Enhancing CV outcomes

: Secondary Prevention Strategies based on TNT & PROVE-IT

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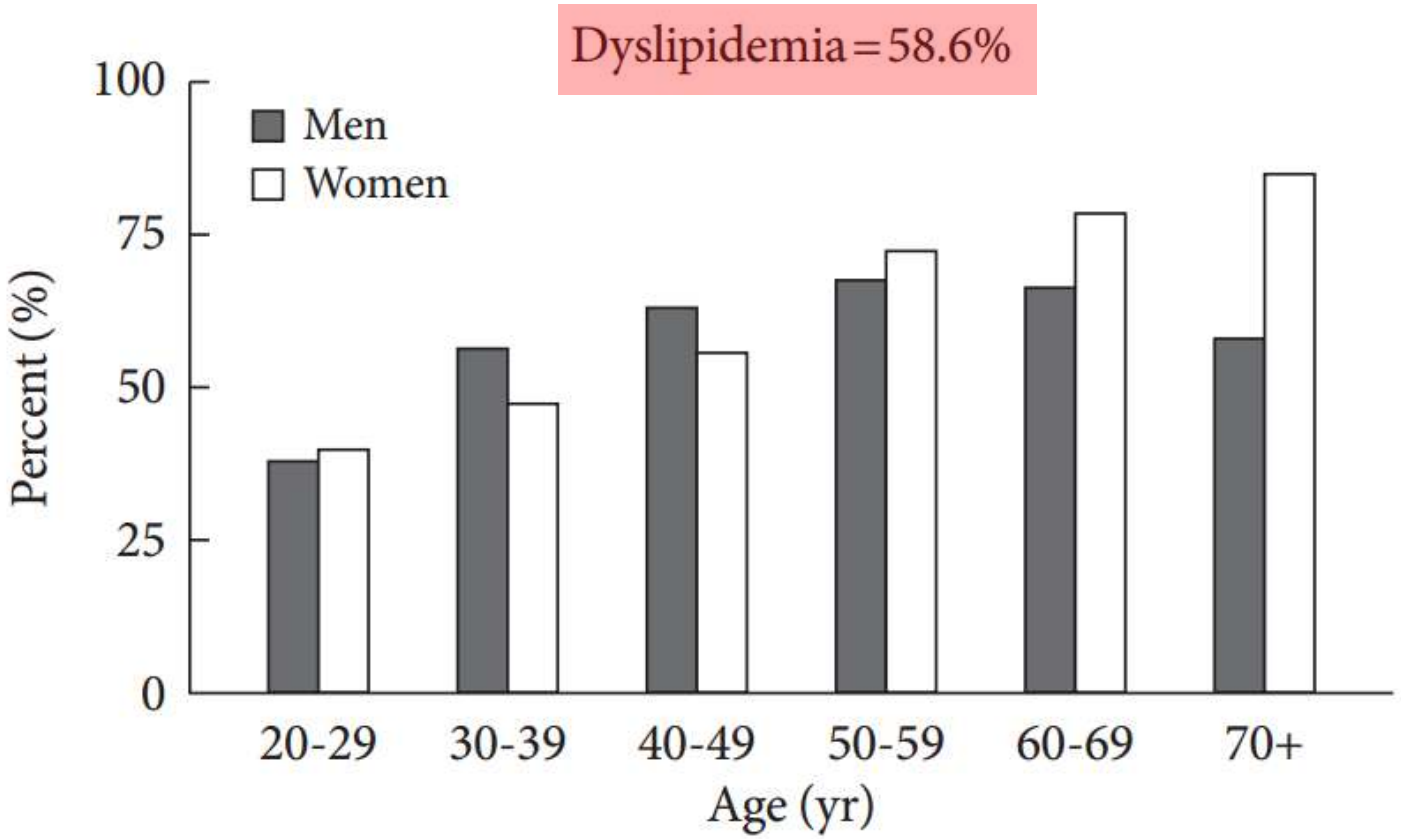
Prevalence of Dyslipidemia in Korea

< Prevalence of dyslipidemia : KNHNES 1998-2010>

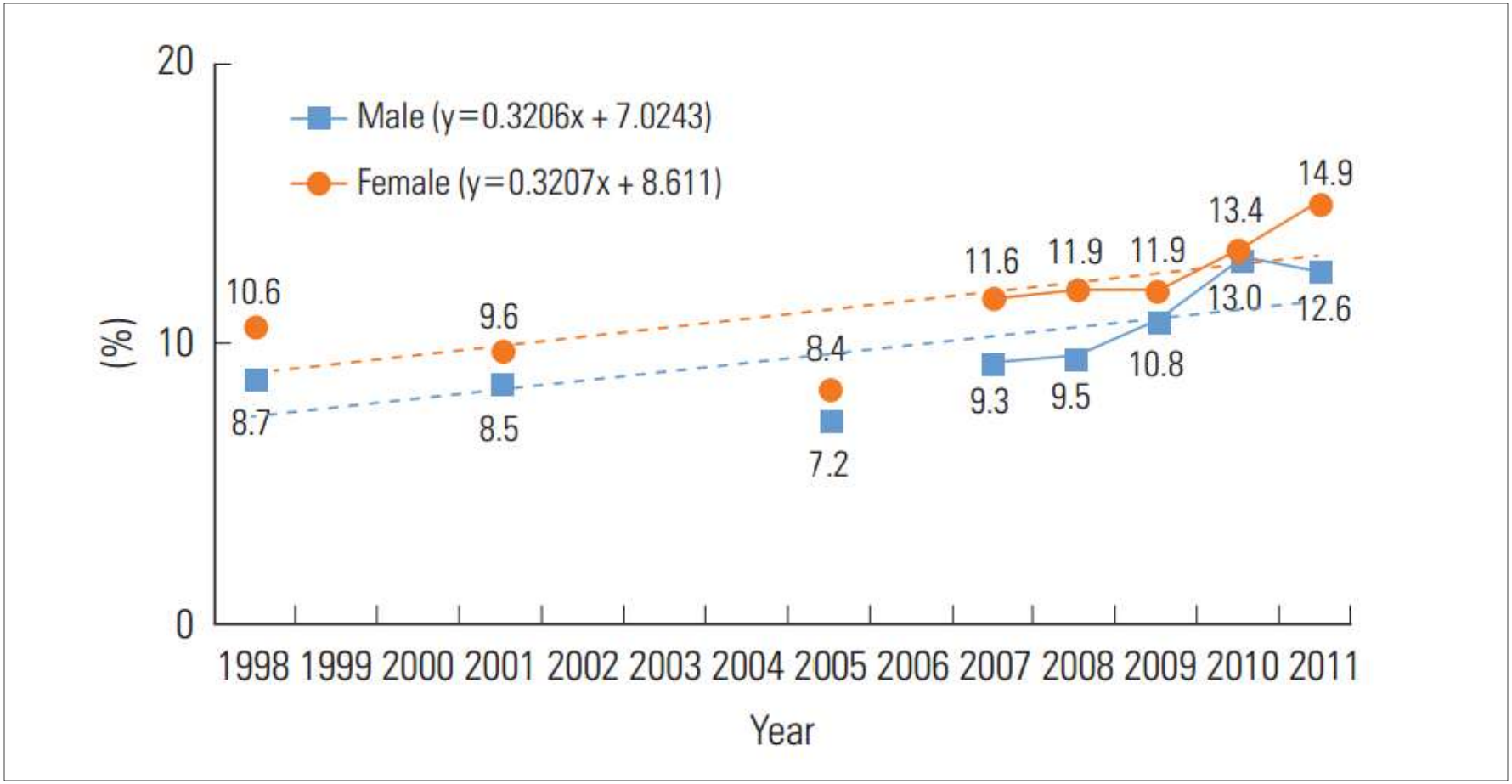


* KNHNES, Korea National Health and Nutrition Examination

Ref. Roh E, et al. Diabetes Metab J. 2013;37(6):433-49.

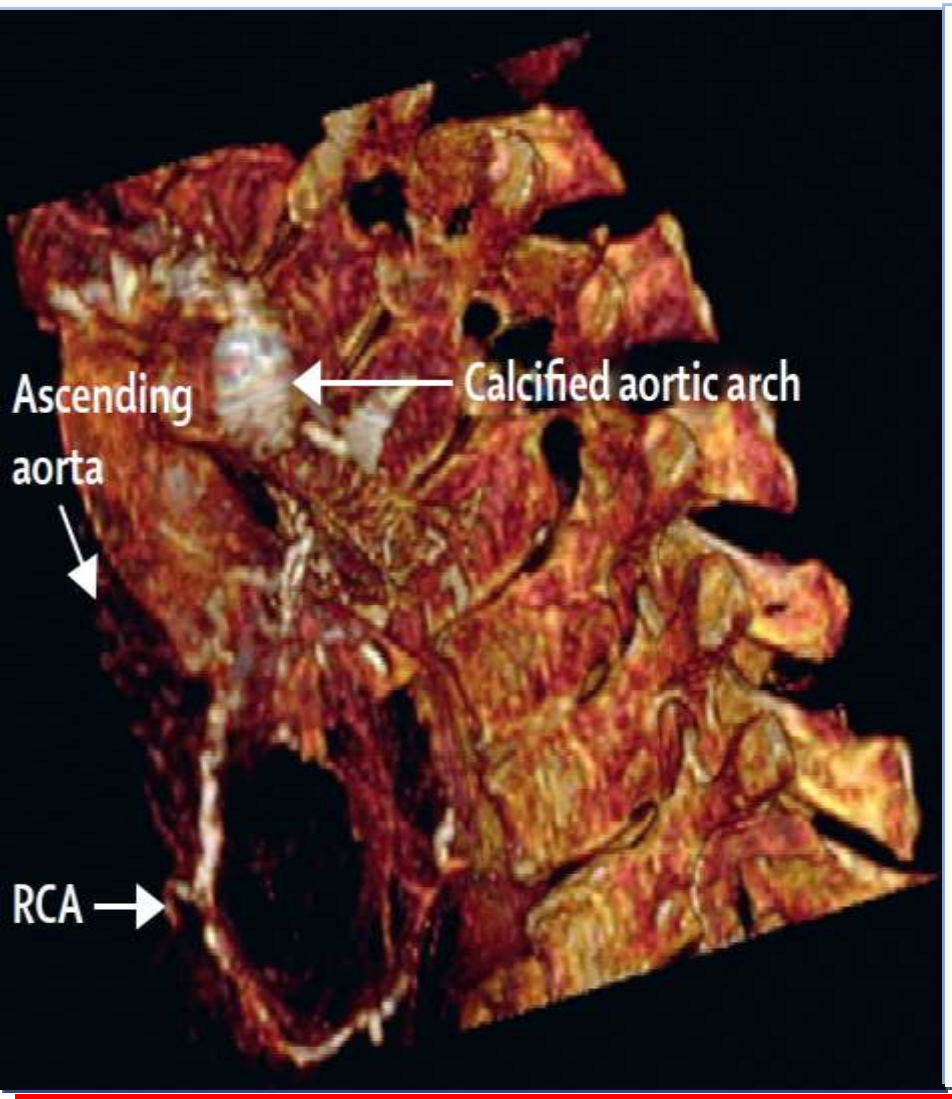
Trend of hypercholesterolemia in Korea

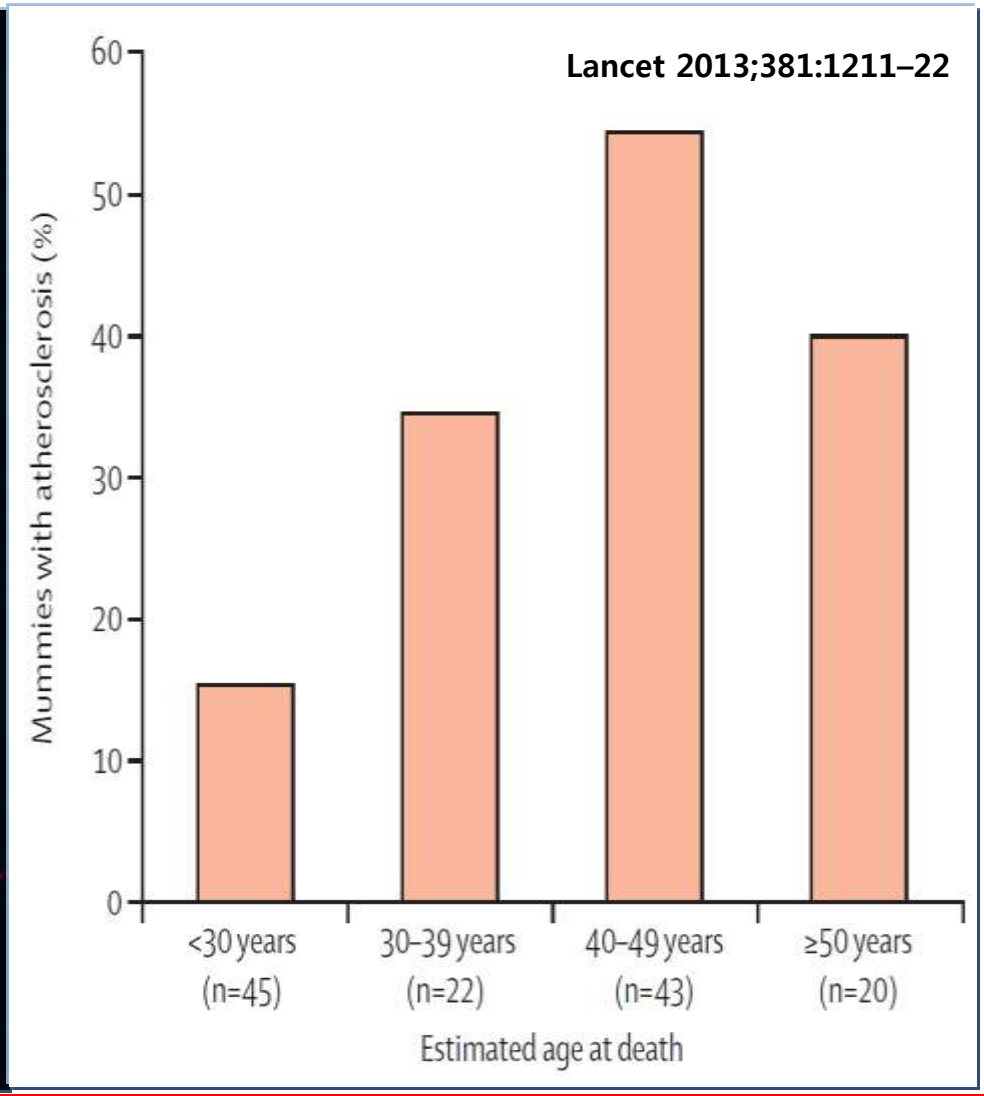
< Prevalence of hypercholesterolemia : Korea health statistics 2011>



Ref. Kim HC, Oh SM. J Prev Med Public Health. 2013;46(4):165-72.

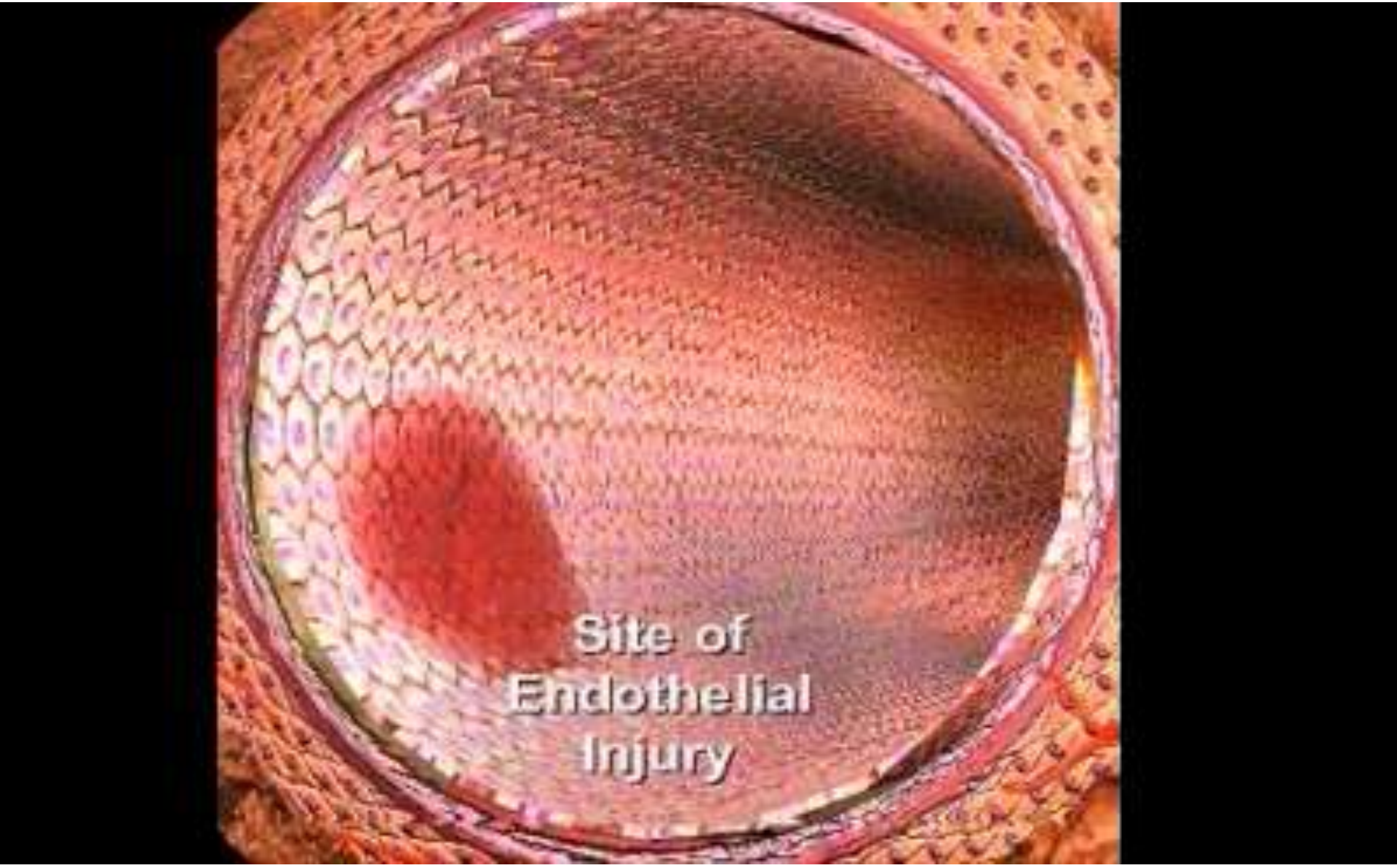
Atherosclerosis across 4,000 years of human history : the Horus study of 4 ancient populations





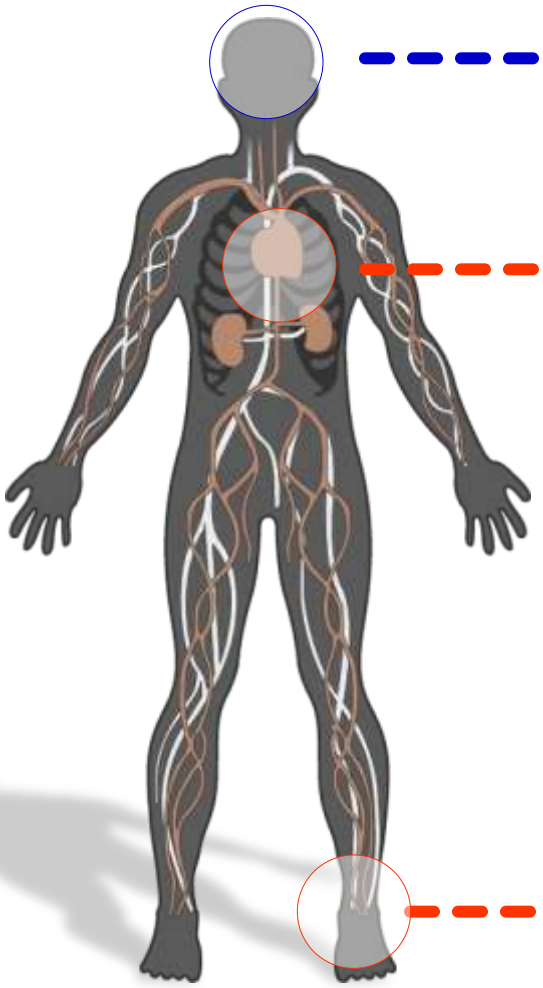
Atherosclerosis was noted in 34% of 137 mummies in 4 preindustrial populations, suggesting that it is an inherent component of human ageing & not characteristic of any specific diet or lifestyle.

