"It takes a Village - to Eradicate Heart Disease"

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State of the Heart Cardiology
Director and Founder

Disclosures

John A Osborne, MD, PhD, FACC

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Everything *is* Bigger in Texas…

Our New Treadmill…

Objectives

- Review and contrast the various tools to assess cardiovascular risk (Framingham and Life-time Risk) and understand how to apply them.
- Learn how to calculate Non-HDL, understand its importance in risk assessment, learn the Guideline-supported goals, and how to apply Non-HDL in a cardiovascular prevention strategy.
- Review the various means to detect early, pre-clinical atherosclerosis, contrast the advantages and disadvantages of these techniques, and be able to understand how use coronary artery calcium scoring to assess risk in a primary prevention population.

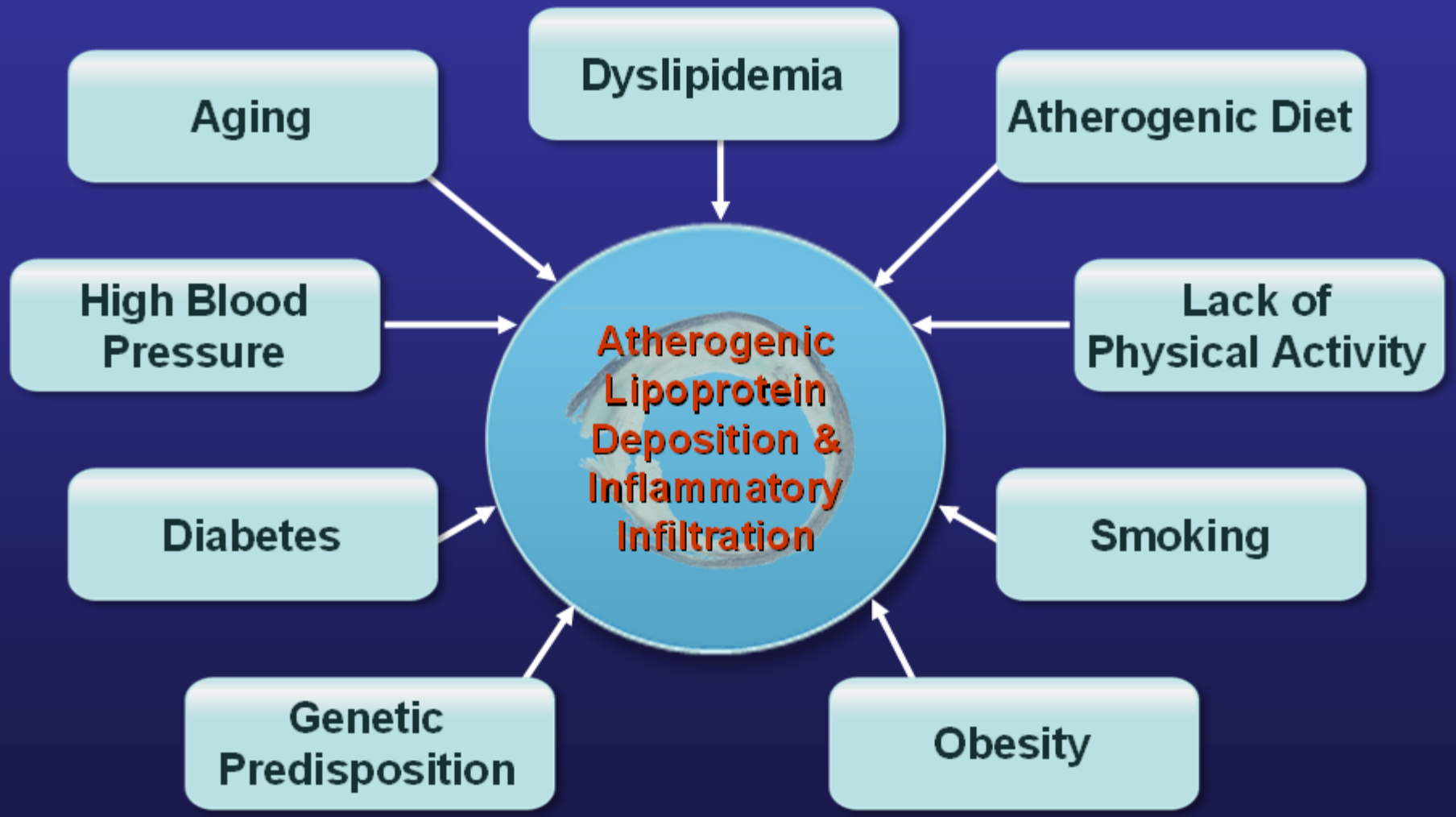
Objectives - Restated

- Get a Life!
- The Coolest, Cheapest, Most Useful Lipid Measurement since Sliced-Spam.
- Do our patients need a “Cardiac Colonoscopy”?

