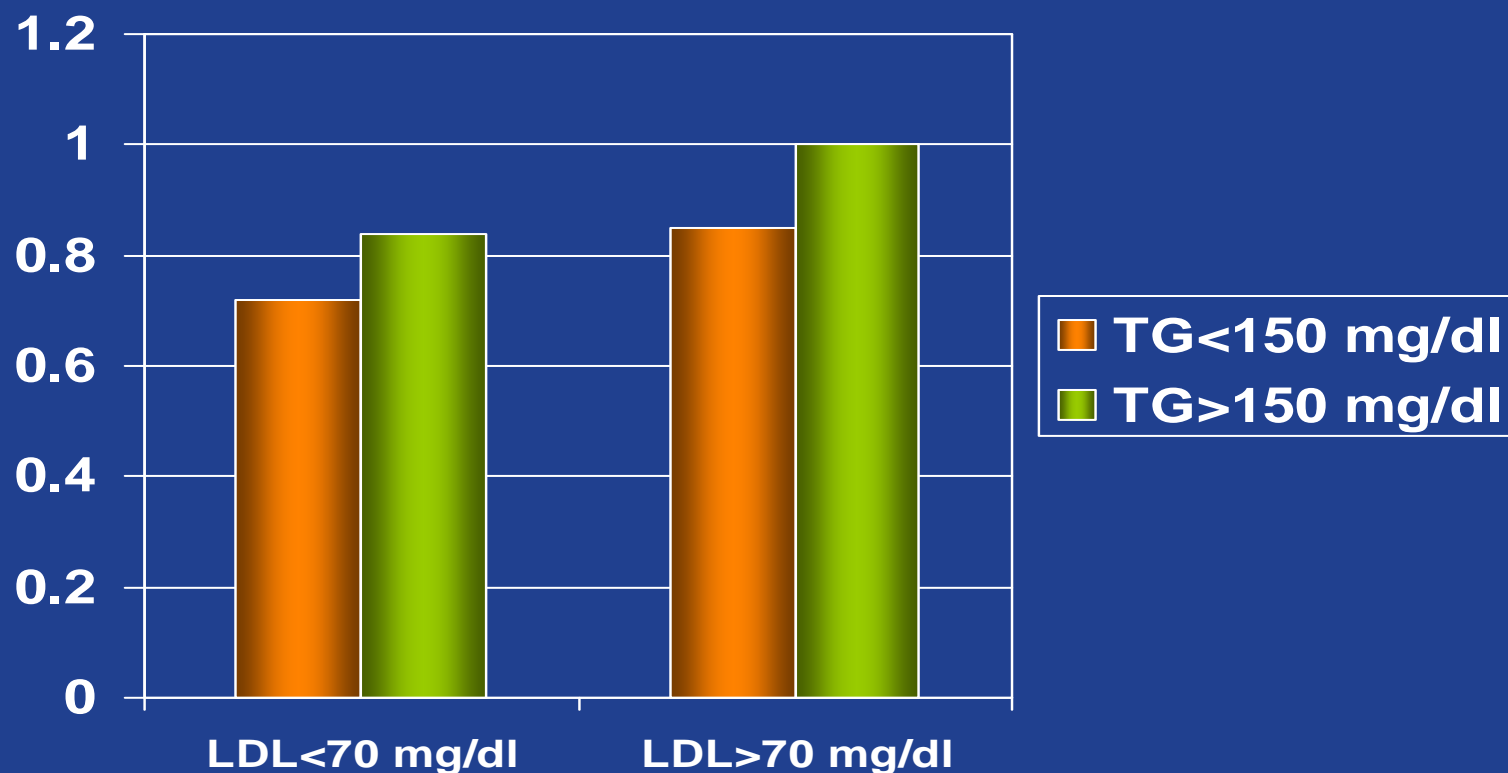
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TG Level Is Significant CVD Risk Factor: Meta-Analysis of 29 Studies



TG Level Remains CVD Risk Factor in Patients On Statins: TNT

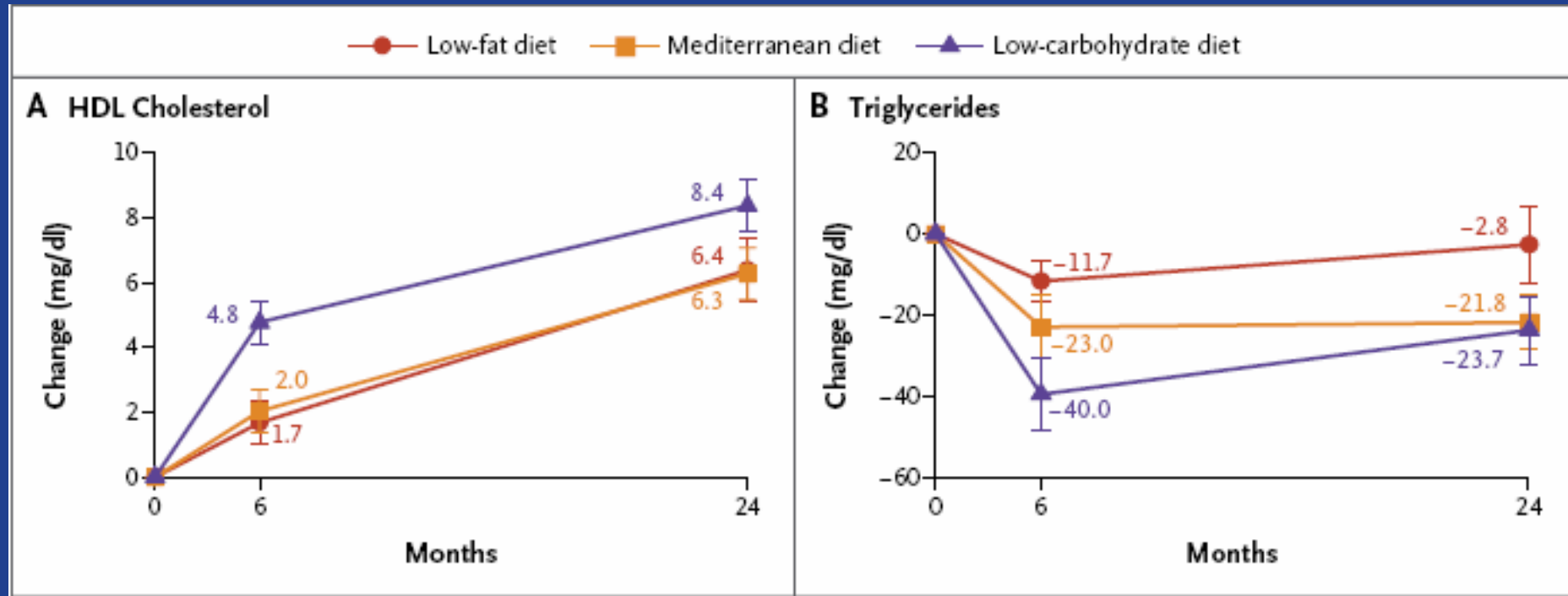
Adjusted HRs of death, MI, and recurrent ACS between 30 days and 2 years of follow-up*



*Adjusted for age, gender, low HDL-C, smoking, HTN, obesity, DM, prior statin therapy, prior ACS, PVD, treatment effect

