Pharmacological Modification of Biomarkers and CV Risk

Jin-Ok Jeong
Cardiovascular Center
Chungnam National University Hospital

The Ideal Biomarker

2007	2011
Sensitive and specific	Either highly sensitive(diagnostic) or Highly specific(treatment effect)
Reflects disease severity	Reflects abnormal physiology/biochemistry
Correlates with prognosis	Prognosis is most meaningful if level i s clinically actionable
Should aid in clinical decision making	Should be used as a basis for specific "biomarker guided-therapy"
Level should decrease following effecti ve therapy	"Bio-monitoring" during treatment is an effective surrogate of improvement

Maisel, JACC 2011

Biomarkers

1. BNP
2. Arterial stiffness
3. LDL/ HDL
4. hs-CRP
5. Lp-PLA
6. Vascular calcification

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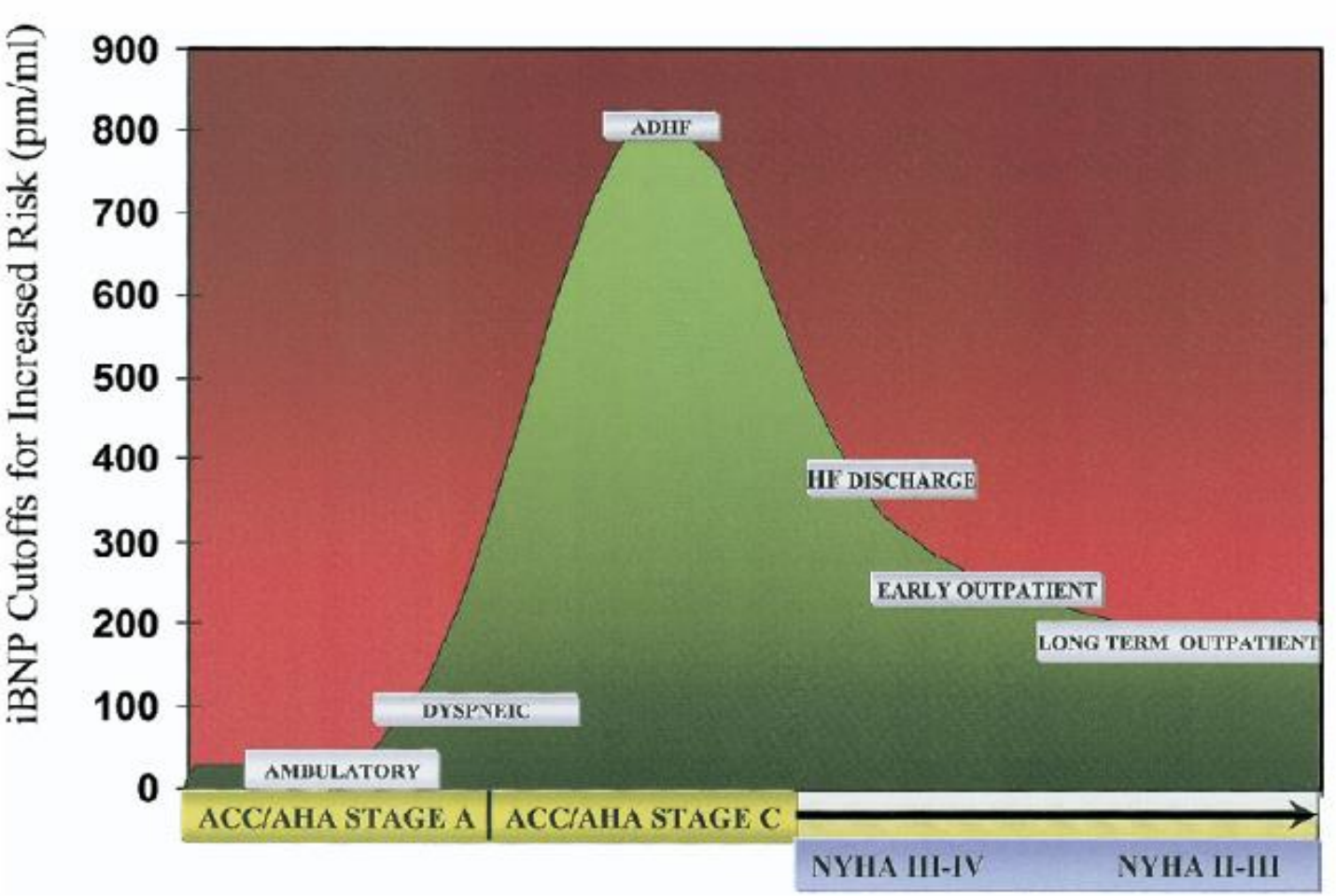
BNP in Heart Failure



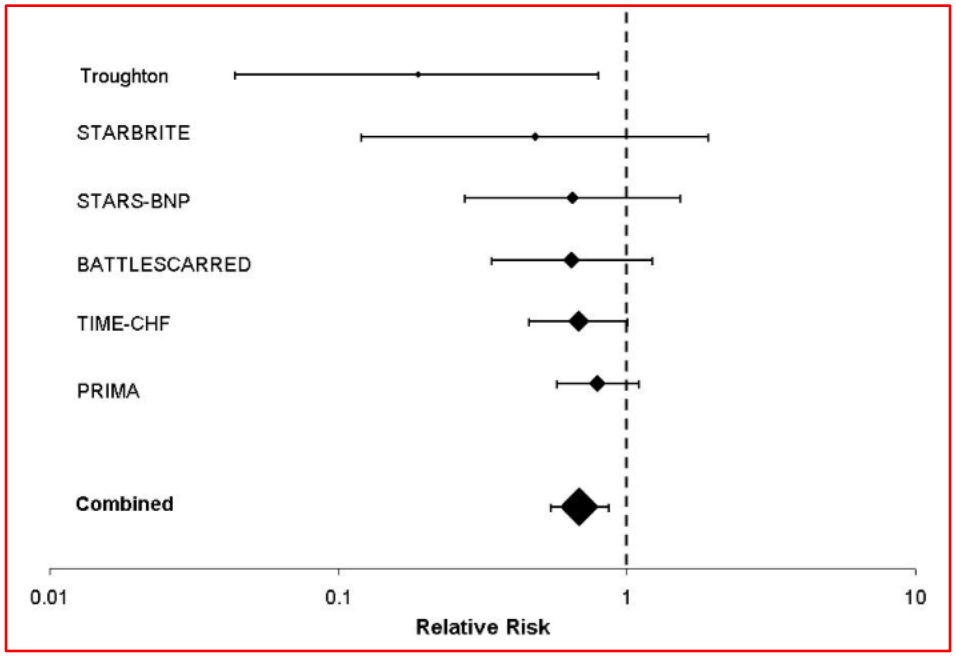
Mills RM. JACC 2008;51:2336

Therapies with Effects on B-Type Natriuretic Peptide Levels

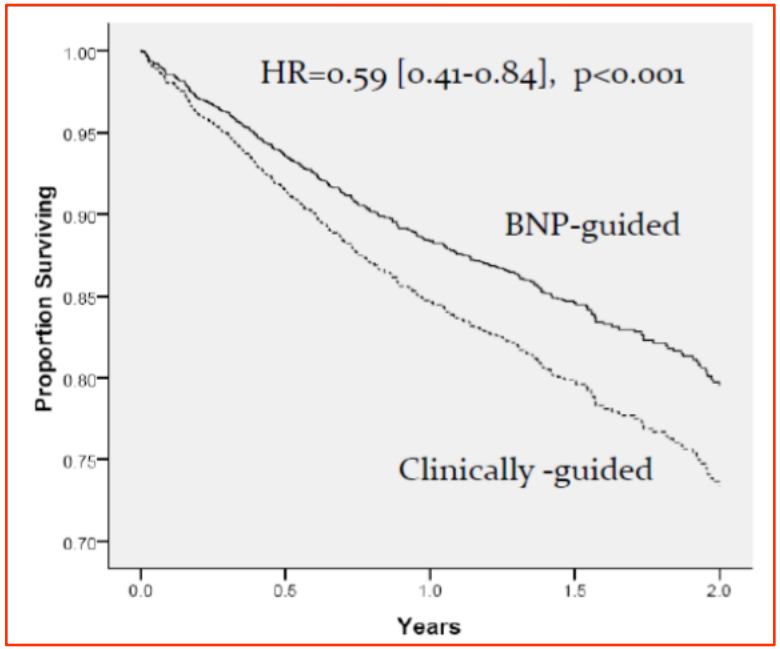
Therapy	Effect on BNP/NT-proBNP
Diuresis	↓
ACE-I	↓
ARB	↓
β-blockers	Some transiently ↑, most ↓
Aldosterone antagonists	↓
BiV pacing	↓
Exercise	↓
Rate control of AF	↓
BNP infusions	↓ N-BNP, ↑BNP then ↓

Guided therapy combined analyses

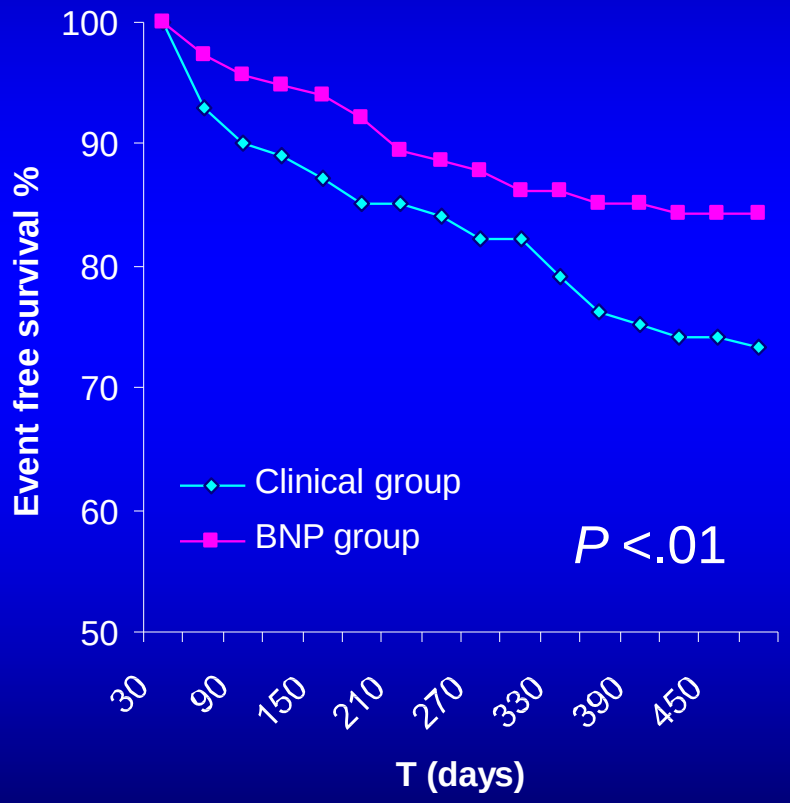
Meta analysis of publication data

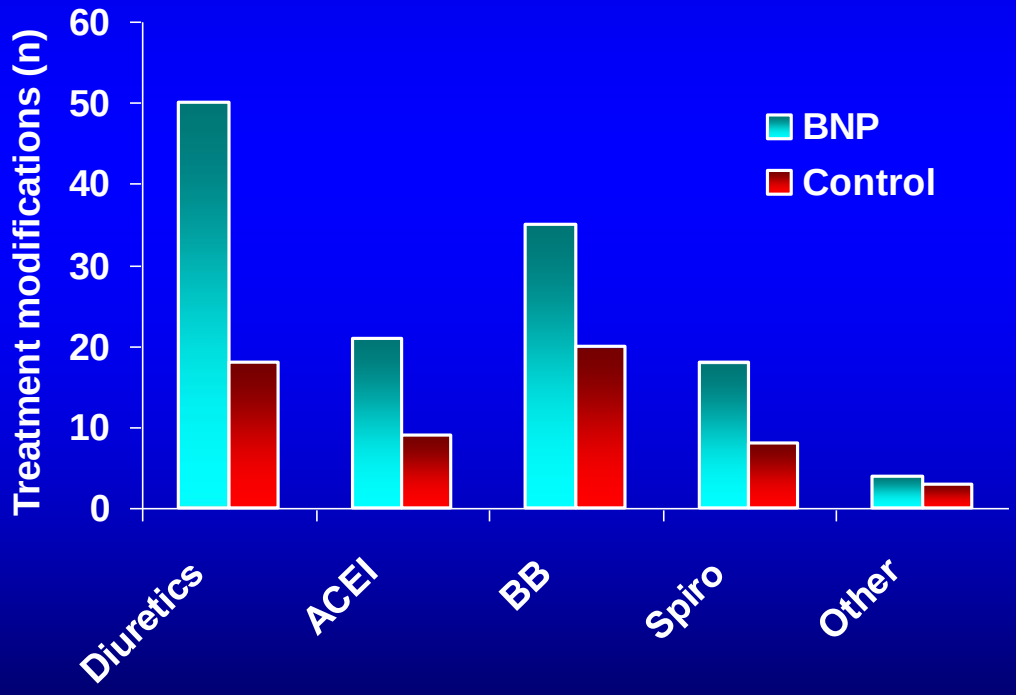


Pooled patient data from all available trials



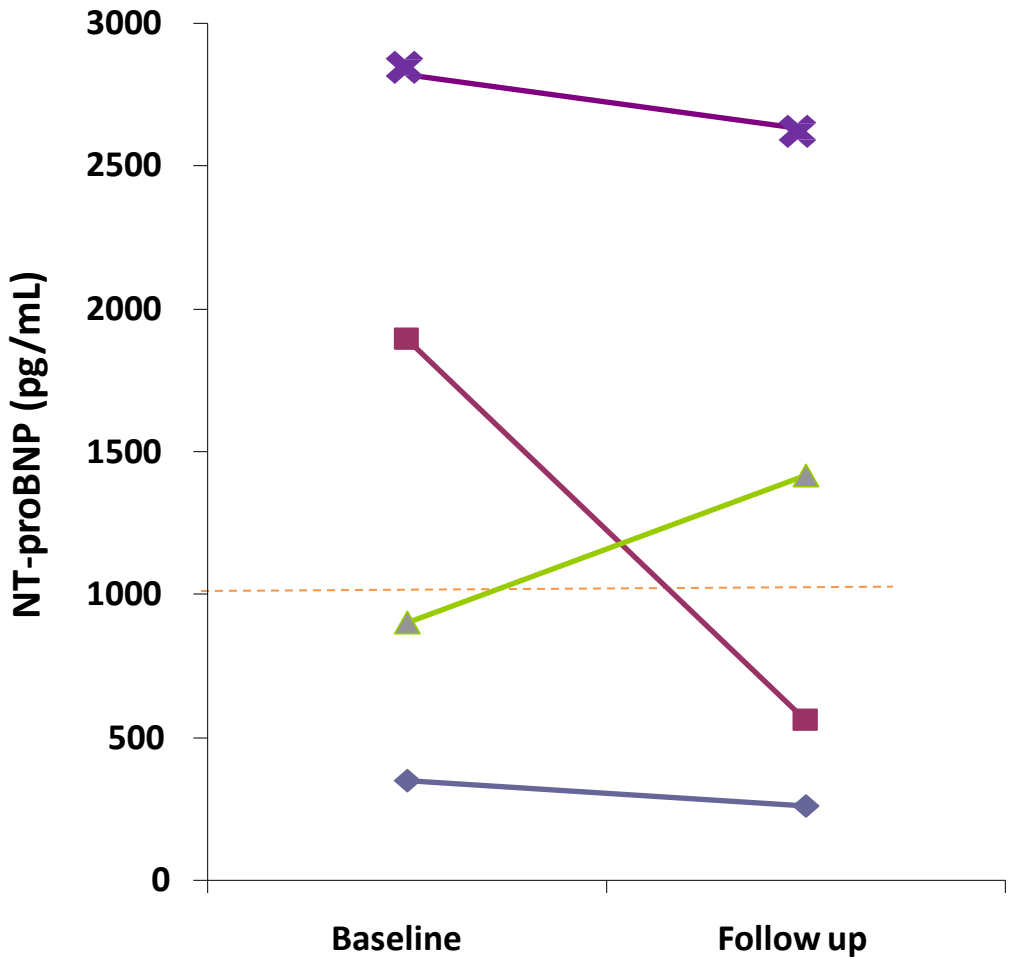
BNP guided HF therapy: STARS





Jourdain, et al, JACC, 2007

Outcomes as a function of response to guided therapy



Group	Mean CV events
High/High	1.57*
Low/High	0.71
High/Low	0.46
Low/Low	0.50

* p = 0.003 versus Low/Low group, p = 0.002 versus High/Low group

Summary of natriuretic peptide testing in ADHF

- Baseline measurement for diagnosis
- Most HF medication decrease BNP (ACEi/ARB, BB, MRA, Diuretics)
- Pre-discharge measurement to assess treatment response:
  - If rise >30%: discharge delayed, ↑Rx
  - If change <30%: possible discharge delay
  - If fall >30%: discharge authorized

Biomarkers

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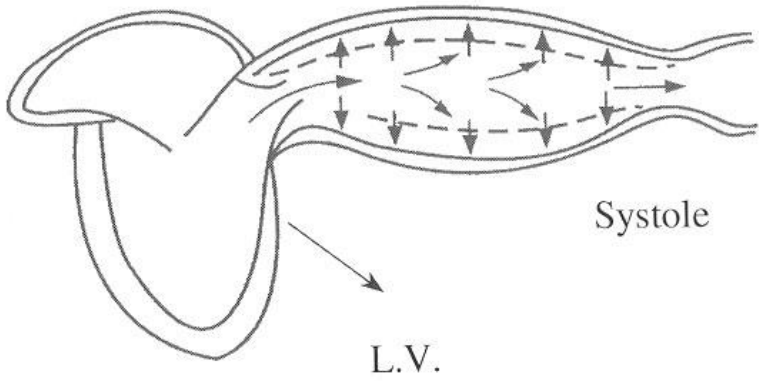
Pulse Wave Velocity