Progression of Atherosclerosis



Secondary Prevention of Cardiovascular Disease

With clinical ASCVD



Stroke or TIA presumed to be of atherosclerotic origin

Stable CHD : history of MI, stable angina,
coronary revascularization
Acute CHD : Acute coronary syndrome (ACS)

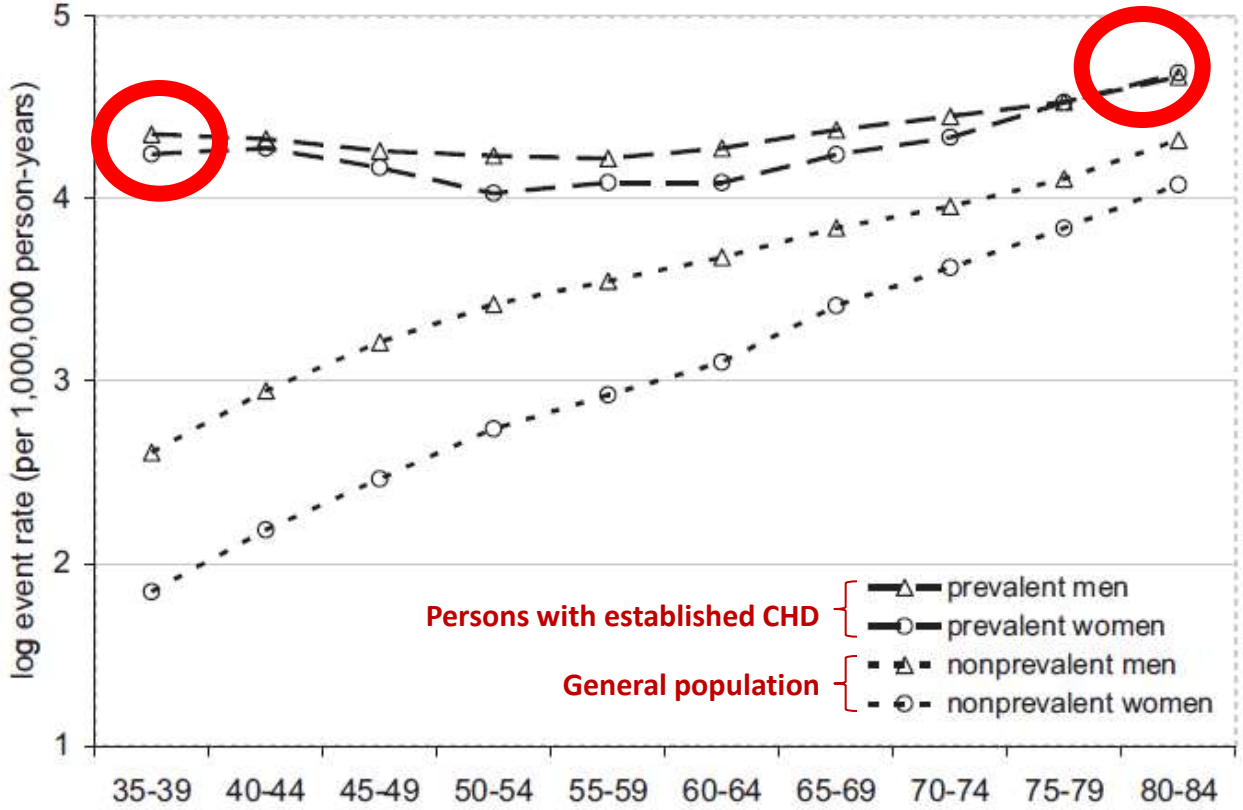
Peripheral arterial disease or revascularization

Ref. Stone NJ, et al. Circulation. published online November 12, 2013.

Persons with established CHD are at much higher risk of recurrent events or death than the general population

A population longitudinal person-based study to examine occurrence of CHD death and nonfatal MI both populations with and without established CHD.

Age-specific rates for major CHD events by disease prevalence and sex for the period 1995 to 2005.



Ref. Briffa TG, et al. Circ Cardiovasc Qual Outcomes. 2011;4:107-113.

More than 40% of major CHD events annually occur in persons with established CHD

The average annual age-standardized prevalence of CHD in the Perth metropolitan region (population 1.6 million) was 28,373 (8.8%) in men and 14,966 (4.0%) in women

Characteristics of Men and Women Ages 35 to 84 Years With and Without Coronary Heart Disease in Perth, Western Australia, Between 1995 and 2005

	Established CHD		CHD Free	
	Men	Women	Men	Women
Average annual population, n	28 373	14 966	313 999	324 409
Average annual prevalence,*† %	8.8	4.0	91.2	96.0
Total nonfatal MI, CHD deaths, n (%)	8335 (43)	4117 (43)	11 121 (57)	5368 (57)
Total CHD deaths, n (%)	4192 (55)	2276 (51)	3470 (45)	2165 (49)
Total nonfatal MI, n (%)	4143 (35)	1841 (36)	7651 (65)	3203 (64)
Average annual crude rates per 100 000 person-years				
Total nonfatal MI+CHD deaths	2686	2513	325	144
CHD deaths	1361	1397	111	63
Nonfatal MI	1325	1116	244	93

*Average prevalence of previous admission for CHD in the past 15 years at June 30 in each calendar year 1995 to 2005.
†Age-standardized.

Ref. Briffa TG, et al. Circ Cardiovasc Qual Outcomes. 2011;4:107-113.

Statin

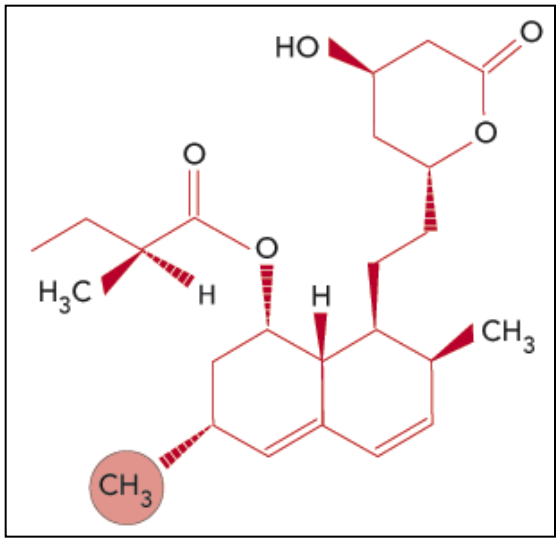
Akira Endo (Sankyo)

First administration of statin

Mevastatin (Sankyo, 1971)

from Penicillium citrinum (of 6,000 fungus/2yr)

Intestinal metaplasia



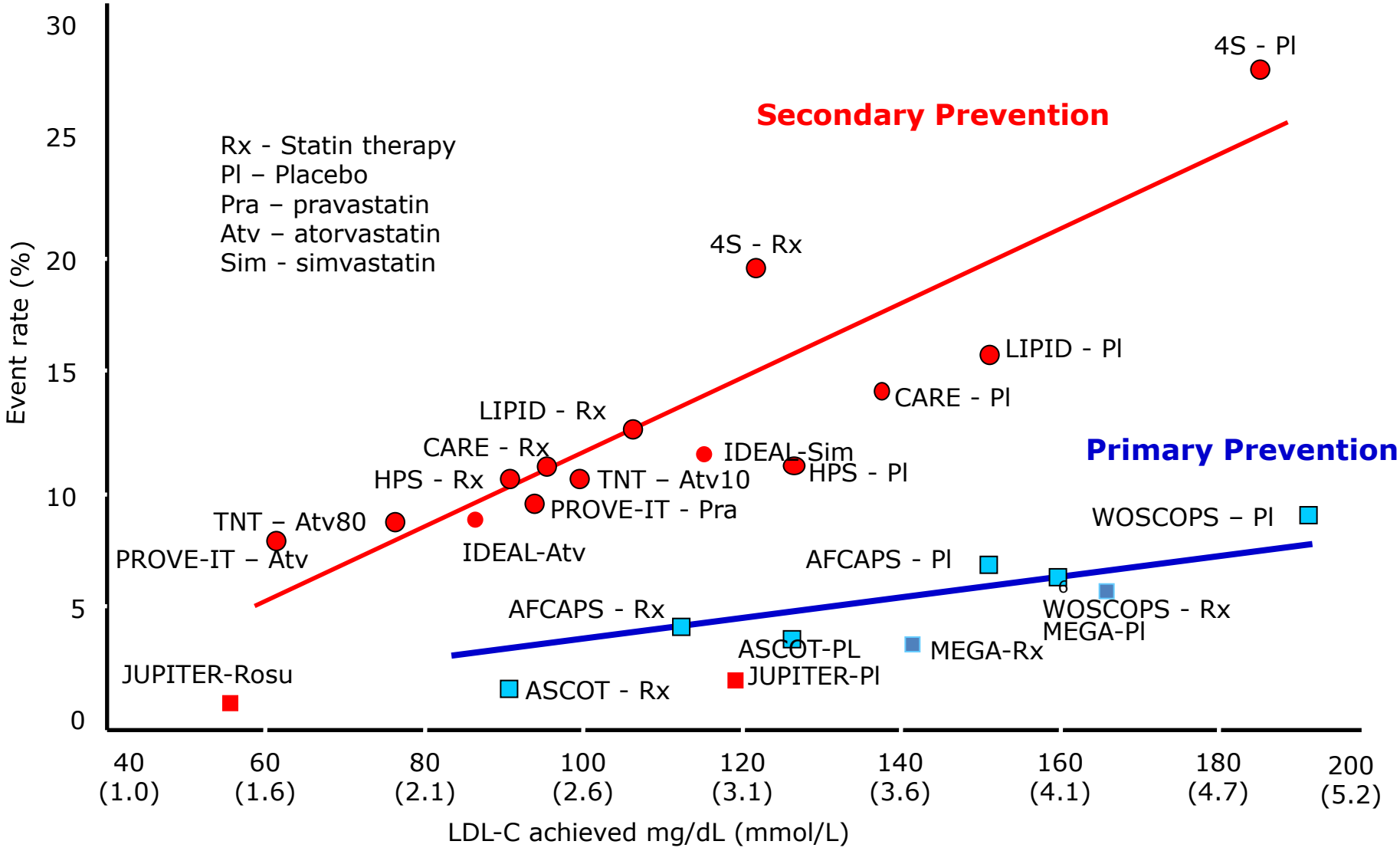
Lovastatin (MSD, 1976)

From Aspergillus terreus

FDA Approval, 1987

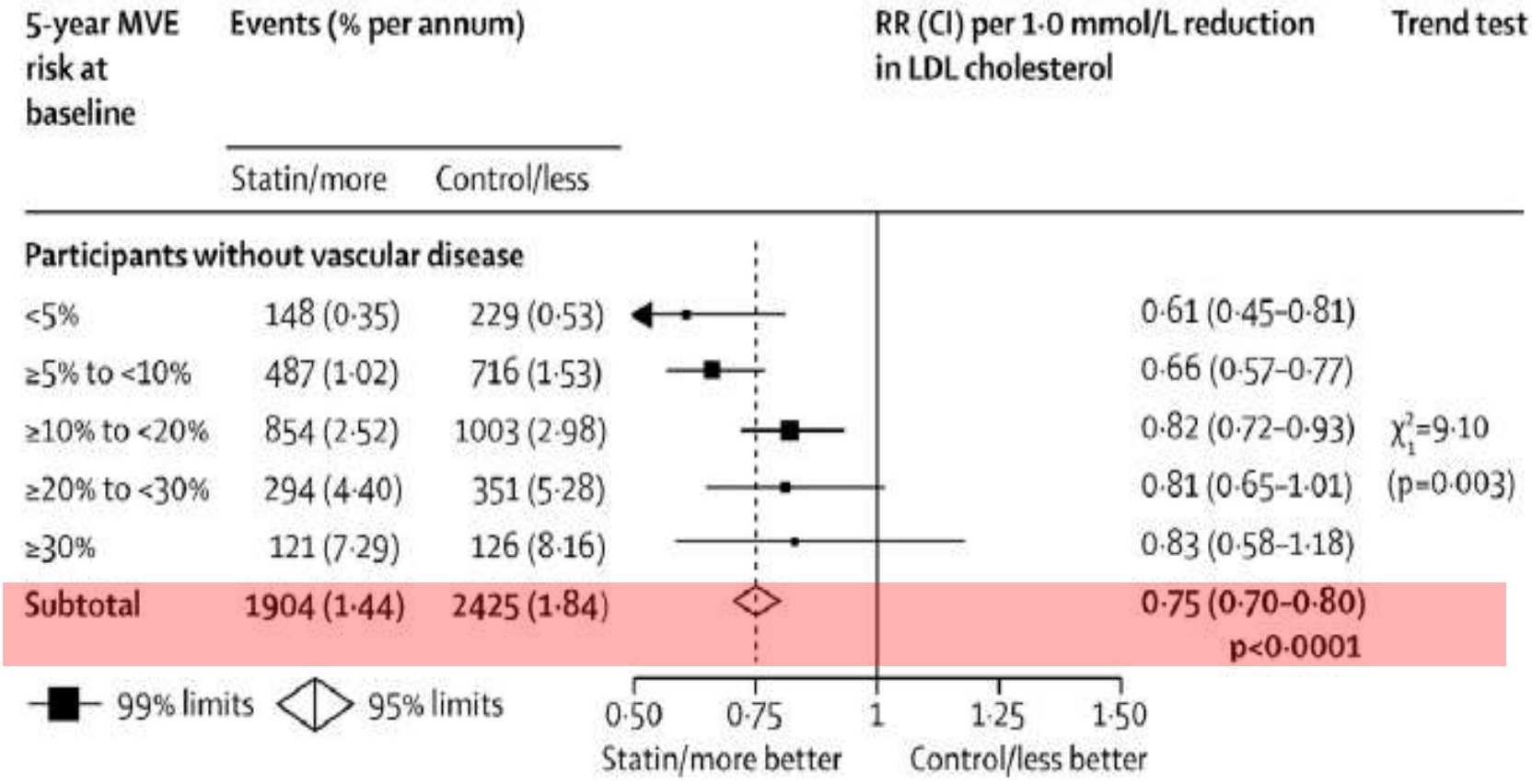
First commercially marketed statin

Established Evidence of "the Lower, the Better"



Exp Opin Emerg Drugs 2004;9(2):269–279, *N Engl J Med* 2005;352:1425–1435. *JAMA* 2005;294:2437; *Lancet* 2006;368:1155