JACC 2008;51:724–30

Diet for Metabolic Dyslipidemia



Outcomes in Fibrate Trials: *Diabetes / Metabolic Syndrome*

	Trial	N	Major CVD Event Rate		Rel. RR	P
			Control	Drug		
Primary Prevention						
HHS*		292	13.0%	3.9%	71%	.005
Secondary Prevention						
BIP†		1470	18.4%	14.1%	25%	.03
VA-HIT‡		769	29.4%	21.2%	32%	.004

Rel. RR indicates relative risk reduction

*Patients with triglycerides >204 mg/dL and an LDL/HDL >5

†Patients with the metabolic syndrome; baseline HDL-C, 33 mg/dL; triglycerides, 170 mg/dL

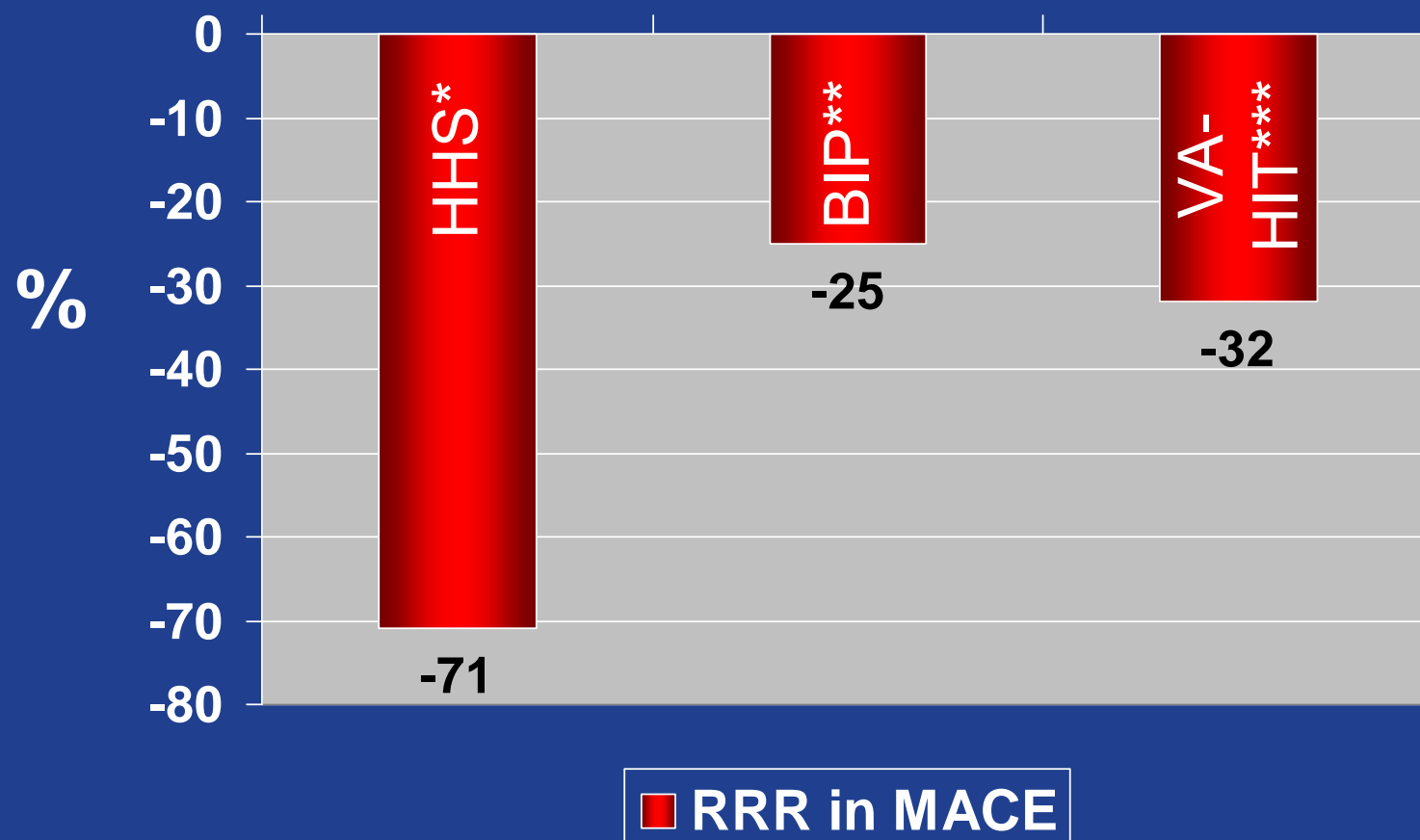
‡Patients with diabetes; baseline HDL-C, 31 mg/dL; triglycerides, 164 mg/dL

* *Circulation*. 1992;85:37-45.

† *Arch Intern Med*. 2005;165:1154-1160.

‡ *Arch Intern Med*. 2002;162:2597-2604.

Fibrate Trials: *Diabetic or Metabolic Syndrome Subanalyses*



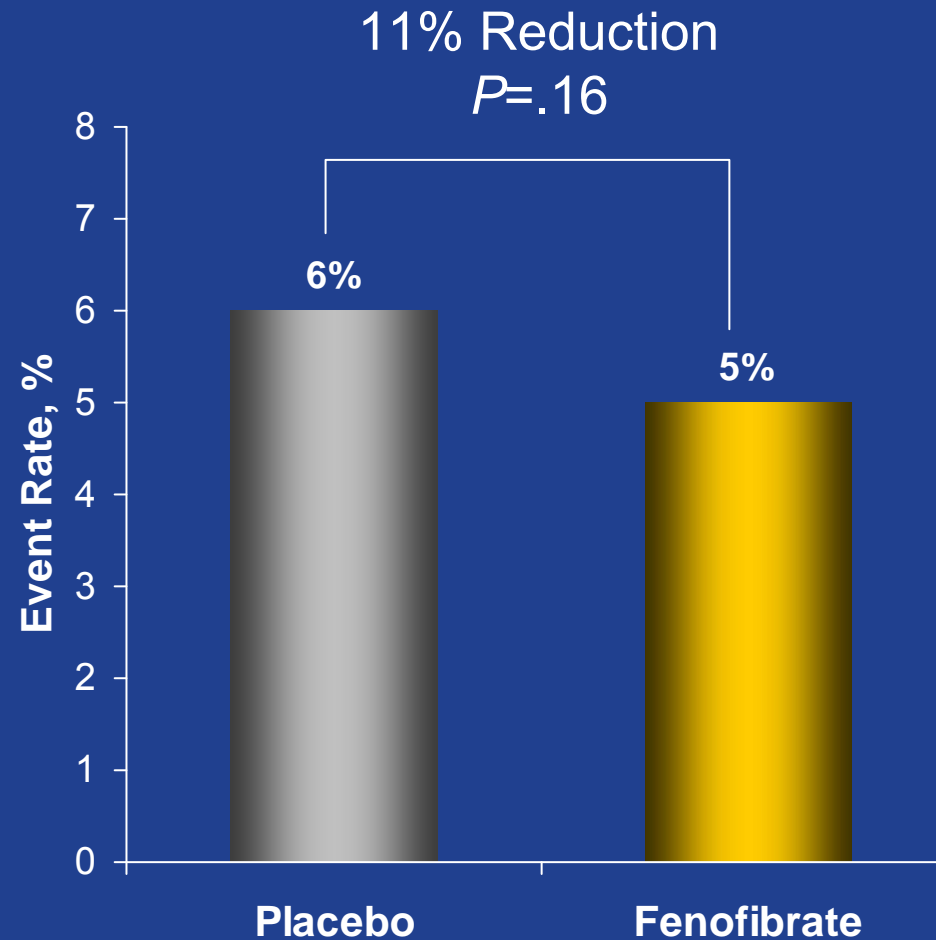
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FIELD: Primary End Point

Nonfatal MI, or CHD Death



Lancet. 2005;366:1849-1861

Fibrates: What's in Store?

