Early Statin Therapy in Acute Coronary Syndrome

The Faster, The Better !

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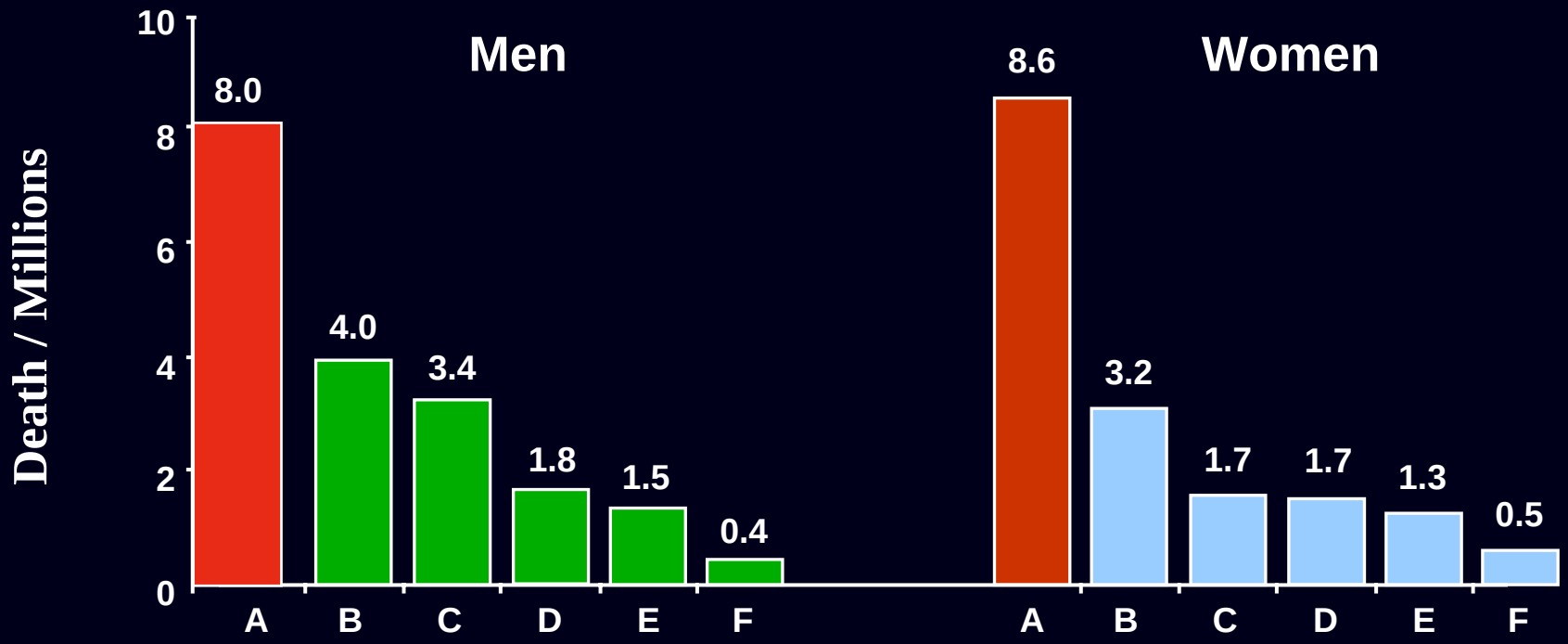
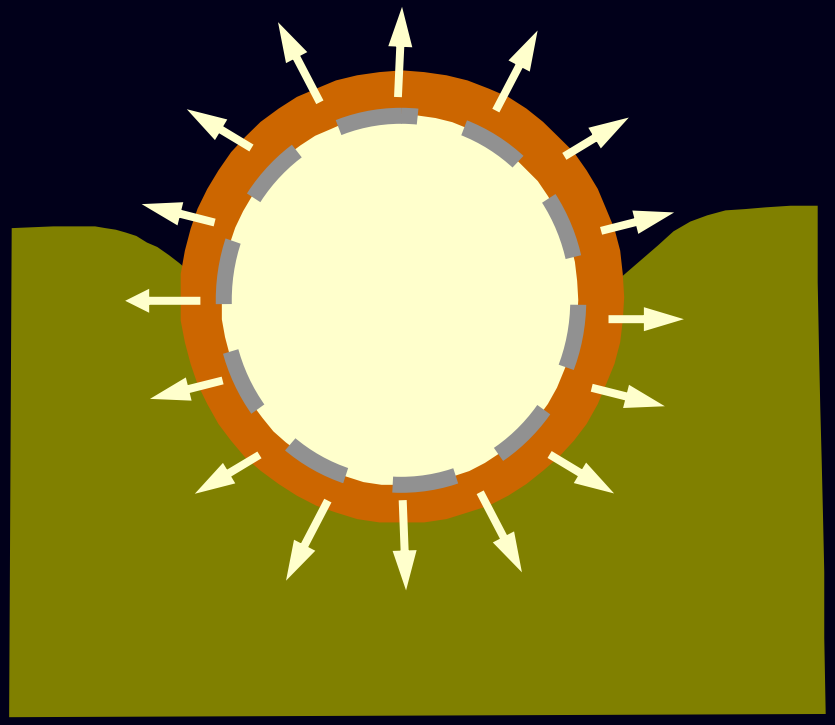
Angioplasty Summit 2005

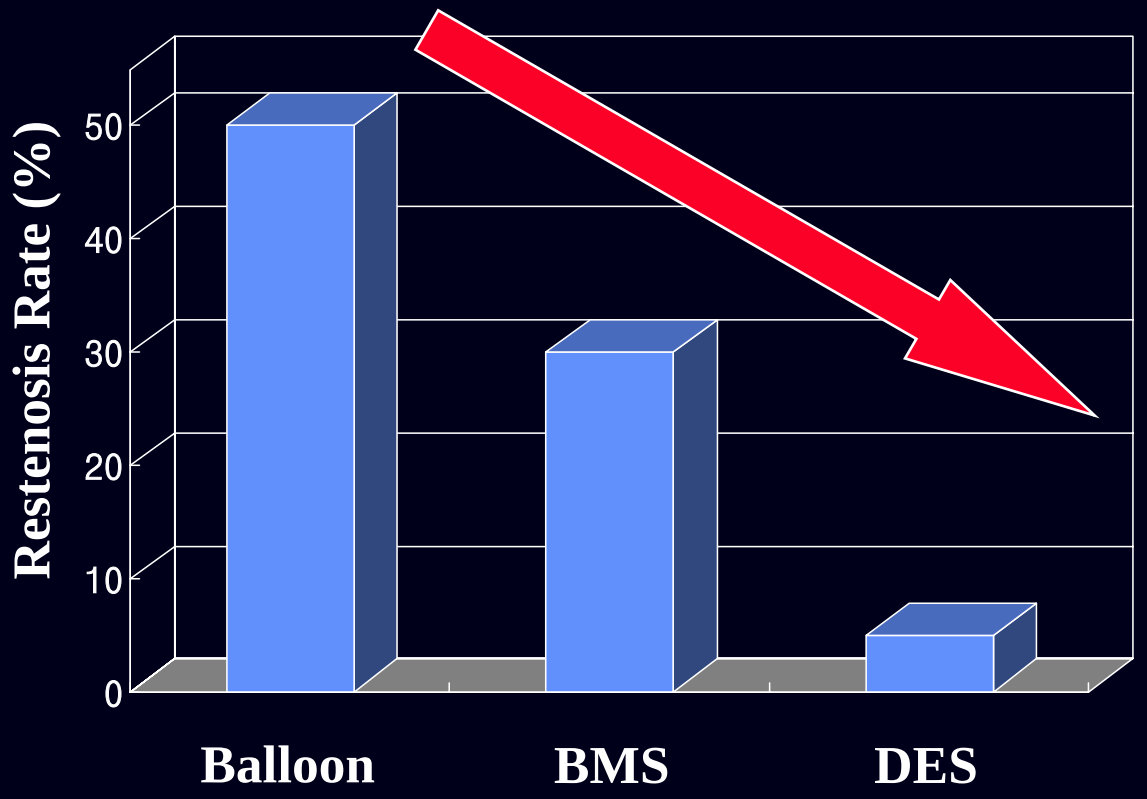
Causes of Death Worldwide, 2001



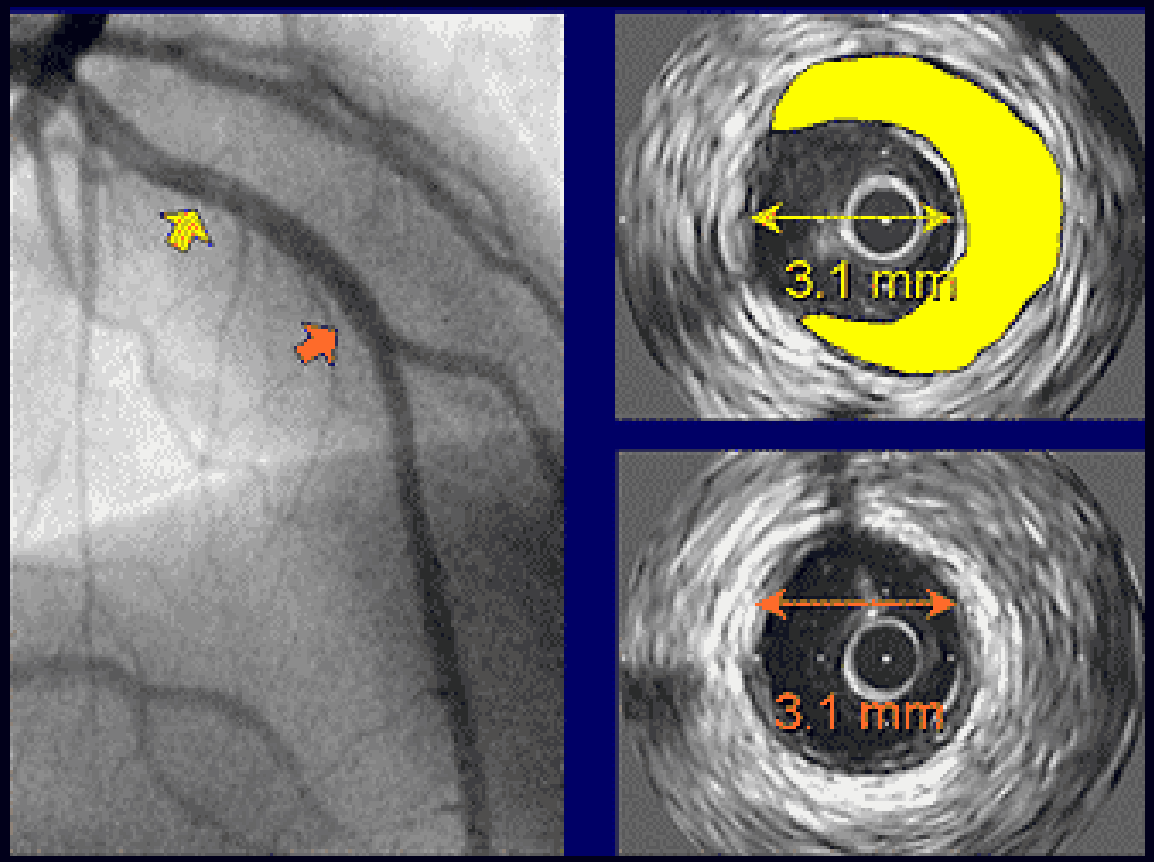
(2001, WHO)