Effects on MACE per 1 mmol/L Reduction in LDL-C

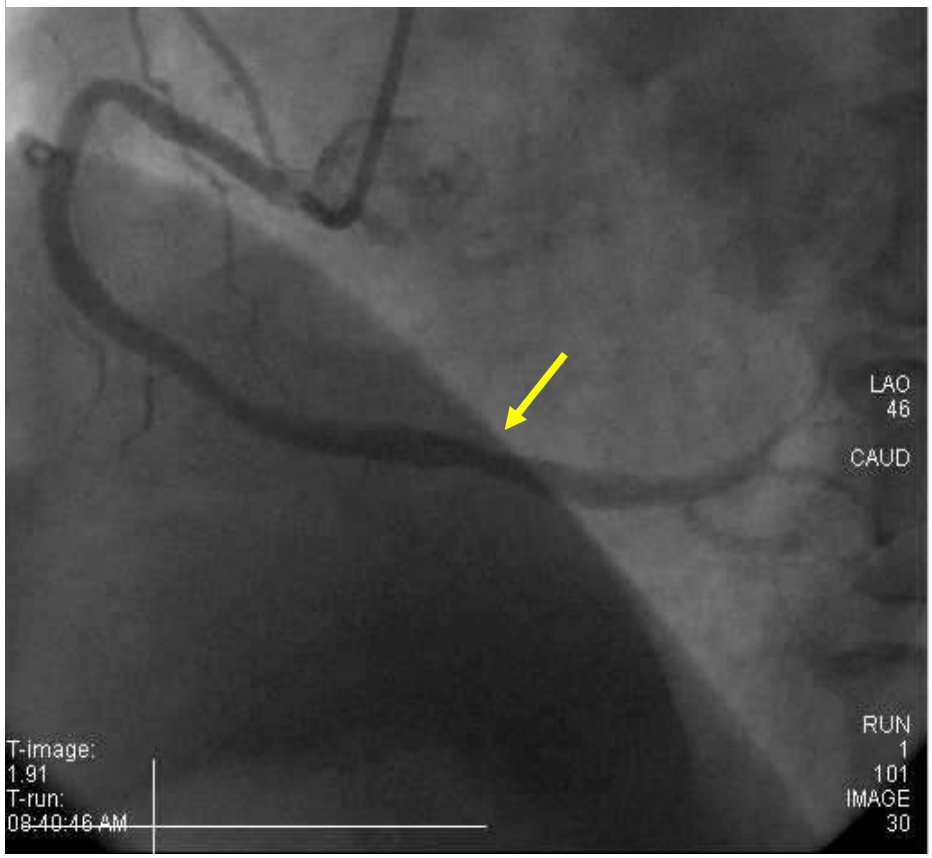


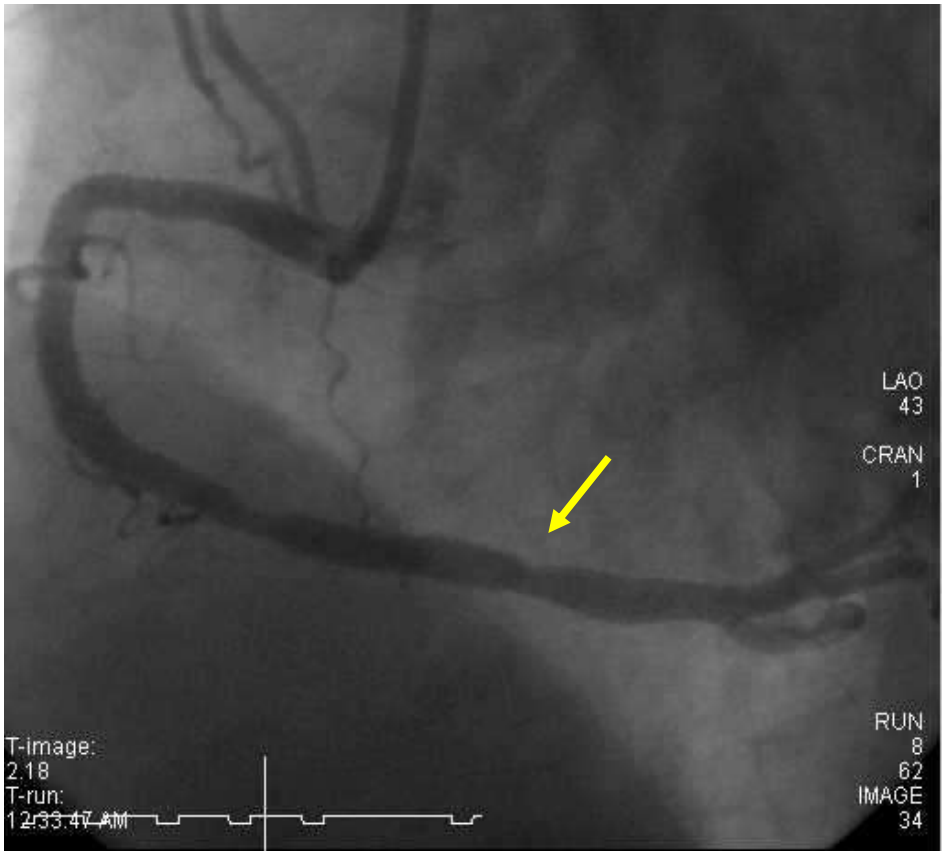
Individual meta-analysis of individuals free of major vascular disease at study entry enrolled in statin trials.
CI = confidence interval; MVE = major vascular event(s); RR = relative risk.
Adapted with permission from Cholesterol Treatment Trialists Collaborators

J Am Coll Cardiol 2014;63:2779–85

Baseline

11M Follow up



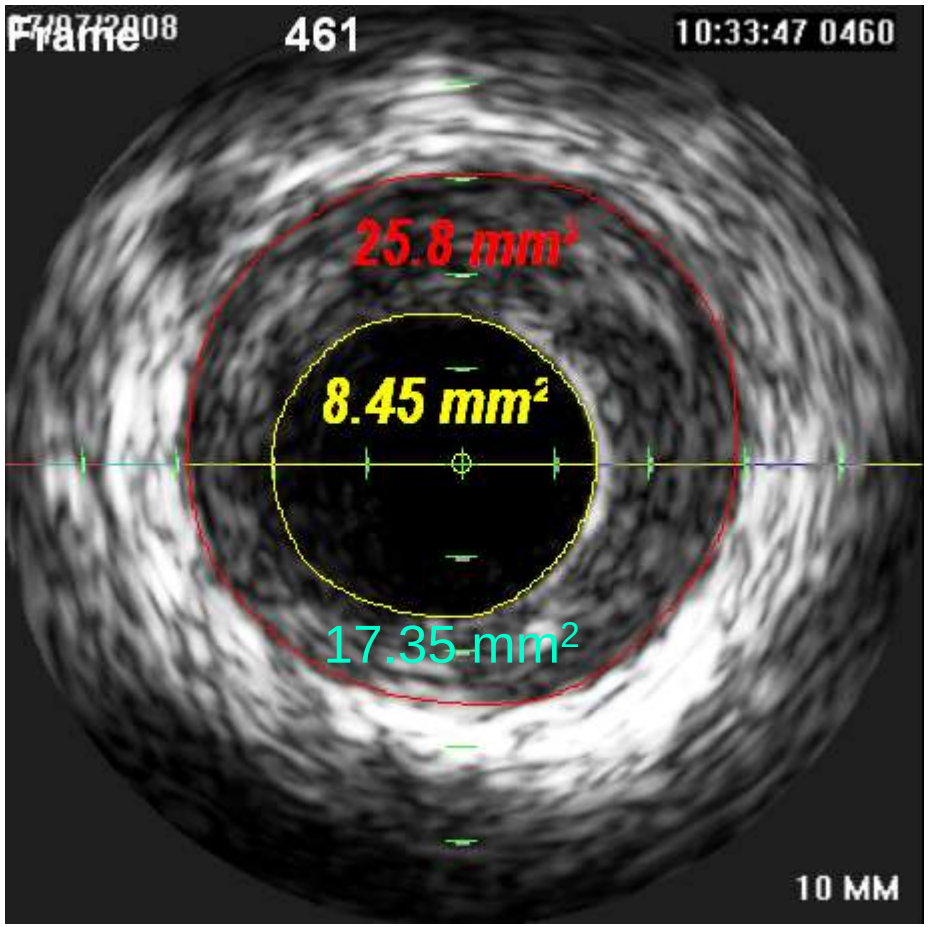


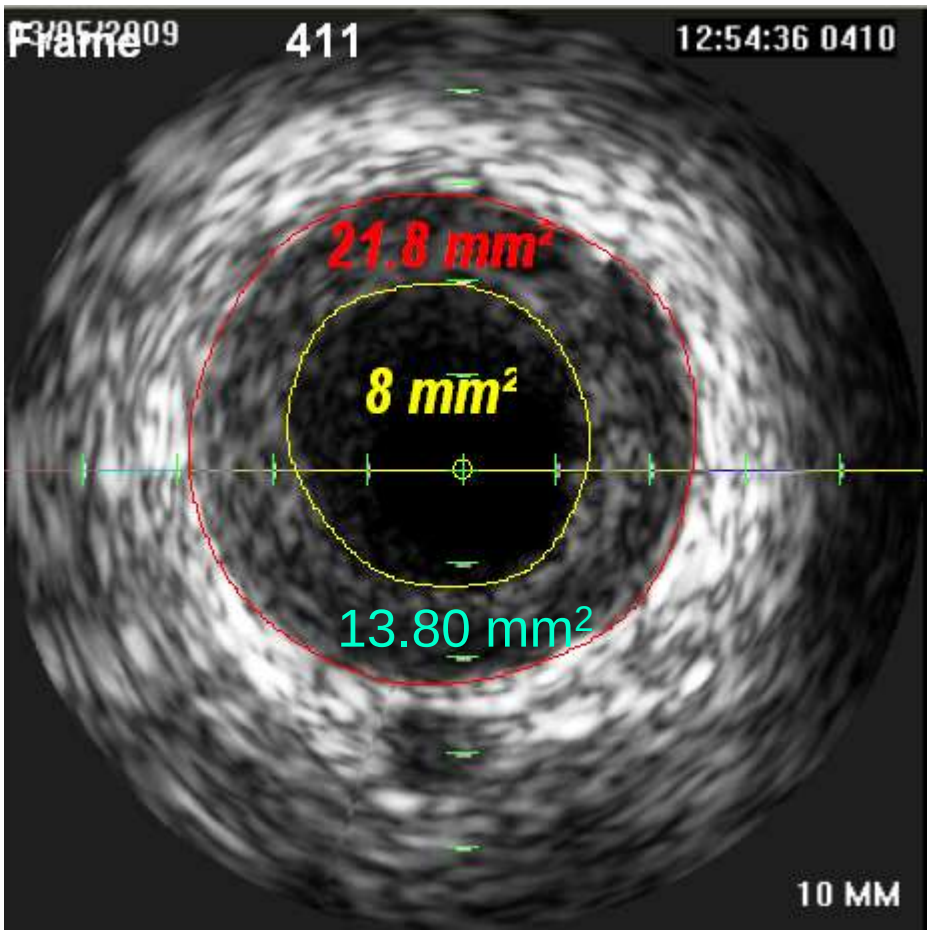
Atorvastatin 40mg/d

Hong YJ et al. Circ J 2011:75;398-406

Baseline

11M Follow up





Plaque burden 67%

Plaque burden 63%

Atorvastatin 40mg/d

Hong YJ et al. Circ J 2011:75;398-406

Circulation Journal
Official Journal of the Japanese Circulation Society
http://www.j-circ.or.jp

ORIGINAL ARTICLE
Ischemic Heart Disease

Comparison of Effects of Rosuvastatin and Atorvastatin on Plaque Regression in Korean Patients With Untreated Intermediate Coronary Stenosis

Young Joon Hong, MD; Myung Ho Jeong, MD; Daisuke Hachinohe, MD; Khurshid Ahmed, MD; Yun Ha Choi; Sook Hee Cho, PhD; Seung Hwan Hwang, MD; Jum Suk Ko, MD; Min Goo Lee, MD; Keun Ho Park, MD; Doo Sun Sim, MD; Nam Sik Yoon, MD; Hyun Ju Yoon, MD; Kye Hun Kim, MD; Hyung Wook Park, MD; Ju Han Kim, MD; Youngkeun Ahn, MD; Jeong Gwan Cho, MD; Jong Chun Park, MD; Jung Chaee Kang, MD

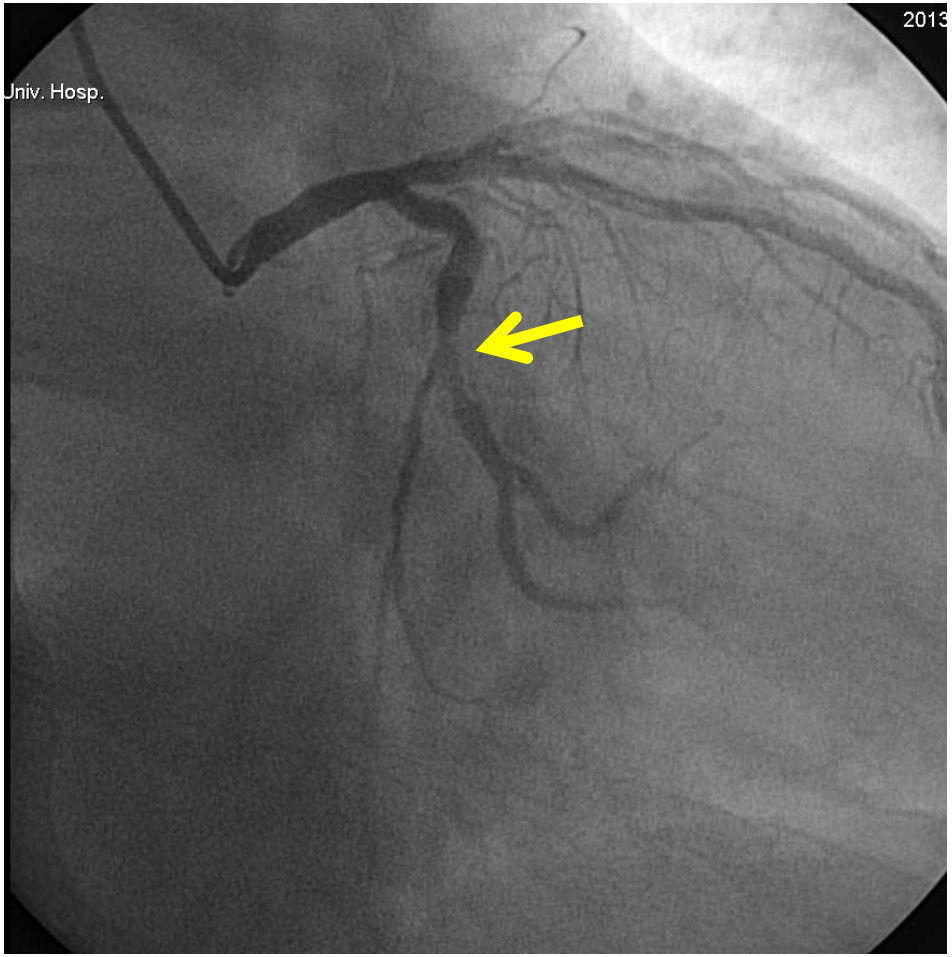
Background: Serial intravascular ultrasound (IVUS) was used to compare the effects of moderate doses of rosuvastatin and atorvastatin on plaque regression in patients with intermediate coronary stenosis.

Methods and Results: This was a prospective, randomized, and comparative study for lipid-lowering therapy with rosuvastatin 20 mg (n=65) and atorvastatin 40 mg (n=63) using serial IVUS (baseline and 11-month follow-up). Efficacy parameters included changes in total atheroma volume (TAV) and percent atheroma volume (PAV) from baseline to follow-up. Changes of TAV (–4.4±7.3 vs. –3.6±6.8 mm^3, P=0.5) and PAV (–0.73±2.05 vs. –0.19±2.00%, P=0.14) from baseline to follow-up were not significantly different between the 2 groups. Plaque was increased in 15% in the rosuvastatin group and in 30% in the atorvastatin group at follow-up (P=0.064). The plaque increase group had higher baseline high-sensitivity C-reactive protein (hs-CRP; 1.28±2.70 mg/dl vs. 0.54±1.16 mg/dl, P=0.034) and higher follow-up low-density lipoprotein cholesterol (LDL-C) (78±24 mg/dl vs. 63±21 mg/dl, P=0.002) compared with the plaque non-increase group. Follow-up LDL-C (odds ratio [OR]=1.038, 95% confidence interval [CI]=1.003–1.060, P=0.036) and baseline hs-CRP (OR=1.025, 95%CI=1.001–1.059, P=0.046), not the type of statin, were the independent predictors of plaque increase at follow-up.

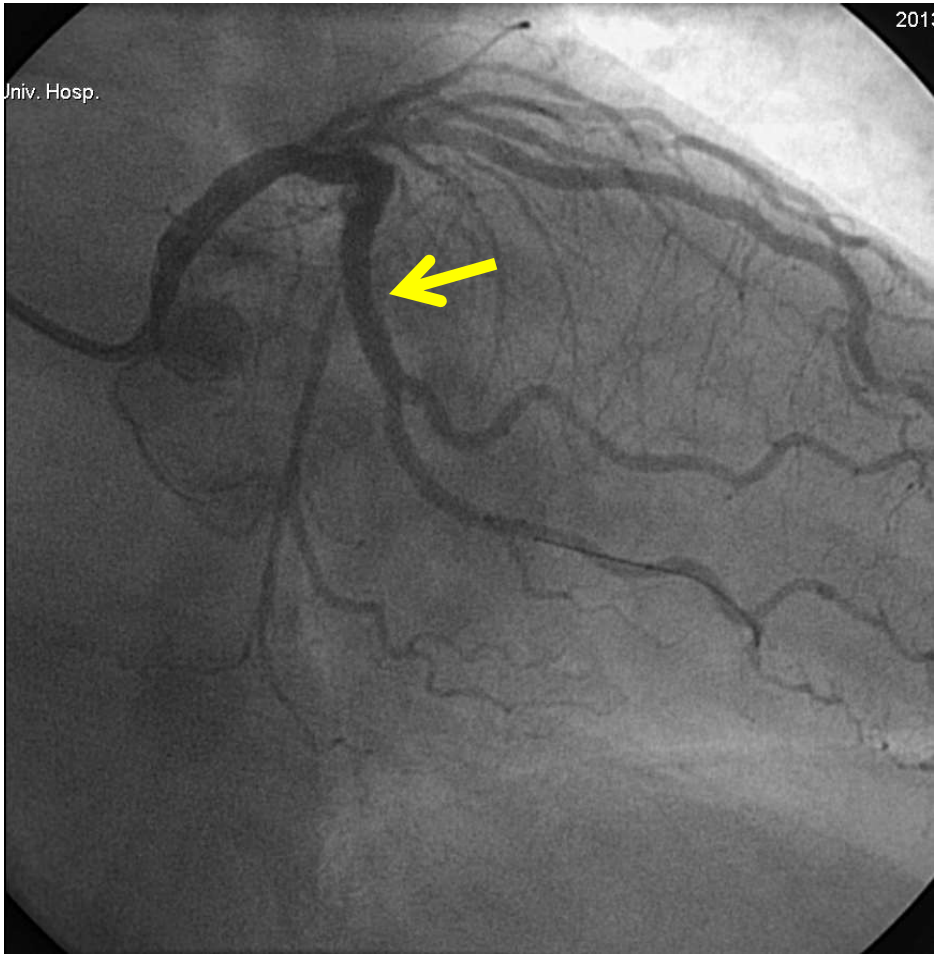
Conclusions: Moderate doses of rosuvastatin and atorvastatin could contribute to effective plaque regression. Follow-up LDL-C and baseline hs-CRP are associated with plaque progression in patients with intermediate coronary stenosis. (*Circ J* 2011; **75:** 398–406)