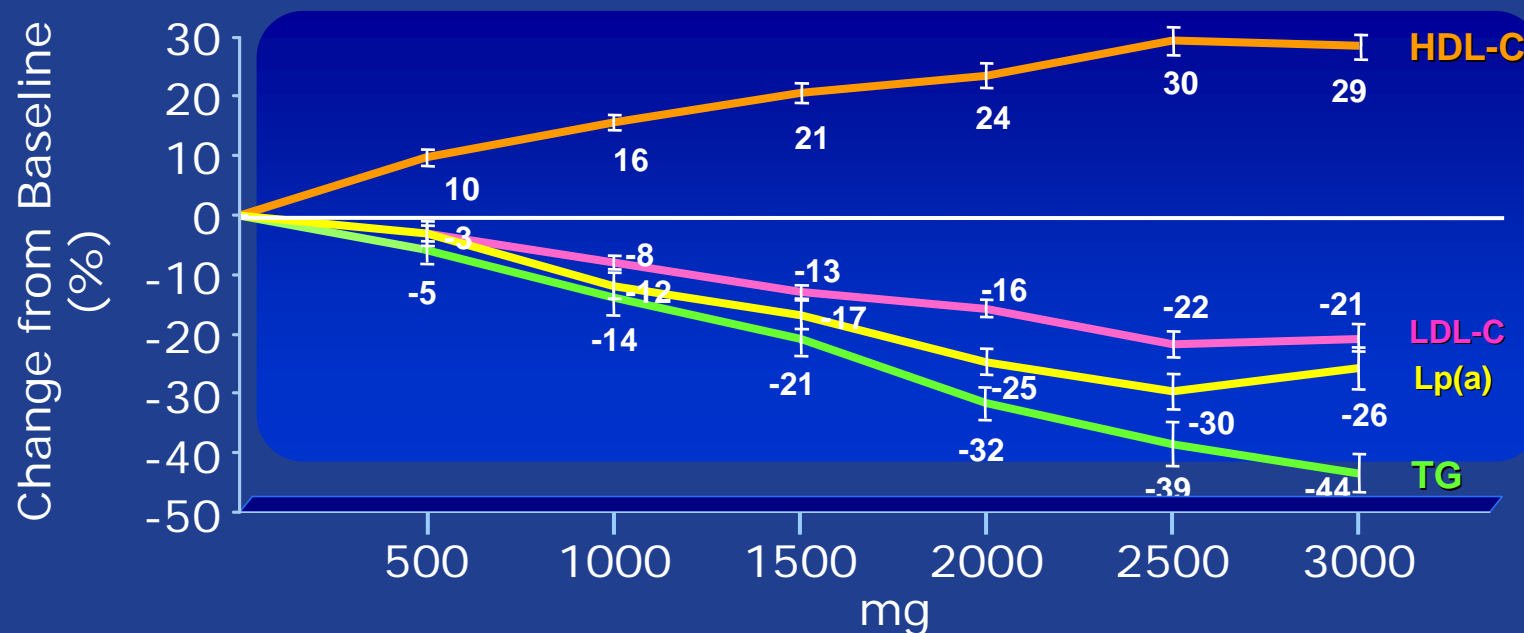
- **ACCORD:**

- Fenofibrate+statin vs. statin in 9750 patients with DM2
- Due 2011

Case Presentation

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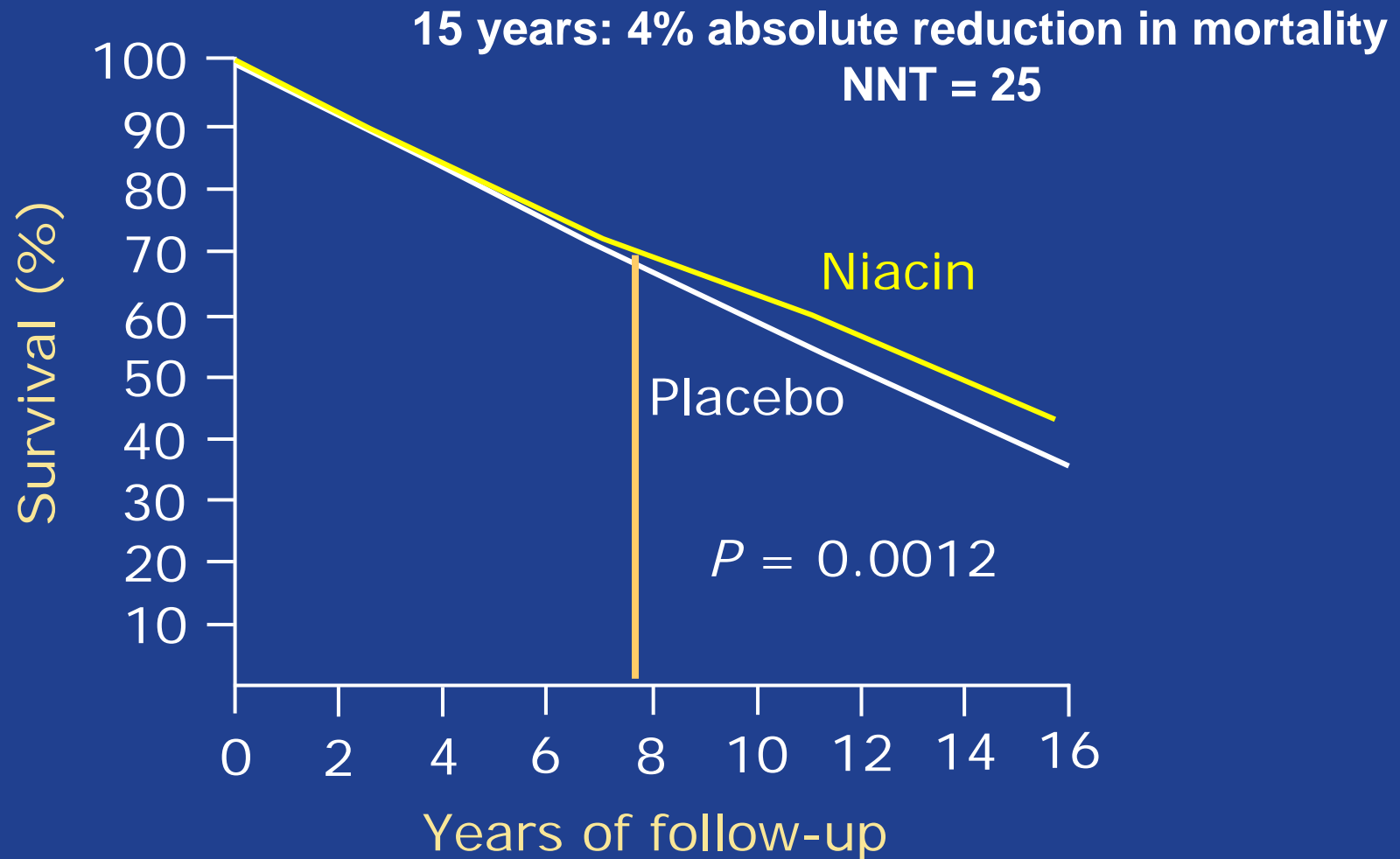
Lipid Effects of Niacin Extended-Release



