



Altas Dosis de Estatinas para Prevenir la Injuria Miocárdica Periprocedimiento

Sugerencias Actuales Basadas en las Evidencias Vigentes



Daniel José Piñeiro

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Presidente, Sociedad Interamericana de Cardiología

Altas Dosis de Estatinas para Prevenir la Injuria Miocárdica Periprocedimiento. Sugerencias Actuales Basadas en las Evidencias Vigentes. Daniel Piñeiro

No tengo relaciones ni tratos comerciales con ninguna compañía farmacéutica o de equipamiento médico, o razones que potencialmente pudiesen afectar la objetividad de mi presentación

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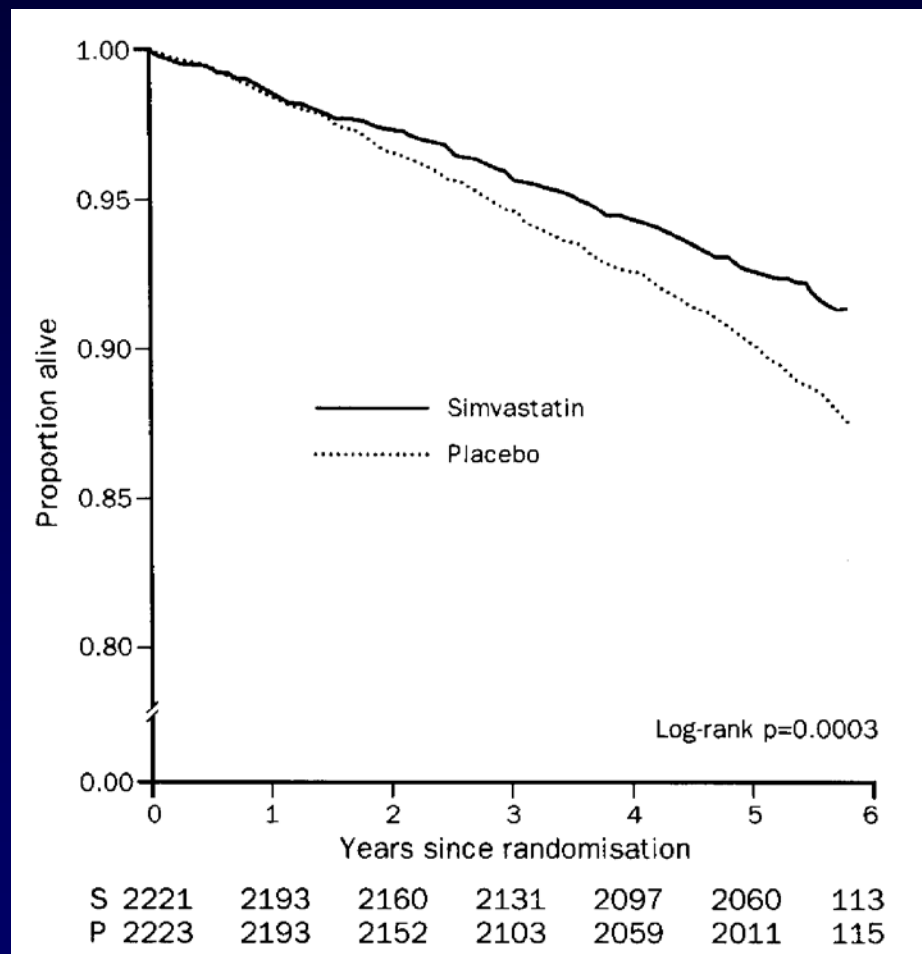
- ¿Cuál es el racional?
- ¿Cuáles son las evidencias?
- ¿Qué dicen las guías?

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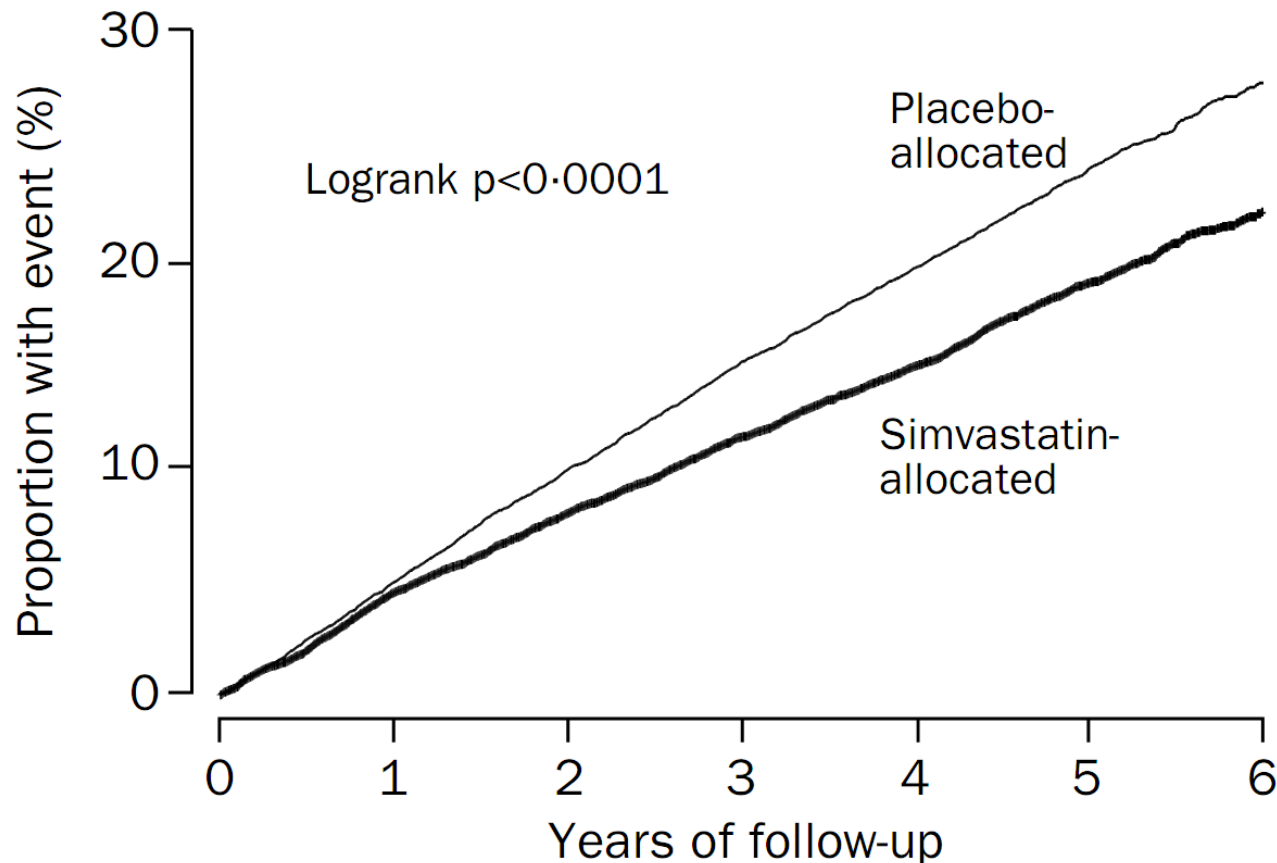
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Randomised Trial of Cholesterol Lowering in 4444 Patients With Coronary Heart Disease: The Scandinavian Simvastatin Survival Study (4S)

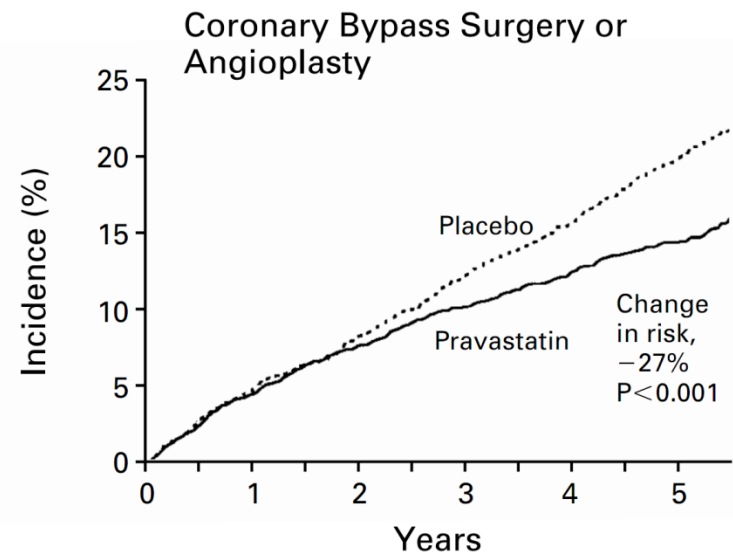
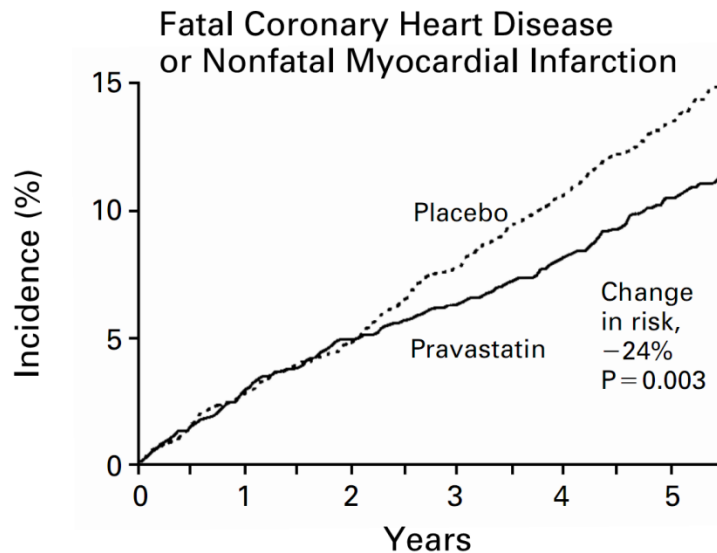


Scandinavian Simvastatin Survival Study Group. Lancet 1994;344:1383-9

MRC/BHF Heart Protection Study of Cholesterol Lowering With Simvastatin in 20536 High-Risk Individuals: A Randomised Placebo-Controlled Trial

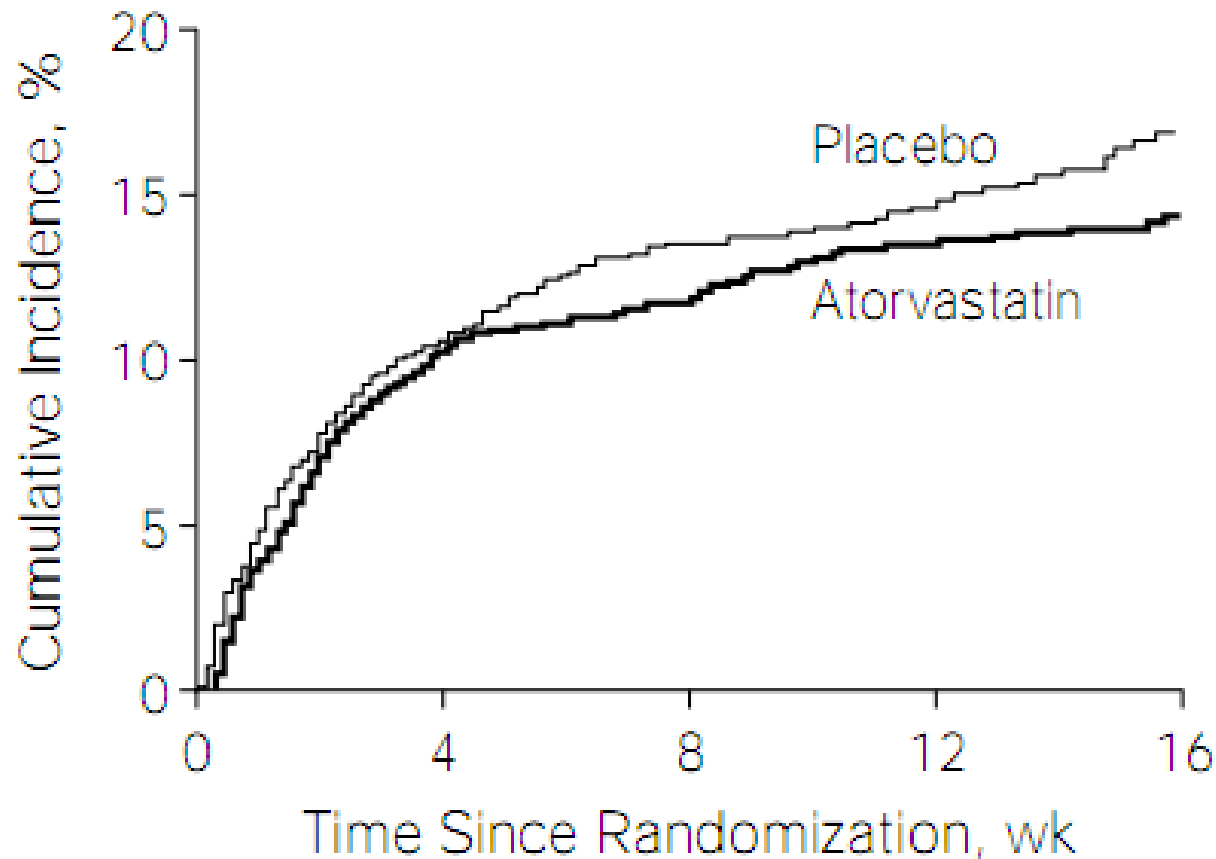


The Effect of Pravastatin on Coronary Events After Myocardial Infarction In Patients With Average Cholesterol Levels