Key Words: Coronary disease; Intravascular ultrasound; Lipid; Plaque

NSTEMI

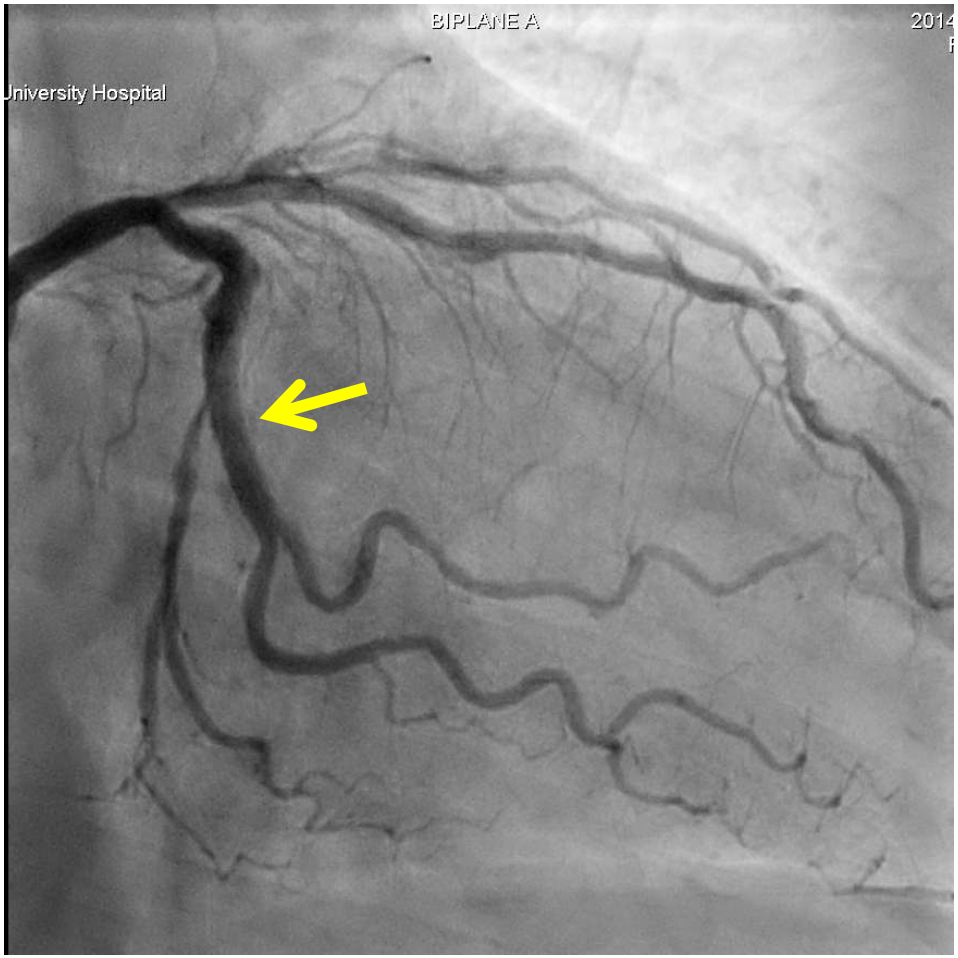


Post-Biomatrix Flex stent



Hong YJ et al. unpublished

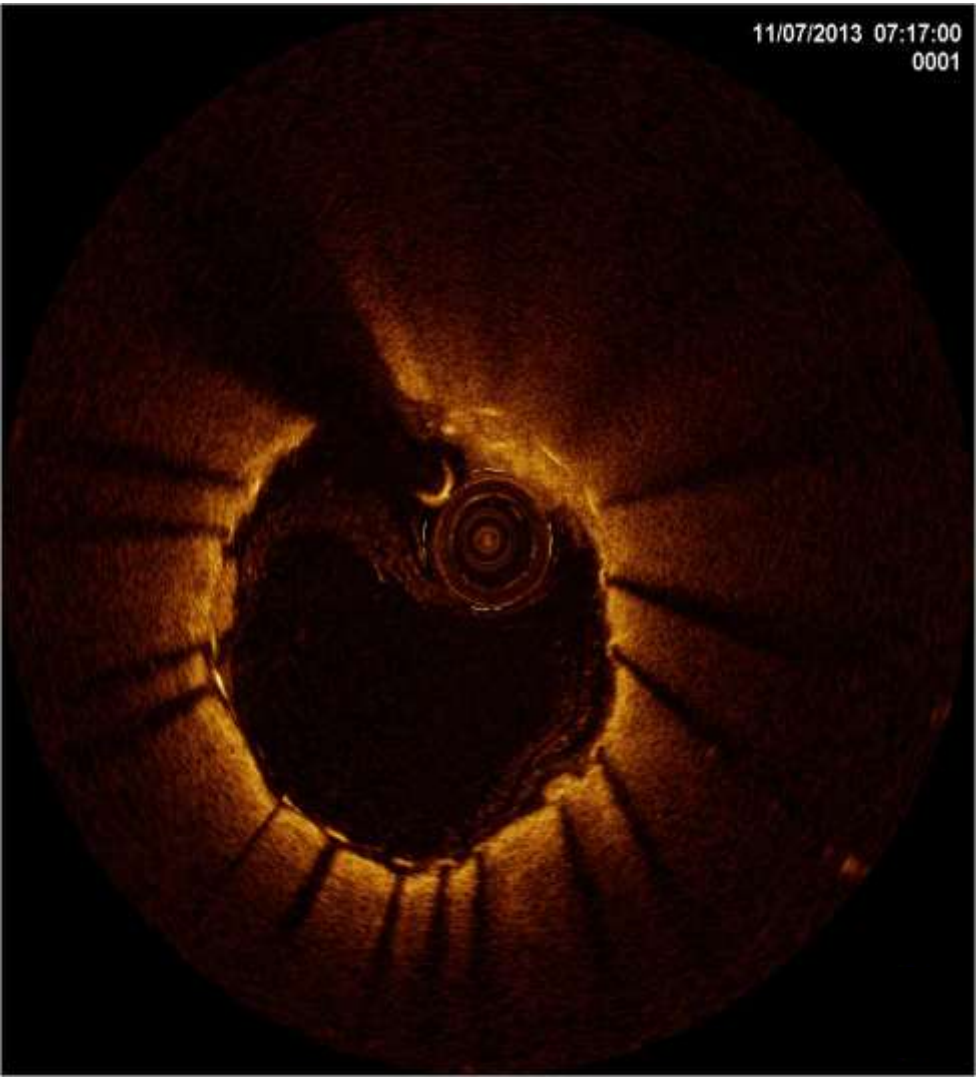
1-Y FU CAG after Tx. with Atorvastatin 40mg

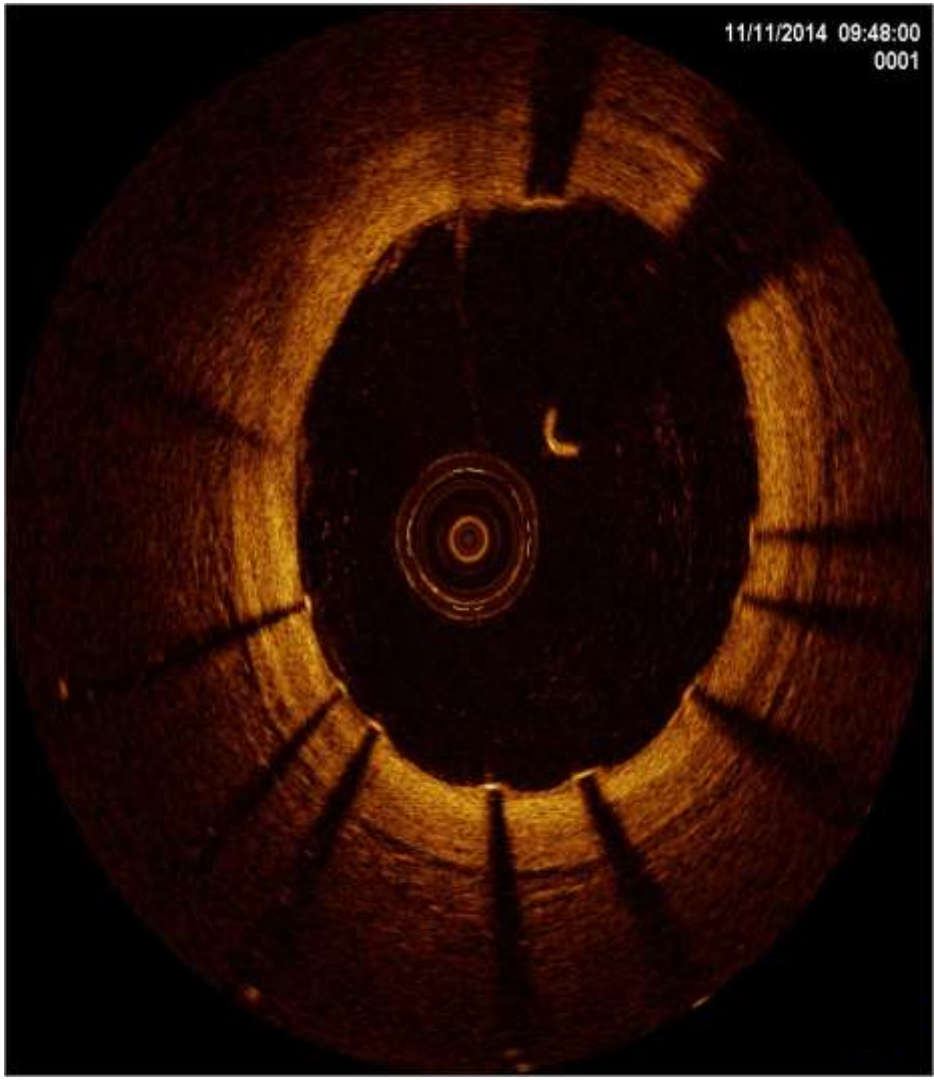


Hong YJ et al. unpublished

Post-stenting OCT

1-Y FU OCT after Tx. with Atorvastatin 40mg





Hong YJ et al. unpublished

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

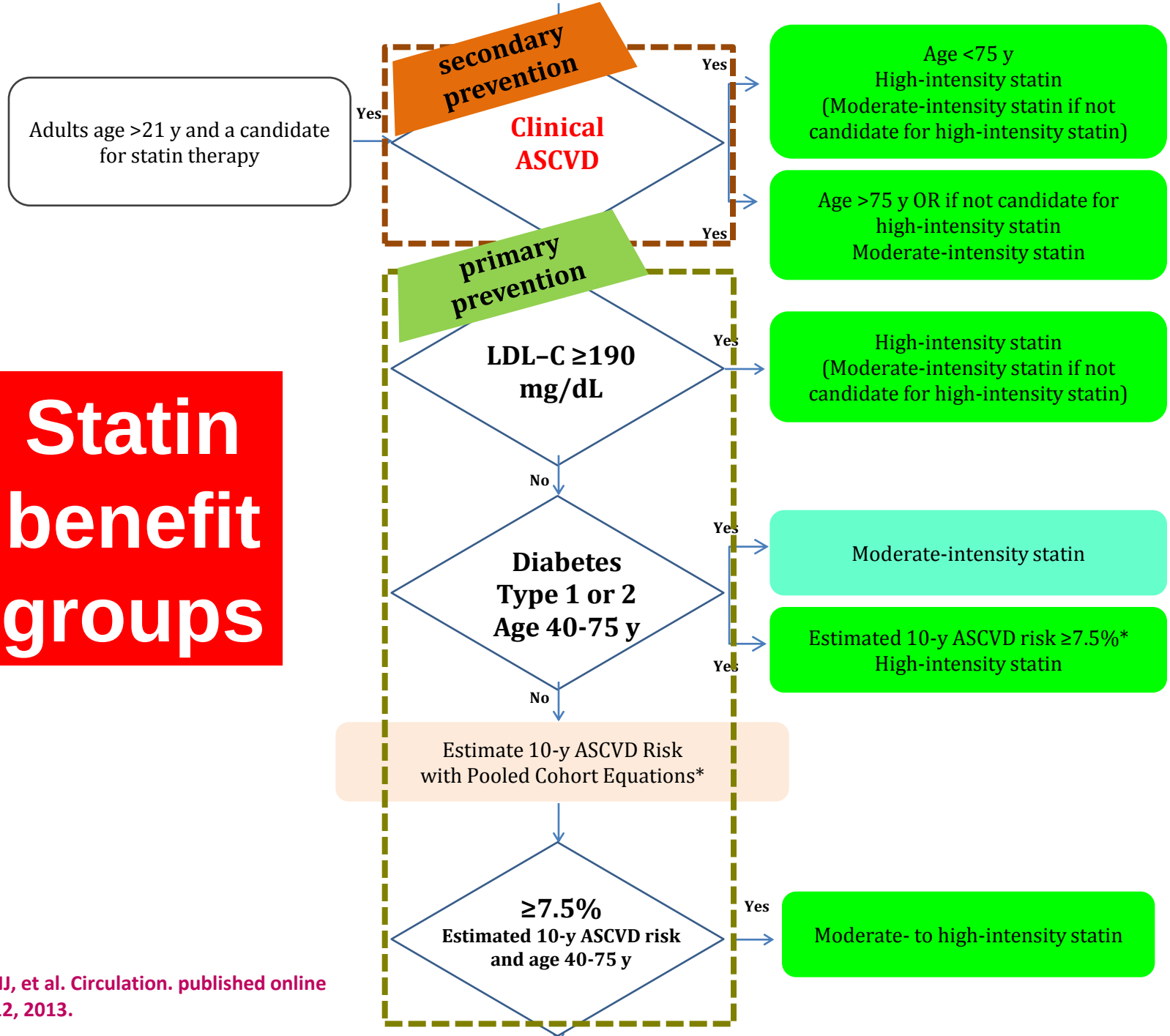
2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Neil J. Stone, Jennifer Robinson, Alice H. Lichtenstein, C. Noel Bairey Merz, Conrad B. Blum, Robert H. Eckel, Anne C. Goldberg, David Gordon, Daniel Levy, Donald M. Lloyd-Jones, Patrick McBride, J. Sanford Schwartz, Susan T. Shero, Sidney C. Smith, Jr, Karol Watson and Peter W.F. Wilson

Circulation. published online November 12, 2013;
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0009-7322. Online ISSN: 1524-4539

Statin benefit groups



Ref. Stone NJ, et al. Circulation. published online November 12, 2013.

2013 ACC/AHA cholesterol guidelines

Clinical ASCVD

Yes → Age ≤ 75 y
High-intensity statin
(Moderate-intensity statin if not candidate for high-intensity statin)

Yes → Age >75 y
OR if not candidate for high-intensity statin
Moderate-intensity statin

* Clinical ASCVD : ACS, or a history of MI, stable or unstable angina, coronary or other arterial revascularization, stroke, TIA, or PAD presumed to be of atherosclerotic origin.

High-Intensity Statin Therapy	**Atorvastatin (40†)–80 mg** Rosuvastatin 20 *(40) mg*
Moderate-Intensity Statin Therapy	**Atorvastatin 10 *(20) mg*** Rosuvastatin (*5) 10 mg* Simvastatin 20–40 mg‡ Pravastatin 40 *(80) mg* Lovastatin 40 mg *Fluvastatin XL 80 mg* Fluvastatin 40 mg bid *Pitavastatin 2–4 mg*

Ref. Stone NJ, et al. Circulation. published online November 12, 2013.

2014 NICE guideline – Lipid modification

established CVD

Yes → Start statin treatment in people with CVD with atorvastatin 80 mg

Yes → Use a lower dose of atorvastatin if any of the following apply:
- potential drug interactions
- high risk of adverse effects
- patient preference.

* CVD disease of the heart and blood vessels caused by the process of atherosclerosis.

Review question	PICO characteristics		Result
What is the clinical and cost effectiveness of statin therapy for adults with established CVD (secondary prevention)?	- Patient	Adults(18 years and over) with established CVD	Atorvastatin 80 mg
	- Intervention	Atorvastatin / Fluvastatin/ Pravastatin /Rosuvastatin /Simvastatin	
	- Comparison	- Low intensity group(pravastatin 10–40 mg or equivalent) - Medium intensity group(simvastatin 40 mg or equivalent) - High intensity group(atorvastatin 80 mg or equivalent)	
	- Outcome	All-cause mortality, CV mortality, Non-fatal MI , Stroke, Quality of life, Adverse event, LDL-cholesterol reduction	

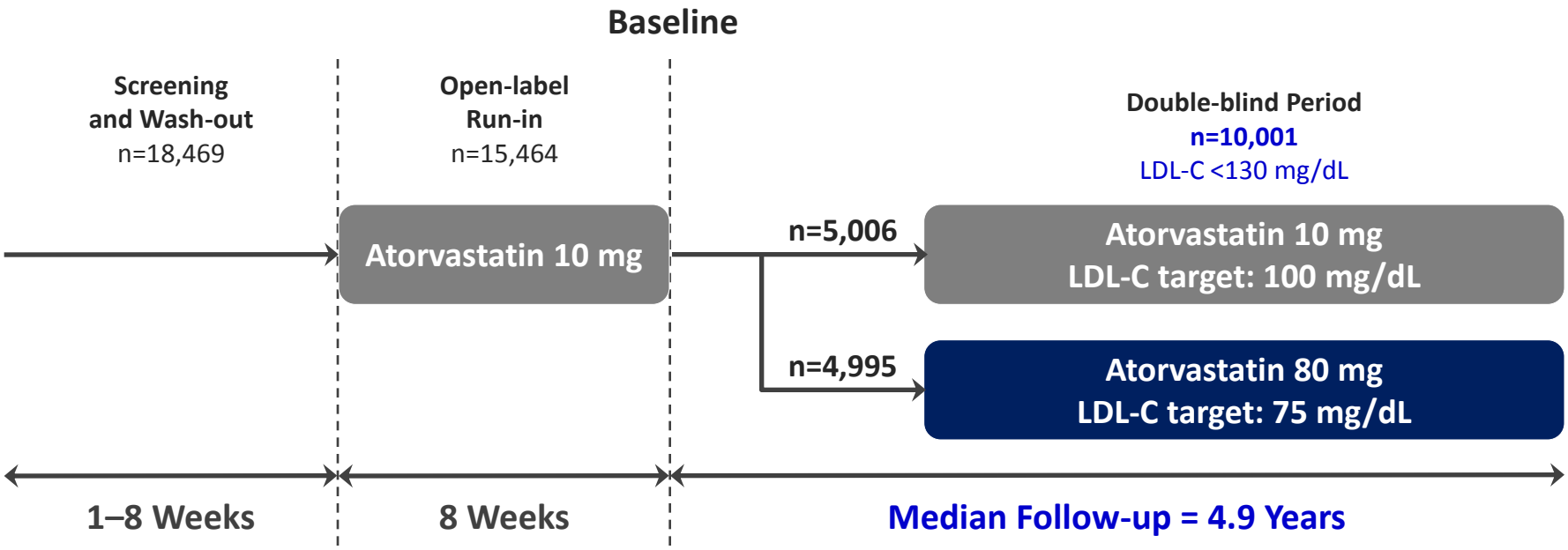
Ref. NICE clinical guideline 181 Accessed August 8, 2014 at http://www.nice.org.uk/

Effect of Atorvastatin 80 mg in patients with stable CHD

TNT, Treating to the New Target

To assess the efficacy and safety of lowering LDL cholesterol levels below 100 mg/dL in patients with stable coronary heart disease

