

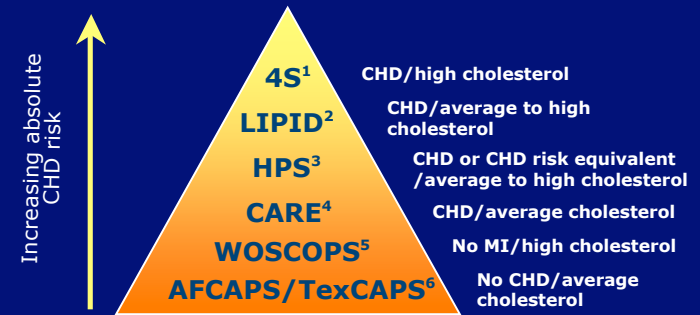
From Vulnerable Plaque to the Vulnerable Patients: A Call to Action

## Evolution of Statin Trials on Vulnerable Plaque

Robert C. Welsh, MD, FRCPC  
 Associate Professor, University of Alberta  
 Chair, Vital Heart Response  
 Director, University of Alberta Cardiology Residency Training Program



## Key statin studies and spectrum of risk



1. The Scandinavian Simvastatin Survival Study Group. *Lancet* 1994;344:1383-1389. 2. The Long-term Intervention with Pravastatin in Ischaemic Disease Study Group. *NEJM* 1998;339:1349-1357. 3. Heart Protection Study Collaborative Group. *Lancet* 2002;360:722. 4. Sacks FM et al. *NEJM* 1996;335:1001-1009. 5. Shepherd J et al. *NEJM* 1995;333:1301-1307. 6. Downs JR et al. *JAMA* 1998;279:1615-1622.

## ASTEROID: Mean baseline and follow-up levels of LDL and HDL cholesterol

Angiographically documented CAD and IVUS

Treatment	LDL-C: baseline (mmol/L)	LDL-C: 24 mo (mmol/L)	p	HDL-C: baseline (mmol/L)	HDL-C: 24 mo (mmol/L)	p
Rosuvastatin 40 mg (n=346)	3.42	1.58	<0.001	1.15	1.29	<0.001

Nissen SE et al. *JAMA* 2006; available at: <http://www.jama.com>.

## ASTEROID: Baseline and follow-up intravascular ultrasound results

IVUS-derived measure	Baseline	24-month follow-up	Absolute change	Relative change (%)
Mean percent atheroma volume (n=349)	39.6	38.6	- 0.98	NA
Mean atheroma volume in the most disease 10-mm subsegment, mm <sup>3</sup> (n=319)	65.1	59.0	- 6.1	- 8.5
Mean normalized total atheroma volume, mm <sup>3</sup> (n=349)	212.2	197.5	- 14.7	- 6.7

Nissen SE et al. *JAMA* 2006; available at: <http://www.jama.com>.

## IDEAL study – primary prevention Changes in lipid parameters

Statin (89%), niacin (65.4%), fibrates (27.0%), and ezetimibe (14%). More than 3/4 of patients received combination lipid-lowering therapy.

Lipid measurement (mg/dL)	Baseline	1 y	p
Total cholesterol	198	160	<0.001
Triglycerides	109	80	<0.001
HDL cholesterol	55	59	<0.001
LDL cholesterol	113	89	<0.001
Apolipoprotein B	90	77	<0.001
Non-HDL cholesterol	143	101	<0.001

Bale BF et al. 2006 International Symposium on Atherosclerosis; June 20, 2006; Rome, Italy.

## IDEAL study Carotid intima-media thickness results

Parameter	Baseline	1 y	p
Common carotid IMT (mm)	0.771±0.118	0.736±0.110	<0.001
Number of plaques	2.0±1.5	1.8±2.0	<0.001
Sum of plaques (plaque burden)	4.2±3.8	3.7±3.4	<0.001

Bale BF et al. 2006 International Symposium on Atherosclerosis; June 20, 2006; Rome, Italy.

## Primary Prevention Summary of treatment effects of statin therapy

Source	Major coronary events	Major cerebrovascular events	All-cause mortality	CHD mortality	Nonfatal MI	Revascularizations
All trials	0.71	0.86	0.92	0.77	0.68	0.66
Overall p	<0.001	0.02	0.09	0.13	<0.001	<0.001

42 848 patients were studied in the meta-analysis, and the mean pretreatment LDL-cholesterol level was 3.78 mmol/L

Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS)  
West of Scotland Coronary Prevention Study (WOSCOPS)  
Pravastatin in Elderly Individuals at Risk of Vascular Disease (PROSPER) study  
Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT-LLT)  
Collaborative Atorvastatin Diabetes Study (CARDS)  
ALLHAT-LLA diabetic subgroup in the Heart Protection Study (HPS).