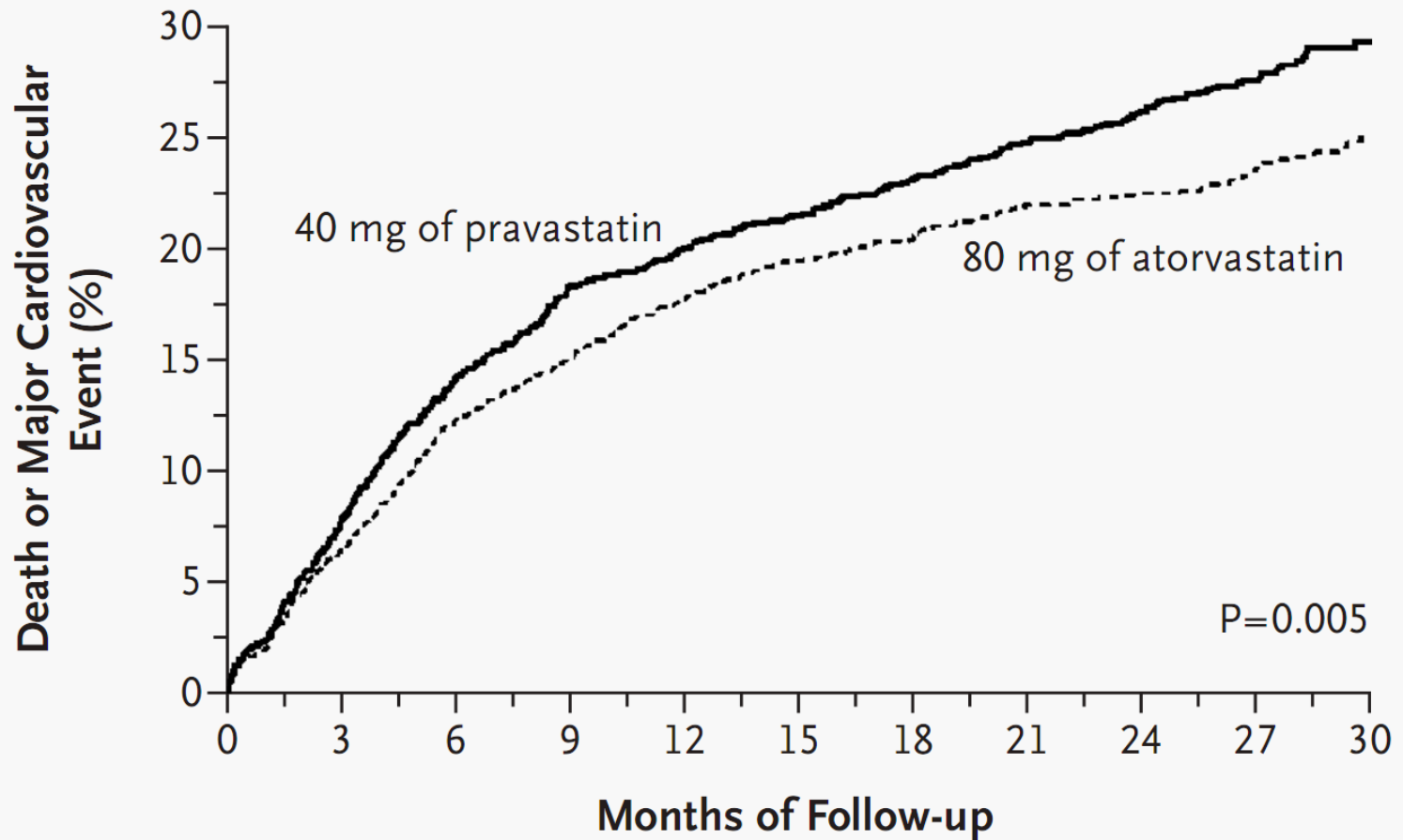


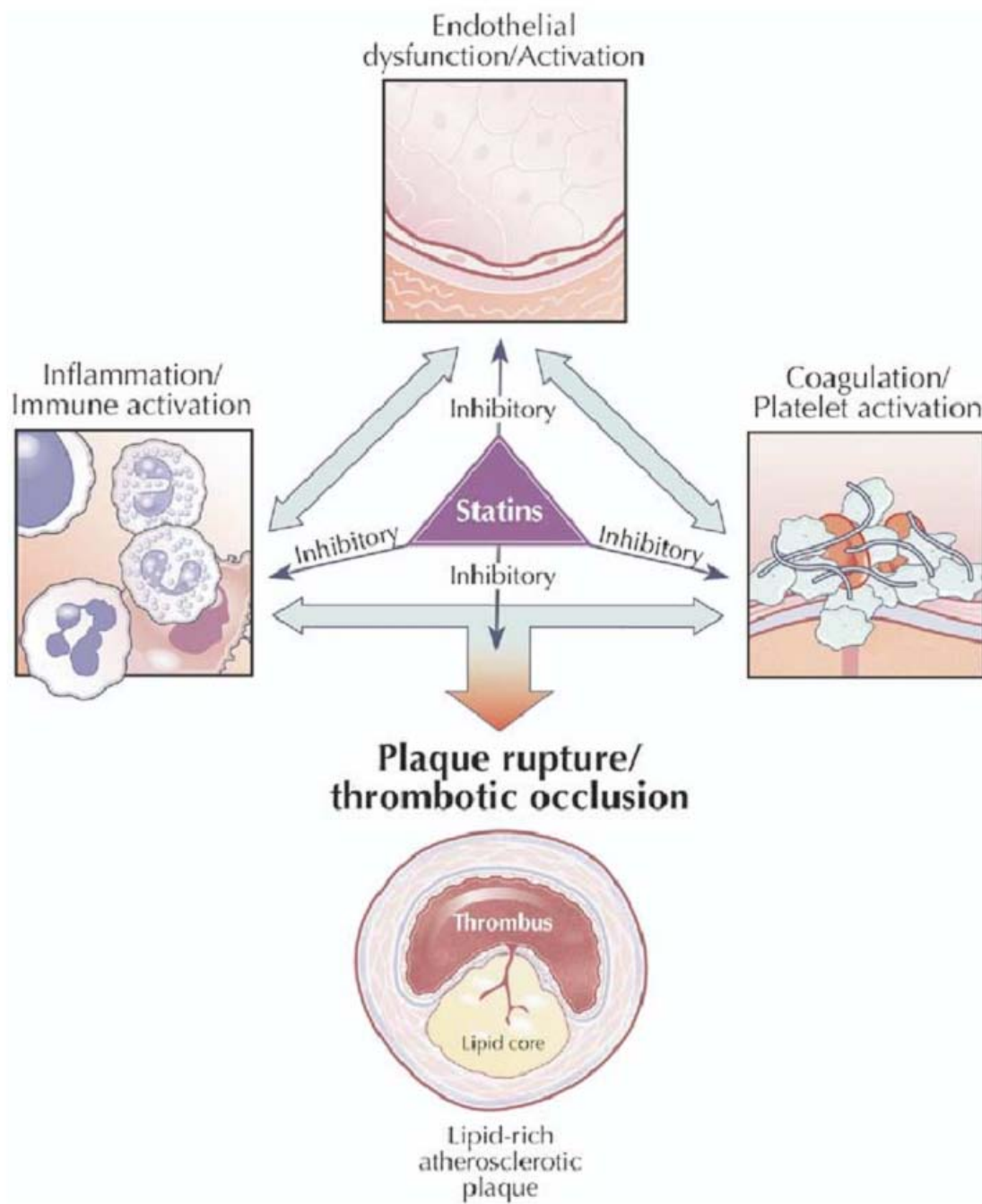
Effect of Atorvastatin on Early Recurrent Ischemic Events in Acute Coronary Syndromes

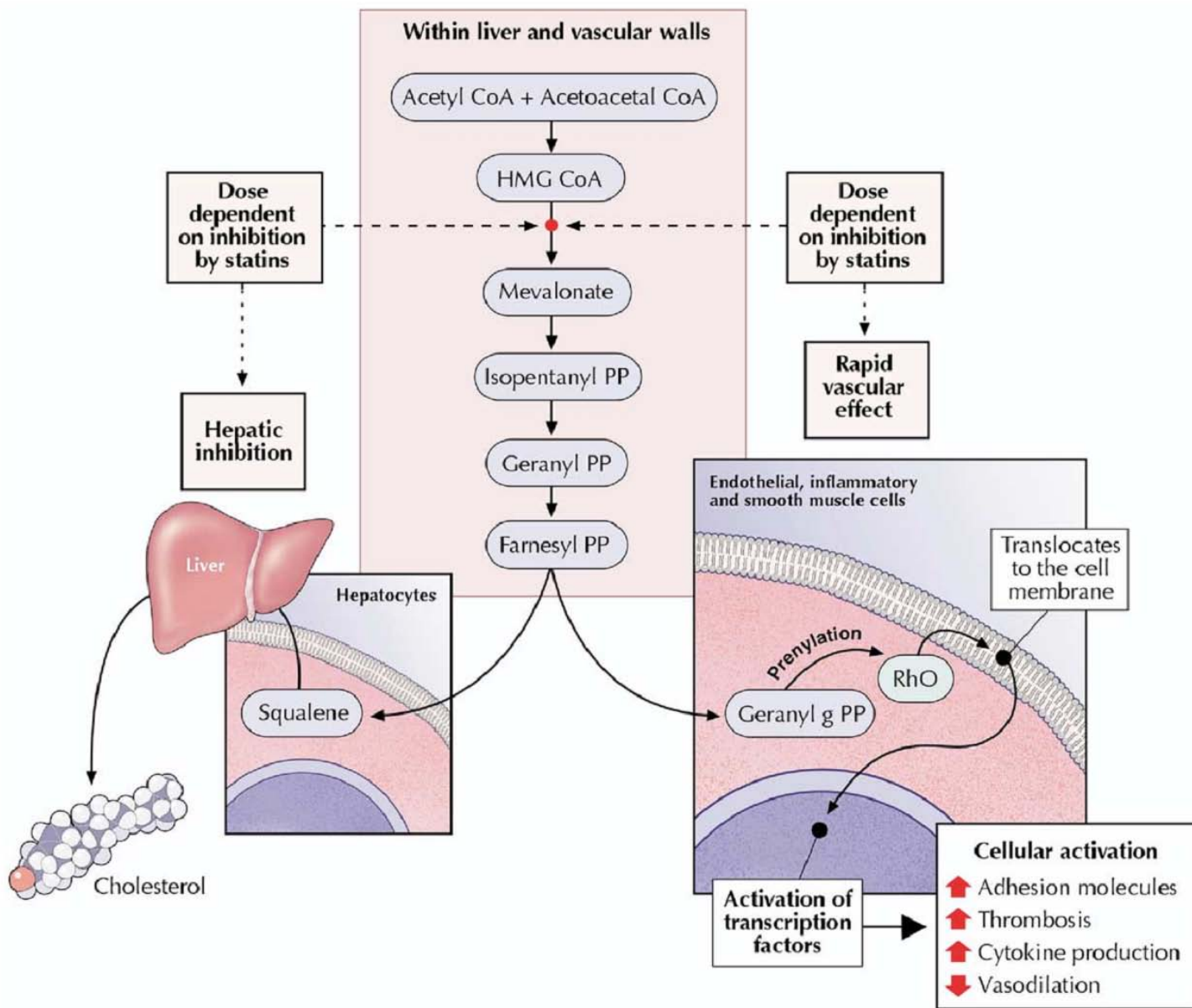
The MIRACLE Study: A Randomized Controlled Trial