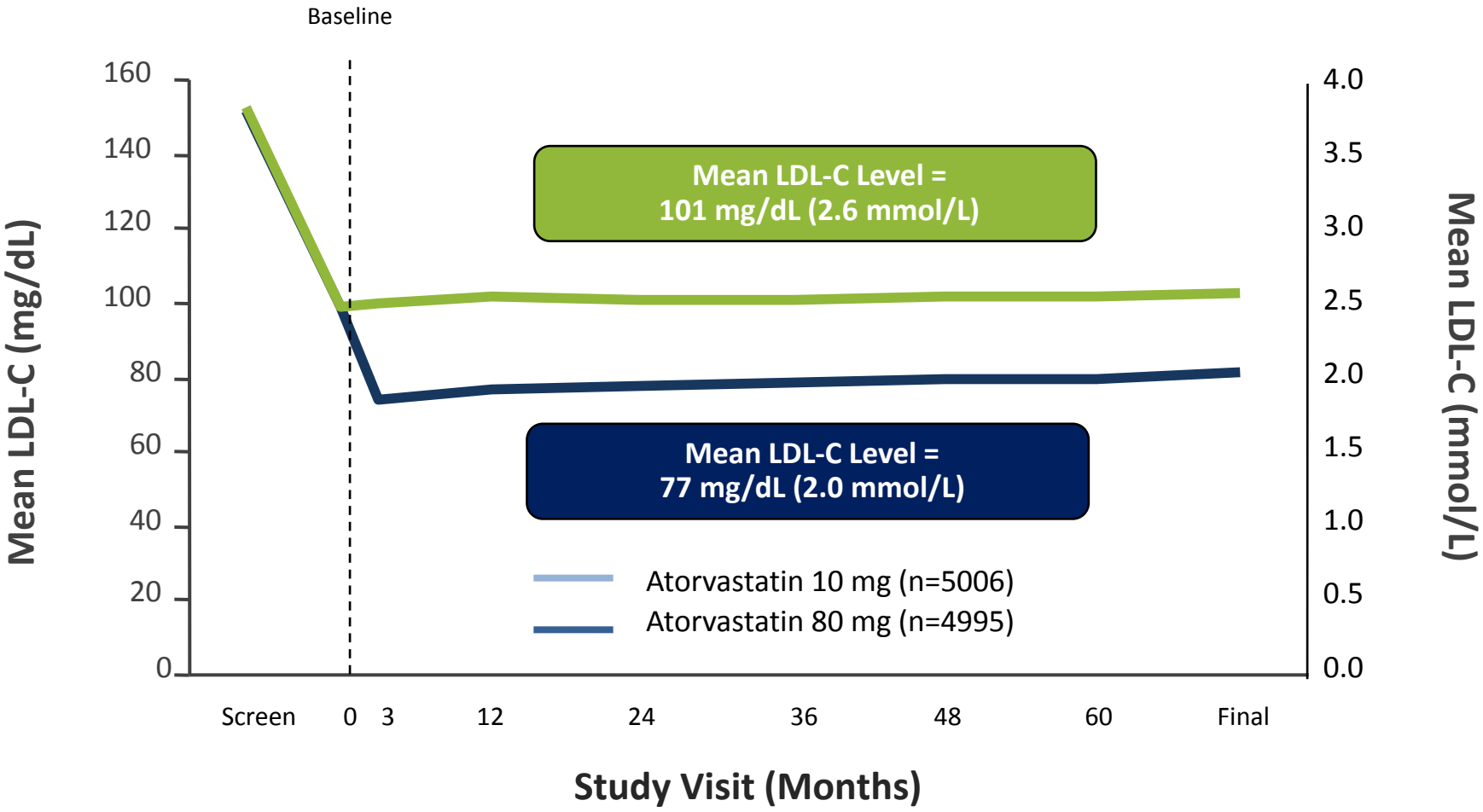
TNT : Study Design



Patient Population	Primary Efficacy Outcome
35-75 yrs with stable CHD LDL-C: 130-250 mg/dL Triglycerides ≤600 mg/dL	Time to occurrence of a major CV event: • CHD death • Nonfatal, non–procedure-related MI • Resuscitated cardiac arrest • Fatal or nonfatal stroke

Ref. Adapted from LaRosa JC, et al. N Engl J Med. 2005;352: 1425-1435

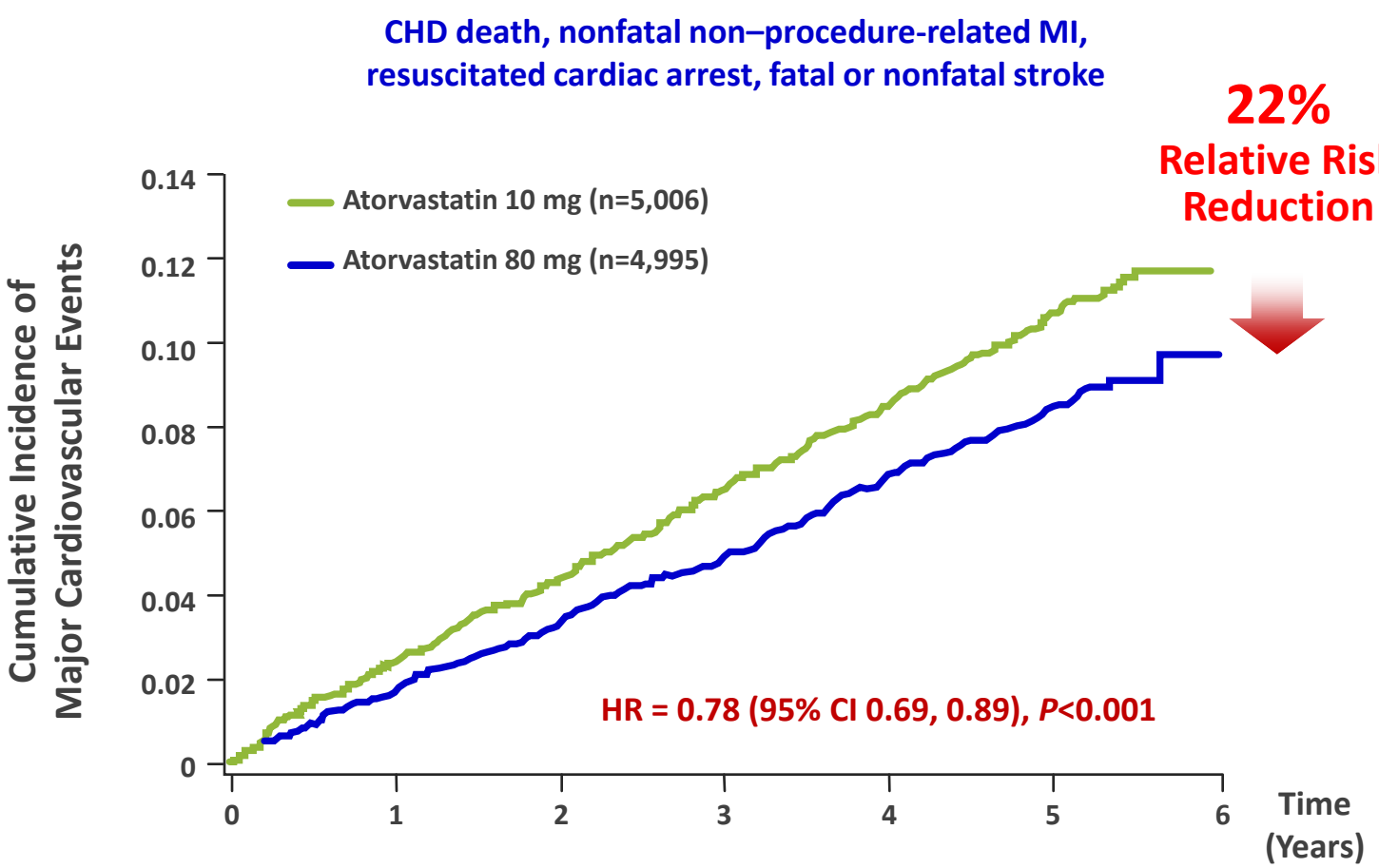
TNT : Changes in Lipid Levels



Ref. Adapted from LaRosa JC, et al. N Engl J Med. 2005;352: 1425-1435

TNT : Primary Efficacy Outcome*

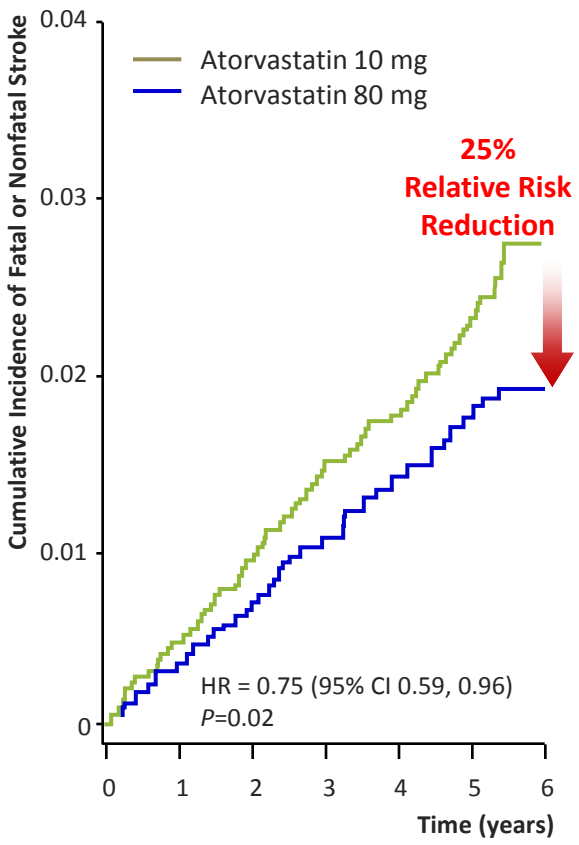
Kaplan–Meier Estimates of the Incidence of the Primary End Point



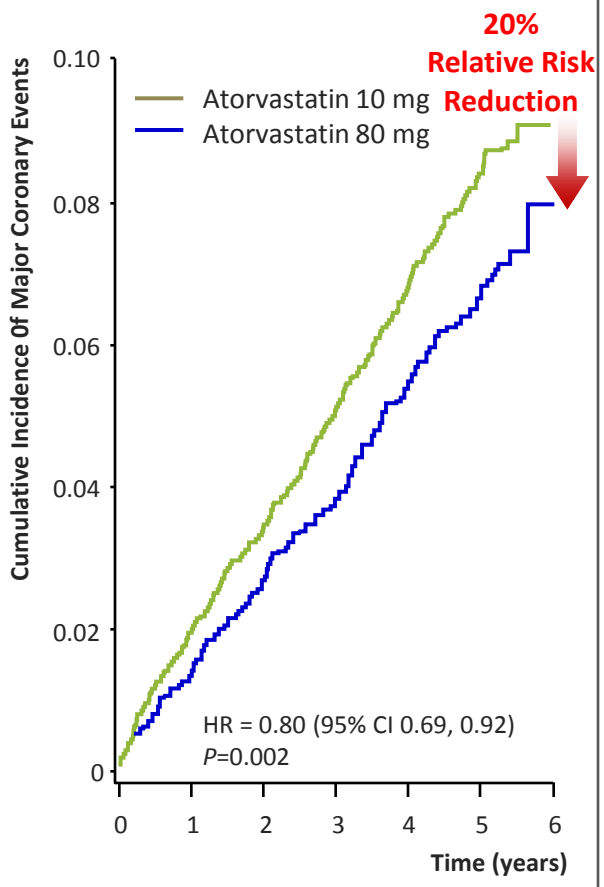
Ref. Adapted from LaRosa JC, et al. N Engl J Med. 2005;352: 1425-1435

TNT : Secondary Efficacy Outcome

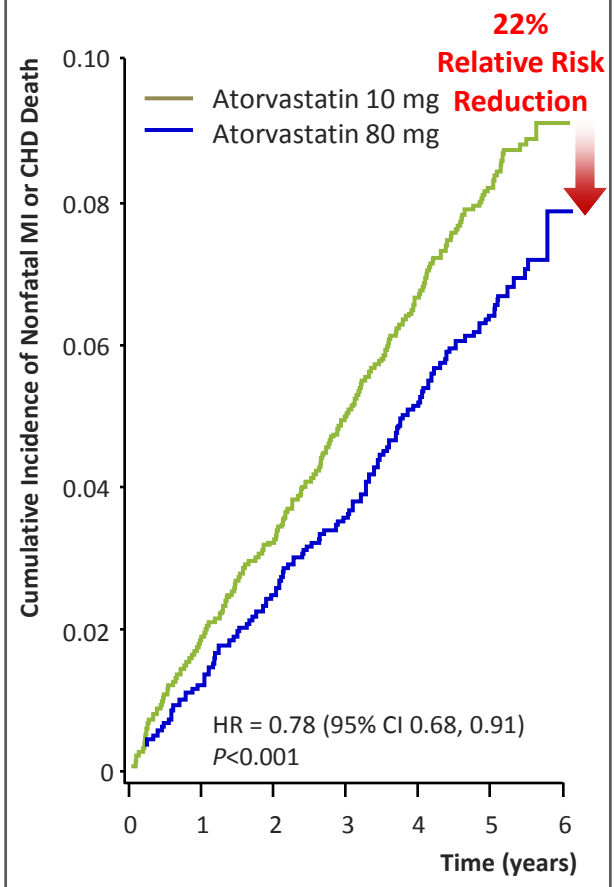
Stroke



Major Coronary Events*



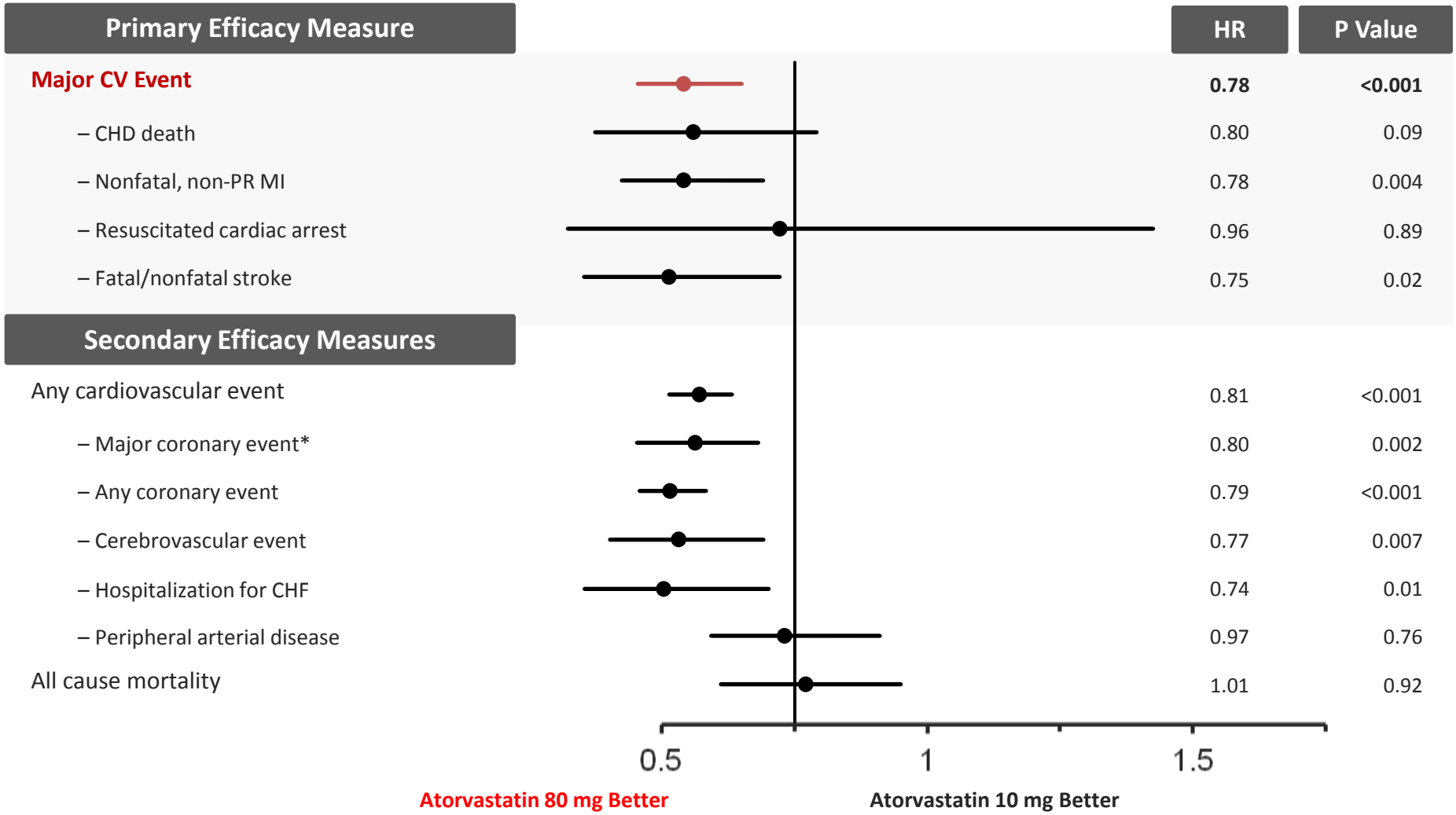
Nonfatal MI or CHD Death



*CHD death, nonfatal non–procedure-related MI, resuscitated cardiac arrest.

Ref. Adapted from LaRosa JC, et al. N Engl J Med. 2005;352: 1425-1435

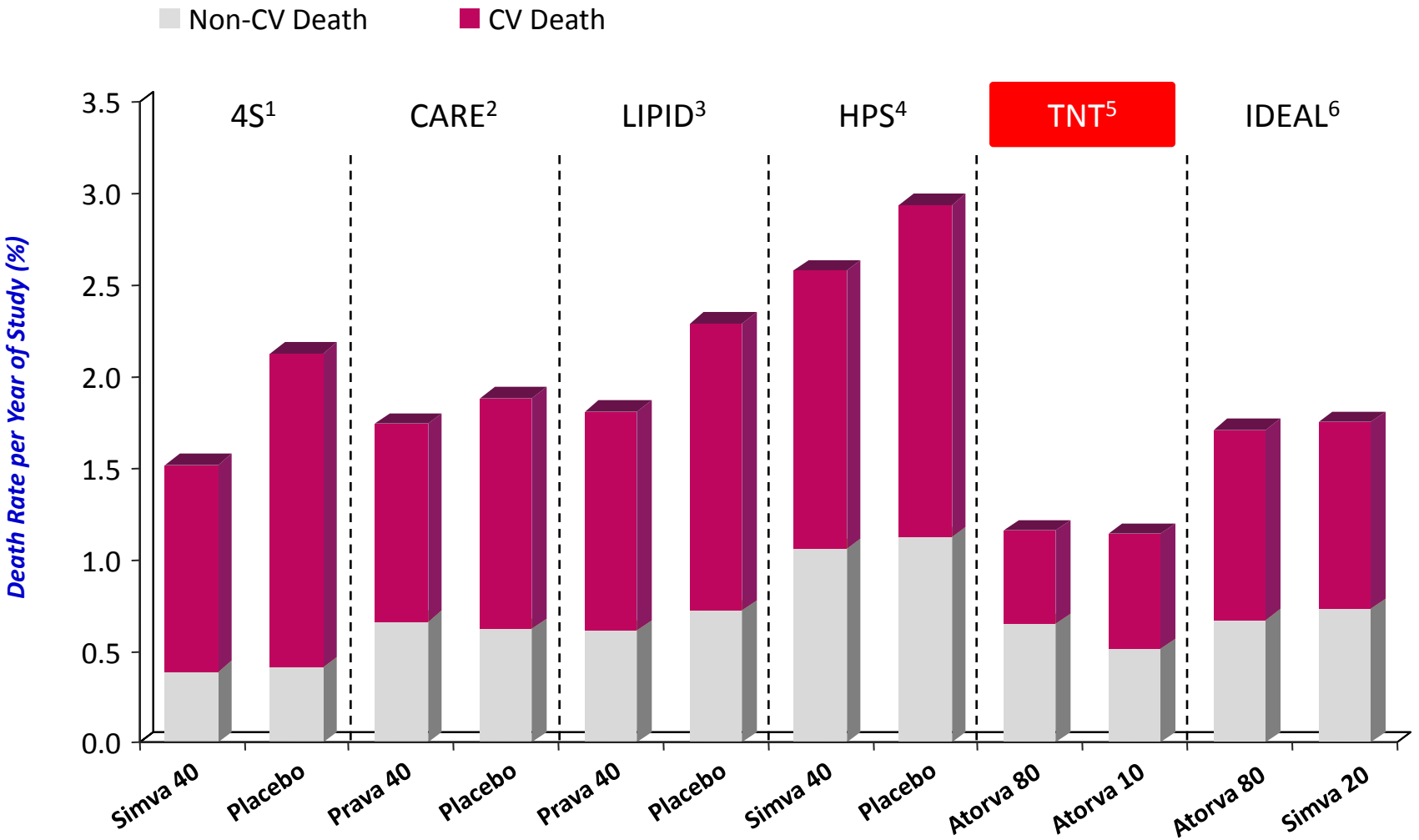
TNT : individual components of outcome



*CHD death, nonfatal non–procedure-related MI, resuscitated cardiac arrest.