- Most potent agent for ↑ HDL: 20%+; nonlinear
- Favorable effects on LDL-particle density
- ↓ LDL (linear), TG, and Lp(a)

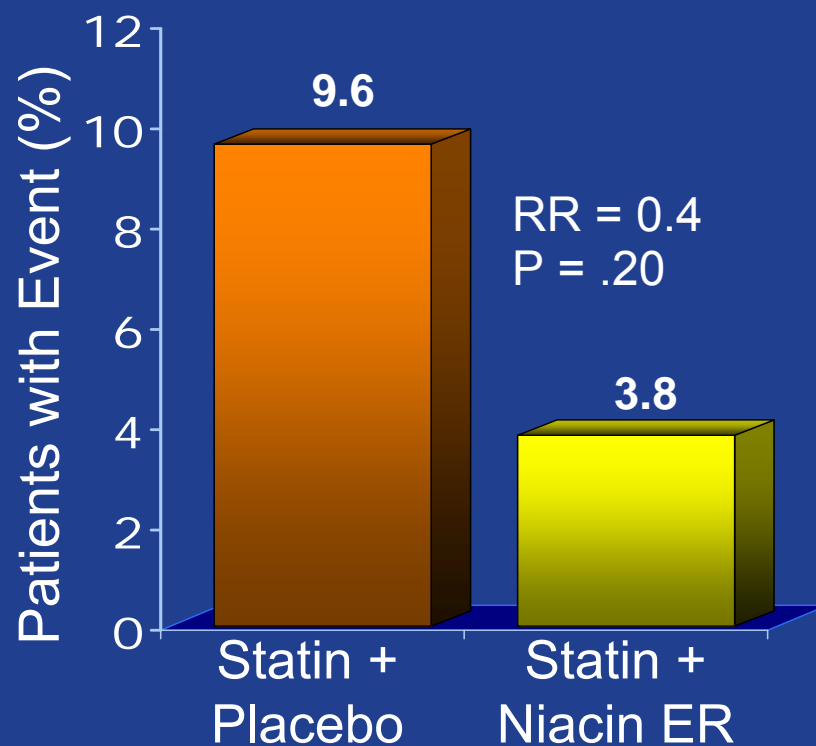
Coronary Drug Project

Long-Term Mortality Benefit of Niacin in Post-MI Patients



NIACIN: Clinical Events

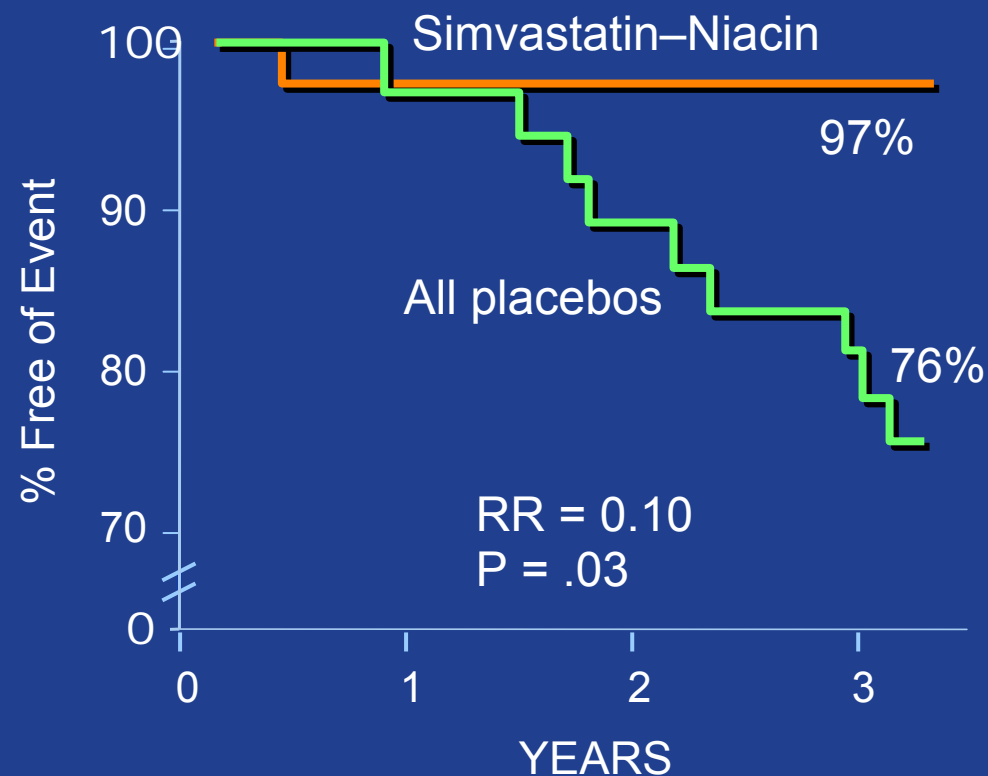
ARBITER 2



Composite End Point (MI, UAP, CVA, Sudden Death, Coronary or peripheral revascularization)

Circulation 2004;110:3512-3517.