Drug-Eluting Stents





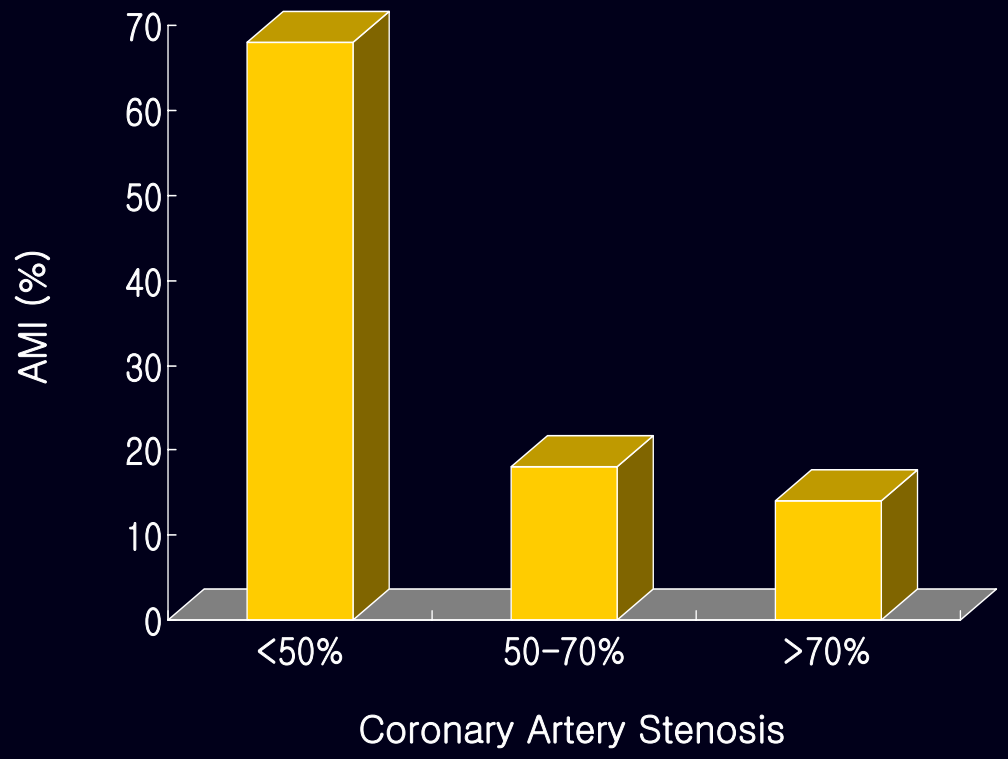
Beyond the Culprit Lesion



- **Atherosclerosis is a diffuse process.**
- **Lack of luminal obstruction does not mean a lack of atherosclerosis**

Circulation 2001;103:2705

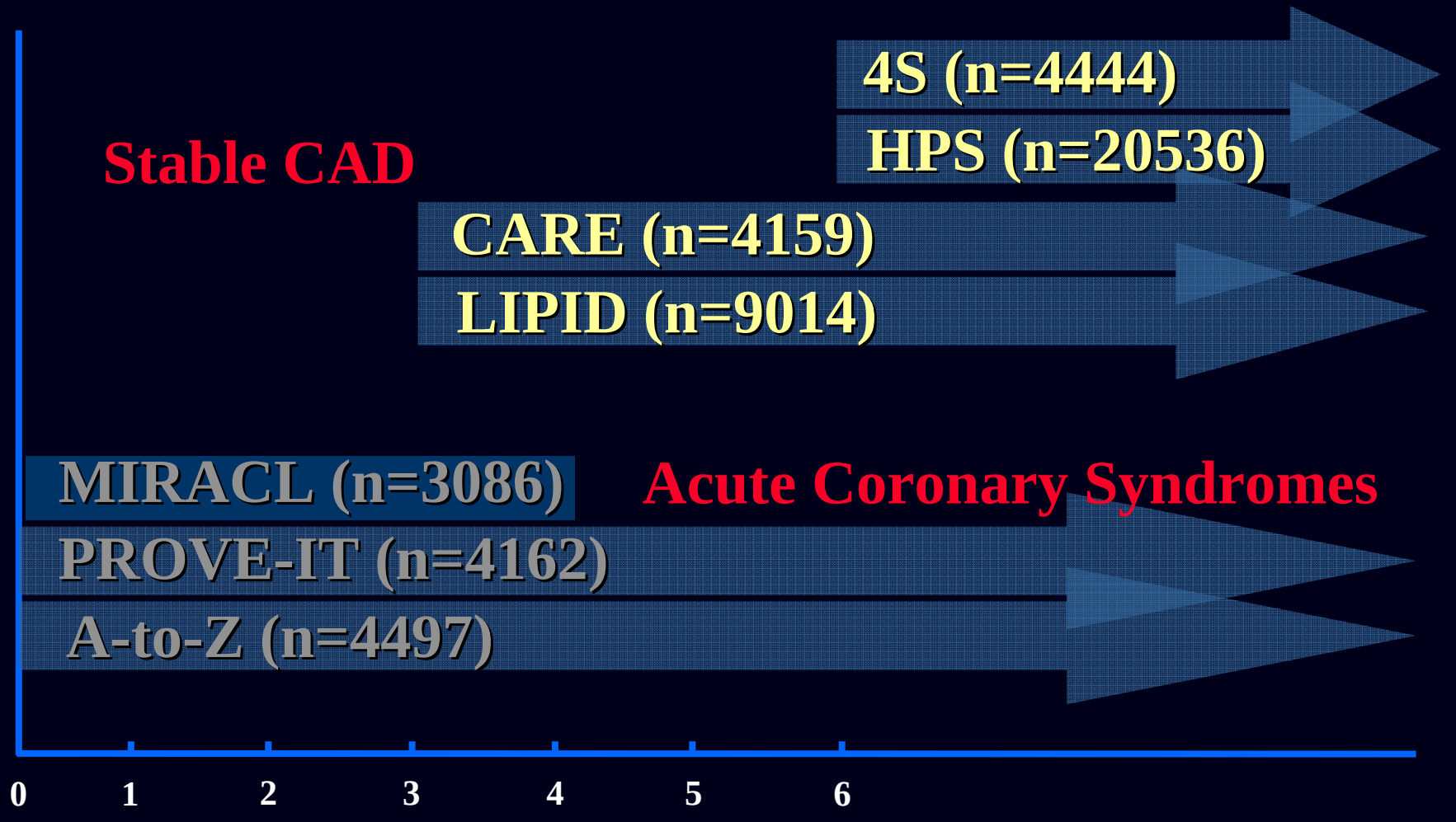
Where Should we go?



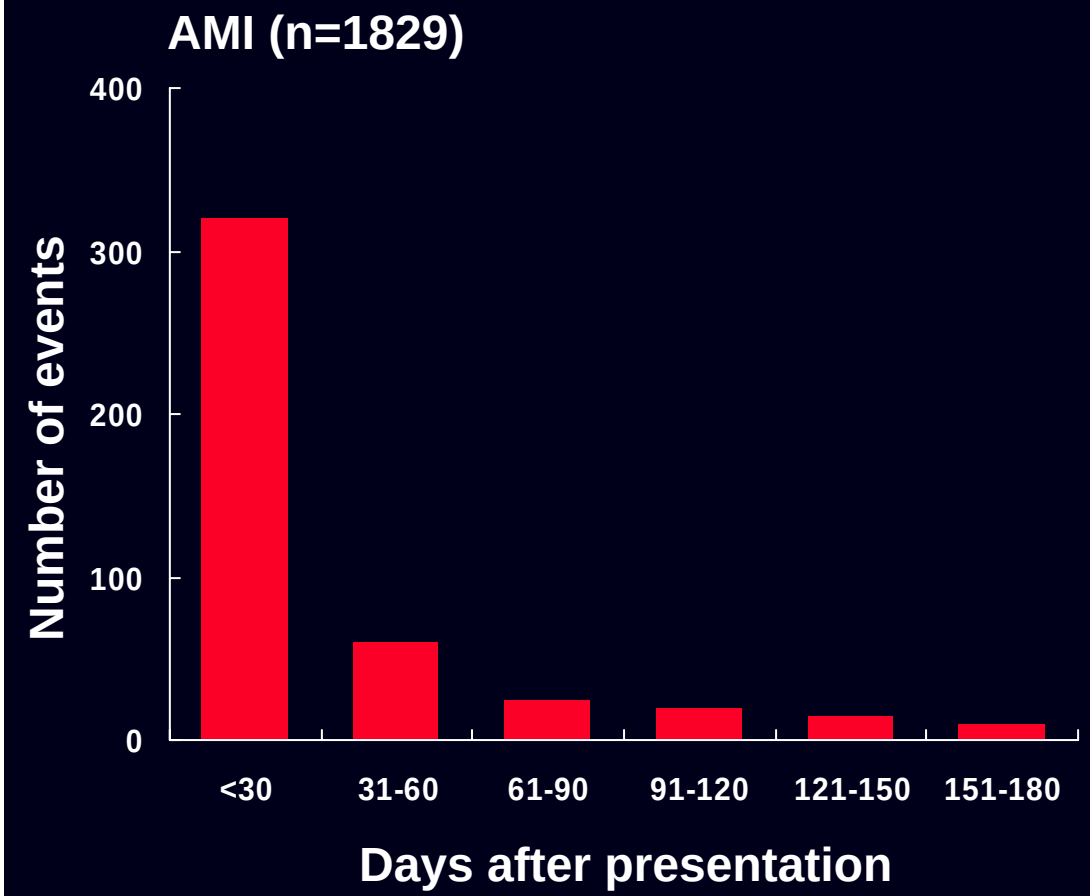
50% of patients with CAD presented with AMI or SCD.

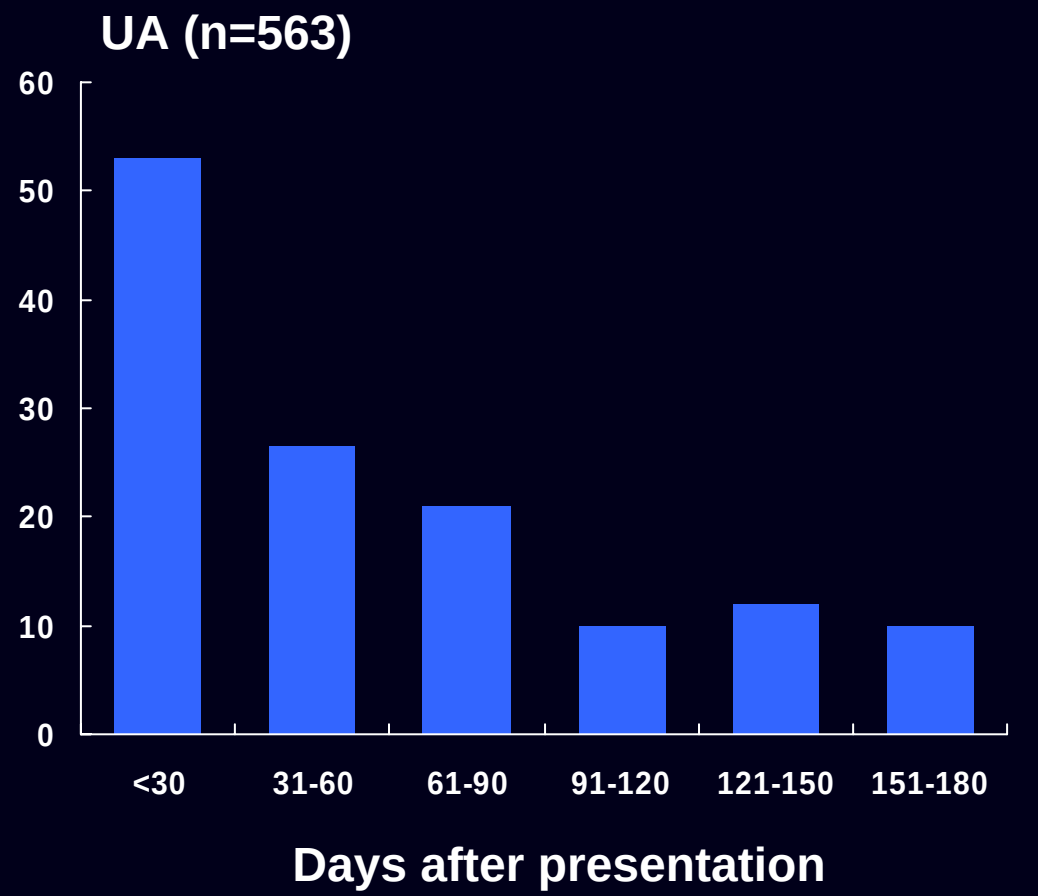
Prevention of acute coronary events must be the primary goal.

