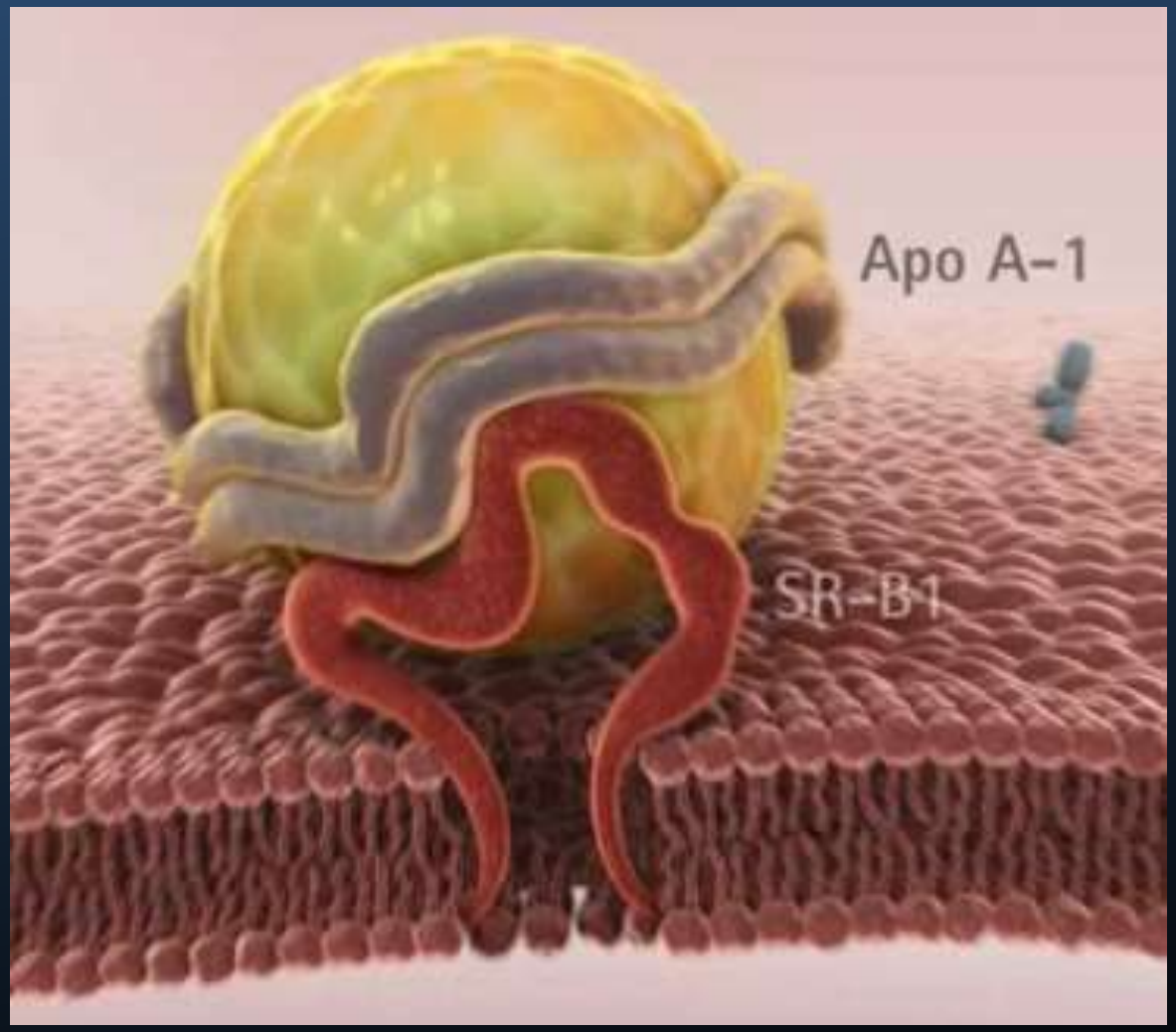
# NEW CONCEPTS IN DYSLIPIDEMIA:DISPELLING 10 COMMON HEALTH “TRUTHS” ABOUT LIPIDS AND RISK ASSESSMENT

Douglas W. Triffon, MD, FACC, FNLA

Scripps Clinic

| Commercial Interest | Nature of Relevant Financial Relationship (Include all those that apply) | | | |
|---|---|---|---|---|
| | What was received | For what role | Self | Spouse/Partner |
| Amarin | Honorarium | Speaker | X | |
| Esperion | Honorarium | Speaker | X | |
| Amgen | Honorarium | Speaker | X | |

# HDL



# HDL-C AND CARDIOVASCULAR RISK

- Cardiovascular risk is inversely related to HDL-C levels.
- The higher the HDL-C the lower the cardiovascular risk.

# FRAMINGHAM STUDY

**TABLE I** Incidence of Coronary Heart Disease by HDL Cholesterol Level—Framingham Study, Exam 11

| HDL Cholesterol Level (mg/dl) | Men | | | Women | | |
|---|---|---|---|---|---|---|
| | Incidence of Coronary Heart Disease | Population at Risk | Rate/1,000 | Incidence of Coronary Heart Disease | Population at Risk | Rate/1,000 |
| All levels | 79 | 1,025 | 77.1 | 63 | 1,445 | 43.6 |
| <25 | 3 | 17 | 176.5 | 0 | 4 | 0.0 |
| 25–34 | 17 | 170 | 100.0 | 11 | 67 | 164.2 |
| 35–44 | 35 | 335 | 104.5 | 12 | 220 | 54.5 |
| 45–54 | 15 | 294 | 51.0 | 19 | 386 | 49.2 |
| 55–64 | 8 | 134 | 59.7 | 14 | 353 | 39.7 |
| 65–74 | 1 | 40 | 25.0 | 3 | 216 | 13.9 |
| 75+ | 0 | 35 | 0 | 4 | 199 | 20.1 |

NOTE: The majority of persons were followed for four years. However, a small number may have been followed for as few as two years or as many as eight years.

American Journal of Medicine, May 1977; vol 62, 707-714

# High-Density Lipoprotein Cholesterol and Cause-Specific Mortality in Individuals Without Previous Cardiovascular Conditions

## The CANHEART Study

Dennis T. Ko, MD, MSc,[a,b,c] David A. Alter, MD, PhD,[a,b,d] Helen Guo, MSc,[a] Maria Koh, MSc,[a] Geoffrey Lau, BHSc candidate,[a] Peter C. Austin, PhD,[a,c] Gillian L. Booth, MD, MSc,[a,c,e] William Hogg, MD, MCISc,[f,g] Cynthia A. Jackevicius, PharmD, MSc,[a,c,h,i] Douglas S. Lee, MD, PhD,[a,c,d] Harindra C. Wijeysundera, MD, PhD,[a,b,c] John T. Wilkins, MD,[k] Jack V. Tu, MD, PhD[a,b,c]

**ABSTRACT**

**BACKGROUND** The prognostic importance of high-density lipoprotein cholesterol (HDL-C) as a specific risk factor for cardiovascular (CV) disease has been challenged by recent clinical trials and genetic studies.

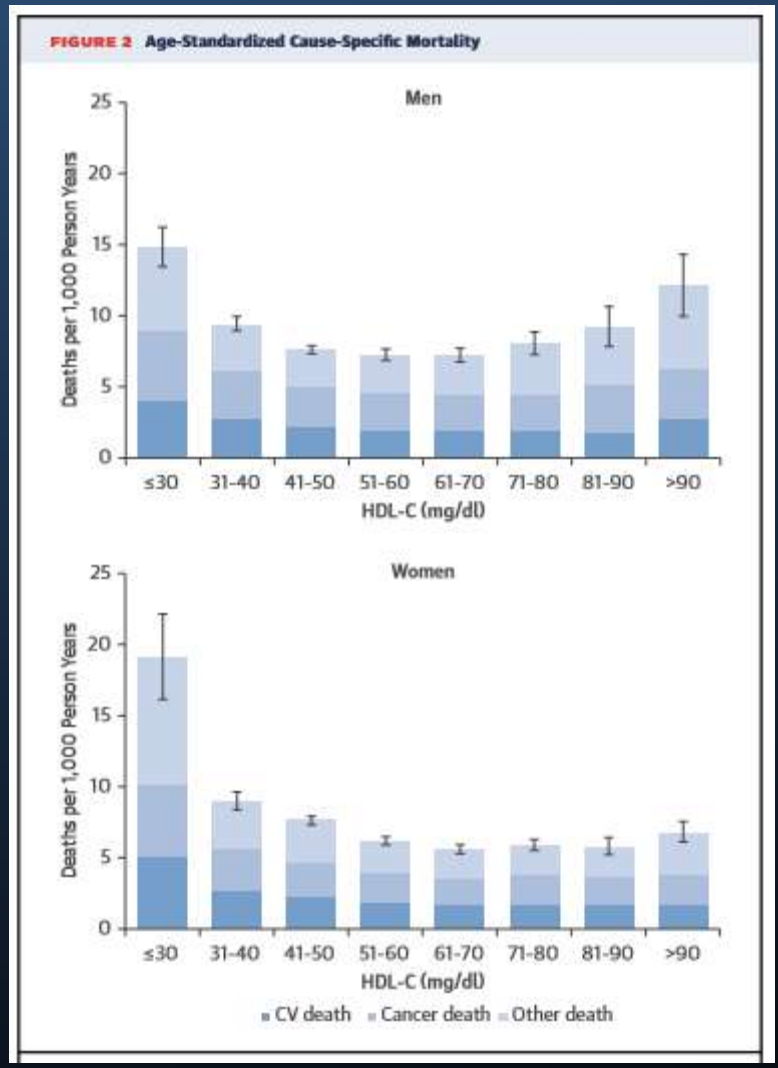
**OBJECTIVES** This study sought to reappraise the association of HDL-C level with CV and non-CV mortality using a "big data" approach.

**METHODS** An observational cohort study was conducted using the CANHEART (Cardiovascular Health in Ambulatory Care Research Team) dataset, which was created by linking together 17 different individual-level data sources. People were included if they were between 40 and 105 years old on January 1, 2008, living in Ontario, Canada, without previous CV conditions or severe comorbidities, and had an outpatient fasting cholesterol measurement in the year prior to the inception date. The primary outcome was cause-specific mortality.

**RESULTS** A total of 631,762 individuals were included. The mean age of our cohort was 57.2 years, 55.4% were women, and mean HDL-C level was 55.2 mg/dl. There were 17,952 deaths during a mean follow-up of 4.9 ± 0.4 years. The overall all-cause mortality rate was 8.1 per 1,000 person-years for men and 6.6 per 1,000 person-years for women. Individuals with lower HDL-C levels were more likely to have low incomes, unhealthy lifestyle, higher triglycerides levels, other cardiac risk factors, and medical comorbidities. Individuals with lower HDL-C levels were independently associated with higher

