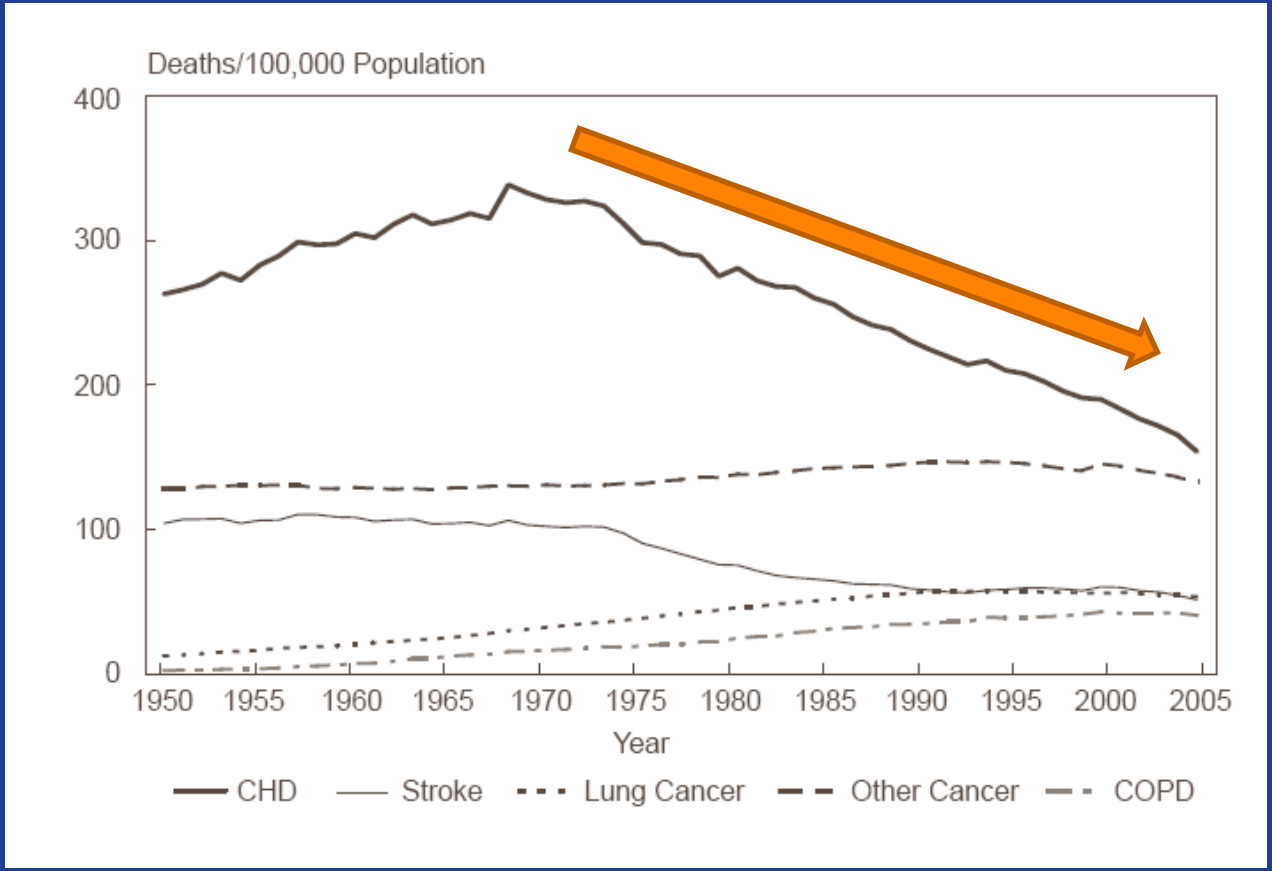
הטיפול בטרשת העורקים ליפידים ודיסליפידמיות

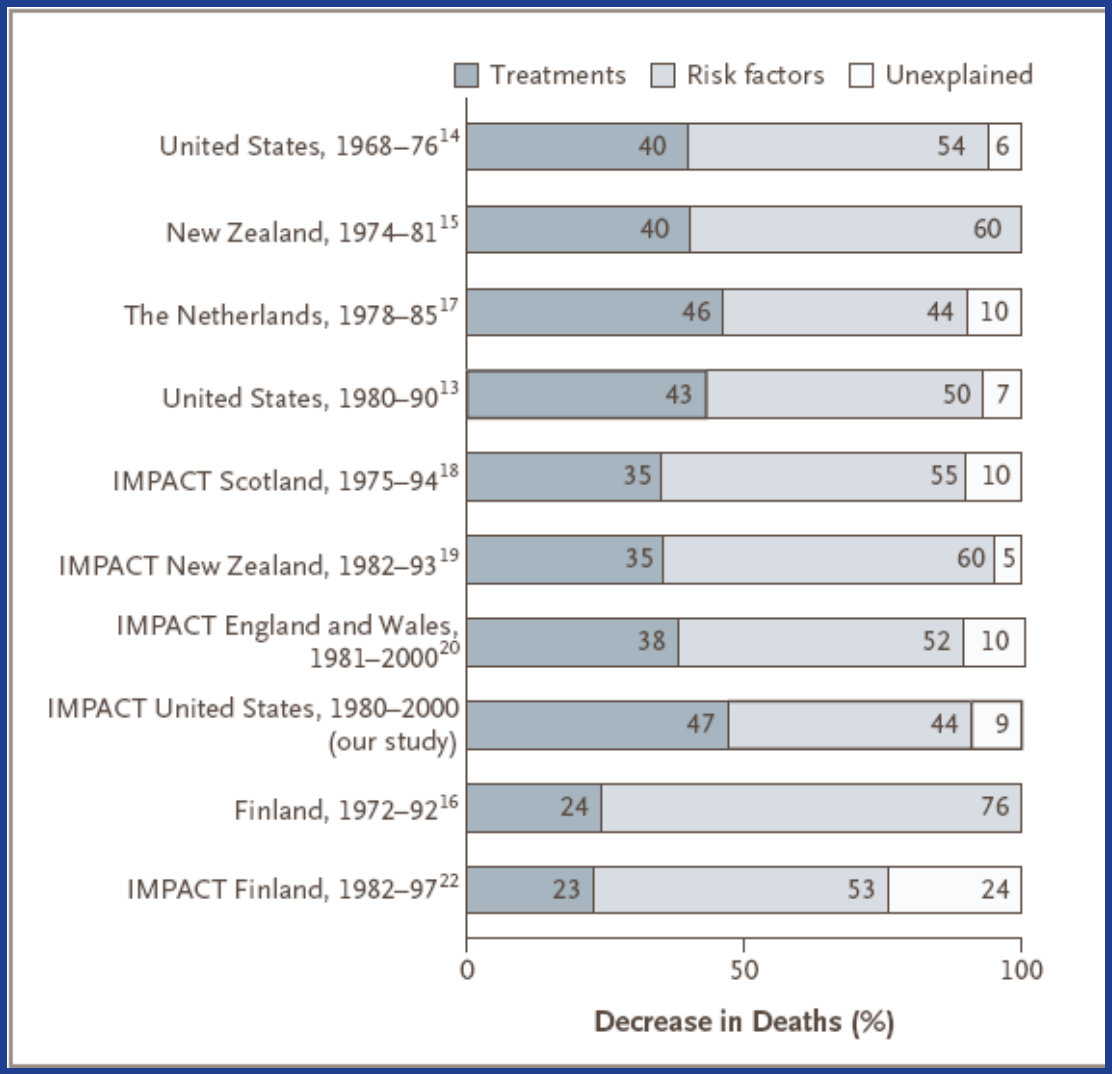
דר' רפי ביצור
מרכז שטרסבורגר לליפידים
המרכז הרפואי ע"ש שיבא, תל השומר

Unadjusted Death Rates for Selected Causes, U.S. 1950–2004



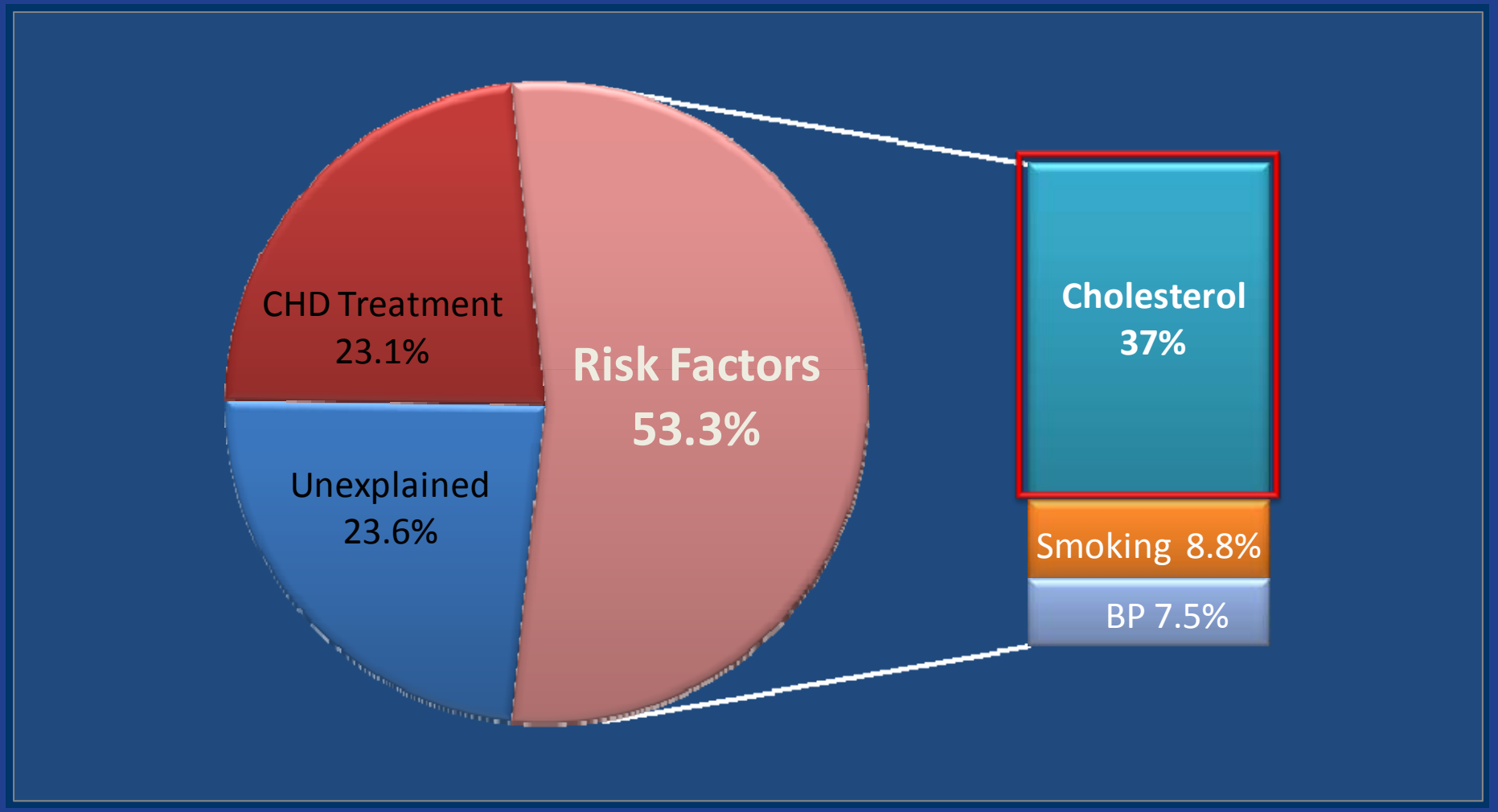
Morbidity and mortality: 2004 chart book on cardiovascular, lung, and blood diseases. Bethesda, MD: National Heart, Lung, and Blood Institute, 2004.

% of the Decrease in Deaths from CHD Attributed to Treatments and Risk-Factors



N Engl J Med 2007;356:2388-98

Reducing CHD Mortality in Finland

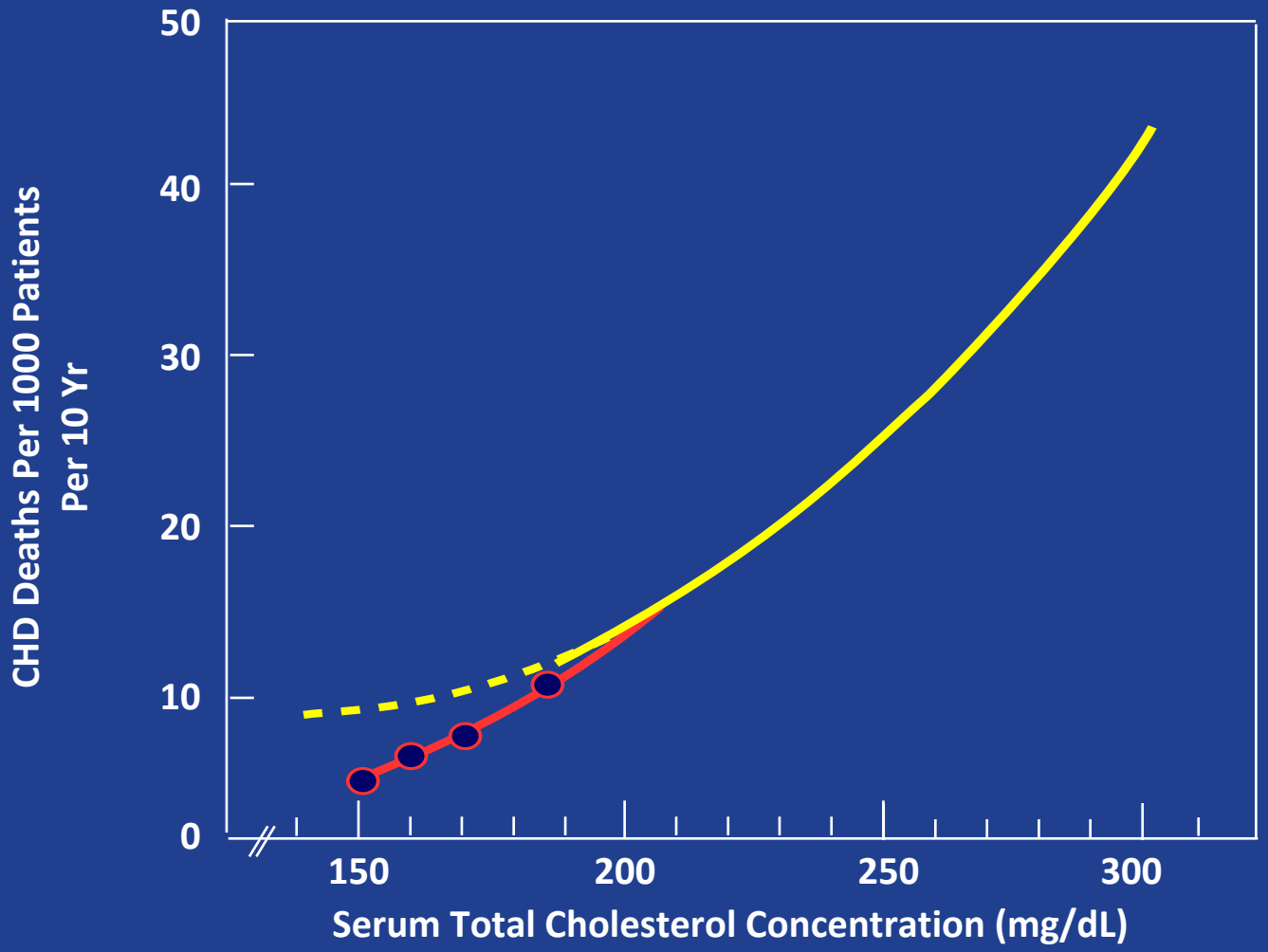


Am J Epidemiol 2005;162:764–773

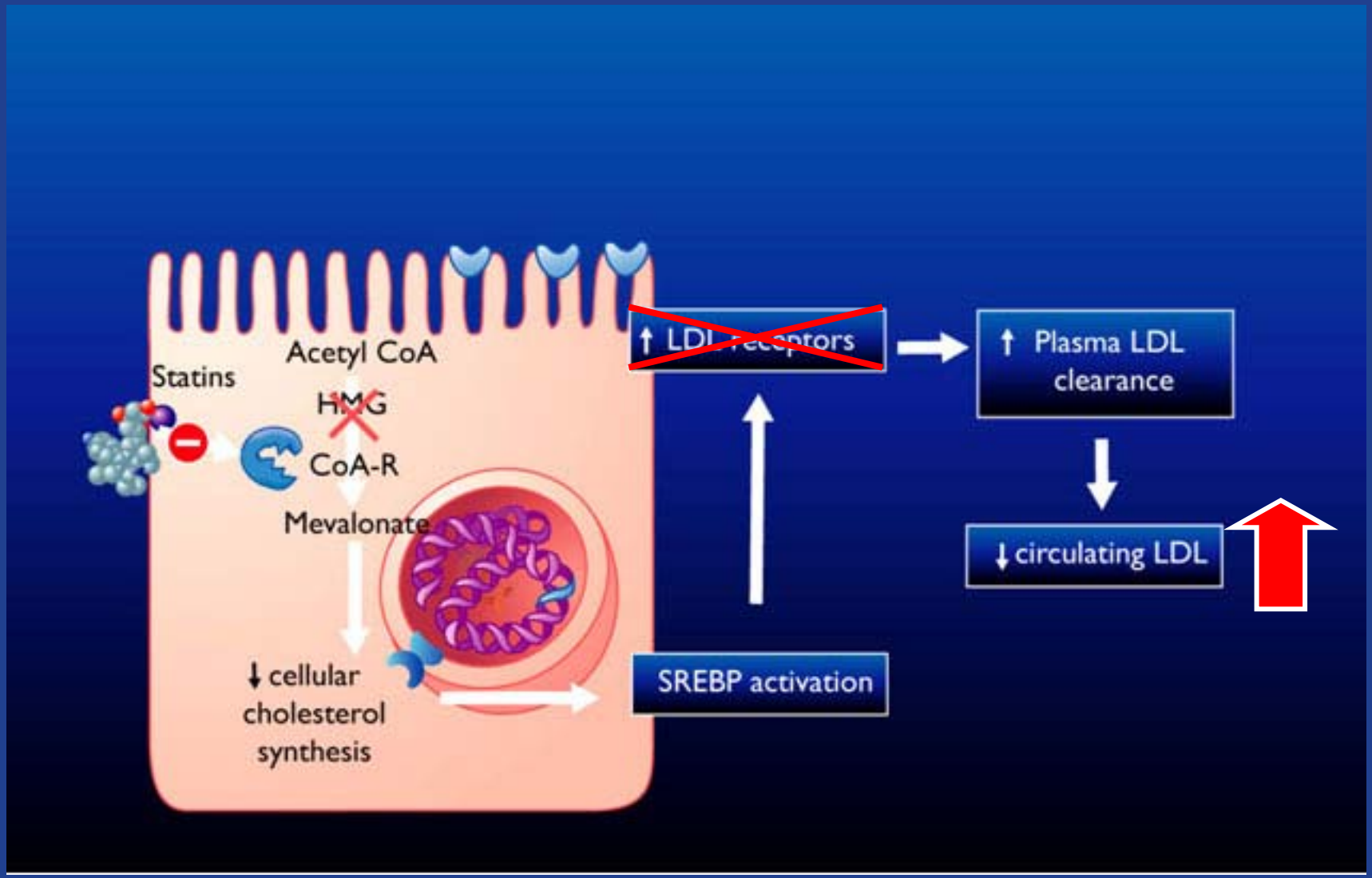
It's The Cholesterol, Stupid

Bill Clinton, 1992 Campaign

CHD Deaths Increase With Rising Total Cholesterol



FH – High Cholesterol, No Other Risk Factors → Early Atherosclerosis



Familial Hypercholesterolemia

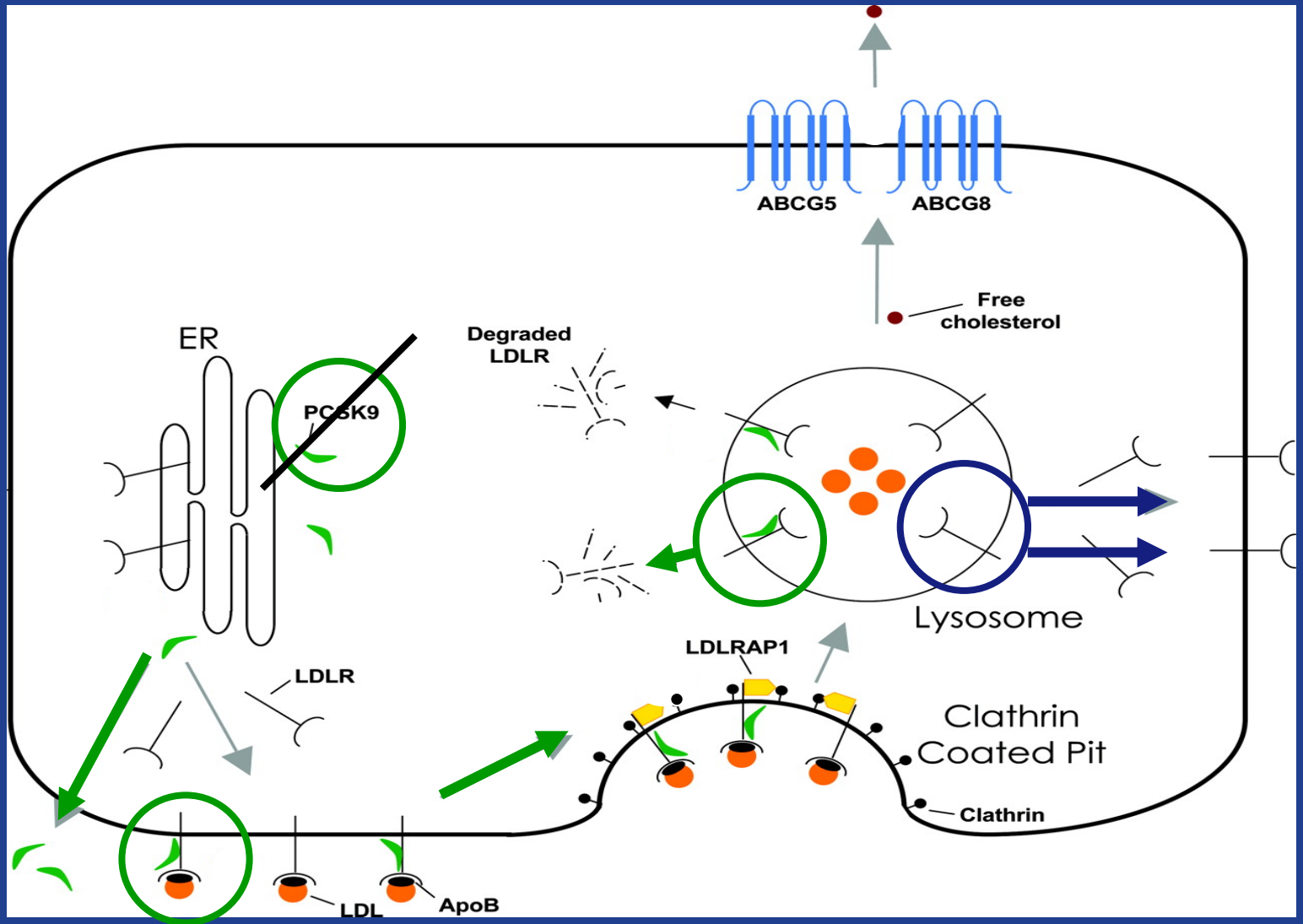
High Cholesterol→ Early Atherosclerosis

	LDL-C (mg/dL)	Mean age at IHD onset
Heterozygous	200-400	45
Homozygous	600-1000	10

No difference in other risk factors

PCSK9 – Degrading LDL-R

proprotein convertase subtilisin/kexin type 9 serine protease

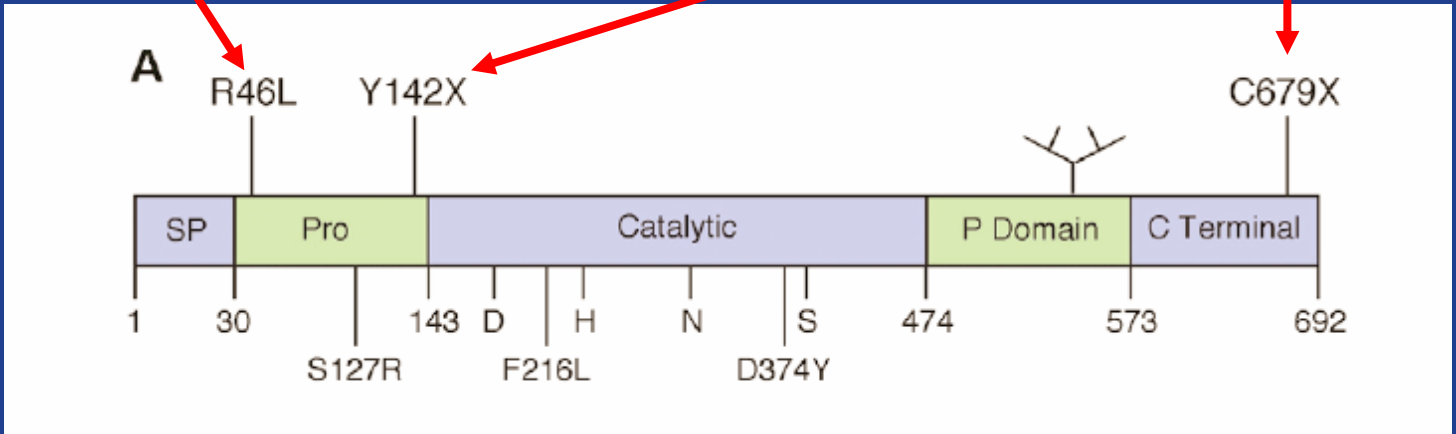


J Clin Endocrinol Metab 2007;92:1581-1589

PCSK9 Mutations

- 3.2% of white subjects
- 21% reduction in mean LDL-C

- 2% of black subjects
- 40% reduction in mean LDL-C



Trends Biochem Sci 2007; 32; 71

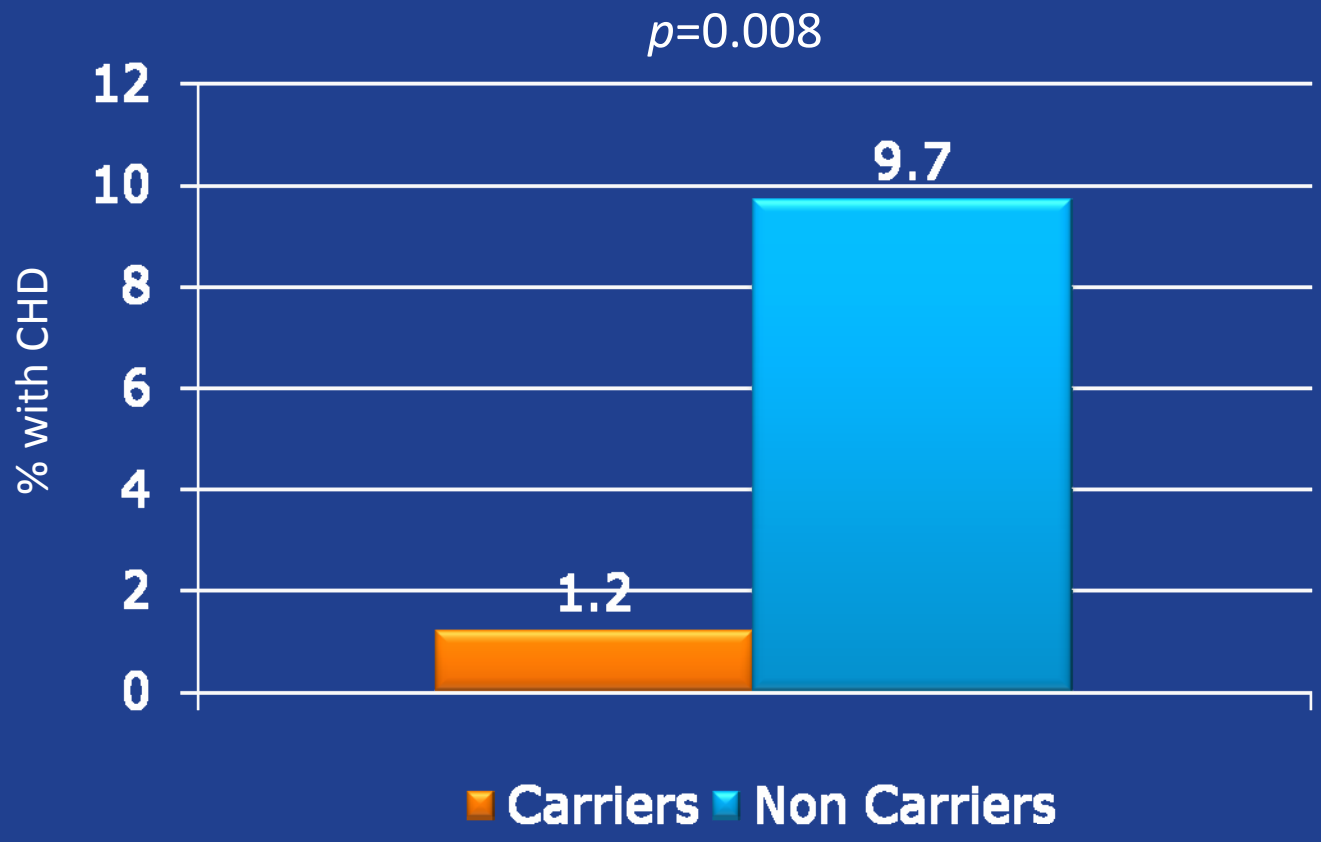
PCSK9 in ARIC (Atherosclerosis Risk in Communities) Study

- Prospective study of atherosclerosis initiated in 1987.
- 15,792 participants
- LDL-C 100 vs. 139 mg/dL in carriers vs. non-carriers
  - ***Low LDL-C from birth***
- No difference in age, sex, TG, HDL-C, BP, smoking, DM