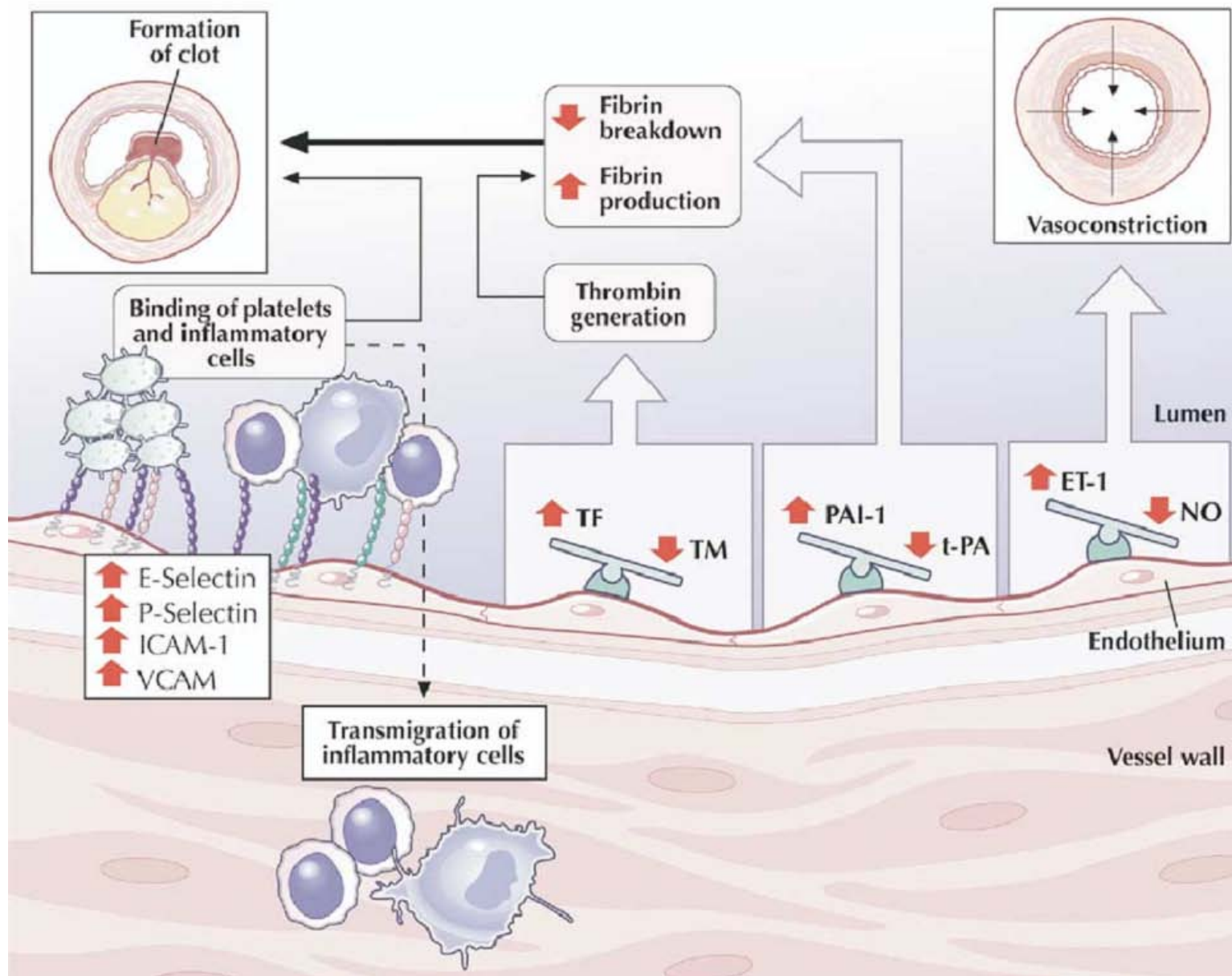


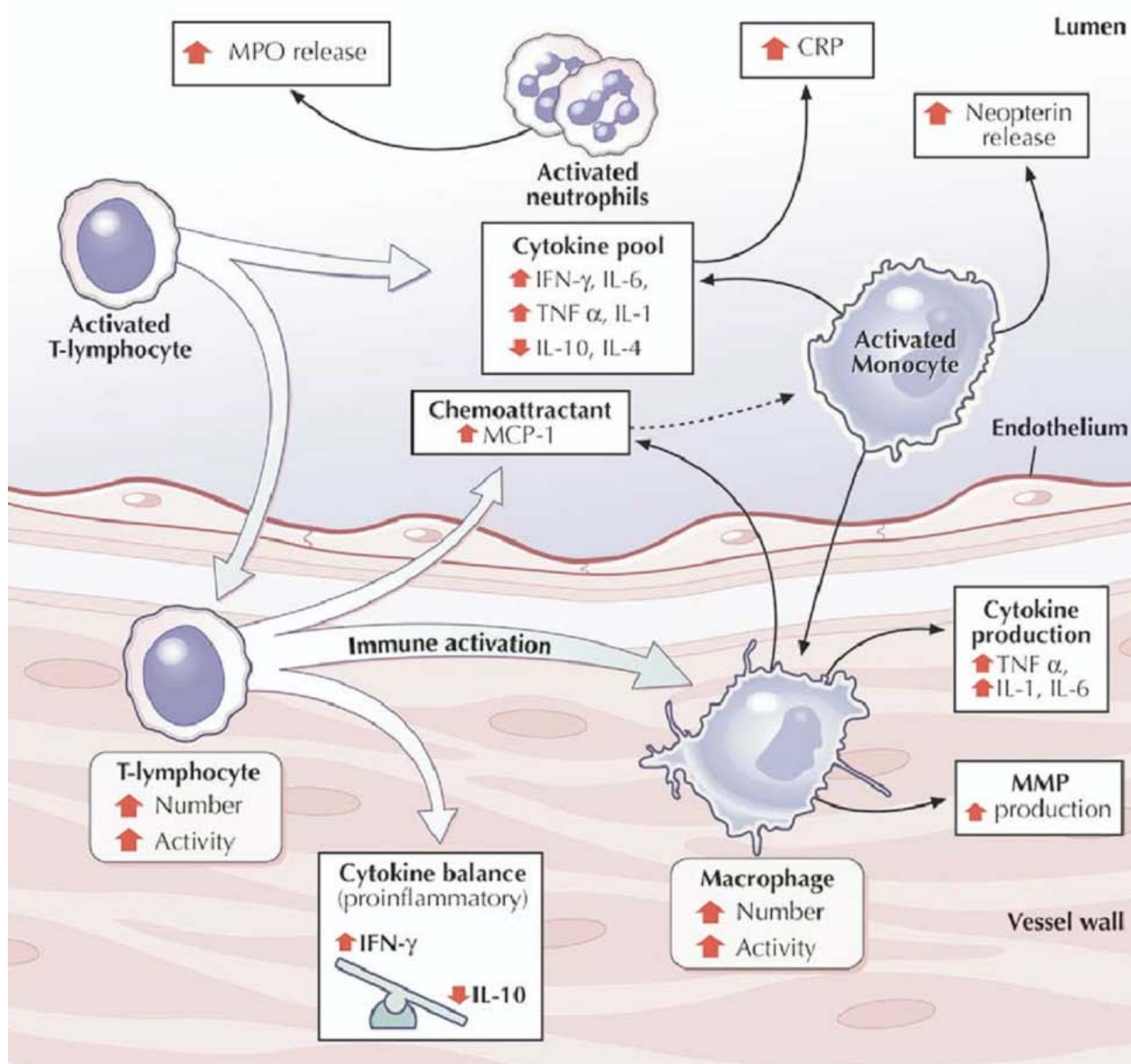
Intensive versus Moderate Lipid Lowering with Statins after Acute Coronary Syndromes











HMG-CoA Reductase Dependent

HMG-CoA Reductase Independent

Cholesterol Dependent

Cholesterol Independent

↓ LDL-C and ↓ oxidized LDL-C

↓ Prenylation
↓ Isoprenoid synthesis
Down-regulation of Rho/rhokinase
↓ NFκB and inflammatory signalling
↓ Expression of MCP-1 by endothelial cells

↓ Foam cell formation

Binding to the lymphocyte function associated antigen, thus preventing binding of lymphocyte to endothelial counter ligand ICAM-1

↓ Macrophage number
↓ Cholesterol rafts for inflammatory signalling
↓ Expression of inflammatory cytokines

↓ Binding of lymphocytes to endothelial receptor ICAM-1
Down-regulation of Th-1 lymphocytes
Cytokine switching from Th-1 to Th-2 type phenotype in lymphocytes
↓ Inflammatory cytokine production/CRP immune modulation

↑ Nitric oxide levels by stabilizing m-RNA

↑ Nitric oxide production

↓ Oxidative stress

↓ Oxidative stress

↓ Expression of adhesion molecules

↓ Endothelial adhesion molecule expression

↓ Platelet activation

↑ Increased TM expression

↓ Tissue factor expression

↑ tPA/PAI-1 ratio

↓ Coagulation factors

? Inactivation of factor Va

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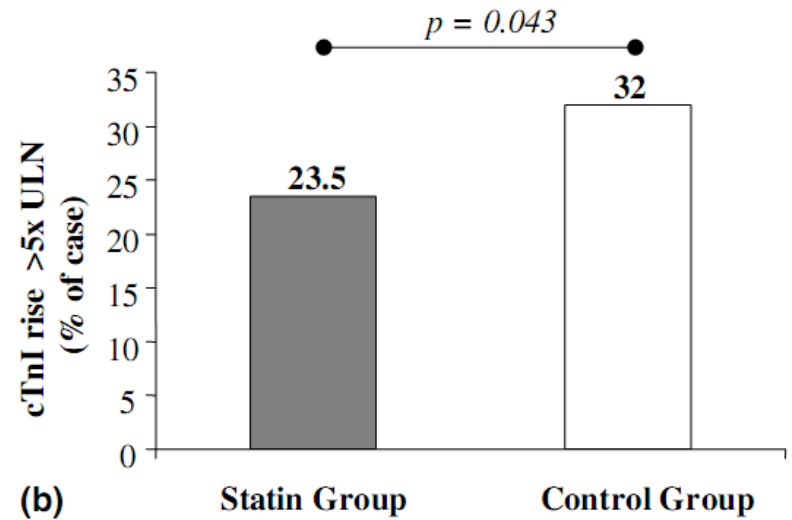
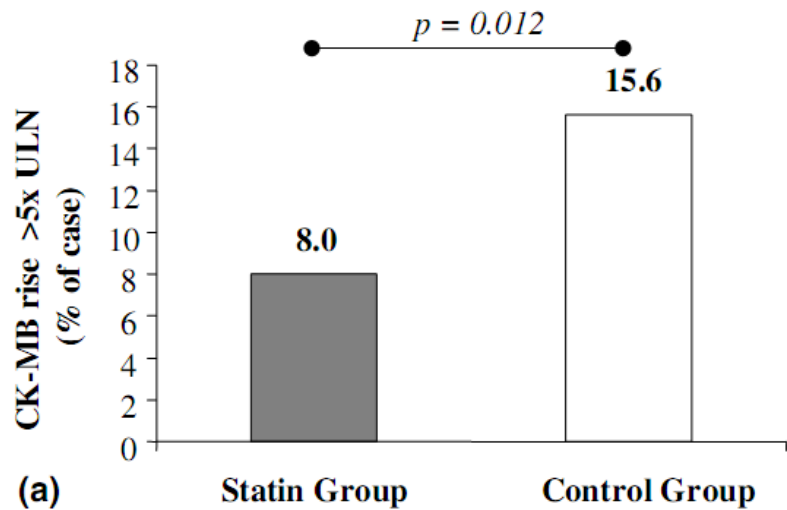
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Clinical research

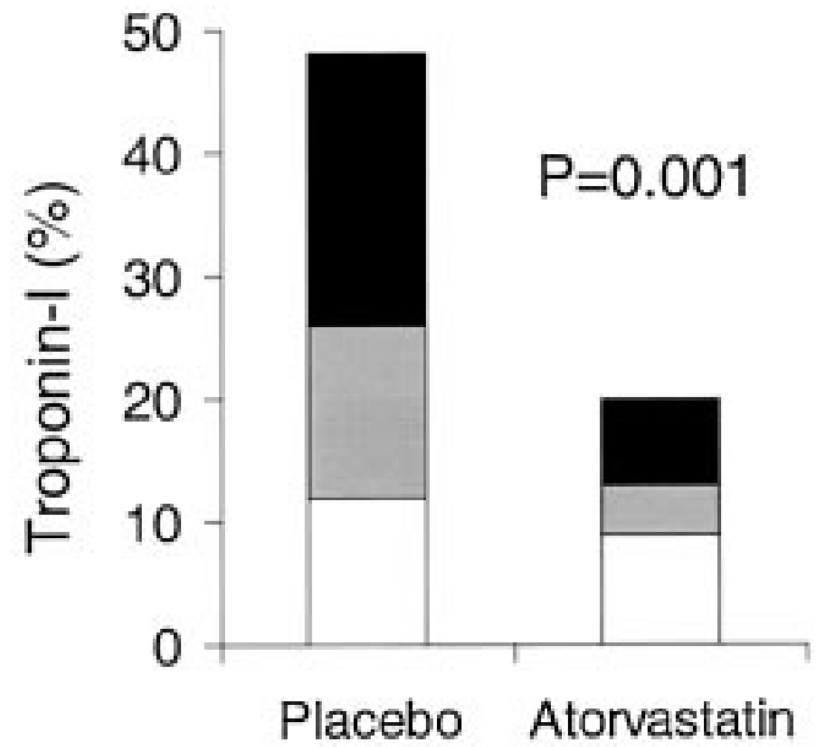
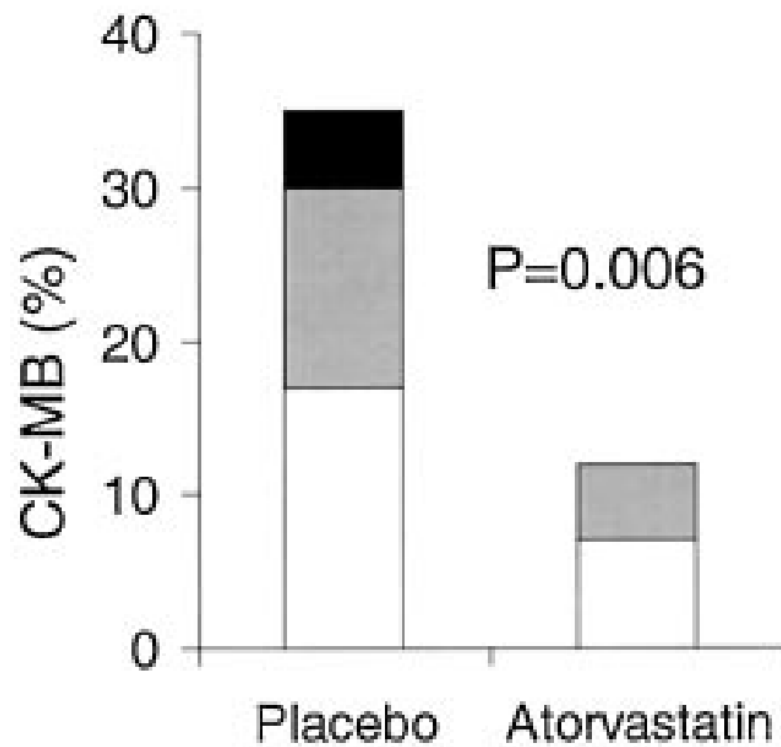
Statin administration before percutaneous coronary intervention: impact on periprocedural myocardial infarction

Carlo Briguori^{a,b,*}, Antonio Colombo^b, Flavio Airoldi^b, Anna Violante^a, Amelia Focaccio^a, Pasquale Balestrieri^a, Pietro Paolo Elia^a, Bruno Golia^a, Stefano Lepore^a, Guido Riviezzo^a, Pierfranco Scarpato^a, Mariateresa Librera^a, Erminio Bonizzoni^c, Bruno Ricciardelli^a

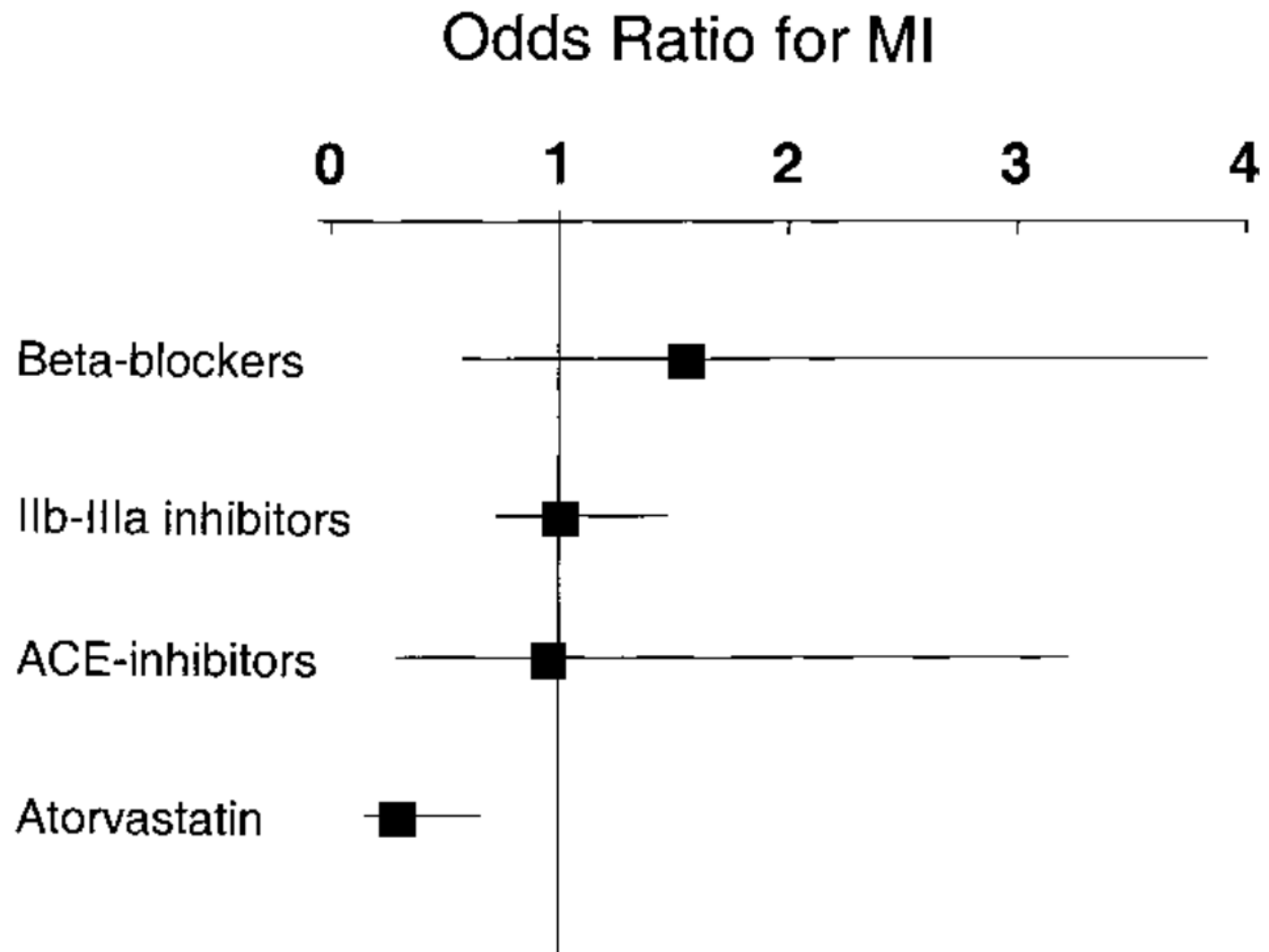


Randomized Trial of Atorvastatin for Reduction of Myocardial Damage During Coronary Intervention : Results From the ARMYDA (Atorvastatin for Reduction of MYocardial Damage during Angioplasty) Study

Vincenzo Pasceri, Giuseppe Patti, Annunziata Nusca, Christian Pristipino, Giuseppe Richichi
and Germano Di Sciascio