- LV contraction → blood ejection into Asc aorta → generate pulse wave



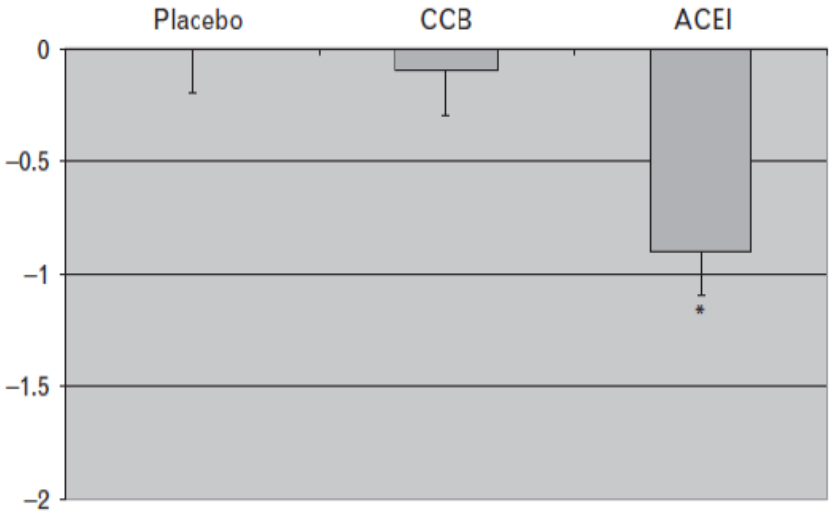
- **Pulse wave velocity**
  - Propagation velocity of pulse wave
  - Index of arterial distensibility and stiffness
  - Higher velocity: higher arterial rigidity, lower distensibility

Raised PWV

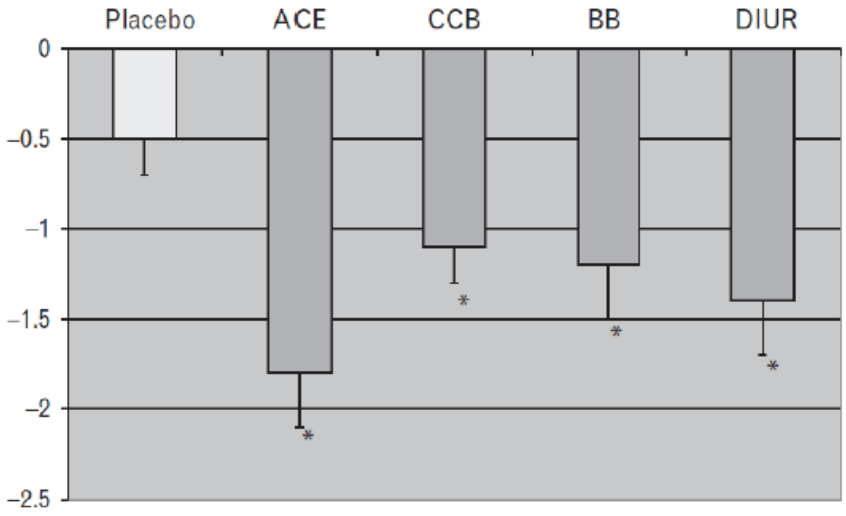
- Established CV risk factors
  - Age, hypercholesterolemia, type II diabetes, sedentary lifestyle
- Independent predictor of CV and all cause mortality in hypertensives
  - 5m/s ↑→ 1.34 all cause mortality, 1.51 CV mortality
  - Aortic PWV >13m/s, strong predictor of CV mortality
- Stroke (relative risk = 1.39 for each 4 m/sec increase) independently of classical CV risk factors

Aortic stiffness is reduced beyond BP lowering

Short term (0-8days)



Long term (1-6months)



Ong KT, et al. J Hypertens 2011;29:1034-42

Anti-hypertensives & Increased Aortic Stiffness

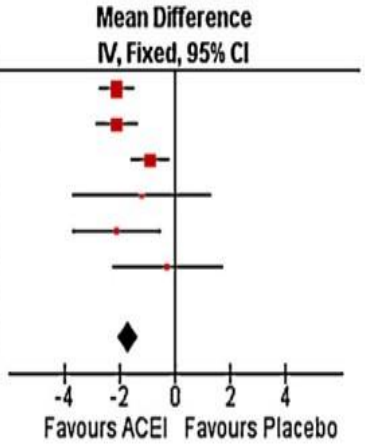
Meta-analysis of RCTs : ACEi vs Placebo

PWV

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Ahimastos 2007	-2.1	0.31	35.3%	-2.10 [-2.71, -1.49]
Ahimastos 2008	-2.1	0.36	26.2%	-2.10 [-2.81, -1.39]
Mitchell 2007	-0.9	0.35	27.7%	-0.90 [-1.59, -0.21]
Rahman 2007 A	-1.2	1.27	2.1%	-1.20 [-3.69, 1.29]
Rahman 2007 B	-2.1	0.8	5.3%	-2.10 [-3.67, -0.53]
Yu 2006	-0.3	1	3.4%	-0.30 [-2.26, 1.66]
Total (95% CI)			**100.0%**	**-1.69 [-2.05, -1.33]**

Heterogeneity: $Chi^2 = 10.48$, df = 5 (P = 0.06); $I^2 = 52\%$

Test for overall effect: Z = 9.16 (P < 0.00001)

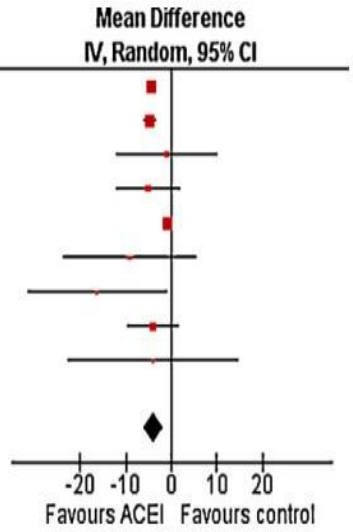


AIx

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Random, 95% CI
Ahimastos 2008	-4.4	0.36	25.2%	-4.40 [-5.11, -3.69]
Dart 2001	-4.7	0.68	23.6%	-4.70 [-6.03, -3.37]
Deary 2002 (F)	-1	5.55	3.4%	-1.00 [-11.88, 9.88]
Deary 2002 (M)	-5	3.48	7.3%	-5.00 [-11.82, 1.82]
Mitchell 2007	-0.9	0.36	25.2%	-0.90 [-1.61, -0.19]
Rahman 2007 A	-9.1	7.41	2.0%	-9.10 [-23.62, 5.42]
Rahman 2007 B	-16.2	7.68	1.9%	-16.20 [-31.25, -1.15]
Tsang 2006	-4	2.75	9.9%	-4.00 [-9.39, 1.39]
Yu 2006	-4	9.39	1.3%	-4.00 [-22.40, 14.40]
Total (95% CI)			**100.0%**	**-3.79 [-5.96, -1.63]**

Heterogeneity: $Tau^2 = 4.70$; $Chi^2 = 59.56$, df = 8 (P < 0.00001); $I^2 = 87\%$

Test for overall effect: Z = 3.43 (P = 0.0006)



Shahin et al. Atherosclerosis 221 (2012) 18–33

ARB improves baPWV independent of BP in type 2 diabetic patients with hypertension.

Candesartan significantly improves baPWV independent of BP.

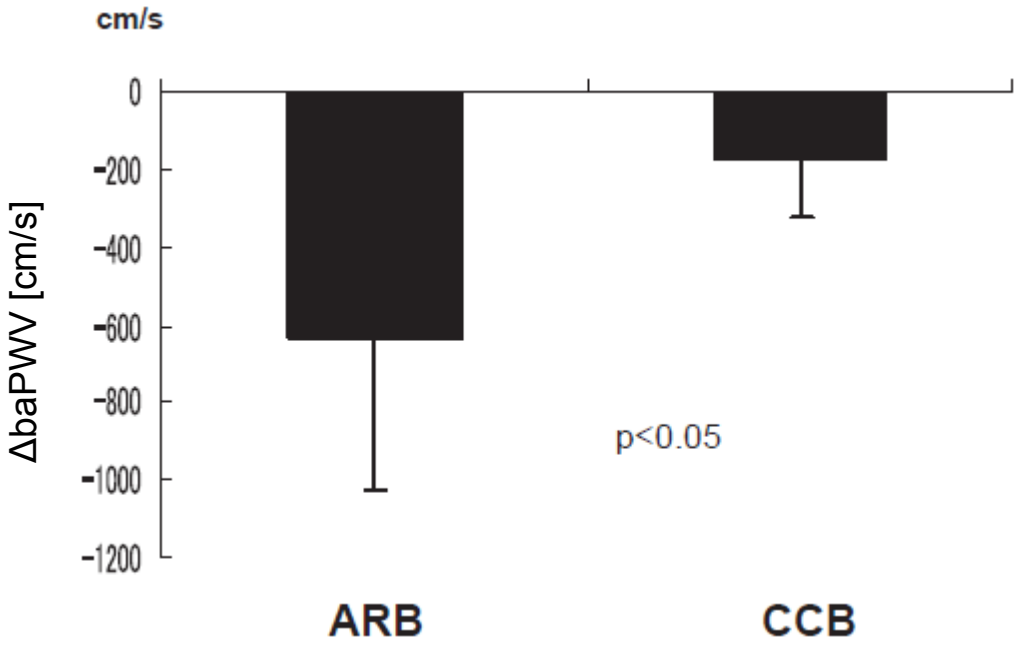


Fig.1 Change in baPWV

Study Data:
22 Type 2 diabetic patients with hypertension received either ARB (candesartan, n = 11) or a calcium channel blocker (amlodipine or nifedipine, n = 11) for 12 weeks.

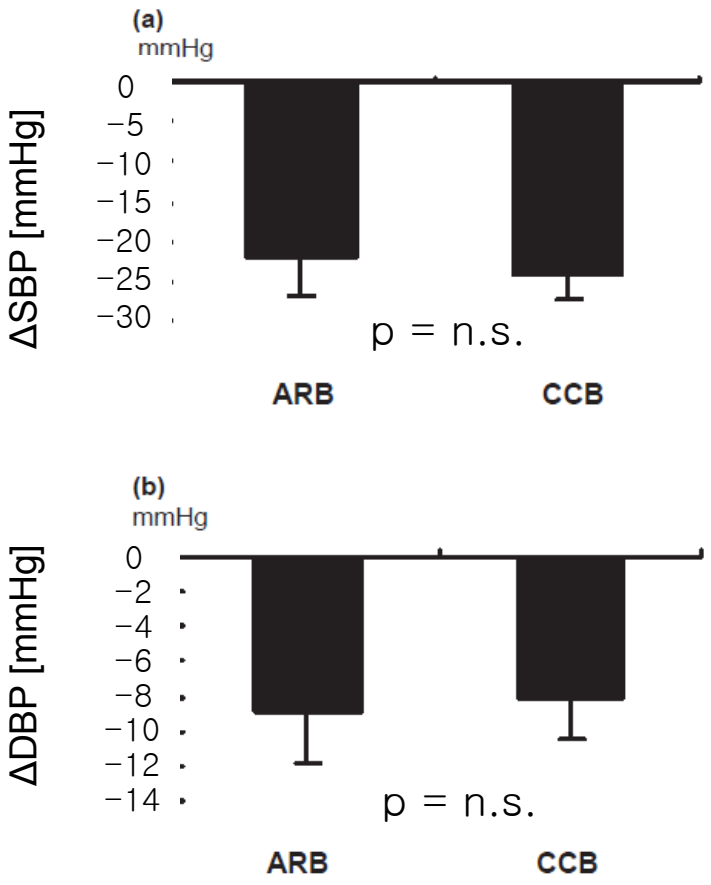
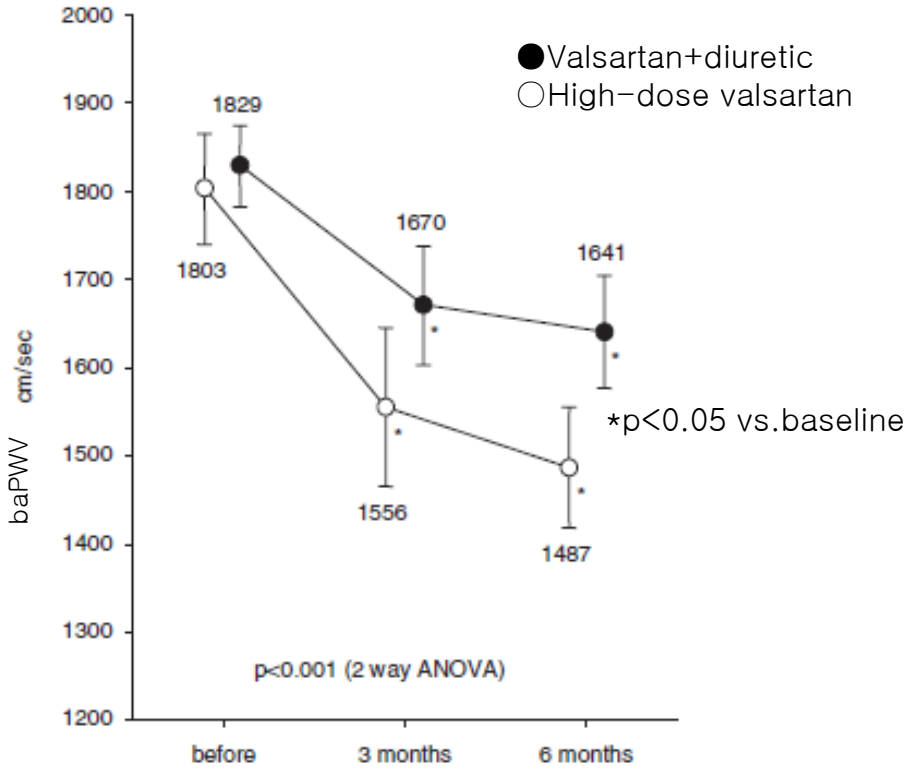


Fig.2 Change in Brachial SBP (a) and Brachial DBP (b)

Ishii H et al., Intern Med. 2008;47(23):2013-8.
Angiotensin II type-I receptor blocker, candesartan, improves brachial-ankle pulse wave velocity independent of its blood pressure lowering effects in type 2 diabetes patients.

Effect of high-dose ARB and ARB plus low-dose diuretic on baPWV

High-dose ARB: valsartan improves baPWV.



Subjects and methods:
Subjects: 43 patients with morning hypertension despite treatment with 80mg valsartan were randomly assigned to receive 160 mg valsartan (n = 22) or 80mg valsartan puls low-dose trichlormethiazide (1mg) (n = 21) for 6 months. Japanese.

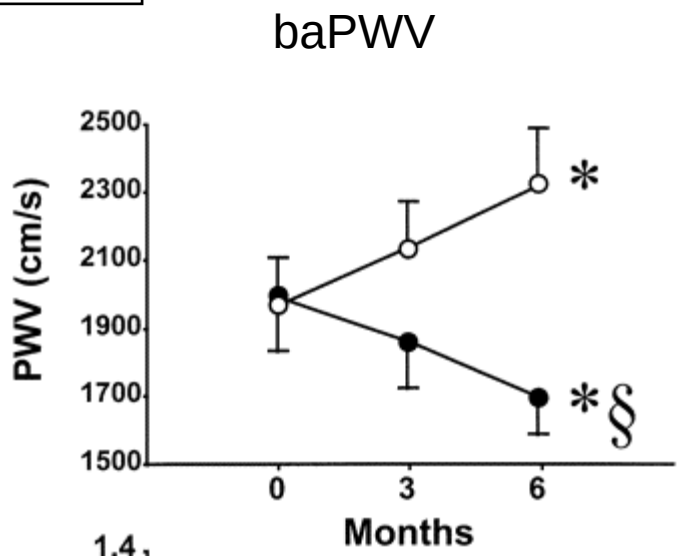
Takami T et al., Hypertens Res. 2009 Oct;32(10):884-8. Epub 2009 Sep 4.
Evaluation of arterial stiffness in morning hypertension under high-dose valsartan compared to valsartan plus low-dose diuretic.

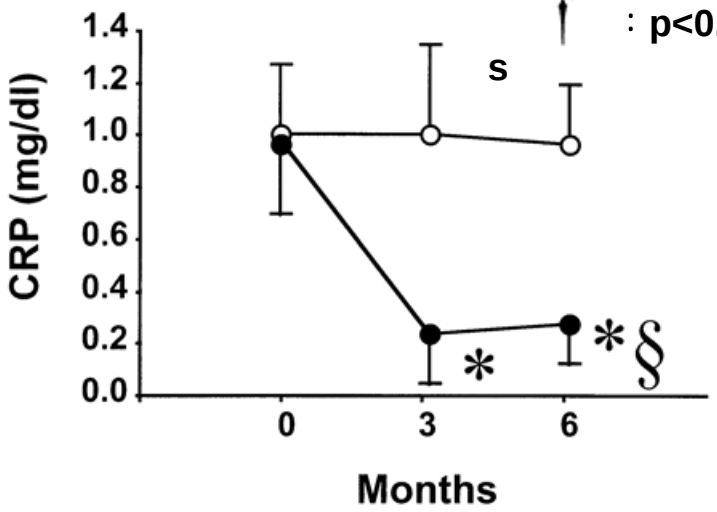
Fluvastatin prevents development of arterial stiffness in hemo-dialysis patients with type 2 diabetes mellitus.

Fluvastatin significantly reduces baPWV and decreases serum concentrations of CRP.

●:Fluvastatin
○:Placebo

* : p<0.05 vs 0 month
§ : p<0.05 vs placebo
† : p<0.05 vs 3 month





Study Data:
Subjects: 22 hemodialysis patients with type 2 diabetes received fluvastatin (20mg/day) or a placebo for 6 month.

Ichihara A et.al., Nephrol Dial Transplant (2002) 17:1513-1517
Fluvastatin prevents development of arterial stiffness in heamodialysis patients with type 2 diabetes mellitus.