N Engl J Med 2006;354:1264-1272

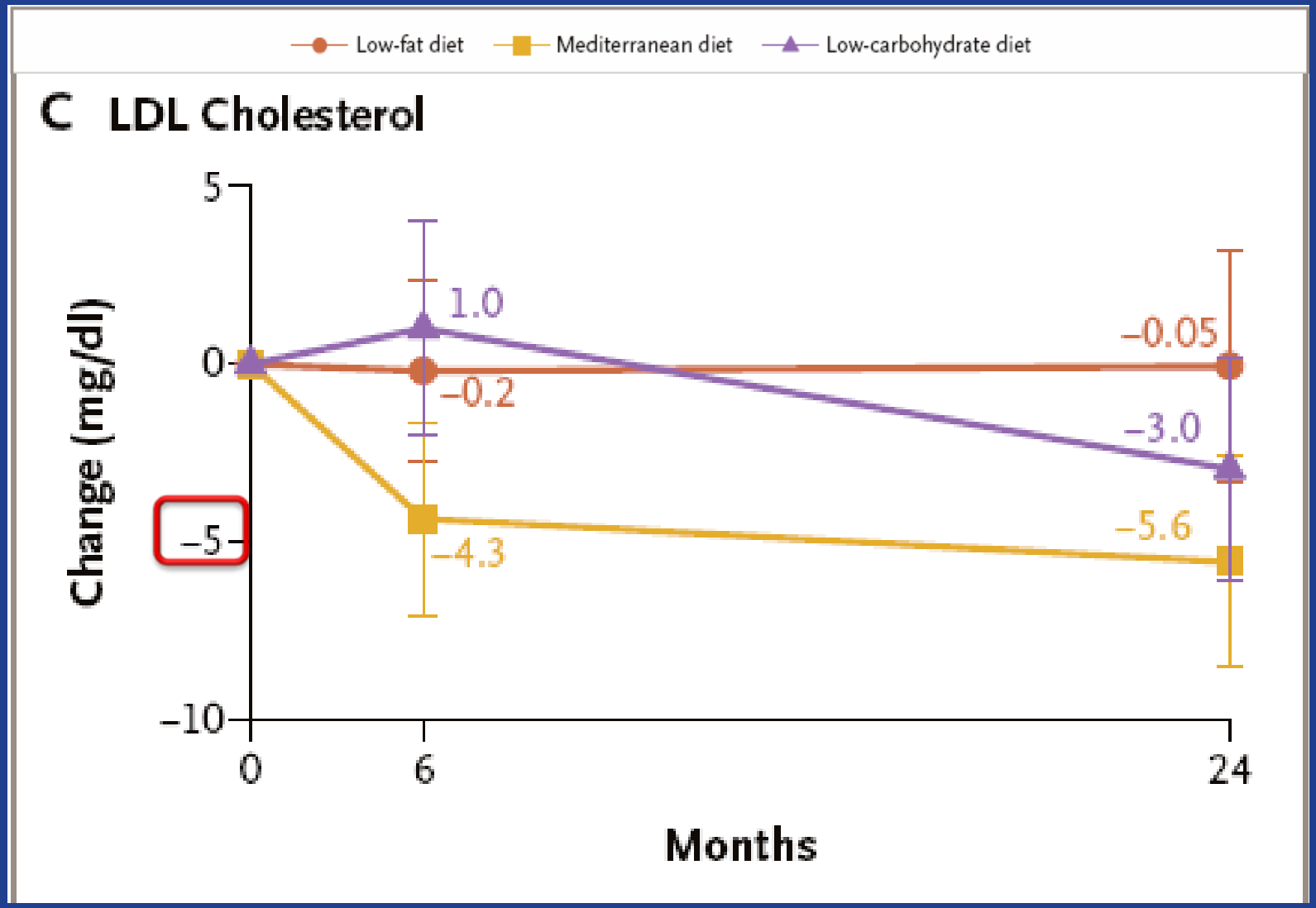
PCSK9 and CHD in ARIC

15 years follow-up: 88% risk reduction



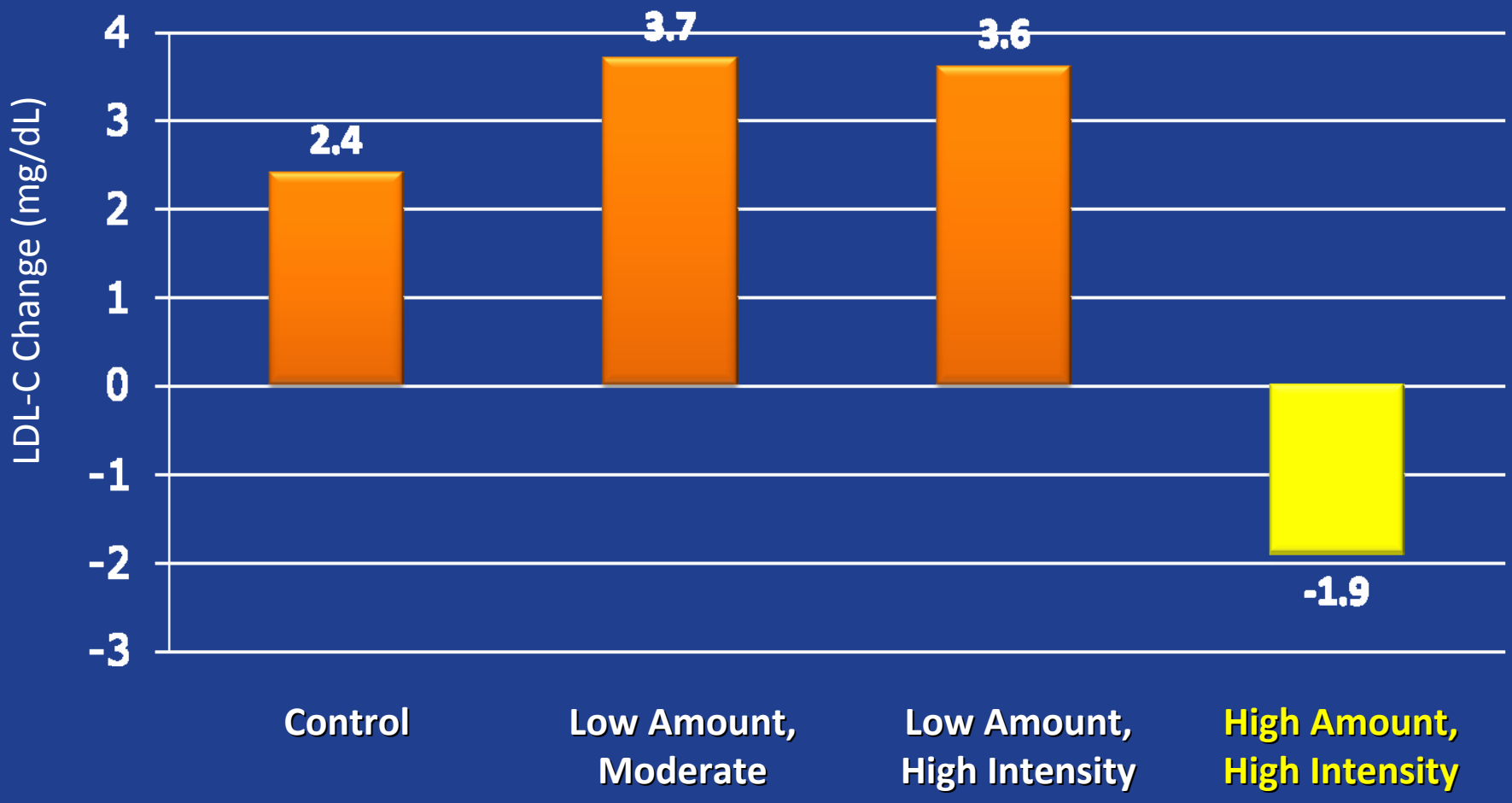
N Engl J Med 2006;354:1264-1272

Low-Carbohydrate, Mediterranean, or Low-Fat Diet



NEJM 2008;359:229-41

Effects of Exercise on LDL-C



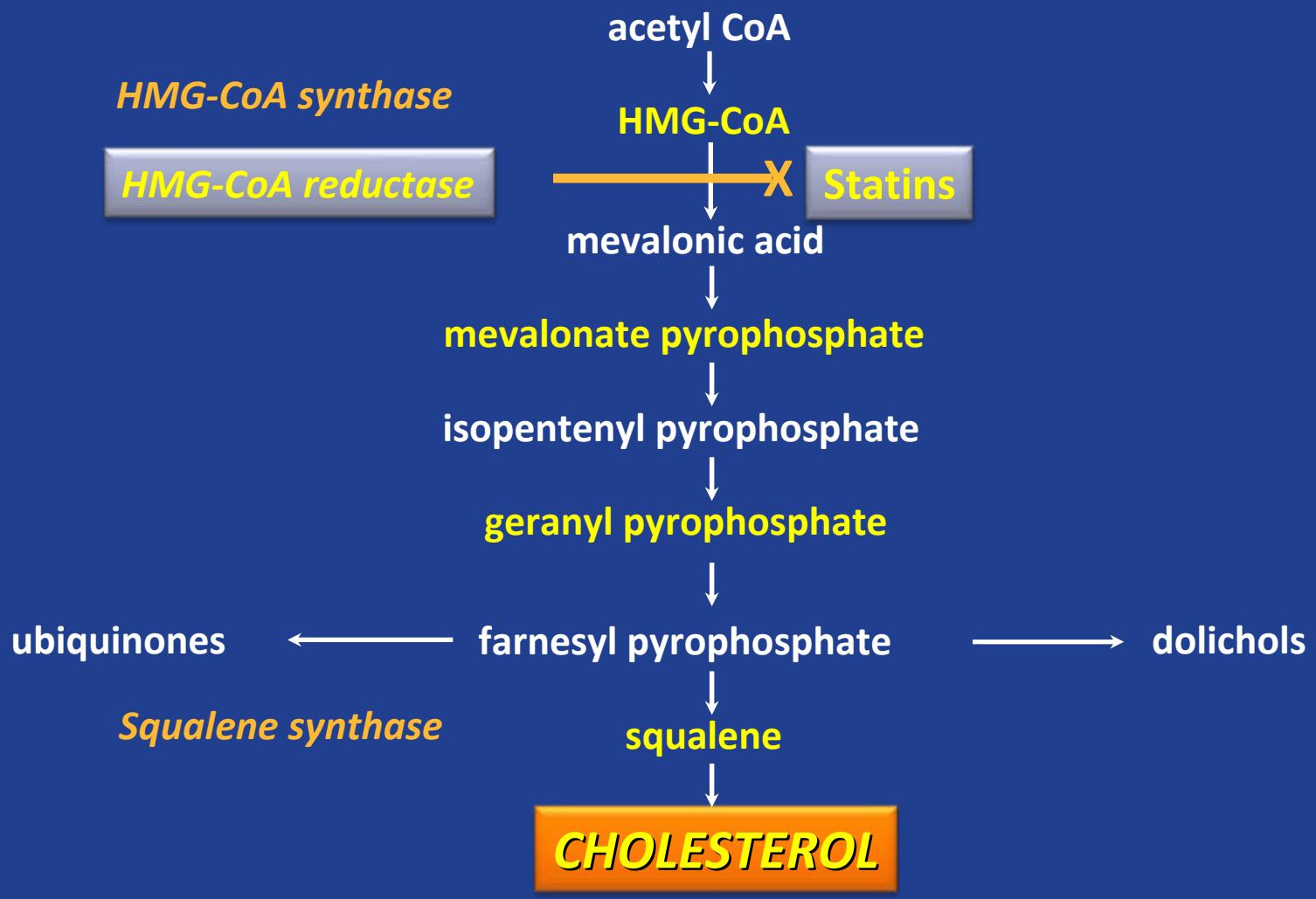
N Engl J Med 2002;347:1483-92

Cholesterol-Lowering Medications

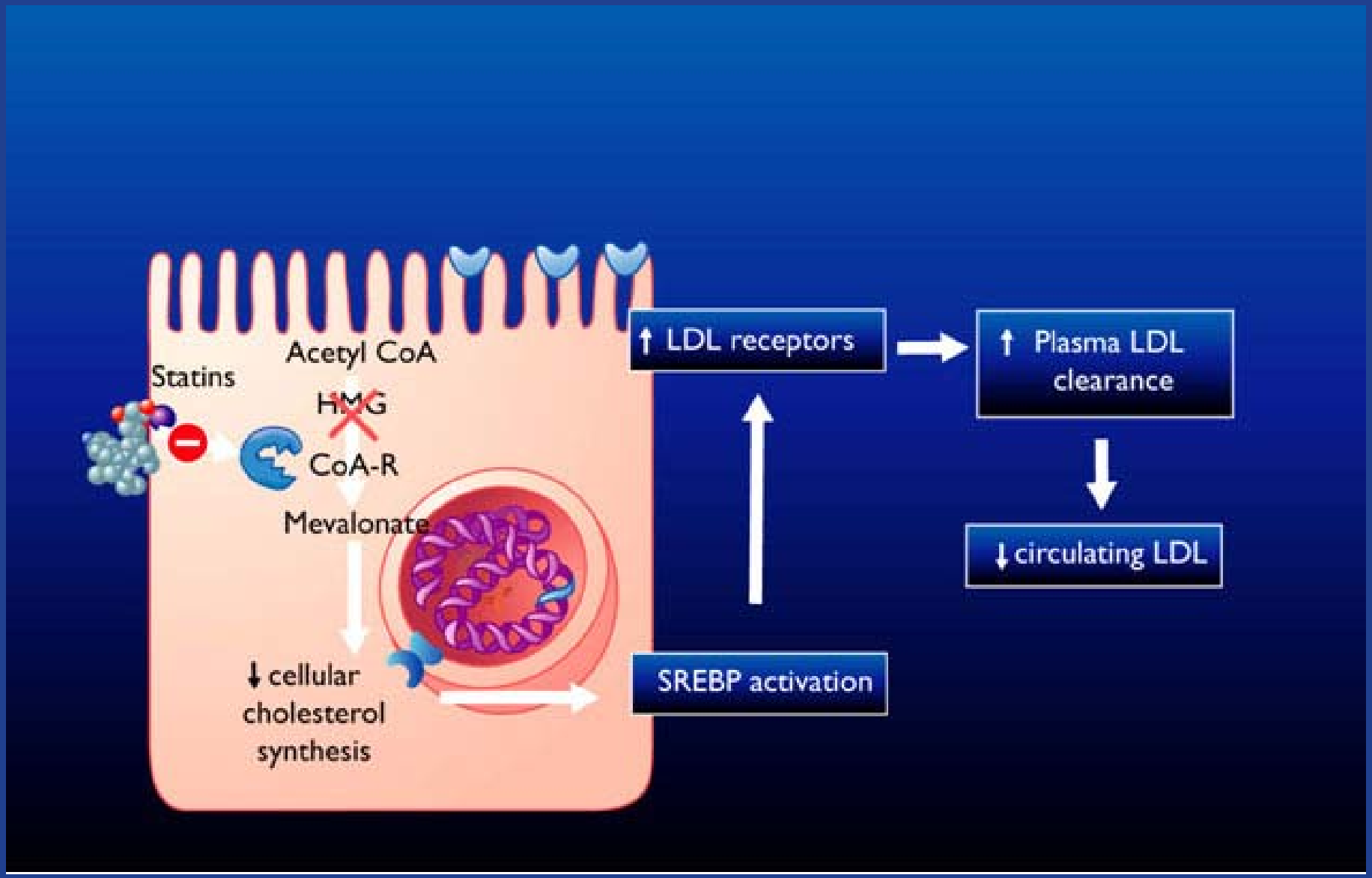
	LDL	HDL	TG	Tolerability
Resins	↓15–30%	↑3-5%	Neutral / ↑	Poor
Statins	↓25-50%	↑6-12%	↓10–20%	Good
Ezetimibe	↓20-25%	↑3-5%	Neutral	Good
Niacin	↓20-25%	↑15-30%	↓10–30%	Reasonable

N Engl J Med 1999;341:498–511.

Mechanism of Action of Statins
Cholesterol Synthesis Pathway



Statins Molecular Mechanisms of Action
SREBP Feedback Control



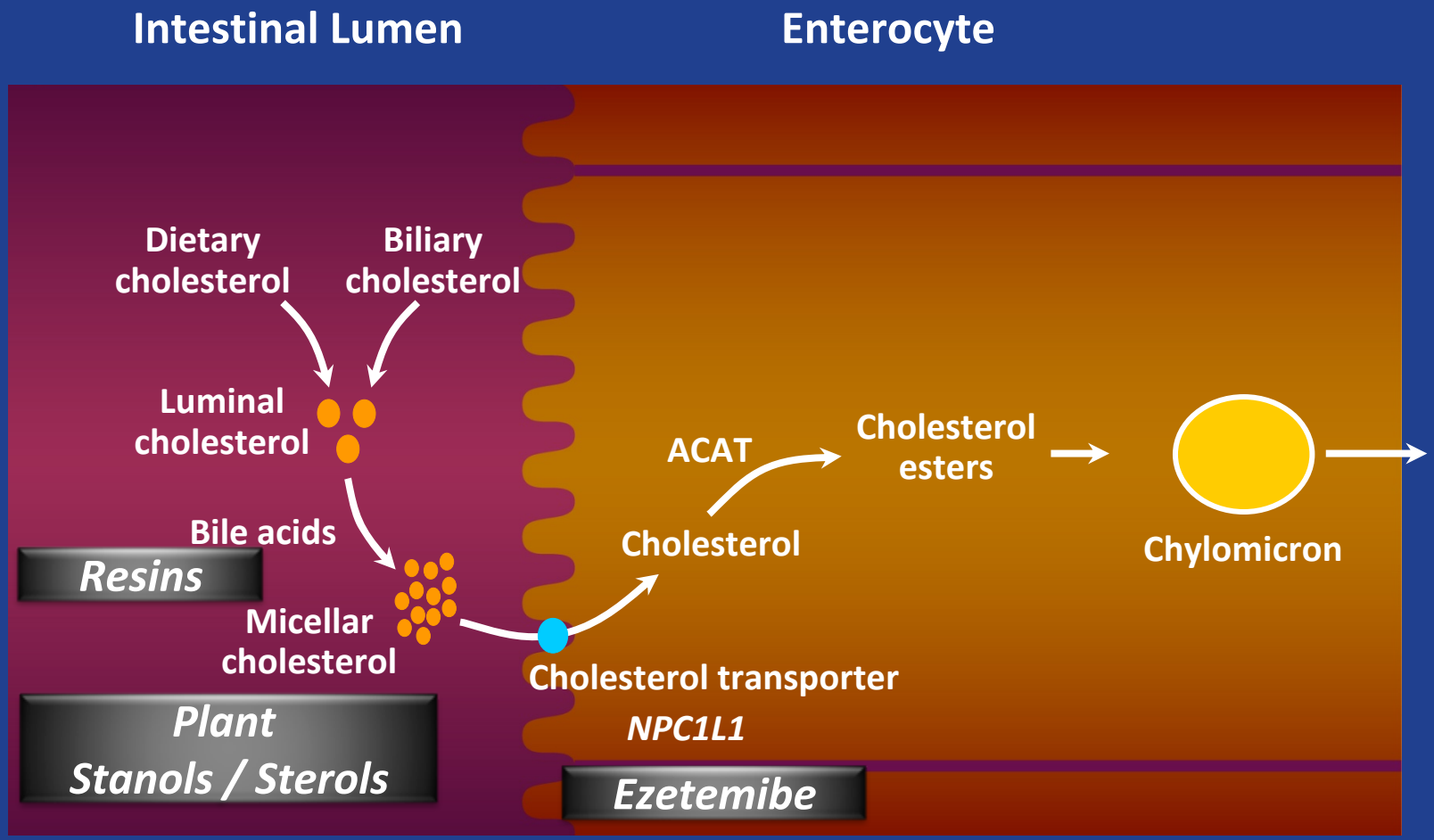
Effects of Statins on Lipids

	LDL-C % change	HDL-C % change	TG % change
Rosuvastati	-56	+10	-22
n	-50	+6	-29
Atorvastatin	-41	+12	-18
Simvastatin	-34	+12	-24
Pravastatin			

Daily dose of 40mg of each drug

N Engl J Med 1999;341:498–511.

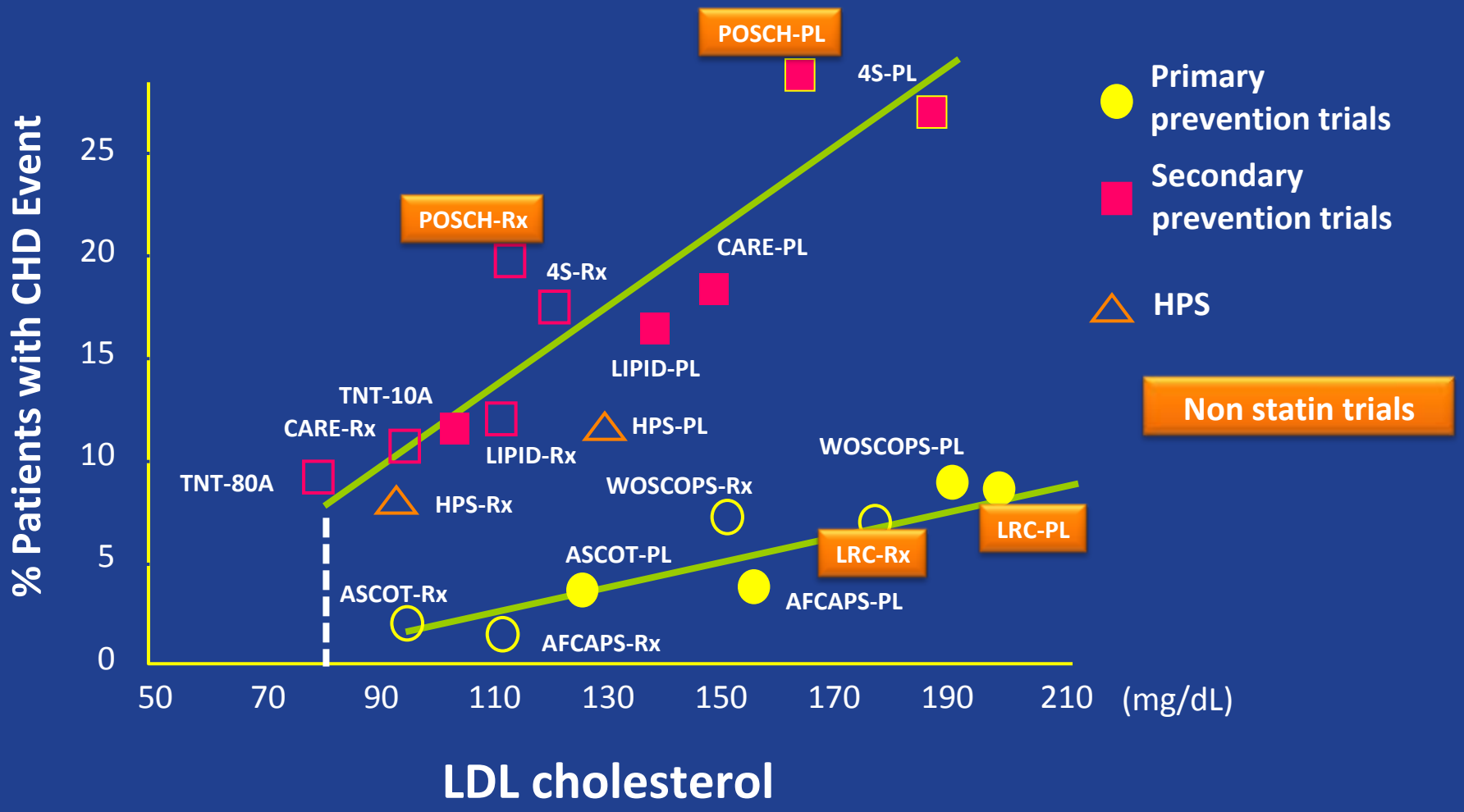
Inhibition of Cholesterol Absorption



ACAT=acyl-coenzyme A:cholesterol acyltransferase; NPC1L1=Niemann-Pick C1 Like 1

Adapted from Gylling H. *Int J Clin Pract.* 2004;58:859–866; Bays H. *Expert Opin Investig Drugs*. 2002;11:1587–1604; Shepherd J. *Eur Heart J. Suppl.* 2001;3(suppl E):E2–E5; Altmann SW et al. *Science.* 2004;303:1201–1204; Davies JP et al. *Genomics.* 2000;65:137–145.

Effect of Lowering LDL-C on CHD Events

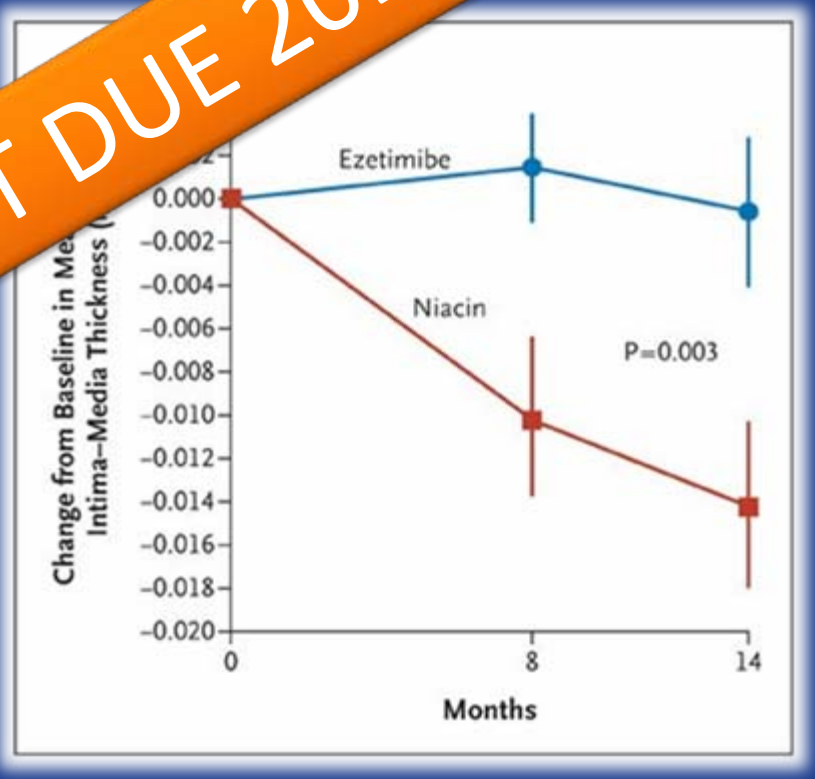


Ballantyne CM. Am J Cardiol. 1998
O'Keefe JH et al, JACC 2004

Ezetimibe

ENHANCE

ARBITE



IMPROVE-IT DUE 2013

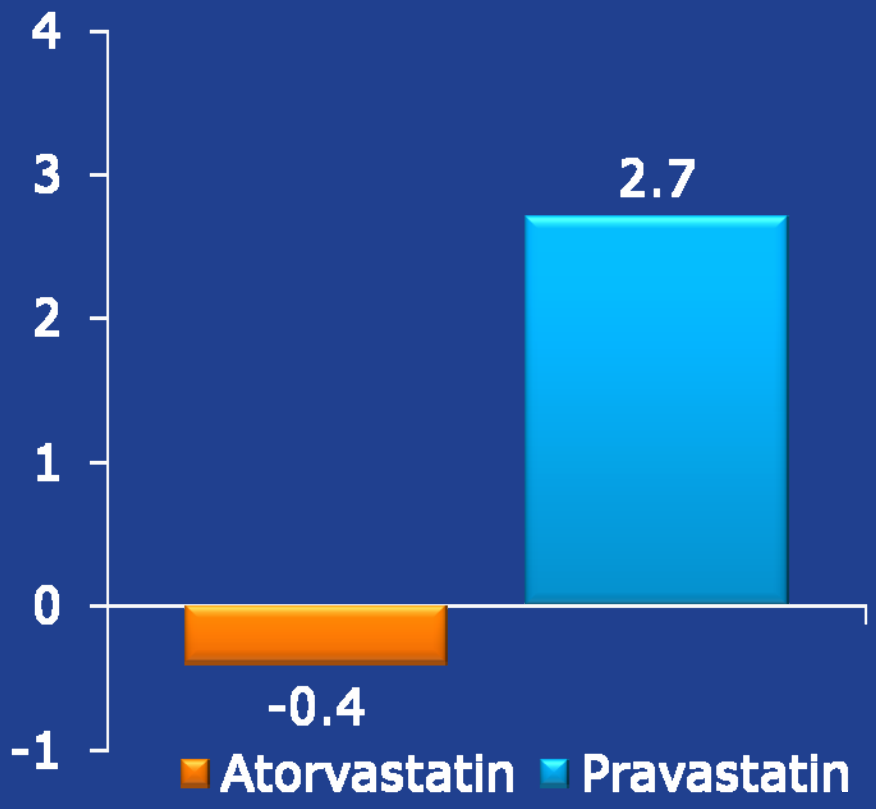
N Engl J Med 2008;358:1431-43

N Engl J Med 2009;361:2113-22

REVERSAL Trial – IVUS analysis
LDL-C 110 vs. 79 mg/dL

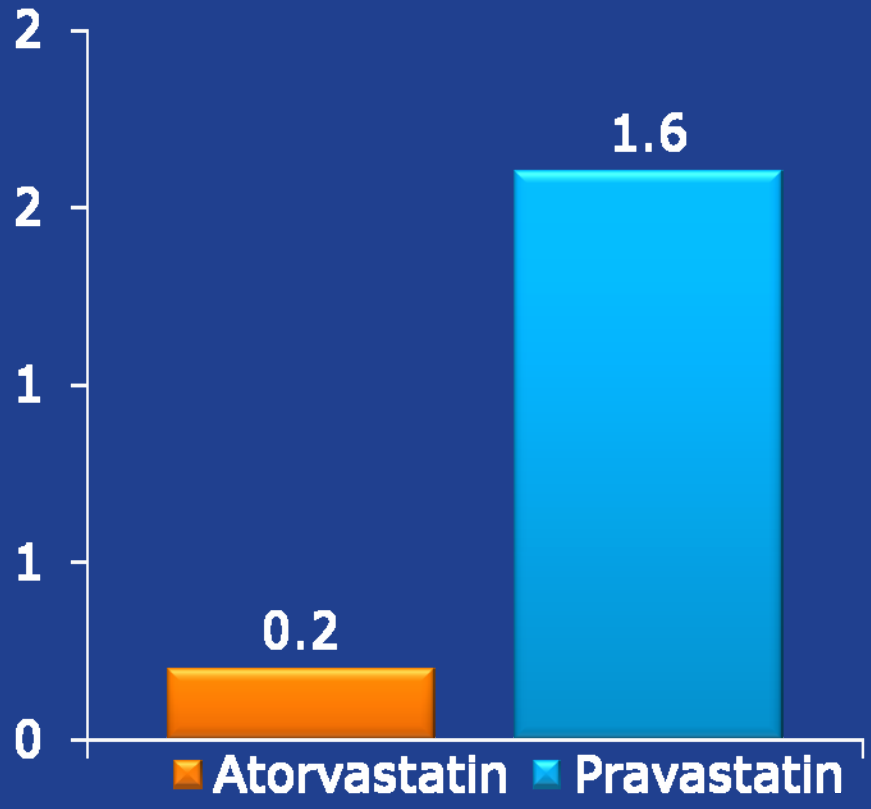
Change in atheroma volume

p=0.02



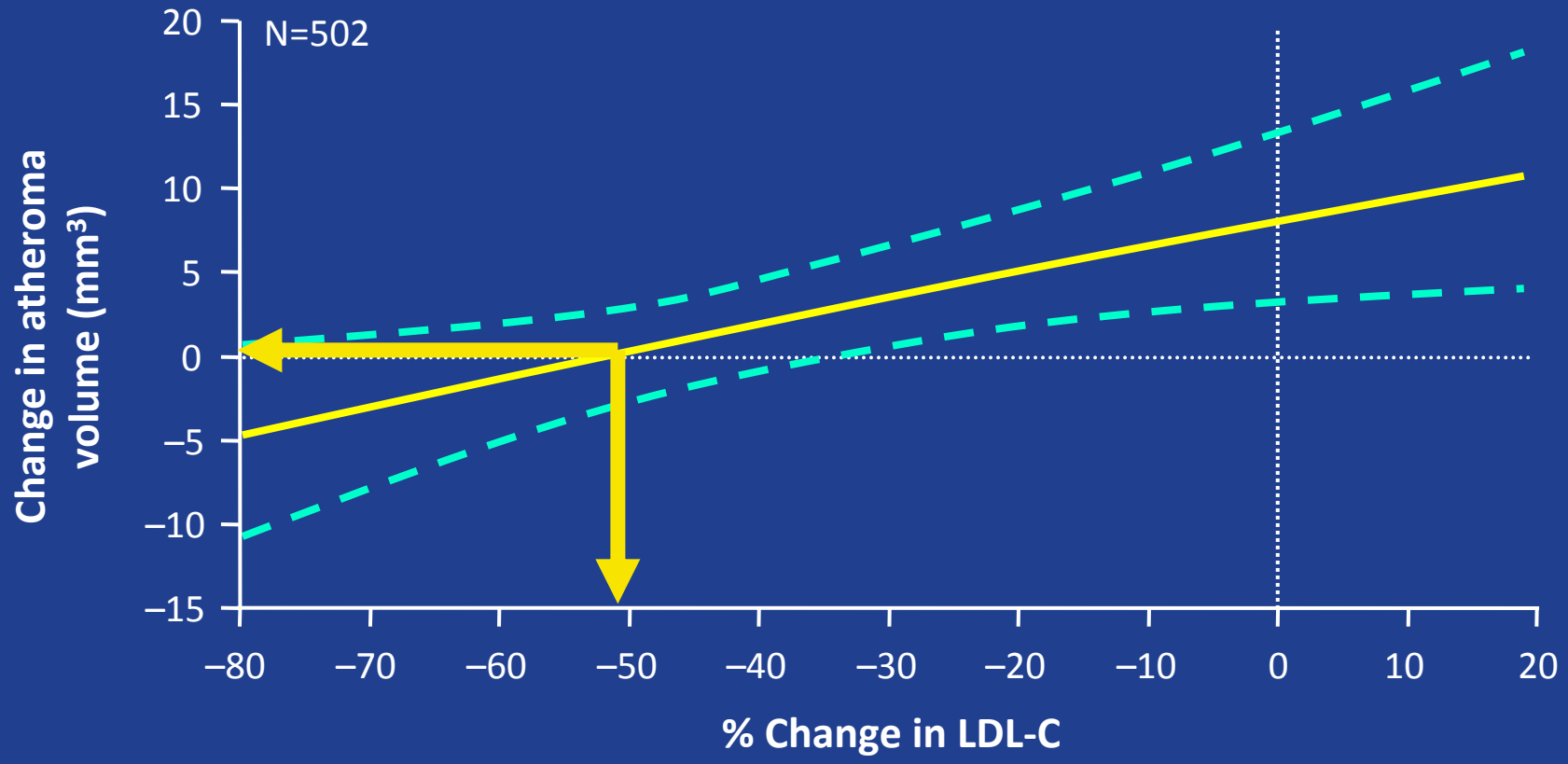
Change in % obstruction volume

p=0.0002



AHA 2003, Orlando, FL

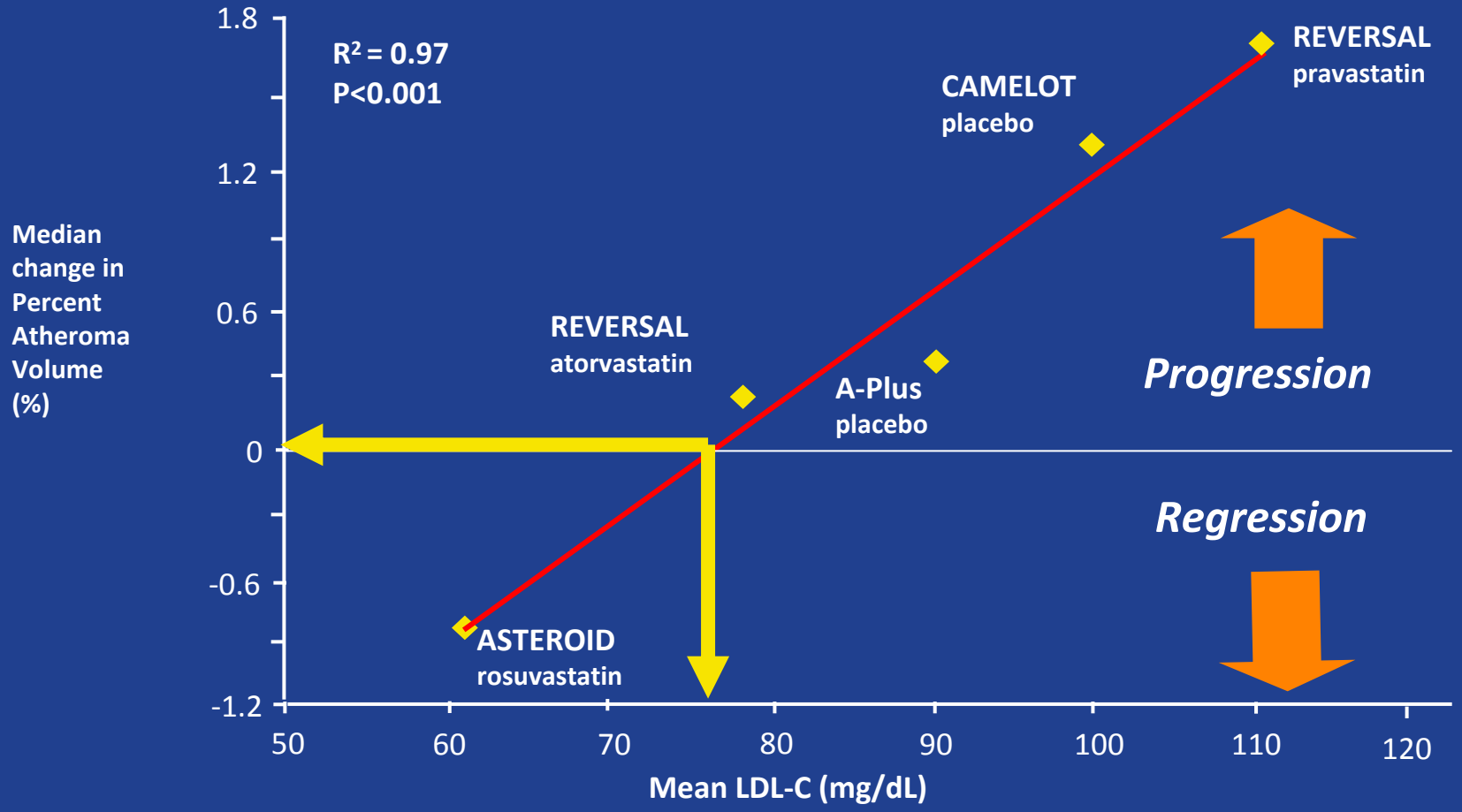
REVERSAL: Relationship Between LDL-C Reduction and Change in Atheroma Volume



The solid blue line indicates the relationship between mean change in LDL-C and change in atheroma volume from linear regression analysis. The dashed green lines indicate the upper and lower 95% confidence limits for the mean values.