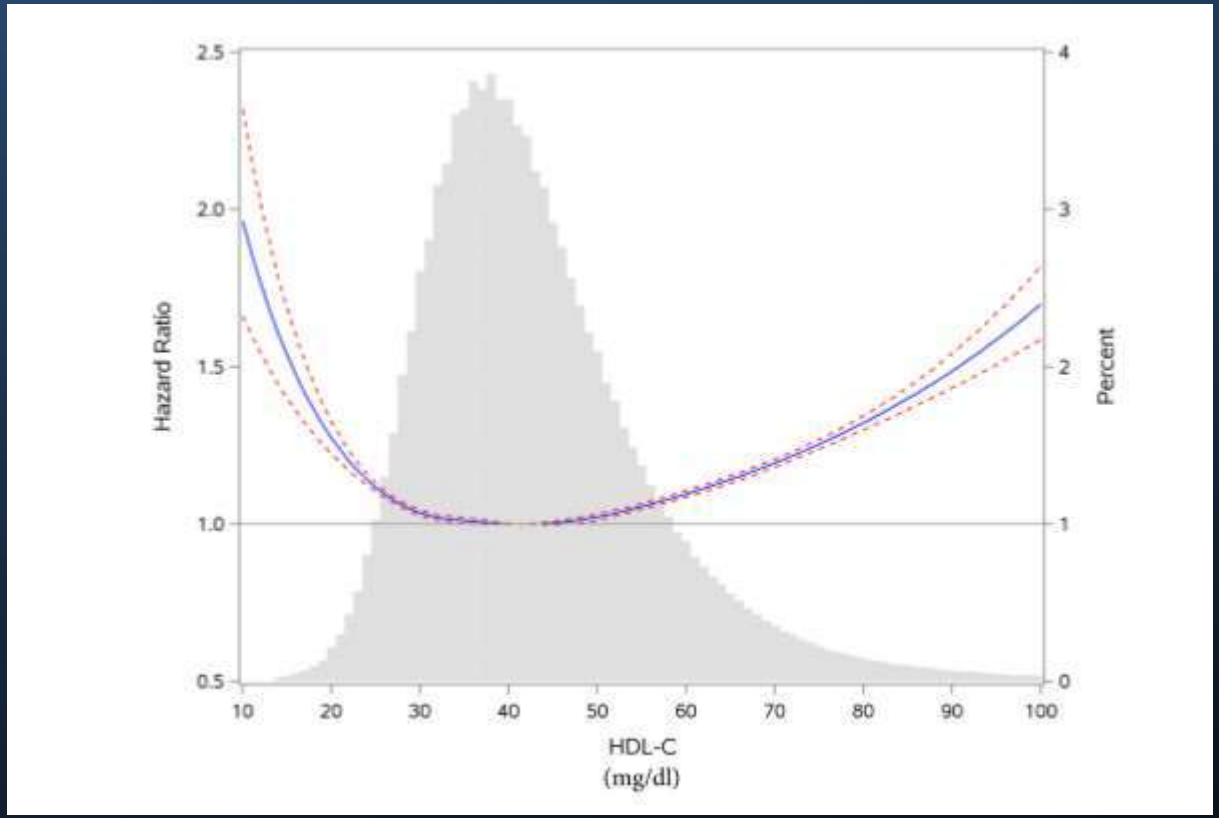
JACC 2016;68;2073-83

# CANHEART STUDY




JACC 2016;68;2073-83

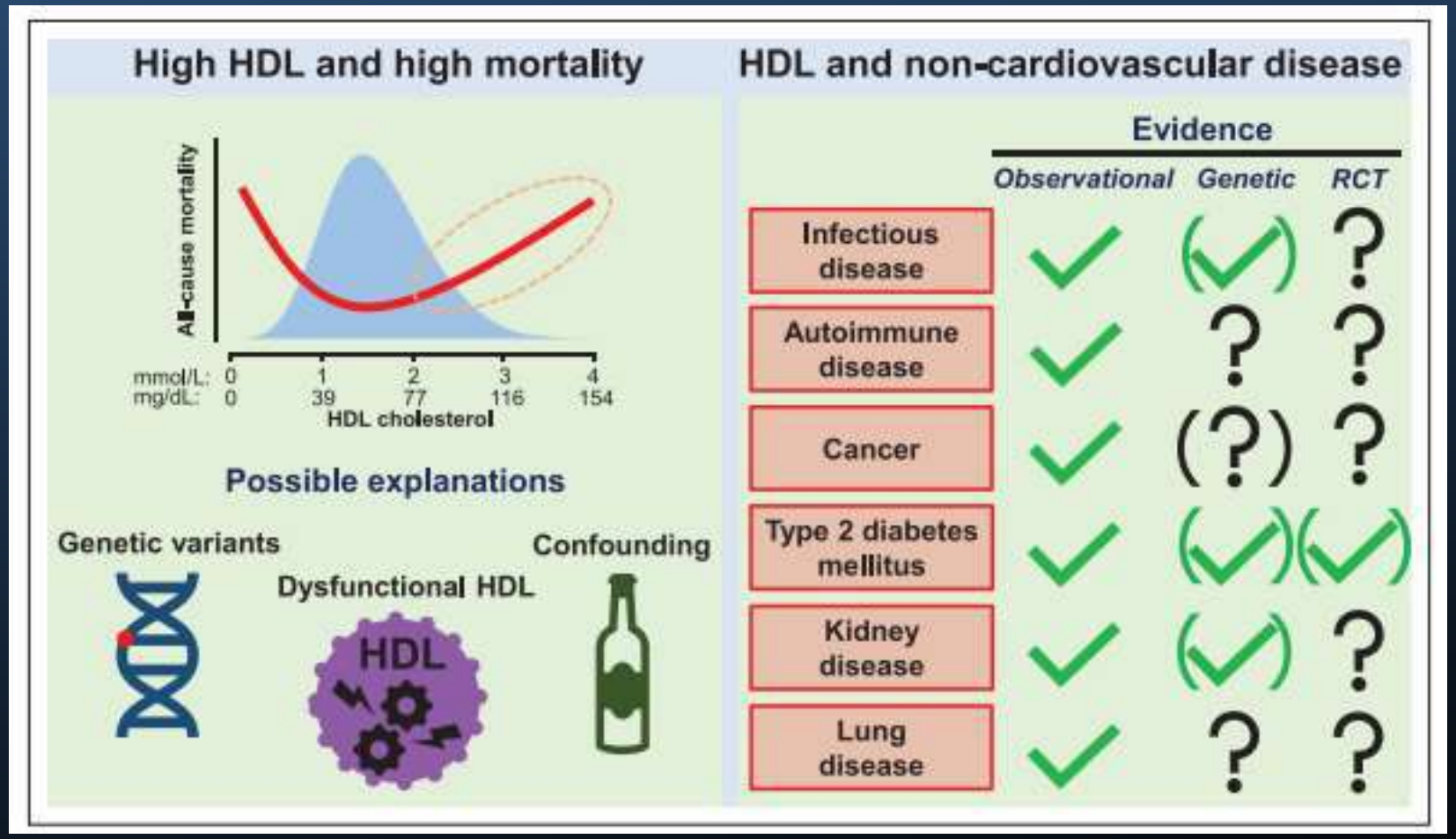
# HDL AND ALL CAUSE MORTALITY




541,682 deaths

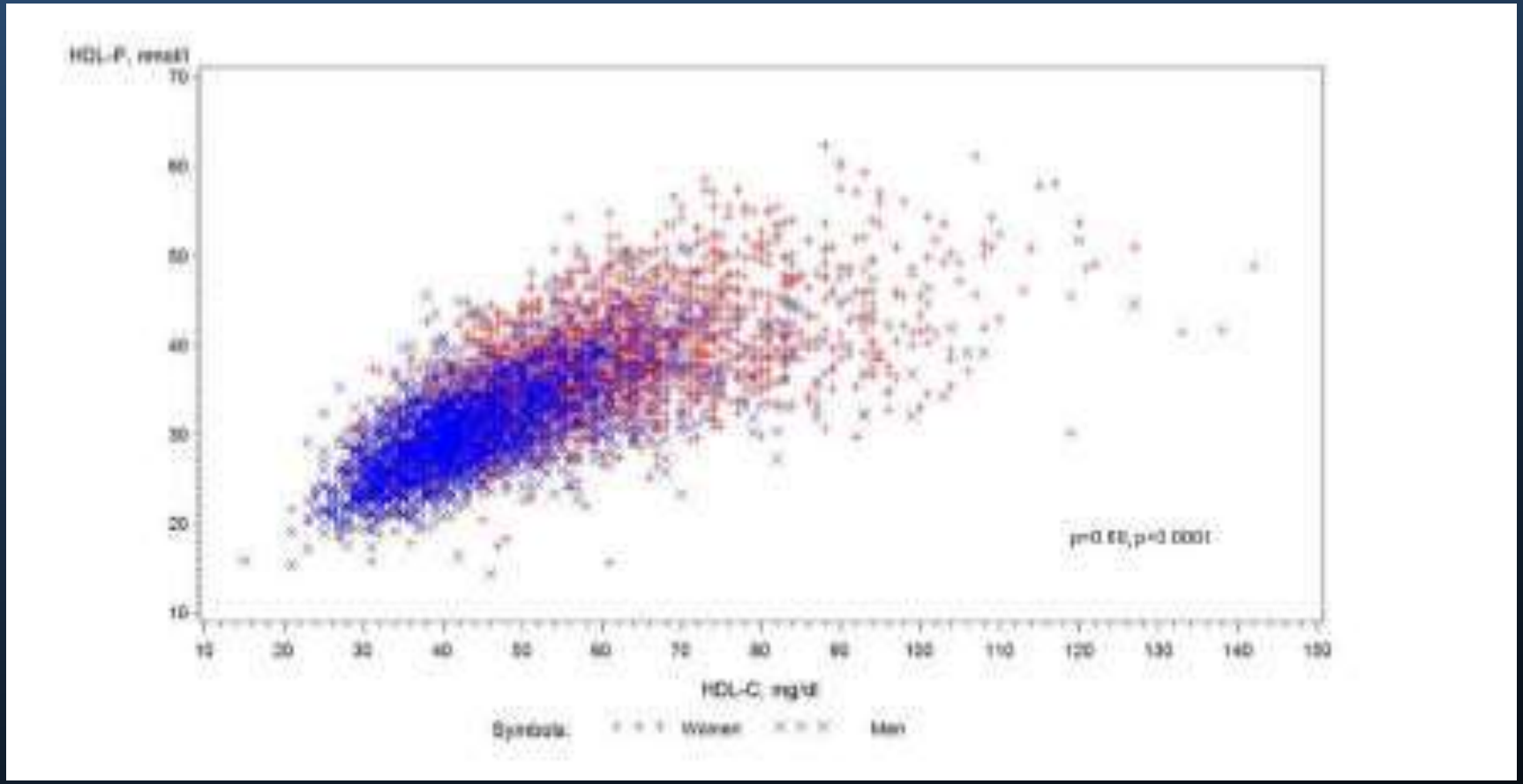
Clin J Am Soc Nephrol 11: 1784–1793, 2016

# HIGH HDL-C AND MORTALITY




Arterioscler Thromb Vasc Biol. 2021;41:128–140. DOI: 10.1161/ATVBAHA.120.314050

# HDL-C VS HDL-P




JACC 2012 Aug 7;(6):508-16

# HDL PARTICLE NUMBER

VA-HIT TRIAL: HDL-P increase by 1 SD decreased CVD 29% over 5 years with no effect from HDL-C

MRFIT: Higher HDL-P reduced CHD death 50% but no effect from HDL-C.

EPIC-NORFOLK :HDL-P in top quartile decreased CAD events by 50%.

HPS: HDL-P was a stronger risk factor for CV events than HDL-C or apo-AI.

MESA: after multi-variate analysis only HDL-P correlated with CV events and HDL-C was not significant.

JUPITOR: HDL-P was significant predictor of CV events in statin treated group and HDL was not

Circulation 125, 2469–2478
Circulation113,1556–1563
Ann. Intern. Med. 150, 84–93
J. Am. Coll. Cardiol. 60, 508–516.
Circulation 128, 1189–1197
Atherosclerosis195,122–128.

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# Cholesterol-Overloaded HDL Particles Are Independently Associated With Progression of Carotid Atherosclerosis in a Cardiovascular Disease-Free Population

## A Community-Based Cohort Study

Yue Qi, MD, PhD, Jie Fan, MD, Jing Liu, MD, PhD, Wei Wang, MD, Miao Wang, MD, Jiayi Sun, MD, Jun Liu, MD, Wuxiang Xie, PhD, Fan Zhao, PhD, Yan Li, MD, Dong Zhao, MD, PhD

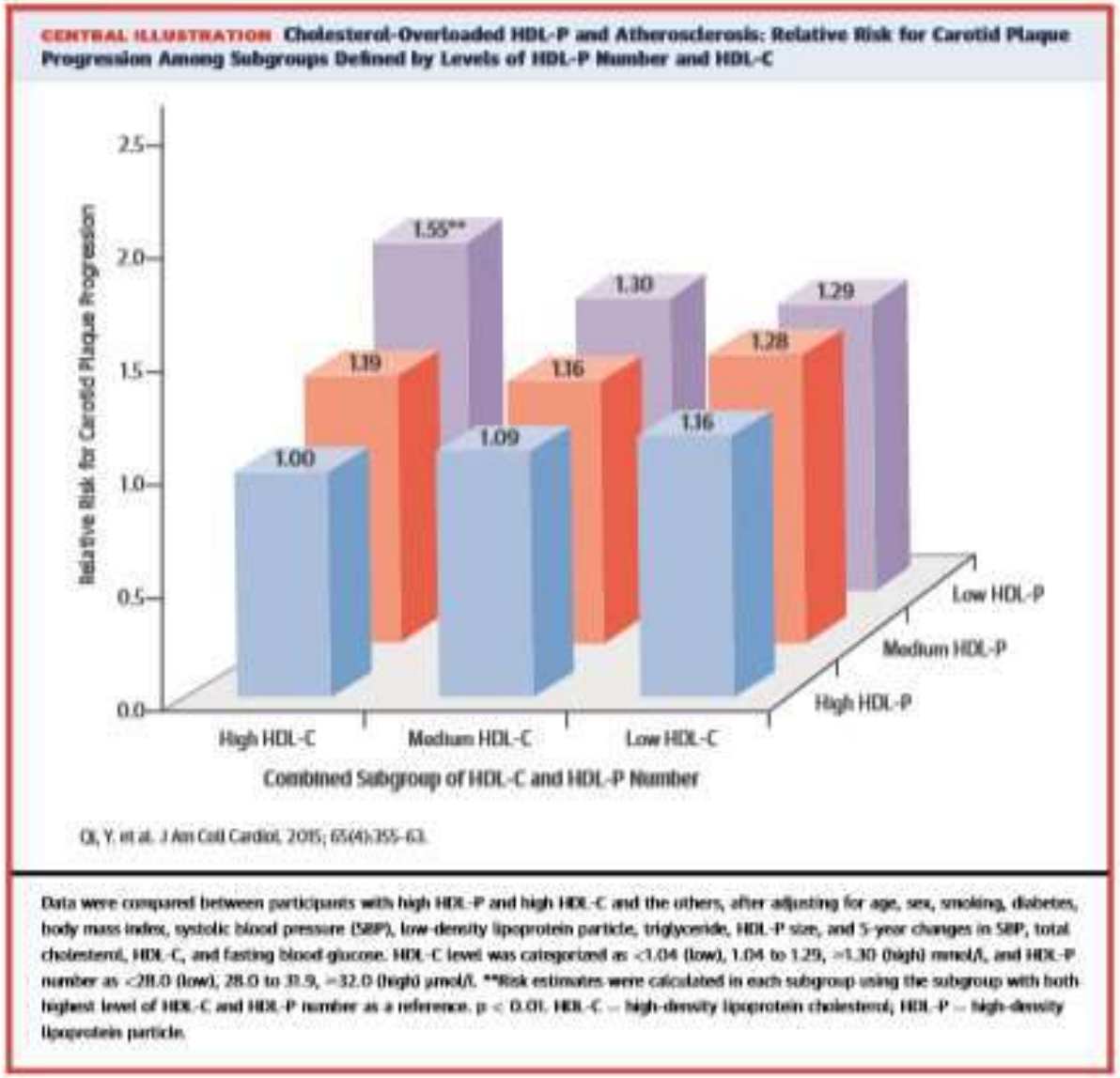
**ABSTRACT**

**BACKGROUND** Cholesterol-overloaded high-density lipoprotein (HDL) particles exert a negative impact on the antiatherogenic function of HDL in experimental studies. However, it remains unclear whether cholesterol-overloaded HDL particle is involved in the development of atherosclerosis in humans.