HATS



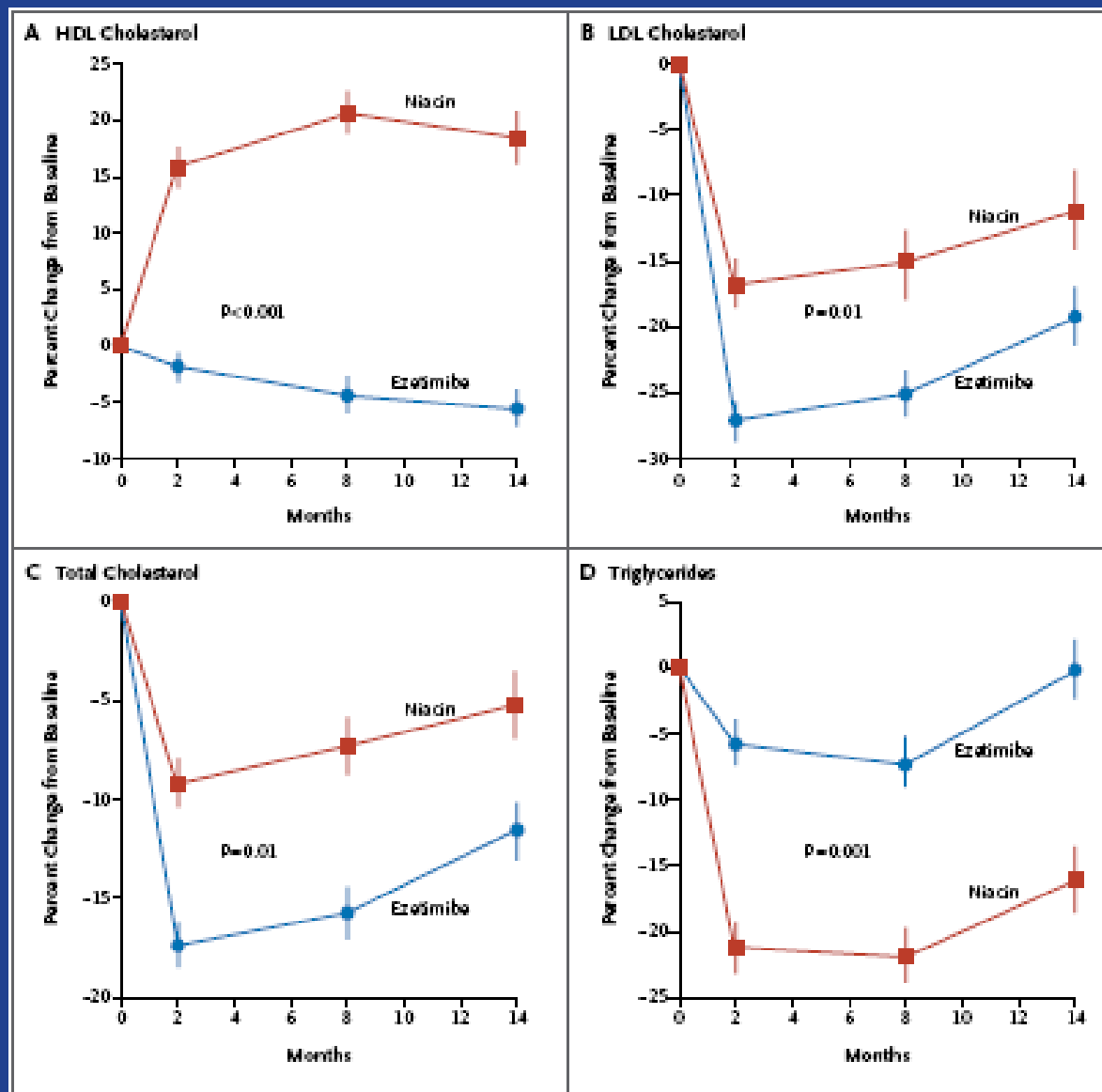
Composite End Point (Death from Coronary Causes, Nonfatal MI, Stroke, or Revascularization for Worsening Ischemia)

NEJM 2001;345:1583-1592

ARBITER-HALTS 6 Study

- 363 CHD/equivalent patients with low HDL-C (<50 mg/dl men, <55 mg/dl women)
 - All on statin with LDL-C < 100 mg/dl
- **Primary end point:** change in cIMT after 14 months
- The trial was terminated early, on the basis of efficacy

ARBITER-HALTS 6 study



Lipids with
niacin (mg/dL)