Effects of Pharmacologic Intervention

- All antihypertensive drugs reduce arterial stiffness (passive decrease of PWV)
- The ability of RAS blockers to reduce arterial stiffness as assessed by PWV seems to be independent to be of their ability to reduce BP
- ACEi and ARBs reduce PWV in the recent meta- analysis
- Statins decrease arterial stiffness

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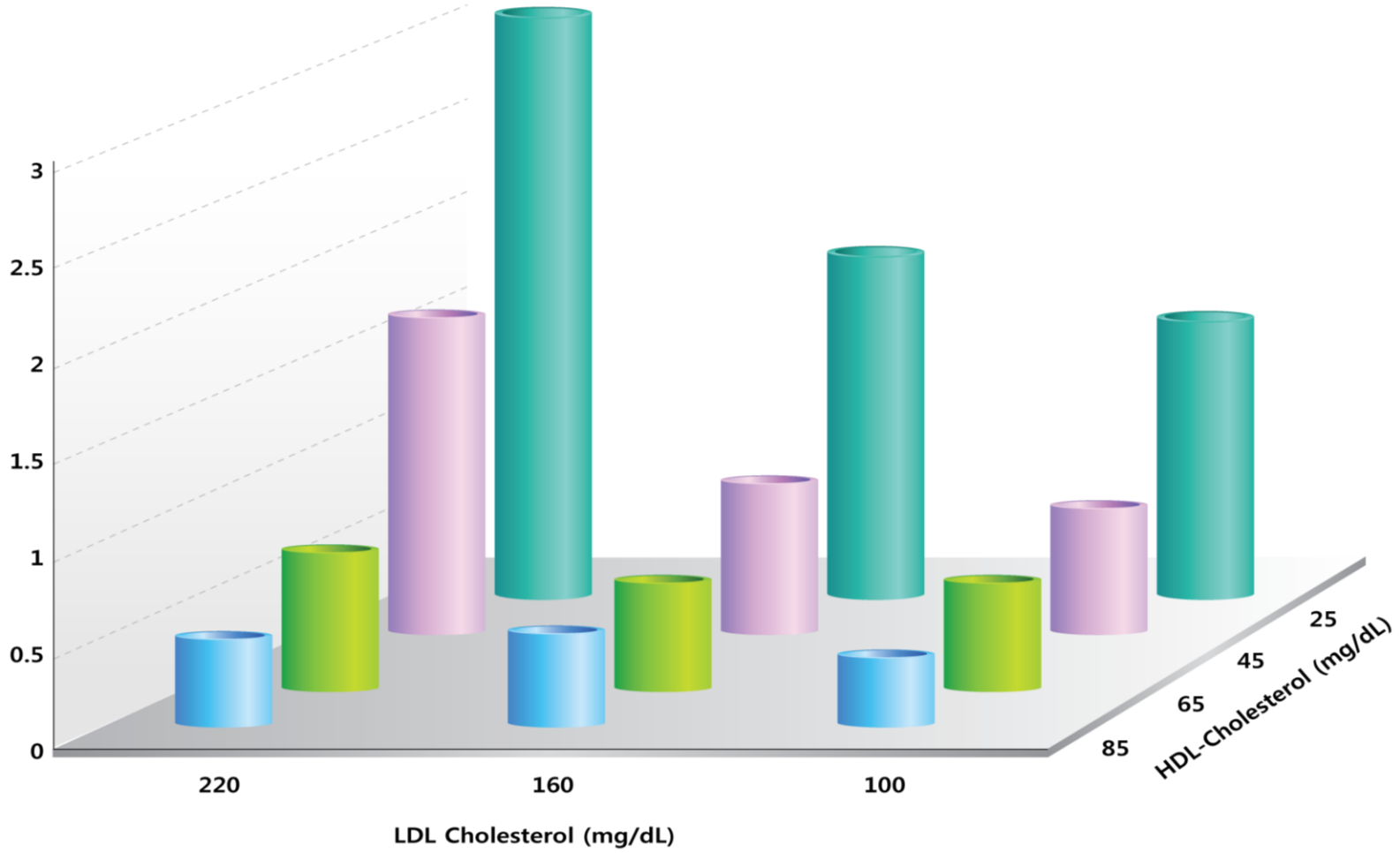
CAD risk as a function of LDL-C and HDL-C
Framingham Heart Study



CASTELLI WP. Am J Cardiol 1998; 82:60-65

Distribution of LDL-C and HDL-C in men with CHD

N=8,500 men with CHD in the U.S. in 1990–92

LDL-C mg/dL	Number	(%)
<100	1,003	13
100–130	2,234	28
131–160	2,711	33
>160	2,139	26

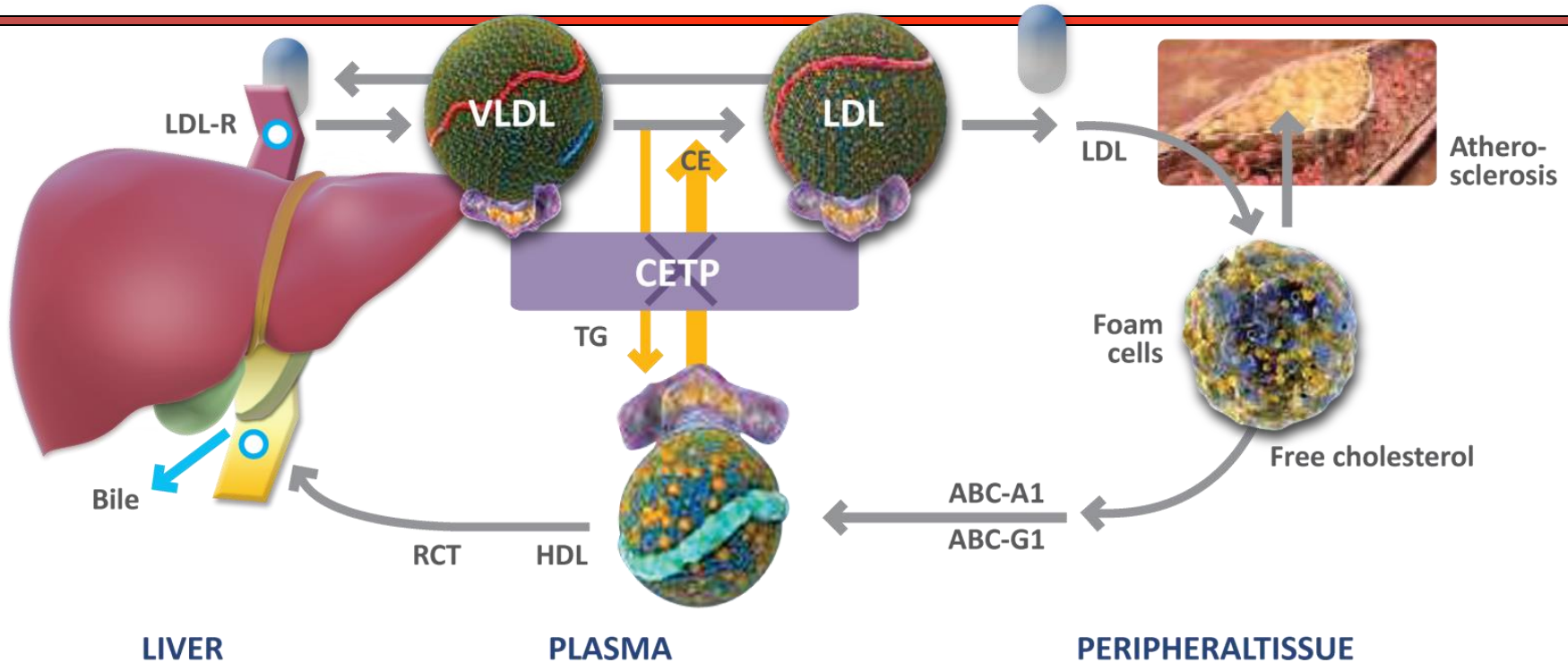
HDL-C mg/dL	Number	(%)
<35	3,286	38
35-40	2,166	25
>40	3,126	36

Veterans Affairs HDL Intervention Trial

- About 40% of CAD patients : LDL cholesterol level below 130 mg/dL.
- 20 to 30% of CAD patients : low HDL cholesterol without high LDL.

Am J Cardiol 1995;75:1196–1201

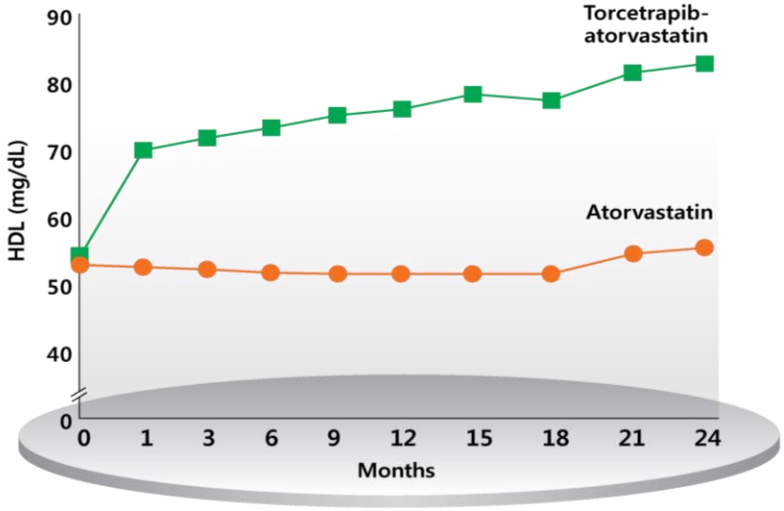
Role of CETP in Lipoprotein Metabolism

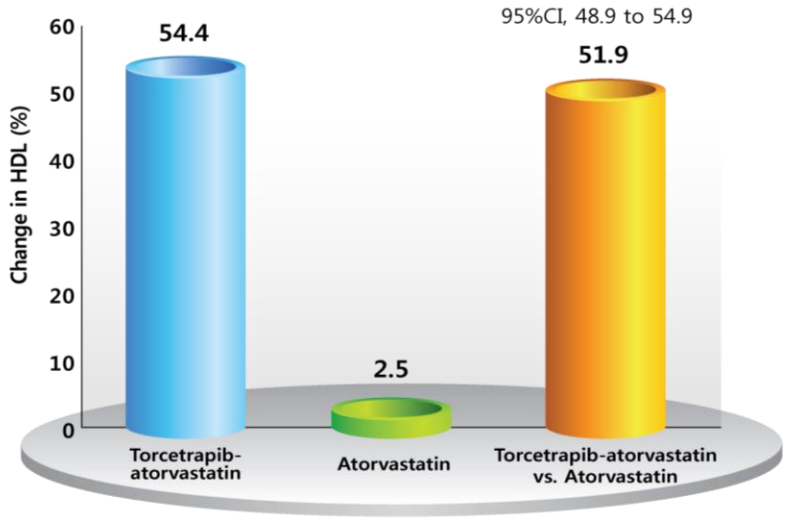


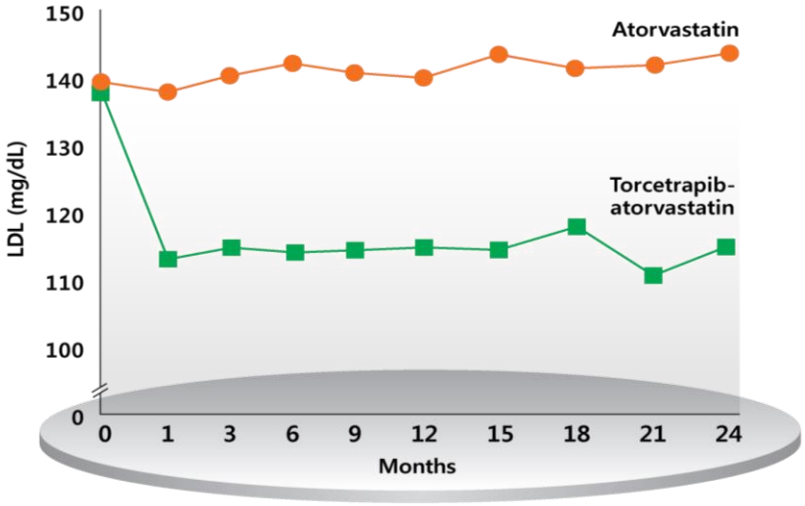
- Human CETP deficiency
  - ↑ in HDL-C (codominant)
- Reducing CETP activity →↓atherosclerosis in animal models

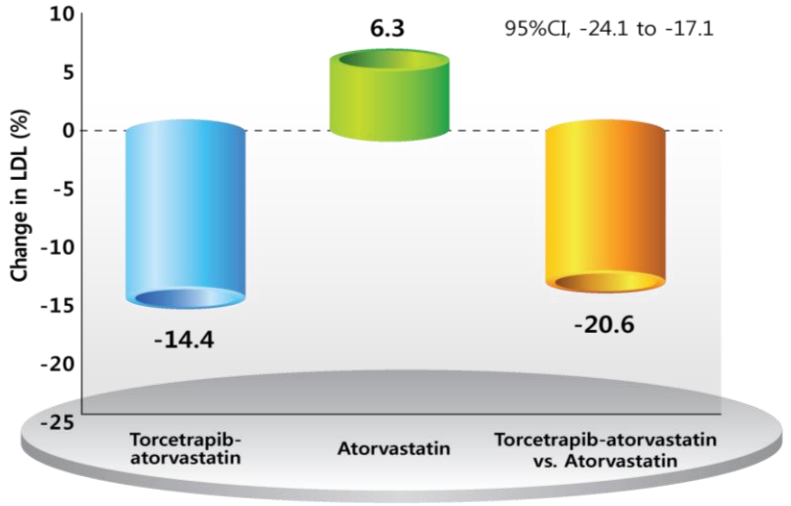
Barter PJ et al. Arterioscler Thromb Vasc Biol. 2003;23:160-167.
Contacos C et al. Atherosclerosis. 1998;141:87-98.
Guerin M et al. Arterioscler Thromb Vasc Biol. 2008;28: 148-154.

ILLUMINATE study : Changes of HDL-C and LDL-C







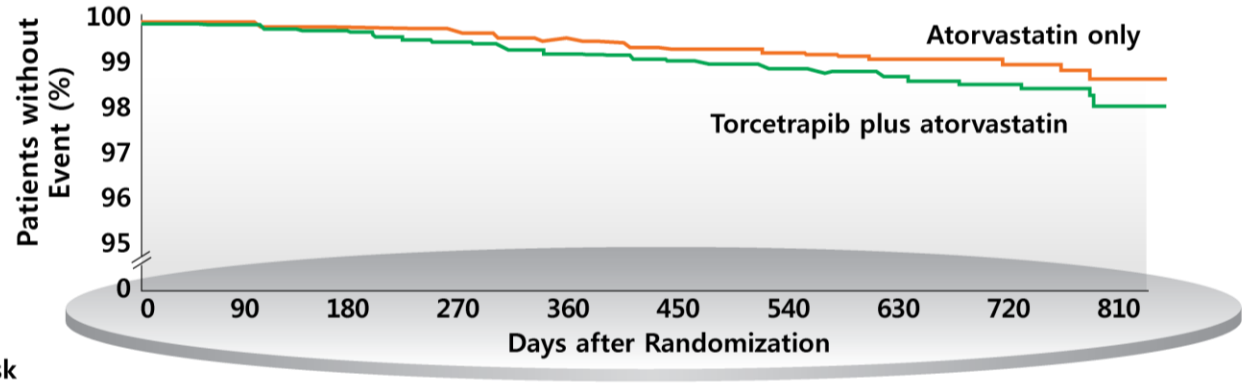


Kastelein JJP et al. NEJM. 2007;356(16):1620-1630

ILLUMINATE study :

Kaplan–Meier Curves for Death from Any Cause and for the Primary Composite Outcome

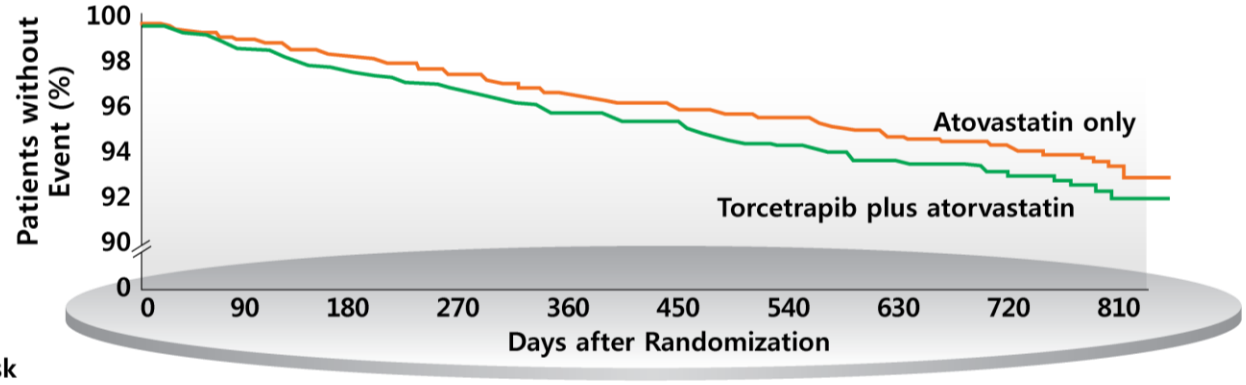
A Death from any Cause



No. at Risk

Atorvastatin only	7534	7530	7521	7509	7487	5833	4043	2078	956	109
Torcetrapib plus atorvastatin	7533	7526	7511	7494	7464	5827	4049	2069	943	114

B Major Cardiovascular Events



No. at Risk

Atorvastatin only	7534	7479	7406	7340	7255	5627	3872	1965	898	103
Torcetrapib plus atorvastatin	7533	7434	7345	7267	7177	5567	3838	1953	888	107

Nissen SE et al. NEJM. 2007;356(8):1304-1316

The Failure of Torcetrapib:
Was it the Molecule or the Mechanism?

↑ Cholesterol efflux via ABCG1

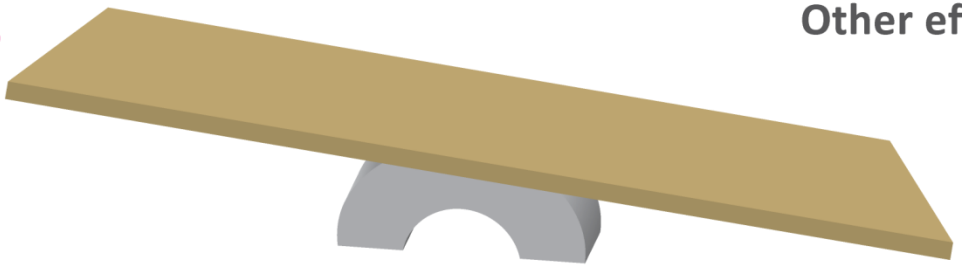
↓ Macrophage foam cells

↓ Coronary Atherosclerosis

↑ Blood pressure
(↑ Aldosterone, ↓ Potassium)

↑ Death from sepsis?
Other effects?