**OBJECTIVES** The objective of this study was to explore whether cholesterol-overloaded HDL particles are associated with the progression of carotid atherosclerosis in a cardiovascular disease-free population.

**METHODS** Baseline HDL particle number was measured using nuclear magnetic resonance spectroscopy in 930 participants ages 45 to 74 years in a community-based cohort study. An estimate of cholesterol molecules per HDL particle (HDL-C/P ratio) was calculated as the ratio of HDL cholesterol to HDL particles. HDL-C/P ratio was categorized as <41.0 (lowest), 41.0 to 46.9, 47.0 to 52.9, and ≥53.0 (highest) using a fixed increment method. Modified Poisson regression was used to assess the association between HDL-C/P ratio and 5-year progression of carotid atherosclerosis as indicated by progression of carotid plaques and change in total plaque area (TPA).

# HDL-C/HDL-P RATIO




JACC vol 65, no 4, 2015;355-63

# TOTAL CHOLESTEROL/HDL-C RATIO

- Total cholesterol/HDL-C ratio is regarded as the best overall measure of lipid risk and is incorporated in all the major cardiovascular risk calculators.

# COMPARISON OF RATIOS

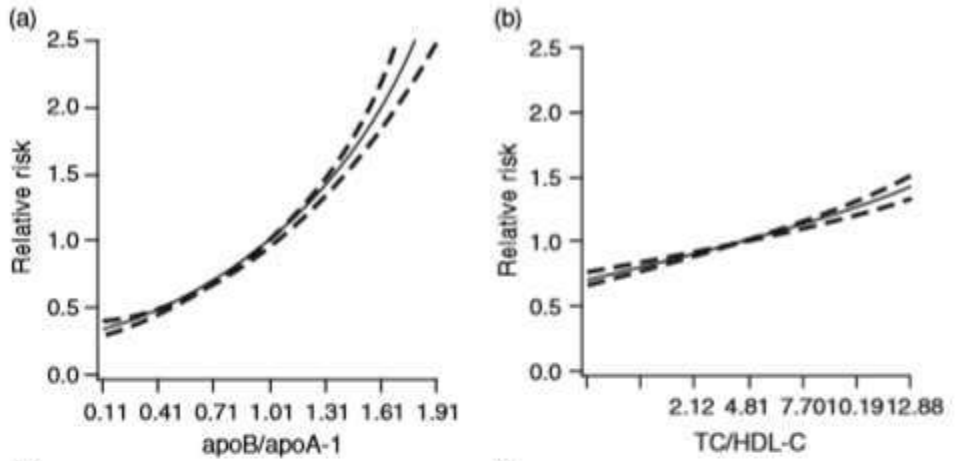



**Fig. 3** apo B/apo A-I ratio versus TC/HDL C ratio in the AMORIS study. Panels (a) and (b) depict the relationship in males between vascular risk and the apo B/apo A-I and TC/HDL C ratios respectively. Panels (c) and (d) present the same data for females. The difference in slopes represents the difference in predictive power between the two ratios.

Journal of Internal Medicine 2006: 259: 247-258

## Coronary Heart Disease

# Low-Density Lipoprotein and High-Density Lipoprotein Particle Subclasses Predict Coronary Events and Are Favorably Changed by Gemfibrozil Therapy in the Veterans Affairs High-Density Lipoprotein Intervention Trial

James D. Otvos, PhD; Dorothea Collins, ScD; David S. Freedman, PhD; Irina Shalaurova, MD; Ernst J. Schaefer, MD; Judith R. McNamara, MT; Hanna E. Bloomfield, MD, MPH; Sander J. Robins, MD

***Background***—Changes in conventional lipid risk factors with gemfibrozil treatment only partially explain the reductions in coronary heart disease (CHD) events experienced by men in the Veterans Affairs High-Density Lipoprotein Intervention Trial (VA-HIT). We examined whether measurement of low-density lipoprotein (LDL) and high-density lipoprotein (HDL) particle subclasses provides additional information relative to CHD risk reduction.

***Methods and Results***—This is a prospective nested case-control study of 364 men with a new CHD event (nonfatal myocardial infarction or cardiac death) during a 5.1-year (median) follow-up and 697 age-matched controls. Nuclear magnetic resonance (NMR) spectroscopy was used to quantify levels of LDL and HDL particle subclasses and mean particle sizes in plasma obtained at baseline and after 7 months of treatment with gemfibrozil or placebo. Odds ratios for a 1-SD increment of each lipoprotein variable were calculated with adjusted logistic regression models. Gemfibrozil treatment increased LDL size and lowered numbers of LDL particles (−5%) while raising numbers of HDL particles (10%) and small HDL subclass particles (21%). Concentrations of these LDL and HDL particles achieved with gemfibrozil were significant, independent predictors of new CHD events. For total LDL and HDL particles, odds ratios predicting CHD benefit were 1.28 (95% CI, 1.12 to 1.47) and 0.71 (95% CI, 0.61 to 0.81), respectively. Mean LDL and HDL particle sizes were not associated with CHD events.

***Conclusions***—The effects of gemfibrozil on NMR-measured LDL and HDL particle subclasses, which are not reflected by conventional lipoprotein cholesterol measures, help to explain the demonstrated benefit of this therapy in patients with low HDL cholesterol. (*Circulation*. 2006;113:1556-1563.)

# VAHIT STUDY

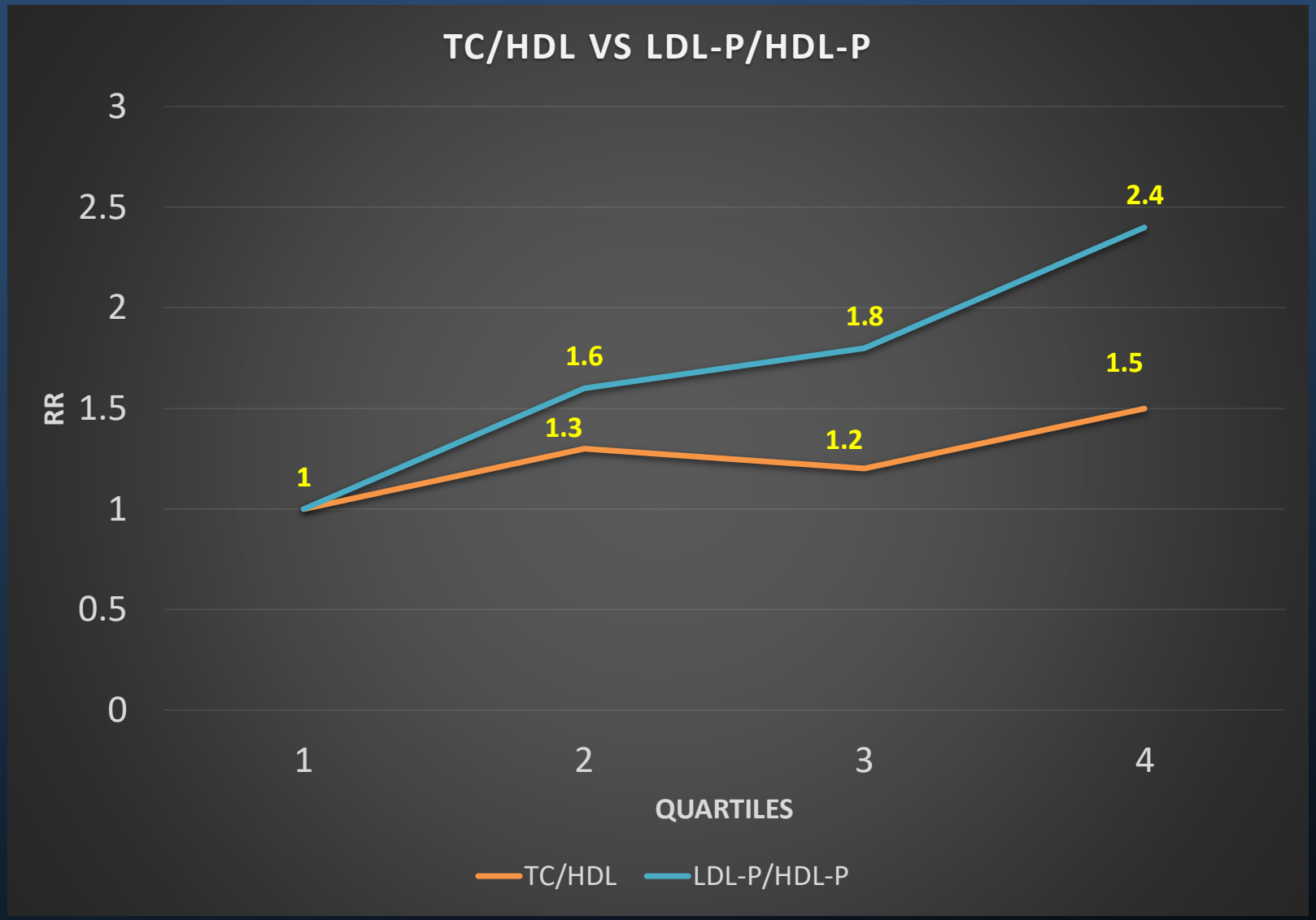
**TABLE 5. Risk of CHD Events According to Quartile of Lipid/Lipoprotein Ratios**

| | Quartile of Plasma Level | | | | |
|---|---|---|---|---|---|
| Ratio | 1 | 2 | 3 | 4 | *P* for Trend |
| TC:HDL-C | | | | | |
| Median (range) | 4.1 (2.1–4.6) | 5.1 (4.6–5.5) | 5.9 (5.5–6.5) | 7.2 (6.5–12.5) | |
| Relative risk* (95% CI) | 1 | 1.3 (0.9–1.7) | 1.2 (0.9–1.6) | 1.5 (1.1–2.0) | 0.27 |
| *P* | | 0.13 | 0.27 | 0.01 | |
| ApoB:ApoA-1 | | | | | |
| Median (range) | 0.66 (0.26–0.73) | 0.79 (0.73–0.85) | 0.90 (0.85–0.97) | 1.1 (0.97–1.9) | |
| Relative risk (95% CI) | 1 | 1.3 (0.9–1.8) | 1.6 (1.2–2.2) | 1.5 (1.1–2.0) | 0.37 |
| *P* | | 0.14 | 0.004 | 0.02 | |
| LDL-P:HDL-P | | | | | |
| Median (range) | 34.4 (13.9–40.5) | 46.4 (40.5–51.2) | 55.3 (51.3–61.2) | 71.0 (61.3–127.7) | |
| Relative risk (95% CI) | 1 | 1.6 (1.2–2.3) | 1.8 (1.3–2.6) | 2.4 (1.8–3.3) | 0.009 |
| *P* | | 0.005 | 0.0005 | <0.0001 | |

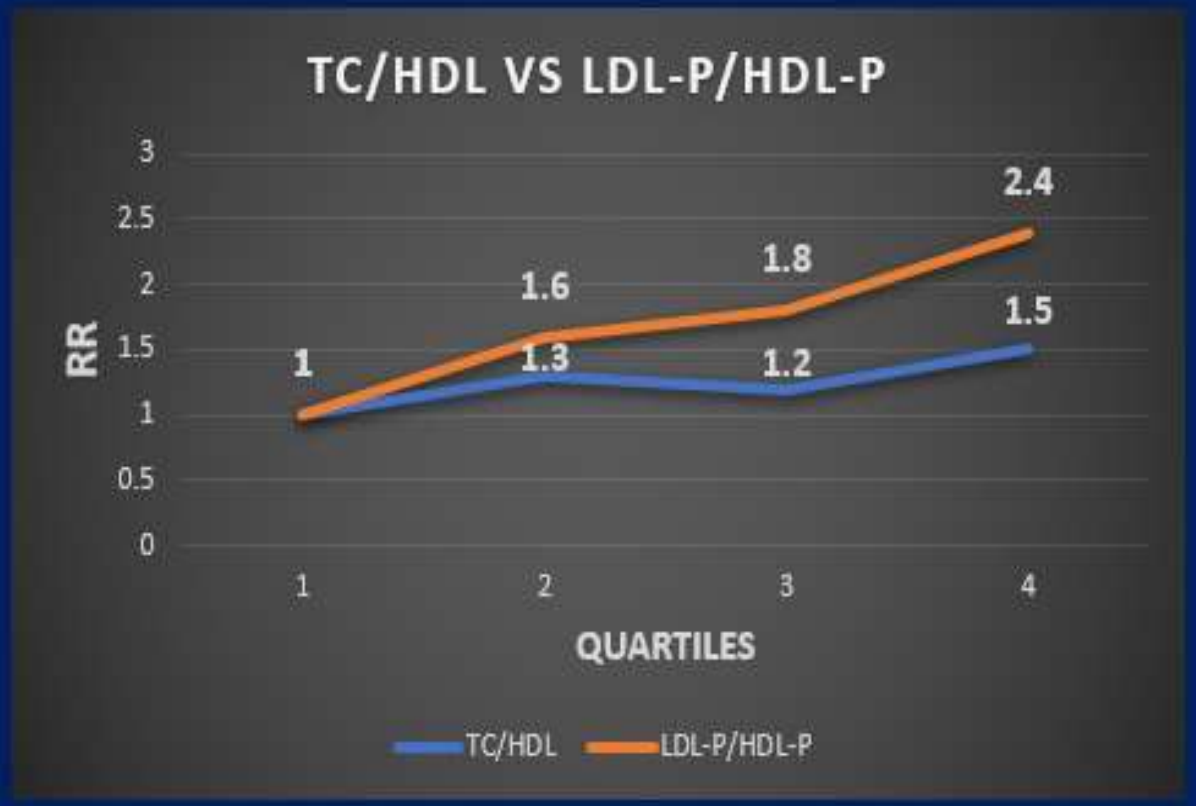
TC indicates triglycerides.