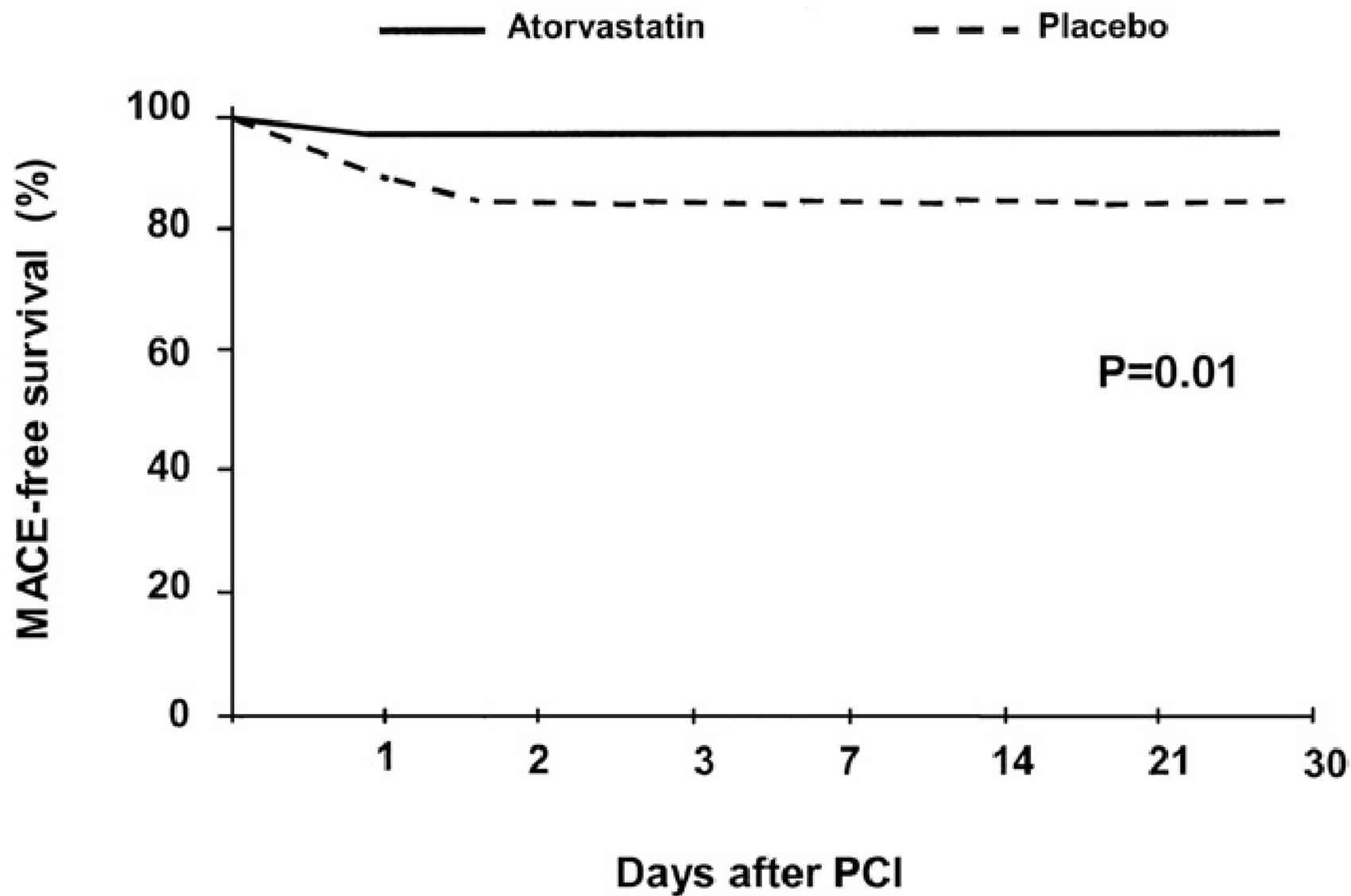
□ > 1 time ▒ 2-5 times ■ >5 times ULN

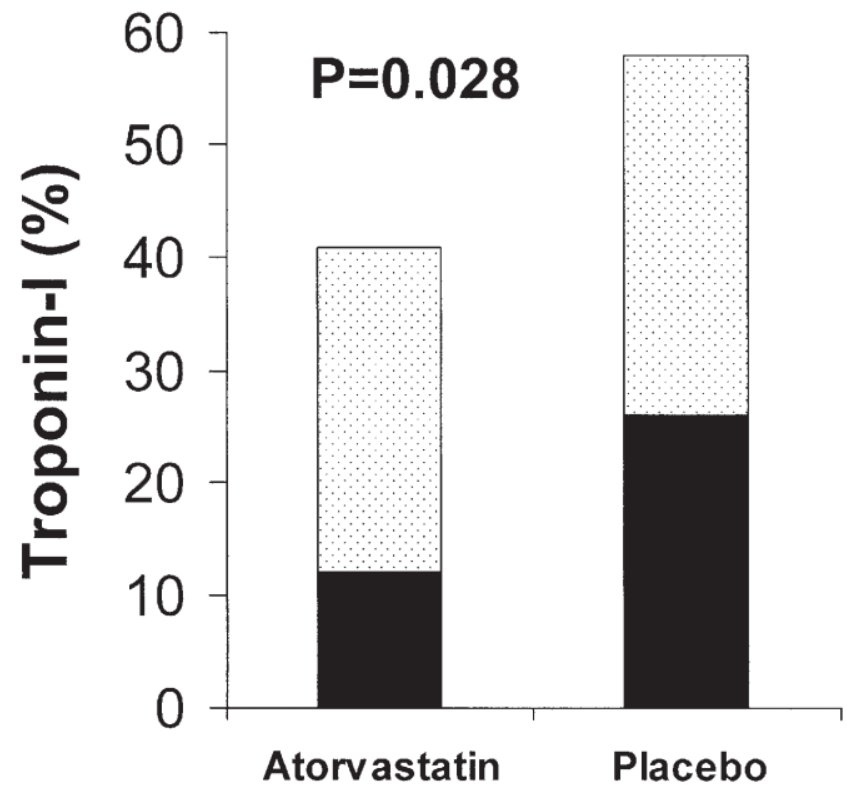
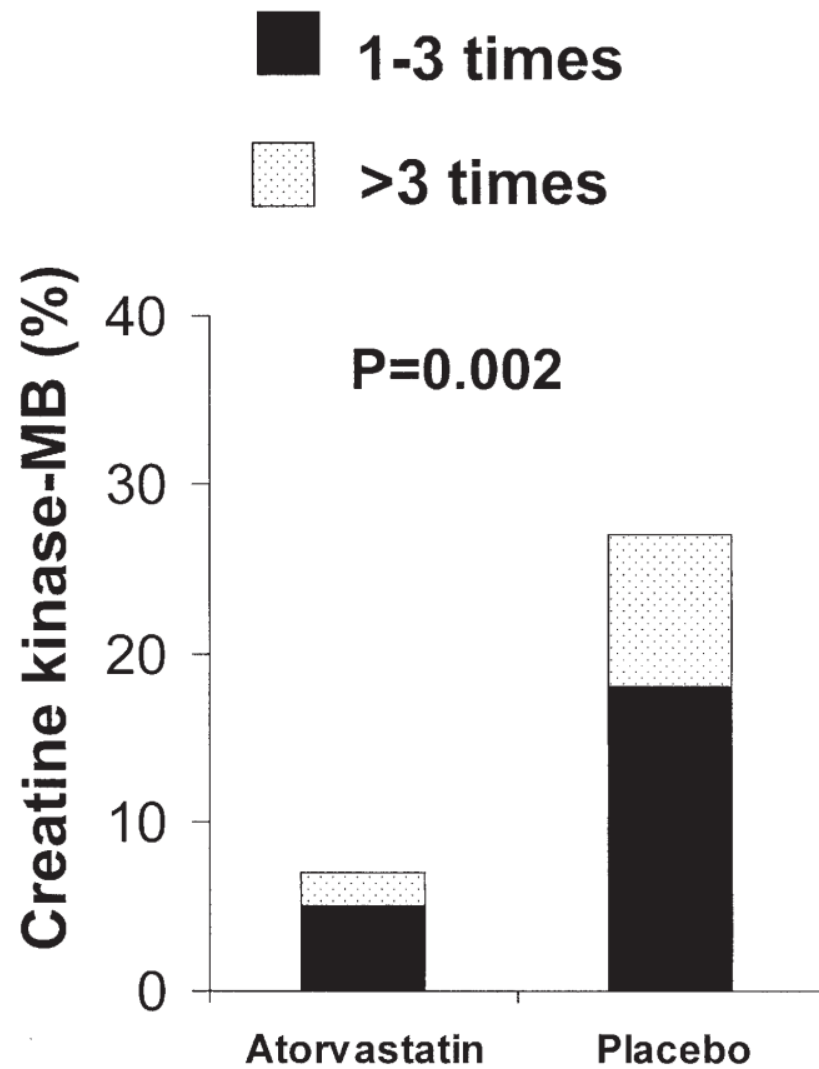


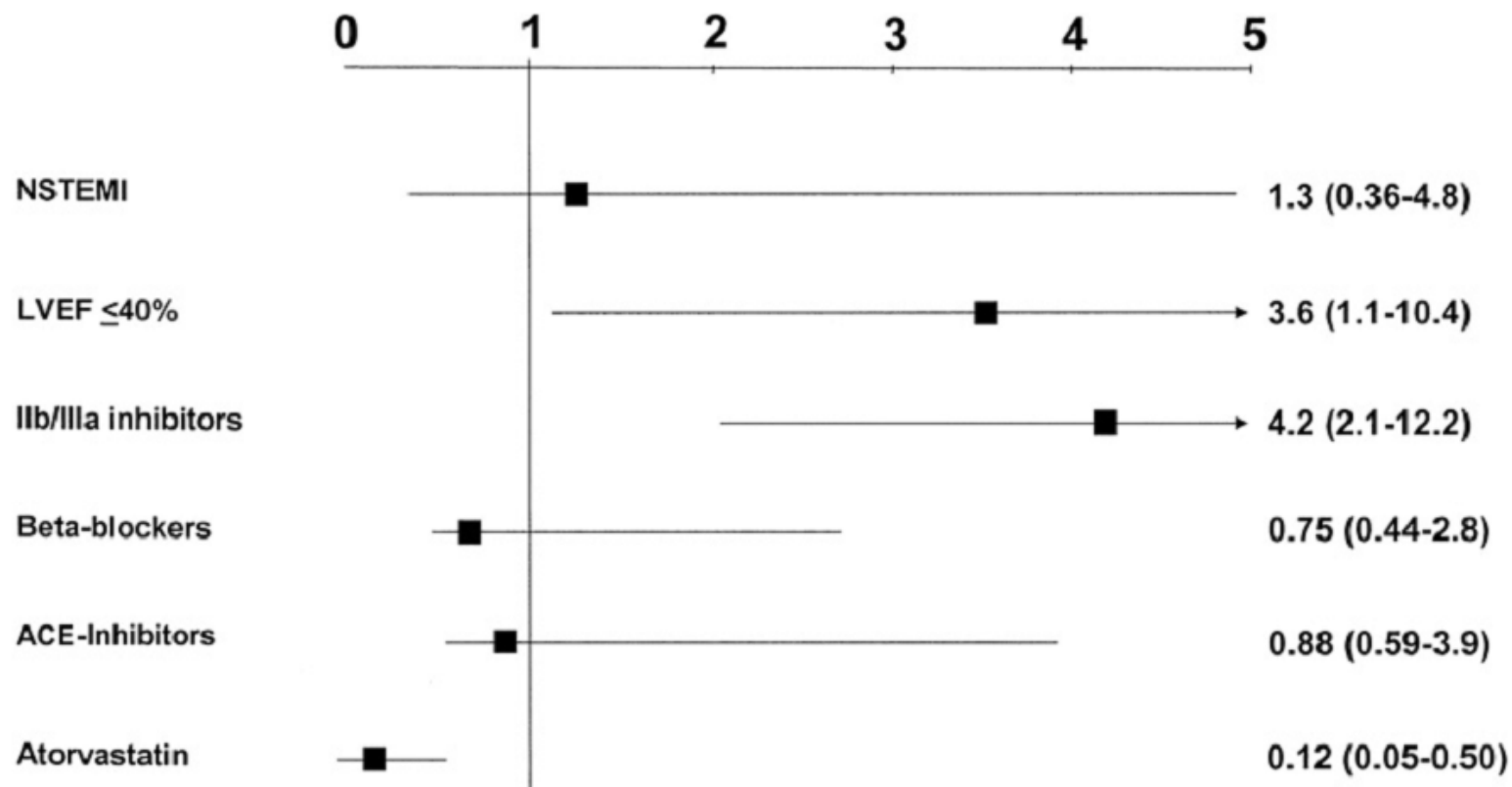
Atorvastatin Pretreatment Improves Outcomes in Patients With Acute Coronary Syndromes Undergoing Early Percutaneous Coronary Intervention

Results of the ARMYDA-ACS Randomized Trial

Giuseppe Patti, MD, FACC,* Vincenzo Pasceri, MD, PhD, FACC,† Giuseppe Colonna, MD,‡
Marco Miglionico, MD,* Dionigi Fischetti, MD,‡ Gennaro Sardella, MD, FACC,§
Antonio Montinaro, MD,‡ Germano Di Sciascio, MD, FACC, FESC*