Statin Therapy in CAD



Recurrent Events after ACS

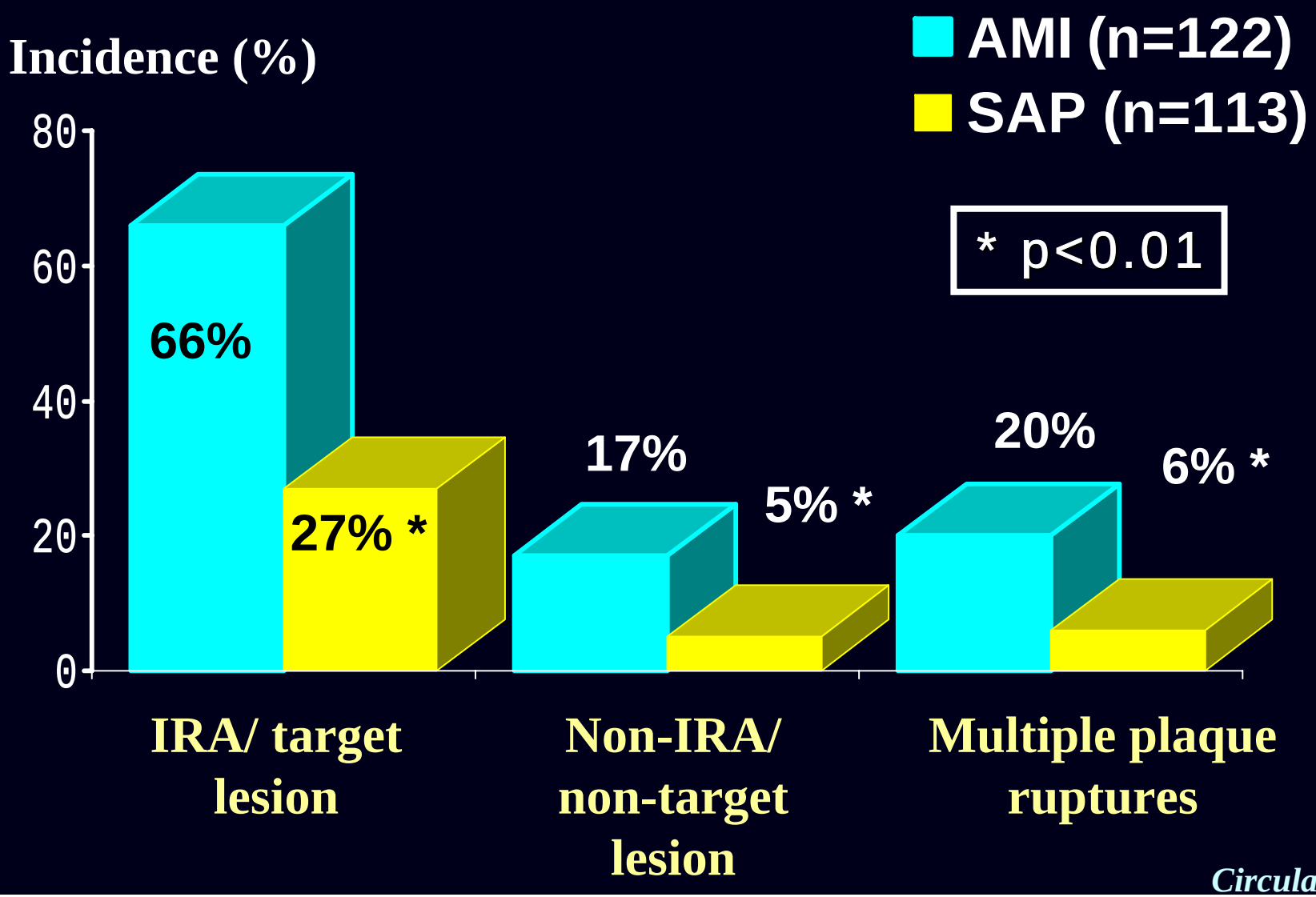




Heart 2003;89:1268

AMC Data

Multiple Plaque Rupture



Circulation2004:110:928

Statin Therapy in ACS

- **Are statins beneficial early post ACS?**
- **Does the degree of LDL lowering matter?**

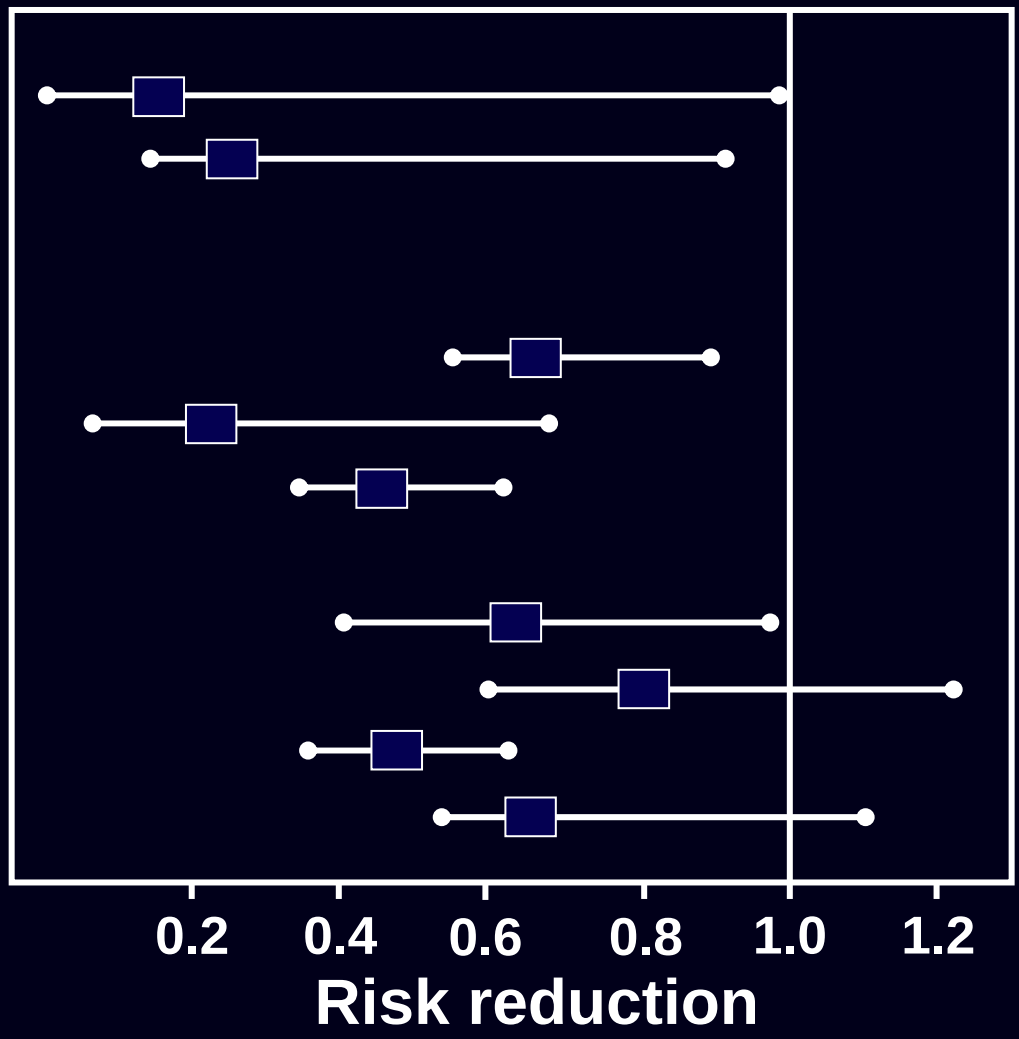
Risk reduction in patients with an ACS treated with lipid-lowering therapy.

Early benefit (in-hospital)
- Mayo Clinic
- PRISM trial

Late benefit (16 wk to 1y)
- Swedish Study
- Mayo Clinic
- PURSUIT/Gusto IIB
- In TIME II
  - prior lipid treatment
  - no prior lipid treatment