*Logistic regression models used on-trial values of lipid/lipoprotein ratios and were adjusted for treatment group, age, hypertension, smoking, body mass index, and diabetes.

Circulation. 2006;113:1556-1563




Circulation. 2006;113:1556-1563




| TC/HDL | 2.5 | 3 | 3.5 | 4 | 4.5 | 5 | 5.5 | 6 | 6.5 | 7 | 7.5 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| RR | 0.42 | 0.68 | 1.05 | 1.33 | 1.72 | 2.05 | 2.43 | 2.69 | 3.11 | 3.35 | 3.77 |
| | | | | | | | | | | | |
| | | | | | | | | | | | |
| LDL-P/HDL- | 17.8 | 24.6 | 34.2 | 41.8 | 52.4 | 61.2 | 71.4 | 78.4 | 90 | 96.2 | 107.4 |
| RR | 0.44 | 0.69 | 1.05 | 1.33 | 1.72 | 2.05 | 2.43 | 2.69 | 3.13 | 3.35 | 3.77 |

Circulation. 2006;113:1556-1563

# LOWER LDL-C IS ALWAYS BETTER

- The patient with the lower LDL-C is always at lower risk.

# Beyond Low-Density Lipoprotein Cholesterol

## Respective Contributions of Non–High-Density Lipoprotein Cholesterol Levels, Triglycerides, and the Total Cholesterol/High-Density Lipoprotein Cholesterol Ratio to Coronary Heart Disease Risk in Apparently Healthy Men and Women

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Jean-Pierre Després, PHD,*‡ Prediman K. Shah, MD,§ John J. P. Kastelein, MD, PHD,‖
Nicholas J. Wareham, MBBS, PHD,# S. Matthijs Boekholdt, MD, PHD,¶ Kay-Tee Khaw, MBBCHIR**

*Québec, Québec, Canada; Los Angeles, California; Amsterdam, the Netherlands; and Cambridge, United Kingdom*

**Objectives** This study was designed to test the hypothesis that at any low-density lipoprotein cholesterol (LDL-C) level, other lipid parameters such as non–high-density lipoprotein cholesterol (HDL-C) levels, triglyceride (TG) levels, and the total cholesterol (TC)/HDL-C are still associated with an increased coronary heart disease (CHD) risk.

**Background** Although LDL-C is considered to be the primary target of lipid-lowering therapy, other parameters of the lipoprotein-lipid profile may more closely associated with CHD risk.

**Methods** In the EPIC (European Prospective Investigation Into Cancer and Nutrition)-Norfolk prospective population study, 21,448 participants without diabetes or CHD between age 45 and 79 years were followed for 11.0 years. A total of 2,086 participants developed CHD during follow-up.

**Results** Among individuals with low LDL-C levels (<100 mg/dl), after adjustment for age, sex, smoking, systolic blood pressure, waist circumference, physical activity, and hormone replacement therapy (in women), those with non–HDL-C >130 mg/dl had a hazard ratio (HR) for future CHD of 1.84 (95% confidence interval [CI]: 1.12 to 3.04) when compared with those with non–HDL-C levels <130 mg/dl. In a similar model, individuals with TG levels >150 mg/dl had an HR of 1.63 (95% CI: 1.02 to 2.59) when compared with those with TG levels <150 mg/dl, and individuals with a TC/HDL-C ratio >5 had an HR of 2.19 (95% CI: 1.22 to 3.93) when compared with those with a TC/HDL-C ratio <5.

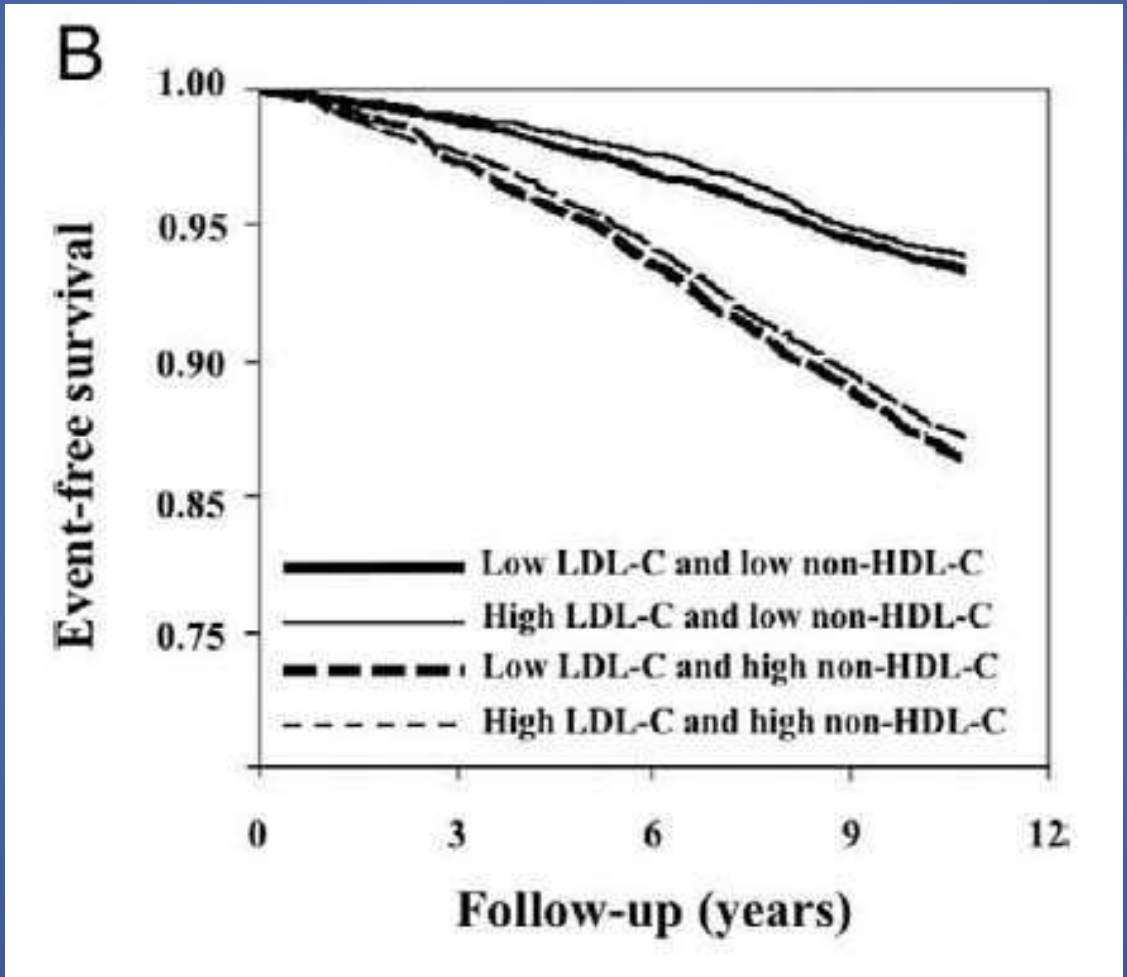
**Conclusions** In this prospective study, independently of their plasma LDL-C levels, participants with high non–HDL-C levels, high TG levels, or with an elevated TC/HDL-C ratio were at increased CHD risk. CHD risk assessment algorithms as well as lipid targets of lipid-lowering trials may also need to consider other easily available parameters such as non–HDL-C. (J Am Coll Cardiol 2010;55:35–41) 

# EPIC-NORFOLK STUDY

- Non-HDL-C was the best predictor of future CHD over the 11 yr follow-up with HR 2.39
- Non-HDL-C HR 2.39
- LDL-C HR 1.22
- TG HR 1.14 (Mean TG 159)
- TC/HDL HR 1.19 (mean HDL 45)

J Am Coll Cardiol 2010;55:35–41

# EPIC-NORFOLK STUDY

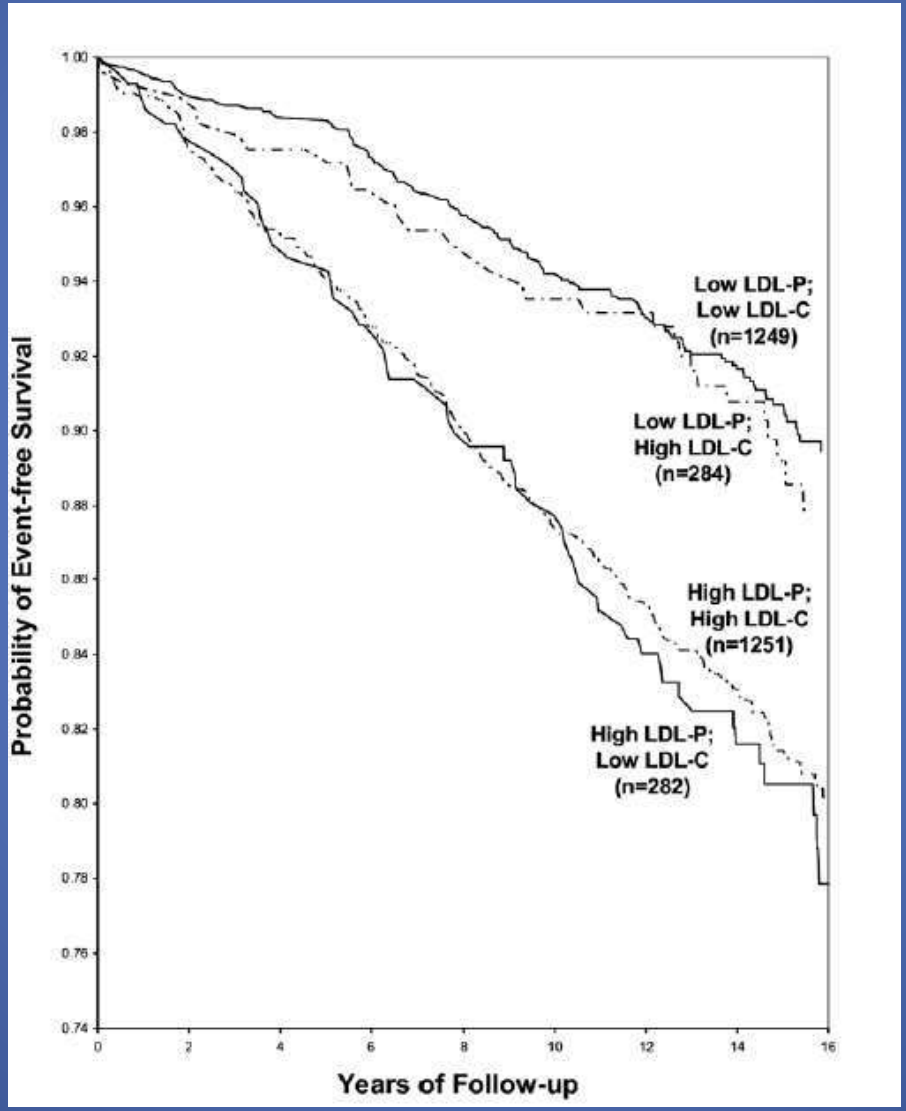



LDL-C < 150.6
Non-HDL > 177.6

TG = 159

J Am Coll Cardiol 2010;55:35–41

# FRAMINGHAM OFFSPRING




Journal of Clinical Lipidology; vol 1, no 6, Dec 2007

# GOAL LDL-C FOR ACS PATIENTS IS LESS THAN 70 MG/DL

- Do all post-ACS patients benefit equally to having an LDL-C under 70 mg/dl?

# Biomarkers and Clinical Cardiovascular Outcomes With Ezetimibe in the IMPROVE-IT Trial

Arman Qamar, MD, MPH,[a] Robert P. Giugliano, MD, SM,[a] Erin A. Bohula, MD, DPhil,[a] Jeong-Gun Park, PhD,[a] Petr Jarolim, MD, PhD,[b] Sabina A. Murphy, MPH,[a] Michael A. Blazing, MD,[c] Robert M. Califf, MD,[d,e,f] Christopher P. Cannon, MD,[a] Eugene Braunwald, MD,[a] David A. Morrow, MD, MPH[a]

## ABSTRACT

**BACKGROUND** Addition of ezetimibe to statin therapy reduces the risk of recurrent cardiovascular (CV) events in patients with prior acute coronary syndrome (ACS). The role of biomarkers in identifying subsets of patients who may derive greater clinical benefit with ezetimibe is unknown.