Thavandiranathan P et al. *Arch Intern Med* 2006; 166:2307-2313.

## Effect of Rosuvastatin on Progression of Carotid Intima Media Thickness in Low Risk Individuals: Results of the METEOR Trial

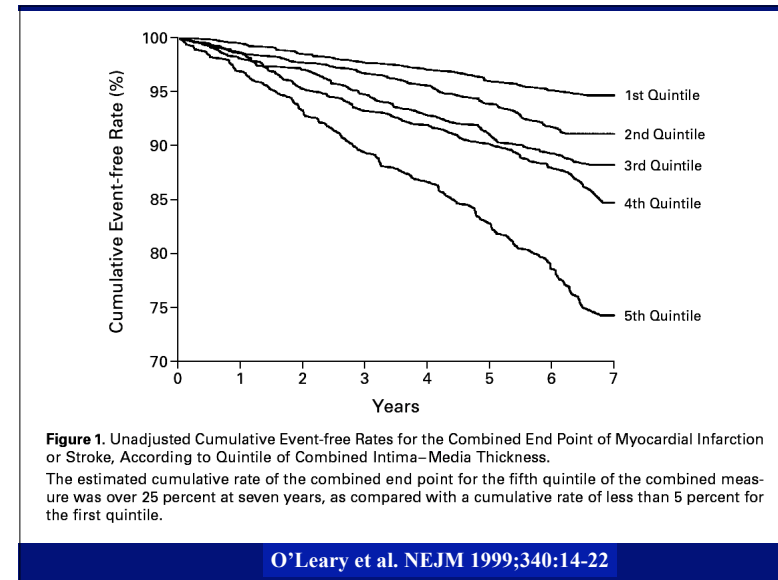
### Measuring Effects on Intima Media Thickness: an Evaluation Of Rosuvastatin

### METEOR

Crouse JR, Raichlen JS, Riley WA, et al. Effect of Rosuvastatin on Progression of carotid intima-media thickness in low-risk individuals with subclinical atherosclerosis: the METEOR trial. *JAMA* 2007; 297: (doi:10.1001/jama.297.12.joc70024)

## Rationale

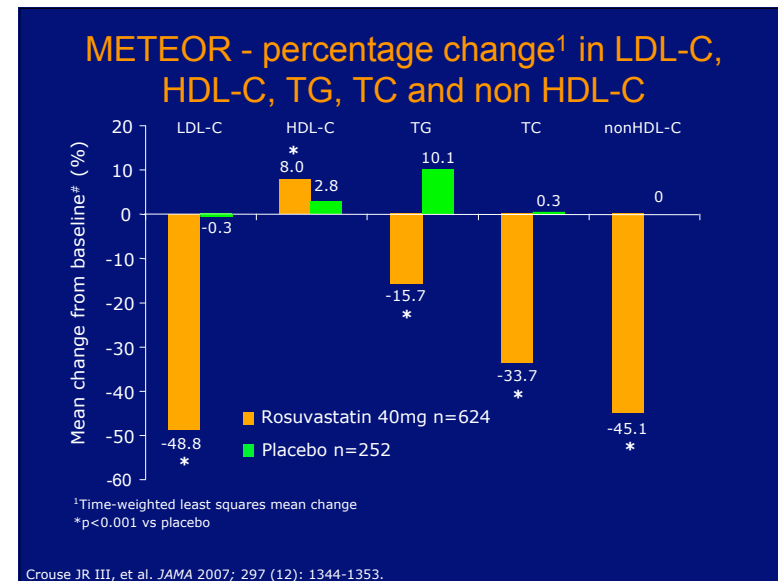
- Carotid intima media thickness (CIMT) is a reliable marker of atherosclerotic burden, relates to cardiovascular risk factors, and predicts future cardiovascular events
- Greater LDL-C reductions with more intensive statin therapy may result in greater effects on atherosclerosis
- Further studies are needed to confirm the effects of efficacious statins in low risk individuals with subclinical disease



## Study Population

### Major inclusion criteria

- Men aged 45–70 years; women aged 55–70 years
- LDL-C 3.1 to <4.9 mmol/L with no coronary heart disease (CHD) risk factor other than age
- LDL-C 3.1 to <4.1 mmol/L with >1 risk factor and a 10-year CHD risk of <10%
- Triglycerides <5.7 mmol/L
- Maximum CIMT of at least 1.2 mm at any site and less than 3.5 mm in all sites



METEOR – Primary Endpoint  
*Change in maximum CIMT for the primary endpoint  
(12 carotid artery sites) estimated from the statistical model*