BENEFICIAL EFFECTS

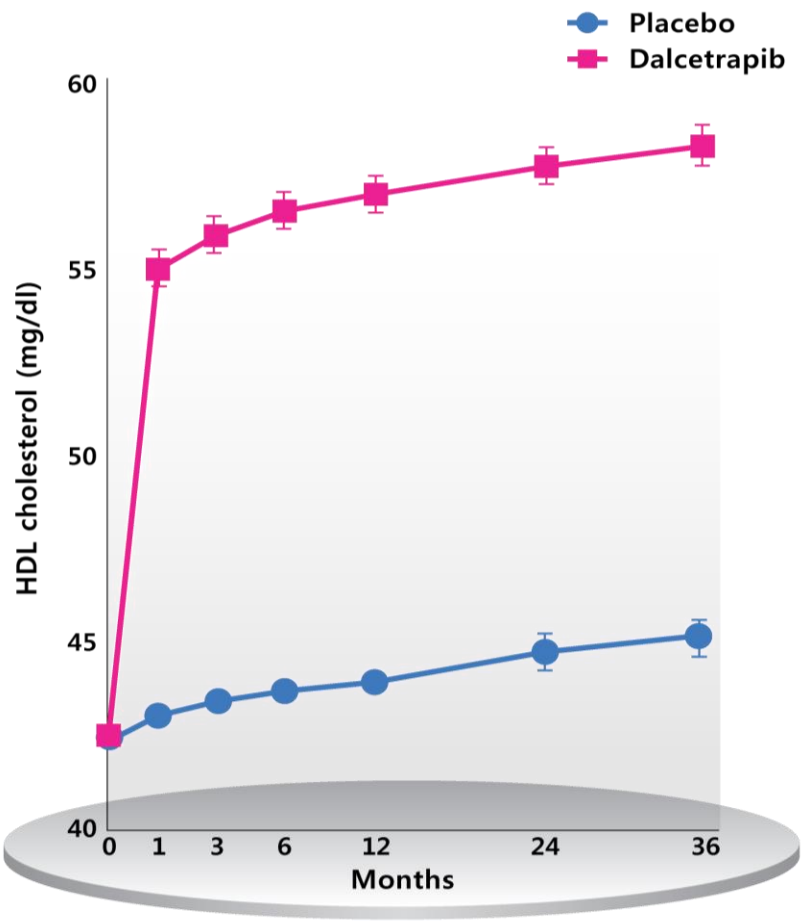


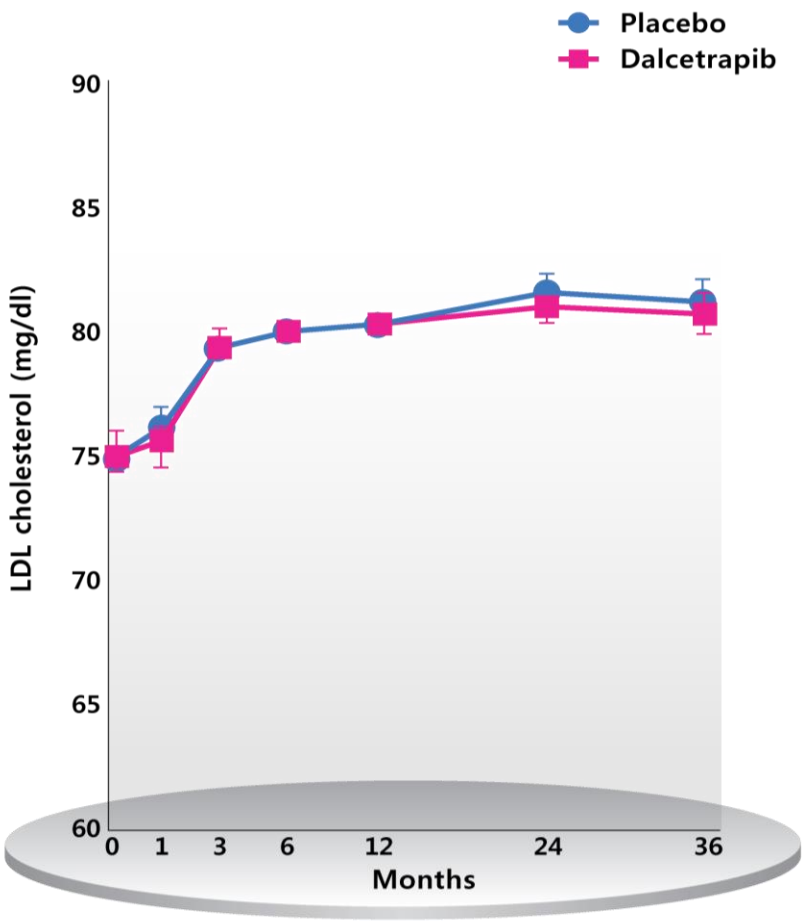
ADVERSE EEFFECTS

TORCETRAPIB

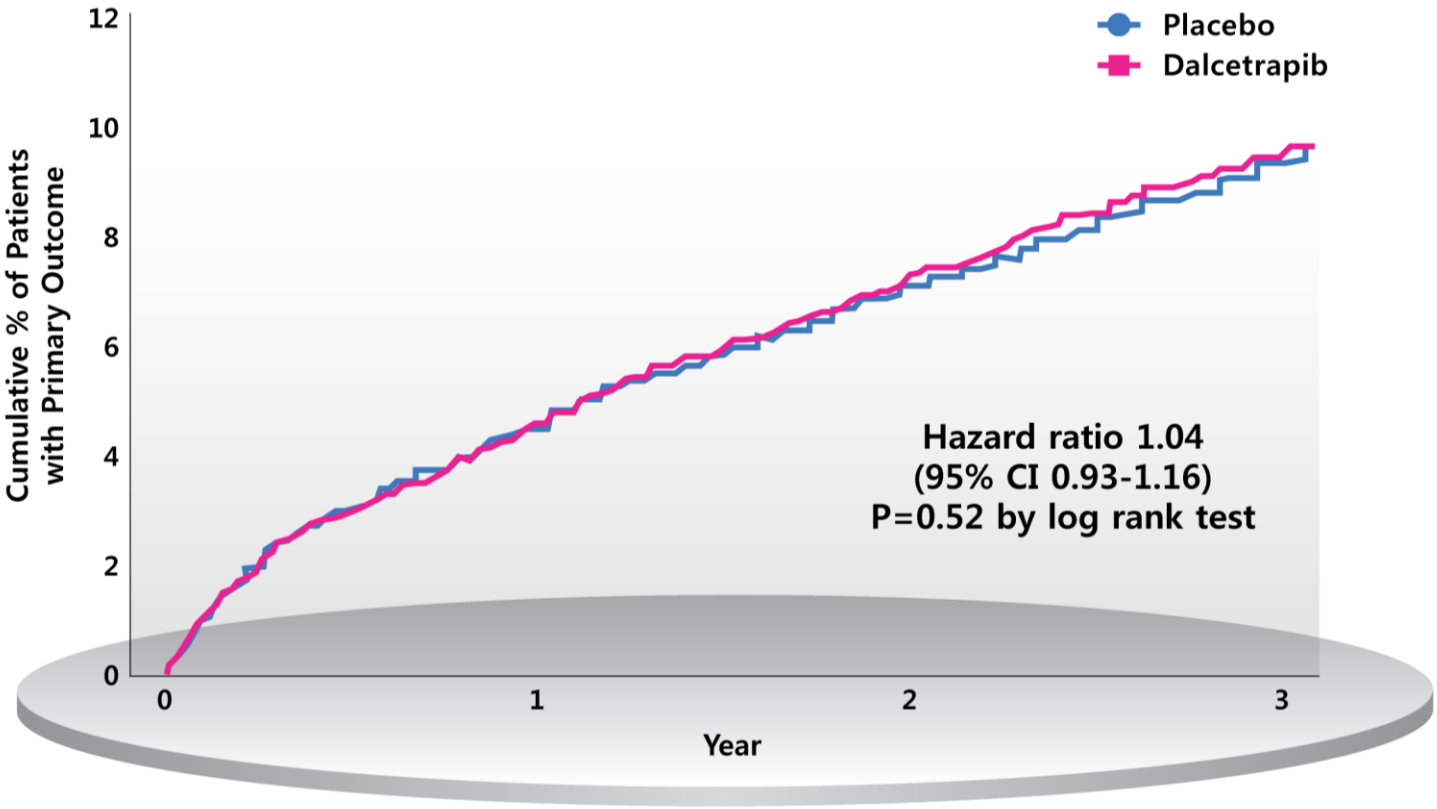
Further clinical trials with CETP inhibitors that do not increase BP or aldosterone are ongoing

DAL-OUTCOMES : HDL-C and LDL-C by treatment group





DAL-OUTCOMES : Primary outcome* by treatment group

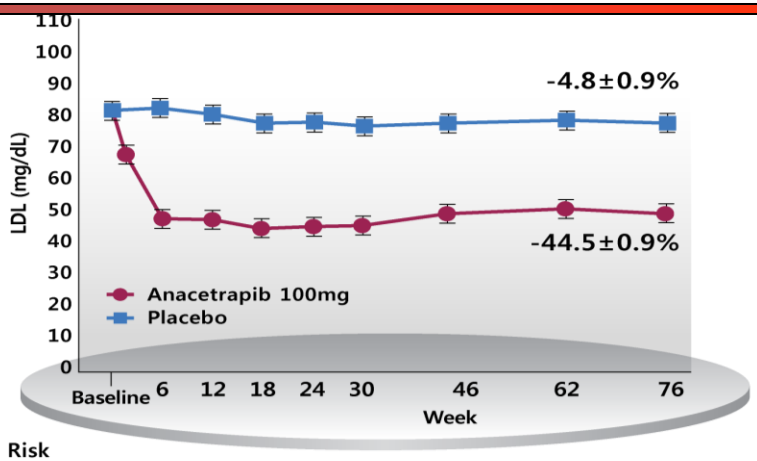


No. at Risk				
Placebo	7933	7386	6551	1743
Dalcetrapib	7938	7372	6495	1736

* Coronary heart dease death, non-fatal MI, ischemic stroke, hospitalization for unstable angina, resuscitated cardiac arrest

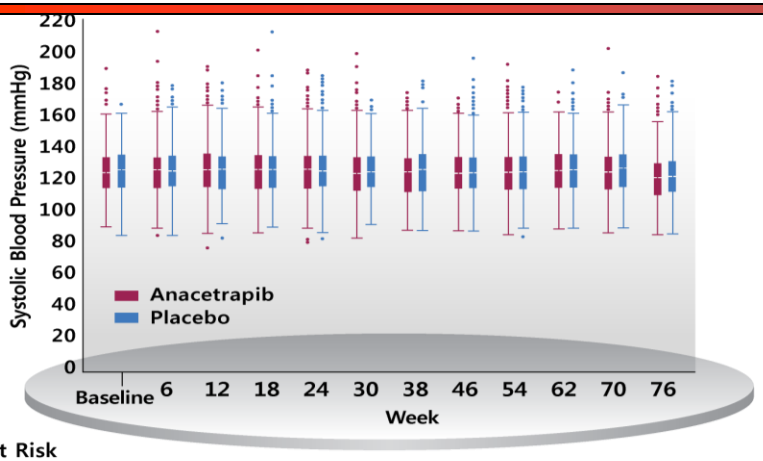
DEFINE study :

Safety of anacetrapib in patients with or at high risk for CHD



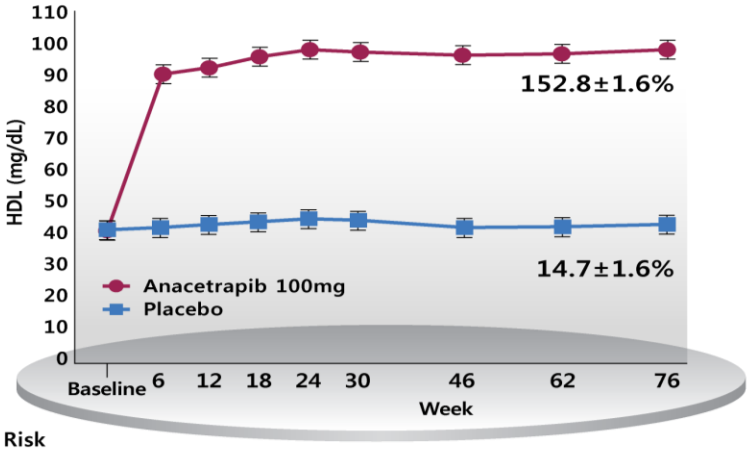
No. at Risk

Anacetrapib	804	771	756	716	687	646	604	568	540
Placebo	803	759	759	741	743	735	711	691	666



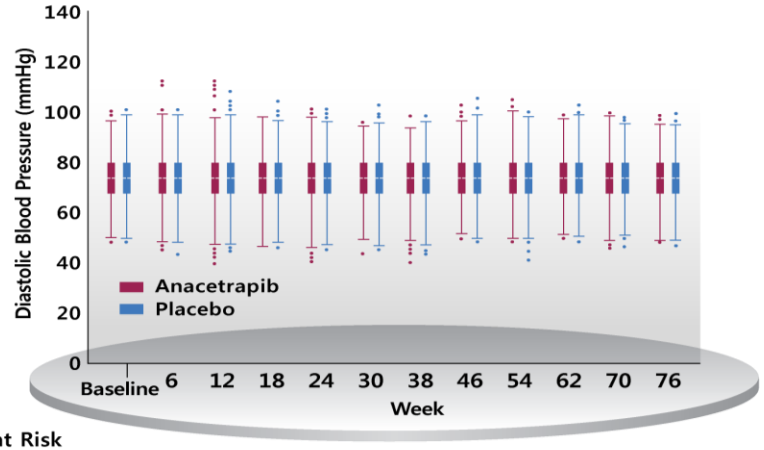
No. at Risk

Anacetrapib	808	801	768	726	694	653	611	595	580	564	551	540
Placebo	804	793	775	751	747	734	723	704	695	683	661	660



No. at Risk

Anacetrapib	807	776	757	718	687	647	607	572	543
Placebo	804	766	761	741	744	736	711	691	666



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DEFINE study - Determining the Efficacy and Tolerability of CETP Inhibition with Anacetrapib

N Engl J Med 2010;363:2406-15

Clinical Trials with CETP Inhibitors

Drug and lipoprotein effects	*Clinical Status*
Torcetrapib: 60% increase in HDL-C 20% decrease in LDL-C	**ILLUMINATE** excess CVD and death ↑ BP
Dalcetrapib: 30% increase in HDL-C no effect on LDL-C	**DAL-OUTCOMES** stopped for futility Slight ↑ in BP, CRP
Anacetrapib: 120% increase in HDL-C 30% decrease in LDL-C	**DEFINE** safety study excluded torcetrapib-like CVD toxicity
Anacetrapib	**REVEAL** study ongoing
Evacetrapib: similar Lp profile to anacetrapib	**ACCELERATE** study ongoing

Summary of CETP inhibitor

➢**The failure of torcetrapib** was likely related to off target adverse cardiovascular effects

➢Lowering of LDL, Lp(a) and VLDL cholesterol levels with potent CETP inhibitors has **strong anti-atherogenic** potential pending outcome trials with Anacetrapib and Evacetrapib

Biomarkers

1. BNP
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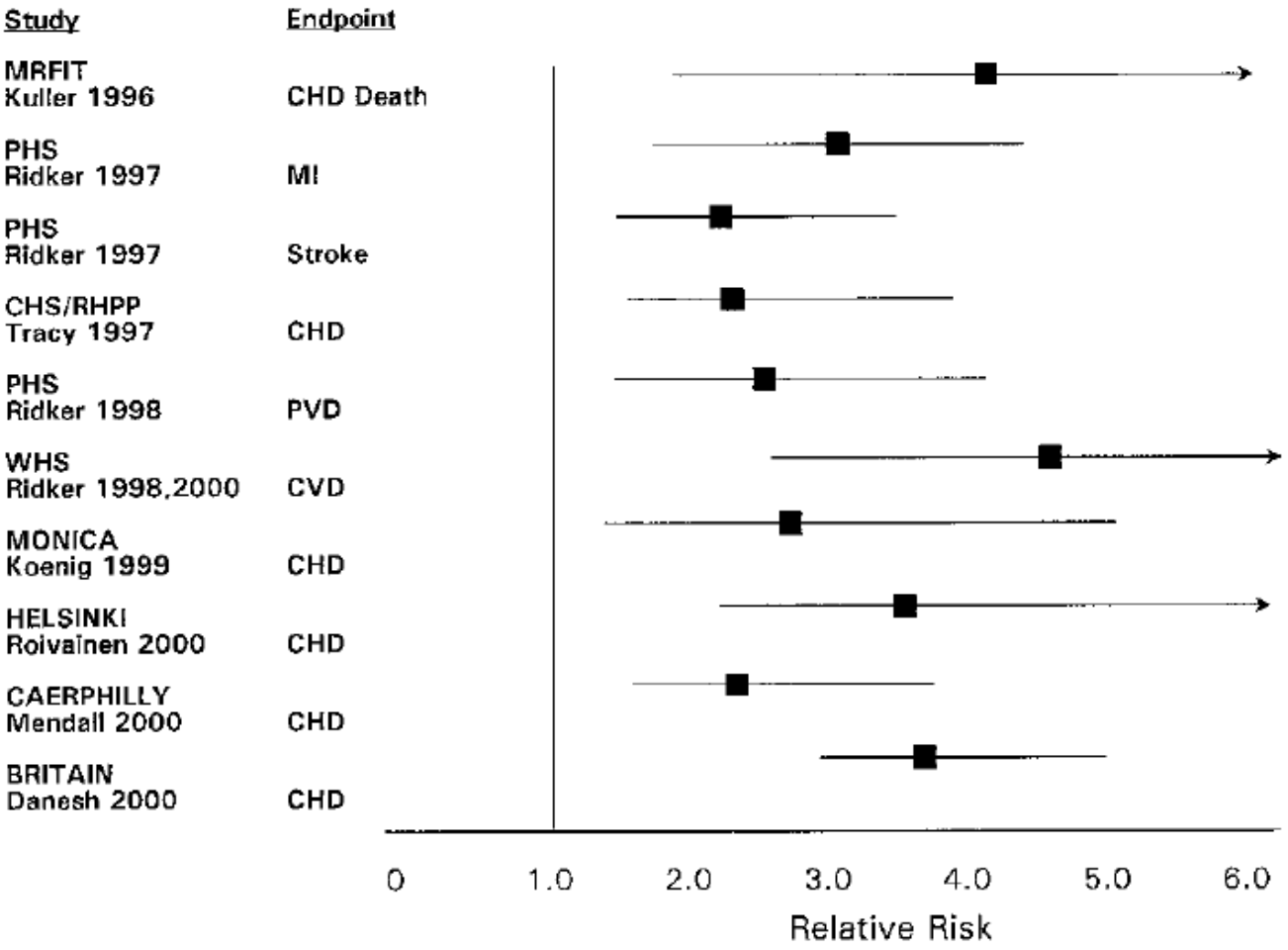
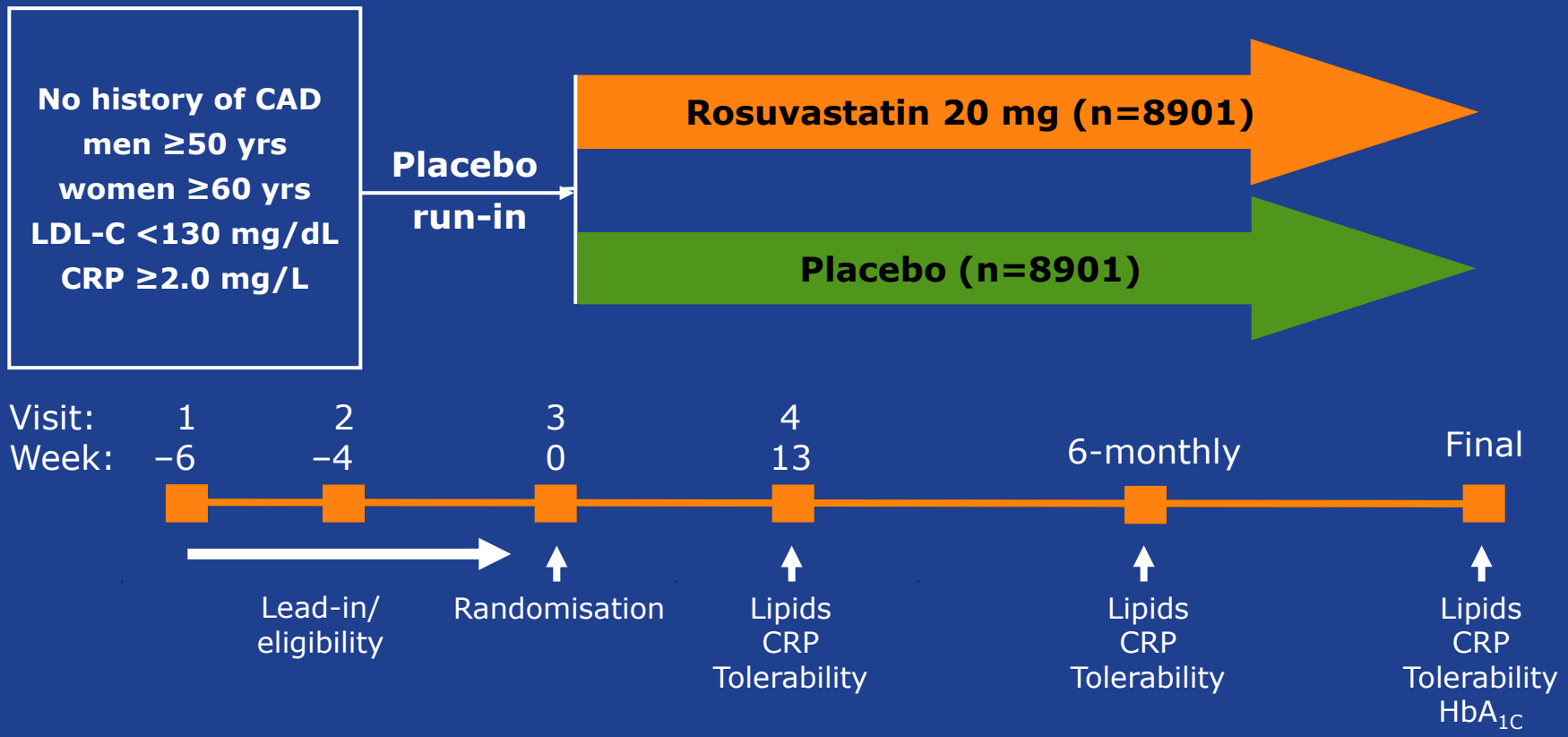
6. Vascular calcification