JAMA 2004;291:1071–1080.

Relationship Between LDL-C and Change in Atheroma Volume for IVUS Trials



JAMA 2006; 295: e-publication ahead of print

HPS: Heart Protection Study

- 20,536 patients, aged 40-80 years,
- CHD, other occlusive arterial disease, DM or >65 year old hypertnsives
- ***Total cholesterol > 135 mg/dL***
- **Mean LDL 131** mg/dL

Lancet 2002; 360: 7–22

HPS: Factorial Treatment Comparisons

Simvastatin (40 mg daily)	vs	Placebo tablets
Vitamins (600 mg E, 250 mg C & 20 mg beta-carotene)	vs	Placebo capsules

5 years average duration of follow-up

Lancet 2002; 360: 7–22

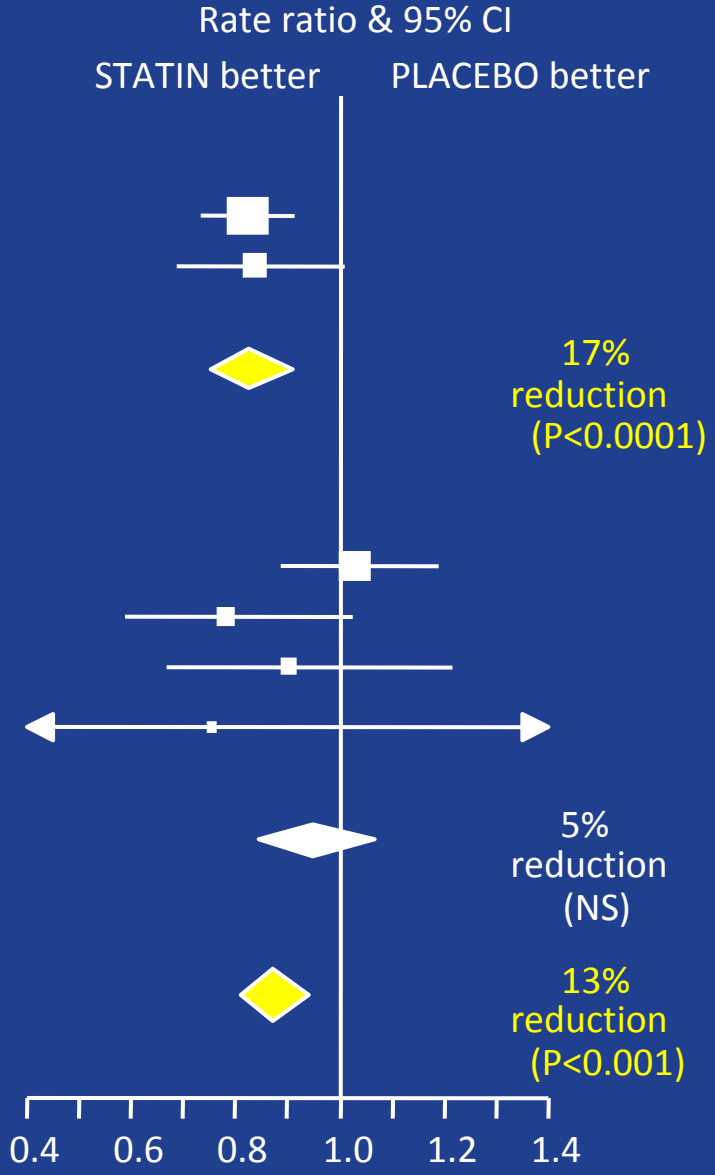
HPS: Average LDL-C Difference by Baseline LDL-C

LDL cholesterol (mg/dl) at entry	SIMVASTATIN (10,269)	PLACEBO (10,267)	Difference in LDL
<116	69	104	-35 ± 0.8
≥116<135	86	123	-37 ± 1.2
≥135	104	143	-39 ± 1.2
ALL PATIENTS	90	127	-37 ± 1.2

Lancet 2002; 360: 7–22

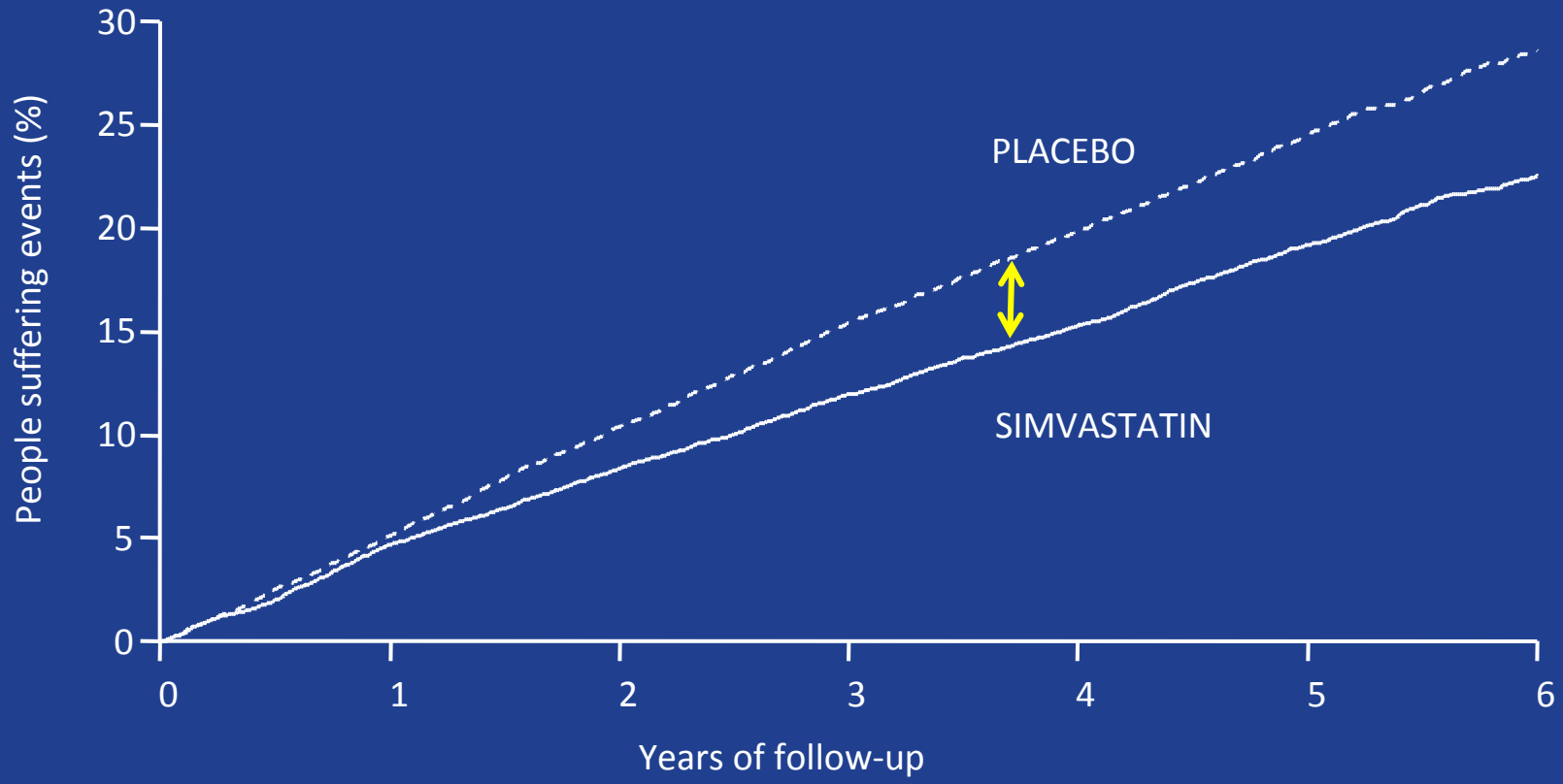
HPS: Cause-specific Mortality

Cause of death	SIMVASTATIN (10269)	PLACEBO (10267)
Vascular		
Coronary	587	707
Other vascular	194	230
ANY VASCULAR	781 (7.6%)	937 (9.1%)
Non-vascular		
Neoplastic	359	345
Respiratory	90	114
Other medical	82	90
Non-medical	16	21
NON-VASCULAR	547 (5.3%)	570 (5.6%)
ALL CAUSES	1328 (12.9%)	1507 (14.7%)



Lancet 2002; 360: 7–22

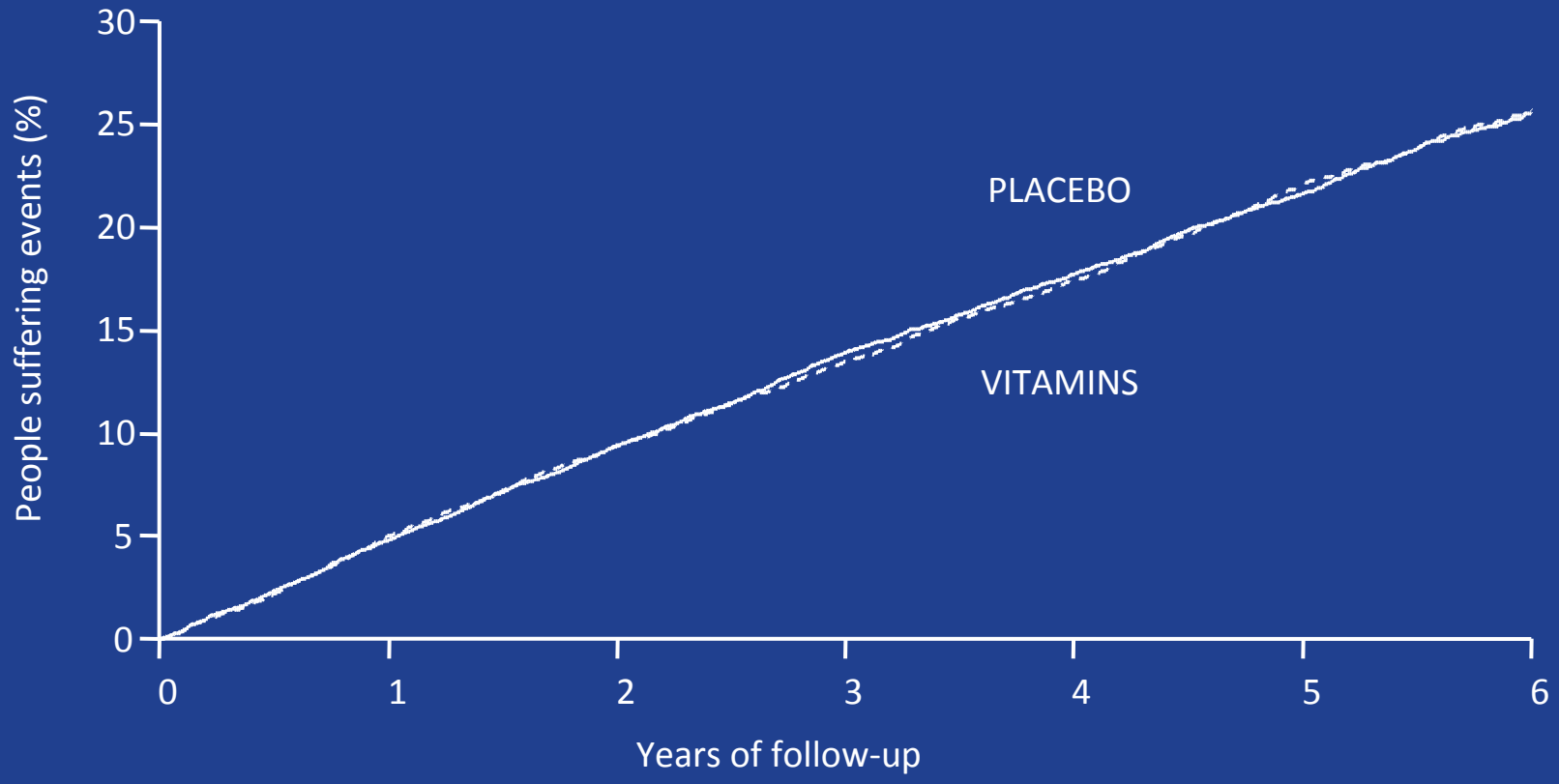
HPS: Major Vascular Event By Year



Benefit/1000 (SE):	5(3)	20(4)	35(5)	46(5)	54(7)	60(18)

Lancet 2002; 360: 7–22

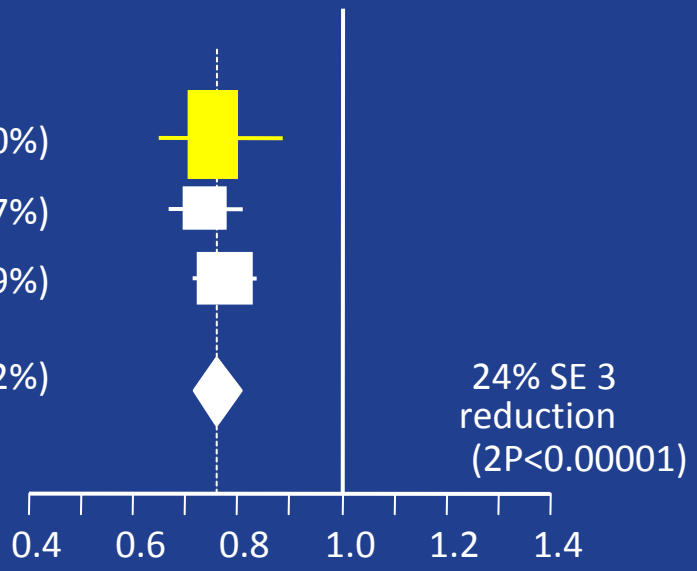
HPS: Major Vascular Event By Year



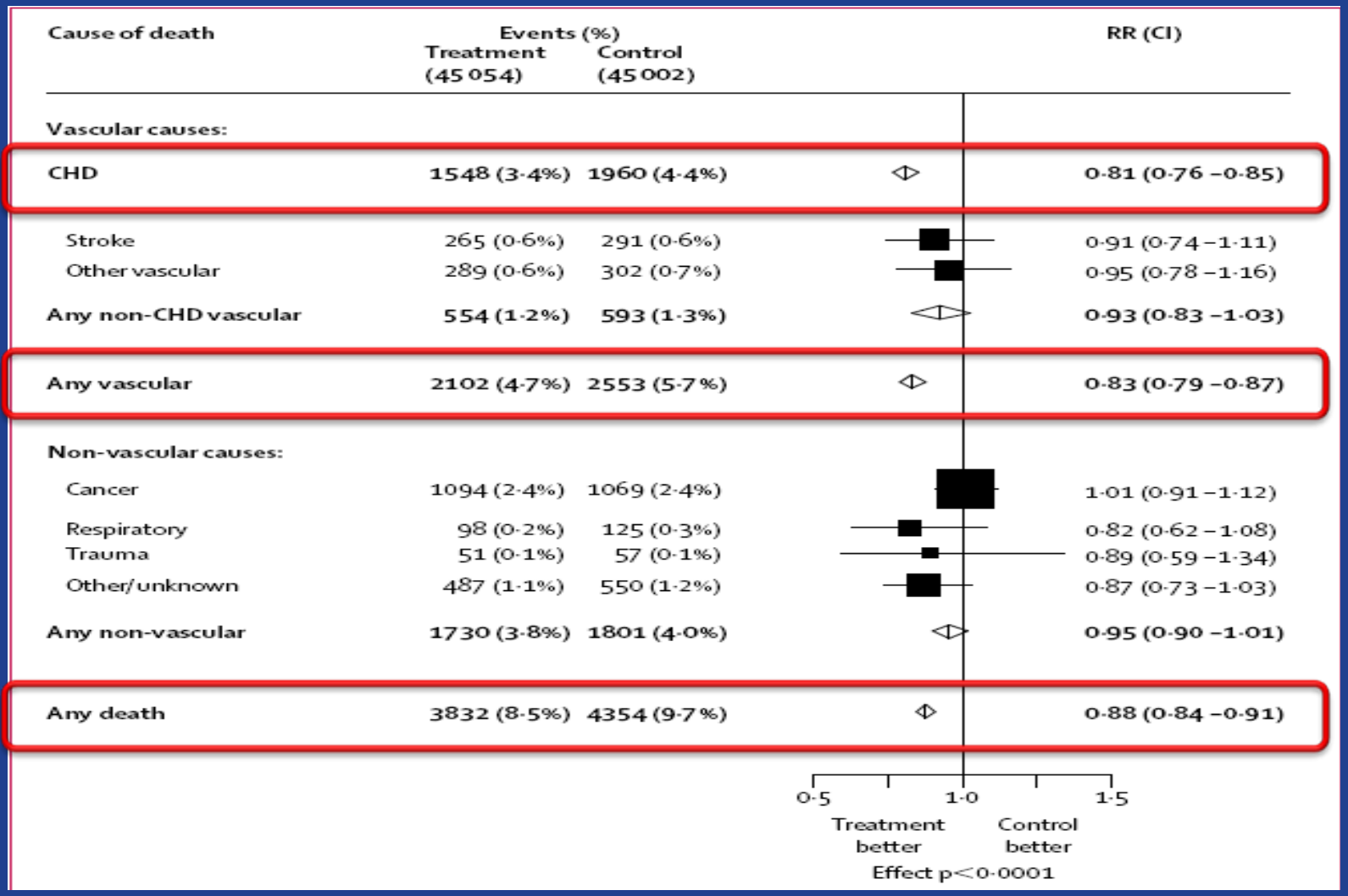
Benefit/1000 (SE):	2(3)	0(4)	-4(5)	-3(5)	4(8)	2(18)

Heart Protection Study: Major Vascular Events by LDL-C

Lipid levels at entry	SIMVASTATIN (10269)		PLACEBO (10267)	
LDL cholesterol (mg/dl)				
< 100	282	(16.4%)	358	(21.0%)
100-130	668	(18.9%)	871	(24.7%)
> 130	1083	(21.6%)	1356	(26.9%)
ALL PATIENTS	2033	(19.8%)	2585	(25.2%)