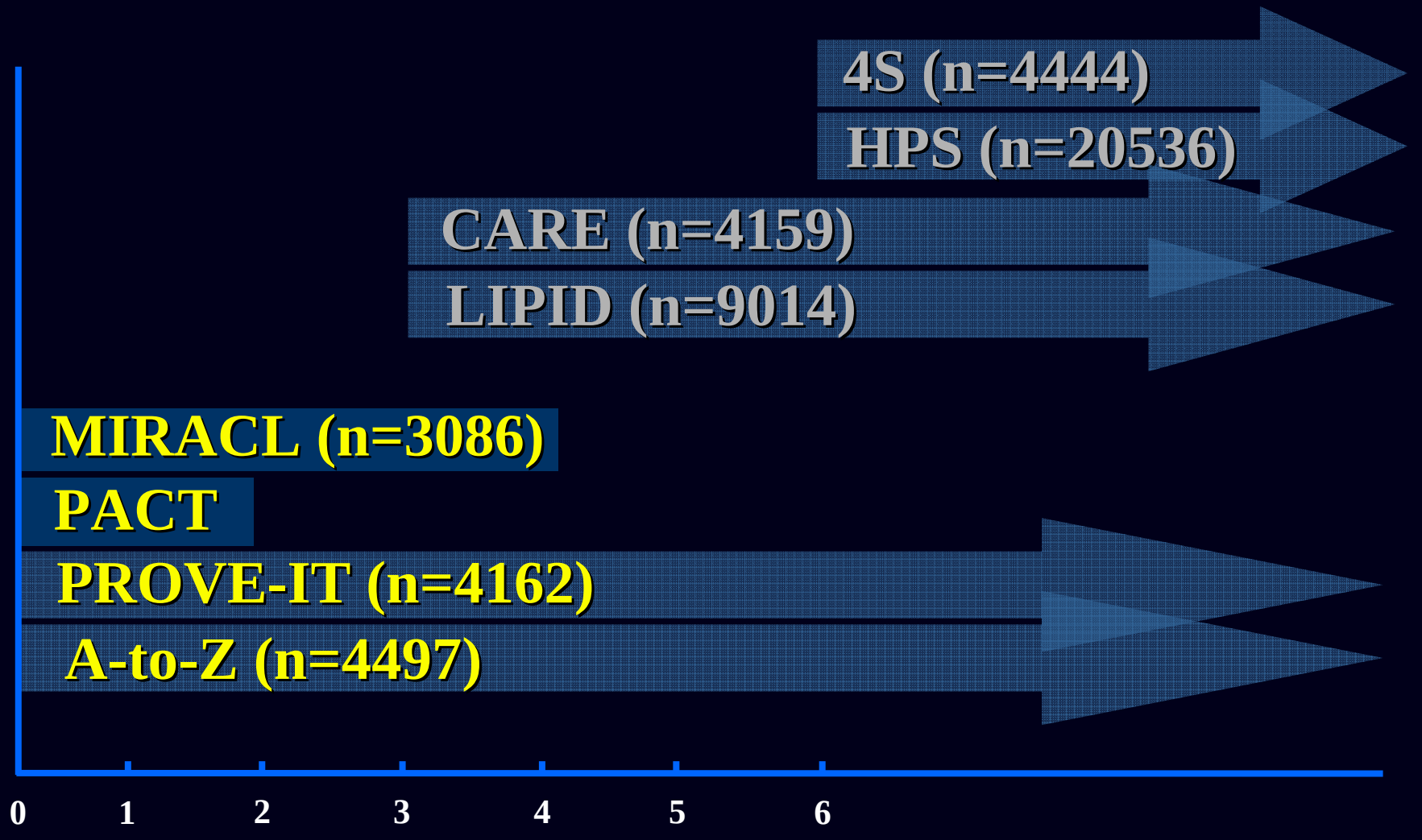
OPUS/TIMI 16

SYMPHONY



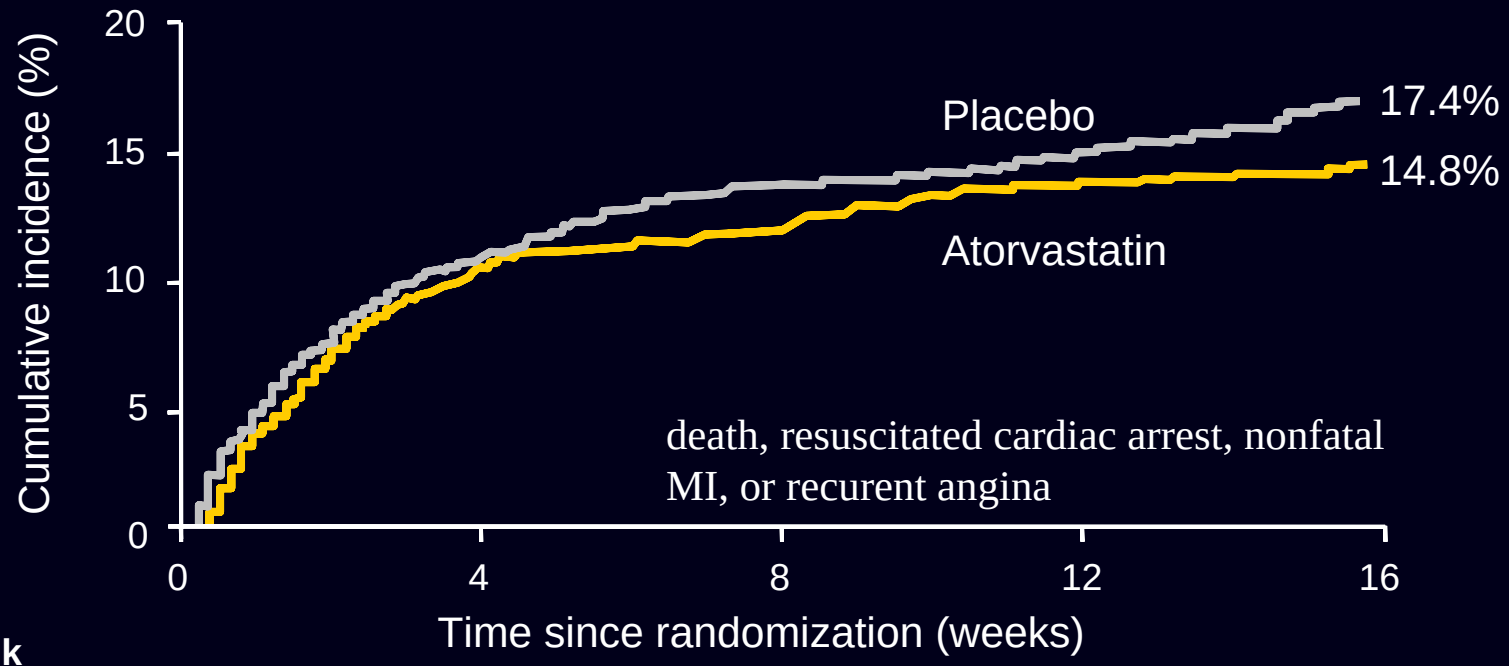
Eur Heart J 2004:6:A32

Early Statin Therapy in ACS



MIRACL: Reductions in Recurrent Ischemic Events

Atorvastatin 80 mg/d over 16 weeks in ACS patients (n=3086)



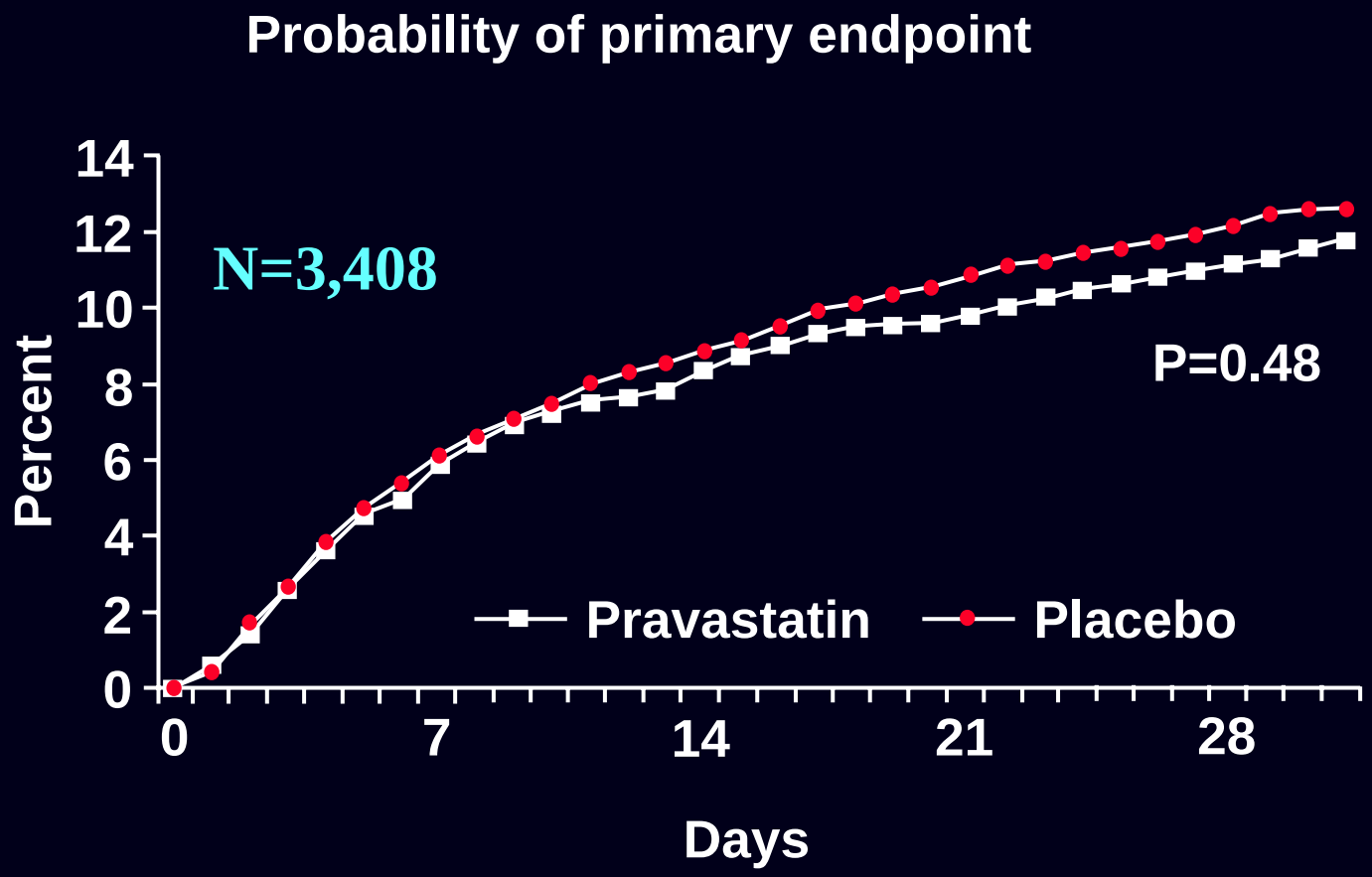
Number at Risk

Atorvastatin	1538	1381	1351	1323	518
Placebo	1548	1384	1338	1318	473

Schwartz GG, et al. *JAMA*. 2001;285:1711-1718.
Kinlay S, et al. *Circulation*. 2003;108:1560-1566.

Effect of Pravastatin Compared With Placebo Initiated Within 24 h of Onset of AMI or uAP

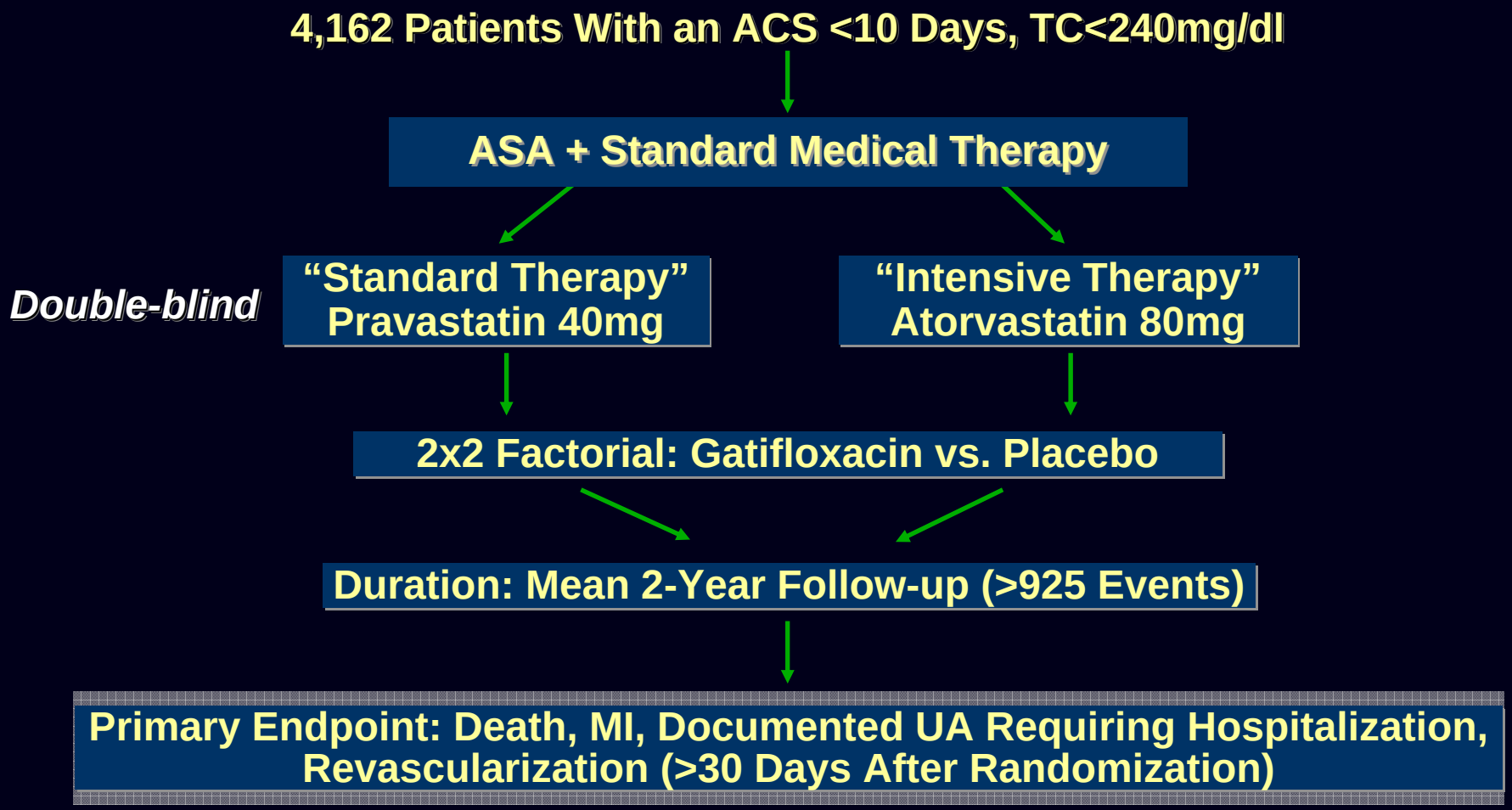
The Pravastatin in Acute Coronary Treatment (PACT) trial