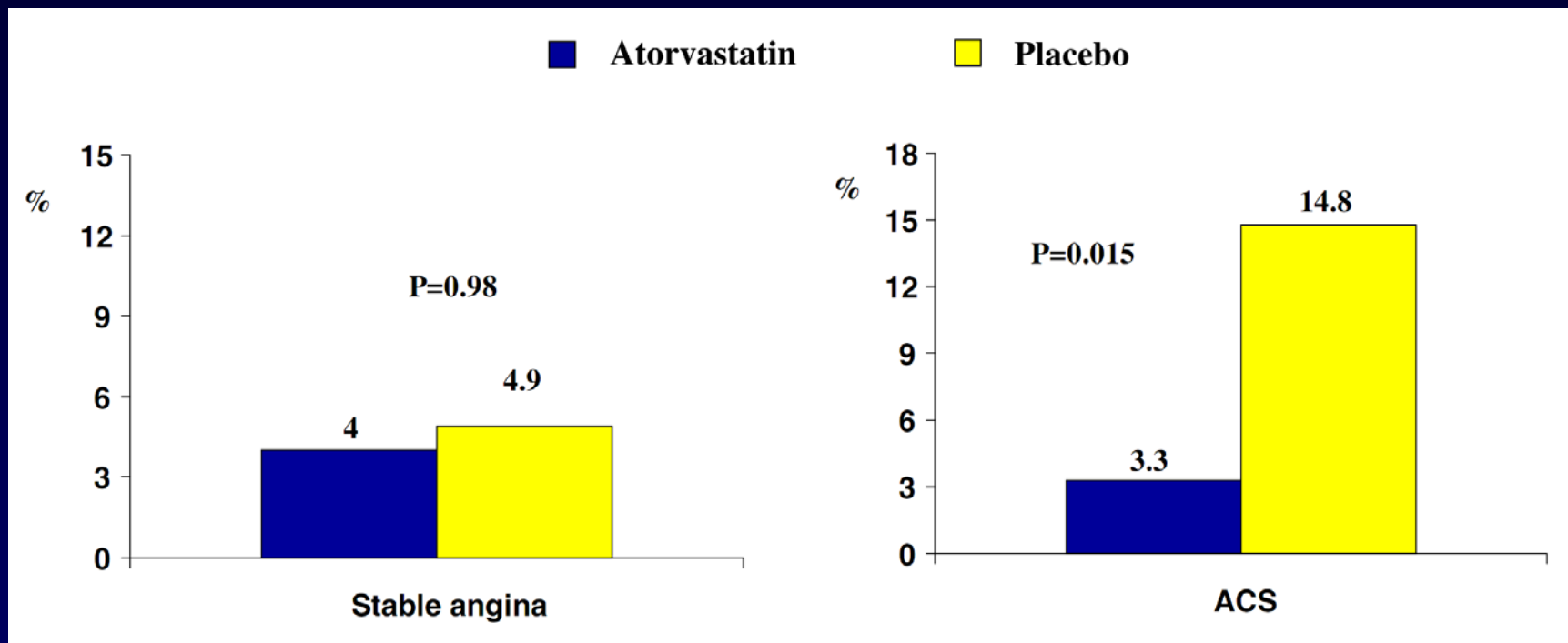
EXPEDITED PUBLICATIONS

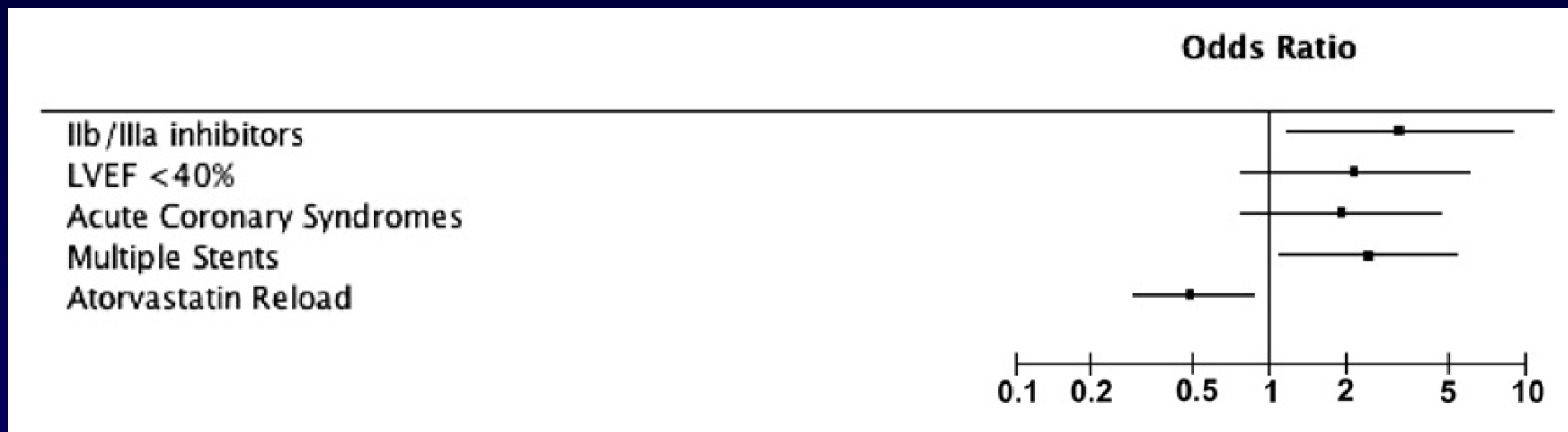
Efficacy of Atorvastatin Reload in Patients on Chronic Statin Therapy Undergoing Percutaneous Coronary Intervention

Results of the ARMYDA-RECAPTURE (Atorvastatin for
Reduction of Myocardial Damage During Angioplasty) Randomized Trial

Germano Di Sciascio, MD,* Giuseppe Patti, MD,* Vincenzo Pasceri, MD,†
Achille Gaspardone, MD,‡ Giuseppe Colonna, MD,§ Antonio Montinaro, MD§

Rome and Lecce, Italy

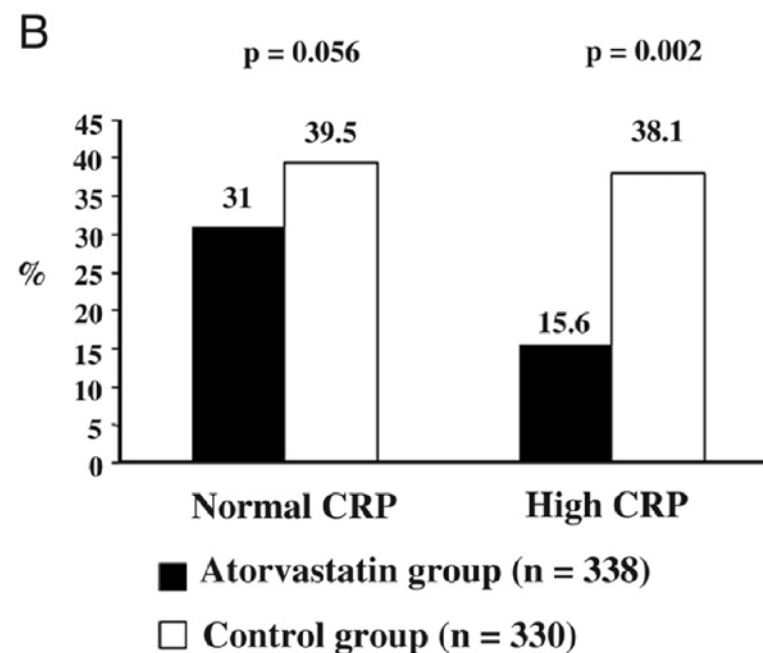
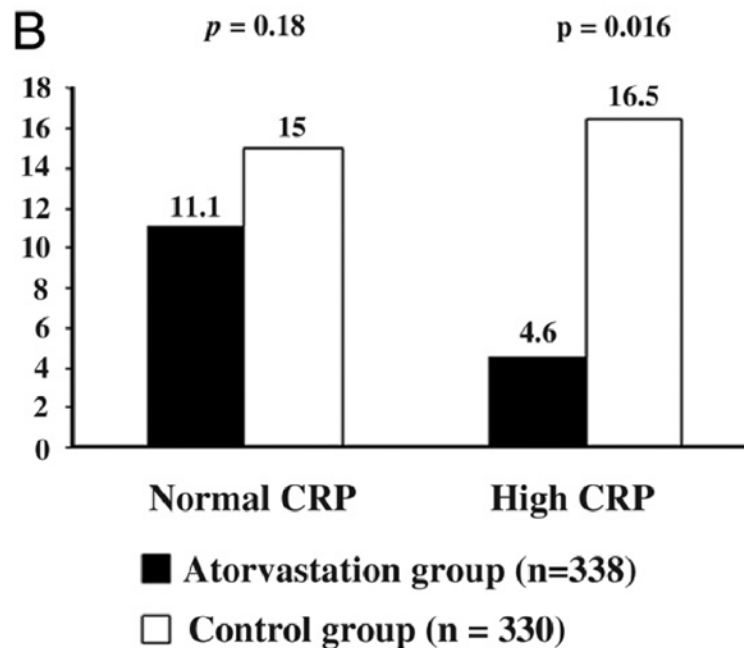
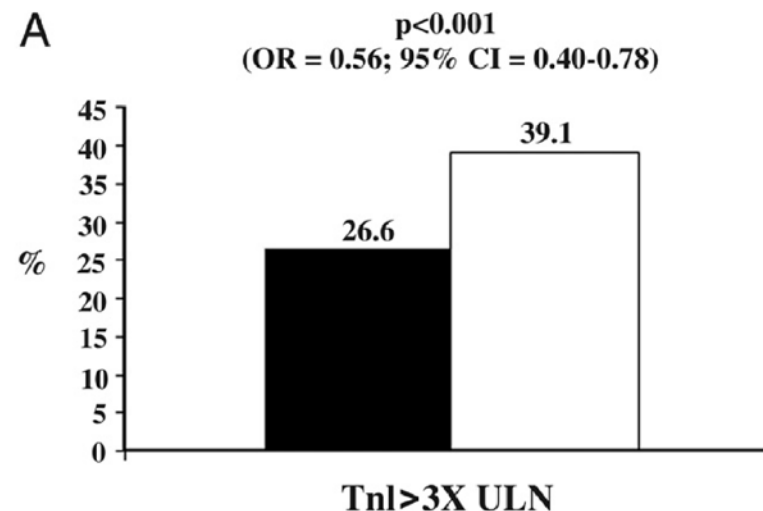
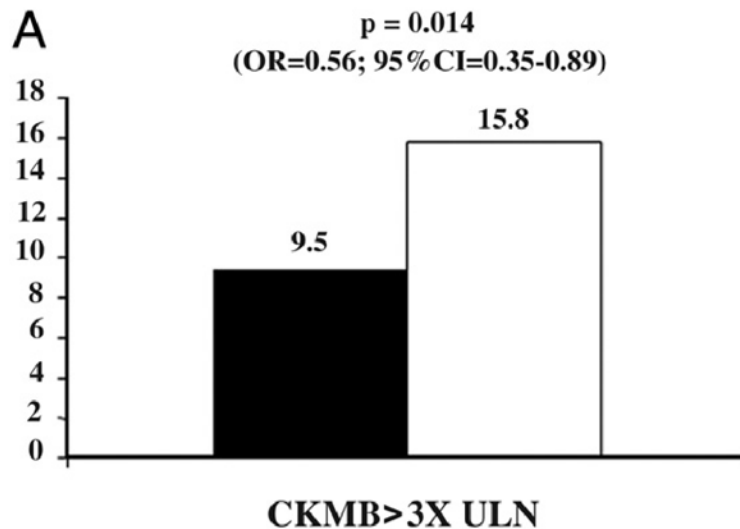




Novel Approaches for Preventing or Limiting Events (Naples) II Trial

Impact of a Single High Loading Dose
of Atorvastatin on Periprocedural Myocardial Infarction

Carlo Briguori, MD, PhD,*† Gabriella Visconti, MD,* Amelia Focaccio, MD,* Bruno Golia, MD,*
Alaide Chieffo, MD,† Alfredo Castelli, MD,† Marco Mussardo, MD,† Matteo Montorfano, MD,†
Bruno Ricciardelli, MD,* Antonio Colombo, MD†