Ref. Adapted from LaRosa JC, et al. N Engl J Med. 2005;352: 1425-1435

Comparison of Non-CV and CV Mortality in Secondary Prevention Studies



Ref. 1. 4S Group. Lancet. 1994;344:1383-9; 2. Sacks FM, et al. N Engl J Med. 1996;335:1001-9; 3. The LIPID Study Group. N Engl J Med. 1998;339:1349-57; 4. HPS Collaborative Group. Lancet. 2002;360:7-22; 5. LaRosa JC, et al. N Engl J Med. 2005;352; 6. Pedersen TR, et al. JAMA. 2005;294:2437-2445.

TNT: Safety Profile

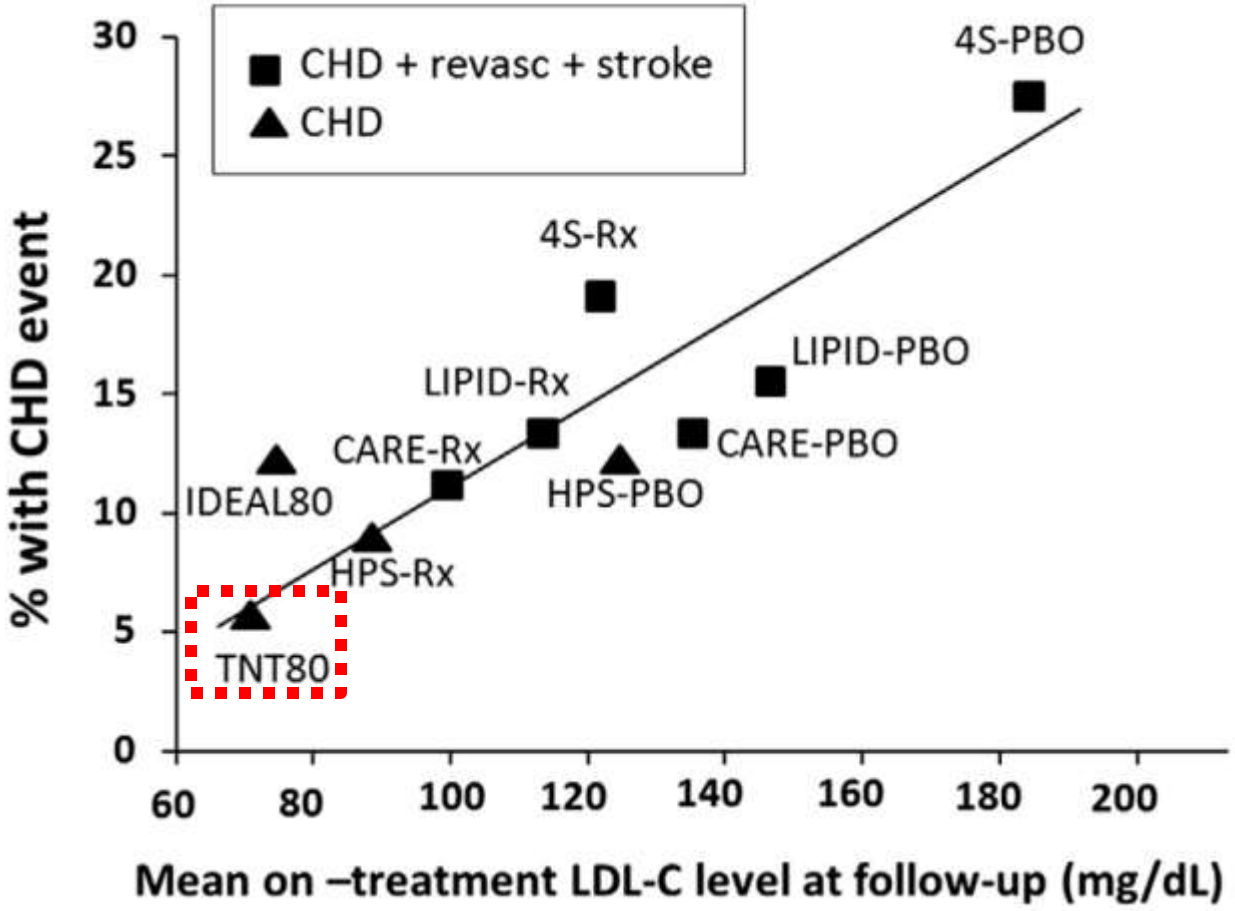
	No. of Patients (%)	
	Atorvastatin 10 mg (n=5,006)	Atorvastatin 80 mg (n=4,995)
Treatment discontinuation due to treatment-related AEs	264 (5.3)	359 (7.2)
Myalgia (treatment-related)	234 (4.7)	241 (4.8)

Intensive lipid-lowering therapy with 80 mg of atorvastatin per day in patients with stable CHD provides significant clinical benefit beyond that afforded by treatment with 10 mg of atorvastatin per day.

*No cases were considered by the investigator with direct responsibility for the patient to be causally related to atorvastatin
†Reported as persistent elevation in ALT, AST, or both on 2 consecutive measures 4-10 days apart

Ref. LaRosa JC, et al. N Engl J Med. 2005;352:1425-1435

The TNT study was the first RCT designed to demonstrate the benefits of lowering LDL-C below 100 mg/dL in stable CHD patients



*Rx, on-treatment arm of study; PBO, placebo arm. 80, 80 mg atorvastatin.

Ref. Adapted from LaRosa JC, et al. N Engl J Med. 2005;352: 1425-1435

TNT allows alterations in NCEP – ATP III 2006 update

NCEP-ATP III 2004 update

Risk Category	LDL-C Goal
High risk: CHD* or CHD risk equivalents† (10-year risk >20%)	<100 mg/dL (optional goal: <70 mg/dL)‖
Moderately high risk: 2+ risk factors‡ (10-year risk 10% to 20%)§§	<130 mg/dL¶
Moderate risk: 2+ risk factors‡ (10-year risk <10%)§§	<130 mg/dL
Lower risk: 0–1 risk factor§	<160 mg/dL

NCEP-ATP III 2006 update

For lipid management:

Assess fasting lipid profile in all patients, and within 24 hours of hospitalization for those with an acute cardiovascular or coronary event. For hospitalized patients, initiate lipid-lowering medication as recommended below before discharge according to the following schedule:

- LDL-C should be <100 mg/dL **I (A)**, **and**
- Further reduction of LDL-C to <70 mg/dL is reasonable. **IIa (A)**
- If baseline LDL-C is ≥100 mg/dL, initiate LDL-lowering drug therapy.§ **I (A)**
- If on-treatment LDL-C is ≥100 mg/dL, intensify LDL-lowering drug therapy (may require LDL-lowering drug combination‖). **I (A)**
- If baseline LDL-C is 70 to 100 mg/dL, it is reasonable to treat to LDL-C <70 mg/dL. **IIa (B)**

2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease

4.2.1.1. Lipid Management

Class I

1. Lifestyle modifications, including daily physical activity and weight management, are strongly recommended for all patients with SIHD.[23,176] (*Level of Evidence: B*)
2. Dietary therapy for all patients should include reduced intake of saturated fats (to <7% of total calories), *trans* fatty acids (to <1% of total calories), and cholesterol (to <200 mg/d).[23,177–180] (*Level of Evidence: B*)
3. In addition to therapeutic lifestyle changes, a moderate or high dose of a statin therapy should be prescribed, in the absence of contraindications or documented adverse effects.[23,163,181–183] (*Level of Evidence: A*)

Class IIa

1. For patients who do not tolerate statins, low-density lipoprotein-cholesterol-lowering therapy with bile acid sequestrants,* niacin,† or both is reasonable.[184,186,187] (*Level of Evidence: B*)

Class I

In addition to therapeutic lifestyle changes, a moderate or high dose of a statin therapy should be prescribed, in the absence of contraindications or documented adverse effects.
(*Level of Evidence: A*)

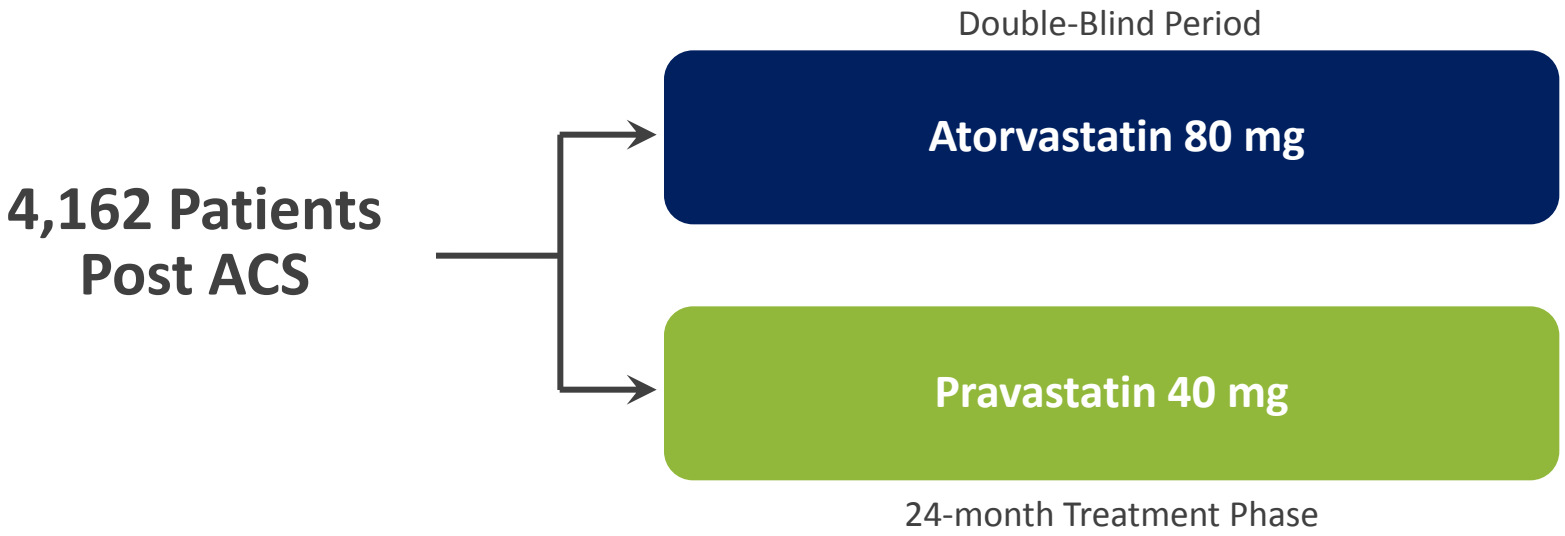
Ref. Fihn SD, et al. Circulation. 2012;126:3097-3137.

Effect of Atorvastatin 80 mg in patients with acute CHD(ACS)

PROVE-IT, Pravastatin or Atorvastatin Evaluation and Infection Therapy

to compare the standard degree of LDL cholesterol lowering to approximately 100 mg/dL with the use of 40 mg of pravastatin daily with more intensive LDL cholesterol lowering to approximately 70 mg/dL with the use of 80 mg of atorvastatin daily as a mean of preventing death or major cardiovascular events in ACS patients

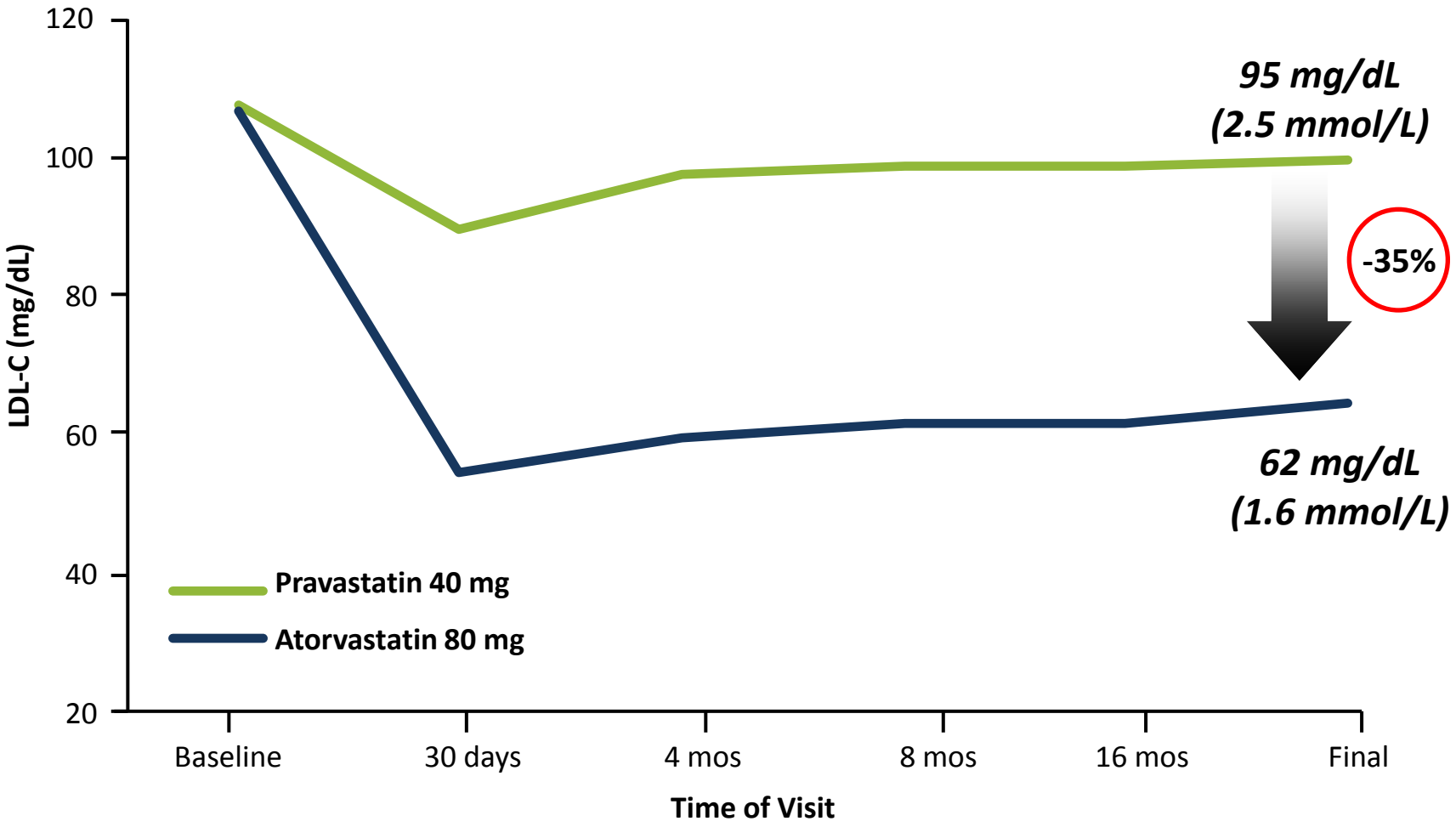
PROVE IT : Study Design



Patient Population	Primary Endpoint
○ 58 y (mean) ○ TC <6.2 mmol/L ○ **Randomized within 10 days of ACS event (mean: 7 days)**	○ Time to Occurrence of: Death, Nonfatal MI, Unstable Angina, Stroke, Revascularization

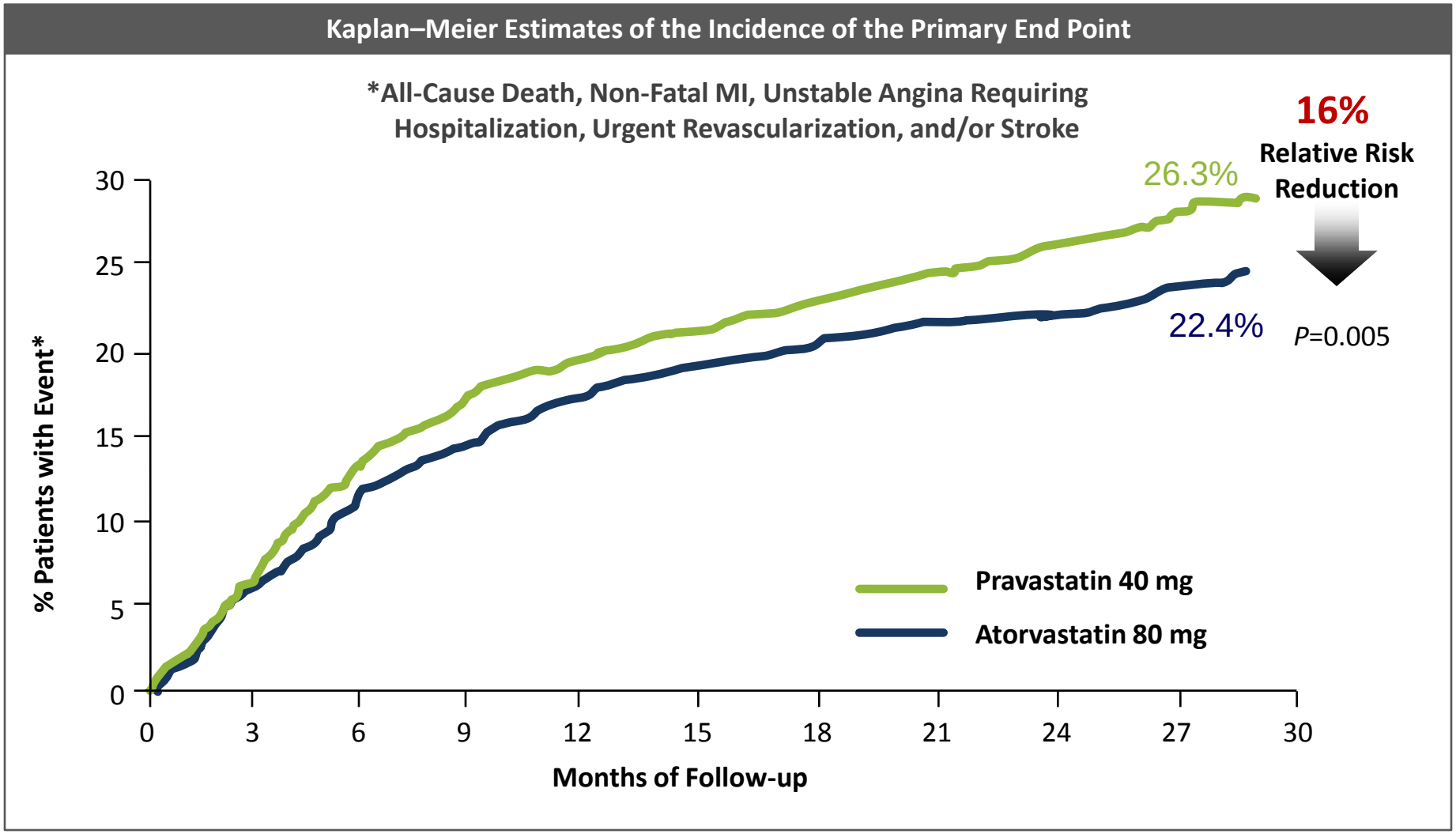
Ref. Adapted from Cannon CP, et al. N Engl J Med. 2004;350:1495-1504.