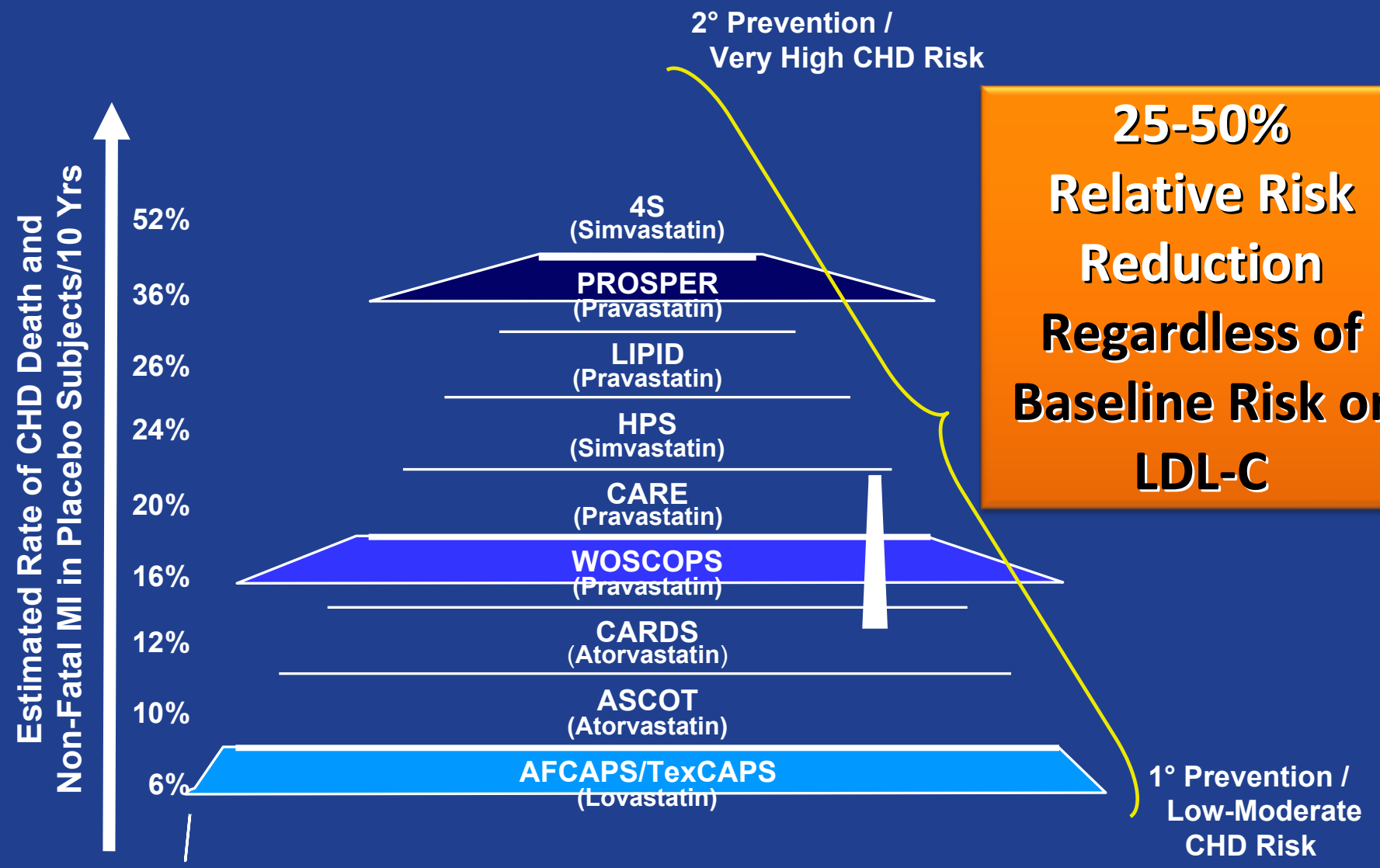


CTT Meta-Analysis: 90,056 Participants in 14 Trials

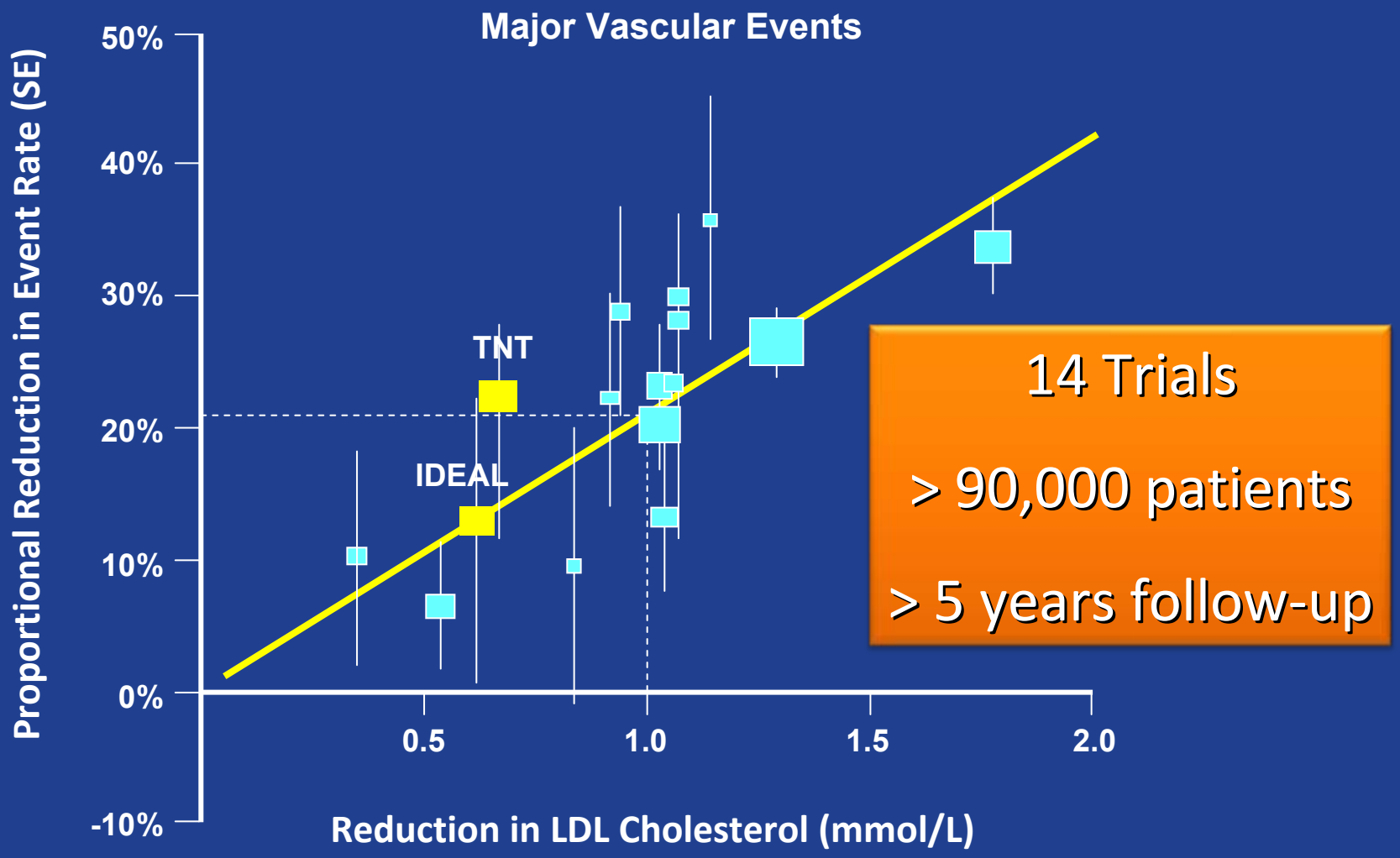


Lancet 2005;366:1267

Statins Benefit Across Risk Groups

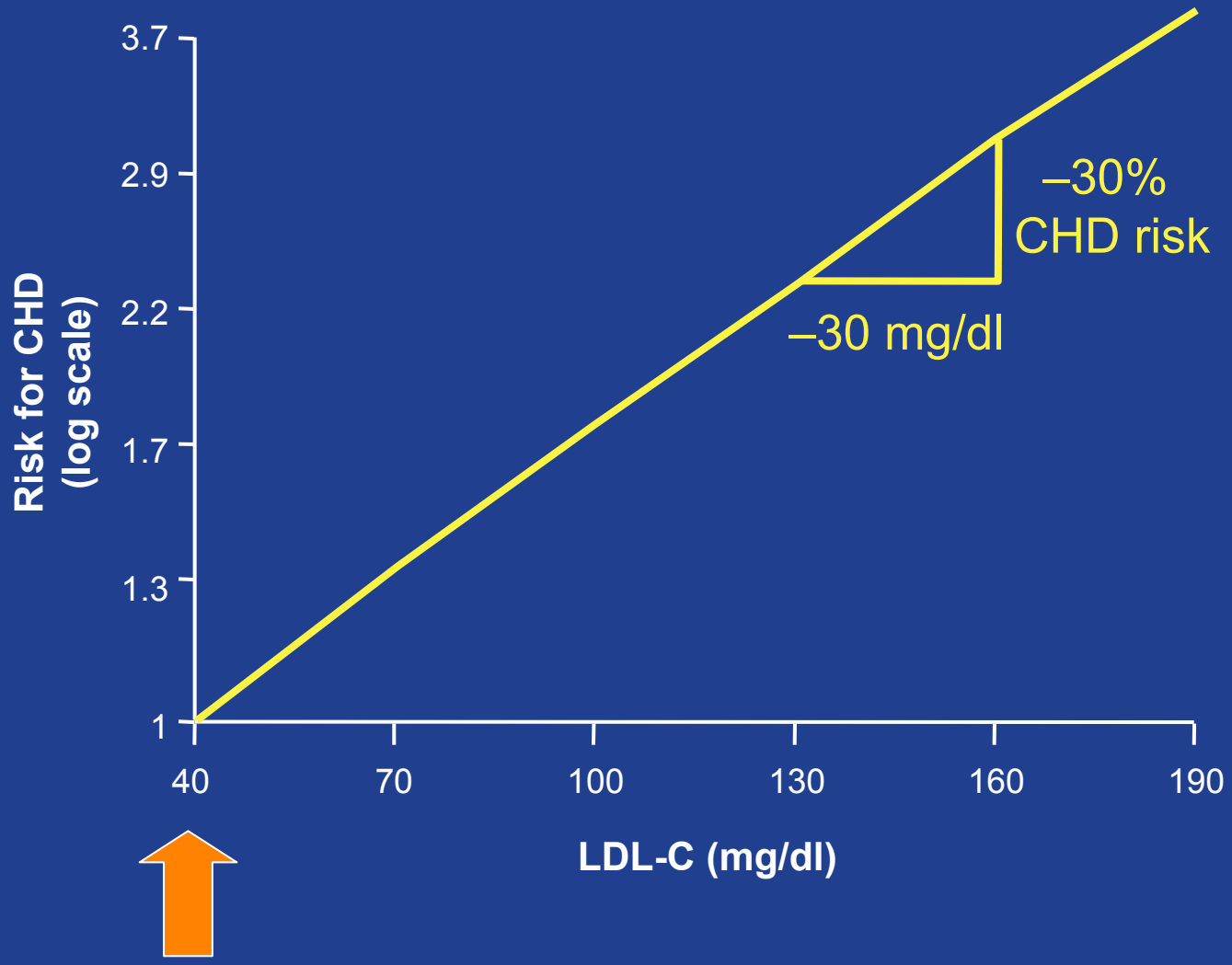


Cholesterol Trialist Collaboration
Meta-Analysis of Dyslipidemia Trials



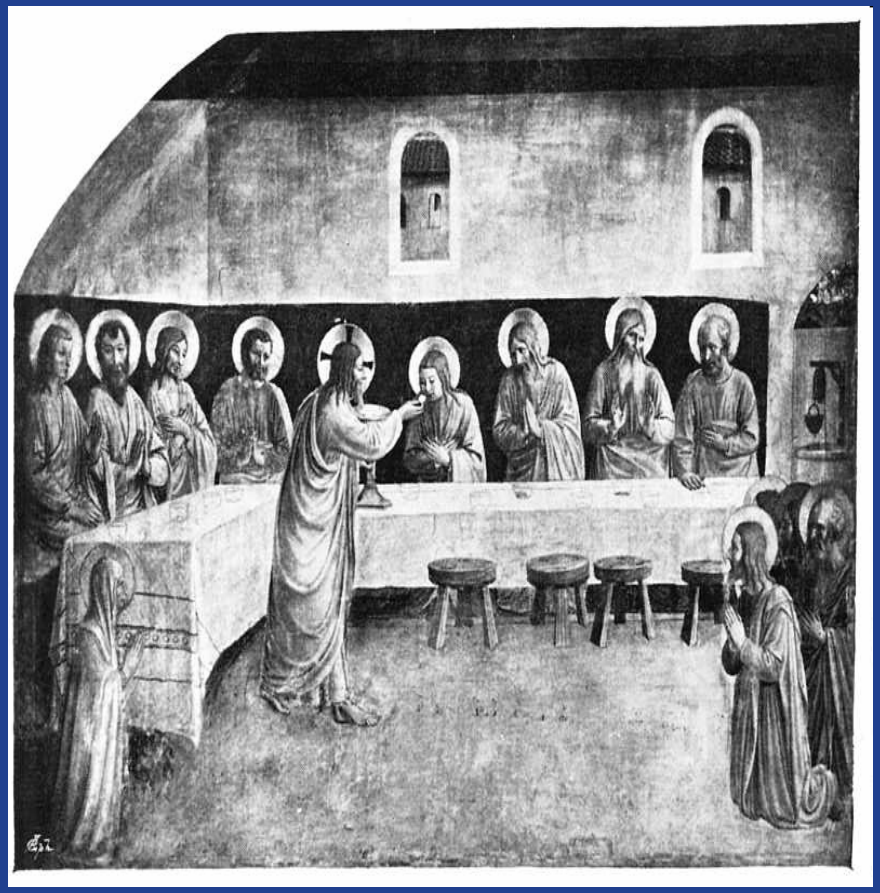
Lancet. 2005; 366:1267-78

Relationship Between LDL-C Levels and Relative Risk for CHD

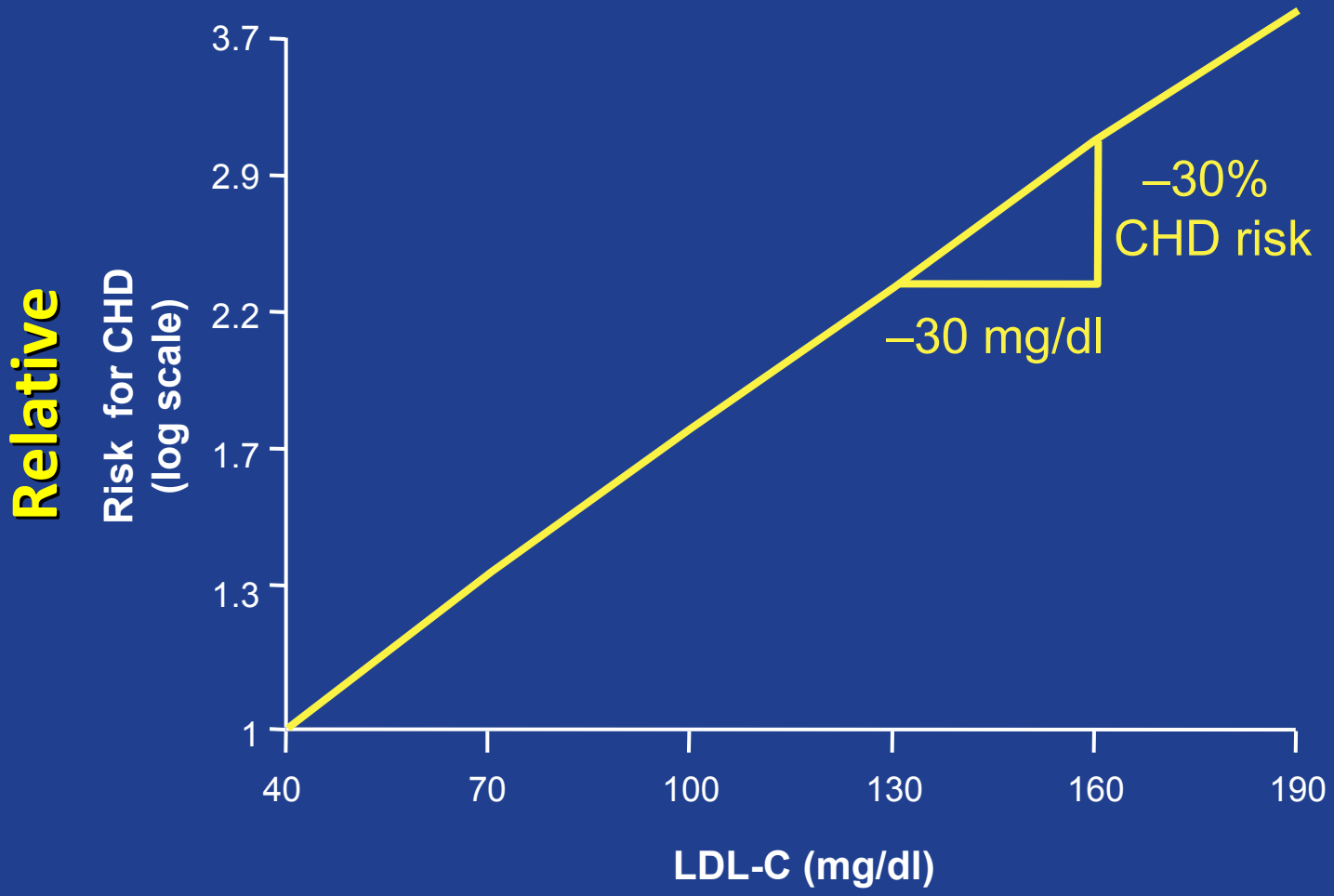


Grundy et al Recent Clinical Trials and NCEP ATP III

If So, Should Everyone Be Treated?



Relationship Between LDL-C Levels and Relative Risk for CHD



Grundy et al Recent Clinical Trials and NCEP ATP III

Malignant Blabbering

	Patient A	Patient B
Risk of disease		
Relative Risk Reduction	50%	50%
Absolute Risk Reduction		
Risk of side effects	1%	1%

ATP III Guidelines

- The intensity of risk-reduction therapy should be adjusted to a person's absolute risk.
- Hence, the first step in selection of LDL-lowering therapy is to assess a person's risk status

Assessing CHD Risk in Men

Age Years	Pts
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

HDL-C (mg/dL)	Pts
> 60	-1
50-59	0
40-49	1
< 40	**2**

Systolic Blood Pressure	Untreated	Treated
<120	0	0
120-129	**0**	1
130-139	1	2
140-159	1	2
≥ 160	2	3

55 yo male
BP 128/80
TC 232
HDL-C 37
LDL-C 167
Non-smoker
No DM

Total Cholesterol (mg/dL)	20-39	40-49	50-59	60-69	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

Cigarette Smoking					
Nonsmoker	0	0	**0**	0	0
Smoker	8	5	3	1	1

CHD Risk Pts	10-Yr CHD Risk
< 0	< 1%
0	1%
1	1%
2	1%
3	1%
4	1%
5	2%
6	2%
7	3%
8	4%
9	5%
10	6%
11	8%
12	10%
13	**12%**
14	16%
15	20%
16	25%
≥ 17	≥ 30%

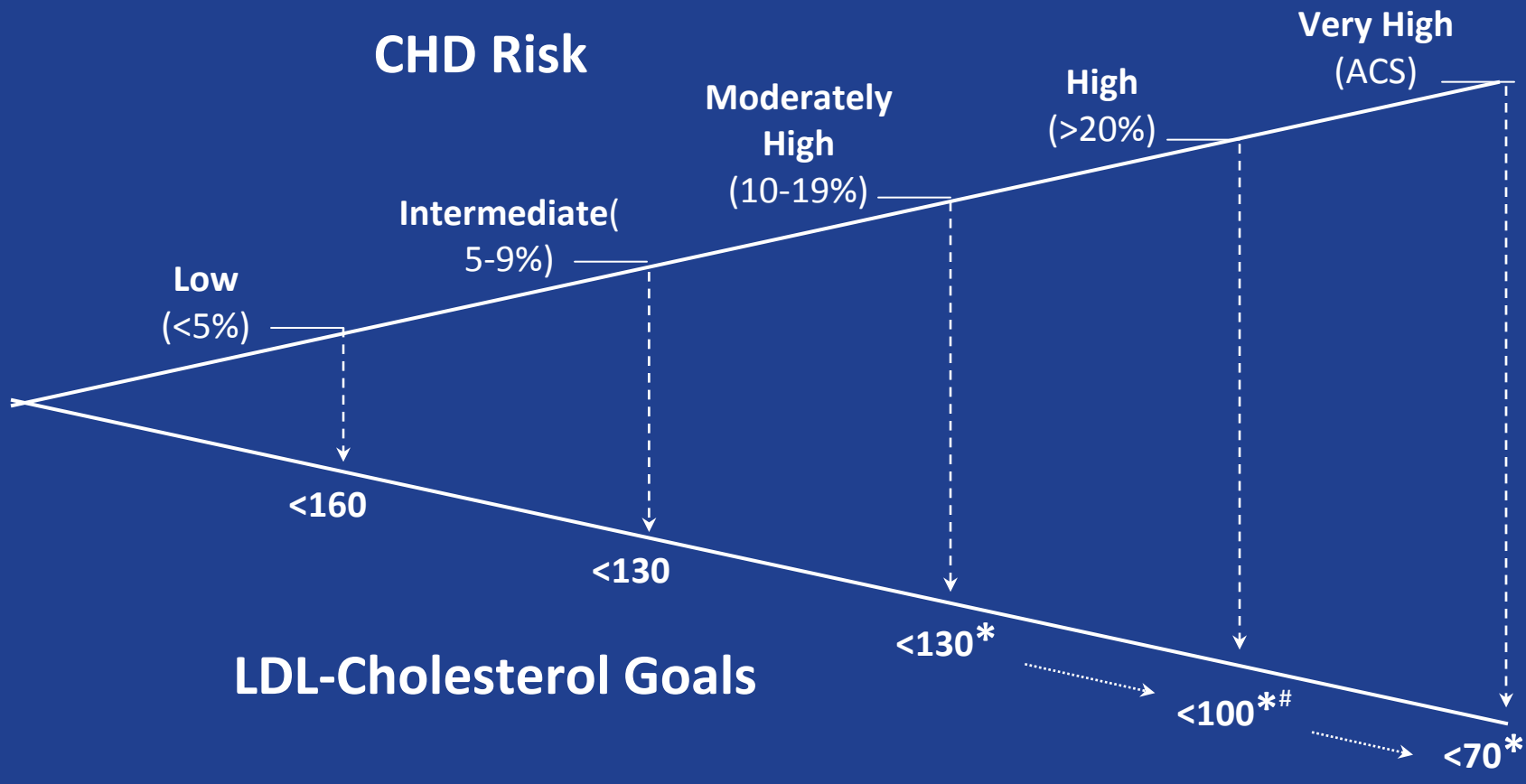
JAMA 2001; 285: 2486-2497

ATP III LDL-C Cutoffs for Therapy

Risk category	LDL-C goal	Initiate lifestyle changes	Drug therapy
High risk: CHD or CHD risk equivalents (10-year risk >20%)	<100 mg/dL (optional <70 mg/dL)	≥100 mg/dL	≥100 mg/dL (consider if LDL-C <100 mg/dL)
Moderate risk: ≥2 risk factors (10-year risk <10%)	<130 mg/dL	≥130 mg/dL	>160 mg/dL
Low risk: ≤1 risk factor	<160 mg/dL	≥160 mg/dL	≥190 mg/dL (consider if LDL-C 160-189 mg/dL)

Grundy SM et al. *Circulation*; available at http://circ.ahajournals.org

Modified ATP III LDL-C Guidelines



* Treat other lifestyle risk factors, metabolic syndrome

Use non-HDL-C for additional drug treatment

Circulation, 2004; 110:227-239

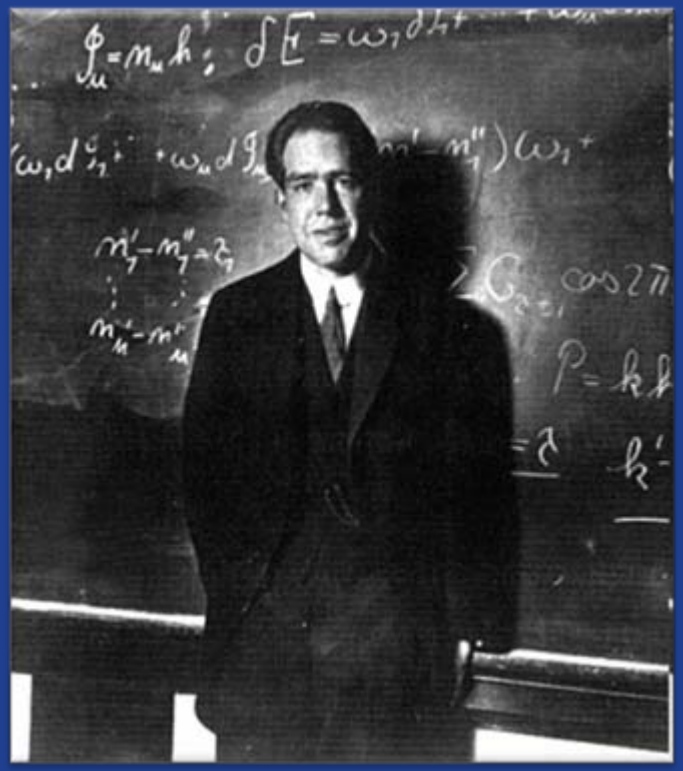
Guidelines: LDL-C Goals in High-Risk Patients

Guideline	LDL-C goal	LDL-C level to initiate TLC	LDL-C level to consider therapy
NCEP ATP III 2001	<100 mg/dL	≥100 mg/dL	≥130 mg/dL

Guidelines: LDL-C Goals in High-Risk Patients

Guideline	LDL-C goal	LDL-C level to initiate TLC	LDL-C level to consider therapy
NCEP ATP III 2004	<100 mg/dL **Optional <70 mg/dL especially in very high-risk patients**	≥100 mg/dL	≥130 mg/dL (100 to 129 mg/dL: drug optional)

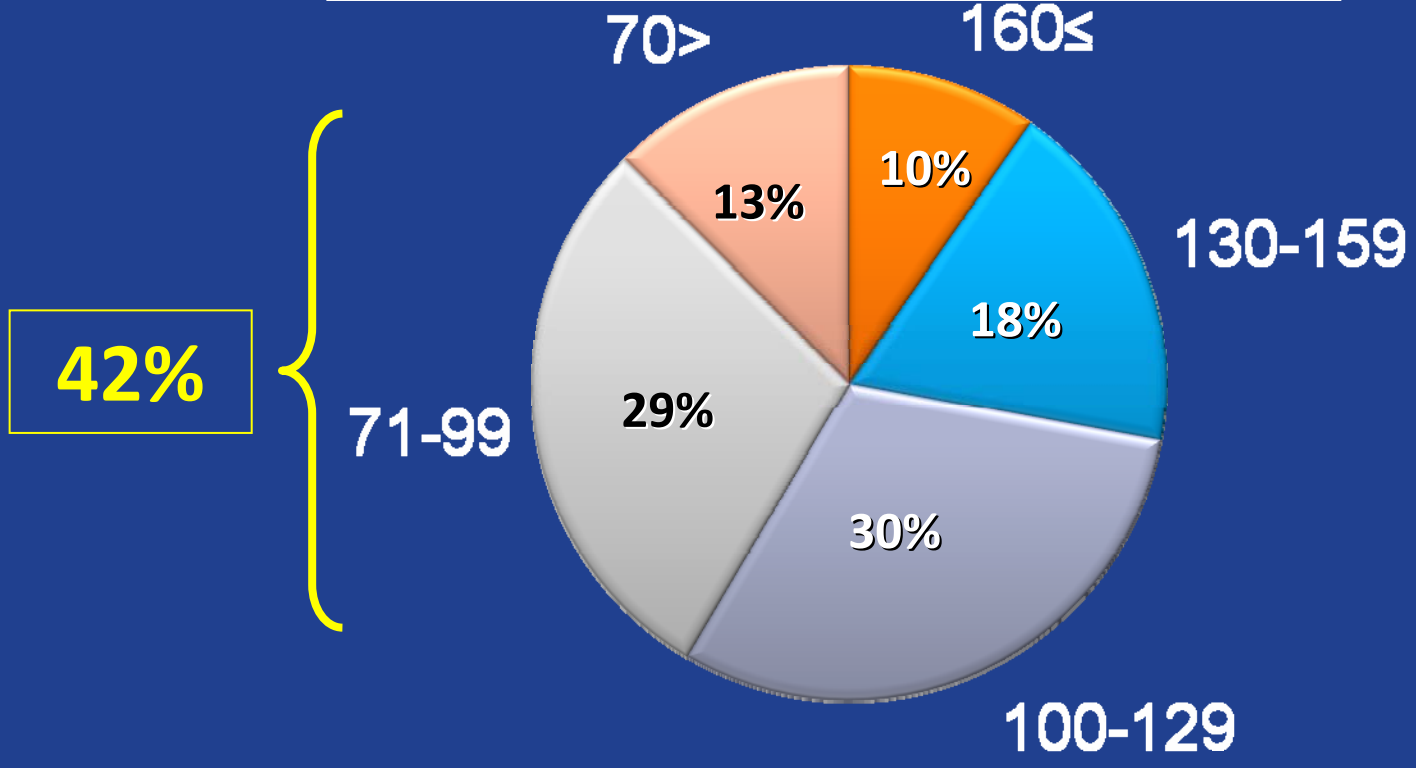
“Prediction Is Very Difficult, Especially If It’s About The Future”



Nils Böhr

LDL-C in Patients Hospitalized with CAD: 48,093 Patients Without History of CAD

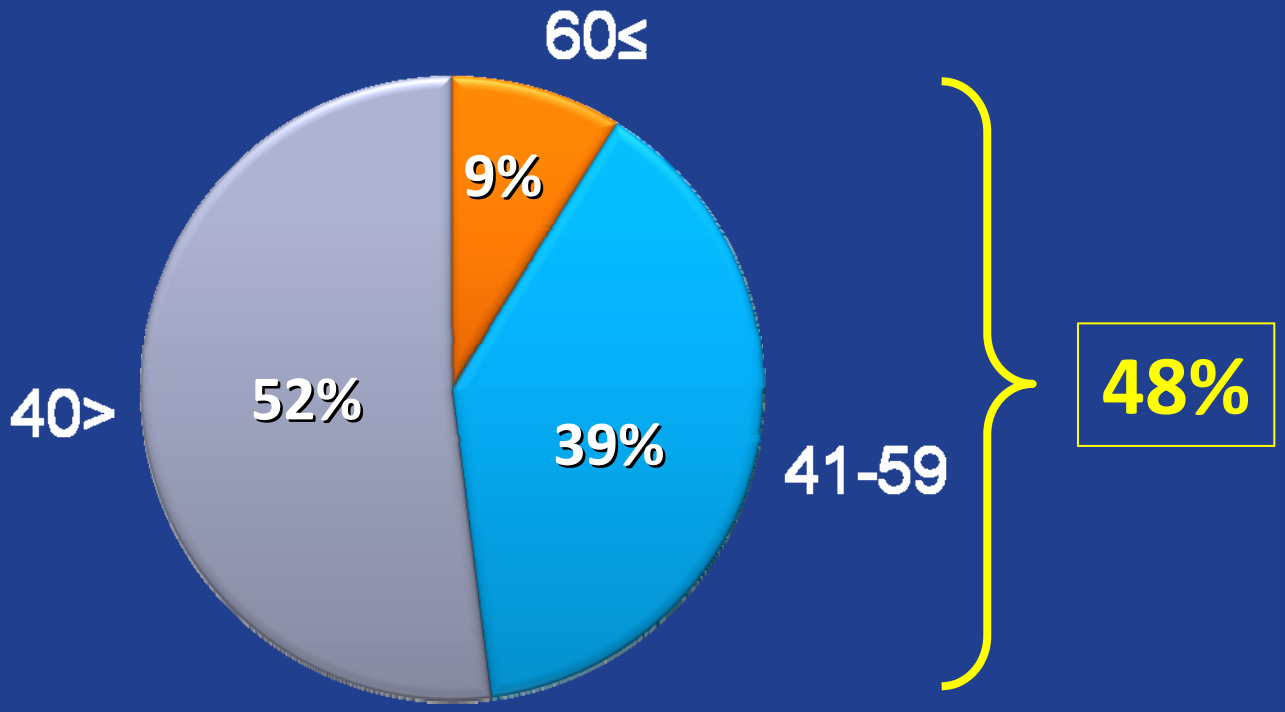
14% on lipid lowering therapy



42% had LDL-C <100 mg/dl

Am Heart J 2009;157:111-7

HDL-C in Patients Hospitalized with CAD: 48,093 Patients Without History of CAD

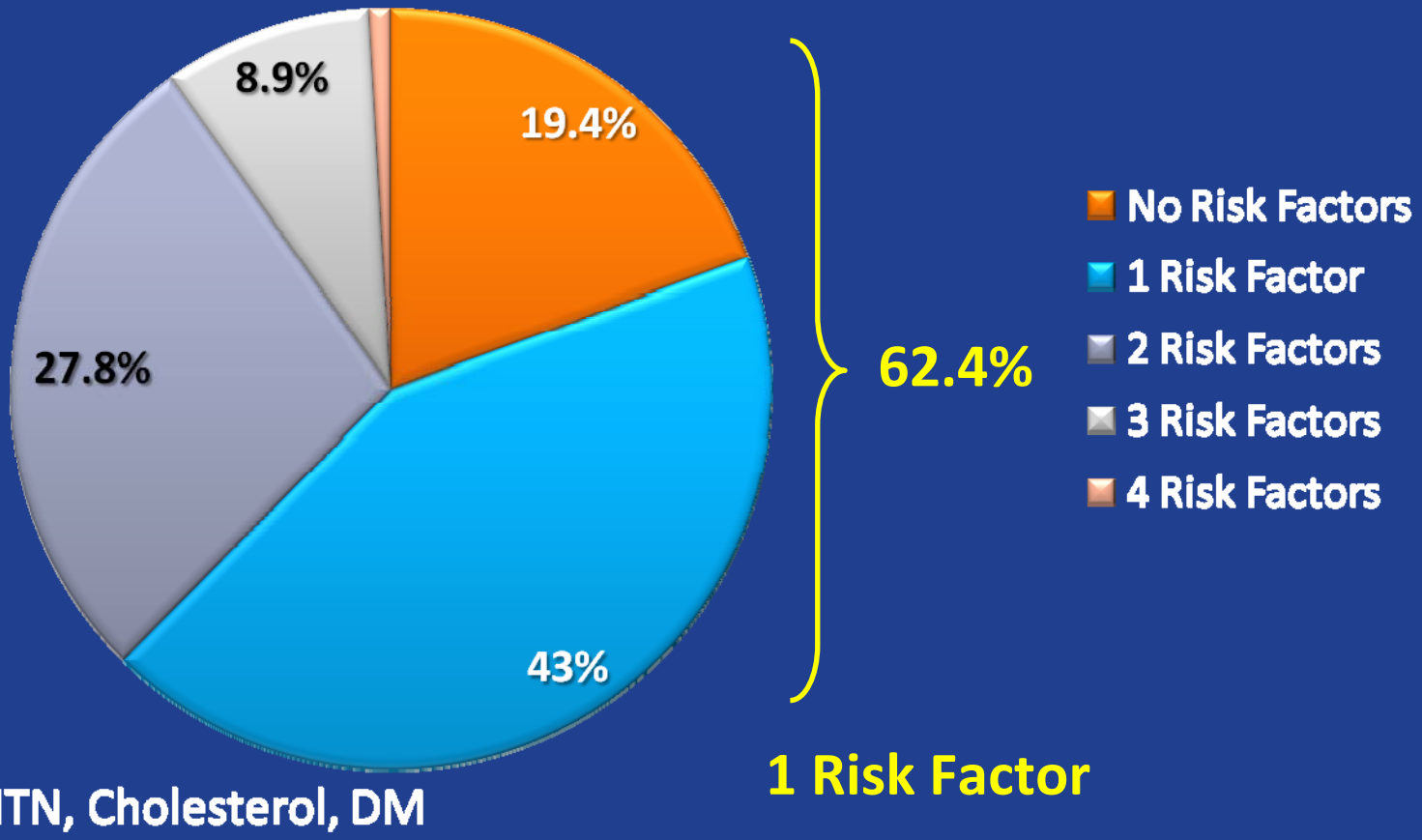


48% had HDL-C >40 mg/dl

Am Heart J 2009;157:111-7

Prevalence of Conventional Risk Factors* in Men with CHD

(14 trials, N = 87,869, mean age 60)

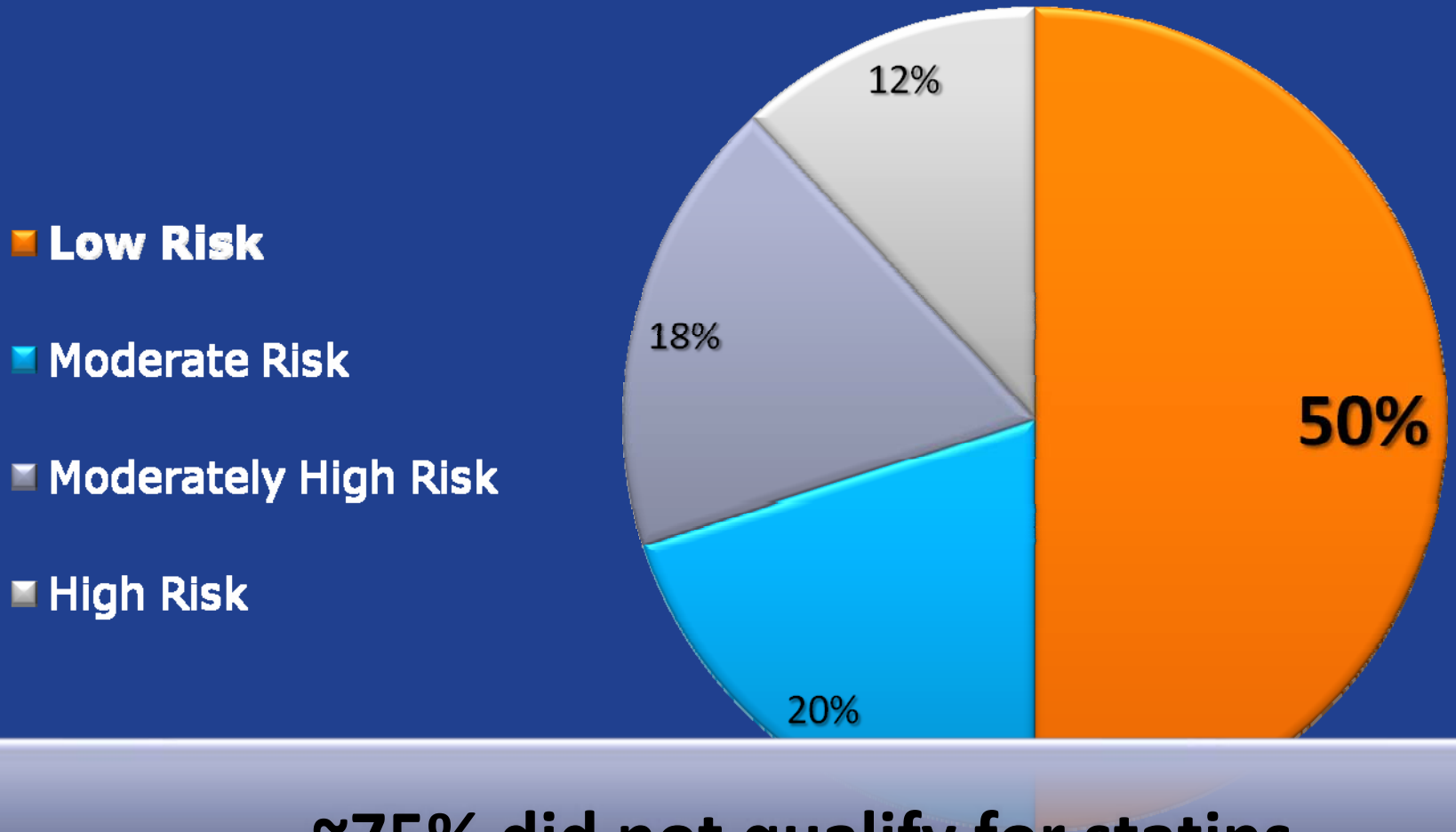


*Smoking, HTN, Cholesterol, DM

JAMA 2003;290:898

How Good Is NCEP ATP III At Predicting MI in Young People?

222 patients with 1st acute MI, no prior CAD, no DM men <55, women <65



~75% did not qualify for statins

JACC 2003;41:1475

"These Data Demonstrate That _____ is An Independent Predictor of MI And Stroke"

hsCRP
sICAM-1
sVCAM-1
P-selectin
E-selectin
IL-1ra, 6, 8, 10, 18
TNF-alpha, TNF-r2
sCD40L
MMP-9
Lp-PLA_2
Myeloperoxidase
Osteoprotegerin
MIC-1
WBC / ESR / albumin

tPA:ag/act
PAI-1:ag/act
D-dimer
Fibrinogen/variants
TAFI
vWF:ag
Factor VII, X, XIII

Homocysteine
ADMA
RAGE

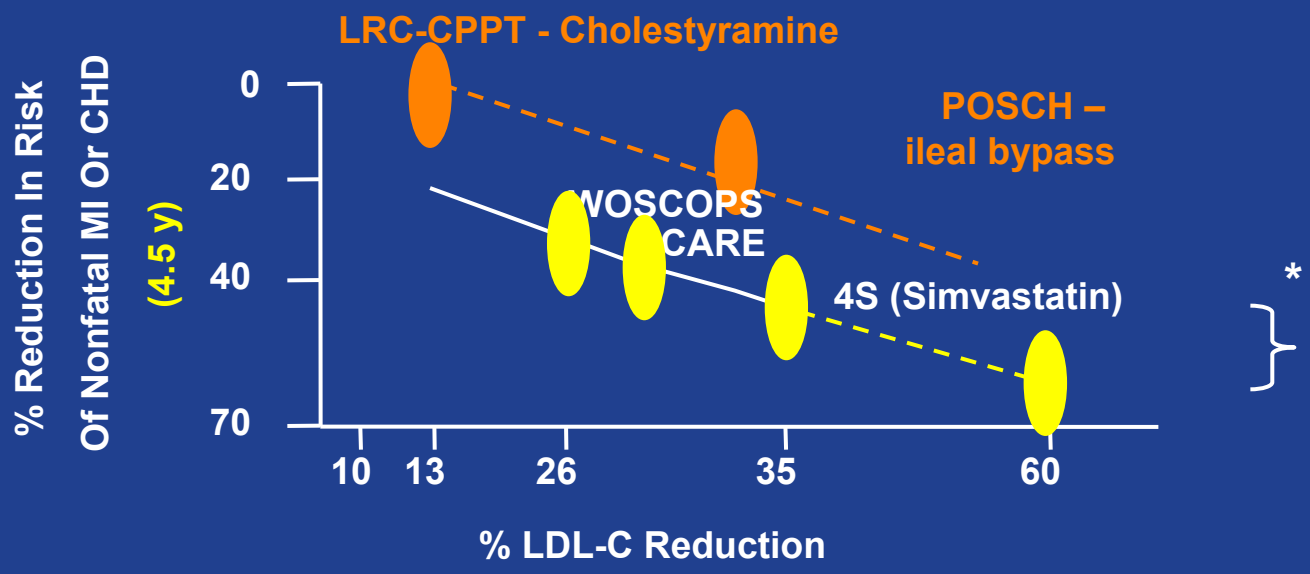
Creatinine
Cystatin C
microalbuminuria

Leptin
Adponectin
Osteopontin

BNP/ANP

LDL, HDL subsets
ILDL / VLDL
Apo A / Apo B
NMR / VAP / A-B
Ox-LDL
Lp(a)
ApoE Genotype

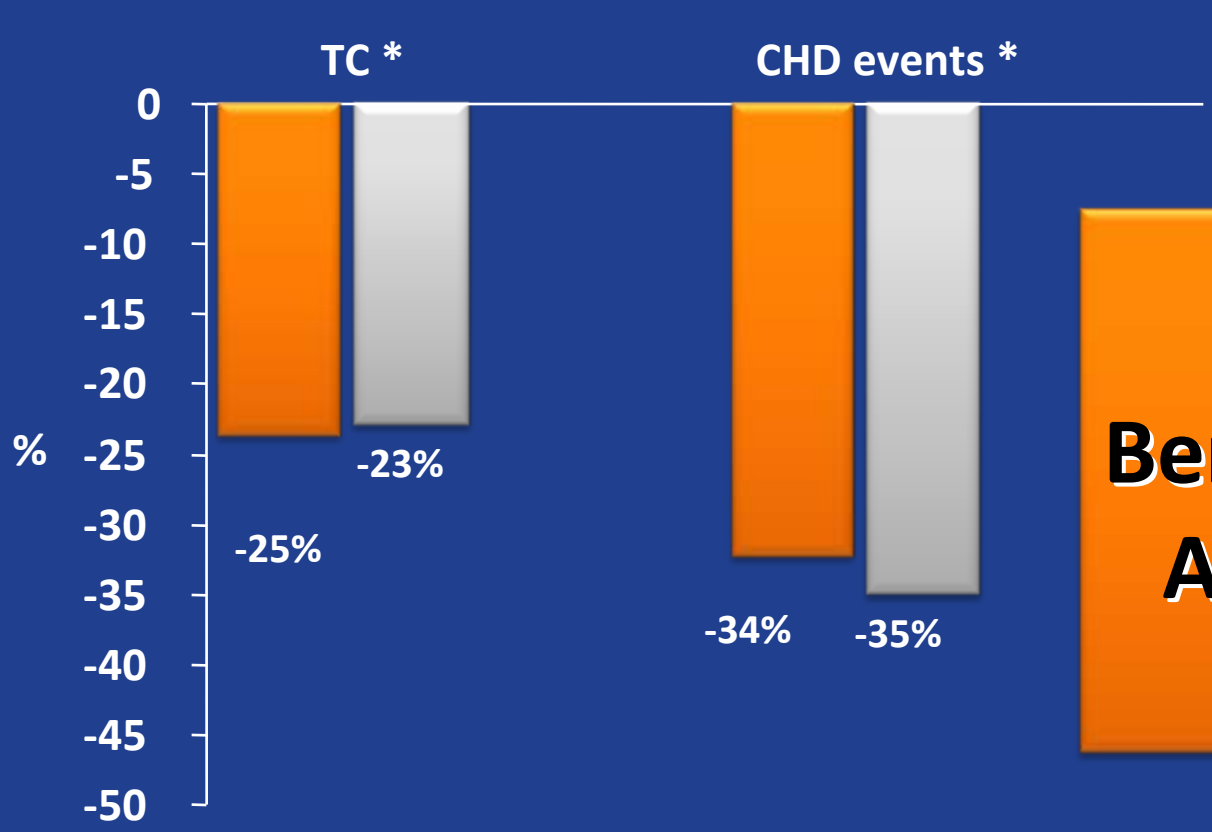
Relation Between LDL-C Reduction And Risk Of Cardiovascular Events



- When outcomes at 4.5 y are considered, beneficial effects of statins occurred more rapidly
- These effects may not be entirely cholesterol dependent; possibly due to pleiotropic effects

Am J Cardiol. 2005;96(suppl):24F.