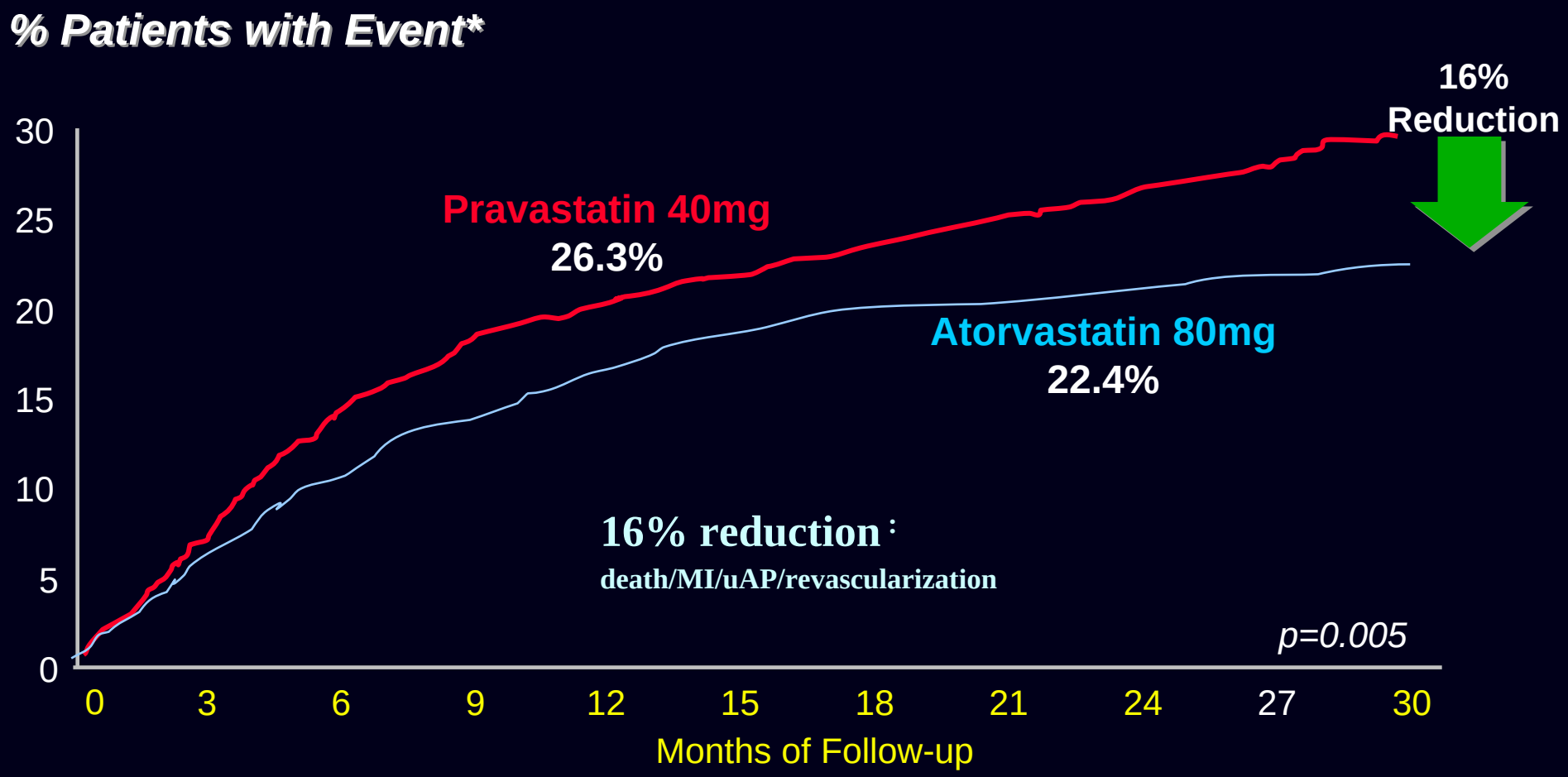
Pravastatin can be safely administered within 24h of the onset of symptoms of an ACS, with a favorable but not significant trend in outcome at 30 days compared with placebo.

AHJ2004:148(1):e2

PROVE-IT


4,162 Patients With an ACS <10 Days, TC<240mg/dl
ASA + Standard Medical Therapy
Double-blind
"Standard Therapy" Pravastatin 40mg
"Intensive Therapy" Atorvastatin 80mg
2x2 Factorial: Gatifloxacin vs. Placebo
Duration: Mean 2-Year Follow-up (>925 Events)
Primary Endpoint: Death, MI, Documented UA Requiring Hospitalization, Revascularization (>30 Days After Randomization)

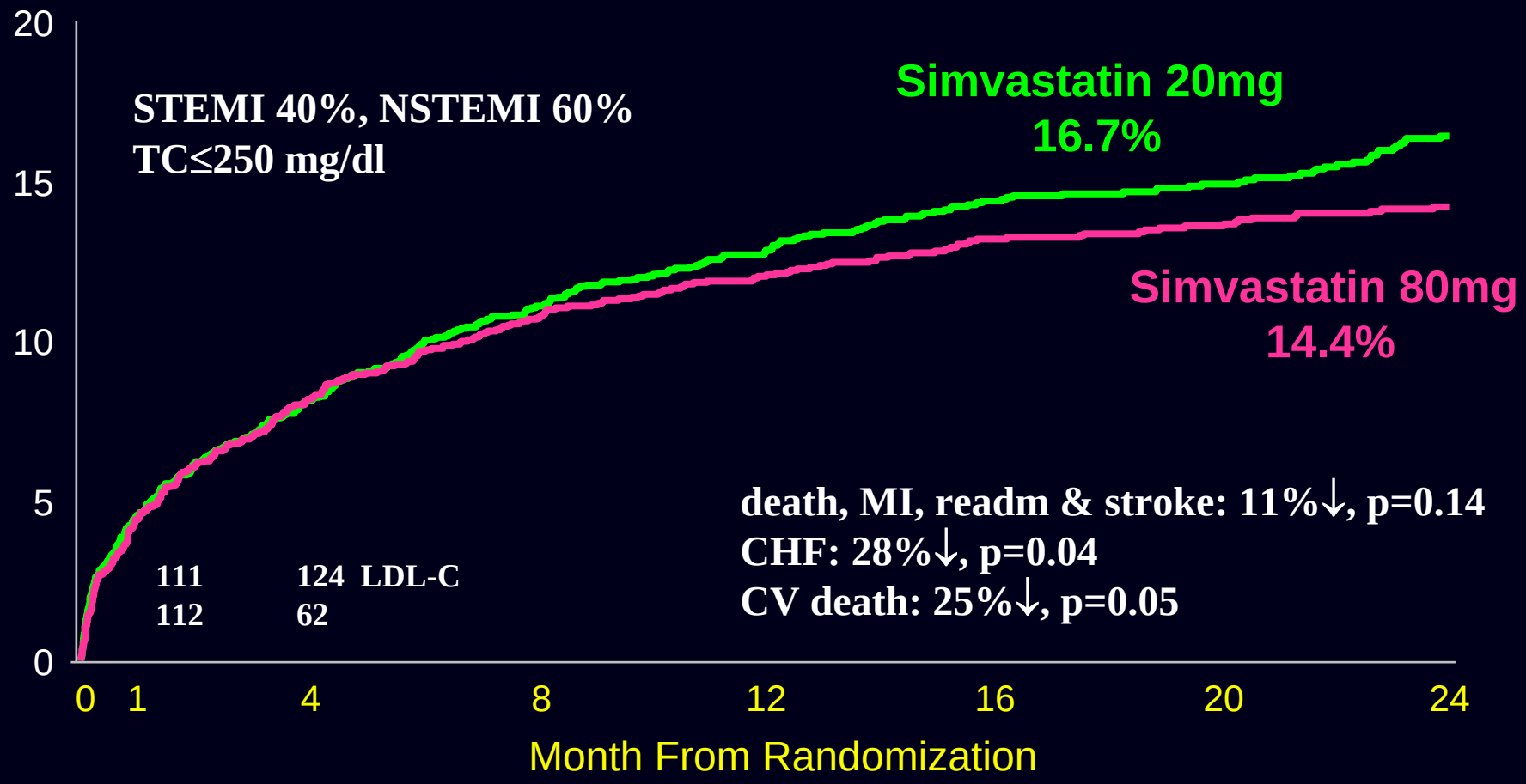
PROVE-IT



- N=4,162 ACS (early invasive-3/4; multiple medications)
- Among patients who have recently had an ACS, an intensive lipid-lowering statin regimen provides greater protection against death or major cardiovascular events than does a standard regimen.

NEJM 2004;350:1495

A to Z in Patients With ACS



- **No early divergence in even rates**
- **A favorable trend toward reduction of MACE.**