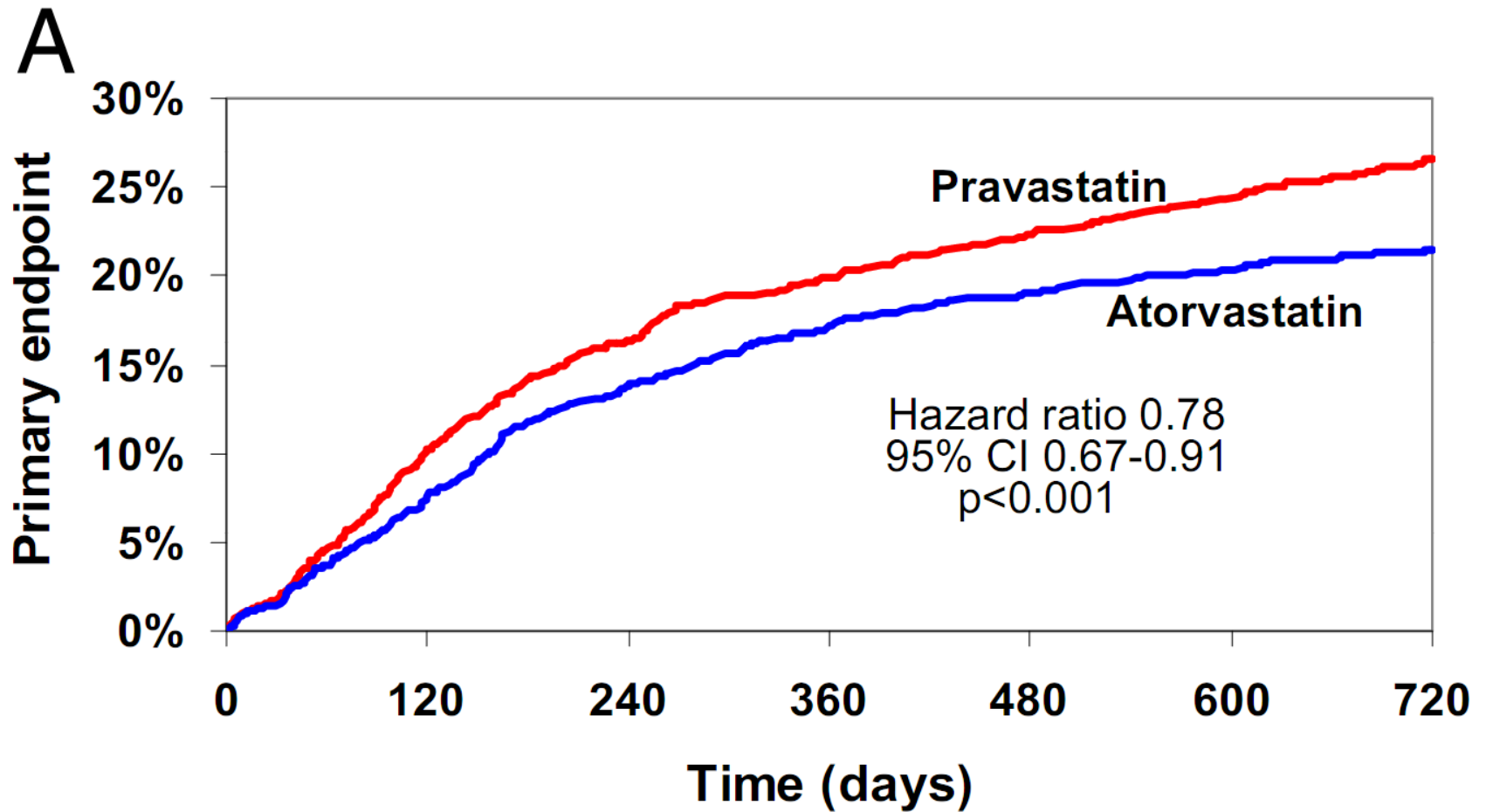


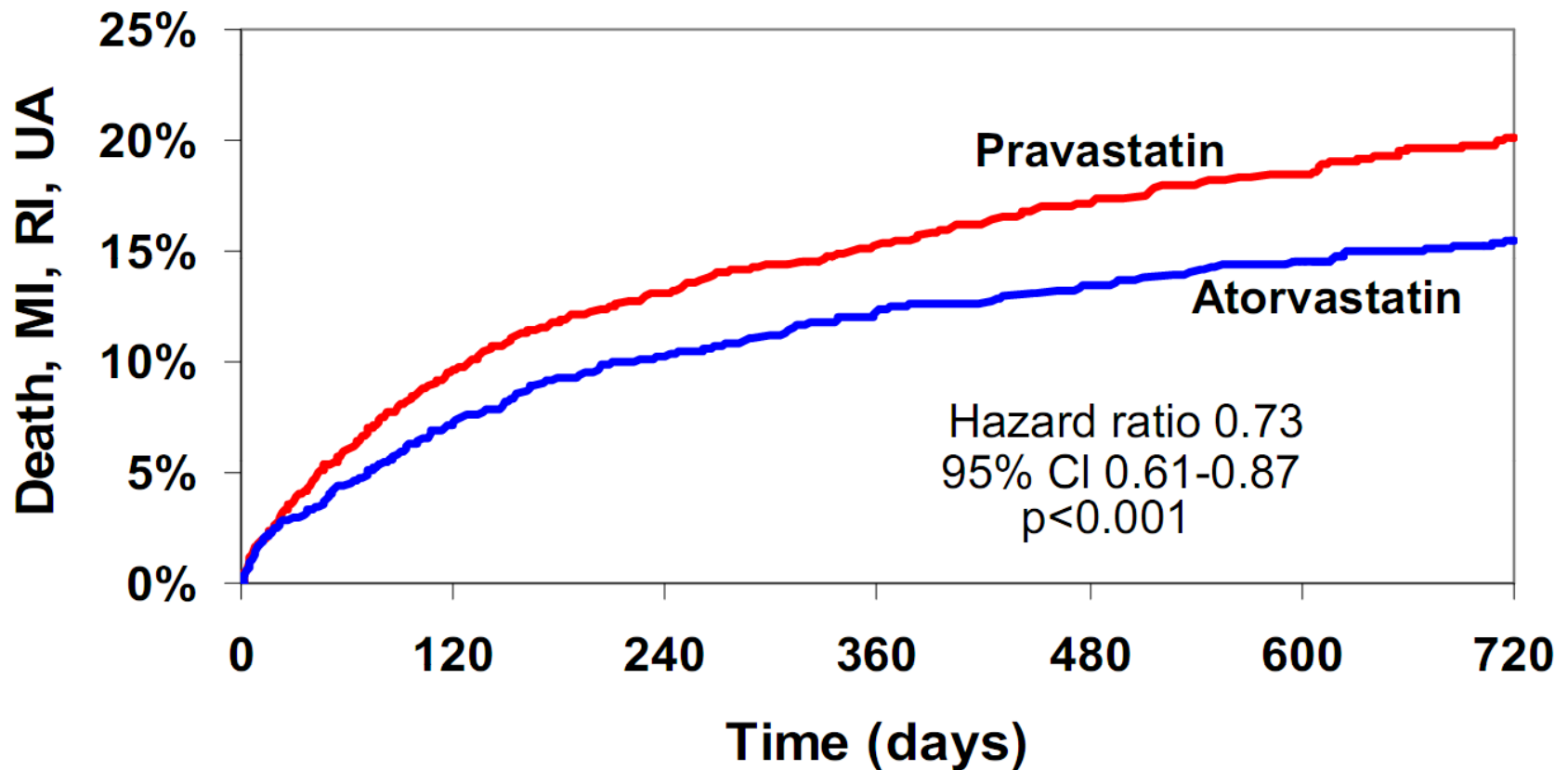
Effect of Intensive Statin Therapy on Clinical Outcomes Among Patients Undergoing Percutaneous Coronary Intervention for Acute Coronary Syndrome

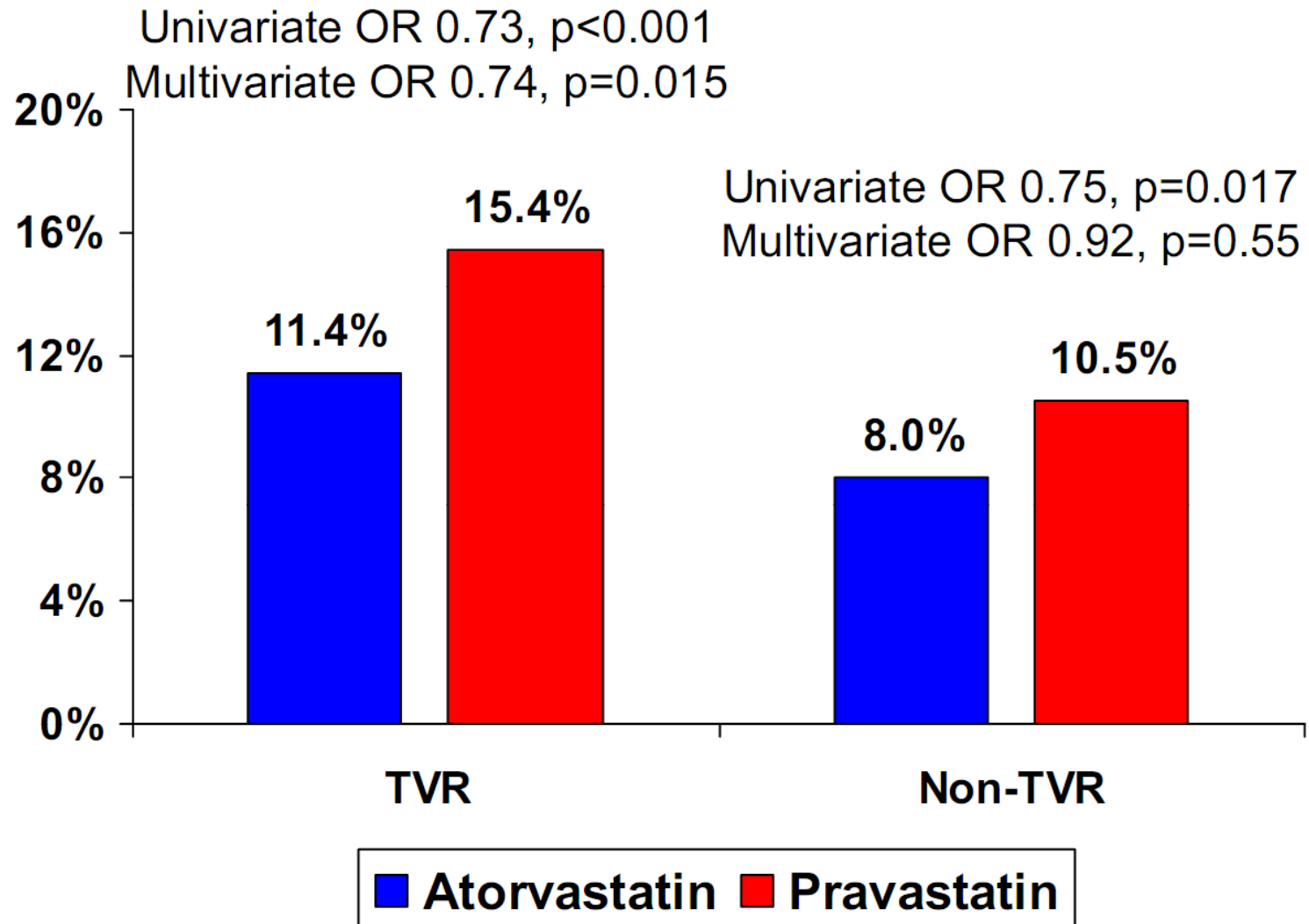
PCI-PROVE IT: A PROVE IT–TIMI 22
(Pravastatin or Atorvastatin Evaluation and Infection Therapy–
Thrombolysis In Myocardial Infarction 22) Substudy

C. Michael Gibson, MS, MD,* Yuri B. Pride, MD,* Claudia P. Hochberg, MD,*
Sarah Sloan, MA, MS,† Marc S. Sabatine, MD, MPH,† Christopher P. Cannon, MD,†
for the TIMI Study Group

Boston, Massachusetts



B





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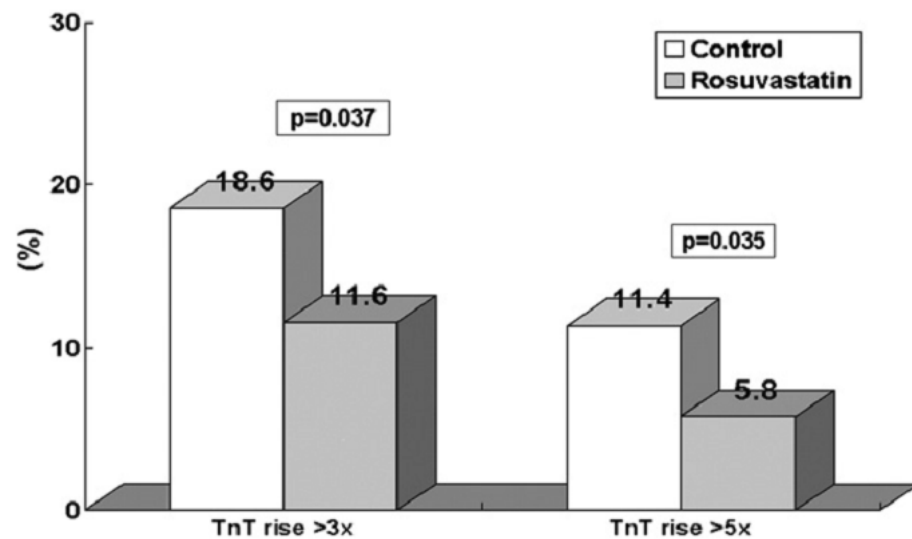
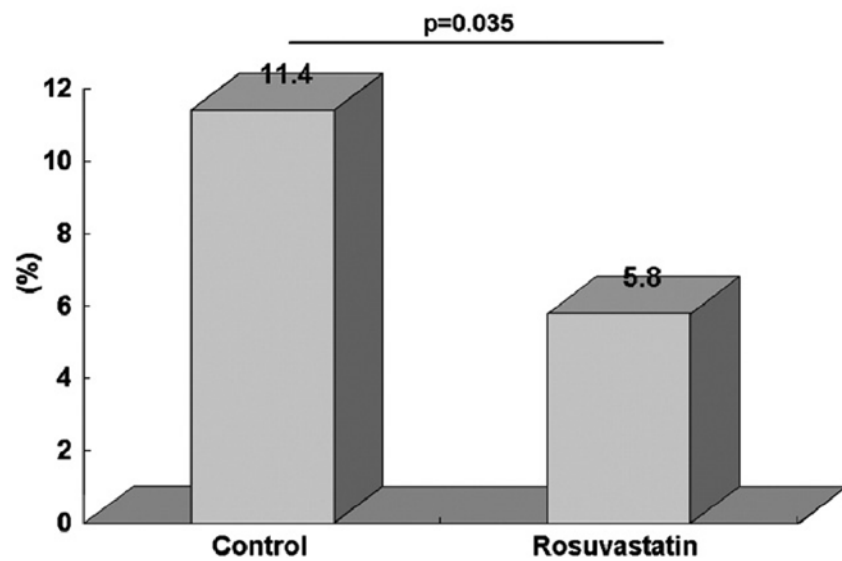
International Journal of Cardiology 137 (2009) 246–251

International Journal of
Cardiology

www.elsevier.com/locate/ijcard

The beneficial effect of high loading dose of rosuvastatin before percutaneous coronary intervention in patients with acute coronary syndrome ☆

Kyeong Ho Yun^a, Myung Ho Jeong^{b,*}, Seok Kyu Oh^a, Sang Jae Rhee^a, Eun Mi Park^a,
Eun Mi Lee^a, Nam Jin Yoo^a, Nam-Ho Kim^a, Young Keun Ahn^b, Jin-Won Jeong^a



QUARTERLY FOCUS ISSUE: PREVENTION/OUTCOMES

Cardiac Intervention and Surgery

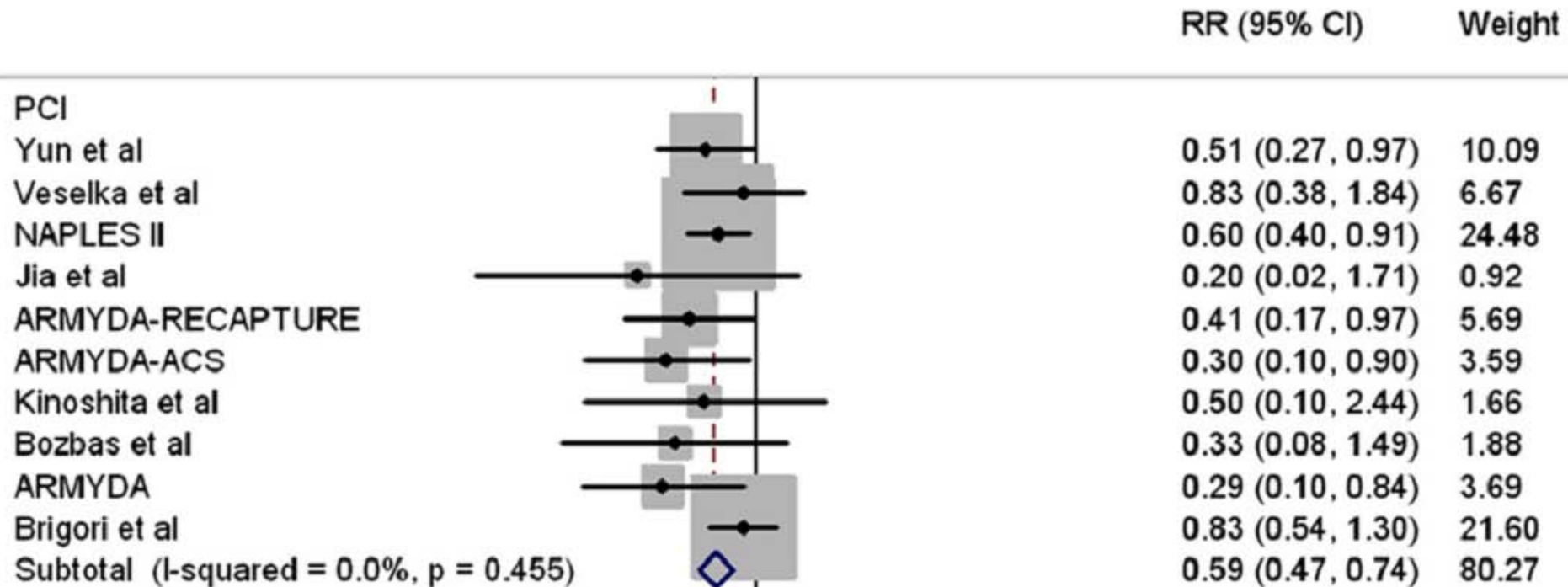
Evidence of Pre-Procedural Statin Therapy

A Meta-Analysis of Randomized Trials

David E. Winchester, MD,* Xuerong Wen, MPH,† Lola Xie, BS,‡ Anthony A. Bavry, MD, MPH*

Gainesville, Florida

Risk Ratios for Post-Procedural Myocardial Infarction



Overall (I-squared = 0.0%, p = 0.734)