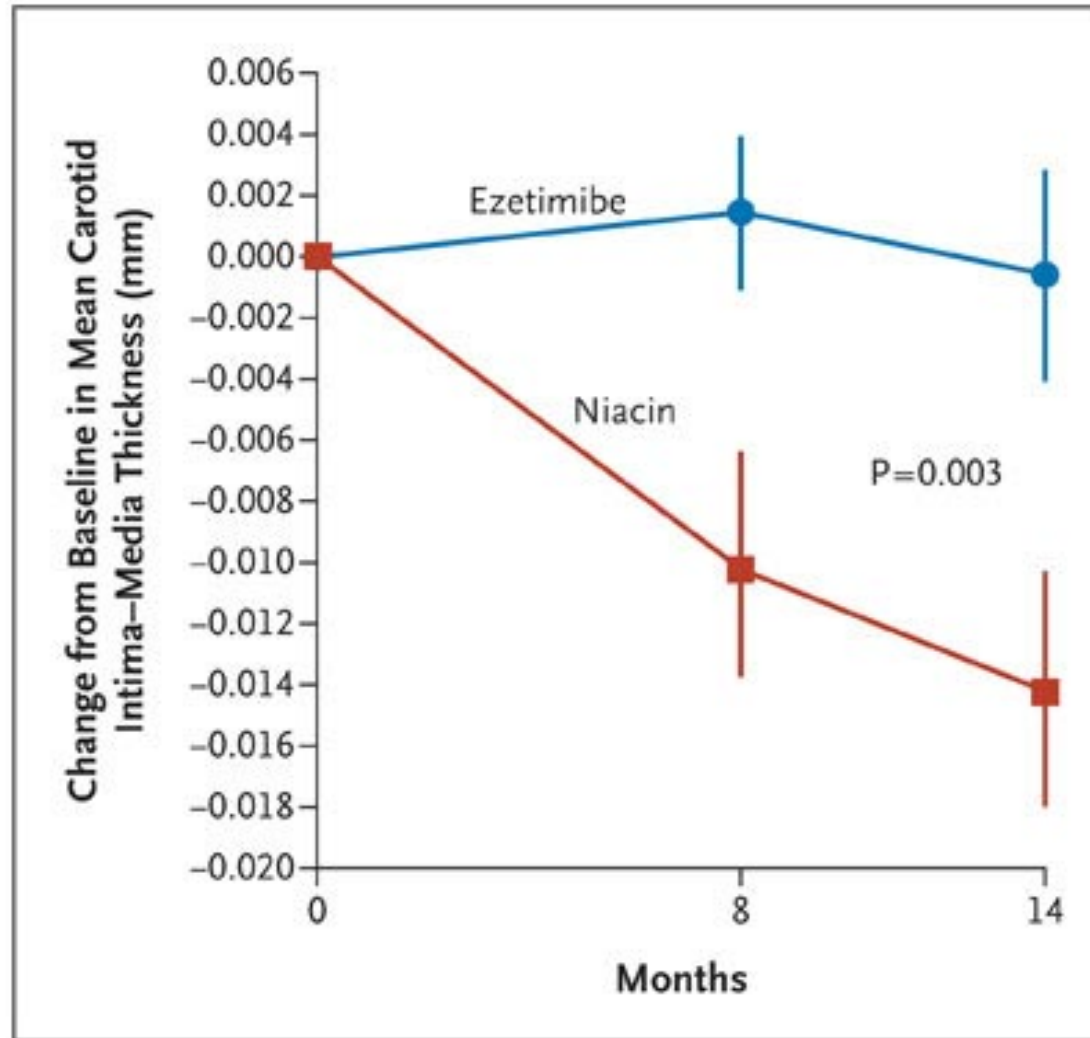
- LDL-C

83 → 73

- HDL-C

43 → 50

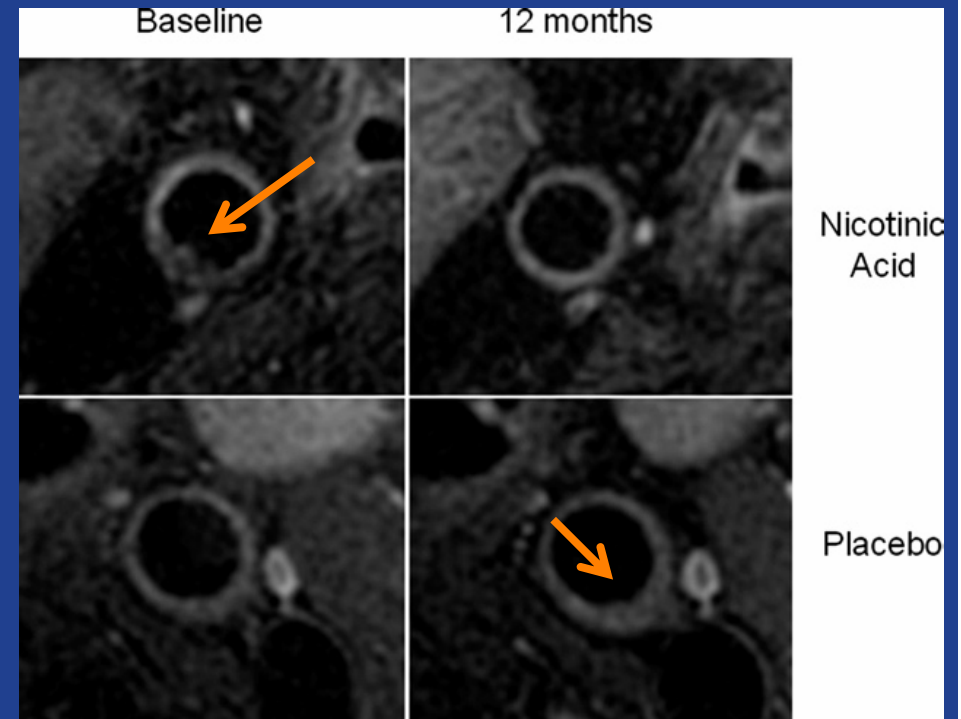
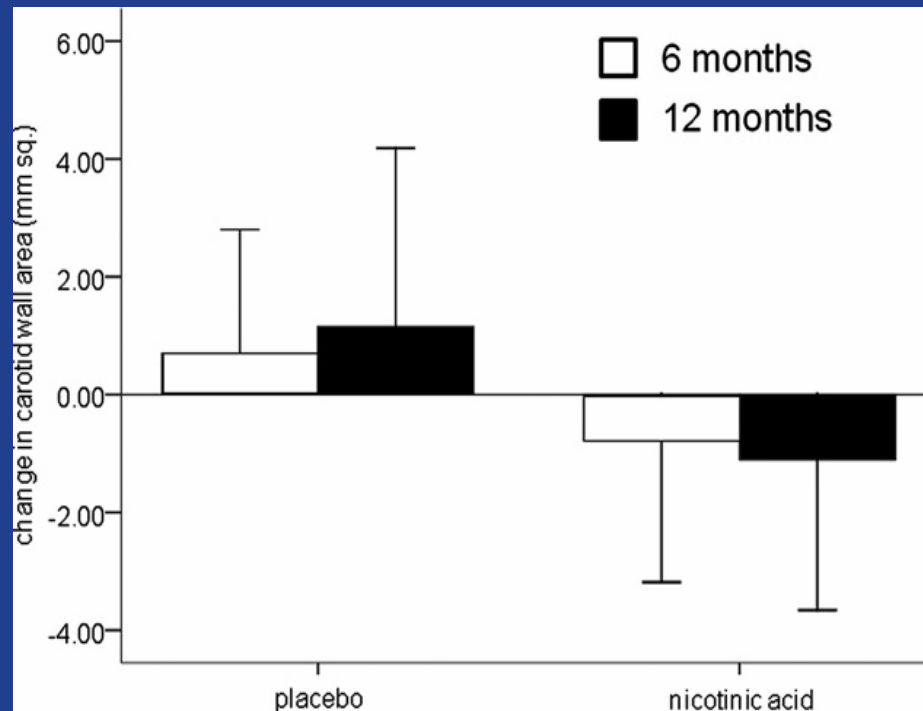
ARBITER-HALTS 6 Study



Oxford Niaspan Study

- 71 statin-treated patients with HDL-C < 40 mg/dl and DM2 + CHD or carotid/peripheral atherosclerosis.
- 2 g daily modified-release NA vs. placebo
- Primary end point: change in carotid artery wall *area* quantified by MRI, after 1 year.

Oxford Niaspan Study



Lipids in niacin group

LDL-C 85 → 69 mg/dL (-19%)

HDL-C 39 → 48 mg/dL (+23%)

Oxford Niaspan Study

- Inverse relationship between the HDL-C and wall area, and no relationship between the LDL-C and wall area.
 - Increases in HDL-C may be beneficial
- Flow-mediated dilation of the brachial artery showed a favorable trend with niacin.
- Aortic distensibility and glyceryl-trinitrate-mediated brachial reactivity did not change significantly with niacin.

NIA Plaque study

- 145 patients with clinically evident atherosclerosis, treated with a statin to ATP III LDL-C targets.
 - Randomized to 1500 mg extended-release niacin or placebo.
- Both arms improved
- No significant difference between the two treatment arms in MRI outcomes, including carotid arterial wall volume and measurements of the lipid core.

NIA Plaque: Change in lipid parameters

Lipid measure (mg/dL)	Statin + placebo, 18 mo	Statin+ER niacin, 18 mo	p (between groups)
LDL-C	77	67	0.03
HDL-C	49	58	<0.001
TG	93	84	0.02

Niacin: What's in Store?