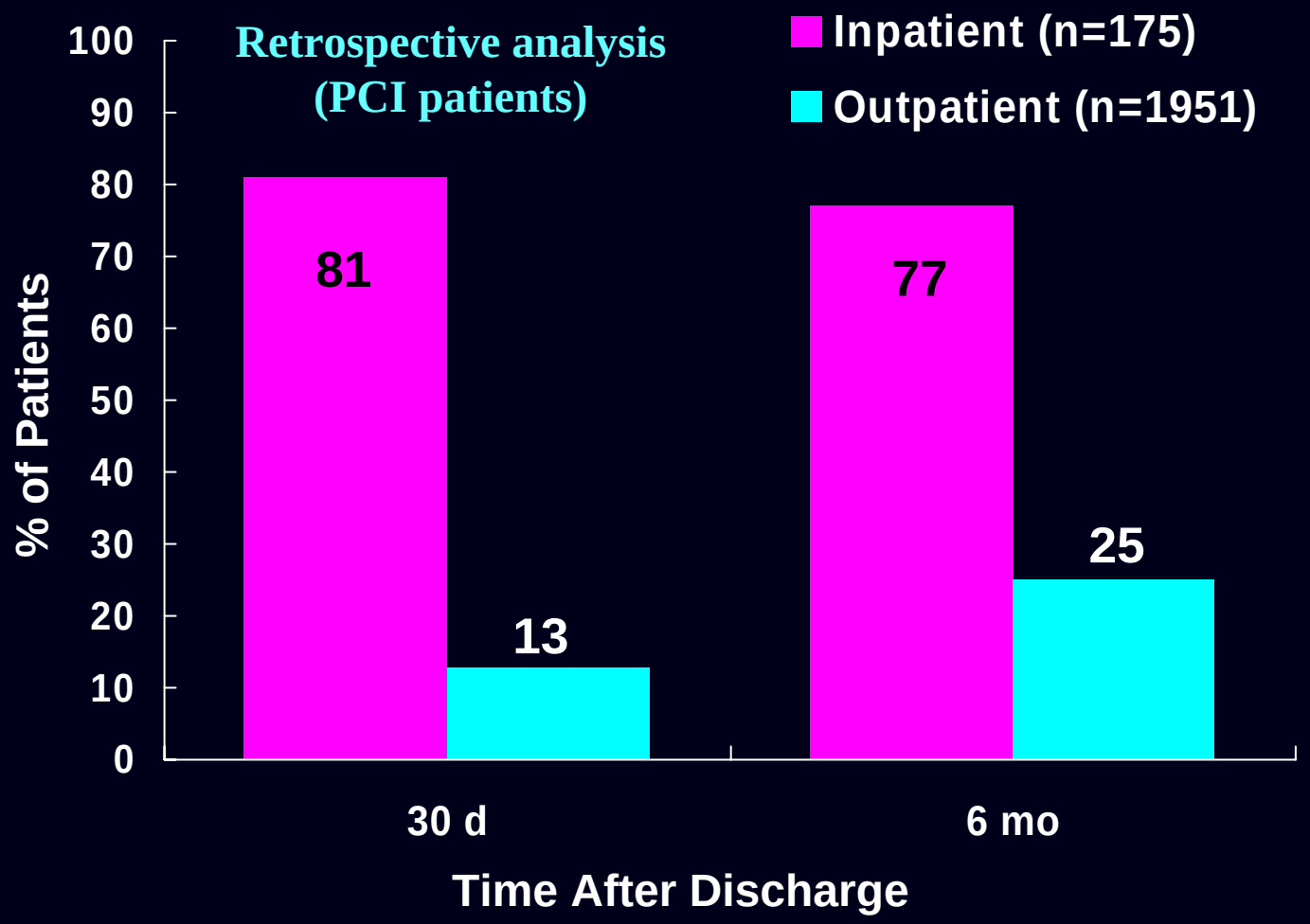
JAMA2004:292:1307

Intensive Statin Therapy in ACS

	A to Z	MIRACL	PROVE-IT
No. of Patients	4,497	3,086	4,162
Δ LDL-C, mg/dl			
Early	62	63	33
Late	15	NA	28
Δ CRP, %	17	34	39
Event reduction, %			
Early	0	16	18
Late	11	NA	16
Myopathic event*	9(0.4%)	0	0

*CK higher than 10 times the upper limit of normal

In-Hospital Initiation of Lipid-Lowering Therapy After Coronary Intervention as a Predictor of Long-term Utilization



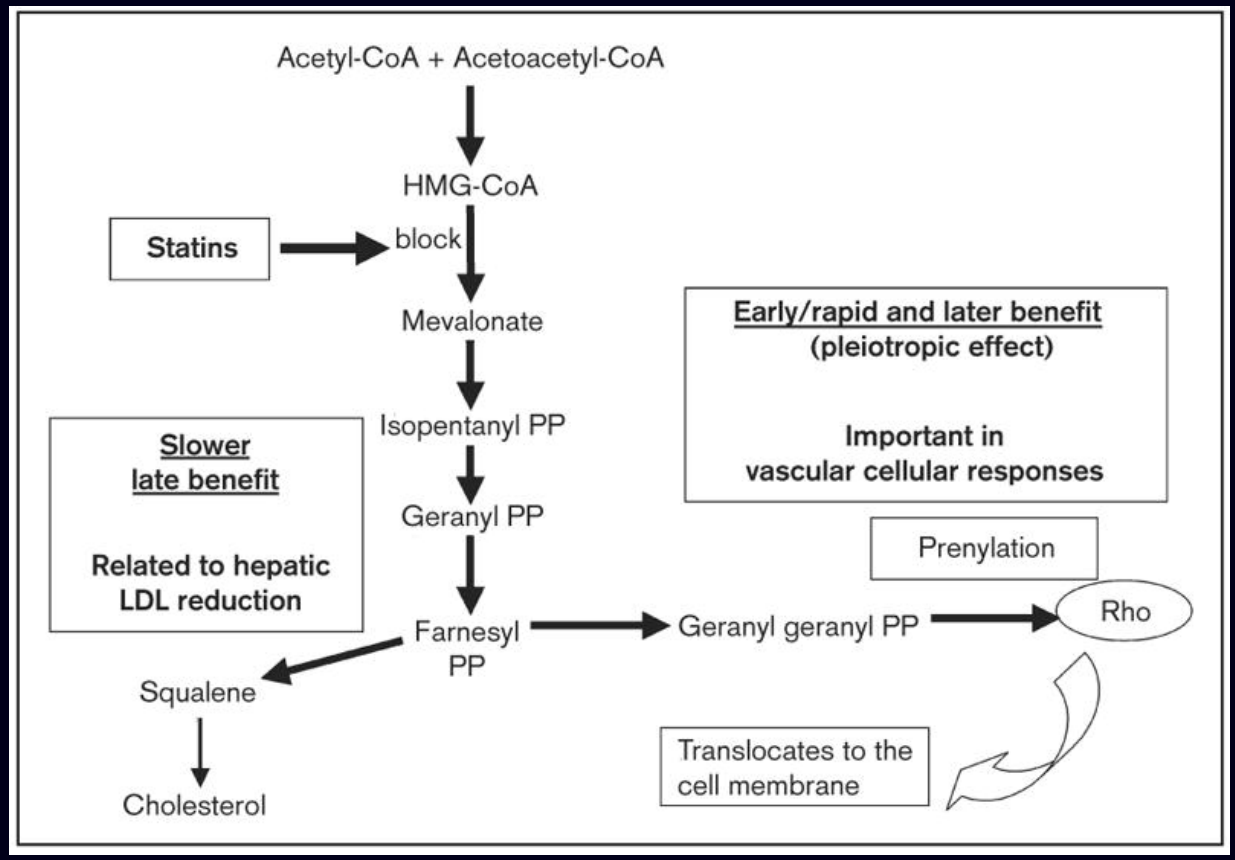
The initiation of lipid-lowering therapy in the inpatient setting increases the rate of its subsequent use, making this an important method of ensuring appropriate secondary prevention

Arch Intern Med 2003; 163: 2576

Summary

- **Early initiation of statin therapy is safe and may have a benefit in the reduction of ischemic events in ACS patients.**
- **Early statin therapy should be considered in all patients admitted with ACS.**

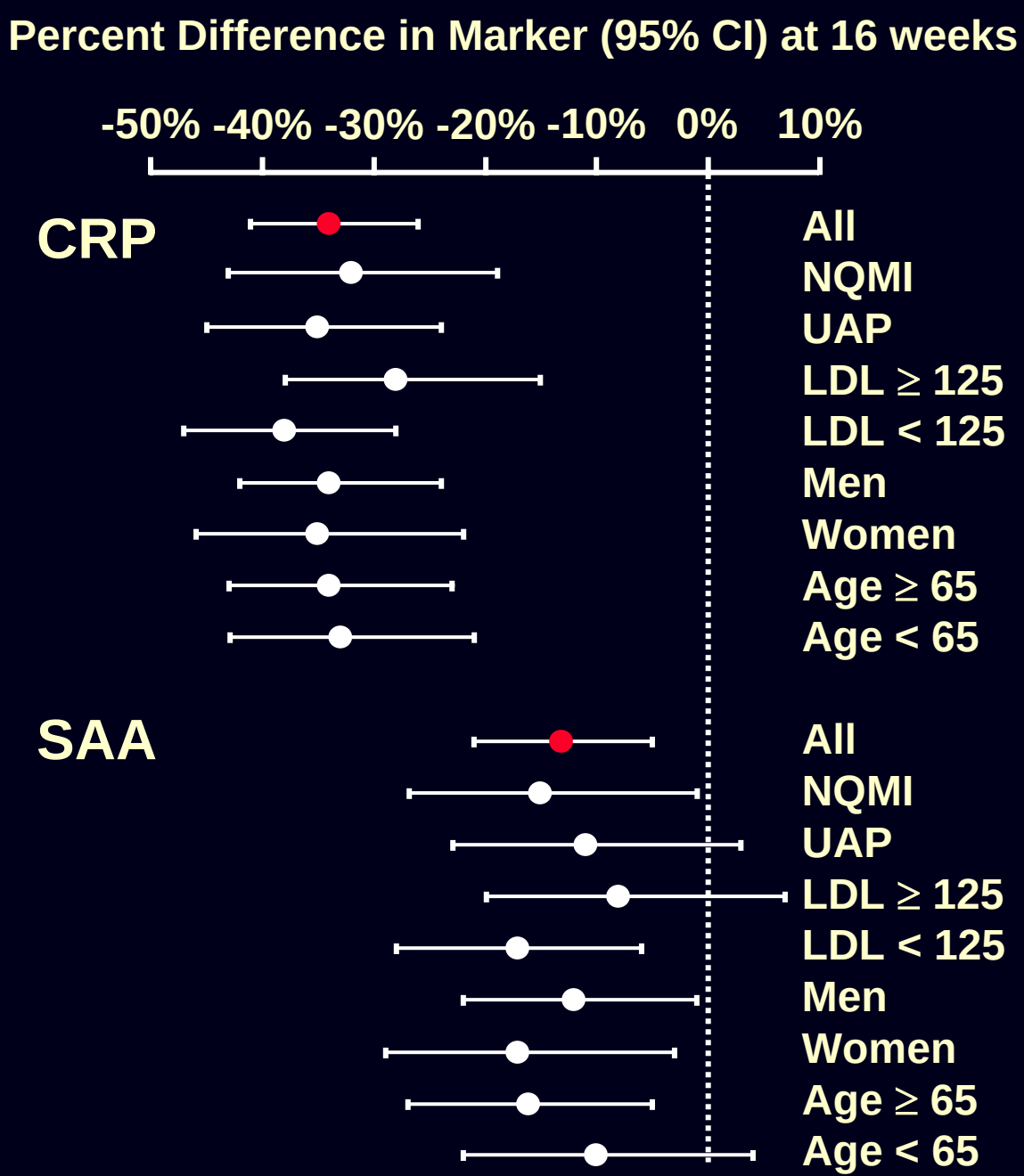
Intensive inhibition of HMG-CoA reductase



HMG-CoA reductase is an ubiquitous enzyme which is present in vascular and inflammatory cells as well as in hepatocytes.

Isoprenoids bind a number of G-proteins such as Rho and Ras by prenylation. Rho activates a number of nuclear TF such as NFkB.