CRP and Coronary Disease



Ridker P. Circulation 2001; 103 (13): 1813-8.

JUPITER;
Justification for the Use of statins in Primary prevention: an Intervention Trial Evaluating Rosuvastatin

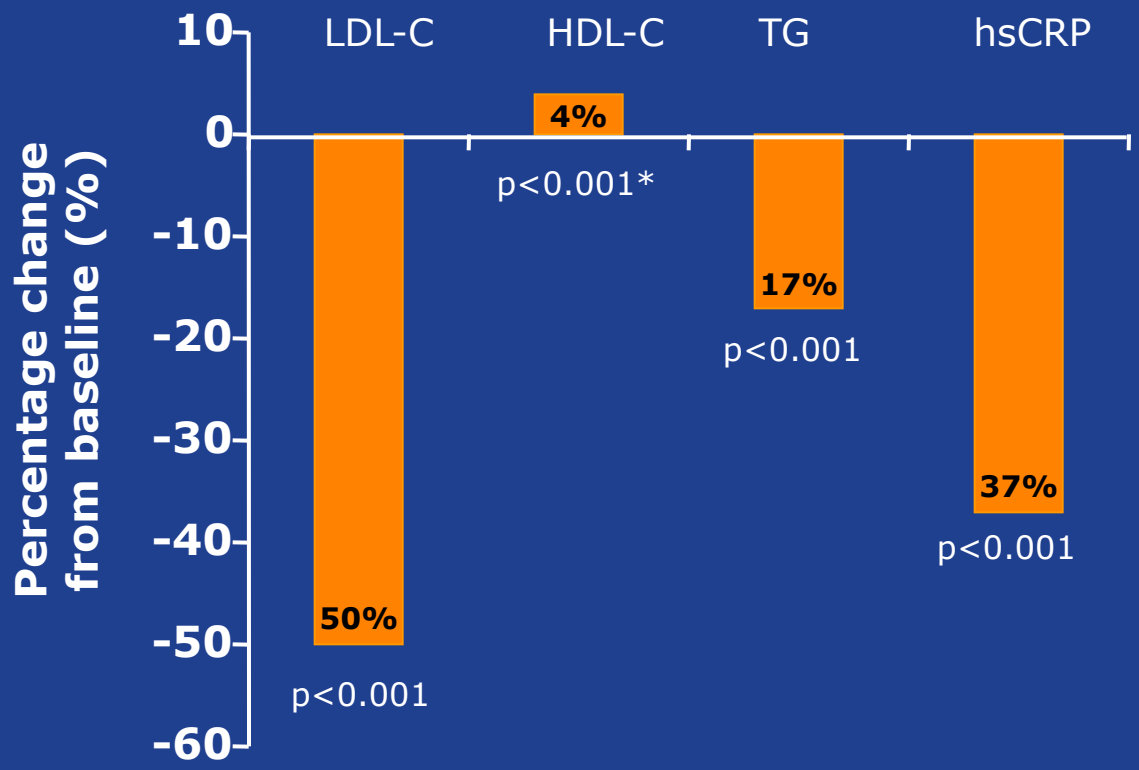


CAD=coronary artery disease; LDL-C=low-density lipoprotein cholesterol; CRP=C-reactive protein; HbA_{1c}=glycated haemoglobin

Ridker P *et al*. *N Eng J Med* 2008;**359**: 2195-2207

JUPITER

Effects on LDL-C, HDL-C, TG and hsCRP at 12 months; Percentage change between rosuvastatin and placebo

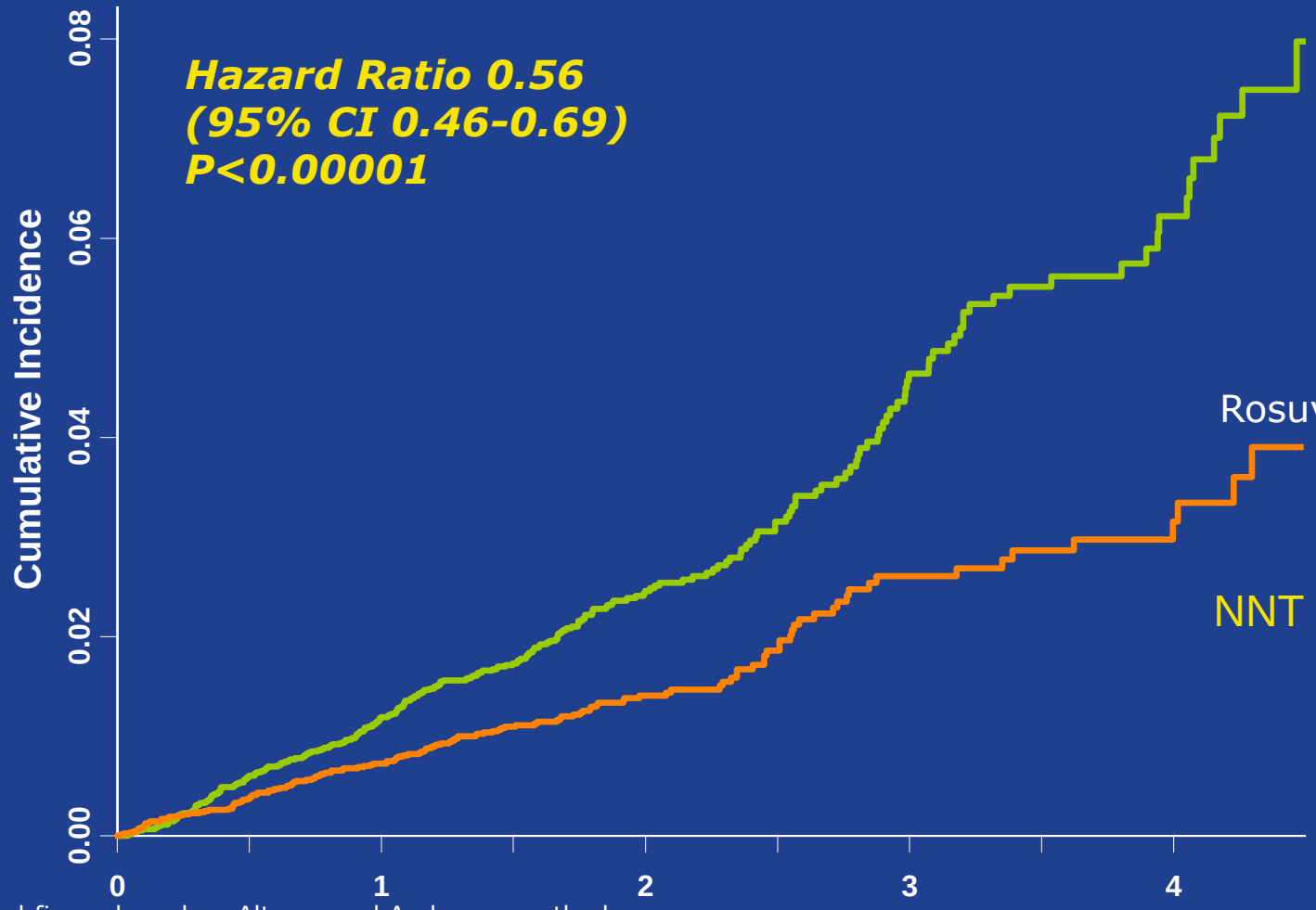


*P-value at study completion (48 months) = 0.34

Ridker P *et al*. *N Eng J Med* 2008;**359**: 2195-2207

JUPITER - Primary Endpoint

(Time to first occurrence of a CV death, non-fatal stroke, non-fatal MI, unstable angina or arterial revascularization)



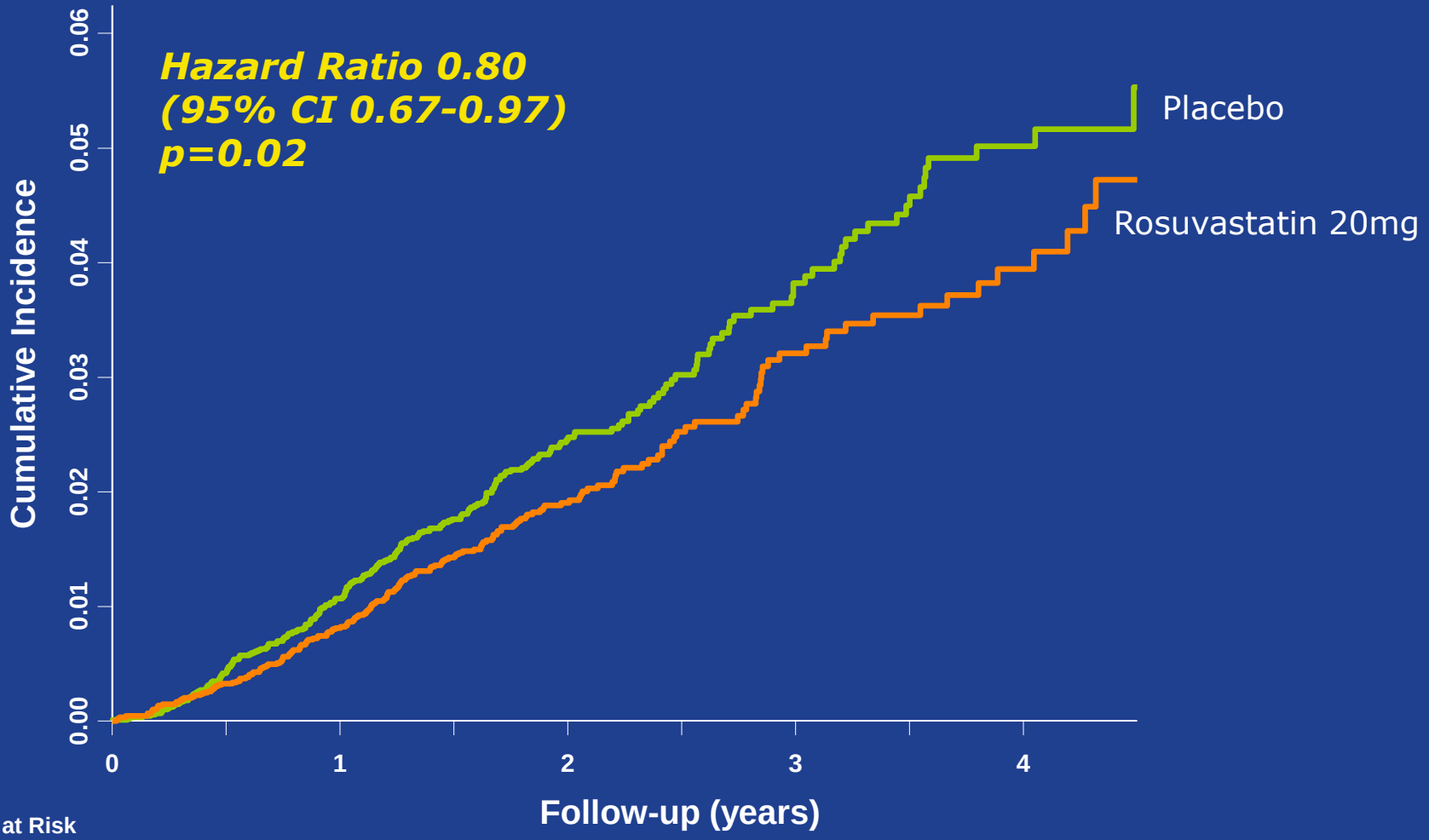
*Extrapolated figure based on Altman and Andersen method

Ridker P *et al*. *N Eng J Med* 2008;**359**: 2195-2207

Number at Risk										
Rosuvastatin	8,901	8,631	8,412	6,540	3,893	1,958	1,353	983	544	157
Placebo	8,901	8,621	8,353	6,508	3,872	1,963	1,333	955	534	174

JUPITER ; Total Mortality

(Death from any cause ; Secondary outcome)



Number at Risk

Rosuvastatin	8,901	8,847	8,787	6,999	4,312	2,268	1,602	1,192	683	227
Placebo	8,901	8,852	8,775	6,987	4,319	2,295	1,614	1,196	684	246

Ridker P *et al*. *N Eng J Med* 2008;**359**: 2195-2207

JUPITER – summary and perspectives

- The JUPITER study included patients with low to normal LDL-C who were at increased CV risk as identified by elevated CRP levels and who did not require statin treatment based on current treatment guidelines
- A 44% reduction in the primary endpoint of major cardiovascular events *(composite of: CV death, MI, stroke, unstable angina, arterial revascularisation)* was observed in patients who received rosuvastatin 20 mg compared with placebo ($p < 0.00001$)
- A 20% reduction in total mortality was observed in patients who received rosuvastatin 20 mg compared with placebo ($p=0.02$), a unique finding for statins in a population without established CHD

Ridker P *et al*. *N Eng J Med* 2008;**359**: 2195-2207

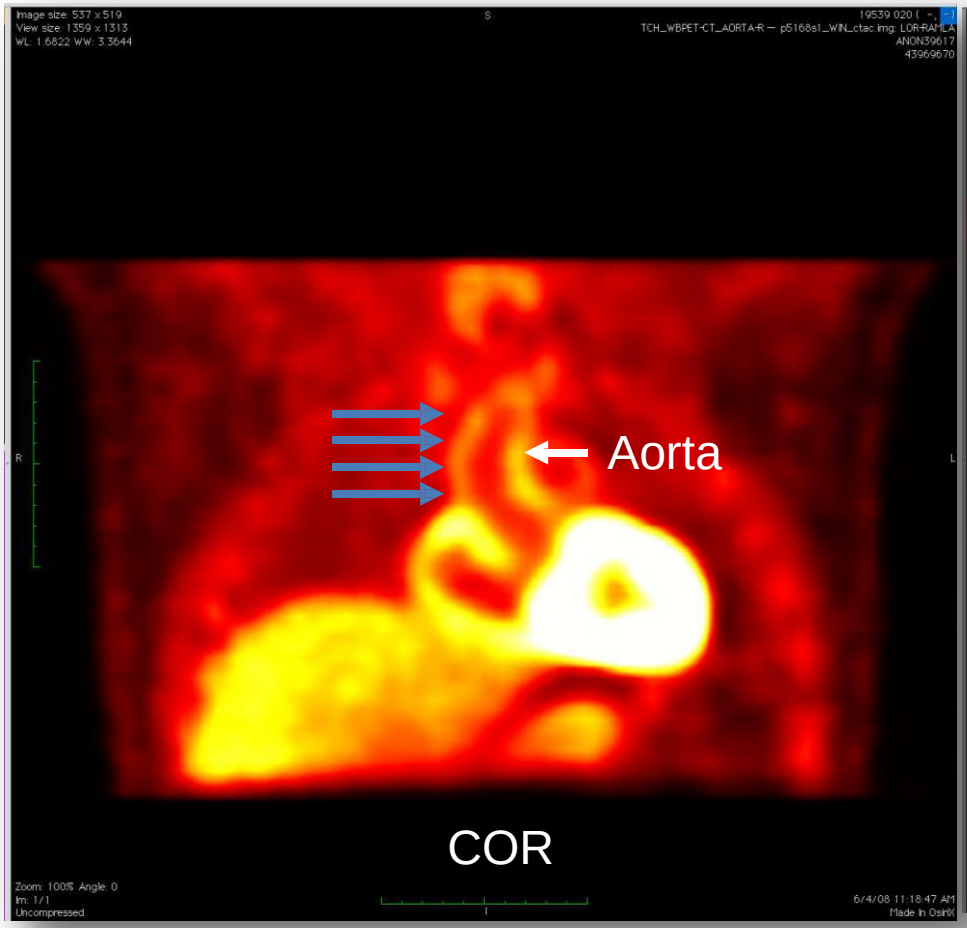
Serum inflammatory biomarkers and plaque inflammation assessed by [18F] - fluorodeoxyglucose positron emission tomography in the dal-PLAQUE study: a post-hoc analysis by baseline features