POSCH: Partial Ileal Bypass



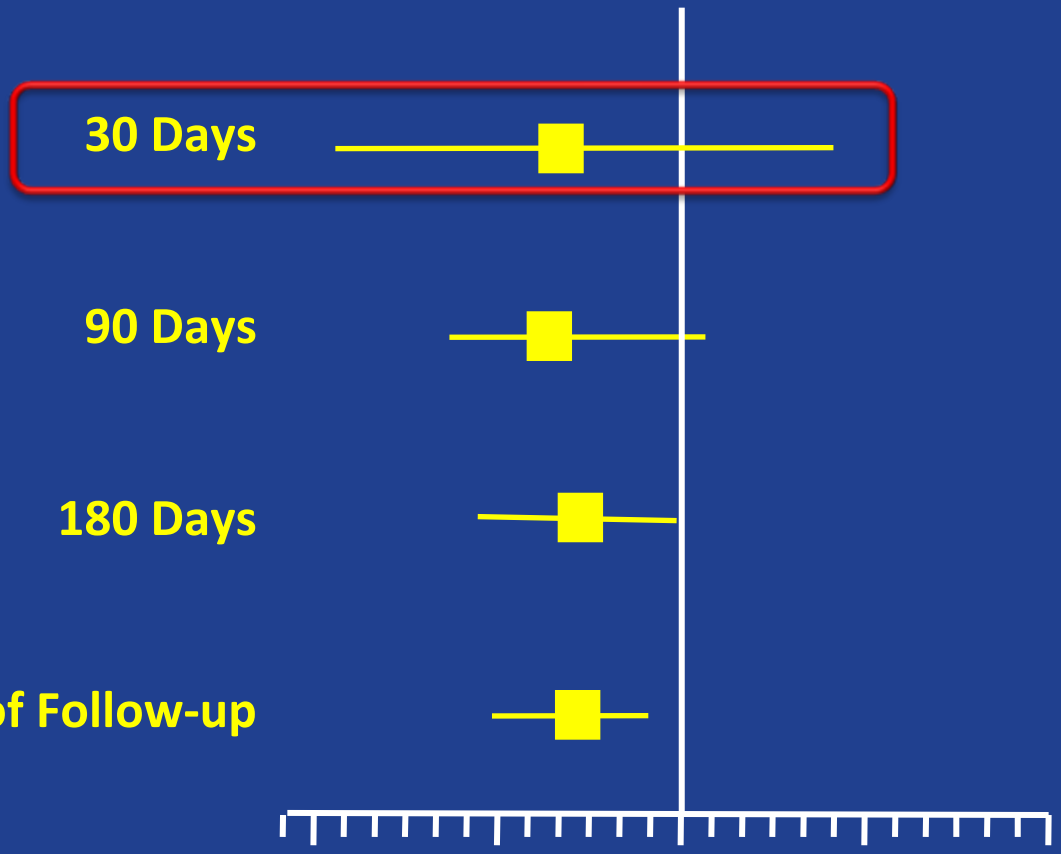
But…

Benefit Significant After 9.7 Vs. ~2 Years

*Net difference between treatment and control groups (*P* values are for events).

Adapted from Levine GN et al. *N Engl J Med.* 1995;332:512-521.

PROVE IT – Rapid Effect
Only LDL-C Reduction?



	Events Rates		
RR	Atorva 80	Prava 40
17%	1.9%	2.2%
18%	6.3%	7.7%
14%	12.2%	14.1%
16%	22.4%	26.3%

Simvastatin vs. Ezetimibe Effect on Endothelial Function

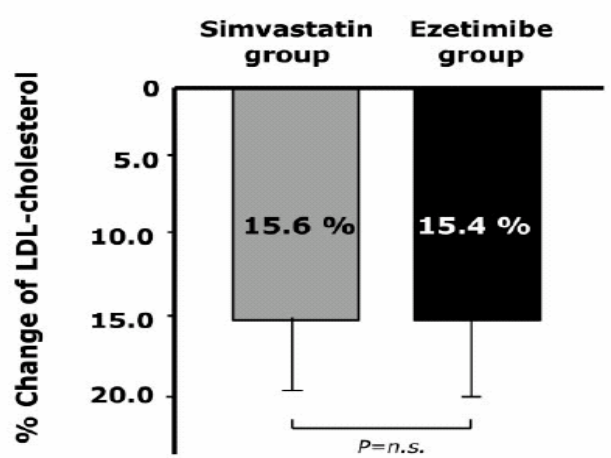
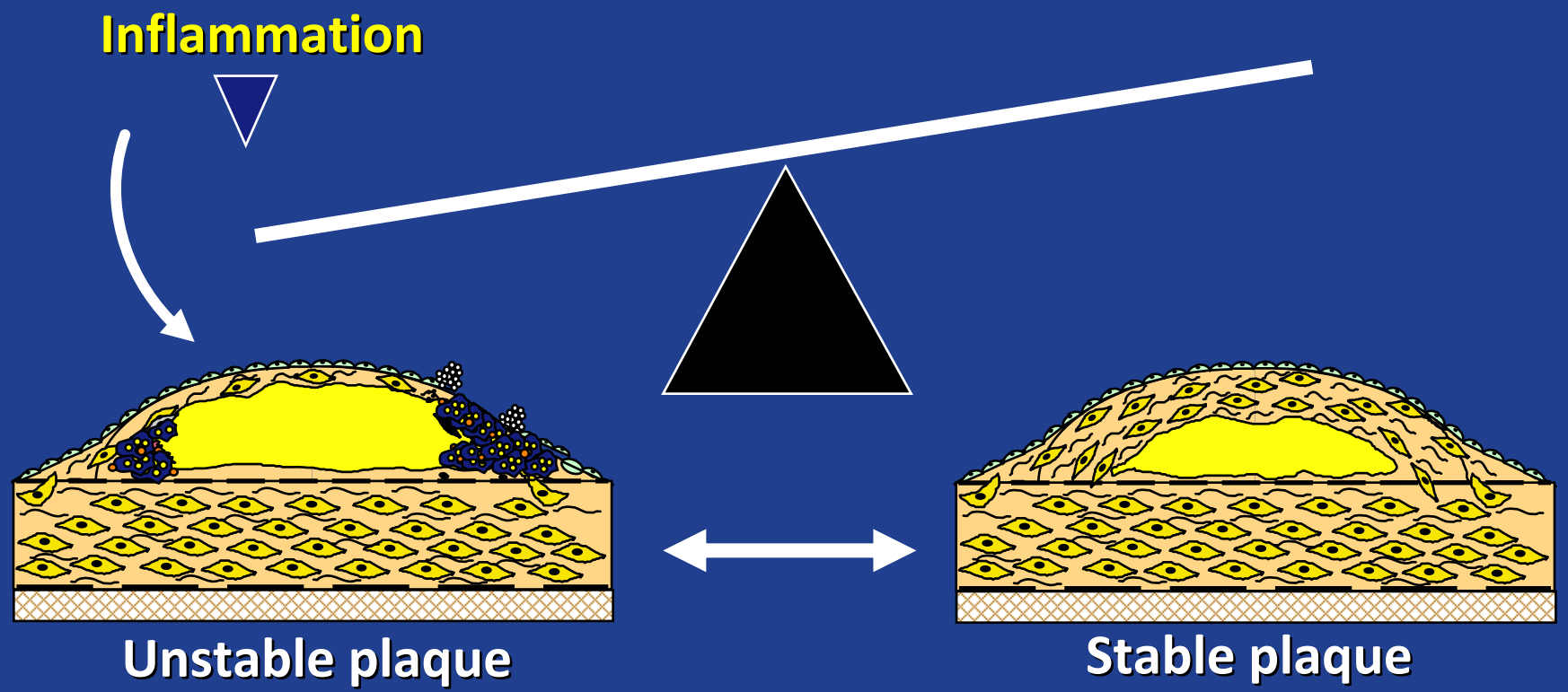


Figure 1. Change in LDL cholesterol serum levels after 4 weeks of treatment with statin (simvastatin, 10 mg/d) or intestinal cholesterol absorption inhibitor ezetimibe (10 mg/d).

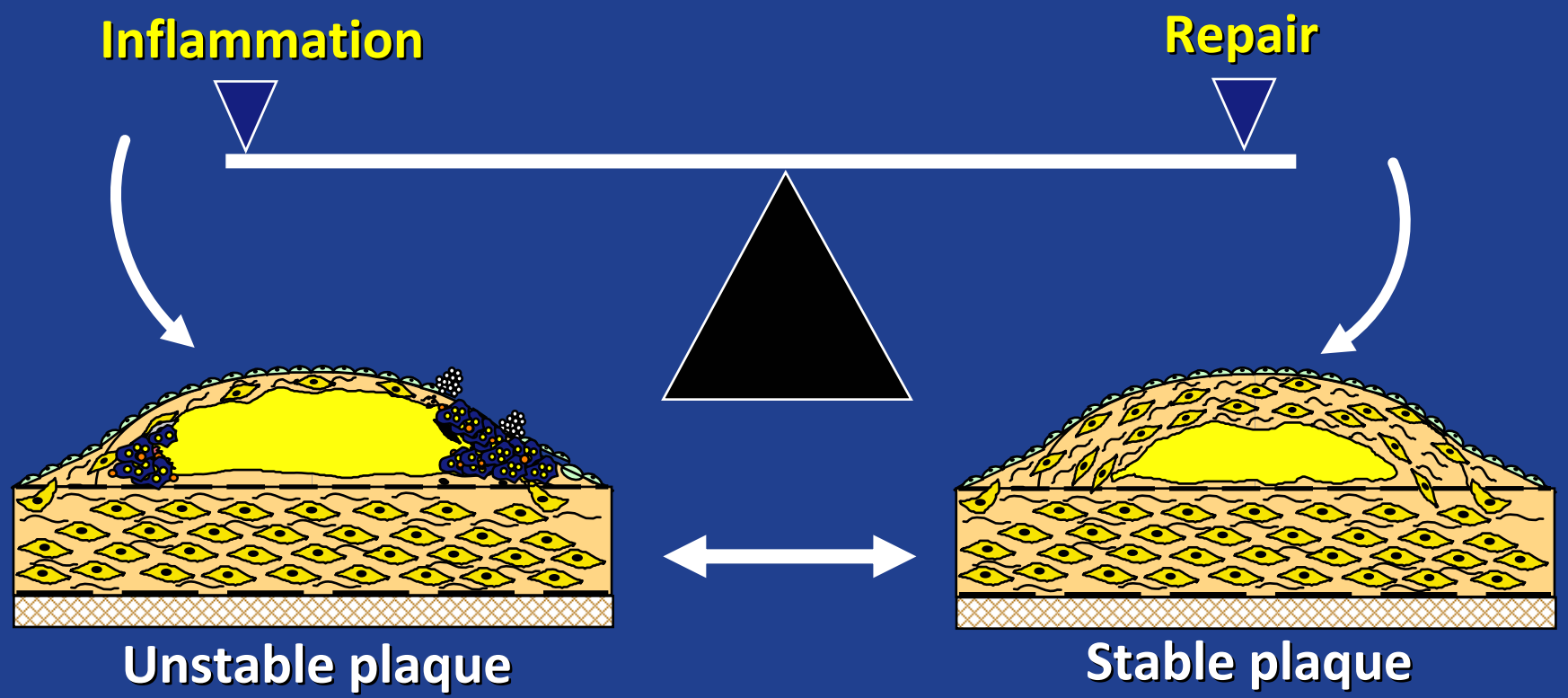
Circulation 2005;111:2356

Balancing the Stability Equation



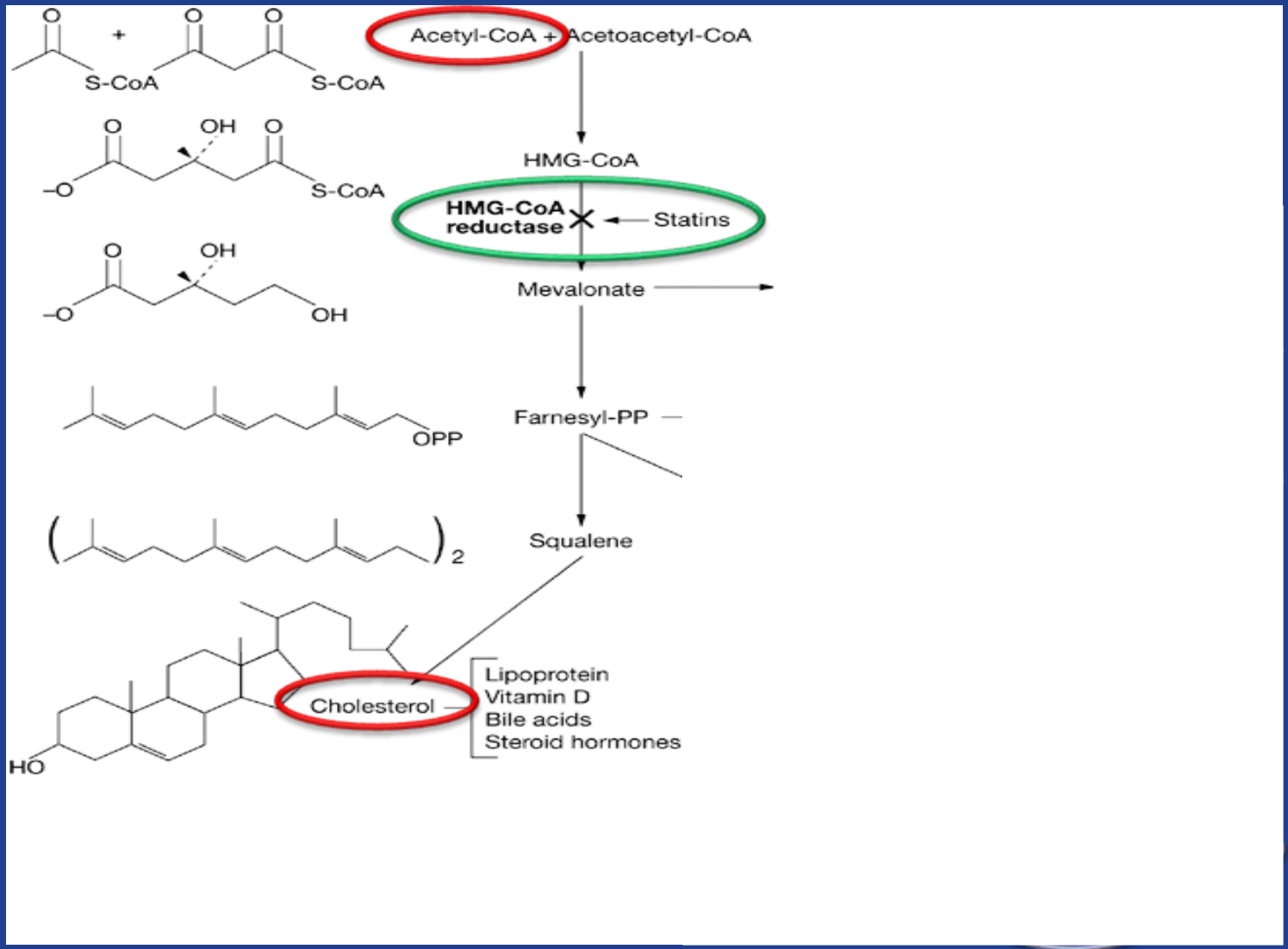
Weissberg, 1999

Balancing the Stability Equation



Weissberg, 1999

Mechanisms Underlying the Pleiotropic Effects of Statins



CRP as a Method to Target Statin Therapy in Primary Prevention: AFCAPS/TexCAPS

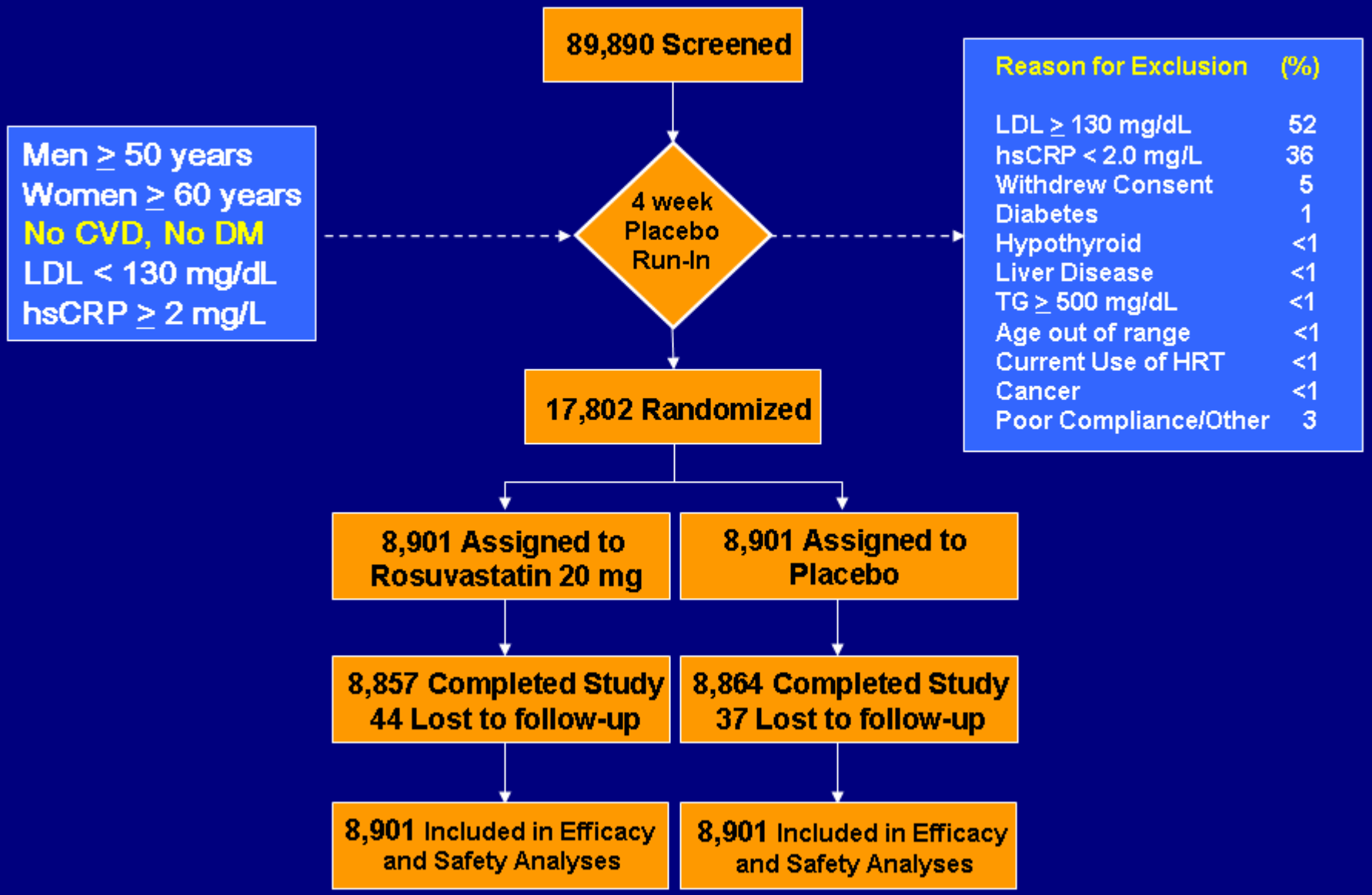
Study Group	Statin	Placebo	NNT	
low LDL-C / low CRP	0.025	0.022	----	No Statin
low LDL-C / high CRP	0.029	0.051	48	?
high LDL-C / low CRP	0.020	0.050	33	Statin
high LDL-C / high CRP	0.038	0.055	58	Statin

Median LDL-C = 149 mg/dL
Median CRP = 1.6 mg/L

NEJM 2001;344:1959-65

JUPITER

Inclusion and Exclusion Criteria, Study Flow



JUPITER
Baseline Blood Levels (median, interquartile range)

	Rosuvastatin (N = 8901)		Placebo (n = 8901)	
hsCRP, mg/L	4.2	(2.8 - 7.1)	4.3	(2.8 - 7.2)
LDL, mg/dL	108	(94 - 119)	108	(94 - 119)
HDL, mg/dL	49	(40 – 60)	49	(40 – 60)
Triglycerides, mg/L	118	(85 - 169)	118	(86 - 169)
Total Cholesterol, mg/dL	186	(168 - 200)	185	(169 - 199)
Glucose, mg/dL	94	(87 – 102)	94	(88 – 102)
HbA1c, %	5.7	(5.4 – 5.9)	5.7	(5.5 – 5.9)

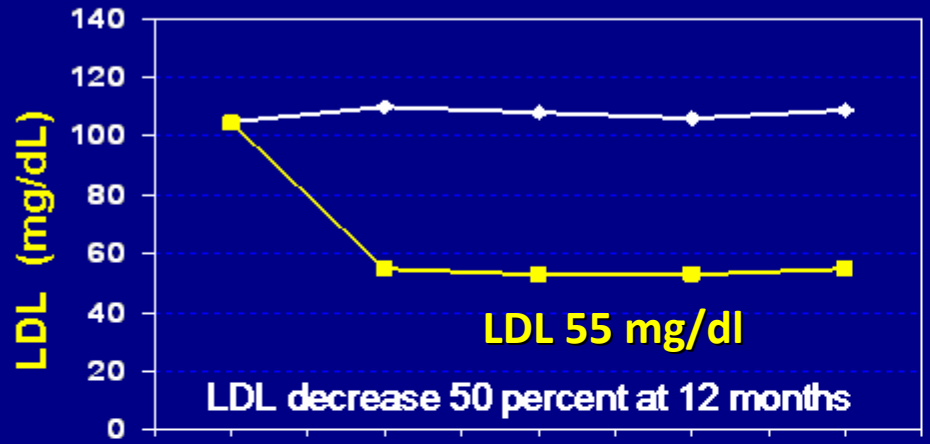
All values are median (interquartile range). [Mean LDL = 104 mg/dL]

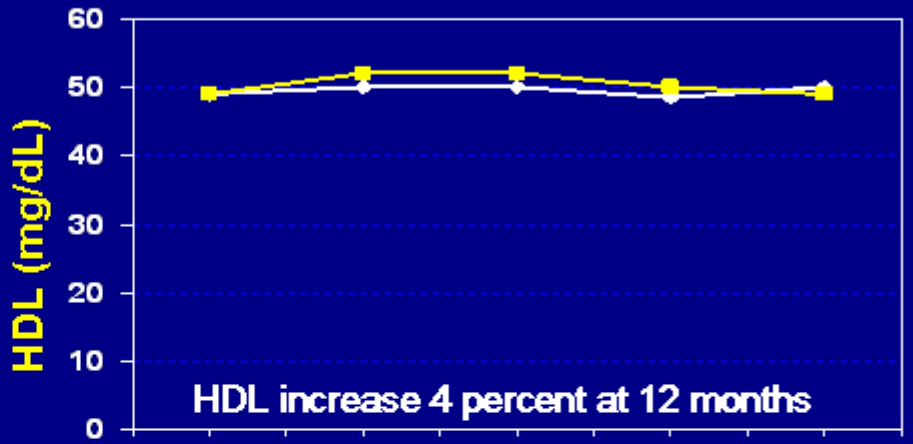
Early Study Termination

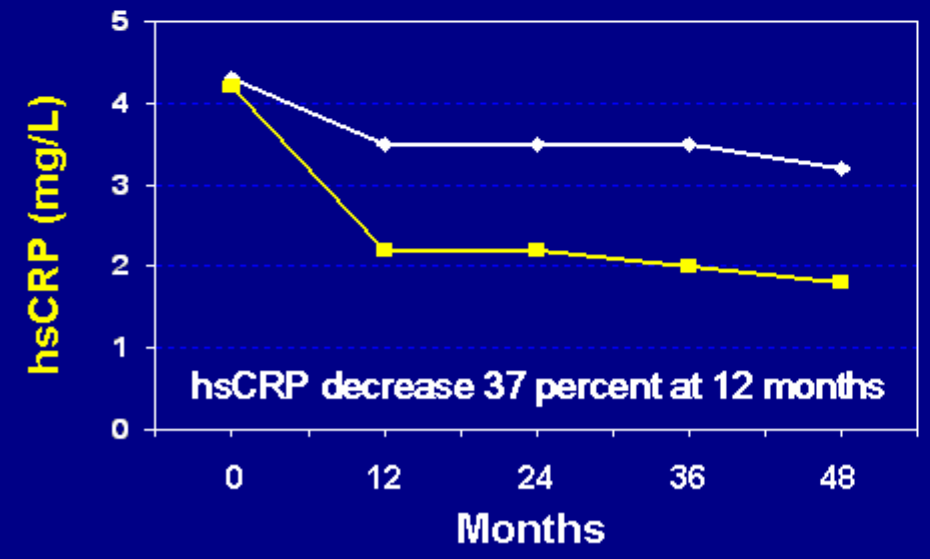
- Designed to continue until 520 primary end points.
- Stopped early when only 393 events had occurred because the DSMB identified benefits to people taking active treatment.
- JUPITER lasted only a median of 1.9 years instead of the planned 4 years.

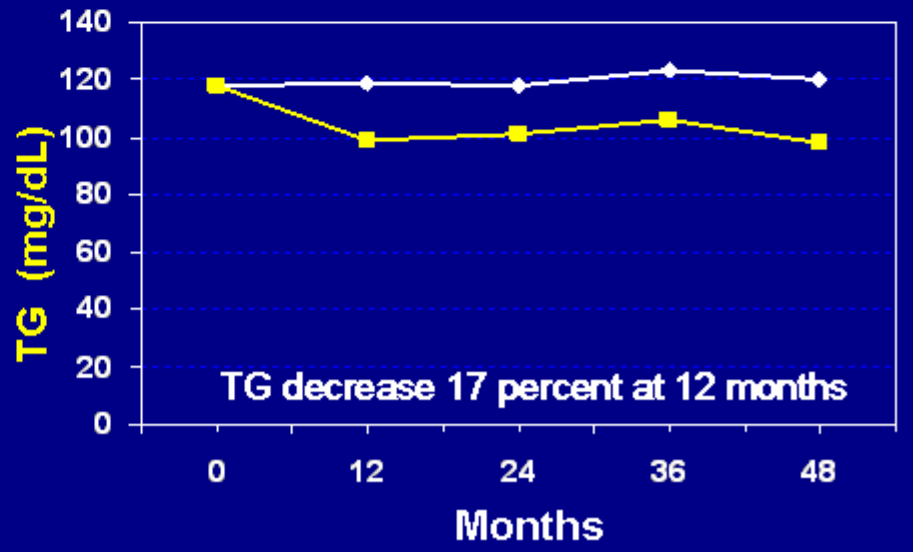
JUPITER

Effects of rosuvastatin 20 mg on LDL, HDL, TG, and hsCRP



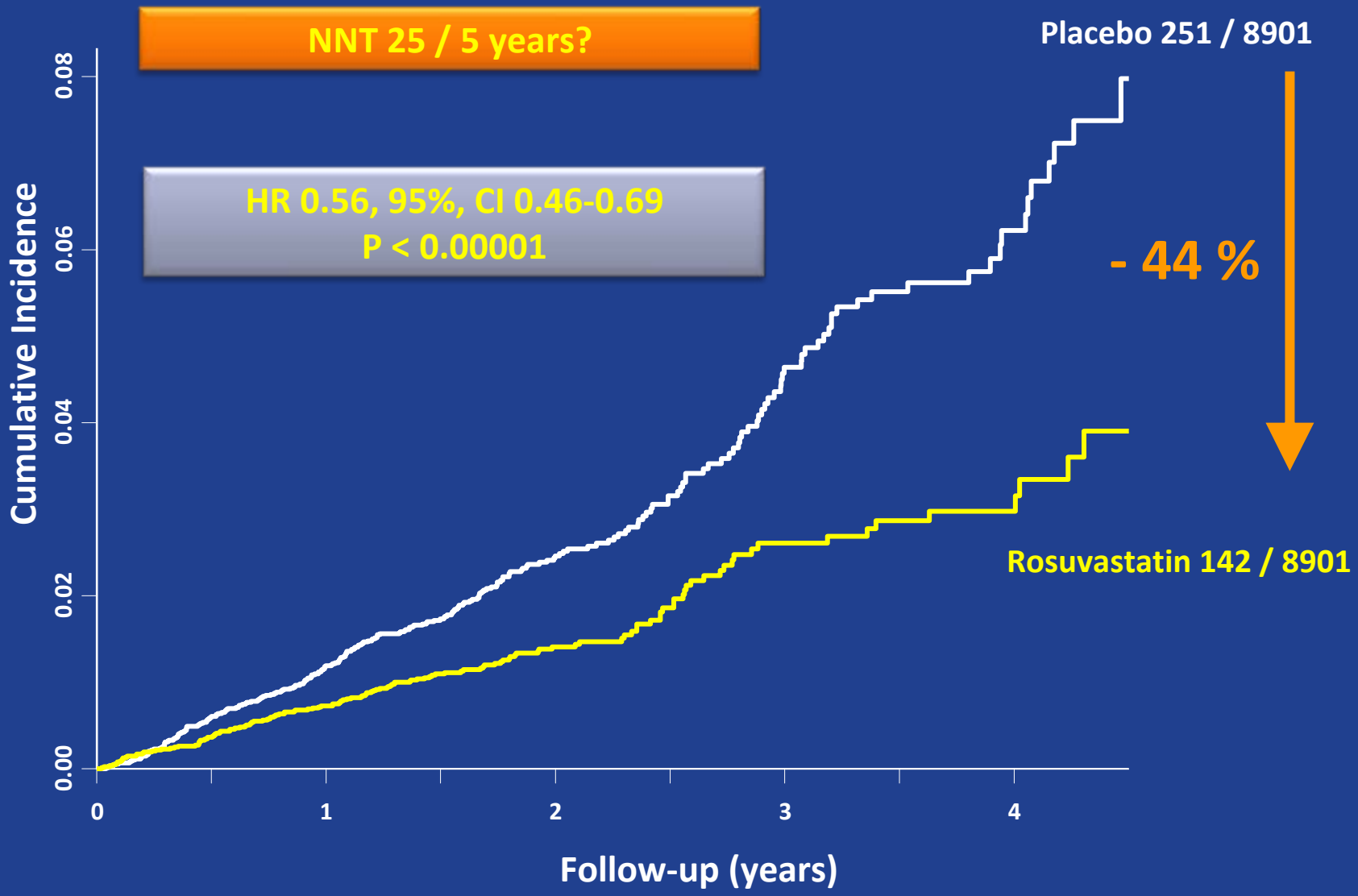






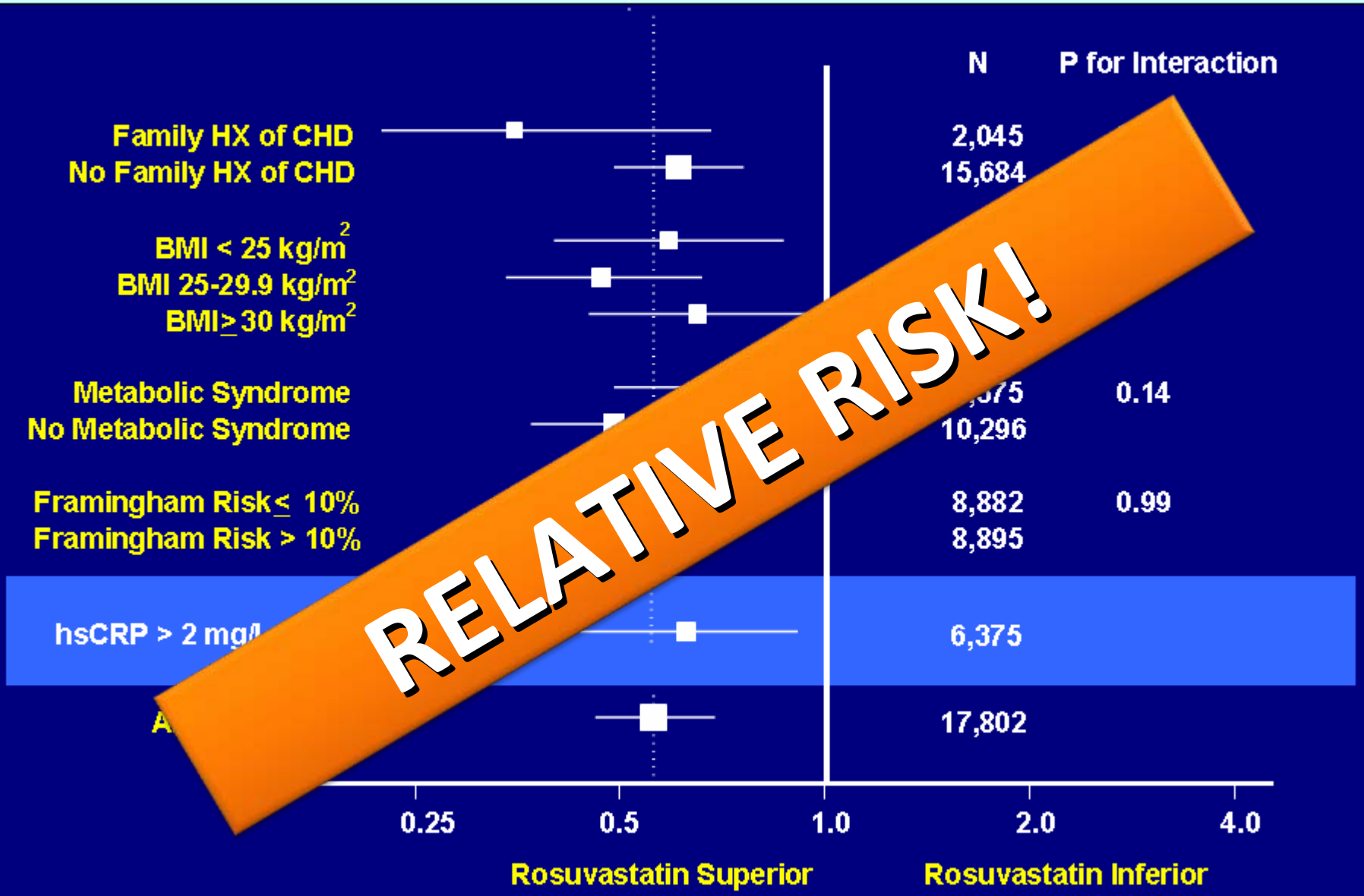
JUPITER Primary Endpoint:

MI, Stroke, UA/Revasc, CV Death



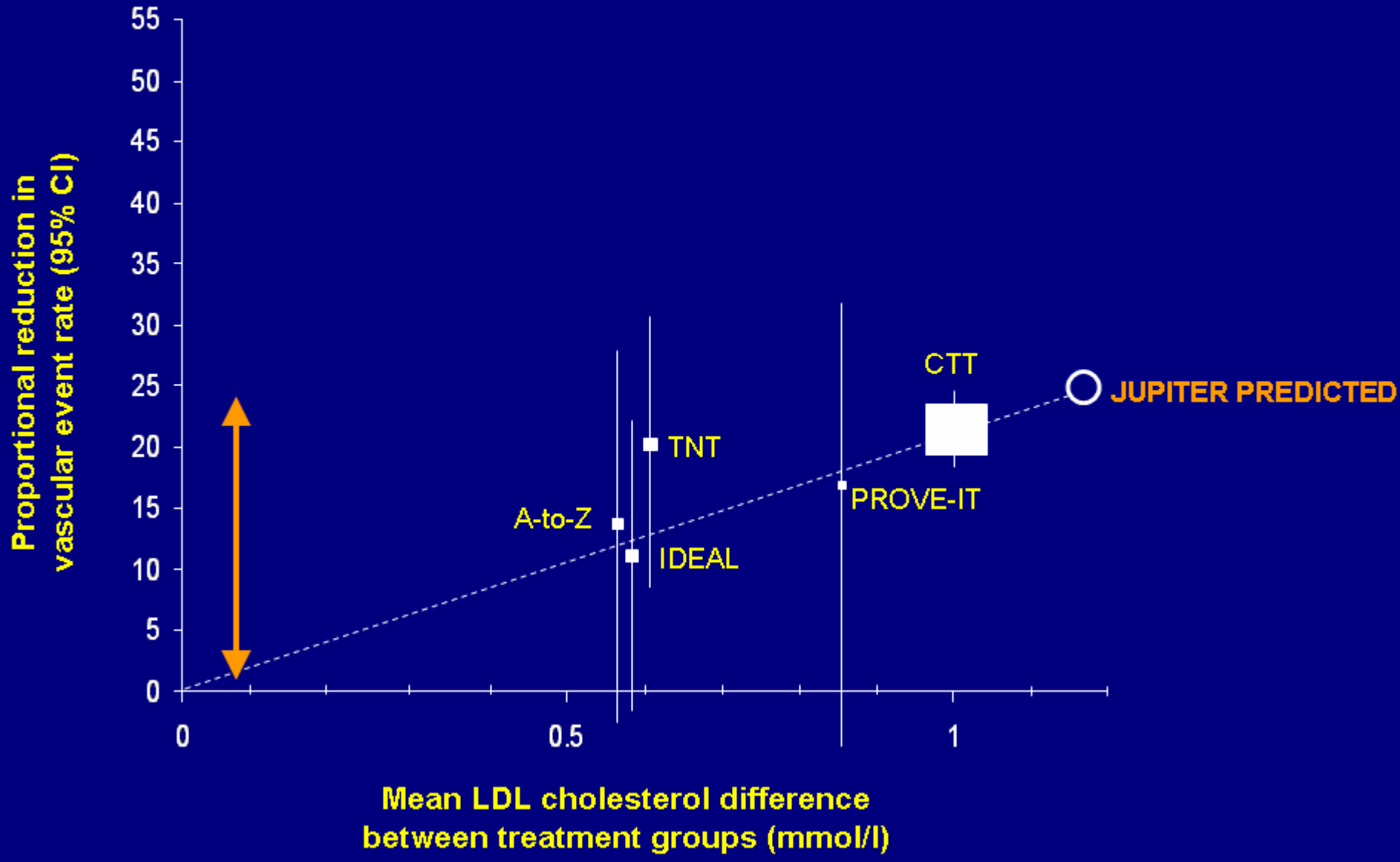
N Engl J Med 2008;359:2195

JUPITER
Primary Endpoint – Subgroup Analysis II



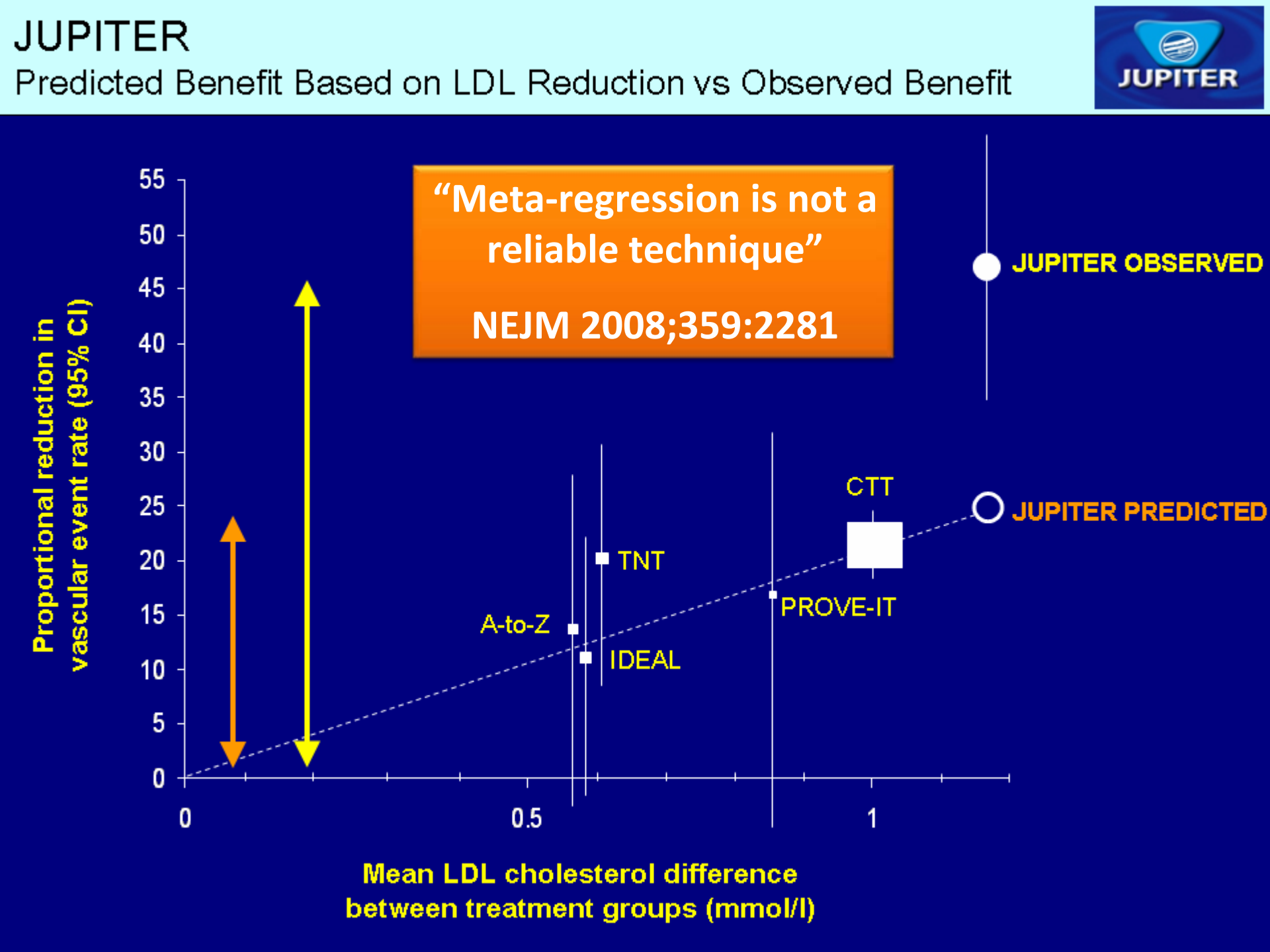
JUPITER

Predicted Benefit Based on LDL Reduction vs Observed Benefit



JUPITER

Predicted Benefit Based on LDL Reduction vs Observed Benefit



JUPITER

Implications for Primary Prevention

A simple evidence based approach to statin therapy for primary prevention.

Among men and women age 50 or over :

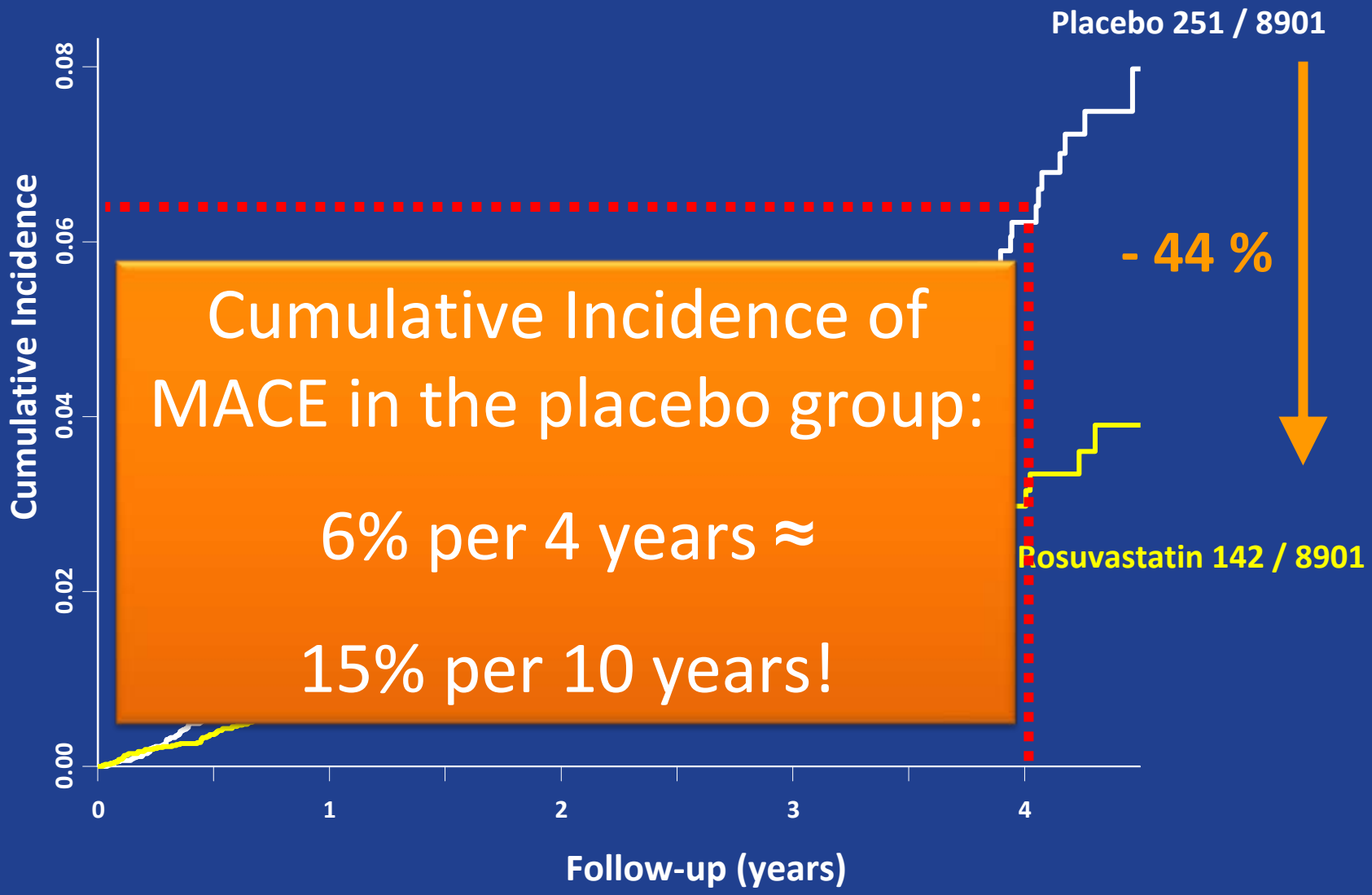
If diabetic, treat
If LDLC > 160 mg/dL, treat
If hsCRP > 2 mg/L, treat

JUPITER: Unanswered Questions

- Not a CRP trial – no low CRP group
  - Simply cholesterol lowering?
- Low risk population?
  - ~50% had metabolic syndrome and/or FRS >10%

JUPITER Primary Endpoint:

MI, Stroke, UA/Revasc, CV Death



Cumulative Incidence of MACE in the placebo group:

6% per 4 years ≈

15% per 10 years!

N Engl J Med 2008;359:2195

ATP III LDL-C Cutoffs for Therapy

Risk category	LDL-C goal	Initiate lifestyle changes	Drug therapy
High risk: CHD or CHD risk equivalents (10-year risk >20%)	<100 mg/dL (optional <70 mg/dL)	≥100 mg/dL	≥100 mg/dL (consider if LDL-C <100 mg/dL)
Moderate risk: ≥2 risk factors (10-year risk <10%)	<130 mg/dL	≥130 mg/dL	>160 mg/dL
Low risk: ≤1 risk factor	<160 mg/dL	≥160 mg/dL	≥190 mg/dL (consider if LDL-C 160-189 mg/dL)

Grundy SM et al. *Circulation*; available at http://circ.ahajournals.org

JUPITER
Adverse Events and Measured Safety Parameters

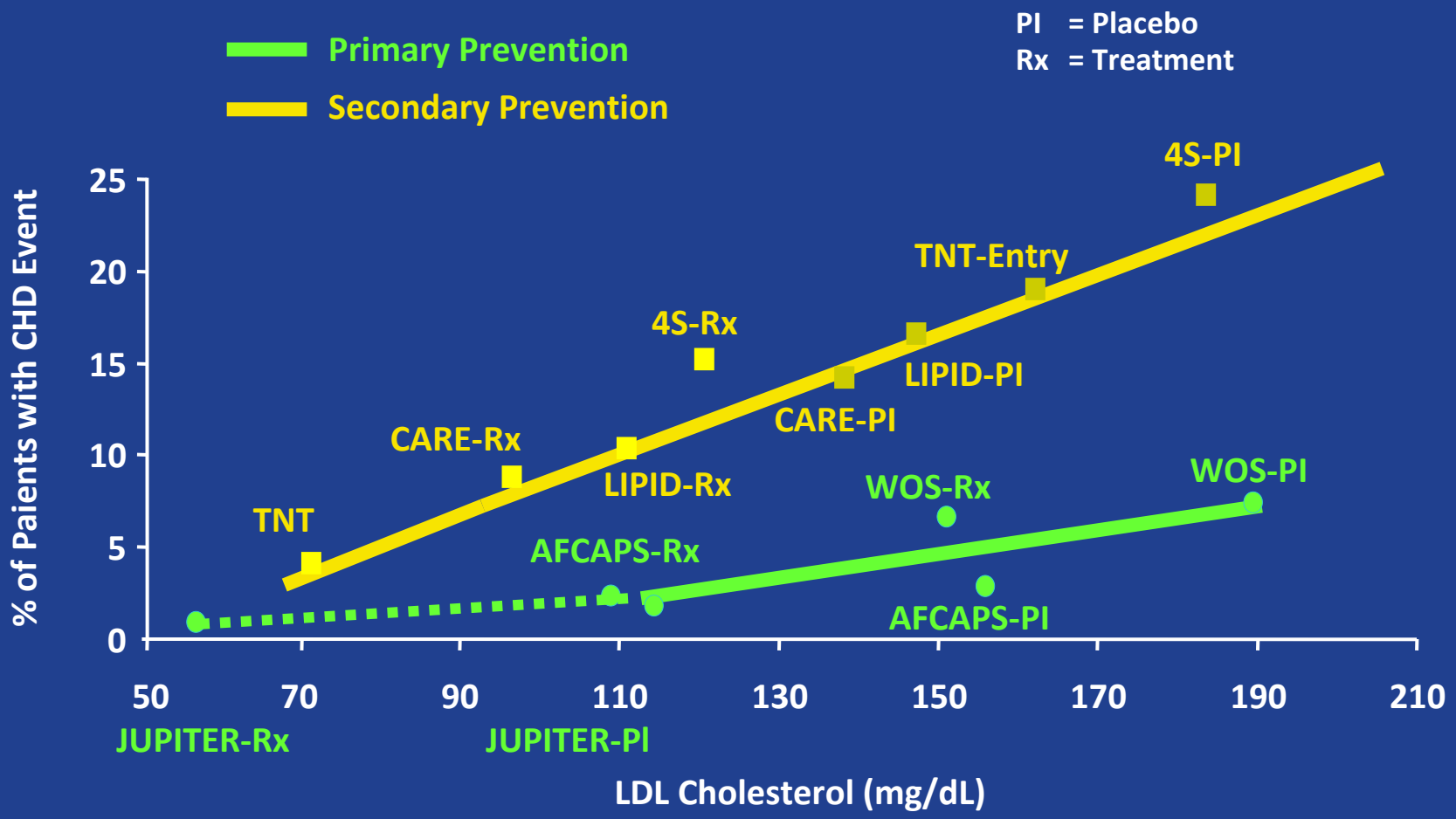
Event	Rosuvastatin	Placebo	P
Any SAE	1,352 (15.2)	1,337 (15.5)	0.60
Muscle weakness	1,421 (16.0)	1,375 (15.4)	0.34
Myopathy	10 (0.1)	9 (0.1)	0.82
Rhabdomyolysis	1 (0.01)*	0 (0.0)	--
Incident Cancer	298 (3.4)	314 (3.5)	0.51
Cancer Deaths	35 (0.4)	58 (0.7)	0.02
Hemorrhagic stroke	6 (0.1)	9 (0.1)	0.44
GFR (ml/min/1.73m^2 at 12 mth)	66.8 (59.1-76.5)	66.6 (58.8-76.2)	0.02
ALT > 3xULN	23 (0.3)	17 (0.2)	0.34

*Occurred after trial completion, trauma induced.
**Physician reported

All values are median (interquartile range) or N (%)

So, Where Are We *Now*?

Relation Between CHD Events and LDL Cholesterol in Statin Trials



AFCAPS: Lovastatin; 4S: Simvastatin
WOS, LIPID, CARE: Pravastatin

Atherosclerosis 1999;143:S17-S21

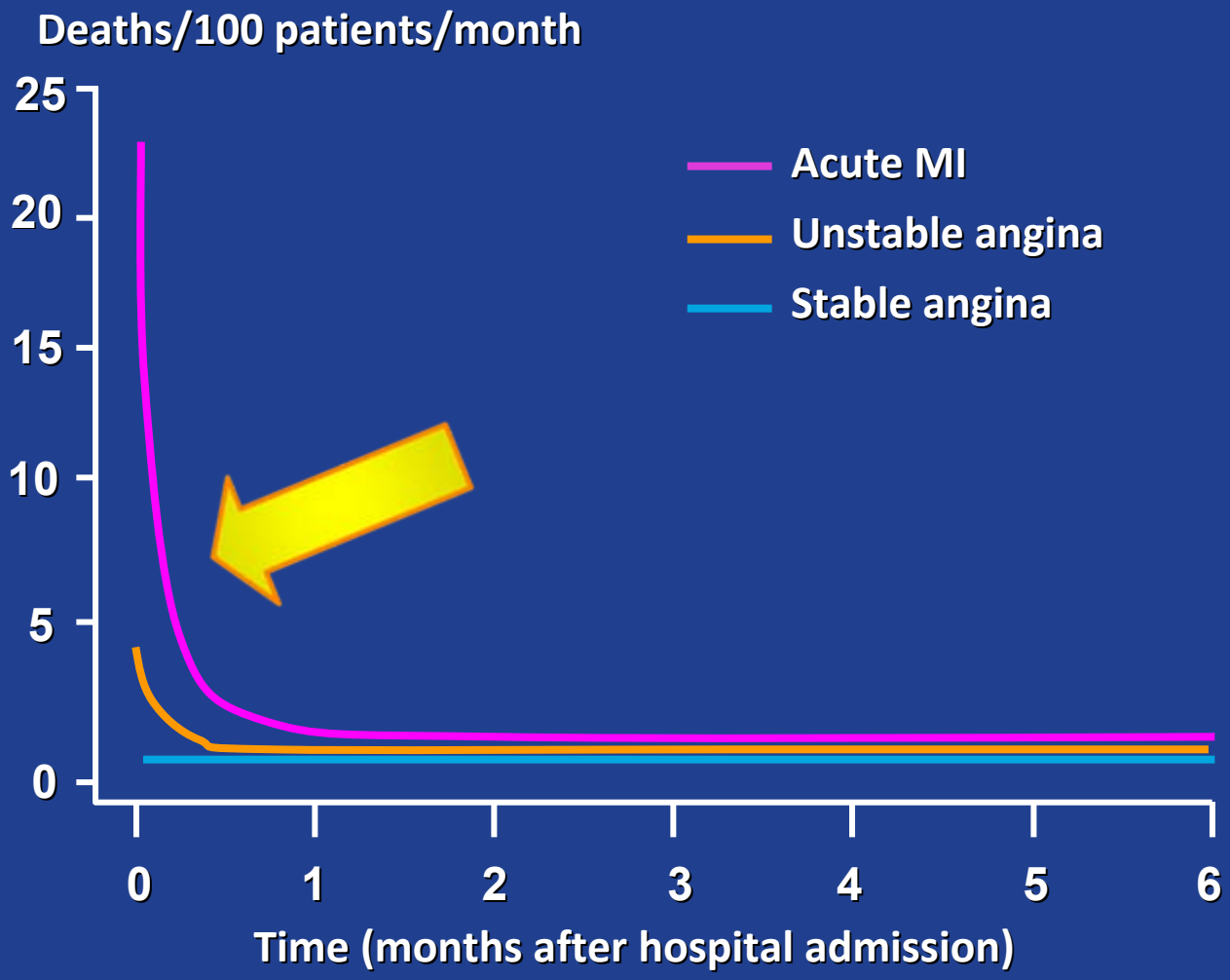
Conclusions - Cholesterol

- Treat the risk, not the LDL!
  - CRP? Other?
- When risk is high, lower is better!
  - "Adults with CHD or multiple risk factors should strive to lower their LDL-C to 50 mg/dL".
  - "It would be reasonable to recommend that an "ideal" LDL-C level should be defined as ≤ 50 mg/dL".

Circulation. 2008;118:672-677

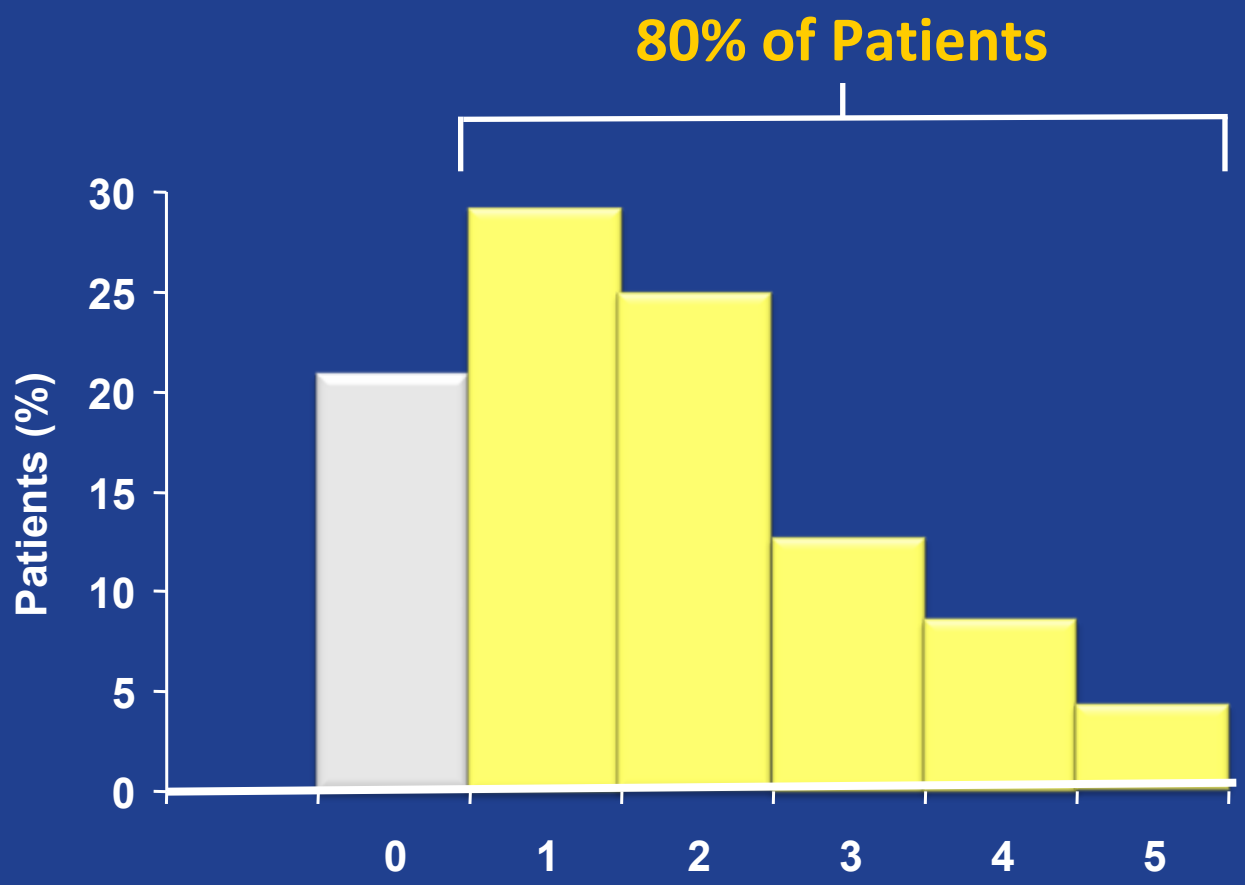
מקרה מיוחד – תסמונת כלילית חדה

Risk Of Death in Patients With CHD is Greatest *Early* After an ACS



Braunwald (1996)

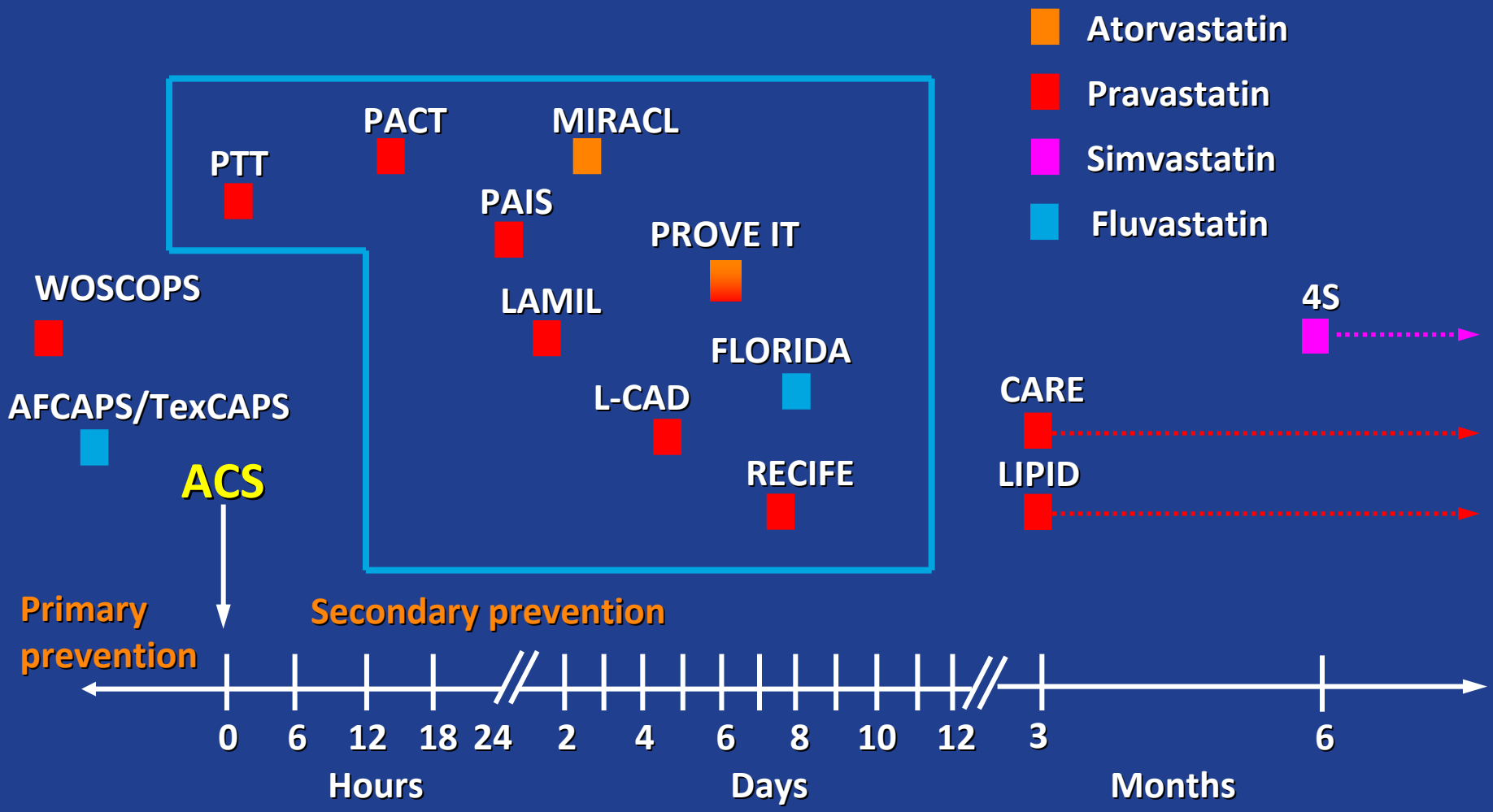
Frequency of Additional "Active" Plaques in Patients With ACS



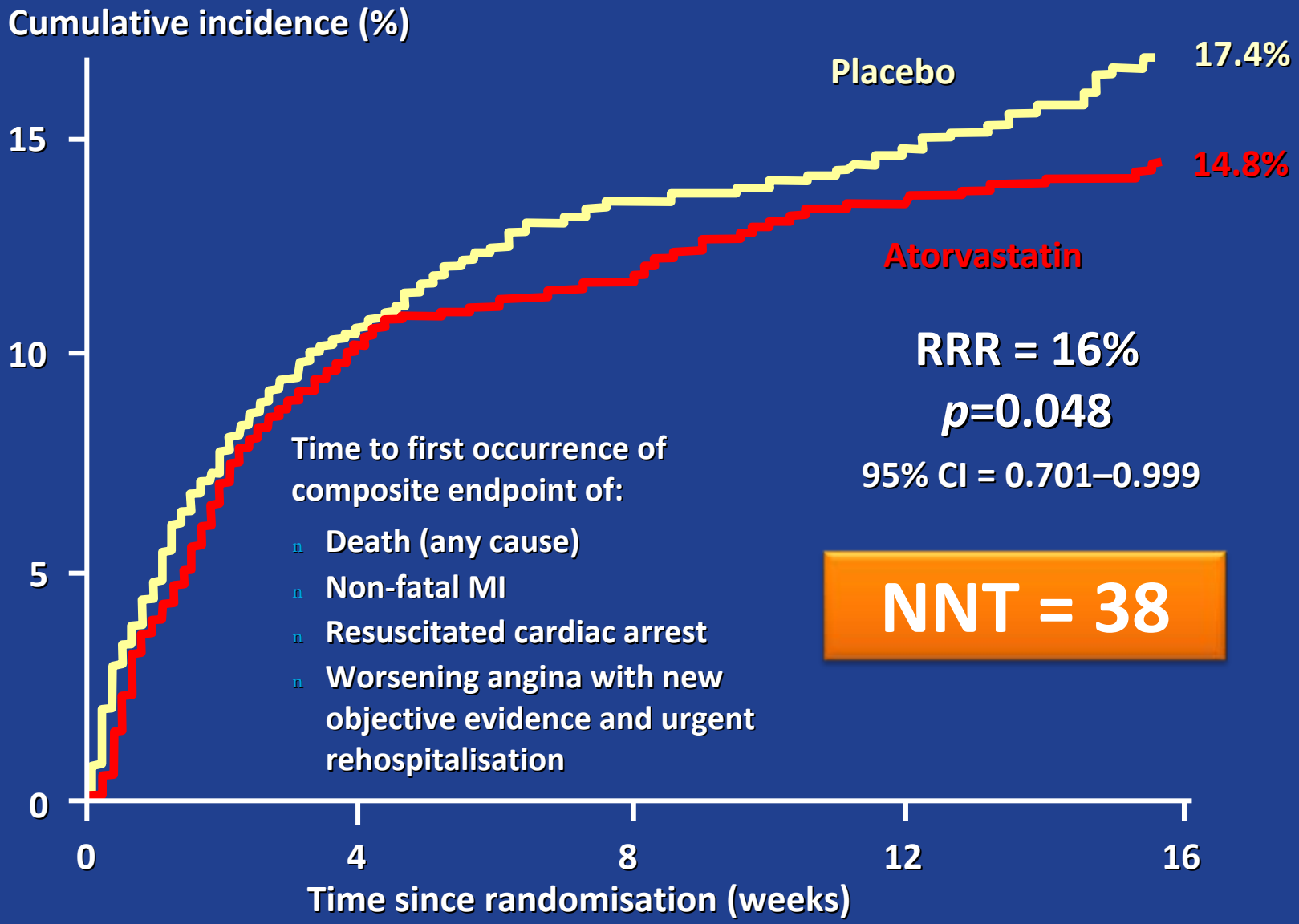
Frequency of multiple active plaque ruptures beyond the culprit lesion.