Curr Opinion Lipidol 2004;15:637



High-Dose Atorvastatin in the MIRACL Study

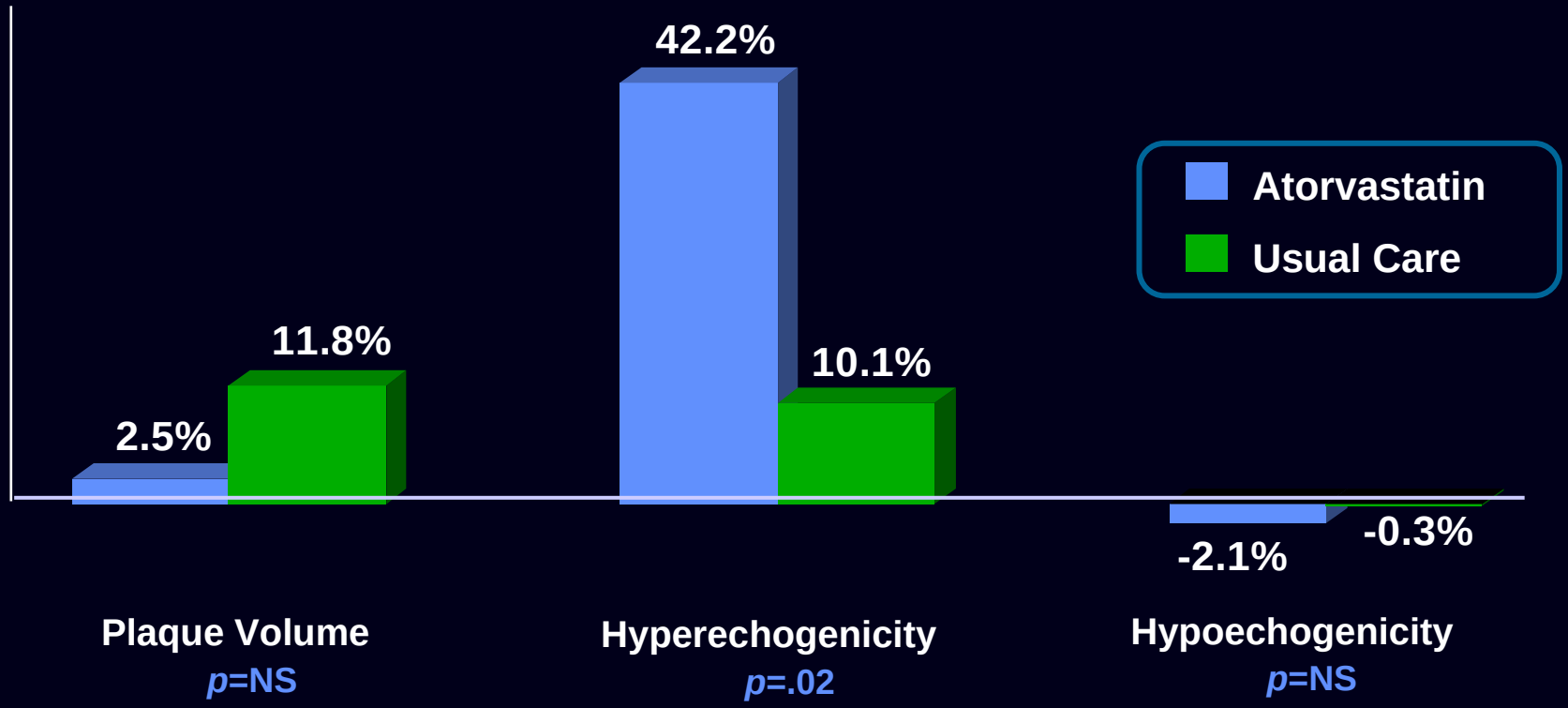
Compared with placebo, atorvastatin significantly reduced CRP and SAA at 16 weeks follow-up.

High-dose atorvastatin potentiated the resolution of inflammation after ACS, reinforce the concept of early lipid lowering soon after ACS.

Circulation 2003;108:1560

Gain Trials

Change After 12 Months of Therapy (%)



The impact of aggressive therapy with atorvastatin (LDL goal of <100 mg/dL) vs moderate therapy (usual care with various statins) on plaque volume and content using ICUS

Circulation 2001;104:387

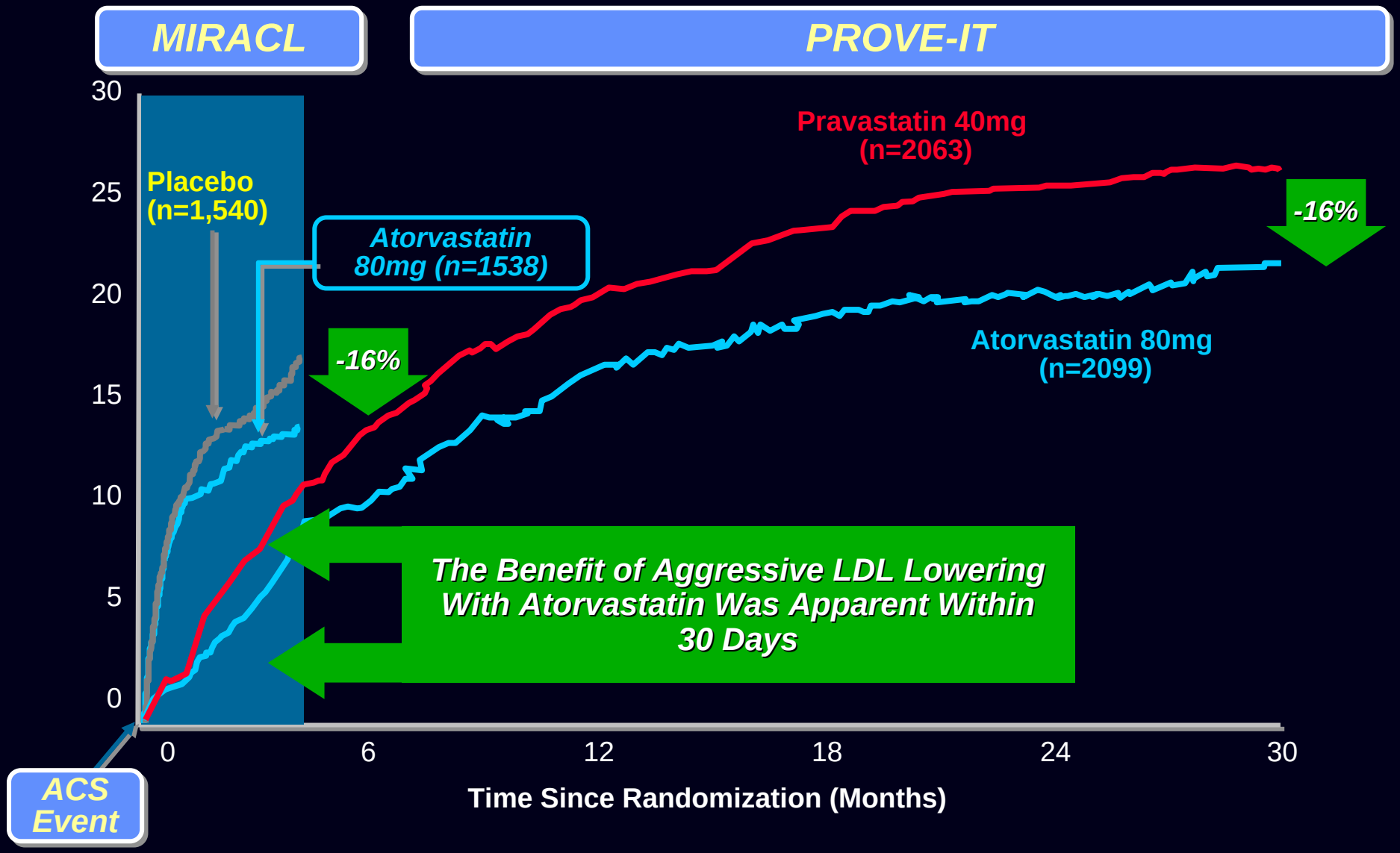
Statin Difference

Are they all the same?

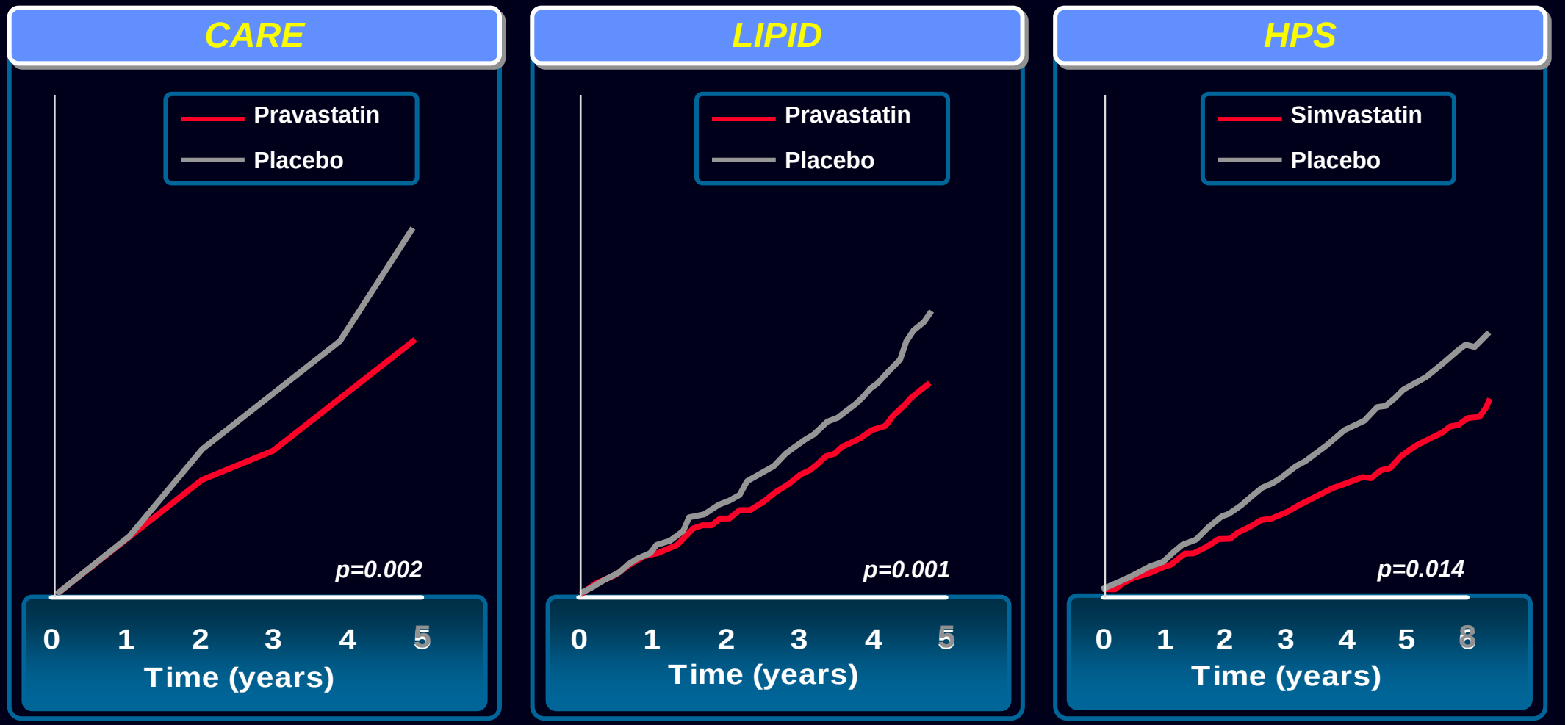
Landmark Clinical Trials:
Statins as a class reduce mortality and morbidity.

PROVE-IT and REVERSAL:
LDL-C reduction alone does not explain all of the differences in efficacy.