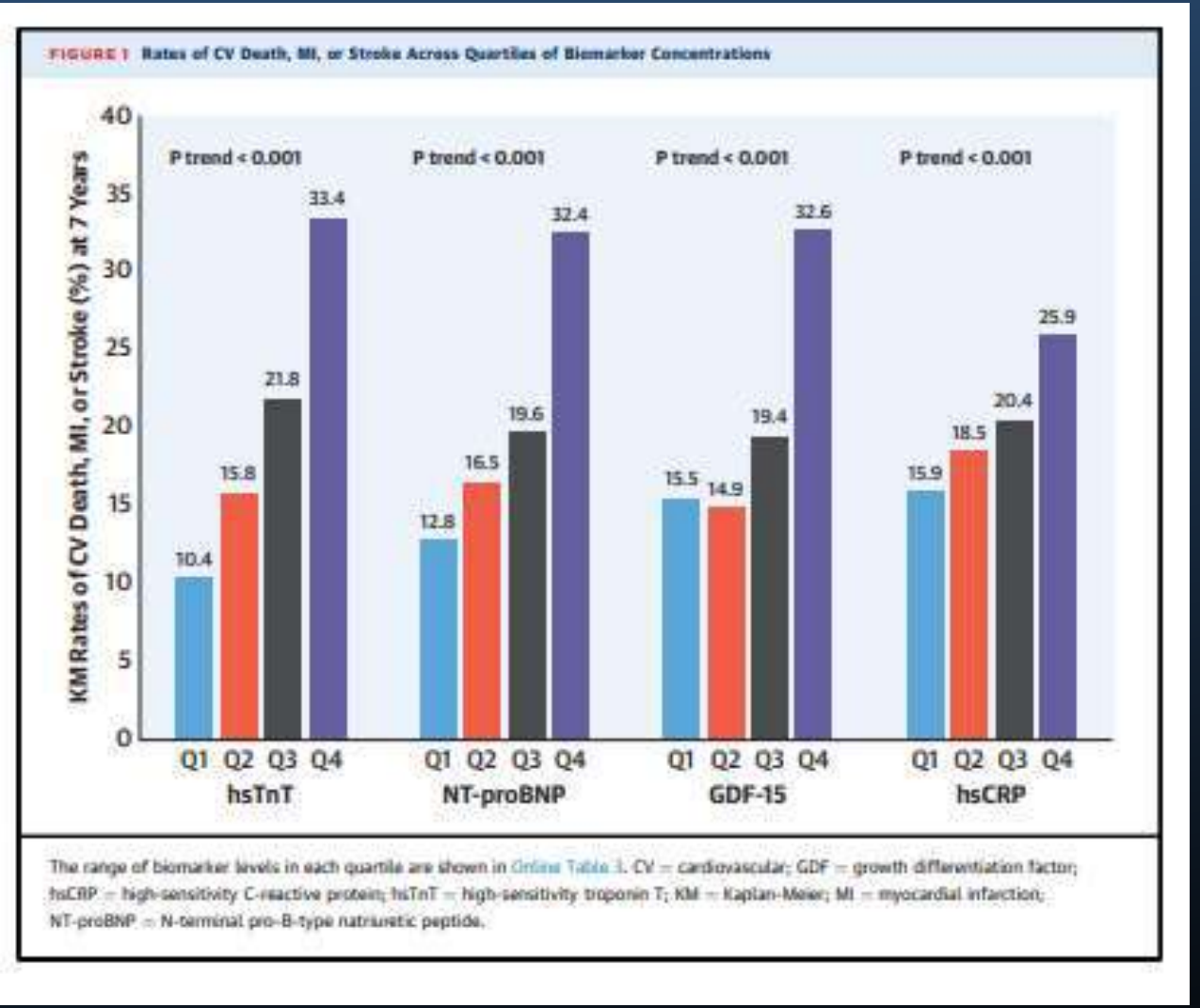
**OBJECTIVES** This study sought to evaluate the role of established CV biomarkers in assessing likely benefit with ezetimibe added to statin therapy in post-ACS patients.

**METHODS** In a pre-specified nested analysis within a randomized, double-blind trial of ezetimibe/simvastatin versus placebo/simvastatin (IMPROVE-IT [Improved Reduction of Outcomes: Vytorin Efficacy International Trial]), high-sensitivity troponin T, N-terminal pro-B-type natriuretic peptide, growth-differentiation factor-15, and high-sensitivity C-reactive protein was measured in 7,195 patients stabilized (1 month post-randomization) after ACS. A multimarker approach based on biomarker values was used to examine the risk of recurrent CV events and clinical benefit with ezetimibe.

**RESULTS** Elevated levels of each biomarker were independently associated with higher risks of CV death/myocardial infarction/stroke and CV death/heart failure ($p_{trend} < 0.001$ for each). There was a pattern of greater absolute risk reduction in CV death/myocardial infarction/stroke with the addition of ezetimibe to statin therapy in patients at higher risk on the basis of biomarker levels. High-risk patients (≥3 biomarkers "positive"; n = 1,437) had an absolute risk difference of −7.3% (95% confidence interval: −13.8% to −0.8%; p = 0.02) with ezetimibe, and intermediate-risk patients (1 to 2 biomarkers positive; n = 3,842) had an absolute risk difference of −4.4% (95% confidence interval: −9.7% to 0.8%), translating into numbers needed to treat at 7 years of 14 and 23, respectively. Low-risk patients (0 biomarkers positive; n = 1,916) did not appear to benefit from the addition of ezetimibe to statin therapy.

**CONCLUSIONS** A biomarker-based strategy identifies a gradient of risk among patients post-ACS, offering the potential to identify higher-risk patients with a correspondingly high absolute benefit from the addition of ezetimibe to statin therapy. (J Am Coll Cardiol 2019;74:1057-68) © 2019 by the American College of Cardiology Foundation.

# IMPROVE-IT TRIAL AND BIOMARKERS




JACC VOL. 74, NO. 8, 2019 Qamar et al. AUGUST 27, 2019:1057 – 68

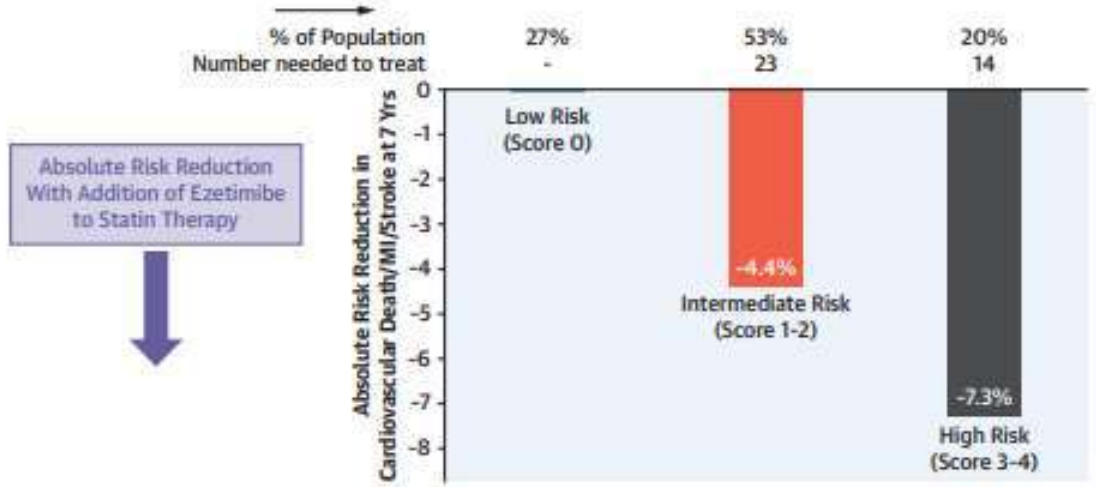
# IMPROVE-IT AND BIOMARKERS

**CENTRAL ILLUSTRATION** **Absolute Risk Reduction and the Number Needed to Treat With the Addition of Ezetimibe to Statin Therapy Across Biomarker-Based Risk Categories**

**Biomarker Score**

*Assign 1 point for each elevated biomarker*

| Biomarker | Points |
|---|---|
| High-sensitivity troponin T ≥14 ng/l | 1 |
| N-terminal pro–B-type natriuretic peptide ≥450 pg/ml | 1 |
| Growth differentiation factor-15 ≥1800 pg/ml | 1 |
| High-sensitivity C-reactive protein ≥2 mg/l | 1 |
| **Maximum Possible Score** | 4 |




Qamar, A. et al. J Am Coll Cardiol. 2019;74(8):1057–68.

A multimarker approach using established cardiac biomarkers identified higher-risk patients who derived a correspondingly high benefit from the addition of ezetimibe to statin therapy. Therapeutic decision making with biomarkers offers the potential to personalize secondary preventive therapy in patients with stable ischemic heart disease. MI = myocardial infarction.

JACC VOL. 74, NO. 8, 2019 Qamar et al. AUGUST 27, 2019:1057 – 68

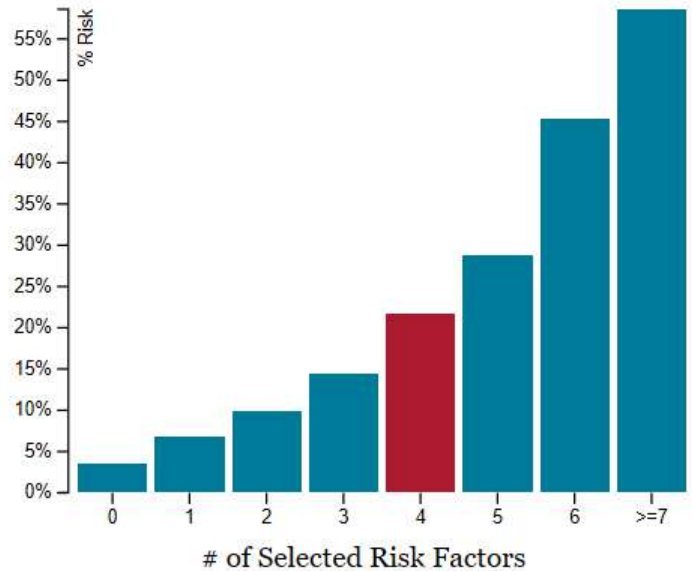
# TIMI Risk Score for Secondary Prevention (TRS 2°P)

## Risk in Patients with Known Atherosclerotic Vascular Disease

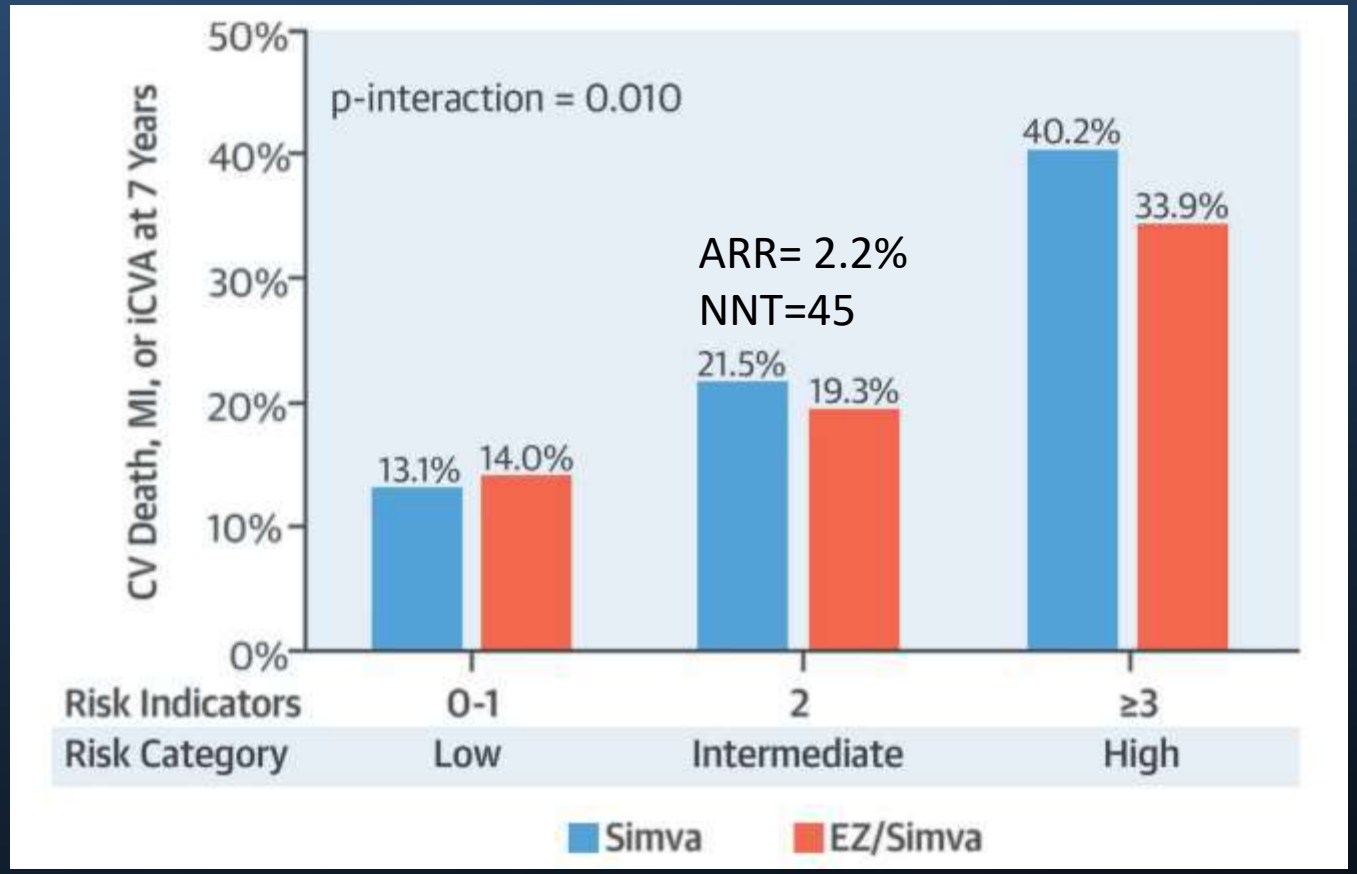
- CHF
- HTN
- Age >= 75
- DM
- Prior Stroke
- Prior CABG
- PAD
- eGFR < 60
- Current Smoking