Circulation. 2002;106:804-808.

Timing Of Statin Therapy Initiation After ACS in Clinical Studies



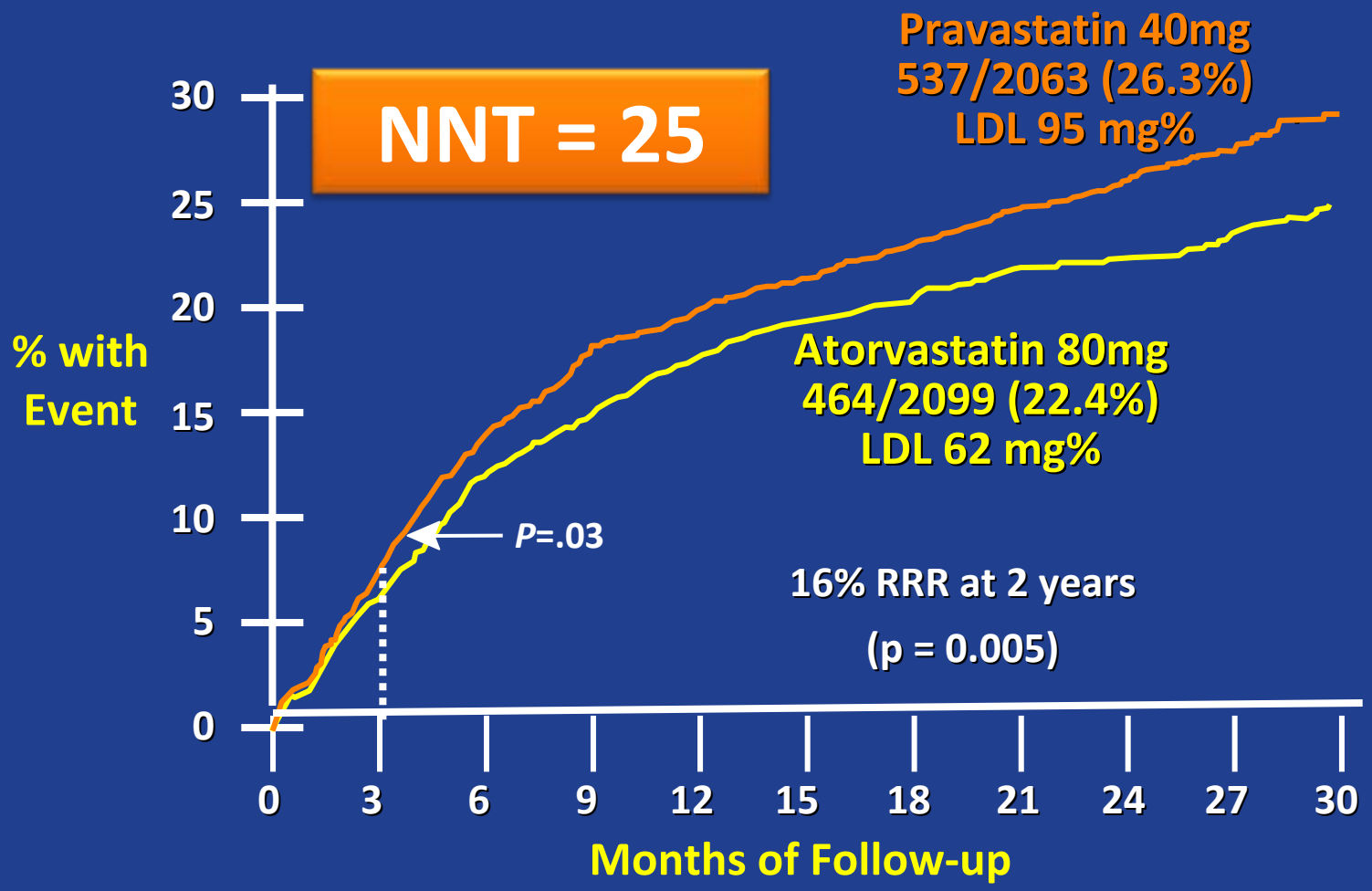
MIRACL: Primary Efficacy Measure



JAMA. 2001;285:1711

PROVE IT - TIMI 22 Results:

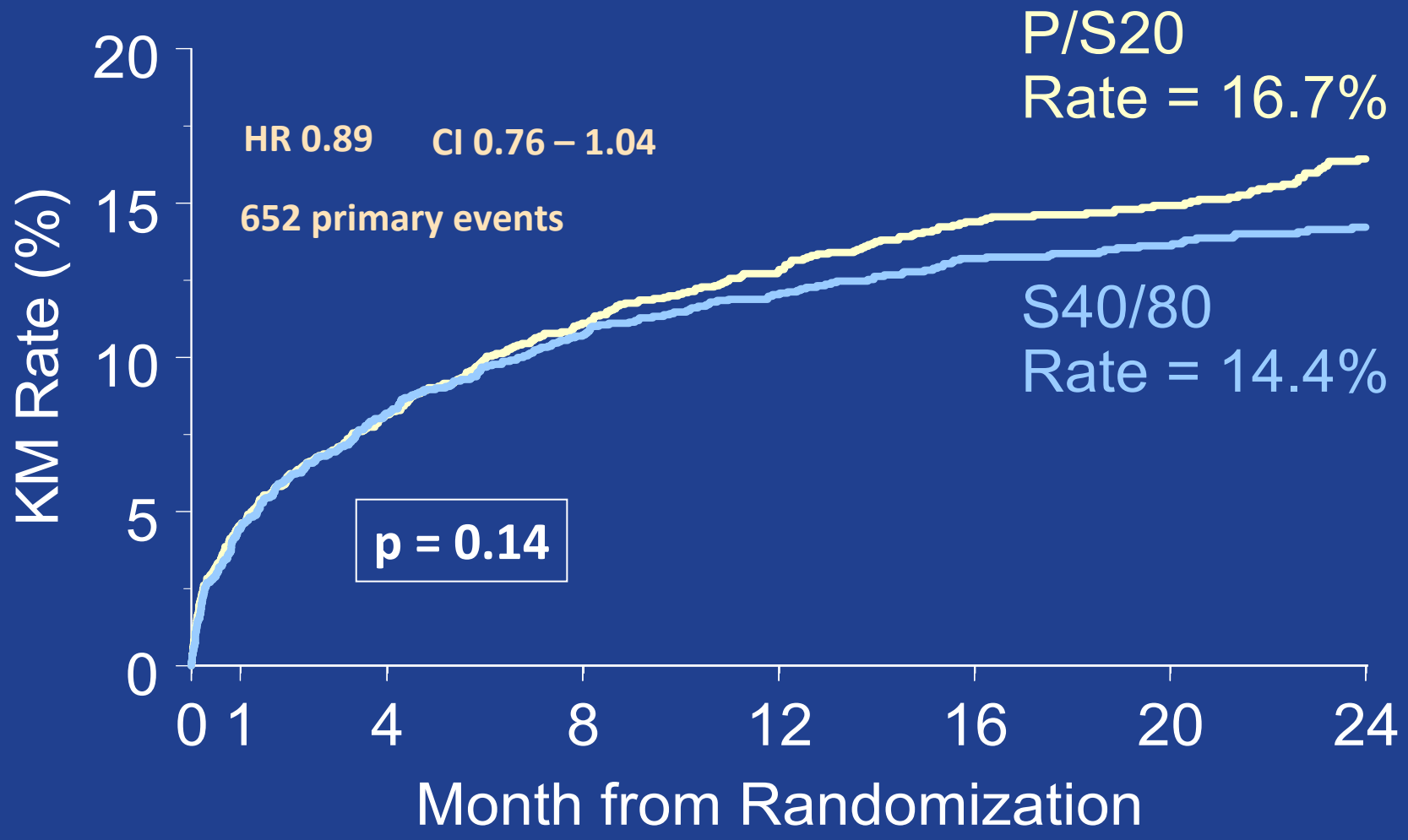
All-Cause Death or Major CV Events



NEJM 2004;350:1495

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.

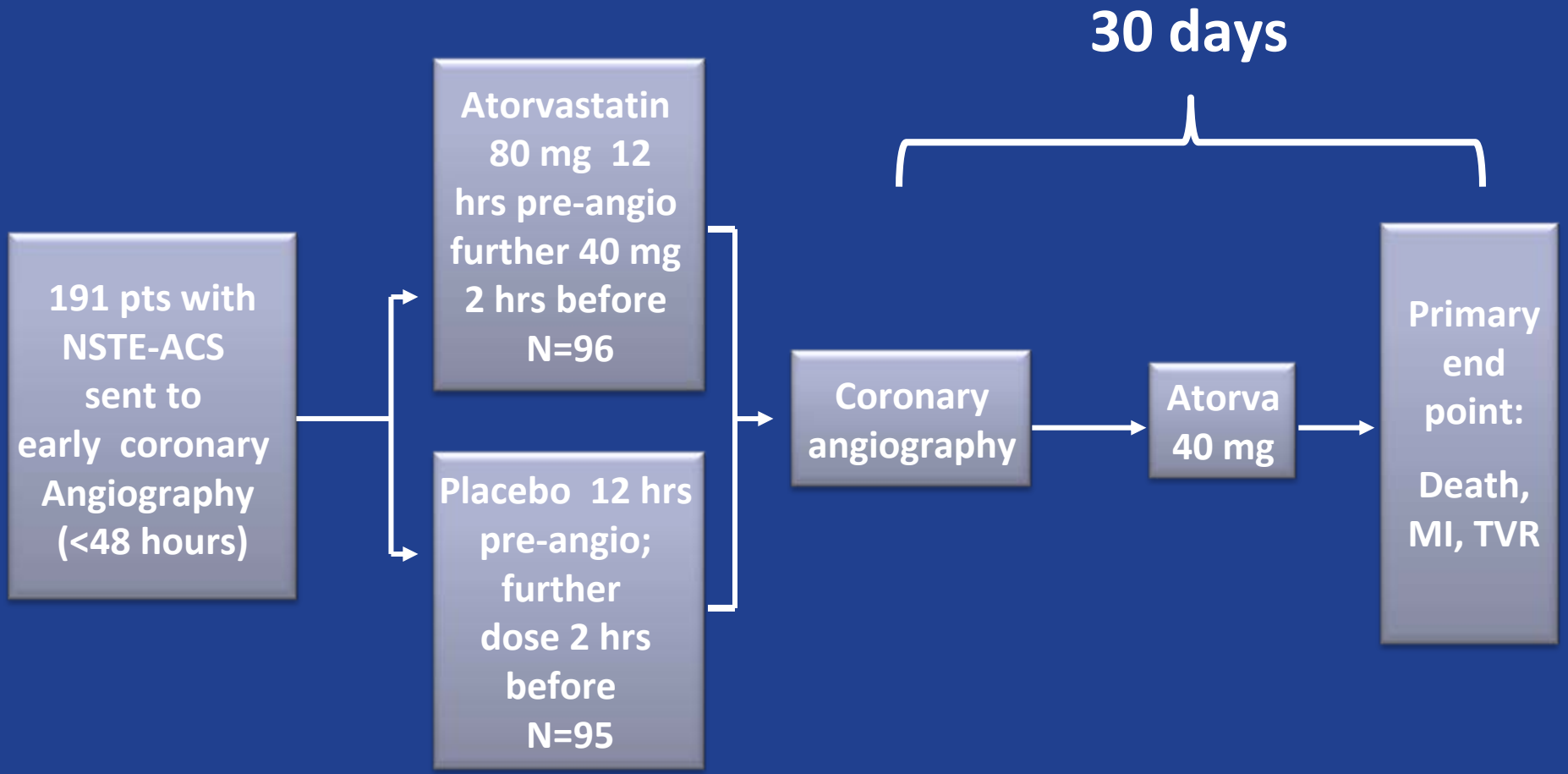
Adapted from Nissen. *JAMA*. 2004;292:1365, with permission.

טיפול בסטטינים בחולים עם תסמונת כלילית חריפה

דו"ח קבוצת עבודה של
האיגוד הקרדיולוגי בישראל

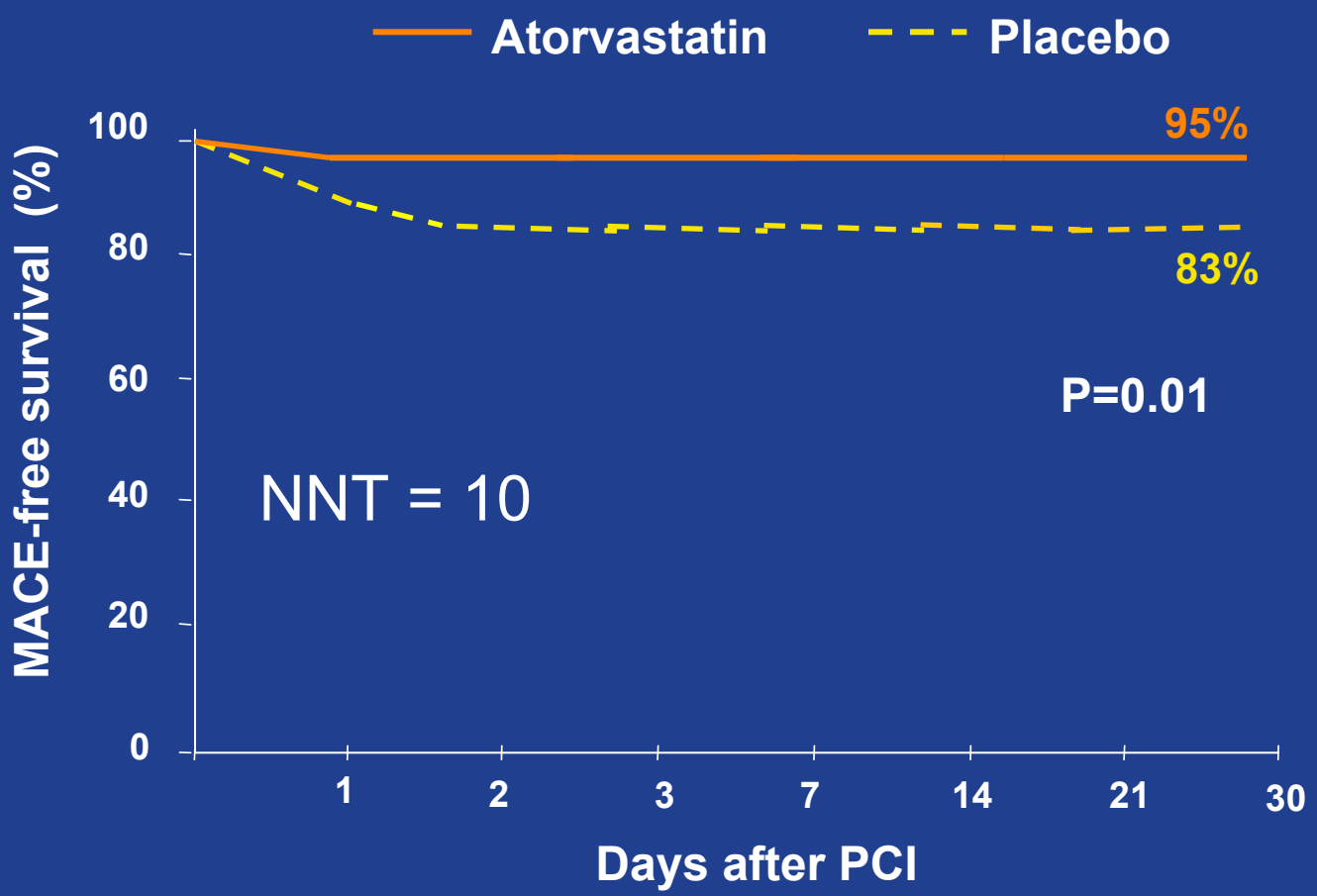
- בחולים לאחר אירוע כלילי חריף, ובהיעדר הוראת נגד, יש לתת טיפול אינטנסיבי בסטטין למשך 6 חודשים לפחות.
- בהמשך יקבע סוג הסטטין ומינונו בהתאם לרמות המטרה של LDL
- בעת כתיבת מסמך זה הטיפול ה"אינטנסיבי" היחיד שיעילותו הוכחה גם בטווח הקצר לאחר הארוע (6 חדשים) הוא אטורבסטטין 80 מ"ג/יום

ARMYDA-ACS: Study Design



JACC 2007;49(12):1272-1278

ARMYDA-ACS: Actuarial Survival curves



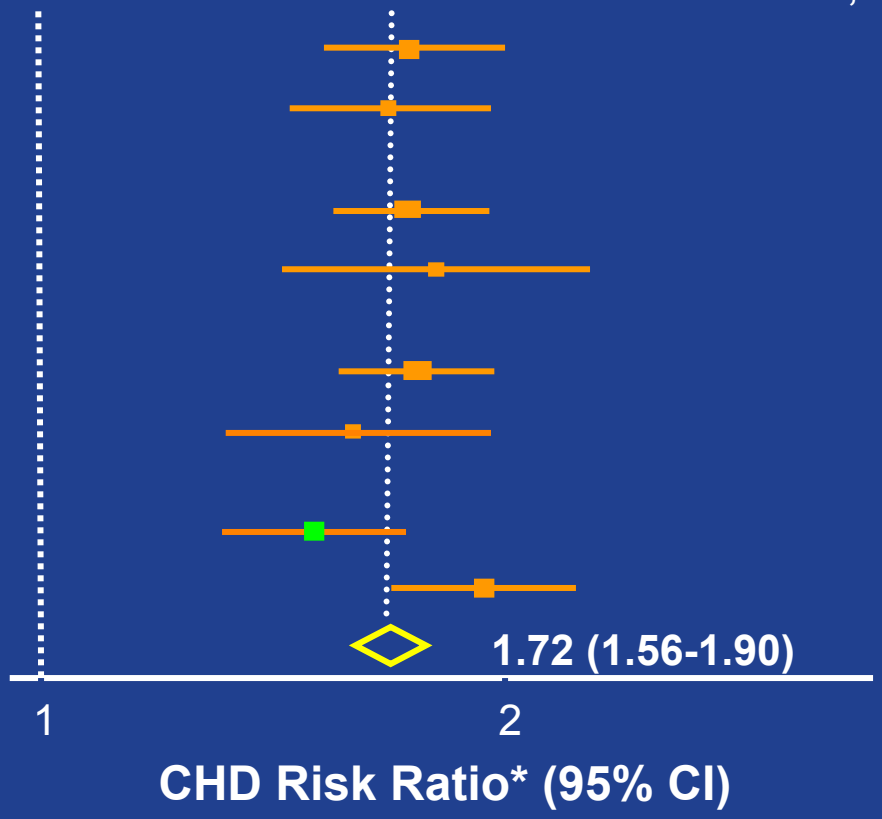
Giuseppe Patti, Vincenzo Pasceri et al. JACC 2007;49(12):1272-1278

מה עם טריגליצרידים ו- HDL?

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

Groups	CHD Cases
Duration of follow-up	
≥10 years	5902
<10 years	4256
Sex	
Male	7728
Female	1994
Fasting status	
Fasting	7484
Nonfasting	2674
Adjusted for HDL	
Yes	4469
No	5689

N = 262,525

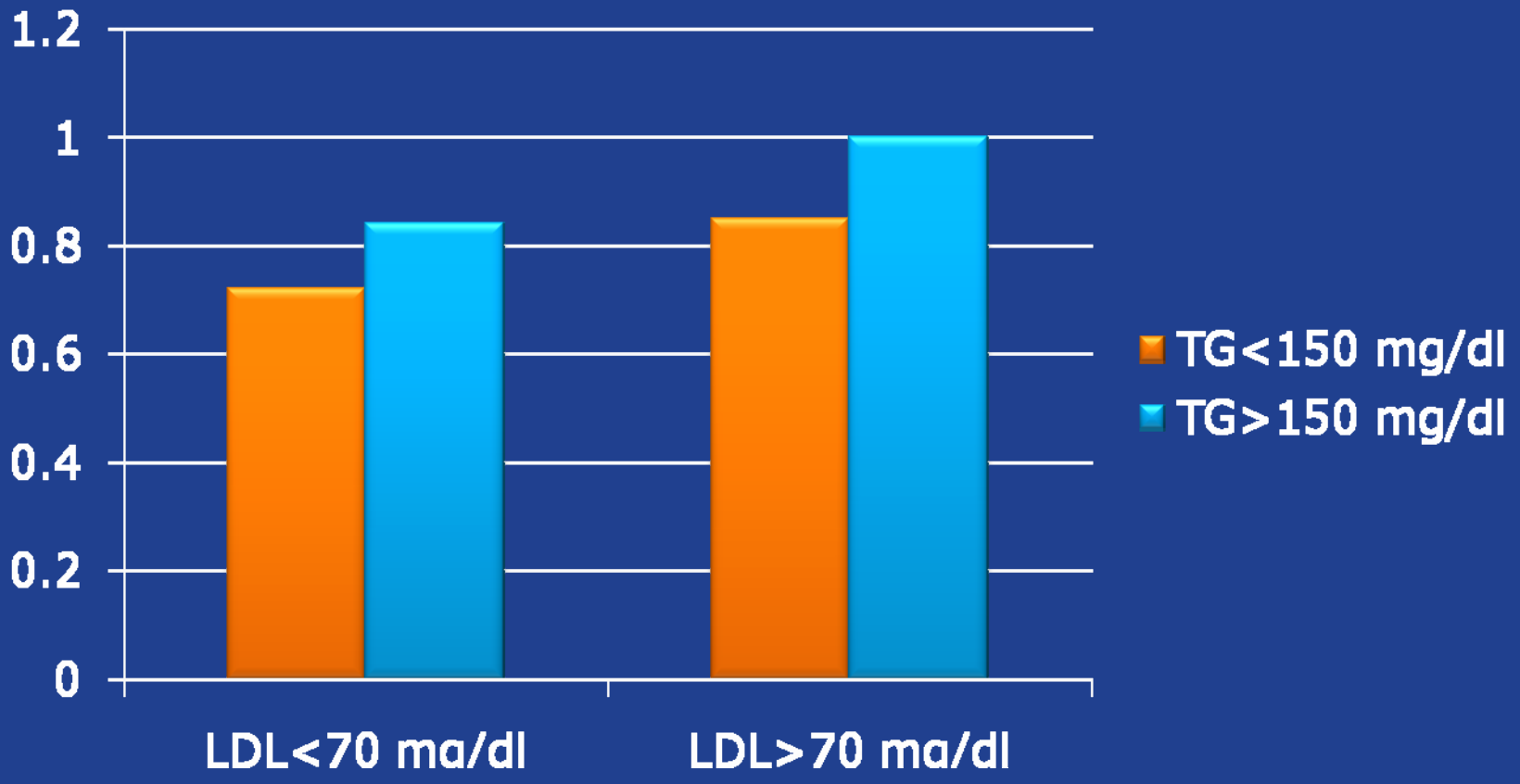


*Individuals in top vs. bottom third of usual log-TG values; adjusted for at least age, sex, smoking status, and lipid concentrations; also adjusted for BP (in most studies).

Circulation. 2007;115:450-458

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*

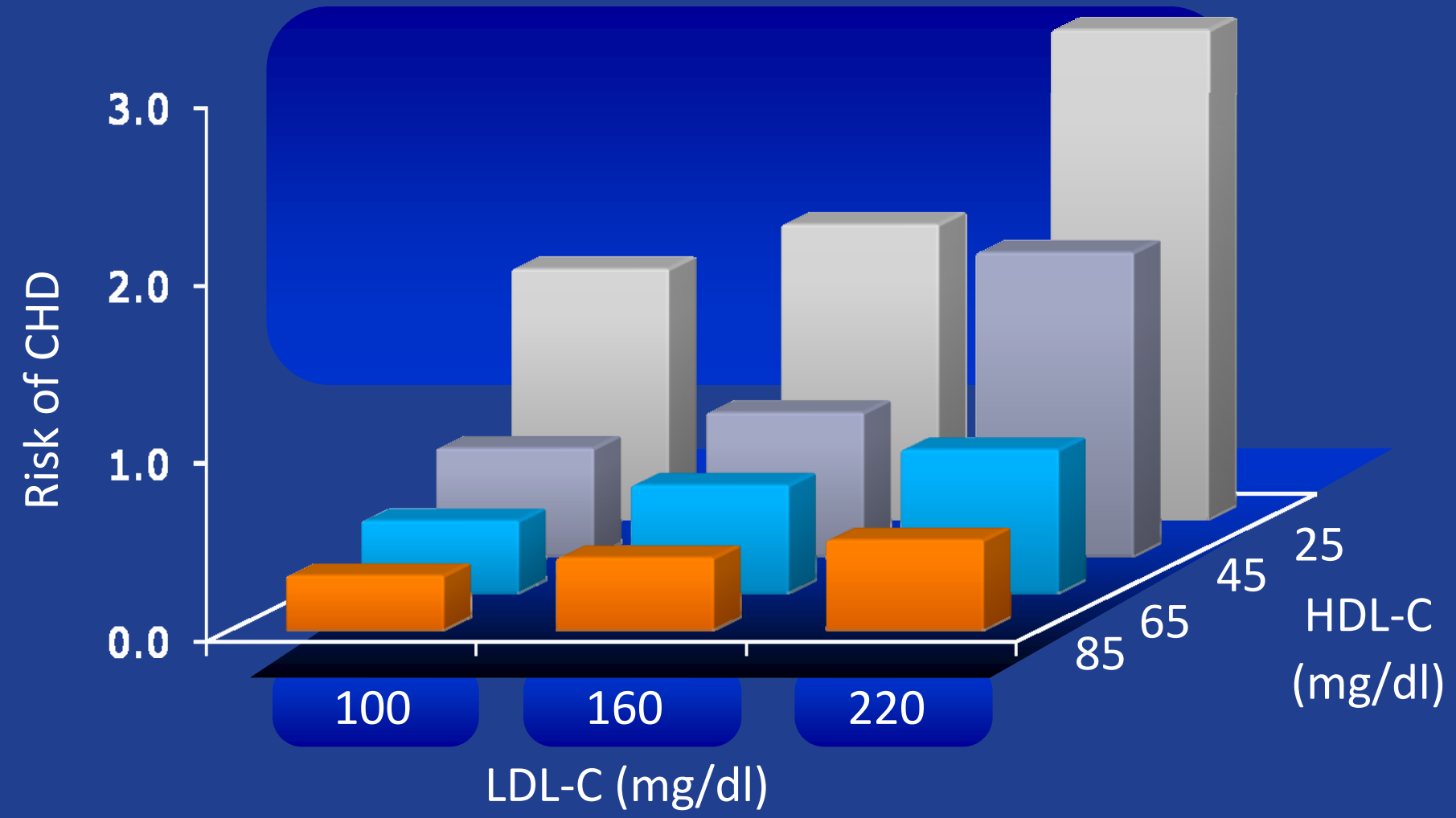


*Adjusted for age, gender, low HDL-C, smoking, HTN, obesity, DM, prior statin therapy, prior ACS, PVD, treatment effect