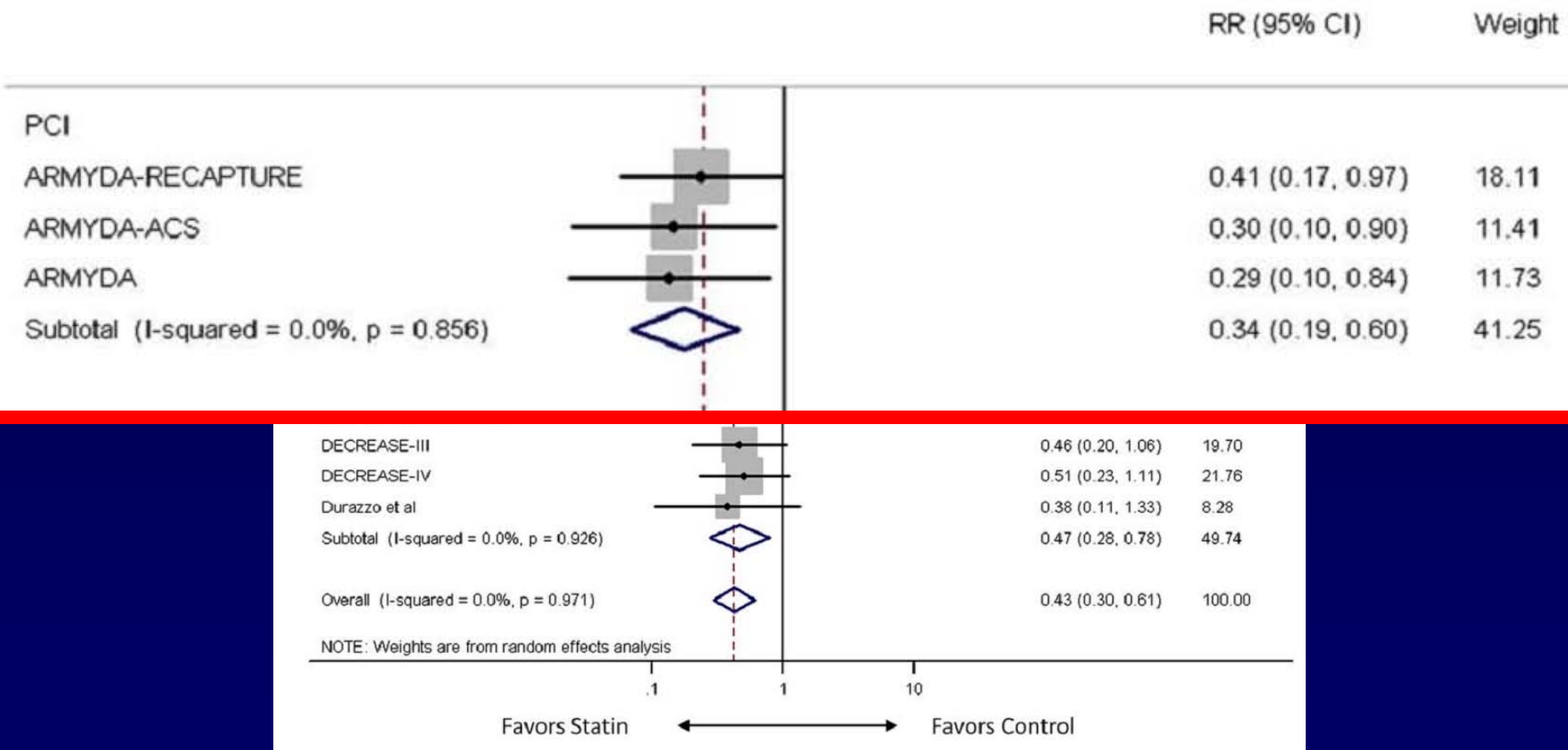
0.57 (0.46, 0.70) 100.00

NOTE: Weights are from random effects analysis

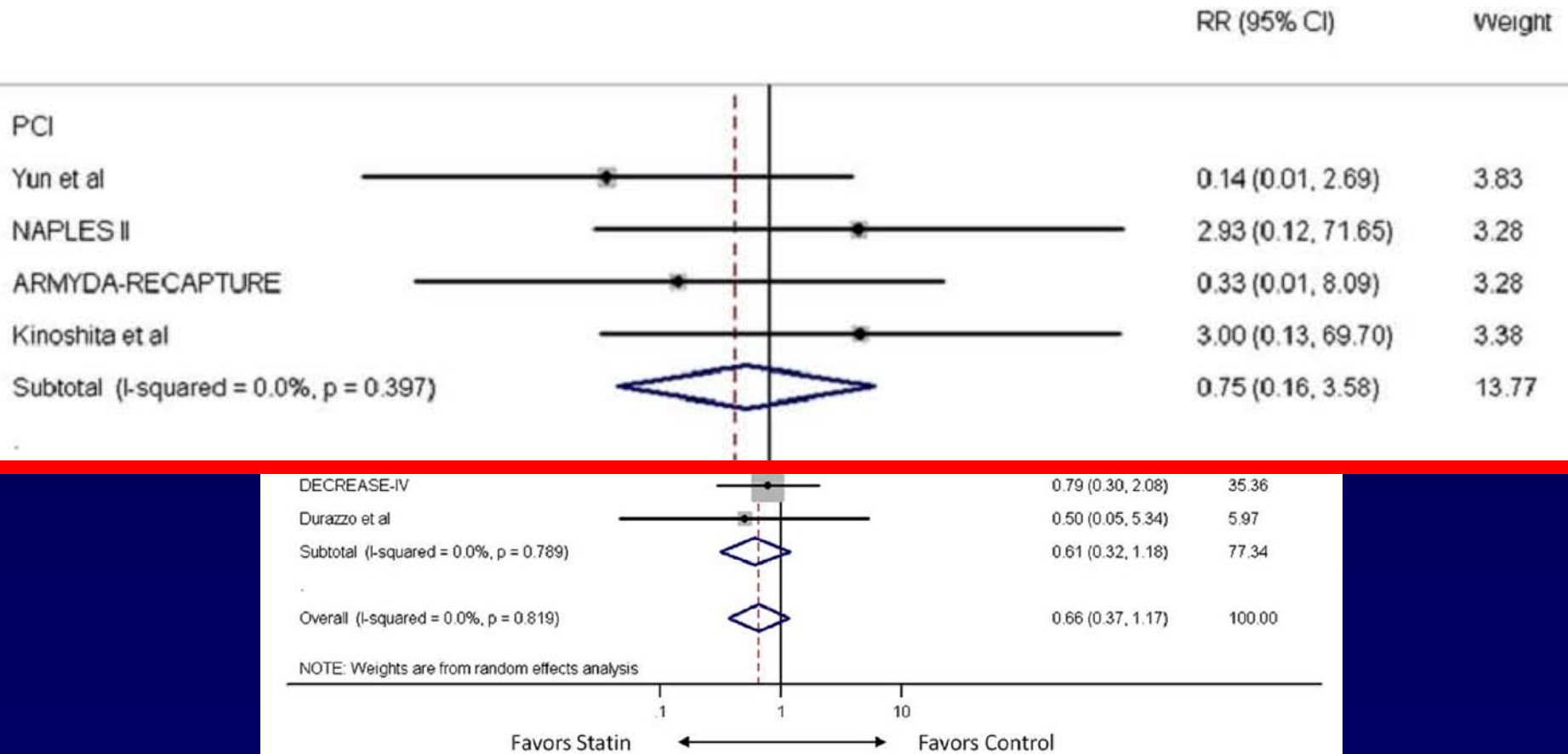
Favors Statin

Favors Control

Risk Ratios for Post-Procedural Myocardial Infarction in Placebo-Controlled Trials



Risk Ratios for Short-Term All-Cause Mortality



Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

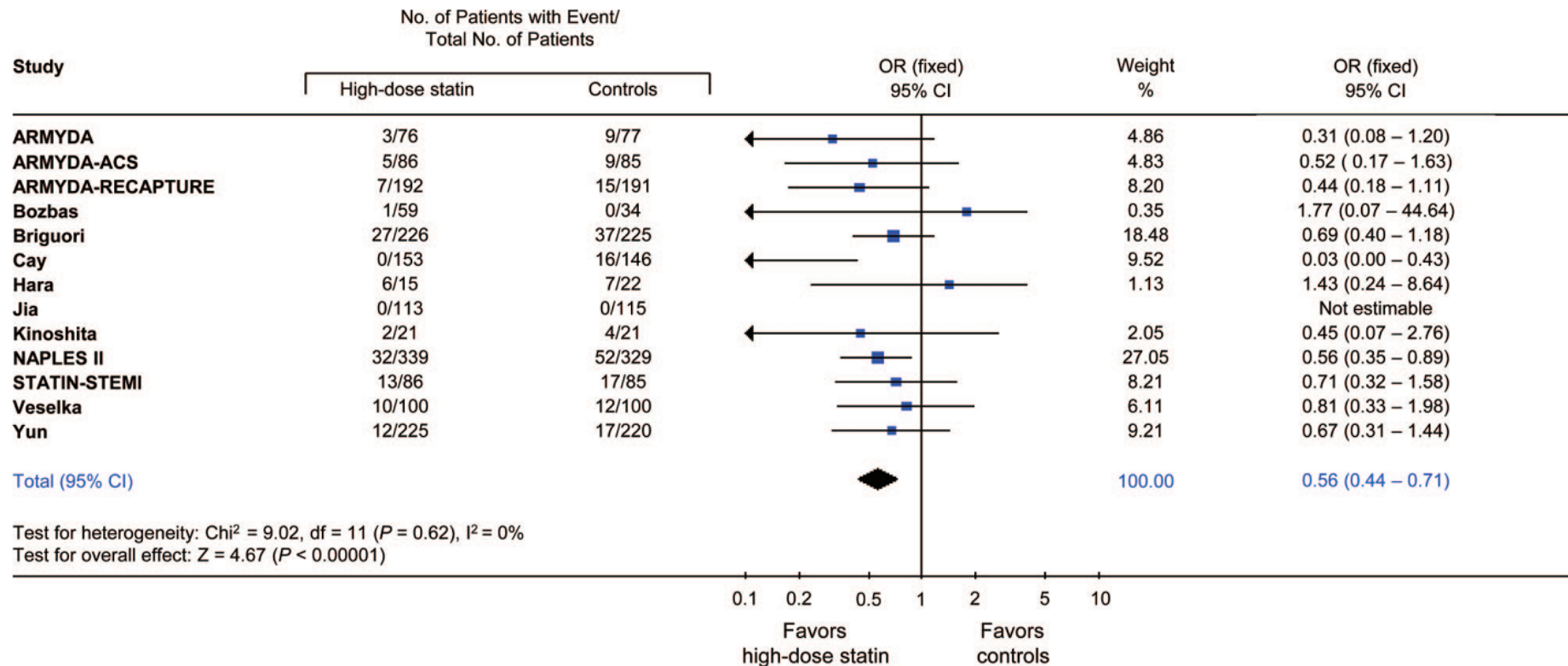


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Association®

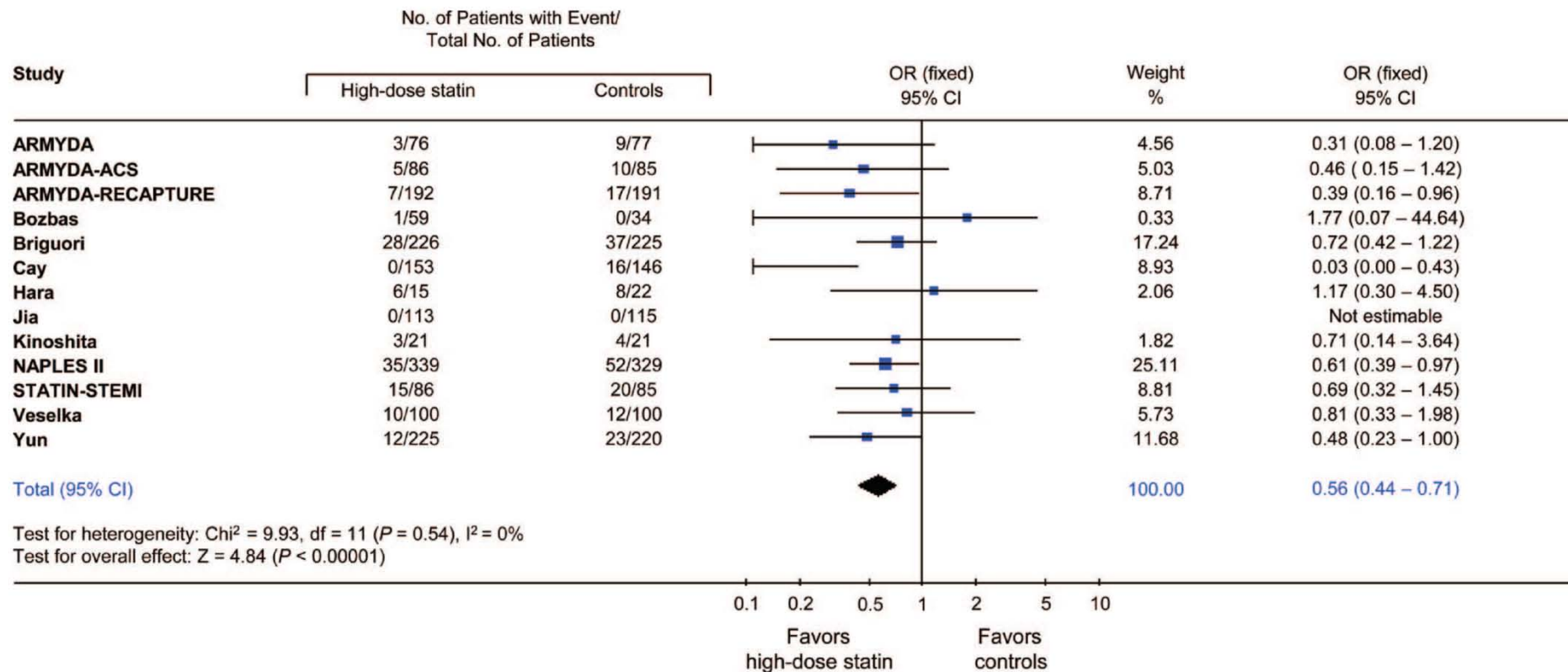
Clinical Benefit of Statin Pretreatment in Patients Undergoing Percutaneous Coronary Intervention : A Collaborative Patient-Level Meta-Analysis of 13 Randomized Studies