**4 Risk Indicators Selected**

**21.8% risk at 3 years of CV death, MI or Ischemic Stroke.**



# TIMI SECONDARY RISK SCORE



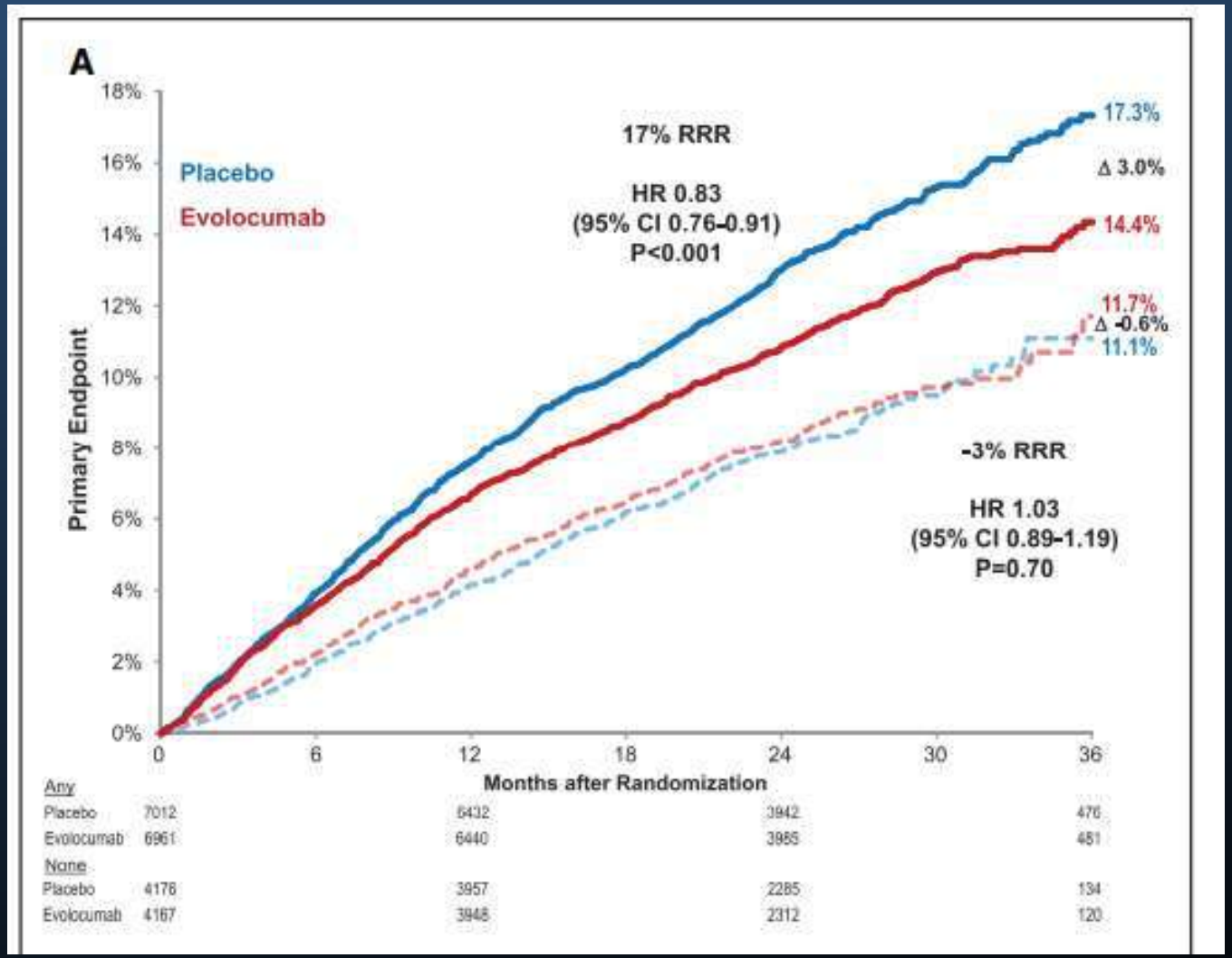

ARR=6.3%
NNT=16

Bohula, E.A. et al. J Am Coll Cardiol. 2017;69(8):911–21

# PCSK9 INHIBITORS AND BENEFIT

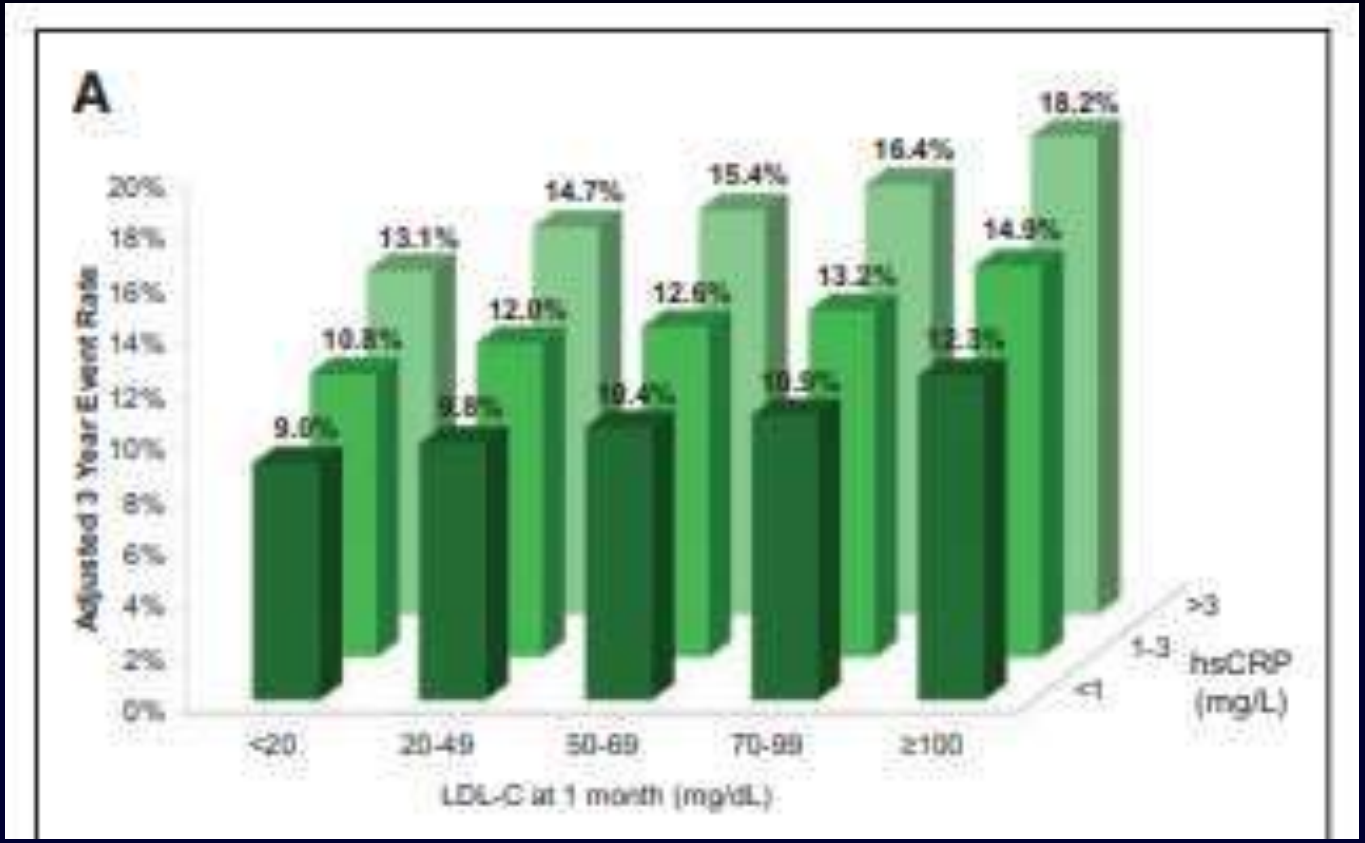
- Do all patients on PCSK9 inhibitors post-MI benefit?