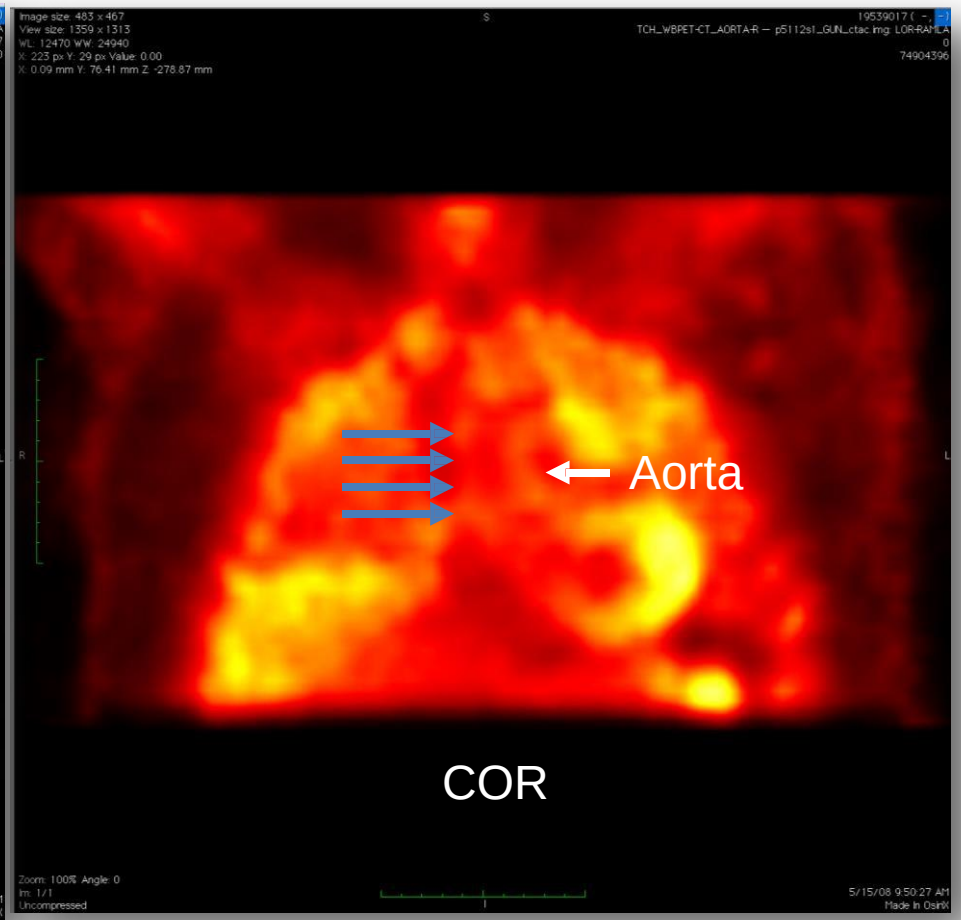
Raphael Duivenvoorden[1], Venkatesh Mani[2], Mark Woodward[3], David Kallend[4], Gabriela Suchankova[4], Valentin Fuster[5], James H.F. Rudd[6], Ahmed Tawakol[7], Michael E. Farkouh[2,8], Zahi A. Fayad[2]

[1]Translational and Molecular Imaging Institute, Mount Sinai School of Medicine, New York, United States of America; [2]Mount Sinai School of Medicine, New York, United States of America; [3]George Institute, University of Sydney, Sydney, Australia; [4]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [5]Cardiovascular Institute, Mount Sinai School of Medicine, New York, United States of America; [6]Division of Cardiovascular Medicine, University of Cambridge, Cambridge, United Kingdom; [7]Massachusetts General Hospital and Harvard Medical School, Boston, United States of America; [8]Peter Munk Cardiac Centre and Li Ka Shing Knowledge Institute, Toronto, Canada

European Society of Cardiology Congress, Munich, Germany, 25-29 Aug 2012

Example of High Versus Low Vascular Inflammation





AX

Results – Difference in MDS_{max} for Highest Versus Lowest Biomarker Tertile

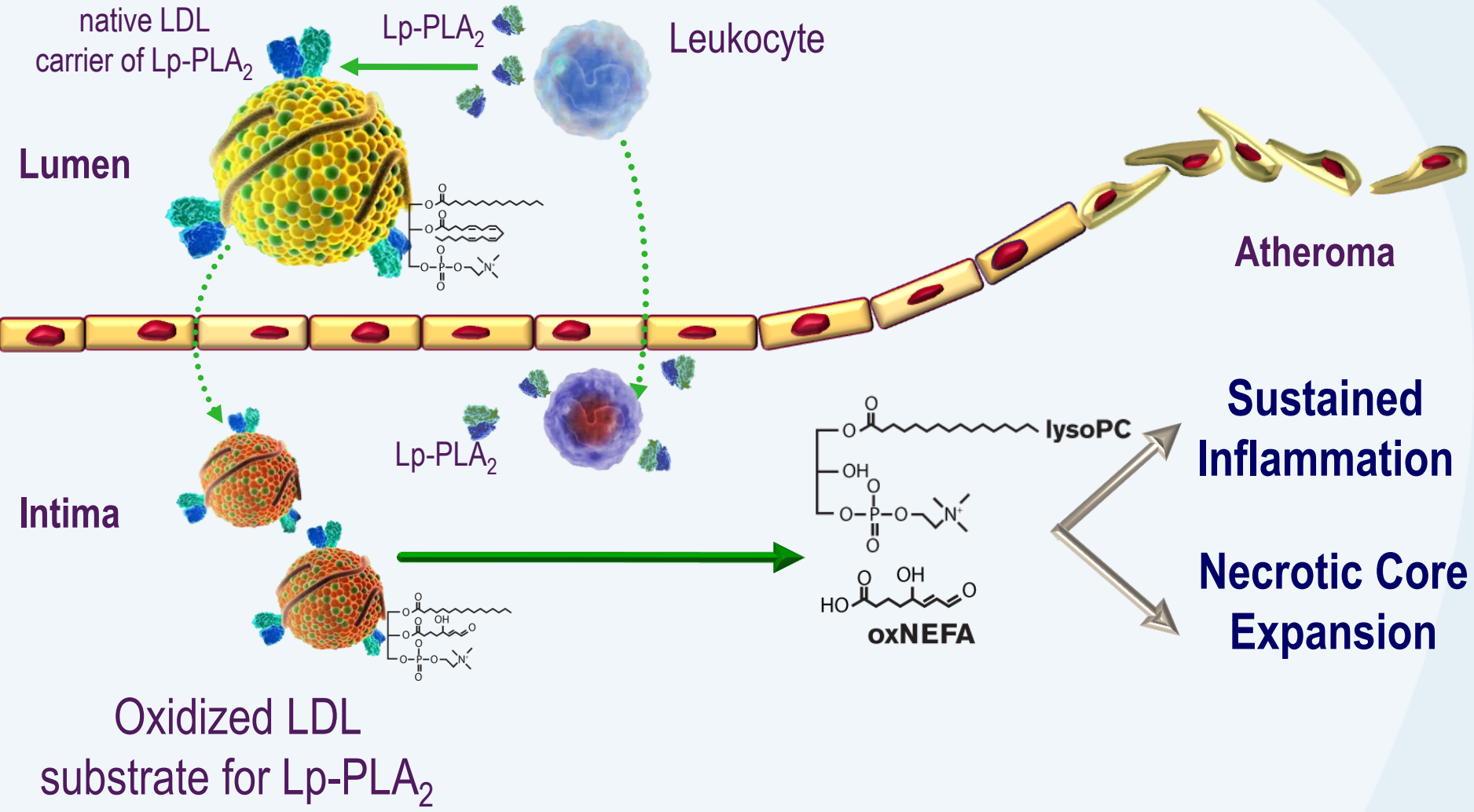
Biomarker	Difference highest versus lowest tertile	*P*-value
hsCRP	0.04	0.82
IL-6	-0.10	0.52
Lp-PLA_2 mass	**0.34**	**0.03***
MMP-3	-0.10	0.53
MMP-9	0.20	0.20
MPO	0.17	0.28
sE-Selectin	-0.04	0.80
sVCAM-1	0.03	0.84
sICAM-1	-0.09	0.57

MDS, most diseased segment; hsCRP, high-sensitivity C-reactive protein; IL-6, interleukin-6; Lp-PLA2, lipoprotein phospholipase A_2; MMP-3, matrix metalloproteinase-3; MMP-9 matrix metalloproteinase-9; MPO, myeloperoxidase; sE-Selectin, soluble E-Selectin; sVCAM-1, soluble vascular cell adhesion molecule; sICAM-1, soluble intracellular adhesion molecule

Biomarkers

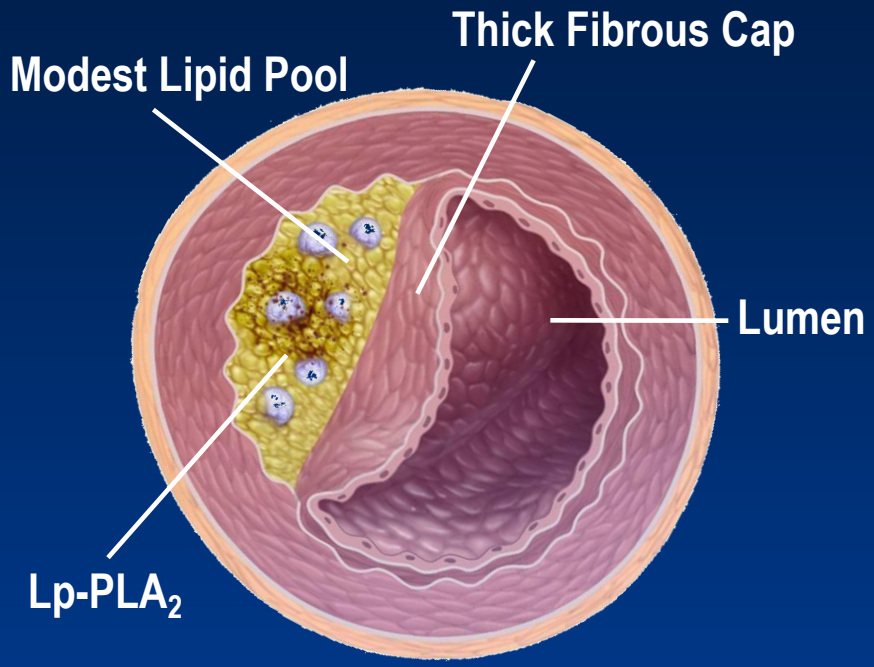
1. BNP
2. LDL/ HDL
3. Arterial stiffness
4. hs-CRP
5. Lp-PLA
6. Vascular calcification

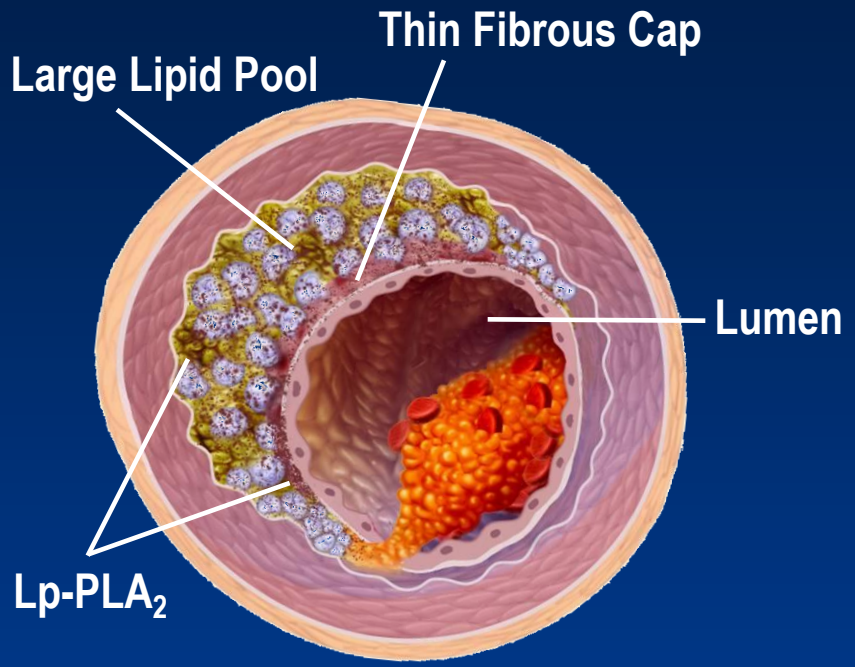
Lipoprotein- associated Phospholipase A_2 (Lp-PLA_2) activity: Background



Macphee, *Biochem J* 1999; Zalewski and Macphee, *ATVB* 2005; Shi *Atherosclerosis* 2007; Kolodgie, *ATVB* 2006

Contrasting histopathological characteristics of a stable versus a vulnerable or ruptured plaque





Stable Plaque

- ✓ Low Lp-PLA_2 content (dark staining)
- ✓ May have significant stenosis
- ✓ Thick fibrous cap / high collagen content
- ✓ Modest lipid pool
- ✓ Few inflammatory cells

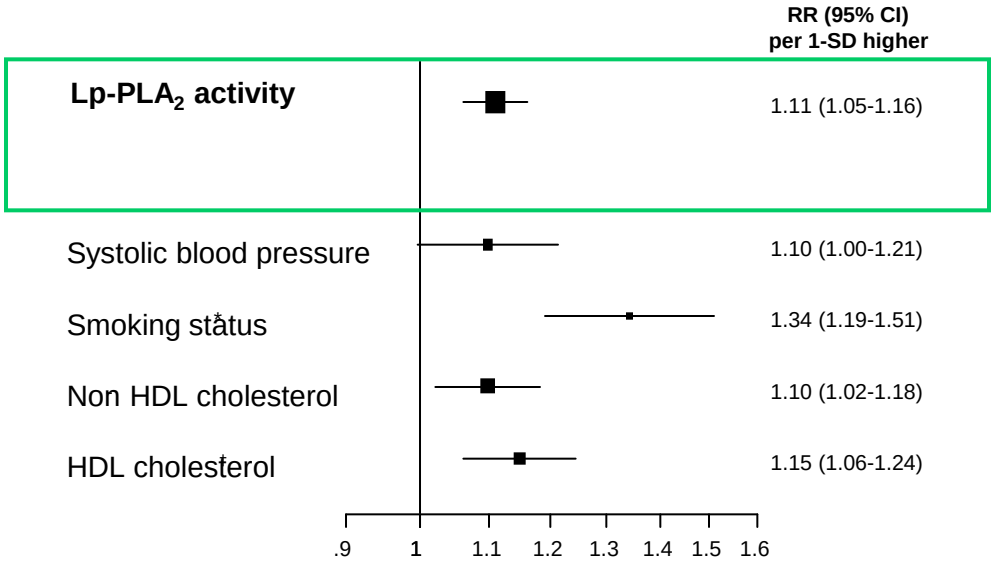
Vulnerable or ruptured Plaque

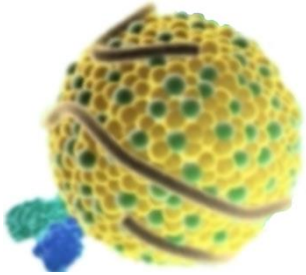
- ✓ High Lp-PLA_2 content (dark staining)
- ✓ May have minimal stenosis
- ✓ Thin fibrous cap / low collagen content
- ✓ Large lipid pool
- ✓ Many inflammatory cells

Corson et al. Am J Card 2008;101(Suppl):41F-50F

Lp-PLA$_2$ and CHD risk: The Lp-PLA$_2$ Studies Collaboration; compared with conventional risk factors

79,036 participants from 32 prospective studies

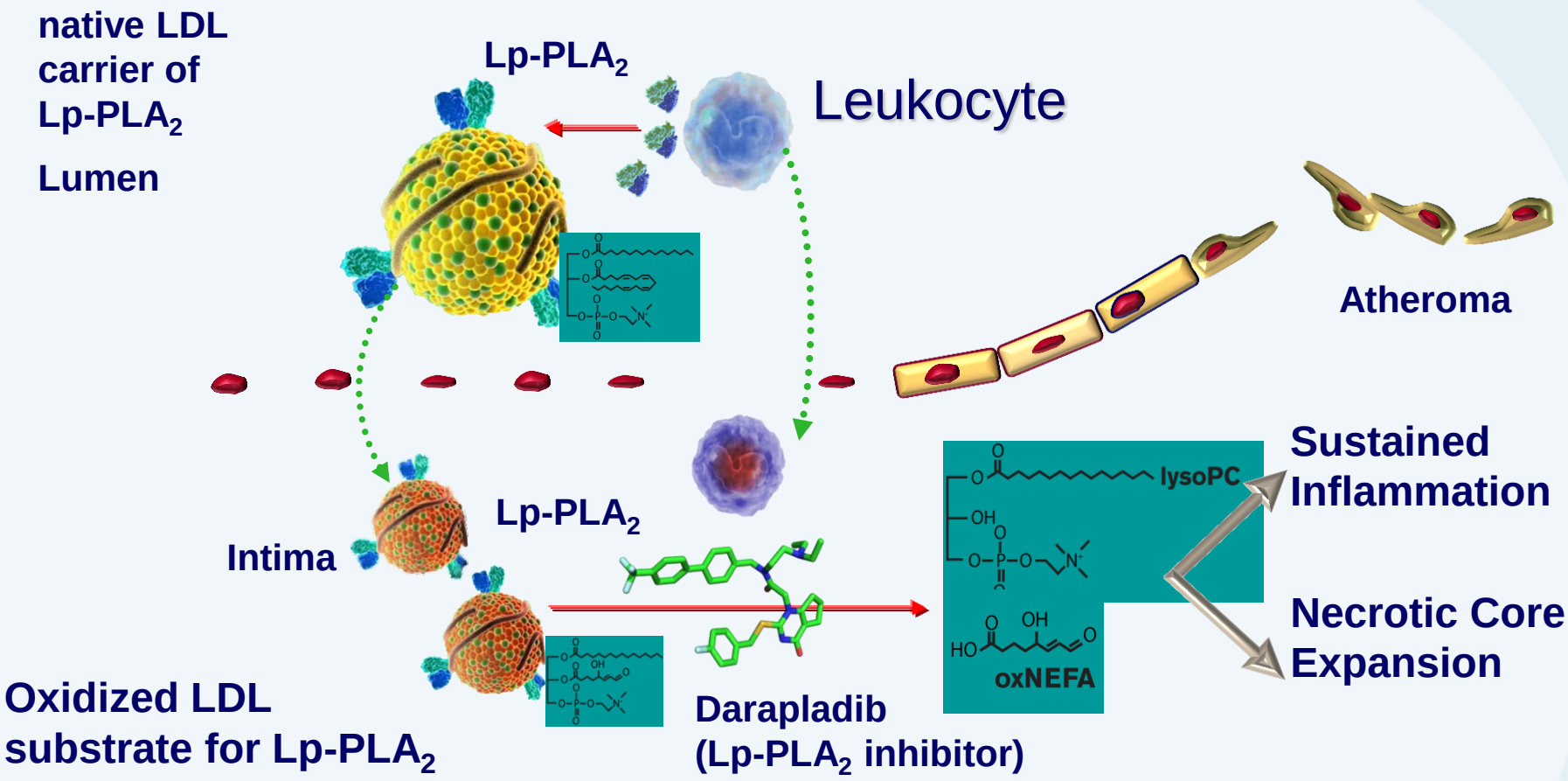




Adjusted for non-lipid and lipid conventional risk factors

LSC *Lancet* 2010; 375:1536

Rationale for targeting Lp-PLA$_2$



Macphee, Biochem J 1999; Zalewski and Macphee. ATVB. 2005;
Shi Atherosclerosis 2007; Kolodgie, ATVB 2006