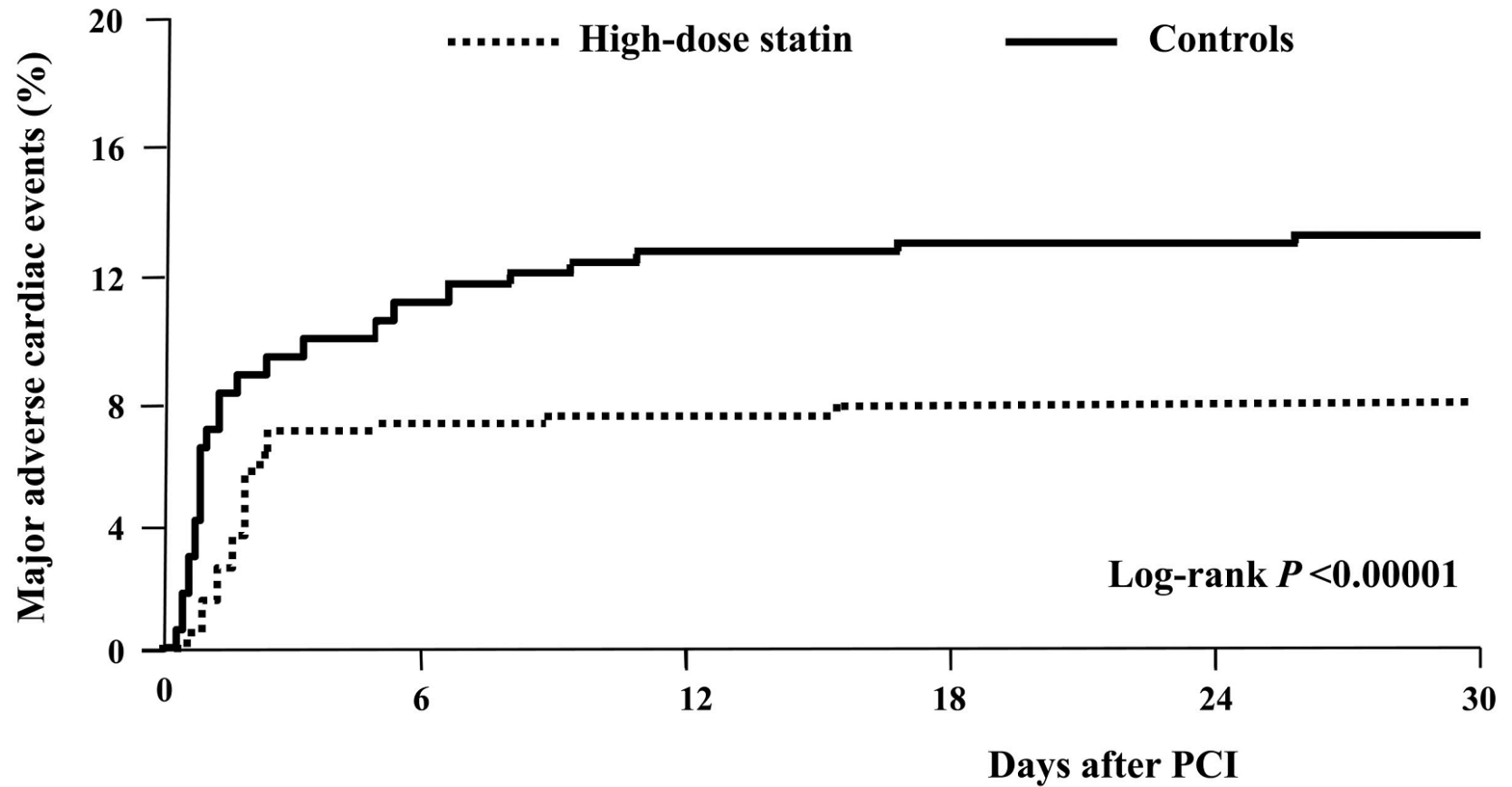
Giuseppe Patti, Christopher P. Cannon, Sabina A. Murphy, Simona Mega, Vincenzo Pasceri, Carlo Briguori, Antonio Colombo, Kyeong Ho Yun, Myung Ho Jeong, Jung-Sun Kim, Donghoon Choi, Huseyin Bozbas, Masayoshi Kinoshita, Keiichi Fukuda, Xin-Wei Jia, Hidehiko Hara, Serkan Cay and Germano Di Sciascio

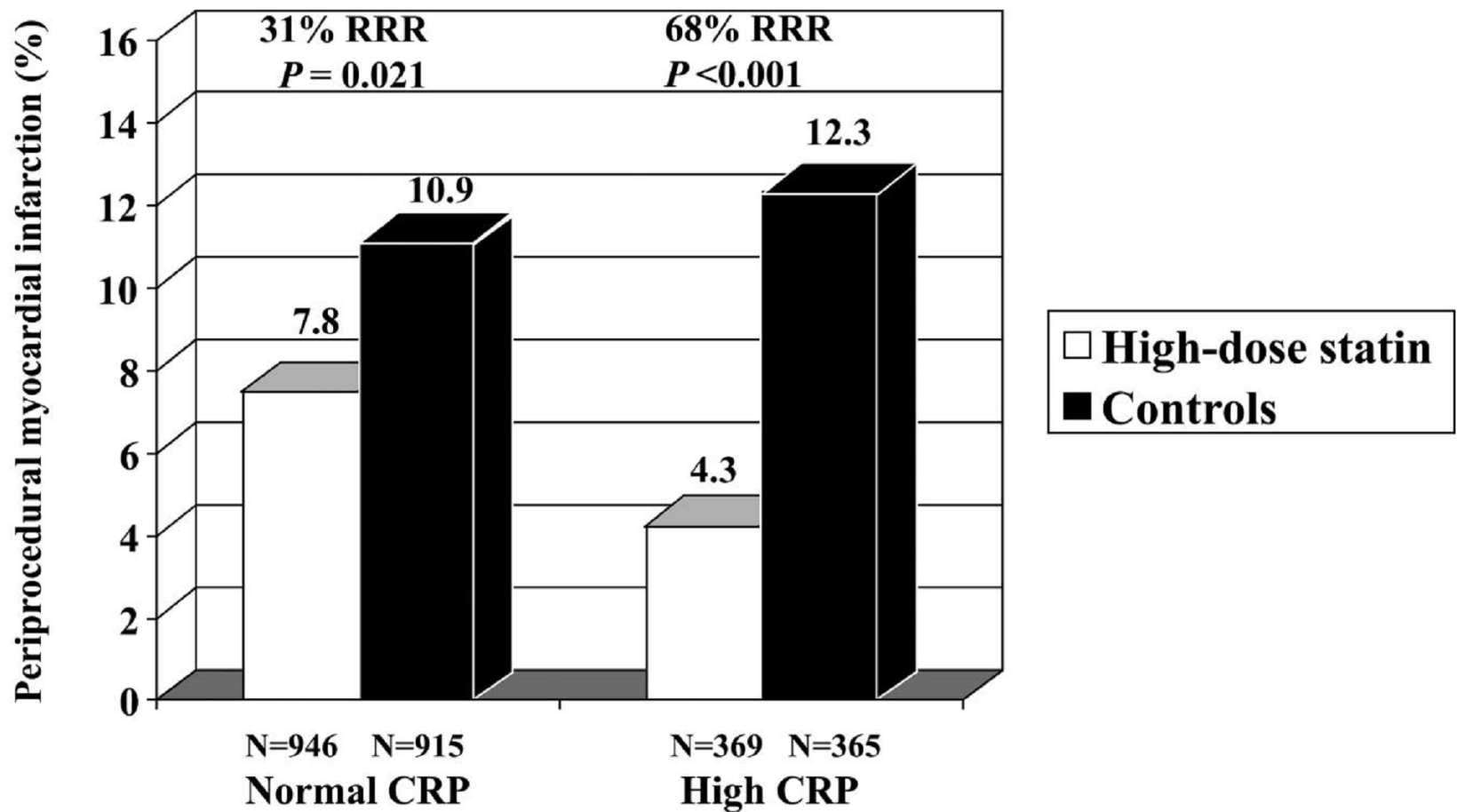
Odds Ratios of Periprocedural Myocardial Infarction in Patients Receiving High-Dose Statin Pretreatment Vs Controls



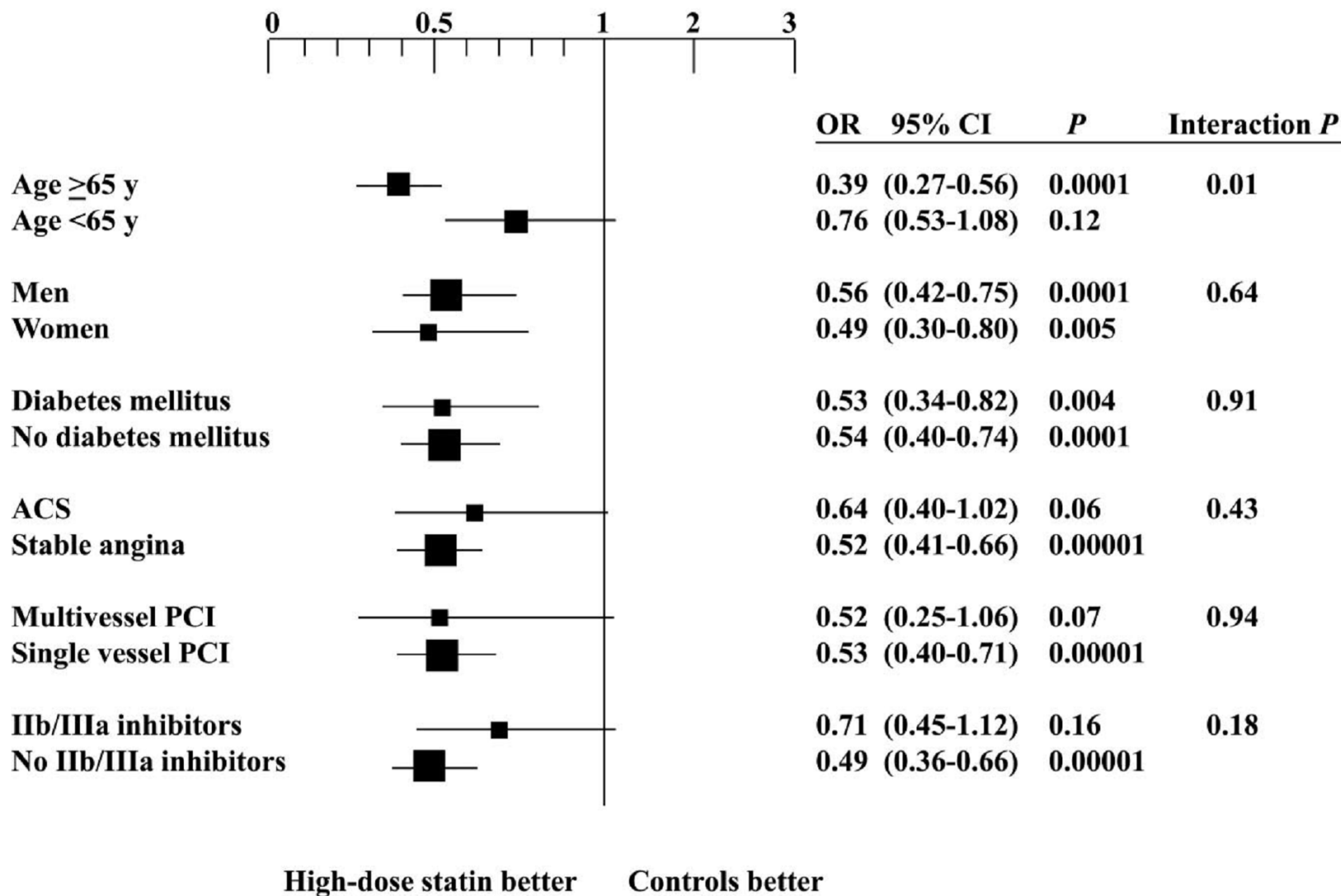
Odds Ratios of Major Adverse Cardiac Events at 30 Days in Patients Receiving High-Dose Statin Pretreatment Vs Controls







Odds ratio for periprocedural myocardial infarction



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PRACTICE GUIDELINE

2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention

A Report of the American College of Cardiology Foundation/American Heart Association
Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions

Table 4. Summary of Recommendations for Preprocedural Considerations and Interventions in Patients Undergoing PCI

Recommendations	COR	LOE	References
Contrast-induced AKI			
Patients should be assessed for risk of contrast-induced AKI before PCI.	I	C	(270,271)
Patients undergoing cardiac catheterization with contrast media should receive adequate preparatory hydration.	I	B	(272-275)
In patients with CKD (creatinine clearance <60 mL/min), the volume of contrast media should be minimized.	I	B	(276-278)
Administration of N-acetyl-L-cysteine is not useful for the prevention of contrast-induced AKI.	III: No Benefit	A	(279-283)
Anaphylactoid reactions			
Patients with prior evidence of an anaphylactoid reaction to contrast media should	I	B	(252,284-286)

Statins

Administration of a high-dose statin is reasonable before PCI to reduce the risk of periprocedural MI.

Bleeding risk			
All patients should be evaluated for risk of bleeding before PCI.	I	C	N/A
CKD			
In patients undergoing PCI, the glomerular filtration rate should be estimated and the dosage of renally cleared medications should be adjusted.	I	B	(298-300)
Aspirin			
Patients already on daily aspirin therapy should take 81 mg to 325 mg before PCI.	I	B	(301-304)
Patients not on aspirin therapy should be given nonenteric aspirin 325 mg before PCI.	I	B	(301,303,304)

4.6. Statin Treatment: Recommendation

CLASS IIa

1. Administration of a high-dose statin is reasonable before PCI to reduce the risk of periprocedural MI. (*Level of Evidence: A for statin-naïve patients [290–296]; Level of Evidence: B for those on chronic statin therapy [297]*)

Conclusiones

1. Cost-effectiveness analysis of the initiation of statin therapy before PCI would likely be very favorable
2. There was no risk excess associated with high-dose loading with statins before the procedure
3. The cost of a few doses of statin is negligible
4. The consistency across the trials and the strength of the effect observed suggest that a strategy of high-dose statin pretreatment should be used routinely in patients undergoing PCI, irrespective of clinical presentation and chronic statin therapy



*"Los analfabetos del siglo
XXI, no serán aquellos
que no sepan leer y
escribir, sino más bien
aquellos que no puedan
aprender, desaprender lo
aprendido y volver a
aprender"*

Toffler A. (1928-)

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XXXIX Congreso
Argentino de Cardiología

Buenos Aires, Argentina



Muchas Gracias

Potential Mechanisms Underlying Early Benefits of Statins Therapy in Pre-PCI

- Anti-inflammation Effect
- Repair and Improvement Endothelial Function
- Anti-platelet Aggregation
- Decrease of Oxidative Stress
- Inhibition of Thrombogenic Responses
- Keep the Plaque Stable

*2011 ACCF/AHA/ SCAI guideline for percutaneous coronary intervention
J Am Col Cardiol 2011;58:e44–122
Lou J. J Interven Cardiol 2012;25:156–162*

Effect of Intensive Statin Therapy on Clinical Outcomes Among Patients Undergoing Percutaneous Coronary Intervention for ACS

- Among patients with ACS who undergo PCI, intensive statin therapy reduces MACE compared with moderate-dose statin therapy.
- The reduction in the incidence of TVR was independent of low-density lipoprotein cholesterol and C-reactive protein lowering and may therefore be due, at least in part, to a pleiotropic effect of high-dose statin therapy

Evidence of Pre-Procedural Statin Therapy

A Meta-Analysis of Randomized Trials

- Statin therapy initiated before invasive procedures reduces post-procedural MI, after both PCI and noncardiac surgical procedures
- Pre-procedural statin therapy should become an increasingly important strategy to improve the safety of invasive procedures