- **HPS2-THRIVE:**

- Niacin and a blocker of PG D2 on top of statin therapy in 20,000 patients

- **AIM-HIGH:**

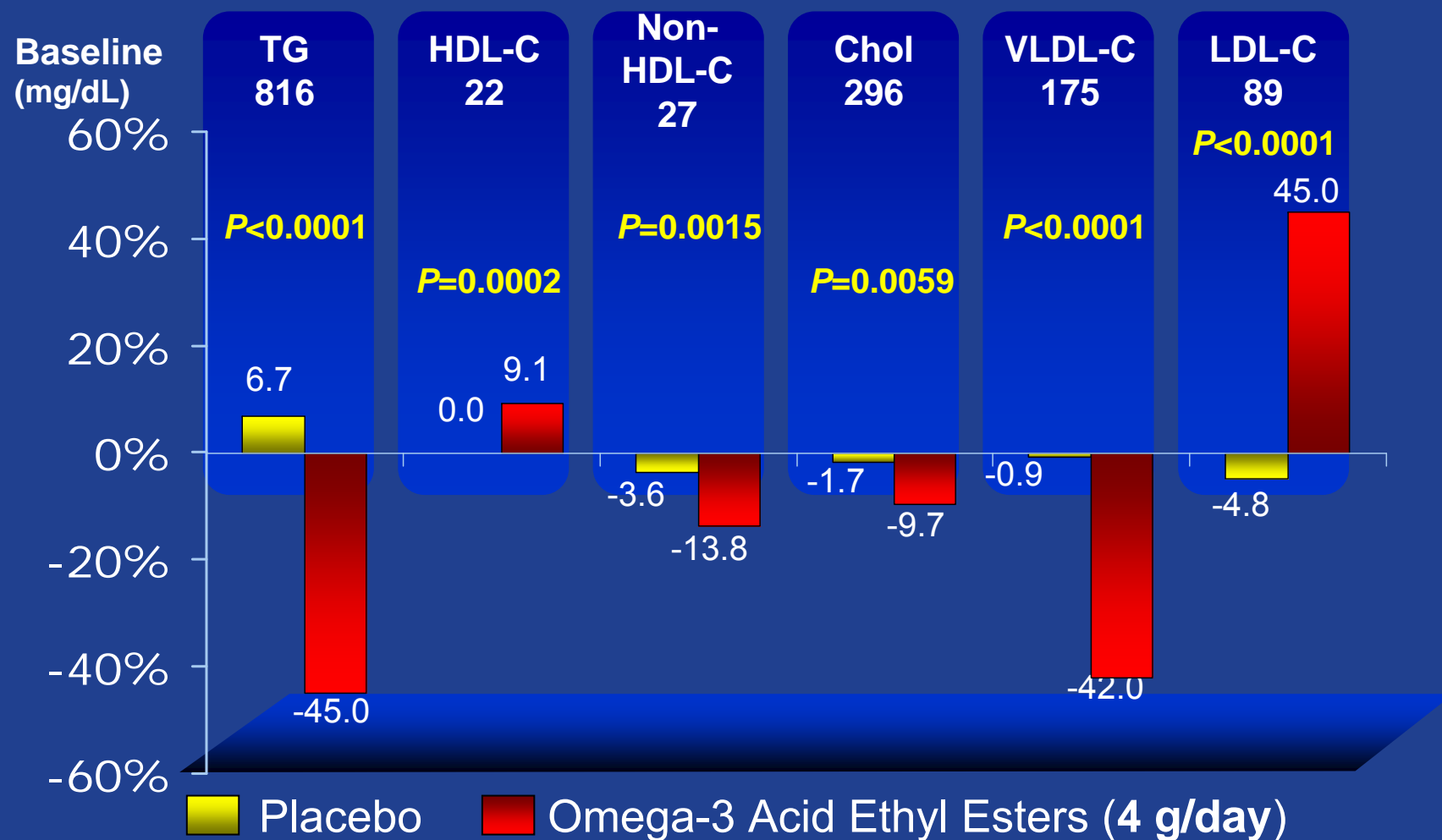
- Simvastatin+Niaspan vs. Simvastatin in 3300 patients with CVD, low HDL and high TG

- Due 2012

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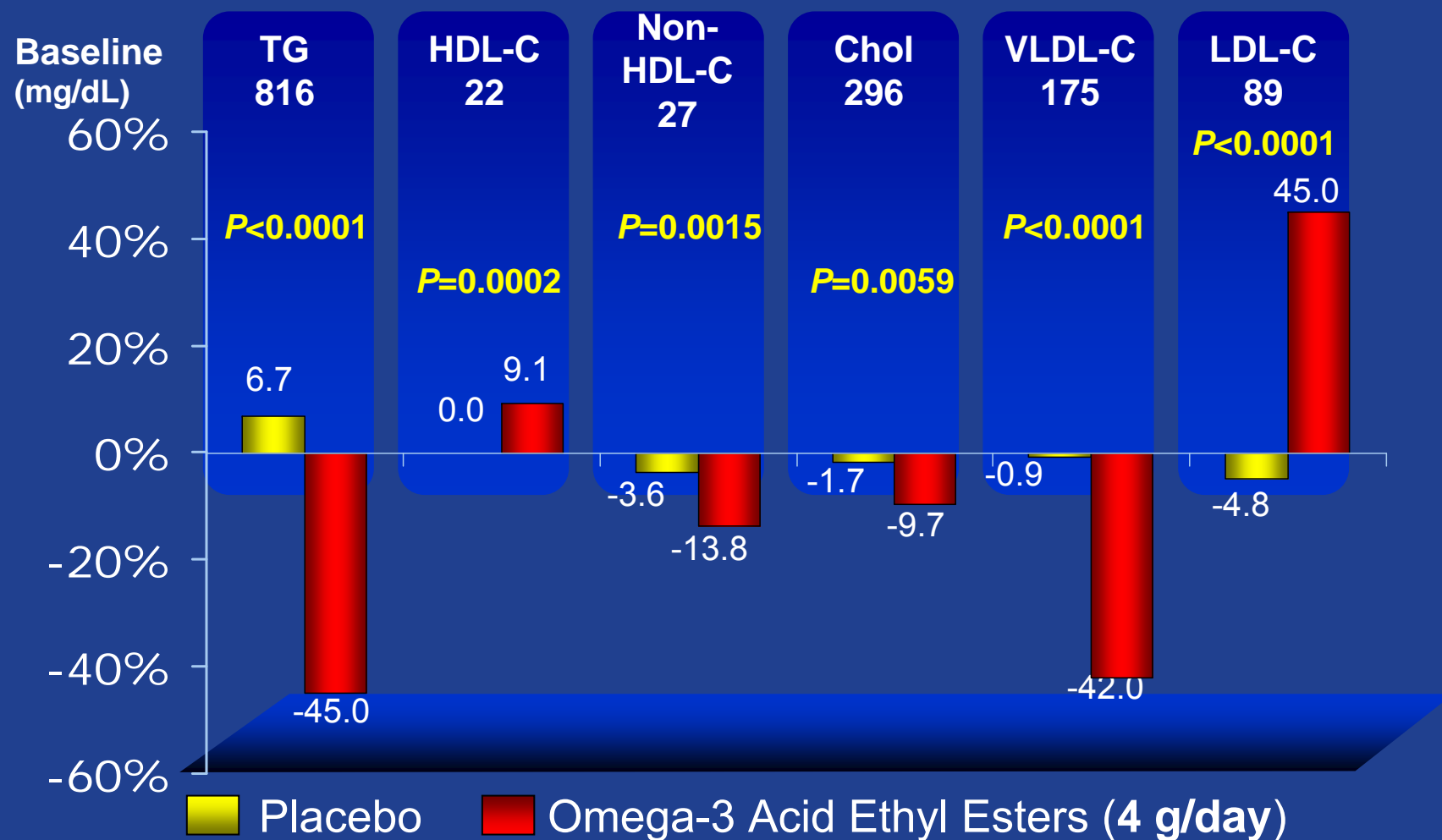
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Omega-3 and Lipids in Patients with TG >500 mg/dl



Pooled analysis: Harris WS et al. *J Cardiovasc Risk* 1997;4:385-391.
Pownall HJ et al. *Atherosclerosis* 1999;143:285-297.