STABILITY Trial

Stabilization of **A**therosclerotic plaque **B**y Initiation of darap**L**ad**I**b **T**herap**Y**

Patients with chronic CHD
(prior MI >1 mth, prior coronary revascularization, multivessel CAD)

Enrichment criteria: ≥60 years of age, diabetes mellitus, low HDL, current smoking, significant renal dysfunction, polyvascular disease

15,828 patients randomized

Darapladib 160mg

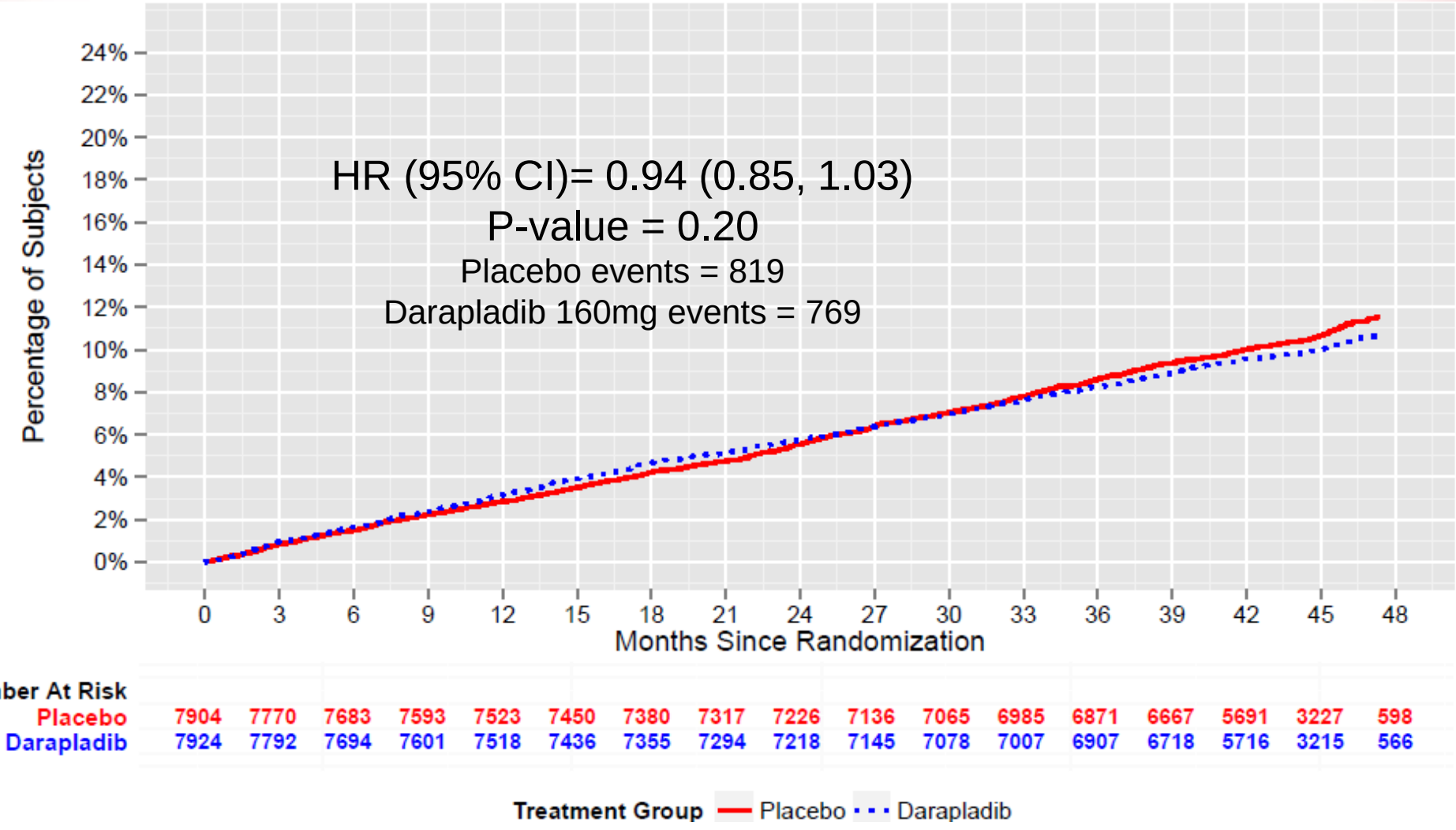
Placebo

Optimized guideline-mandated treatment

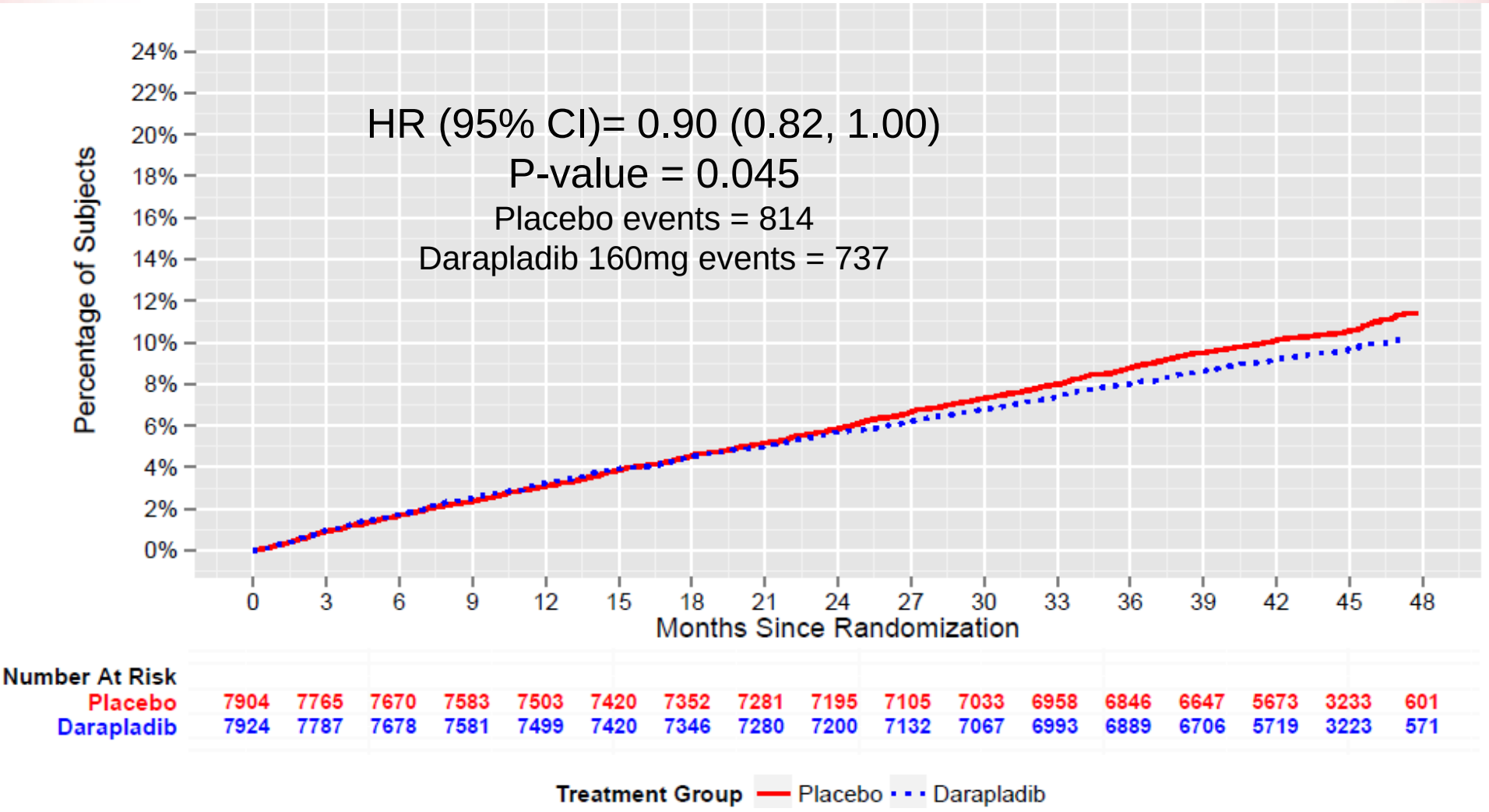
median follow-up 3.7 years , 1588 events

Primary endpoint: composite of CV death, MI, stroke
Secondary endpoints: major coronary events, total coronary events

Primary Endpoint:
Time to First Occurrence CV Death, MI, Stroke

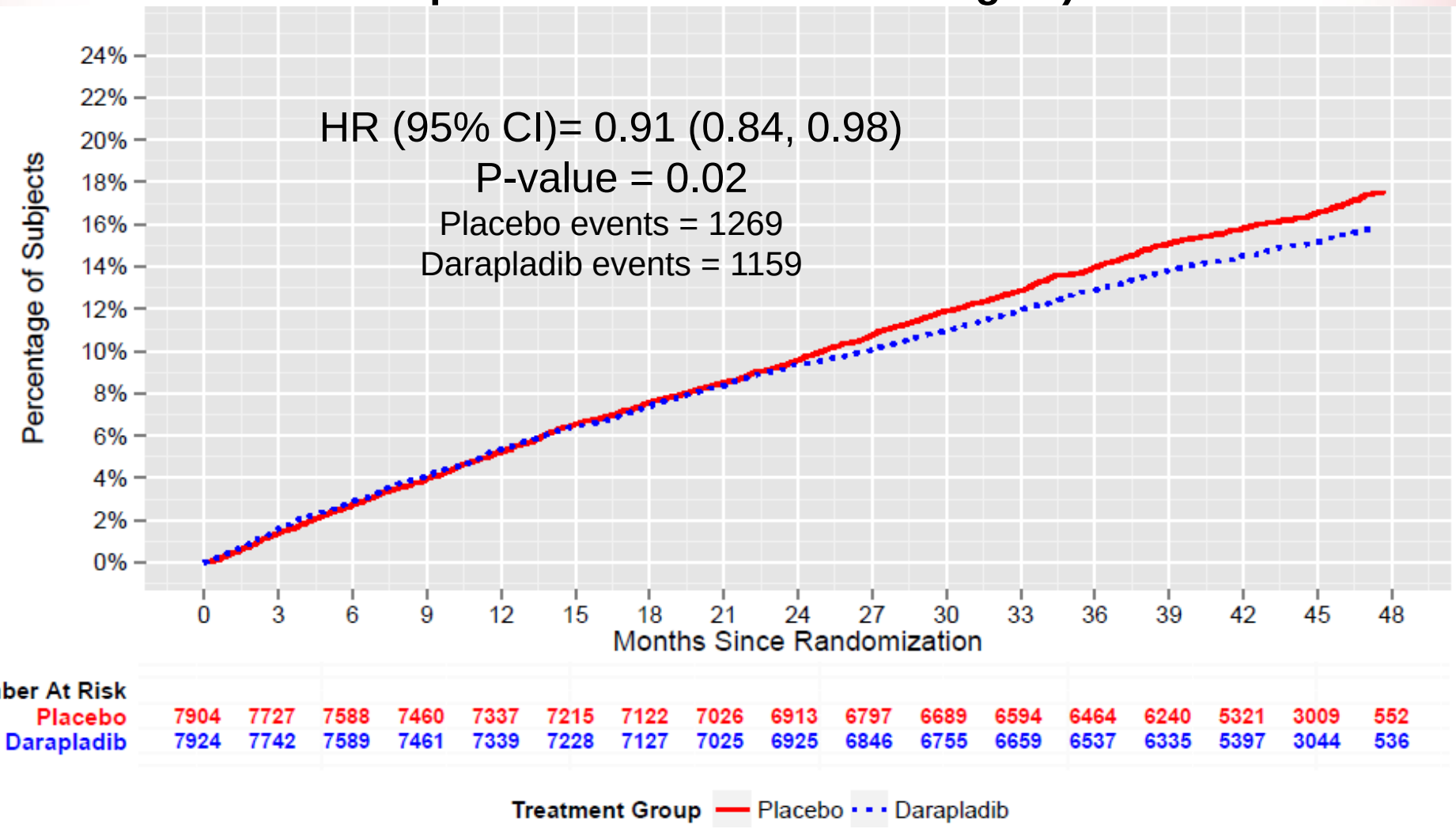


Time to First Occurrence Major Coronary Events
(CHD Death, MI, Urgent Coronary Revascularization)



Time to First Occurrence Total Coronary Events

(CHD Death, MI, Any Coronary Revascularization, Hospitalization for Unstable Angina)



Summary of STABILITY

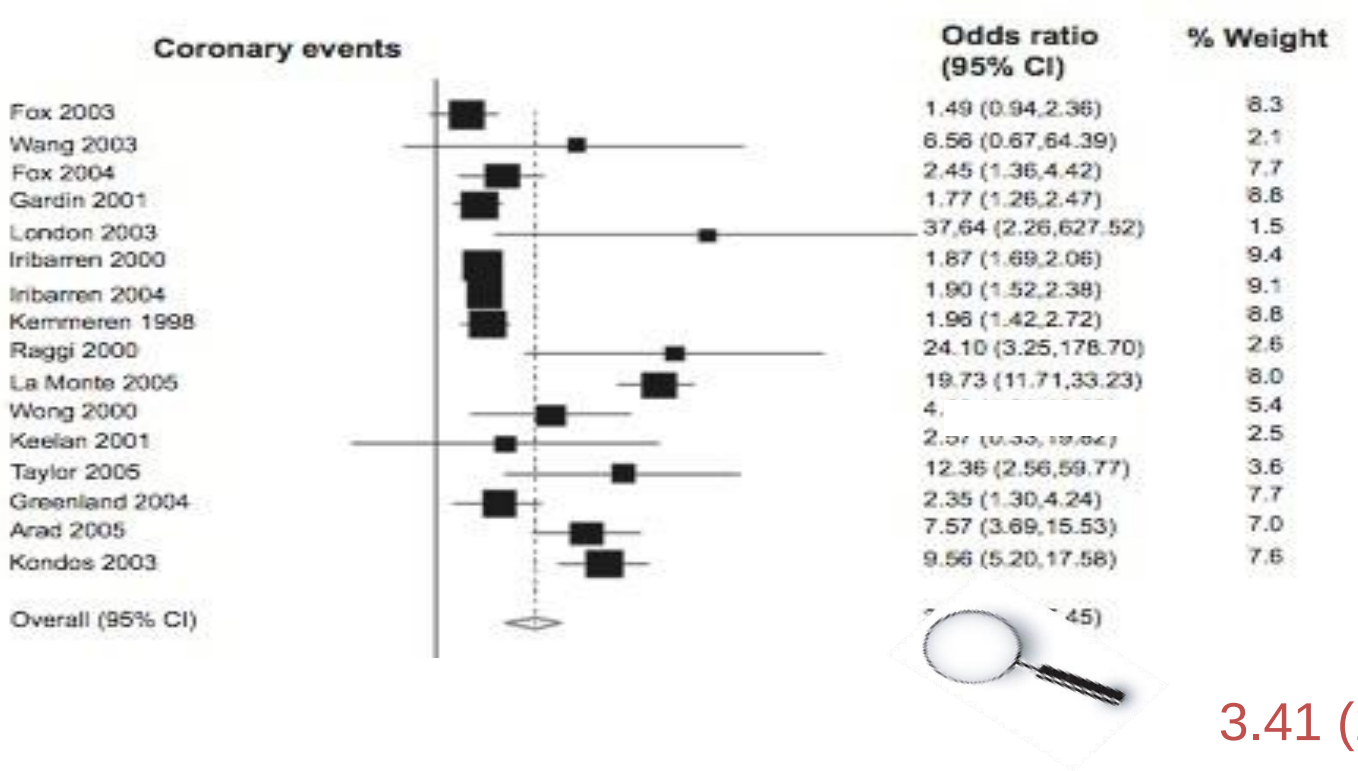
- Did not significantly reduce the incidence of the primary composite endpoint of CV death, MI or stroke
- There was on effect on stroke or total mortality
- Reduced the prespecified coronary-specific secondary endpoints of major coronary events (1% absolute) and total coronary events (1.5% absolute) with nominal significance ($p<0.05$)
- Further analyses of the trial results in subgroups based on biomarkers, including Lp-PLA_2 levels, and genetics will explore if darapladib might be useful in specific patient subsets

- SOLID trial (ACS); coming soon

Biomarkers

1. BNP
2. LDL/ HDL
3. hs-CRP
4. Arterial stiffness
5. Lp-PLA
6. Vascular calcification

Vascular calcification as a marker of increased cardiovascular risk: a meta-analysis