# CLINICAL BENEFIT OF PCSK9 INHIBITORS BY SEVERITY AND EXTENT OF CAD




Circulation. 2018;138:756–766. DOI: 10.1161/CIRCULATIONAHA.118.034309

# LDL RISK AND CRP RISK IN THE FOURIER TRIAL

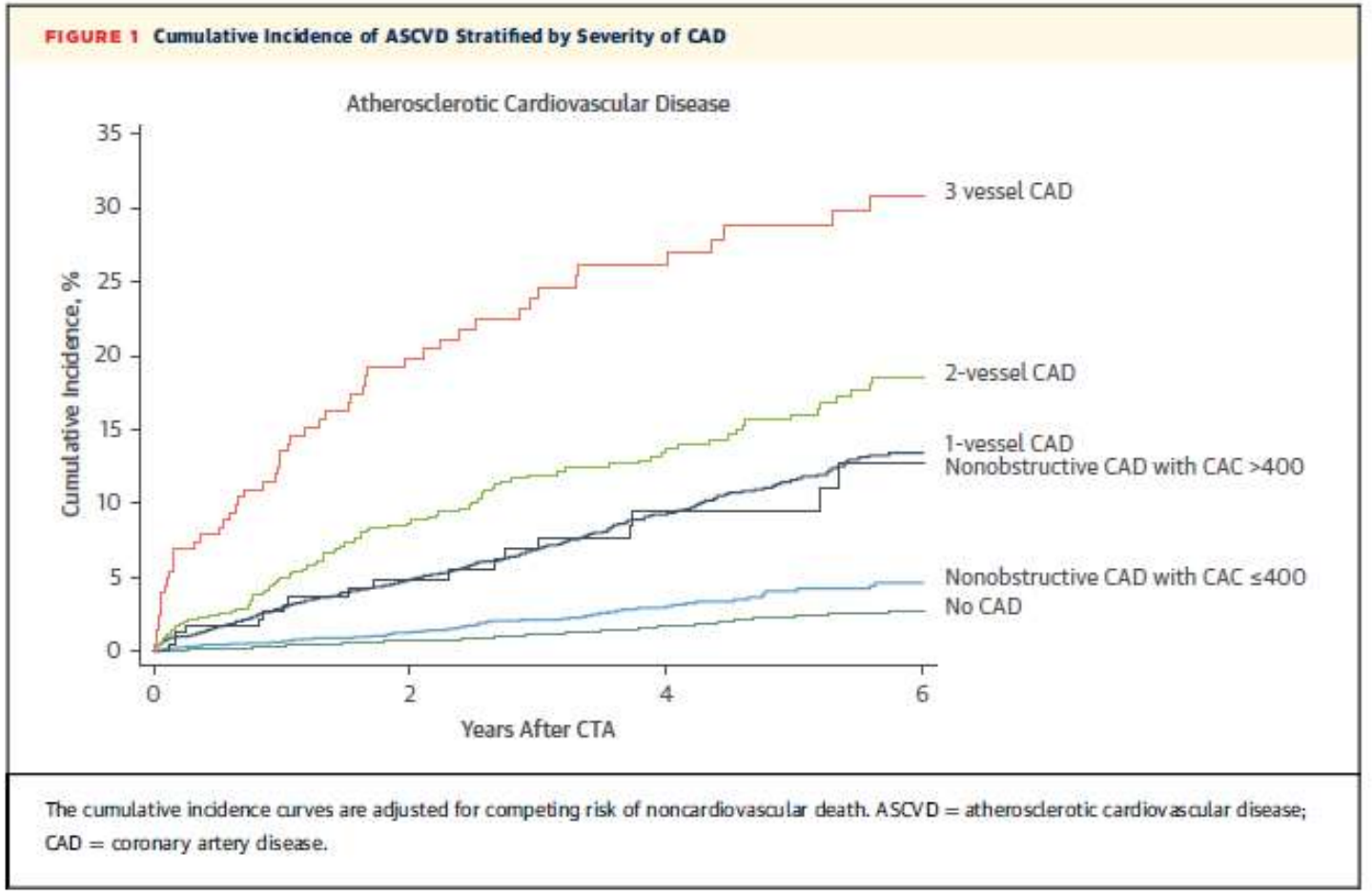



*Circulation.* 2018;137:00–00. DOI: 10.1161/CIRCULATIONAHA.118.034032

# 10 YEAR CARDIOVASCULAR RISK AND LDL-C

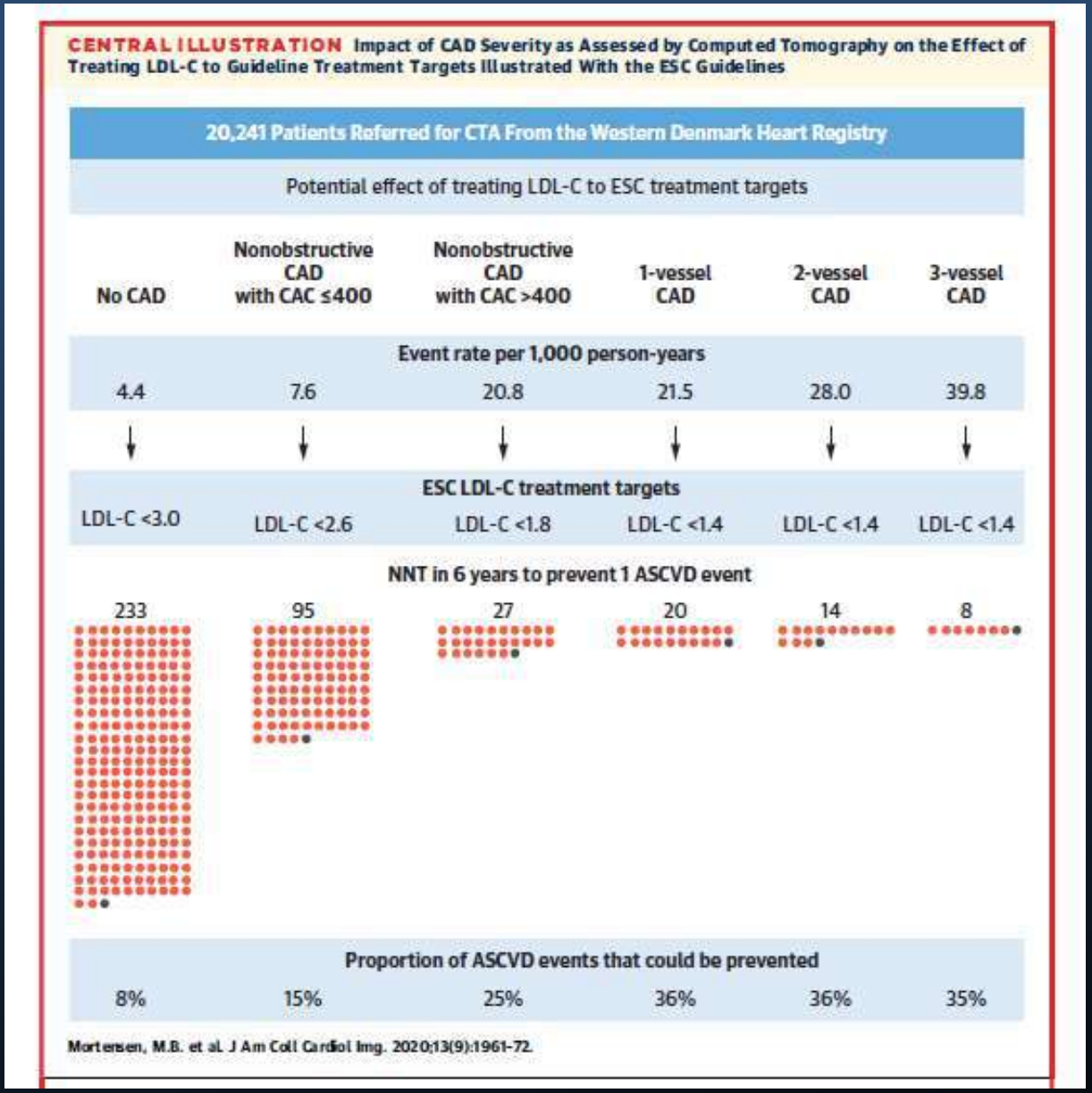
- Most major lipid guidelines recommend calculating 10 year cardiovascular risk and assessing LDL-C levels to direct intensity of lipid lowering therapy.
- Does this approach identify and appropriately treat those patients who benefit the most from aggressive treatment?

# CAD Severity on Cardiac CTA Identifies Patients With Most Benefit of Treating LDL-Cholesterol to ACC/AHA and ESC/EAS Targets



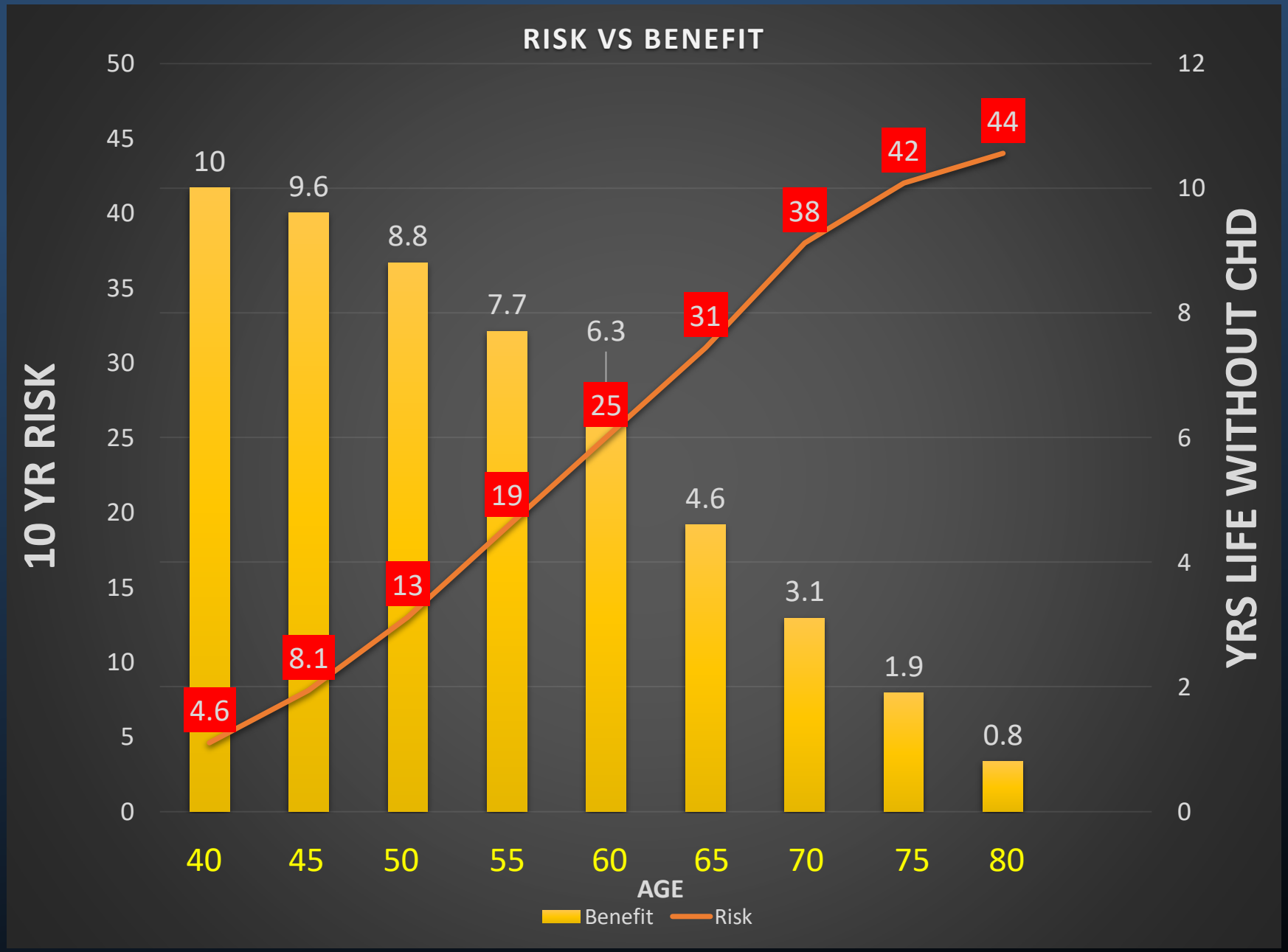

20,241 symptomatic patients undergoing diagnostic CTA from the Western Denmark Heart Registry

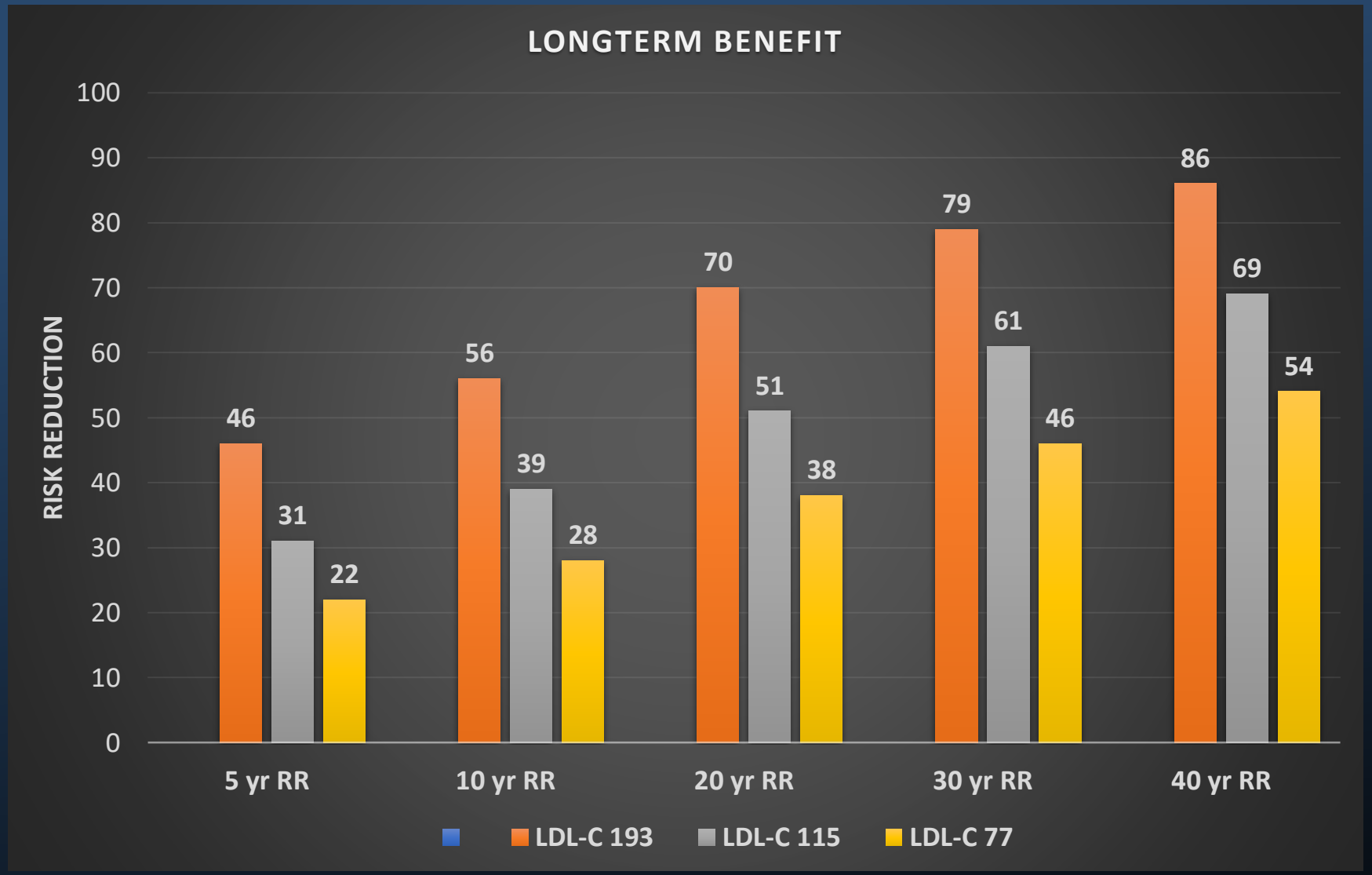
J Am Coll Cardiol Img 2020;13:1961–72




LDL 55 mg/dl

J Am Coll Cardiol Img 2020;13:1961–72


RISK VS BENEFIT
10 YR RISK
YRS LIFE WITHOUT CHD
50
45
40
35
30
25
20
15
10
5
0
12
10
8
6
4
2
0
10
9.6
8.8
7.7
6.3
4.6
3.1
1.9
0.8
4.6
8.1
13
19
25
31
38
42
44
40
45
50
55
60
65
70
75
80
AGE
Benefit
Risk




European Heart Journal (2017) 38,2459-2472

# Prevalence, Impact, and Predictive Value of Detecting Subclinical Coronary and Carotid Atherosclerosis in Asymptomatic Adults

## The BioImage Study

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**ABSTRACT**

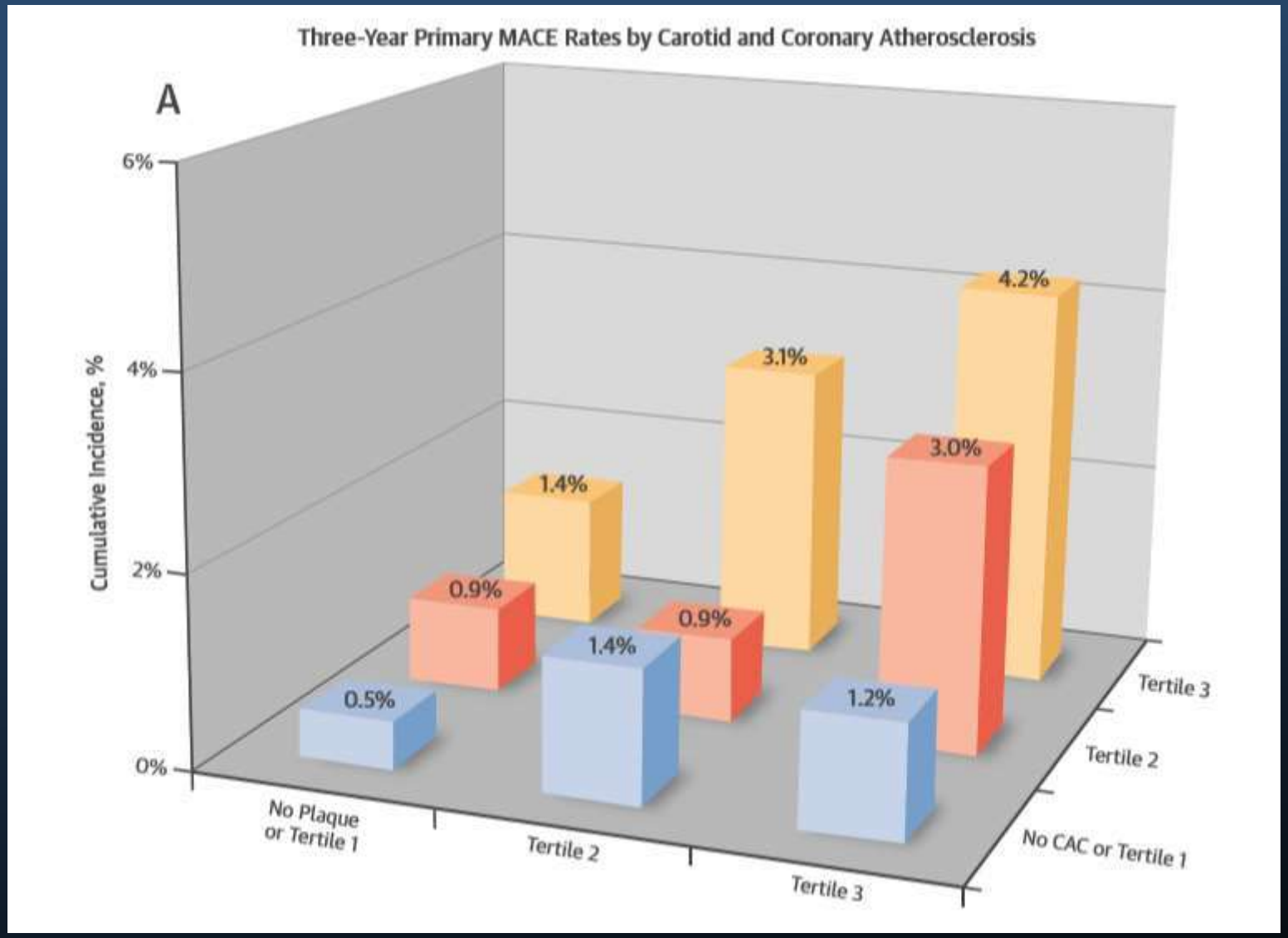
**BACKGROUND** Although recent studies suggest that measuring coronary artery calcification (CAC) may be superior to indirect atherosclerotic markers in predicting cardiac risk, there are limited data evaluating imaging-based biomarkers that directly quantify atherosclerosis in different vascular beds performed in a single cohort.