PROVE IT : Changes in LDL-C



Ref. Adapted from Cannon CP, et al. N Engl J Med. 2004;350:1495-1504.

PROVE IT: Primary End Point*



Ref. Adapted from Cannon CP, et al. N Engl J Med. 2004;350:1495-1504.

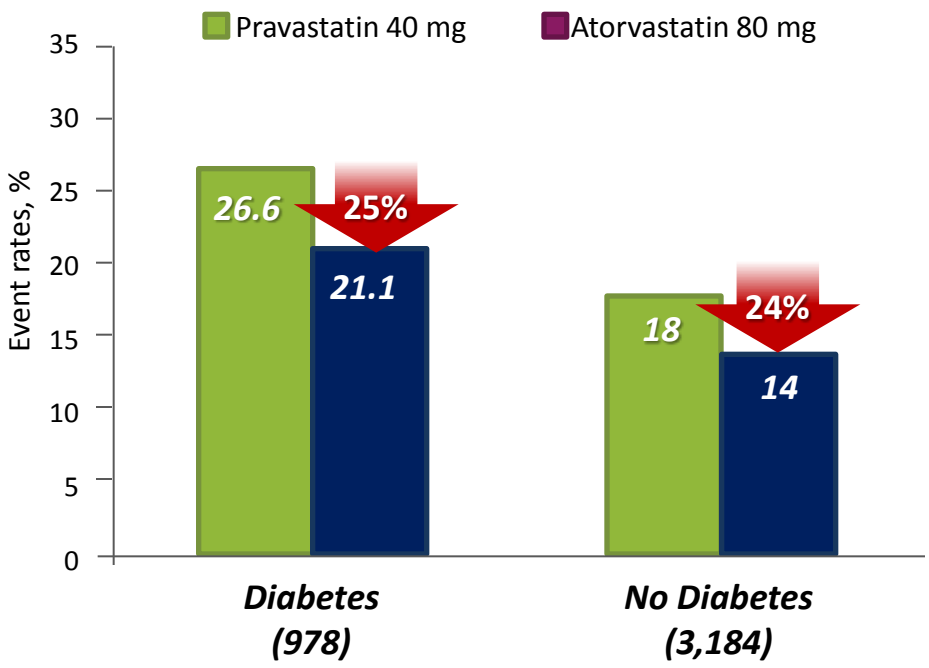
PROVE IT(DM) : Triple endpoint

978 Patients
aged ≥ 18 years
with DM, ACS

- Pravastatin 40 mg/day
- Atorvastatin 80 mg/day

- Triple endpoint : Death, MI, UA requiring rehospitalization
- Mean follow-up = 24 months

Kaplan–Meier rate of the triple endpoint by 2 years in diabetic vs.non-diabetic patients

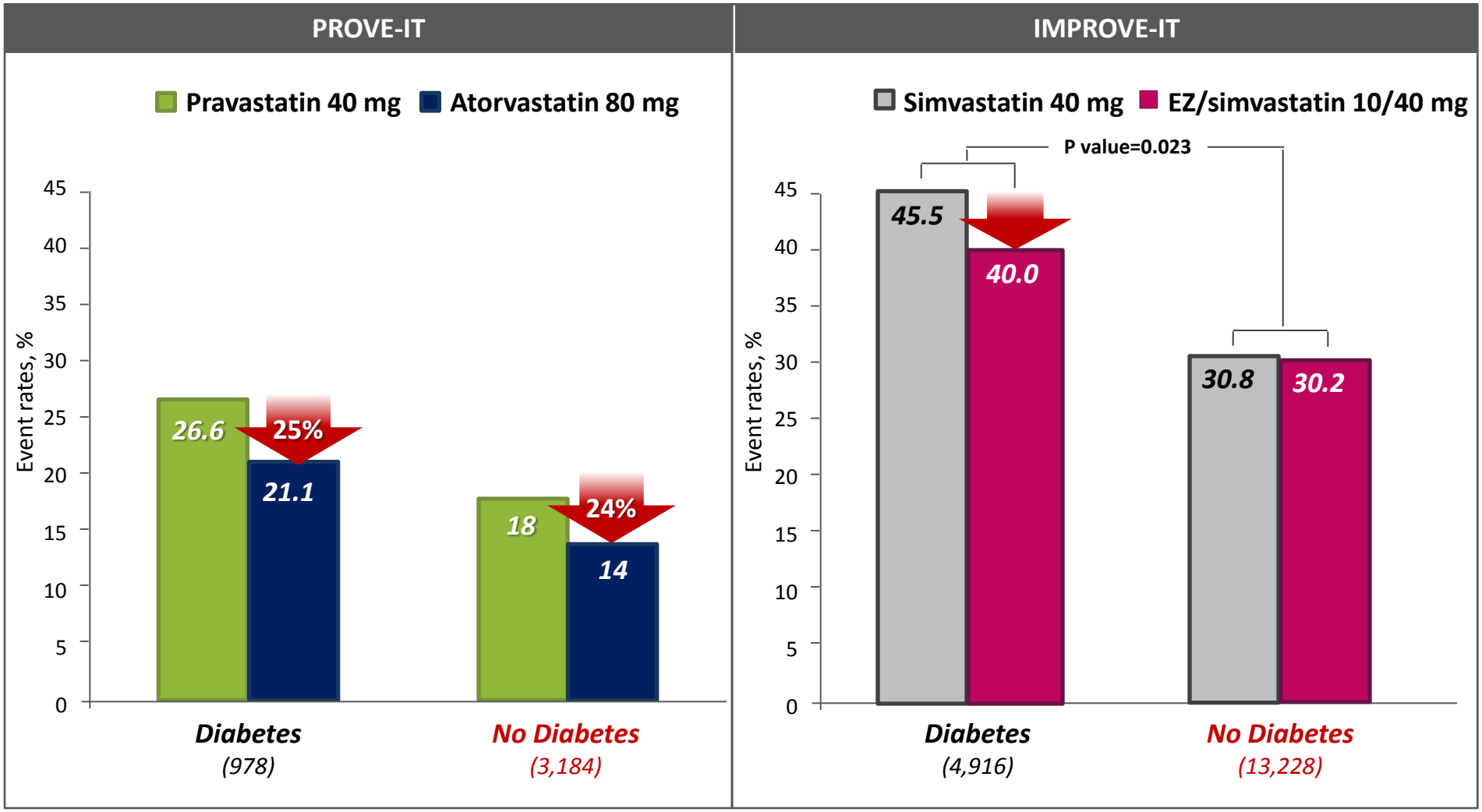


DM HR=0.75(0.58-0.97), p=0.03

no DM HR=0.76(0.64-0.90), p=0.002

Ref. Adapted from Ahmed S, et al. Eur Heart J 2006;27:2323-9.

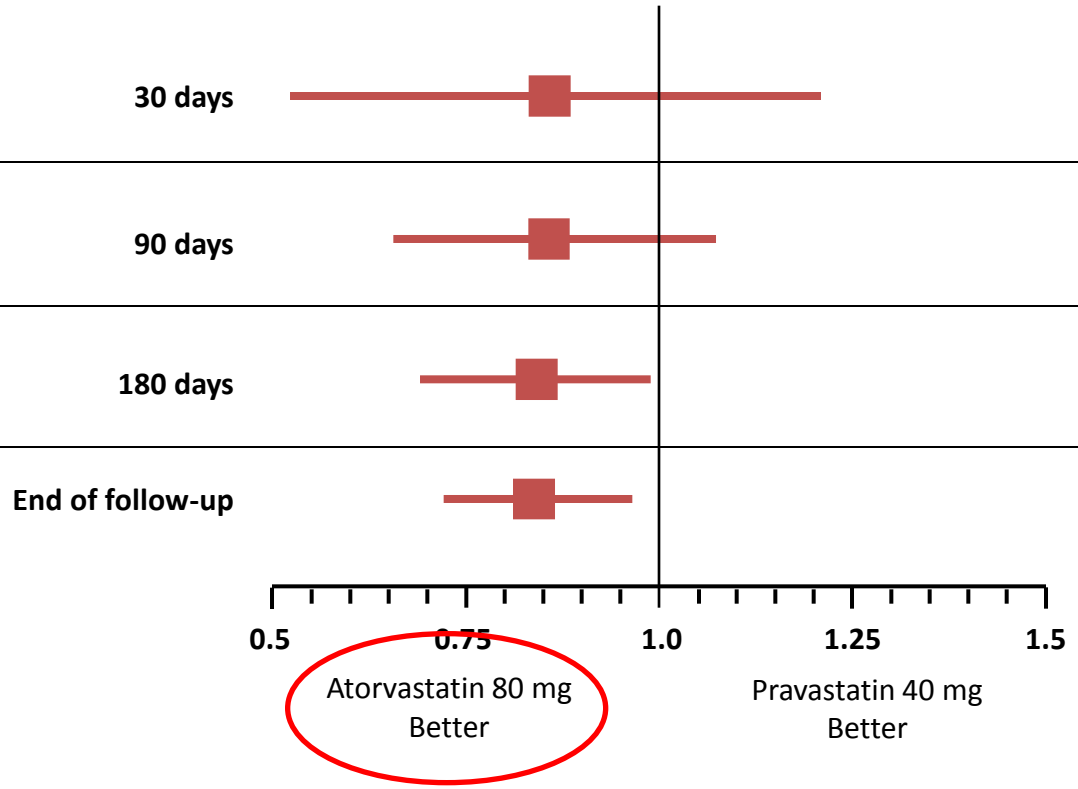
Intensive Atorvastatin vs Ezetimibe/Simvastatin in ACS patient with DM, without DM



Ref. Adapted from Ahmed S, et al. Eur Heart J 2006;27:2323-9.

PROVE IT: The benefit of high-dose atorvastatin as compared with standard-dose pravastatin emerged as early as 30 days and was consistent over time

Primary Endpoint Over Time

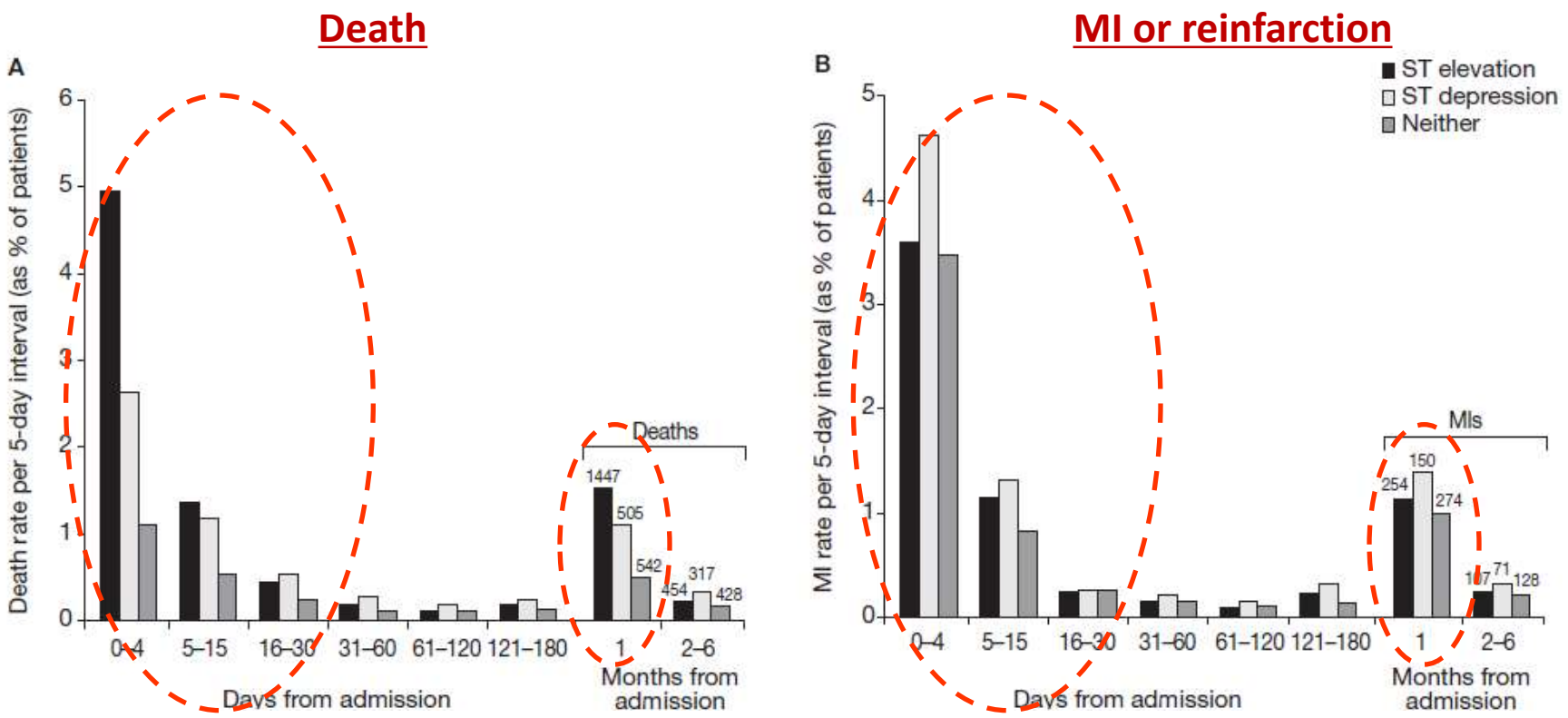


Event Rates		
RR	Atorvastatin 80 mg	Pravastatin 40 mg
17%	1.9%	2.2%
18%	6.3%	7.7%
14%	12.2%	14.1%
16%	22.4%	26.3%

Ref. Adapted from Cannon CP, et al. N Engl J Med. 2004;350:1495-1504.

Most of Death and Recurrence in Patients with ACS Occurred During 1 Month from Admission

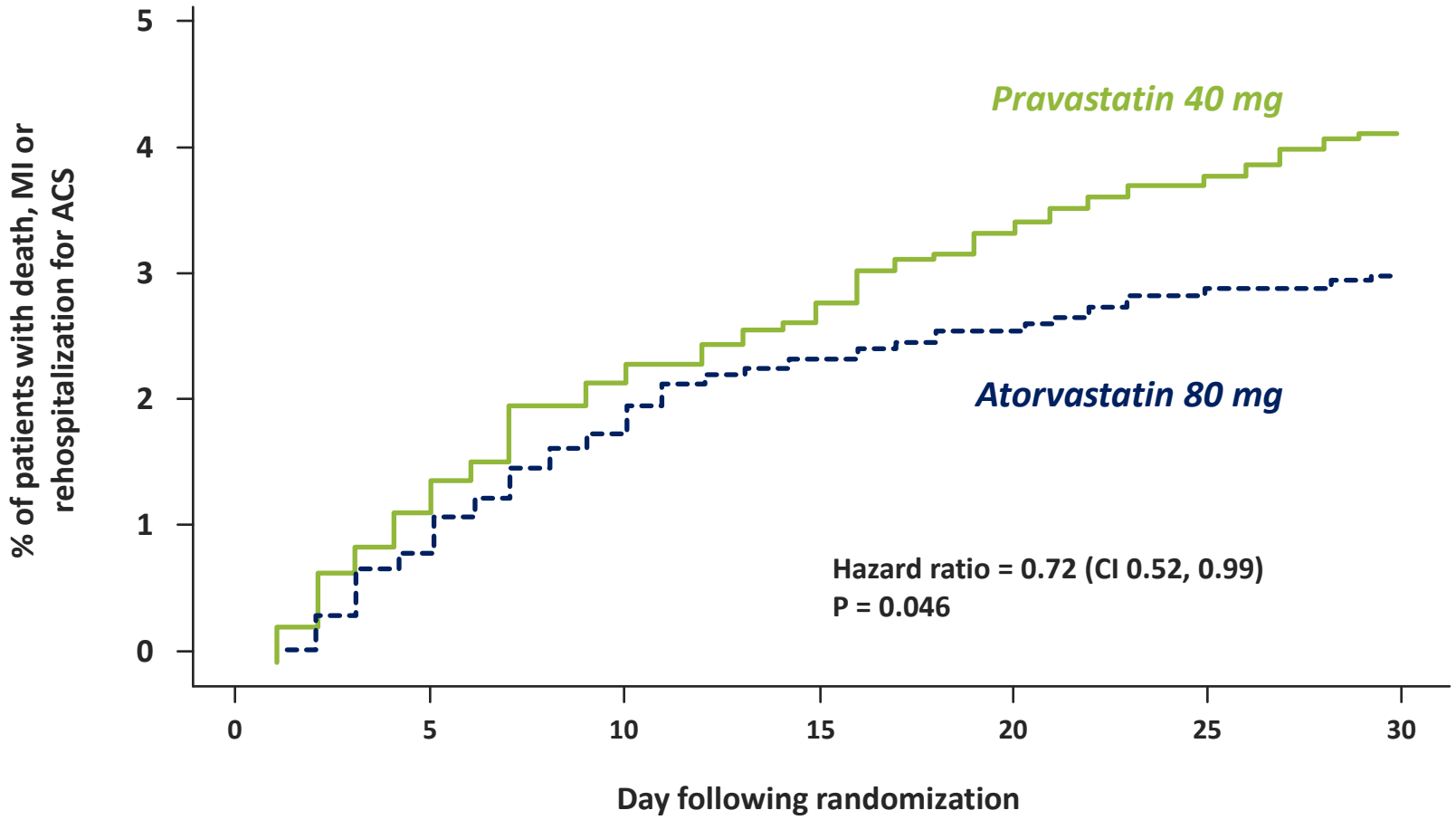
Event rates by time interval in patients presenting with acute coronary syndromes.