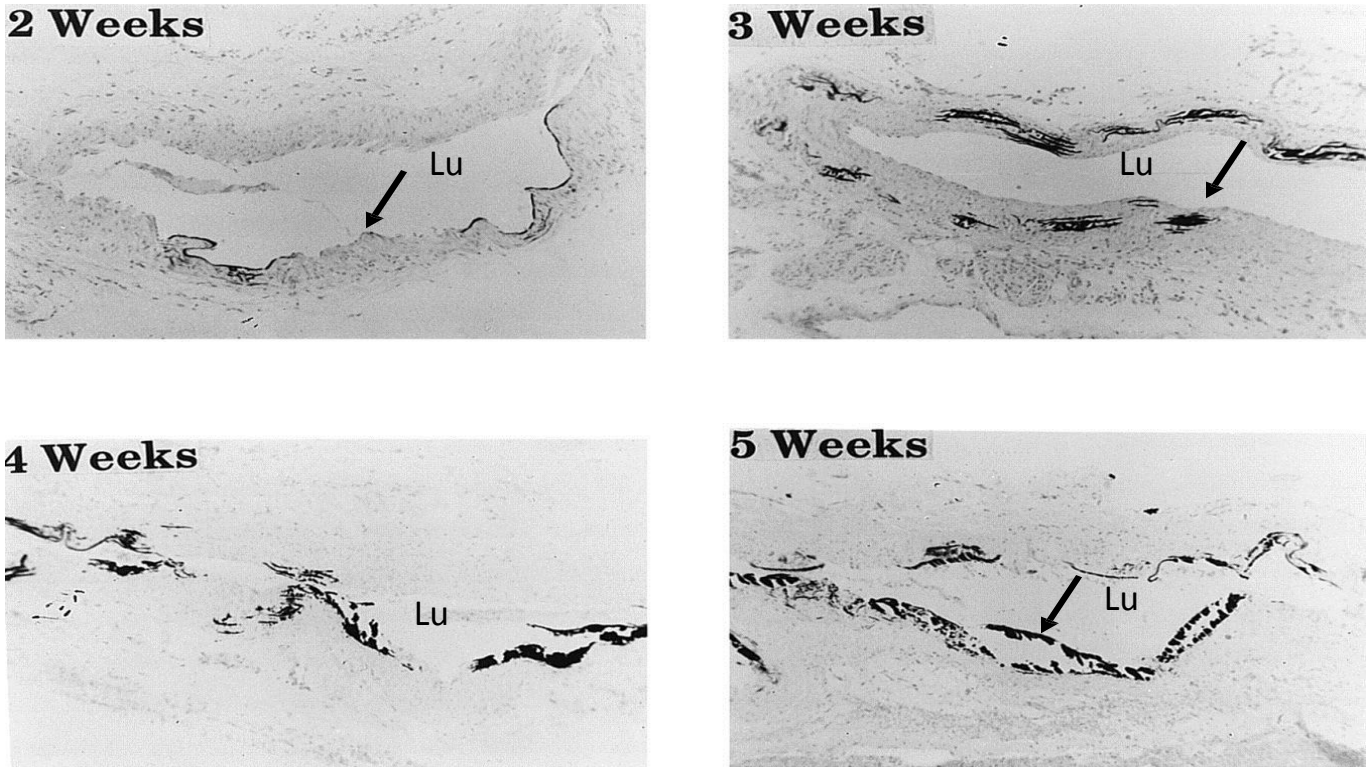
3.41 (2.71 – 4.30)

Rennenberg et al. Vascular health and risk management 2009

Coronary artery calcium is a better predictor of cardiovascular events than the Framingham risk score and can help to reclassify asymptomatic individuals into high-risk or low-risk categories

Alexopoulos et al. Nature Reviews Cardiology 2009

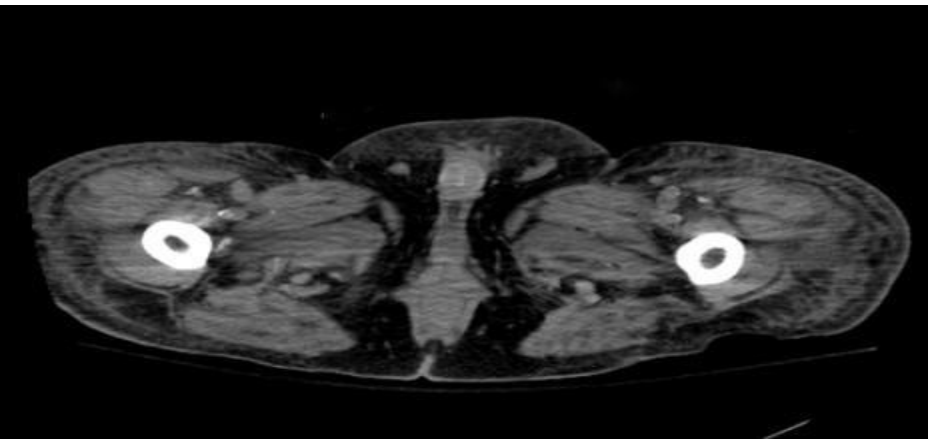
Warfarin causes rapid calcification of the elastic lamellae in rat arteries



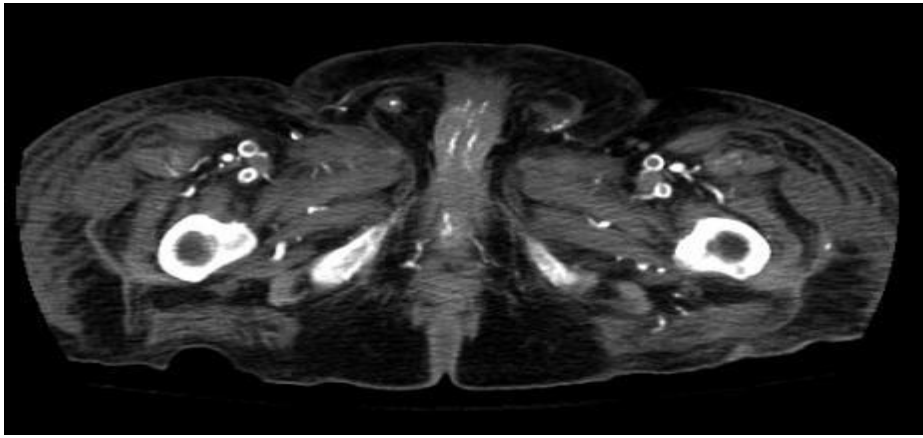
Warfarin induced artery calcification is promoted by increases in serum calcium or phosphate. Strong upregulation of MGP at sites of calcification, though in the inactive uncarboxylated form

Price et al. ATVB 1998

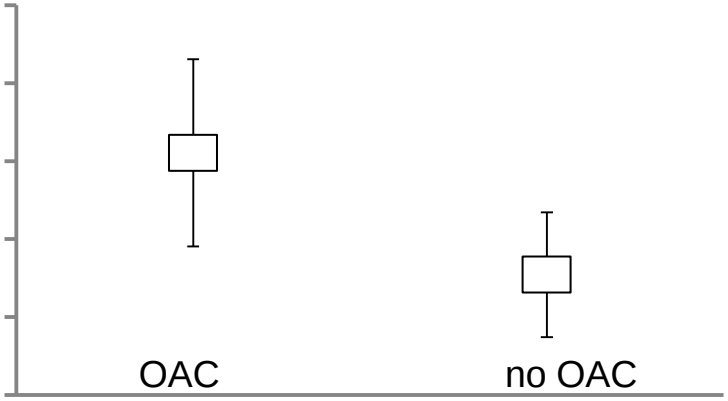
Warfarin induced calcifications



Before coumarin Tx

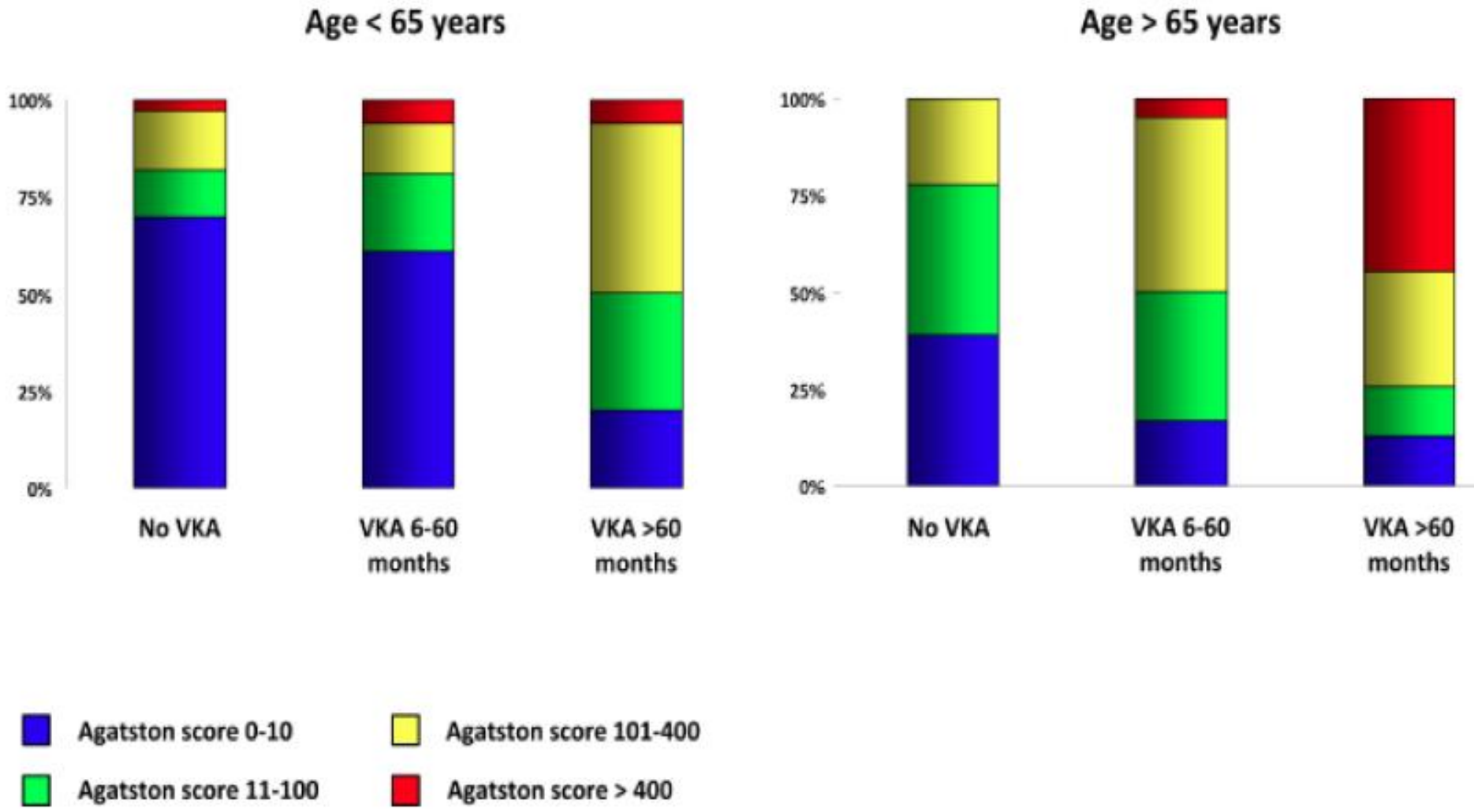


9 months after start of coumarin Tx



Schurgers et al. Blood, Nov 2004

Low-risk AF patients on VKA treatment

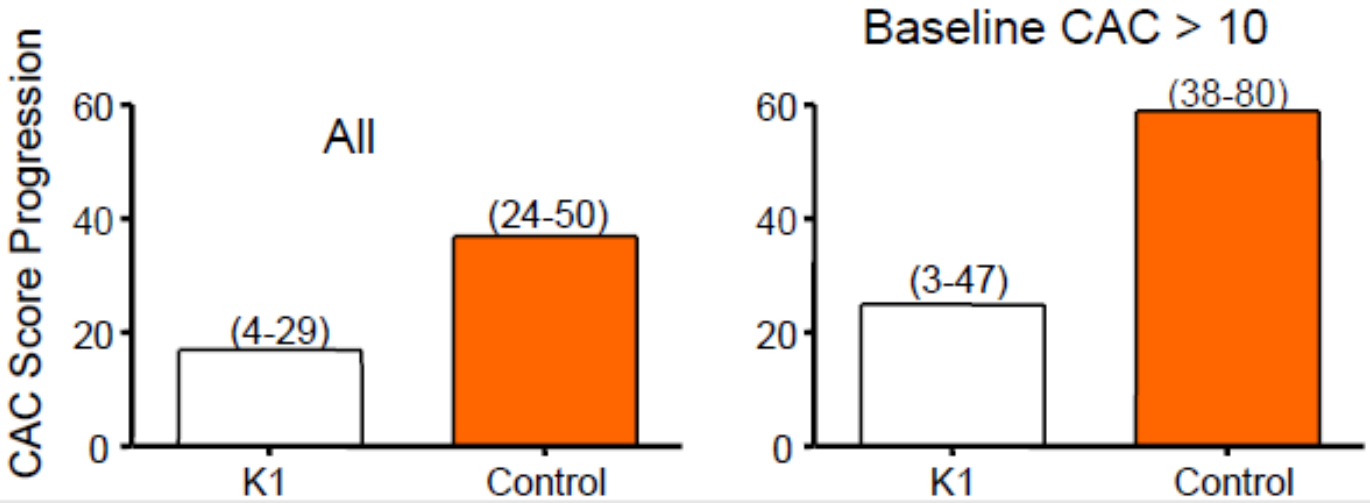


Weijs et al. Eur Heart J 2011

Vitamin K supplementation reduces progression of VC

Design: n= 388, mean age 68 years, 500µg K1 supplementation daily
Endpoint: Coronary artery calcification (CAC) progression over 3 y.

Results: Significant differences were only apparent after secondary analysis, restricted to patients >85% adherent to supplementation (n = 367).



K1 supplementation slows the progression of CAC in healthy older adults with preexisting CAC, independent of its effect on total MGP concentrations.
No difference in CV morbidity / mortality between the groups.

Shea et al. AJCN 2009

VitaK-CAC Study
- Design -

Population

- CAC-patients (n = 200)
- Not on VKA
- CAC score >100; < 400

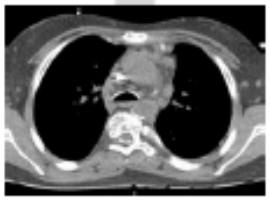
randomised (1:1)

follow-up = 2.0 years

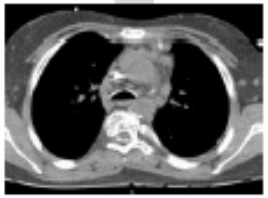
Standard therapy + placebo (n = 100)

Standard therapy + Vitamin K2 (360) (n =100)

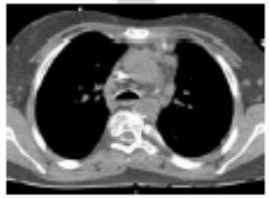
Week 0



Week 52



Week 104



- End points: primary = progress of coronary calcification
  secondary = vascular stiffness and biomarkers

Aortic stenosis - Study
- Design -

Population

- AS-patients (n = 200)
- Not on VKA
- AVC score > 50

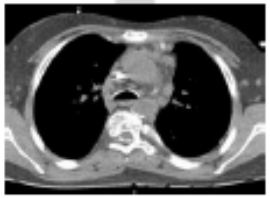
randomised (1:1)

Standard therapy + placebo (n = 100)

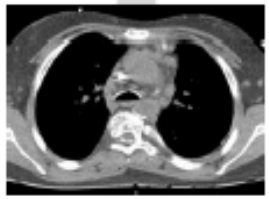
Standard therapy + Vitamin K1 (2mg) (n =100)

follow-up = 1.0 years

Week 0



Week 52



- End points: primary = progress of aortic valve calcification and CAC

  secondary = Echocardiography and biomarkers

ASCVD Risk Calculator

Search "ACC/AHA Prevention Guidelines risk calcul

American Heart Association.

AMERICAN COLLEGE of CARDIOLOGY

The American Heart Association and the American College of Cardiolog
provide a series of new cardiovascular prevention guidelines for the as
cardiovascular risk, lifestyle modifications that reduce risk, management
cholesterol, and management of increased body weight in adults. To
implementation of these guidelines, the new Pooled Cohort Equations CV
and additional Prevention Guideline Tools are available below. Others ma
and available in the near future.

2013 Prevention Guidelines Tools

CV RISK CALCULATOR

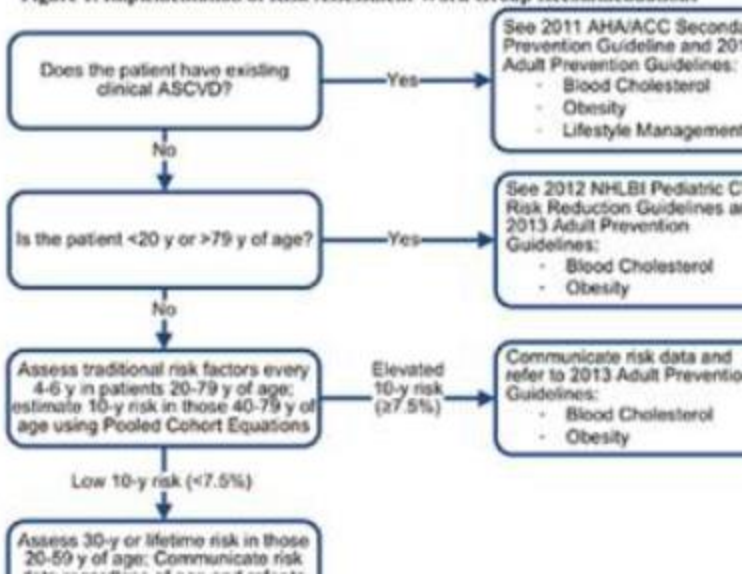
DOWNLOAD CV RISK CALCULATOR

This downloadable spreadsheet is a companion tool to the 2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk. The spreadsheet enables health care providers and patients to estimate 10-year and lifetime risks for atherosclerotic cardiovascular disease (ASCVD), defined as coronary death or nonfatal myocardial infarction, or fatal or nonfatal stroke, based on the Pooled Cohort Equations and the work of Lloyd-Jones, et al., respectively. The information required to estimate ASCVD risk includes age, sex, race, total cholesterol, HDL cholesterol, systolic blood pressure, blood pressure lowering medication use, diabetes status, and smoking status.

Estimates of 10-year risk for ASCVD are based on data from multiple community-based populations and are applicable to African-American and non-Hispanic white men and women 40 through 79 years of age. For other ethnic groups, we recommend use of the equations for non-Hispanic whites, though these estimates may underestimate the risk for persons from some race/ethnic groups, especially American Indians, some Asian Americans (e.g., of south Asian ancestry), and some Hispanics (e.g., Puerto Ricans), and may overestimate the risk for others, including some Asian Americans (e.g., of east Asian ancestry) and some Hispanics (e.g., Mexican Americans).

Estimates of lifetime risk for ASCVD are provided for adults 20 through 59 years of age and are shown as the lifetime risk for ASCVD for a 50-year old without ASCVD who has the risk

Figure 1. Implementation of Risk Assessment Work Group Recommendations



10-year ASCVD risk

Gender(M/F);
Age(20~79);
Race(White/African American/Other;
Total cholesterol(mg/dl, 130-320);
HDL cholesterol(mg/dl, 20-100);
Systolic BP(90~200);
Treatment for HT(Y/N);
Diabetes(Y/N);
Smoker(Y/N);

Conclusions

➢구관이 명관이다....

- The use of some biomarker(esp. natriuretic peptides) to objectively guide HF therapy is a promising approach
- Direct modification of biomarker still need development and proof through more large RCT

감사합니다