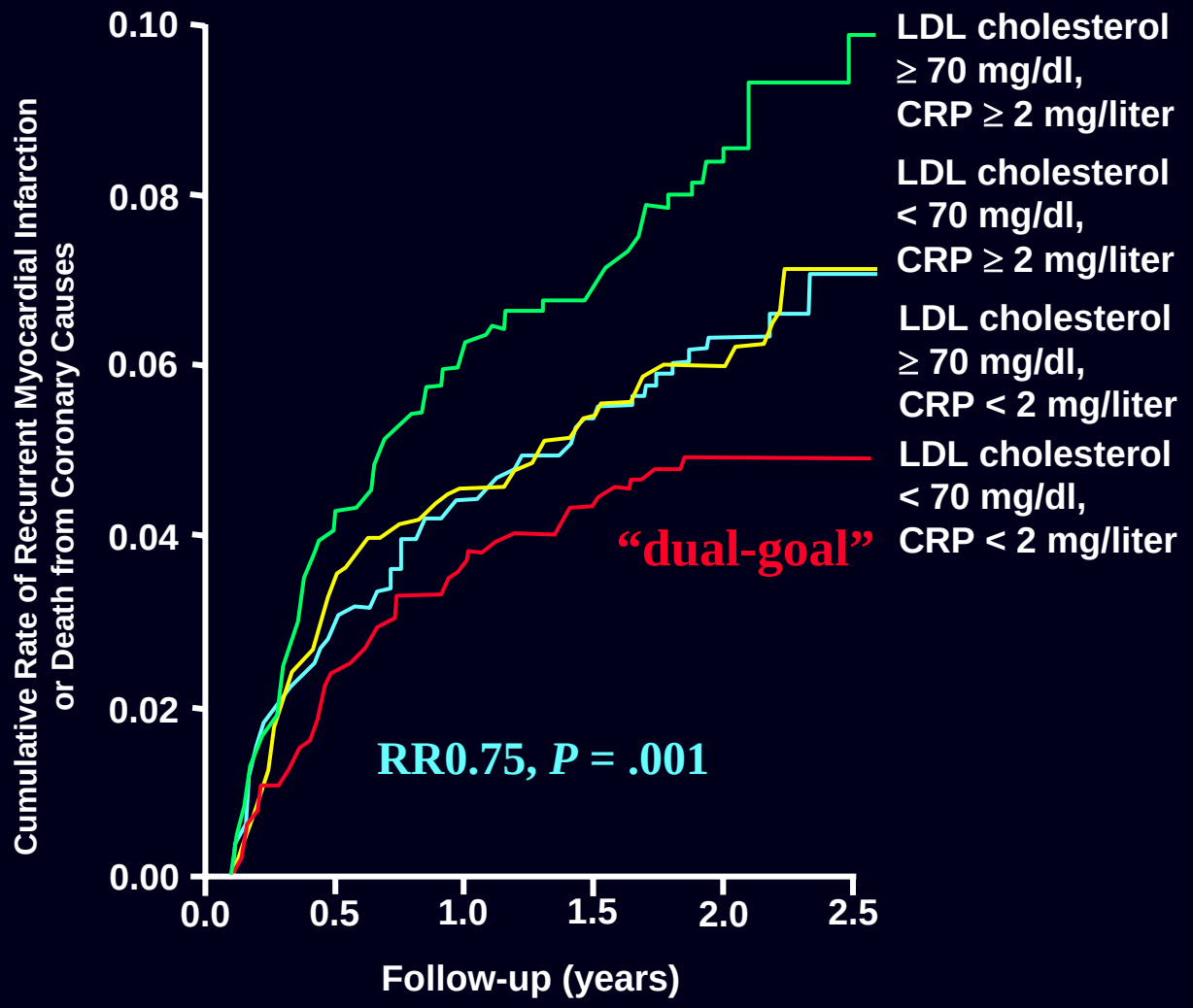
Early Benefits of Atorvastatin in ACS



Early Benefits Not Seen With Pravastatin or Simvastatin in Secondary Prevention



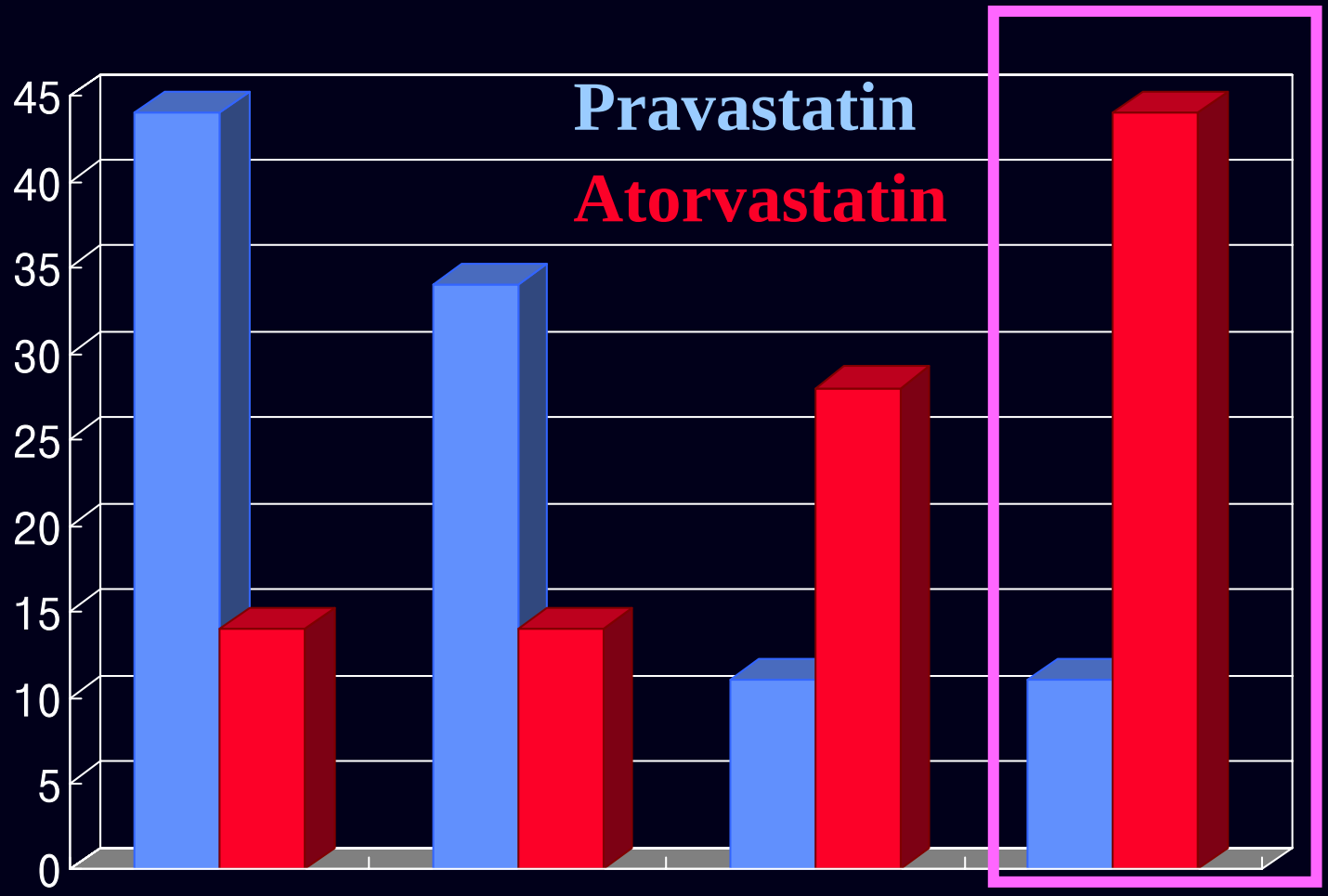
PROVE-IT: CRP Analysis



Patients who have low CRP levels after statin therapy have better clinical outcomes than those with higher CRP levels, regardless of the resultant level of LDL cholesterol.

N Engl J Med 2005;352:20

PROVE-IT: CRP Analysis

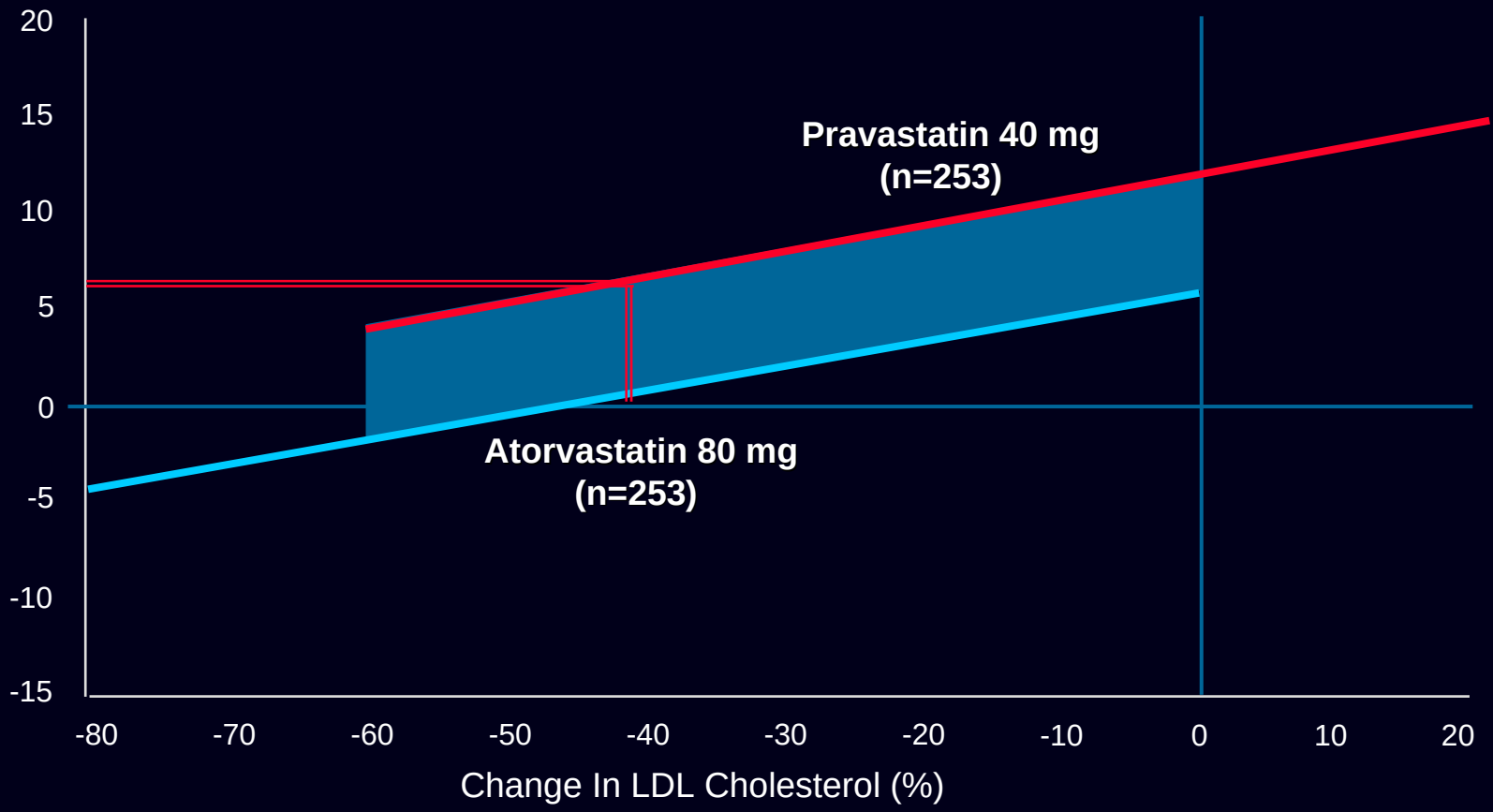


Probability to Get in the Best Group: 4-Fold Difference!

REVERSAL

Good Evidence of Statin Difference

Change in Atheroma Volume (mm^3)



The progression rate at any level of LDL-C reduction was lower with atorvastatin compared with pravastatin.

Statin Differences

- **Head-to-head comparison**

  There is no doubt that all statins have had an immense impact on the way we manage patients with CAD.

  Recent clinical data suggest that they are not equally effective for all patient subsets.

Conclusions

- **Overall, statin therapy should be initiated in the setting of ACS, regardless of plasma lipid values.**
- **The results of recent clinical trials herald the beginning of a new era of intensive statin therapy.**