**OBJECTIVES** The BioImage Study (A Clinical Study of Burden of Atherosclerotic Disease in an At-Risk Population) sought to identify imaging biomarkers that predict near-term (3-year) atherothrombotic events.

**METHODS** The BioImage Study enrolled 5,808 asymptomatic U.S. adults (mean age: 69 years, 56.5% female) in a prospective cohort evaluating the role of vascular imaging on cardiovascular risk prediction. All patients were evaluated by CAC and novel 3-dimensional carotid ultrasound. Plaque areas from both carotid arteries were summed as the carotid plaque burden (cPB). The primary endpoint was the composite of major adverse cardiac events (MACE) (cardiovascular death, myocardial infarction, and ischemic stroke). A broader secondary MACE endpoint also included all-cause death, unstable angina, and coronary revascularization.

**RESULTS** Over a median follow-up of 2.7 years, MACE occurred in 216 patients (4.2%), of which 82 (1.5%) were primary events. After adjustment for risk factors, and compared with individuals without any cPB, hazard ratios for MACE were 0.78 (95% confidence interval [CI]: 0.31 to 1.91), 1.45 (95% CI: 0.67 to 3.14), and 2.36 (95% CI: 1.13 to 4.92) with increasing cPB tertile, with similar results for CAC. Net reclassification significantly improved with either cPB (0.23) or CAC (0.25). MACE rates increased simultaneously with higher levels of both cPB and CAC.

**CONCLUSIONS** Detection of subclinical carotid or coronary atherosclerosis improves risk predictions and reclassification compared with conventional risk factors, with comparable results for either modality. Cost-effective analyses are warranted to define the optimal roles of these complementary techniques. (BioImage Study: A Clinical Study of Burden of Atherosclerotic Disease in an At-Risk Population; NCT00738725) (J Am Coll Cardiol 2015;65:1065–74) © 2015 by the American College of Cardiology Foundation.




JACC 2015:65, 1064-74

# POLYGENE RISK SCORE AND BENEFIT OF CHOLESTEROL LOWERING

- Cardiovascular risk may vary by  30-60% dependent on genetic risk factors that are not reflected in traditional clinical risk factors.
- Analysis of polygenetic risk score in JUPITER, ASCOT, CARE, and PROVE-IT trials revealed 71% greater benefit of cholesterol lowering in subjects with high polygene score vs low polygene risk score.

Lancet 2015 June 6: 385(9984): 2264-2271

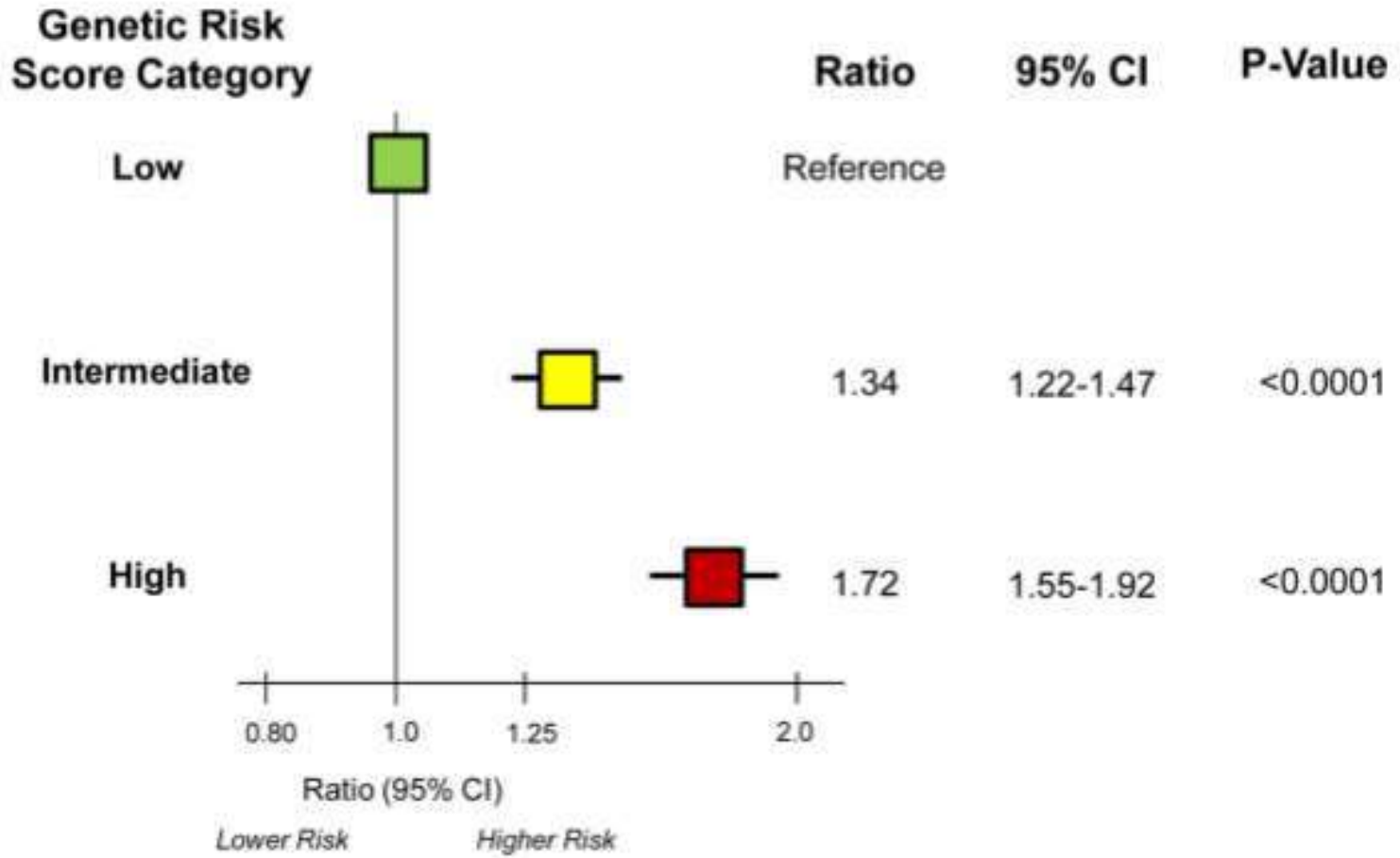



**Figure 1. Summary of Risk of Coronary Heart Disease Across Genetic Risk Score Categories in Primary and Secondary Prevention Populations**

The boxes indicate the point estimates and the horizontal lines the 95% confidence intervals.

Lancet 2015 June 6: 385(9984): 2264-2271

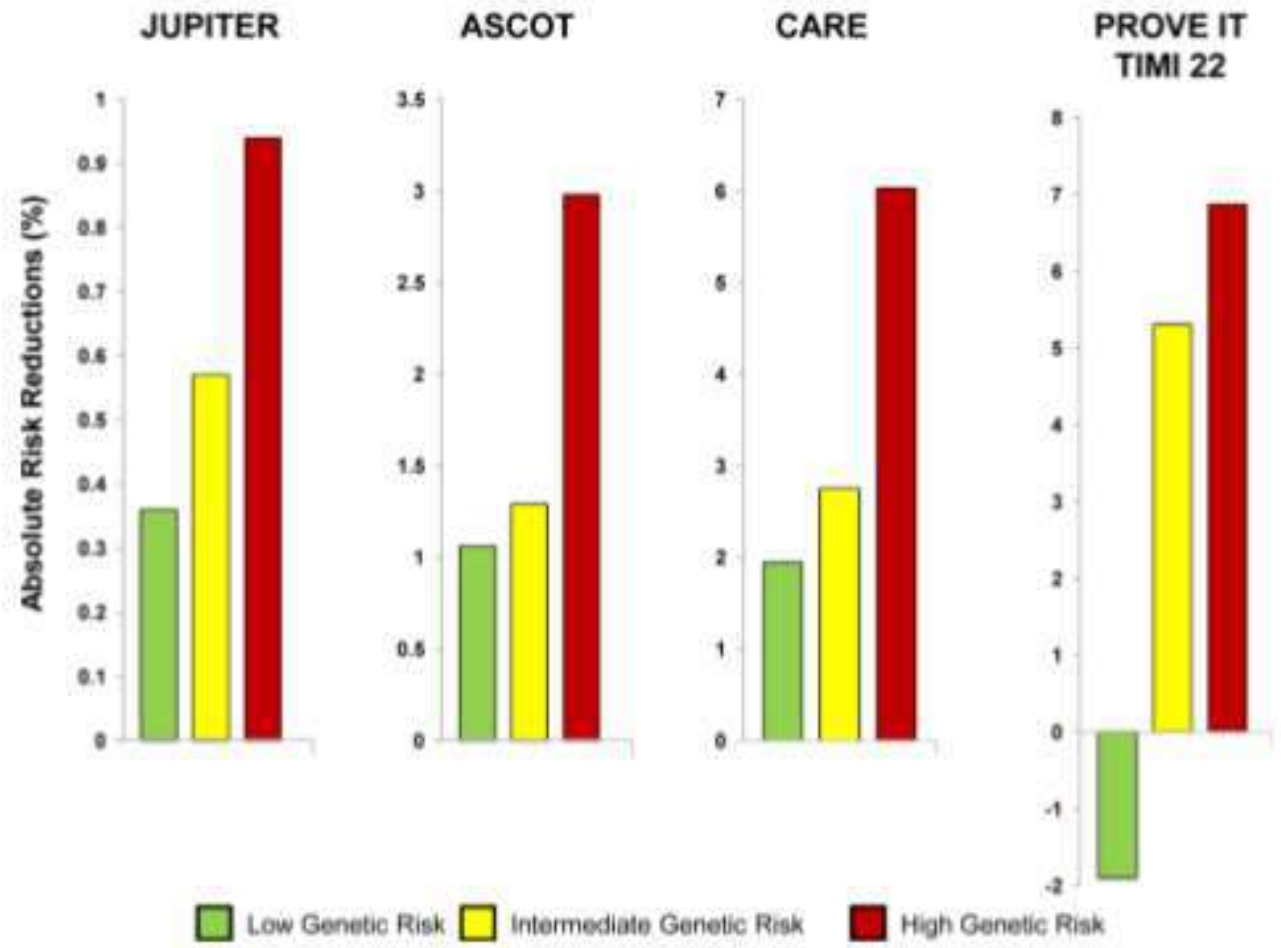



**Figure 3. Absolute Risk Reductions of Coronary Heart Disease with Statin Therapy across Genetic Risk Score Categories**

In PROVE IT-TIMI 22, the control group is moderate intensity statin therapy (pravastatin 40 mg) and the statin group is high intensity statin therapy (atorvastatin 80 mg).

Lancet 2015 June 6: 385(9984): 2264-2271

# POLYGENE RISK SCORE AND AGE FOR CORONARY CALCIUM SCREENING

| AGE RECOMMENDED FOR CAC SCORE MEN | | | | | |
|---|---|---|---|---|---|
| PRS | 2 | 1 | AVE | -1 | -2 |
| AGE | 37 | 40 | 42.9 | 46 | 49 |

| AGE RECOMMENDED FOR CAC SCORE WOMEN | | | | | |
|---|---|---|---|---|---|
| PRS | 2 | 1 | AVE | -1 | -2 |
| AGE | 49 | 52 | 55 | 58 | 61 |

JCCT 13(2019) P203-210

# SUMMARY

- HDL-C
- HDL-P
- TC/HDL RATIO
- LDL-P/HDL-P RATIO
- LDL-C lower is not always better
- All patients benefit from LDL-C < 70 mg/dl
- PCSK9 inhibitors benefit is predicted by LDL-C alone
- Cardiovascular risk is missed by calculators vs CTA
- Calcium score of zero is zero risk
- Low risk may be high risk if polygene risk is high