JACC 2008;51:724–30

Low HDL-C is an Independent Predictor of CHD Risk Even When LDL-C is Low

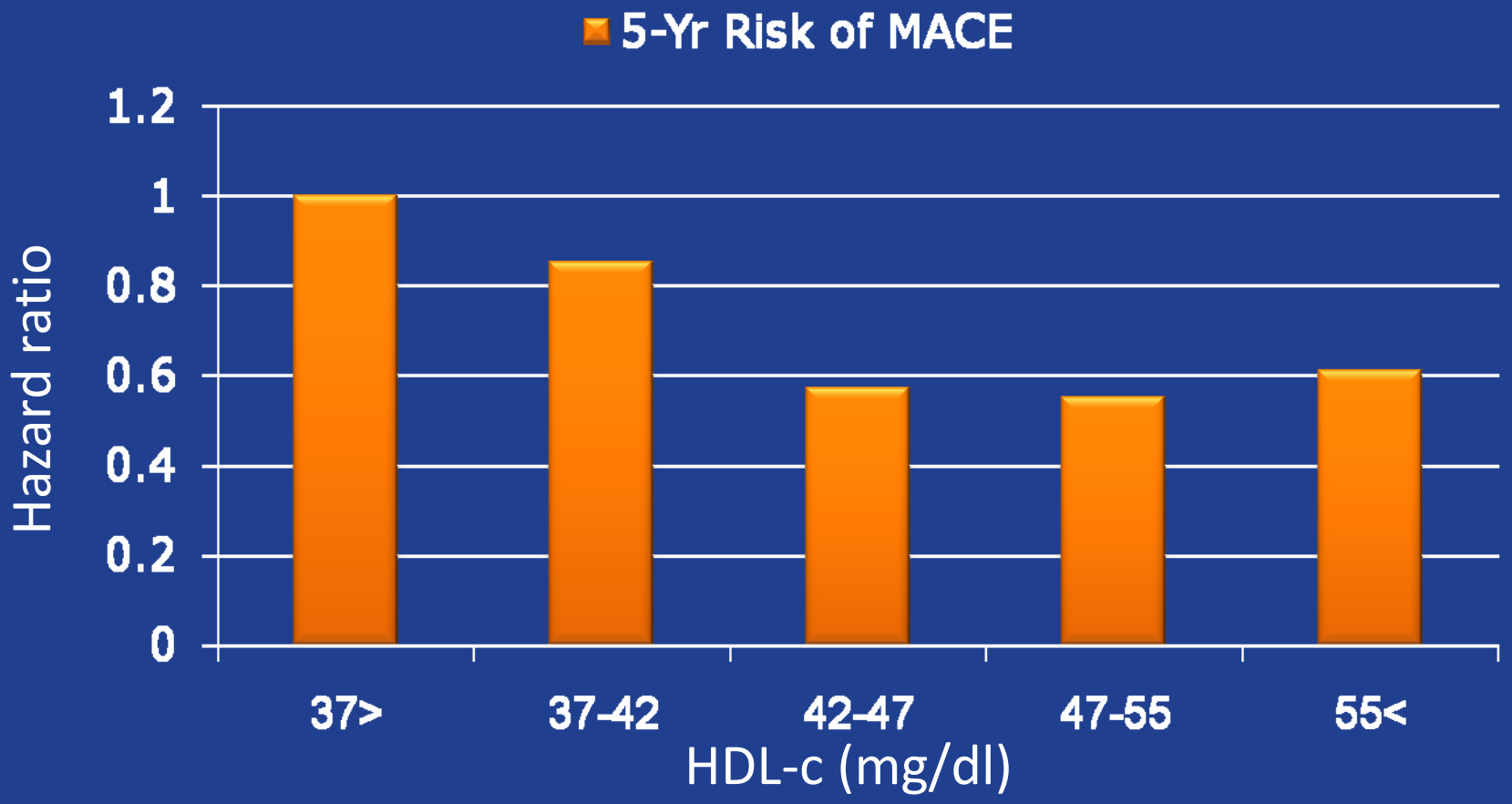
Framingham Heart Study



Am J Med 1977;62:707-714

HDL-c Levels and MACE in Patients Treated With Statins to LDL-c < 70 mg/dl

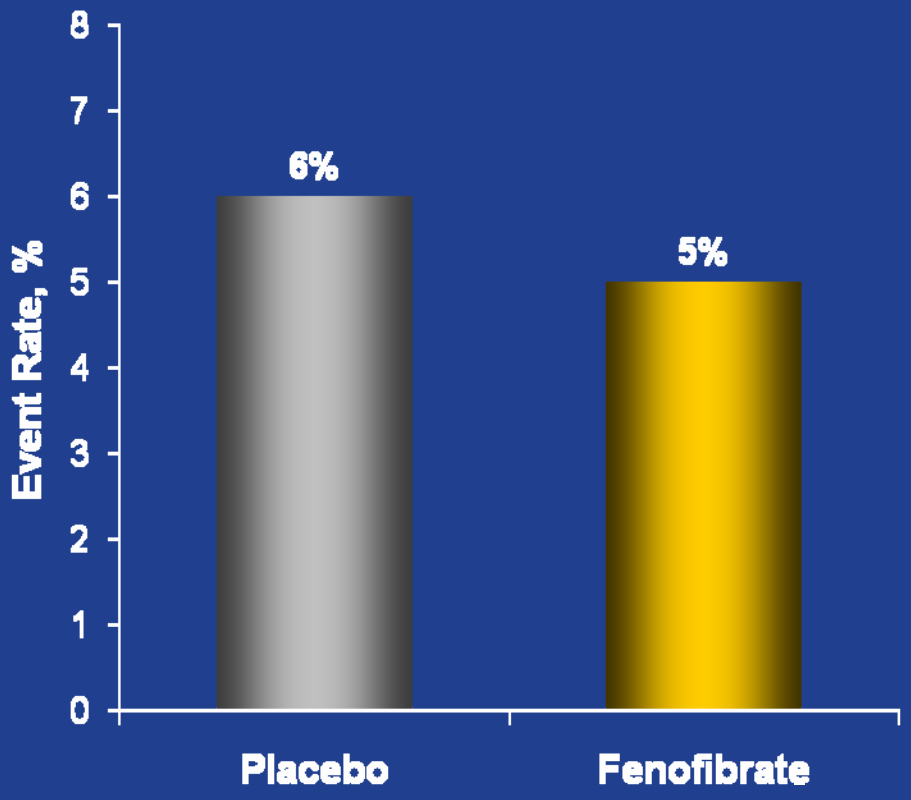
TNT



NEJM 2007;357:1301-10

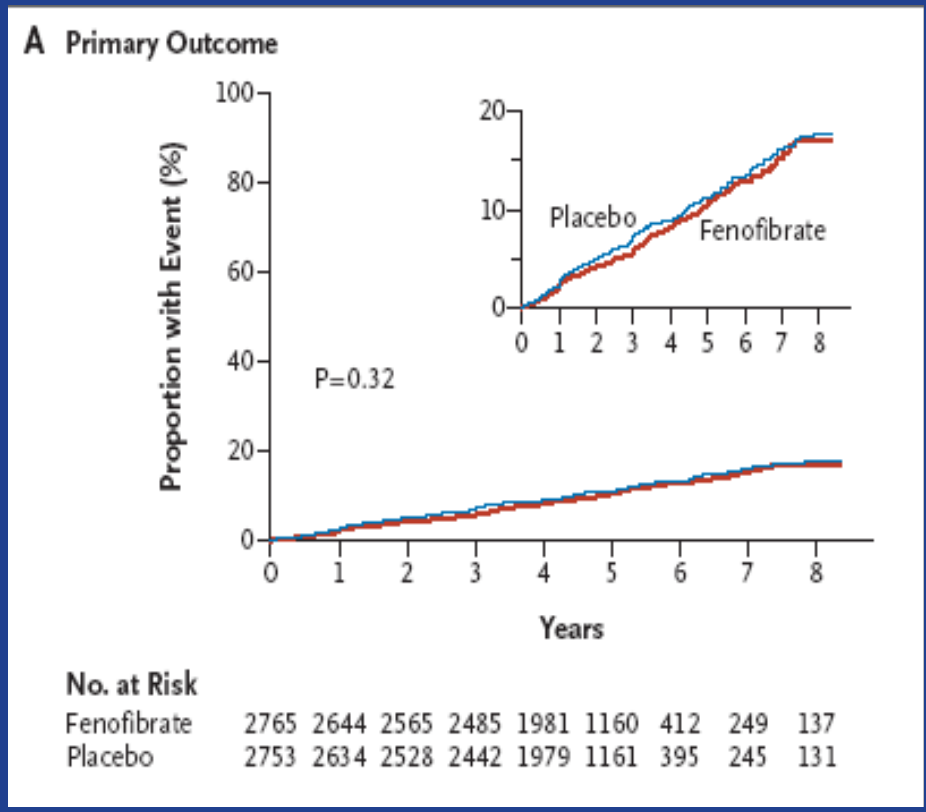
Fibrates and Cardiovascular Outcomes

FIELD



Lancet. 2005;366:1849-1861

ACCORD

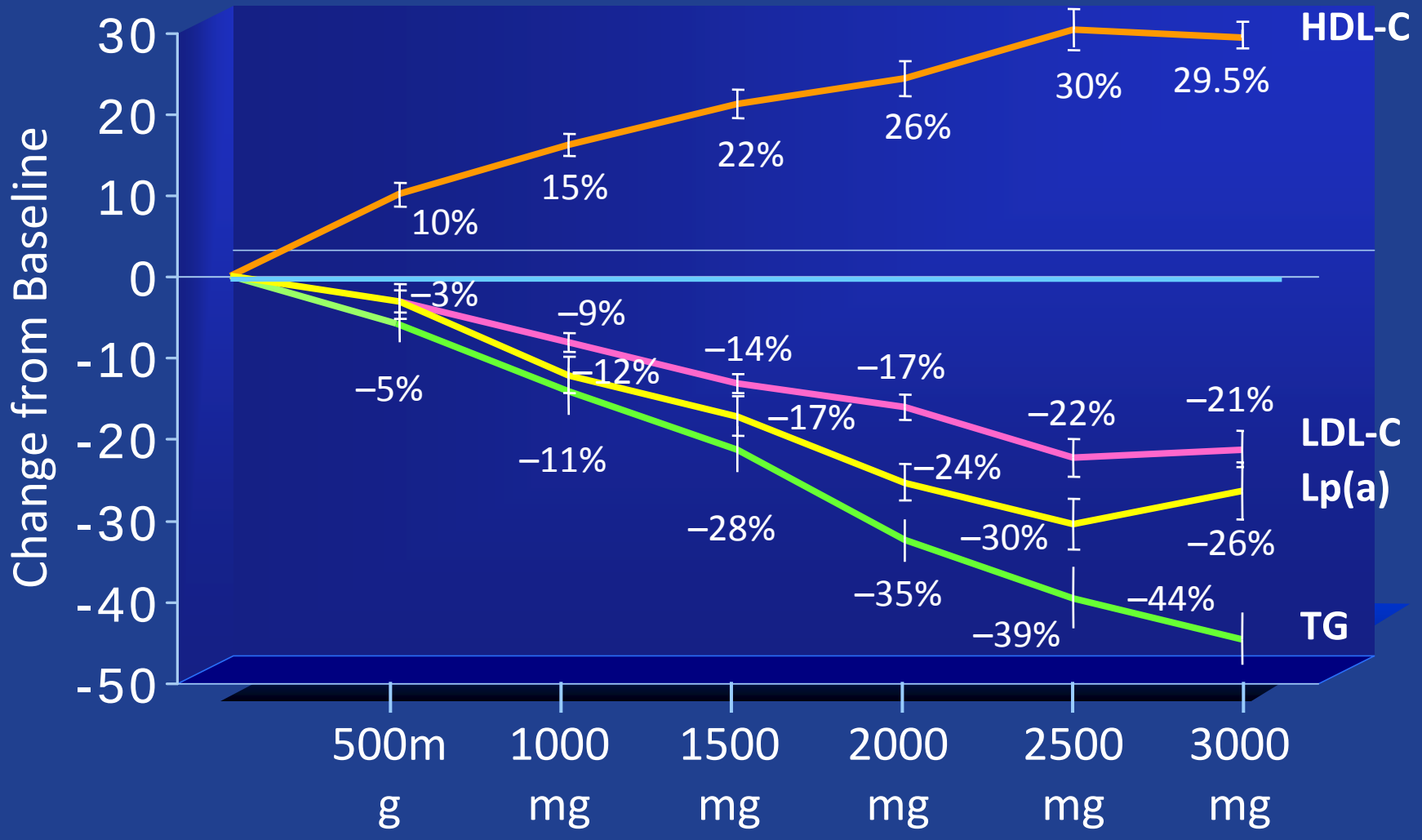


NEJM Published online March 14, 2010

Fibrates in Metabolic Dyslipidemia

Trial (Drug)	Primary Endpoint: Entire Cohort (P-value)	Lipid Subgroup Criterion	Primary Endpoint: Subgroup
HHS (Gemfibrozil)	-34% (0.02)	**TG > 200 mg/dl LDL-C/HDL-C > 5.0**	**-71%**
BIP (Bezafibrate)	-7.3% (0.24)	**TG ≥ 200 mg/dl**	**-39.5%**
VA-HIT (Gemfibrozil)	-22% (0.006)	**DM Patients; baseline HDL-C 31 mg/dL; TG 164 mg/dL**	**-32%**
FIELD (Fenofibrate)	-11% (0.16)	**TG ≥ 204mg/dl HDL-C < 42 mg/dl**	**-27%**
ACCORD (Fenofibrate)	-8% (0.32)	**TG ≥ 204 mg/dl HDL-C ≤ 34 mg/dl**	**-31%**

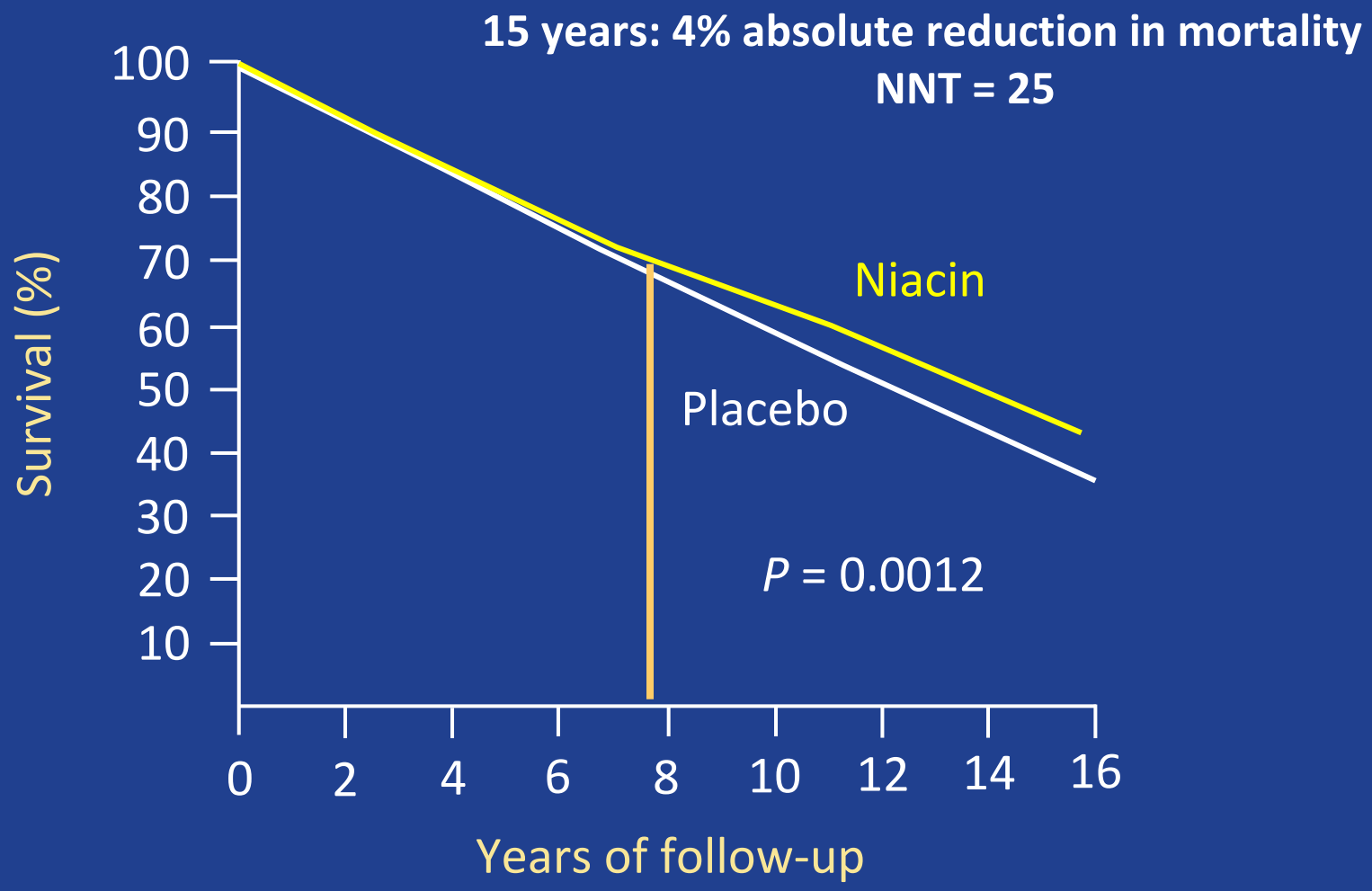
Efficacy of Extended-Release Niacin



Am J Cardiol 2000;85:1100-1105.

Coronary Drug Project

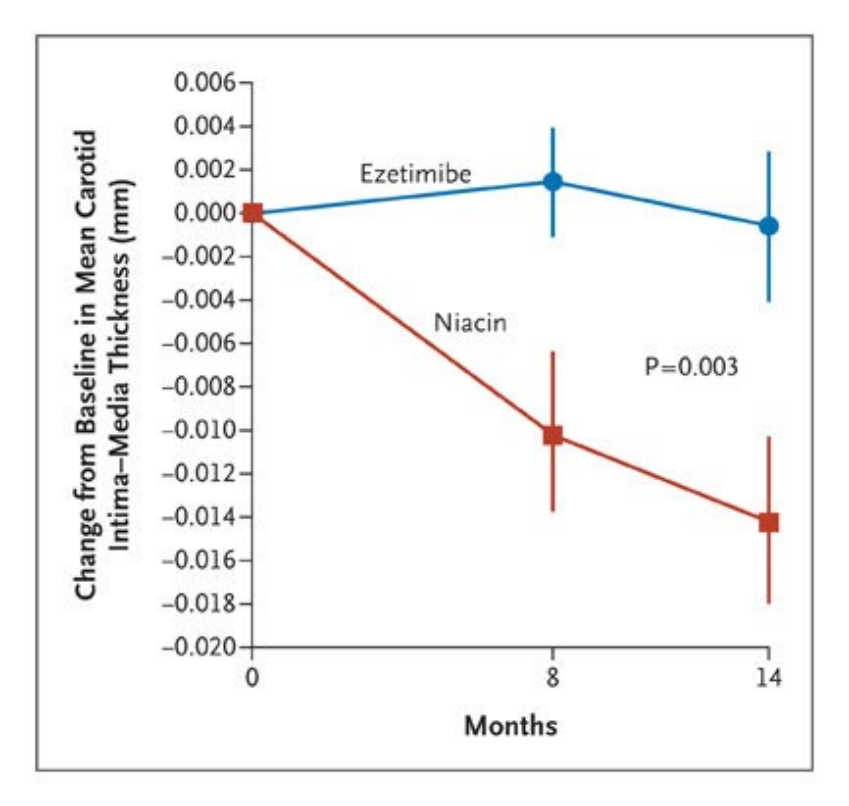
Long-Term Mortality Benefit of Niacin in Post-MI Patients



J Am Coll Cardiol 1986;8:1245–1255

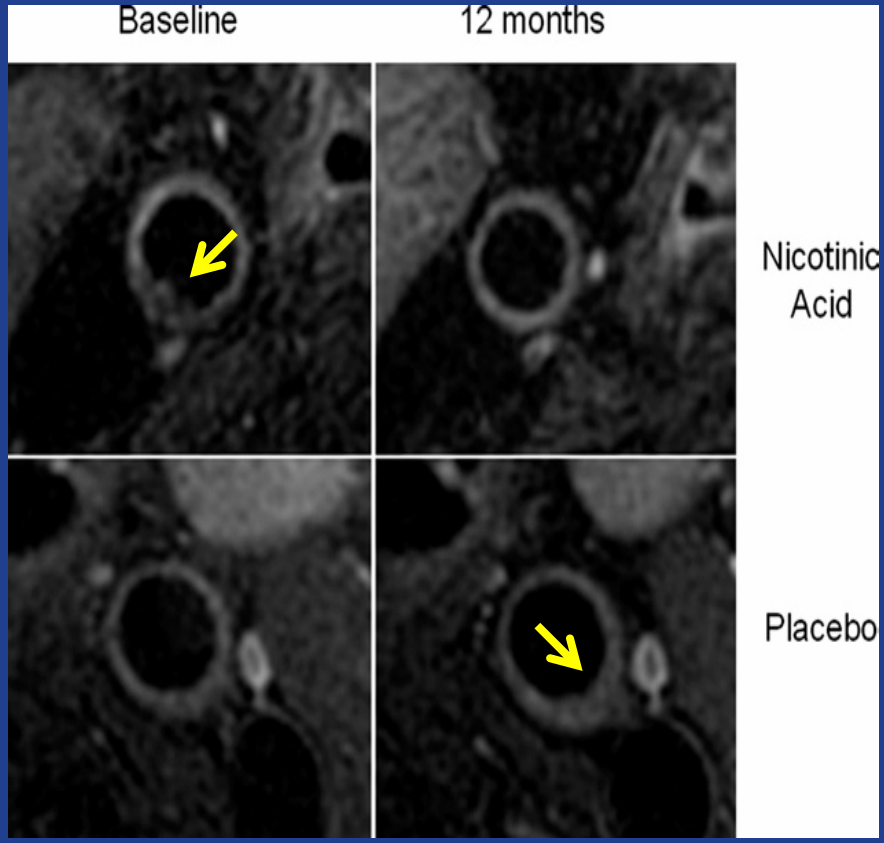
Niacin Imaging Studies

ARBITER-HALTS



N Engl J Med 2009;361.

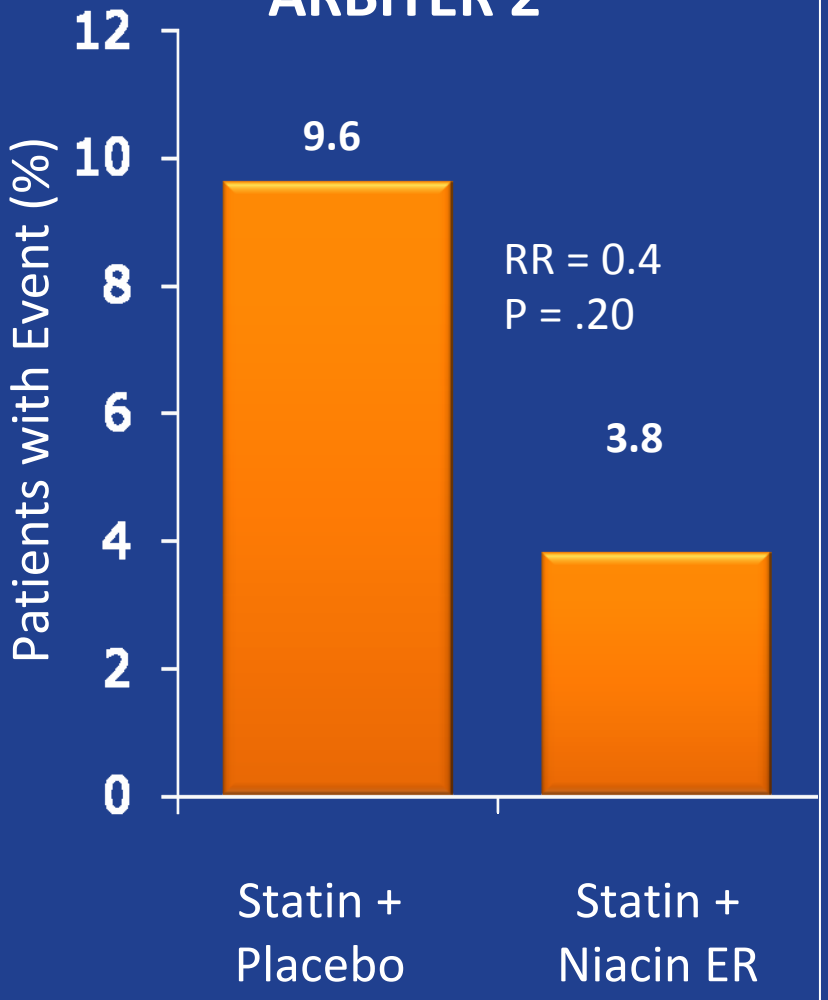
Oxford Niaspan Study



J Am Coll Cardiol 2009;54:1787–94

NIACIN: Clinical Events

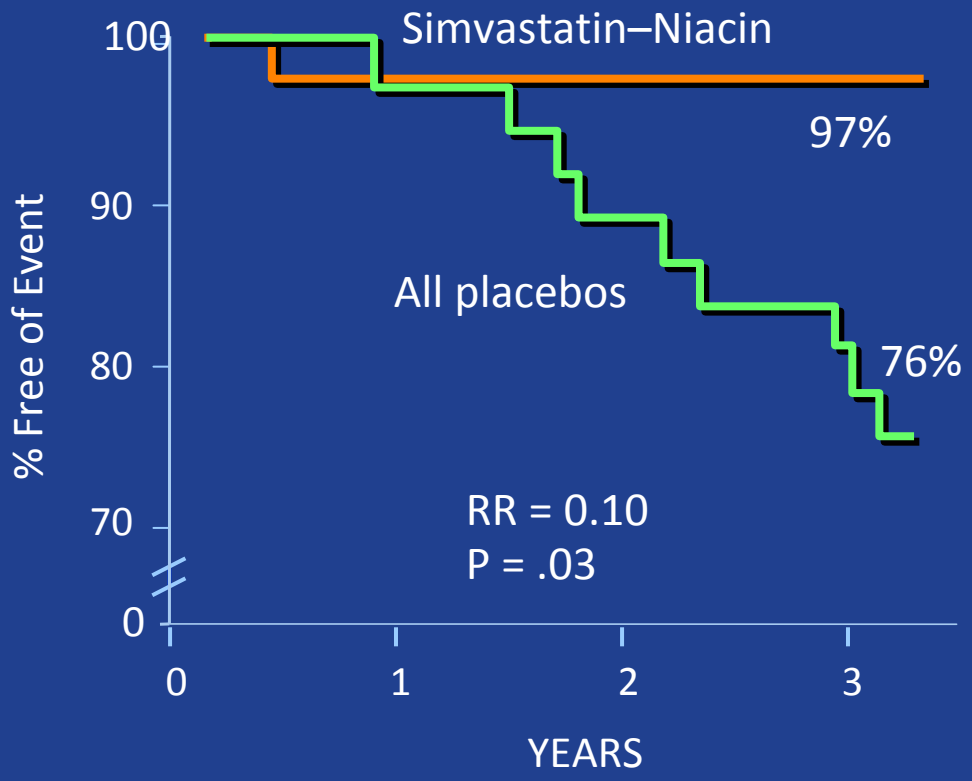
ARBITER 2



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

Circulation 2004;110:3512-3517.

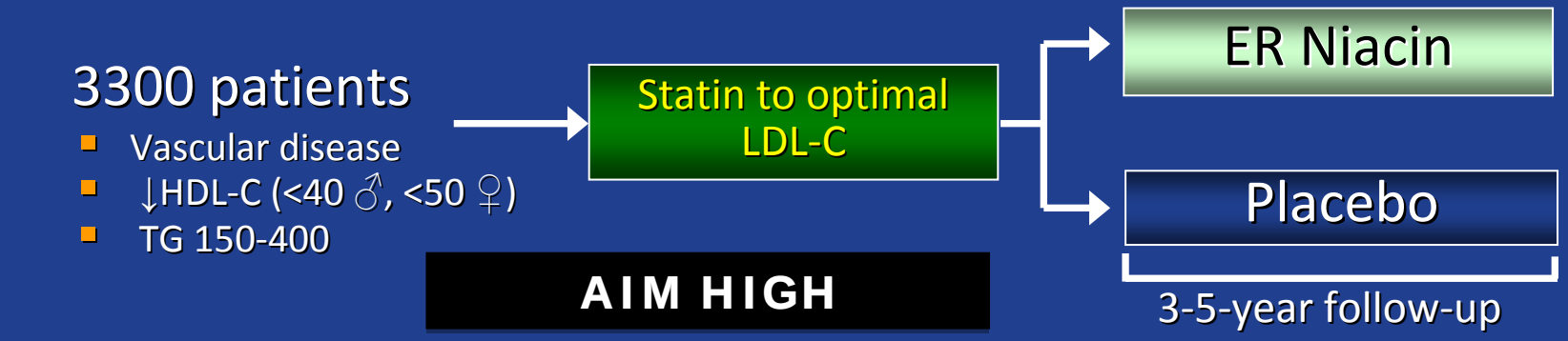
HATS



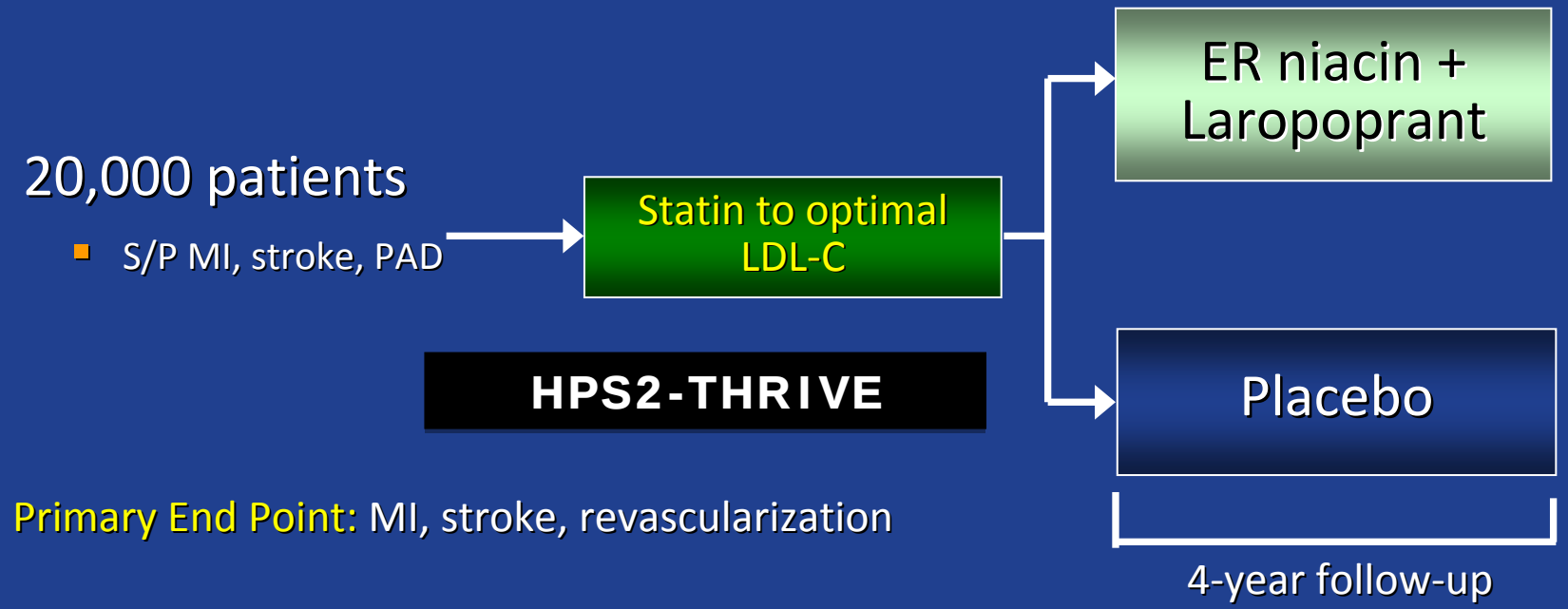
Composite End Point (Death from Coronary Causes, Nonfatal MI, Stroke, or Revascularization for Worsening Ischemia)

NEJM 2001;345:1583-1592

Niacin: Ongoing Studies Due ~ 2012



Primary End Point: CHD death, MI, stroke, ACS



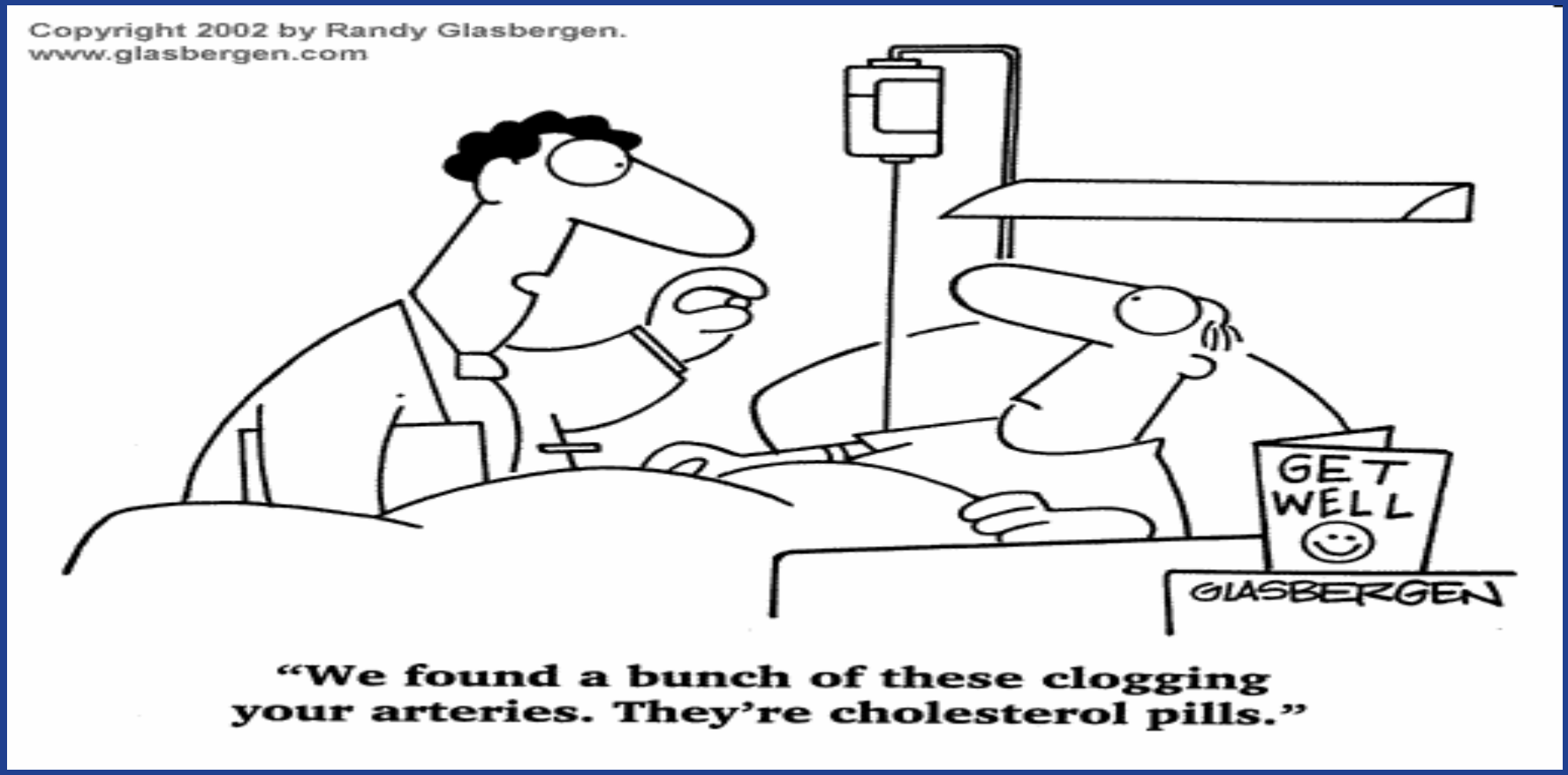
Primary End Point: MI, stroke, revascularization

Future Prospects

Summing up, it is clear the future holds great opportunities. It also holds pitfalls. The trick will be to avoid the pitfalls, seize the opportunities, and get back home by six o'clock .

Woody Allen

תודה רבה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"We found a bunch of these clogging your arteries. They're cholesterol pills."