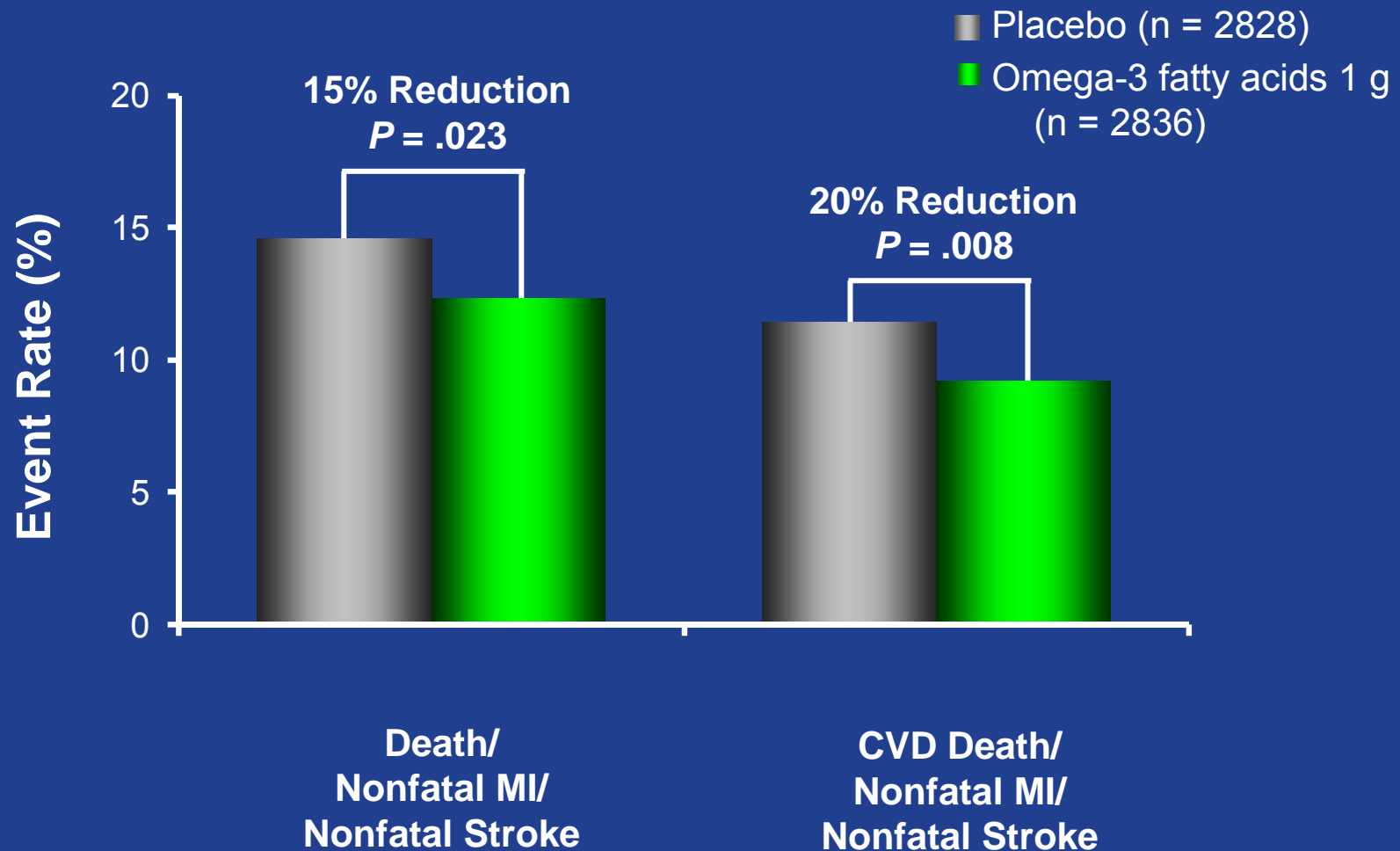
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Dietary Supplementation With Omega-3 Fatty Acids After MI

GISSI-Prevenzione

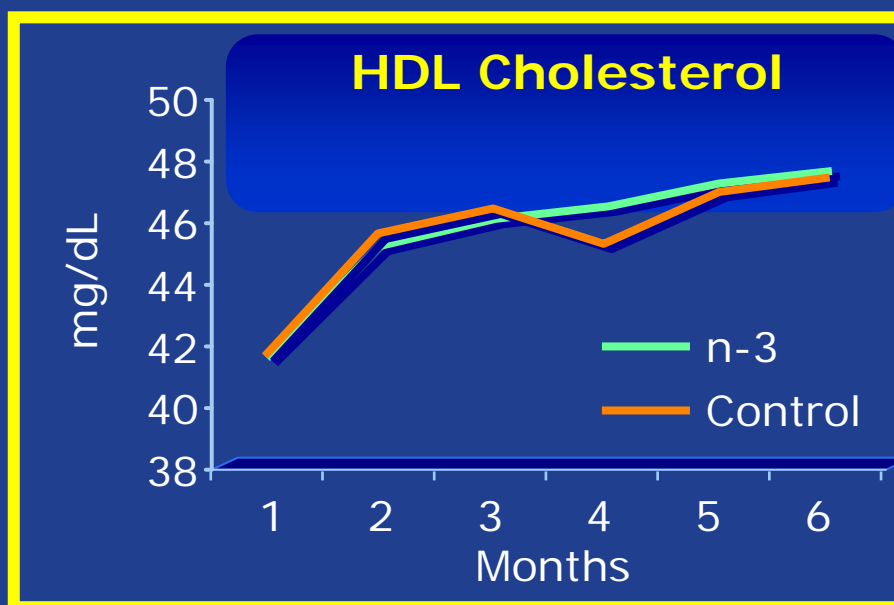


Lancet. 1999;354:447-455.

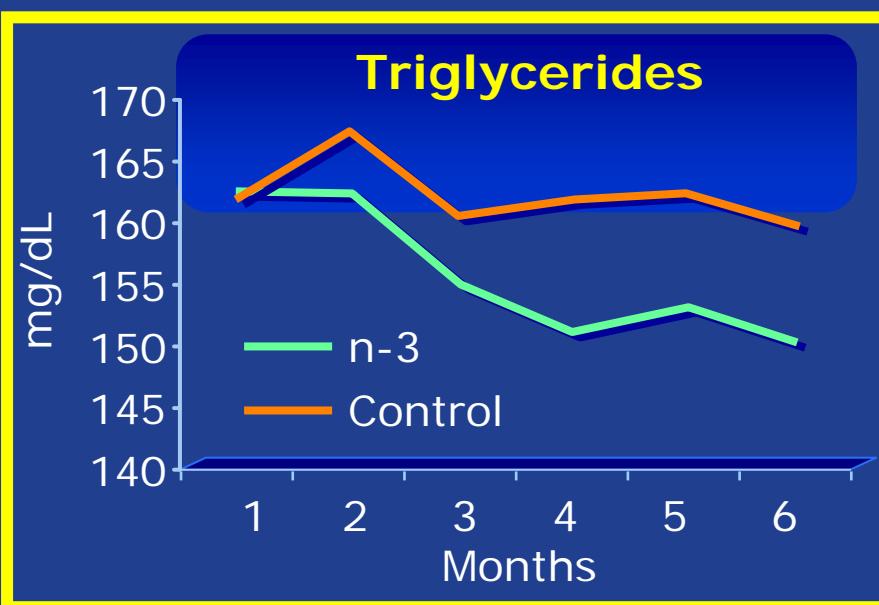
GISSI-Prevenzione:

Effects of EPA+DHA on Serum Lipids

No Difference



5% Difference



Circulation 2002;105:1897-1903.

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