Ref. Adapted from Fox KA, et al. Nat Clin Pract Cardiovasc Med. 2008;5(9):580-9.

Intensive statin therapy early after ACS leads to a reduction in clinical events at 30 days

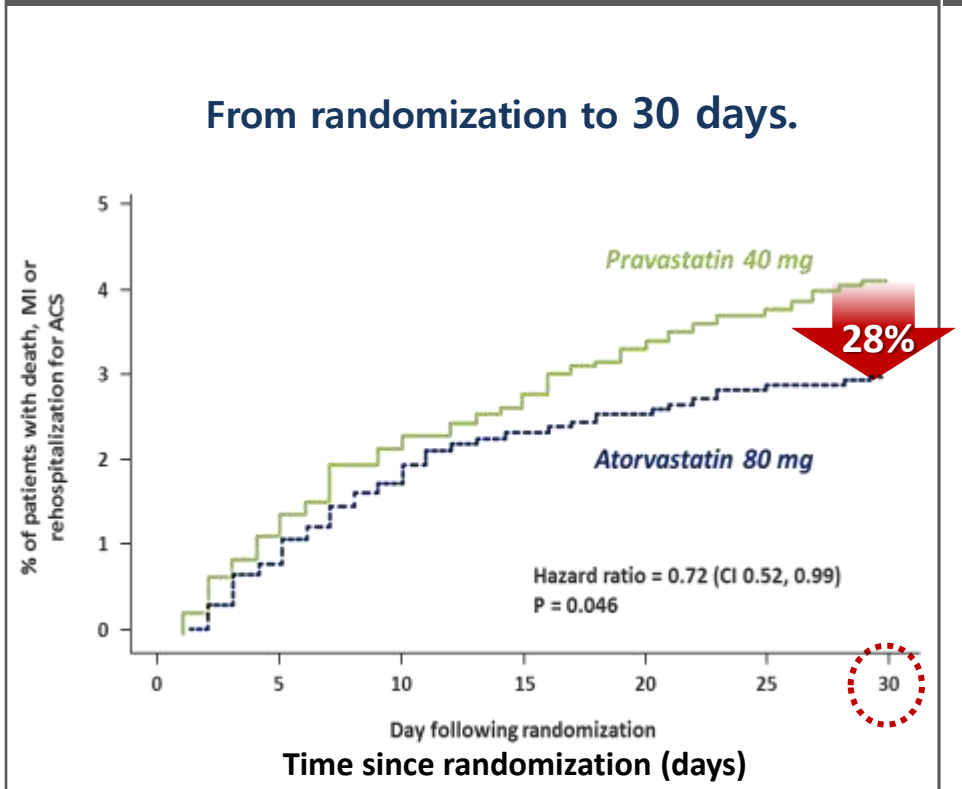
Kaplan-Meier estimates of the composite end point of death, MI, or rehospitalization with recurrent ACS from randomization to 30 days.



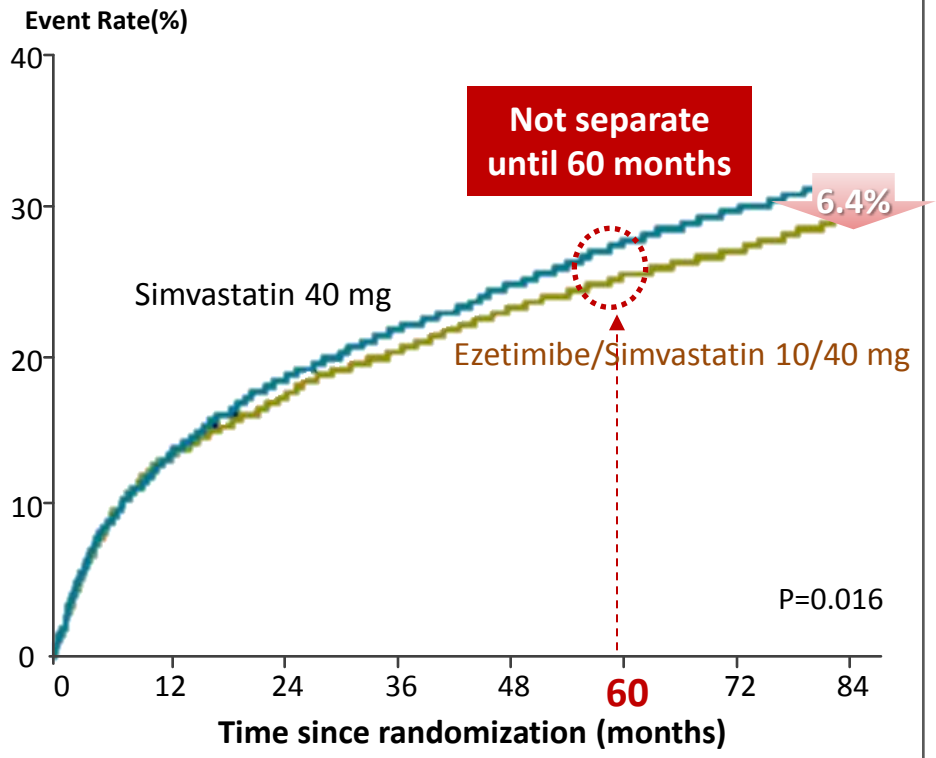
Ref. Adapted from Ray KK, et al. J Am Coll Cardiol 2005;46:1405–10

Intensive Atorvastatin vs Ezetimibe/Simvastatin in patient with ACS

PROVE-IT : death, MI, or rehospitalization



IMPROVE-IT

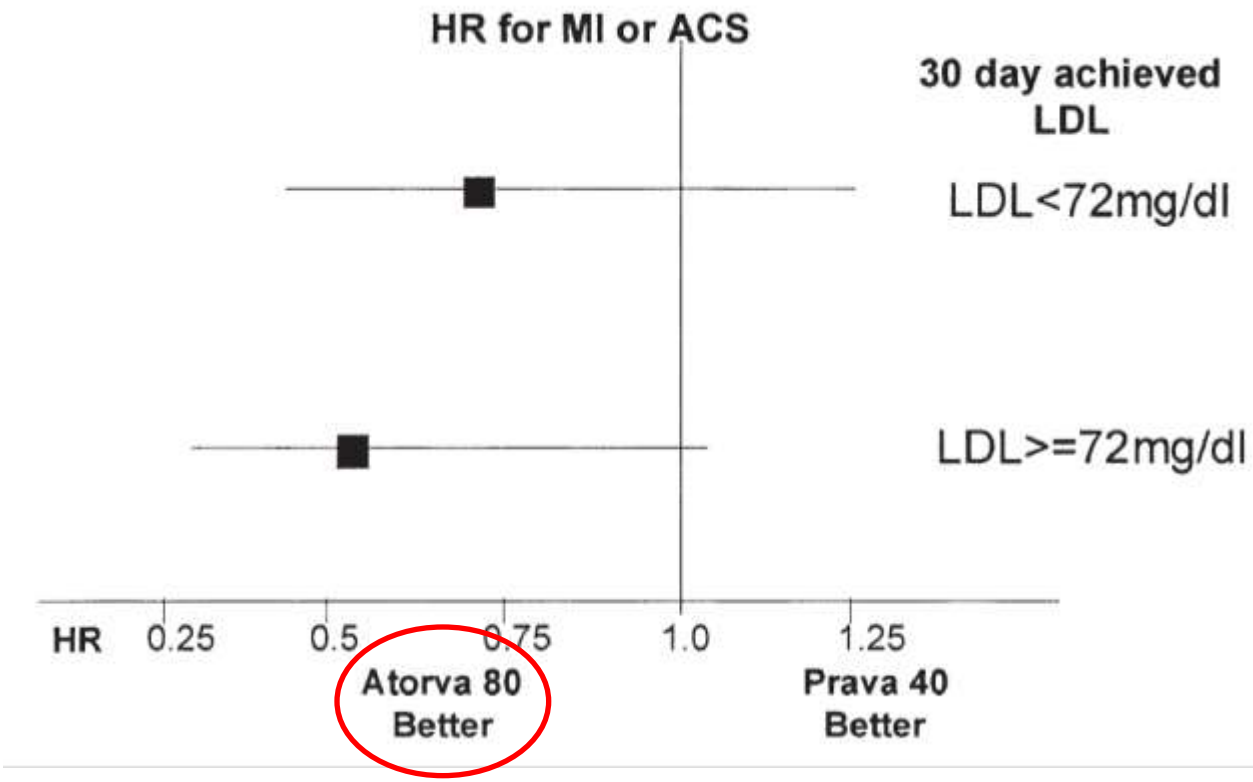


At 30 days vs after 60 month

Ref. Adapted from Ray KK, et al. J Am Coll Cardiol 2005;46:1405–10

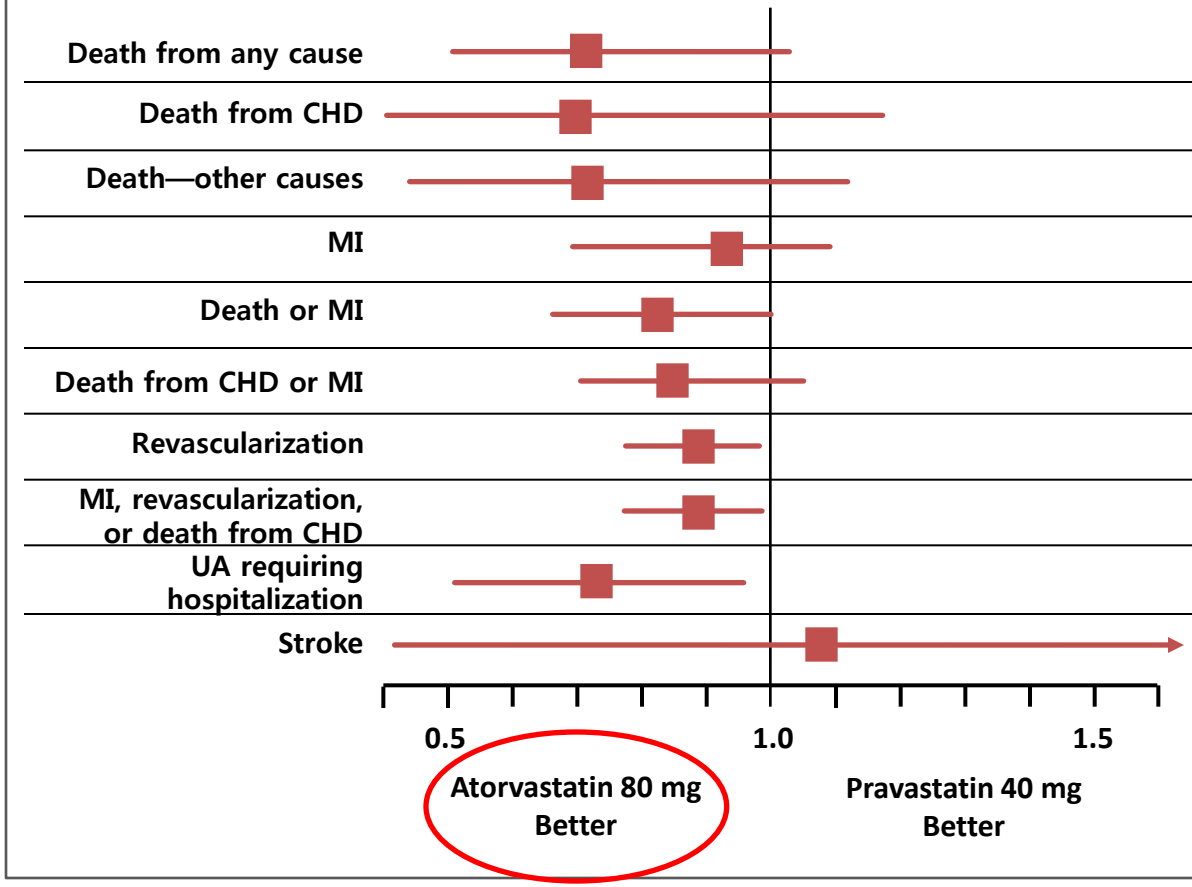
Early Benefits of Intensive Statin Therapy at 30 days were present irrespective of LDL-C reduction

Risk of MI or recurrent ACS within 30 days by median day-30 LDL-C



Ref. Adapted from Cannon CP, et al. JACC 2006;48:843–53.

PROVE IT : Reductions in Major Cardiac End Points (2-Y Event Rates)



2-Y Event Rates			
	RR	Atorvastatin 80 mg	Pravastatin 40 mg
Death from any cause	28%	2.2%	3.2%
Death from CHD	30%	1.1%	1.4%
Death—other causes	27%	1.2%	1.8%
MI	13%	6.6%	7.4%
Death or MI	18%	8.3%	10.0%
Death from CHD or MI	16%	7.2%	8.3%
Revascularization	14%	16.3%	18.8%
MI, revascularization, or death from CHD	14%	19.7%	22.3%
UA requiring hospitalization	29%	3.8%	5.1%
Stroke	-9%	1.0%	1.0%

Ref. Adapted from Cannon CP, et al. N Engl J Med. 2004;350:1495-1504.

PROVE IT : Safety Profile

	No. of Patients (%)	
	Atorvastatin 80 mg (n=2099)	Pravastatin 40 mg (n=2063)
Treatment discontinuation due to AEs*	13.8%†	10.9%†
Myopathy	NR	NR

Among patients who have recently had an acute coronary syndrome, an intensive lipid-lowering statin regimen provides greater protection against death or major cardiovascular events than does a standard regimen.

NR, not reported
ALT, alanine aminotransferase
ULN, upper limit of normal
*elevated liver-enzyme levels, elevated creatinine kinase levels, drug-related side effect, myalgia or arthralgia, or other adverse event
†calculated based on number of patients that started statin treatment (N=2086 for atorvastatin; N=2054 for pravastatin)

Ref. Adapted from Cannon CP, et al. N Engl J Med. 2004;350:1495-1504.

2012 ACCF/AHA Guidelines for the Management of Patients With Unstable Angina/NSTEMI

5.2.7. Lipid Management

Class I

1. The following lipid recommendations are beneficial:
   a. Lipid management should include assessment of a fasting lipid profile for all patients, within 24 h of hospitalization. *(Level of Evidence: C)*
   b. Hydroxymethyl glutaryl-coenzyme A reductase inhibitors (statins), in the absence of contraindications, regardless of baseline LDL-C and diet modification, should be given to post-UA/NSTEMI patients, including postrevascularization patients. *(Level of Evidence: A)*
   c. For hospitalized patients, lipid-lowering medications should be initiated before discharge. *(Level of Evidence: A)*
   d. For UA/NSTEMI patients with elevated LDL-C (greater than or equal to 100 mg per dL), cholesterol-lowering therapy should be initiated or intensified to achieve an LDL-C of less than 100 mg per dL. *(Level of Evidence: A)* Further titration to less than 70 mg per dL is reasonable. (*Class IIa, Level of Evidence: A*)
   e. Therapeutic options to reduce non–HDL-CII are recommended, including more intense LDL-C–lowering therapy. *(Level of Evidence: B)*
   f. Dietary therapy for all patients should include reduced intake of saturated fats (to less than 7% of total calories), cholesterol (to less than 200 mg per d), and trans fat (to less than 1% of energy). *(Level of Evidence: B)*
   g. Promoting daily physical activity and weight management are recommended. *(Level of Evidence: B)*
2. Treatment of triglycerides and non–HDL-C is useful, including the following:
   a. If triglycerides are 200 to 499 mg per dL, non–HDL-CII should be less than 130 mg per dL. *(Level of Evidence: B)*
   b. If triglycerides are greater than or equal to 500 mg per dL,¶¶ therapeutic options to prevent pancreatitis are fibrate## or niacin## before LDL-lowering therapy is recommended. It is also recommended that LDL-C be treated to goal after triglyceride-lowering therapy. Achievement of a non–HDL-CII less than 130 mg per dL (ie, 30 mg per dL greater than LDL-C target) if possible is recommended. *(Level of Evidence: C)*

Ref. Anderson JL, et al. Circulation. published online April 29, 2013.

2013 ACCF/AHA Guideline for the Management of STEMI

8.3. Lipid Management: Recommendations

CLASS I

1. High-intensity statin therapy should be initiated or continued in all patients with STEMI and no contraindications to its use (434–436). (*Level of Evidence: B*)

Ref. O'Gara PT, et al. J Am Coll Cardiol. 2013;61(4):e78-e140.

Evidence in 2013 ACC/AHA guideline update

Clinical ASCVD

Yes

Age ≤ 75 y ➡ High-intensity statin
(if not candidate ➡ Moderate-intensity statin)

Evidence statement 6

In adult with CHD/CVD, fixed high intensity statin treatment (atorvastatin 40-80 mg) that achieved a mean LDL-C 67-79 mg/dL reduced the RR for CHD/CVD events more than fixed lower-dose statin treatment that achieved a mean LDL-C 97-102 mg/dL. In these trials, the mean LDL-C levels achieved differed by 23-30 mg/dL, or 22%-30%, between the 2 groups. Simvastatin 80 mg did not decrease CVD events compared with simvastatin 20-40 mg	**H**	***Secondary Prevention***	**Benefit:** **TNT**(46), IDEAL(47), **PROVE-IT(48)** **Lower LDL-C reduction, no benefit :** A-Z(119), ACCORD(14) **No difference in LDL-C between groups :** (SEARCH (128) not included in CQ1)

Conclusion

- **Patients with established CHD are at much higher risk of recurrent events or death than the general population.**
- **Intensive statin therapy with atorvastatin 80 mg/d in patients with stable CHD provides significant clinical benefit compared with atorvastatin 10 mg/d.**
- **The TNT study was the first RCT designed to demonstrate the benefits of lowering LDL-C well below 100 mg/dL in stable CHD patients.**

Conclusion

- **In the PROVE IT trial, Intensive statin therapy with atorvastatin 80 mg/d in patients post-ACS provides significant clinical benefits compared to pravastatin 40 mg/d and leads to a reduction in clinical events at 30 days, consistent with greater early pleiotropic effects.**

- **The TNT and PROVE IT studies are the important evidences of major guidelines on secondary prevention for CHD.**

Thank You For Your Attention