The Challenge of Assessing Cardiovascular Risk…

- Complex disease with many overlapping and interacting “Risk Factors”
- Should we focus on Moderate-Term Risk (10 year risk) or should we instead focus on Lifetime Risk?
- Should we focus on the predisposing “Risk Factors” to understand who has “The Disease” or should we determine directly if the patient has “The Disease”?

Biology of Atherosclerosis: Contributing Factors[1–3]



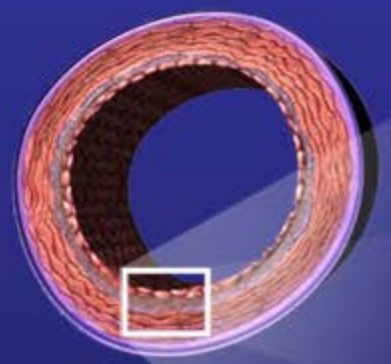
1. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *Circulation.* 2002;106:3143–3421. **2.** Wilson PW et al. *Circulation.* 1998;97:1837–1847. **3.** Hubert HB et al. *Circulation.* 1983;67:968–977.

Get a Life!

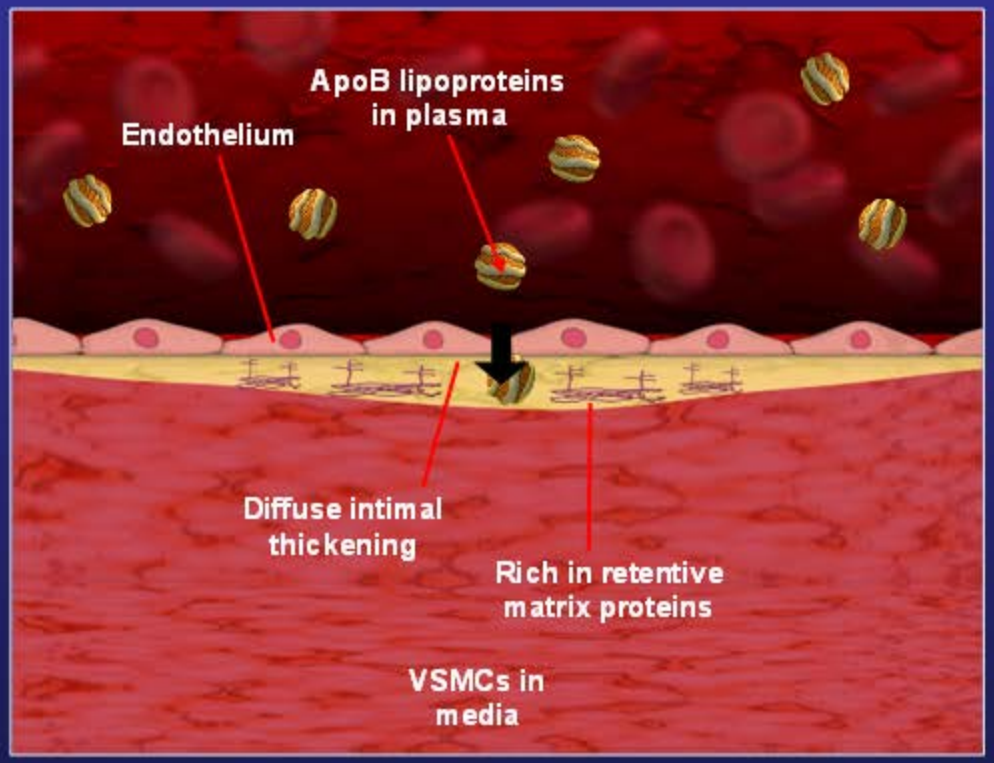
The Problems with Framingham..

- Focuses on 10-year CV Risk, not lifetime
- Clearly underestimates risk in the young(er) and women
- Not designed to assess risk in those less than 40
- Does not take into account family history
- Based on a homogenous, small, white-middle class population of suburban Boston.
- A population-based model to be used decide upon therapy at the individual level.

Prelesional Susceptible Area of the Arterial Wall: Response-to-Retention Model[1]



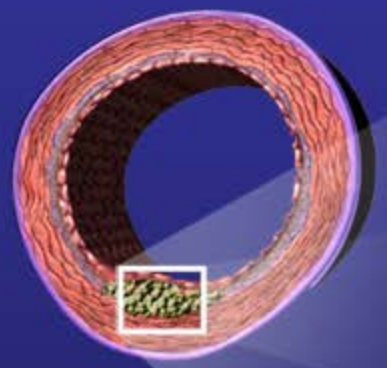
- Early stage of atherosclerosis
- Diffuse intimal thickening
- No lipids or macrophages in endothelium



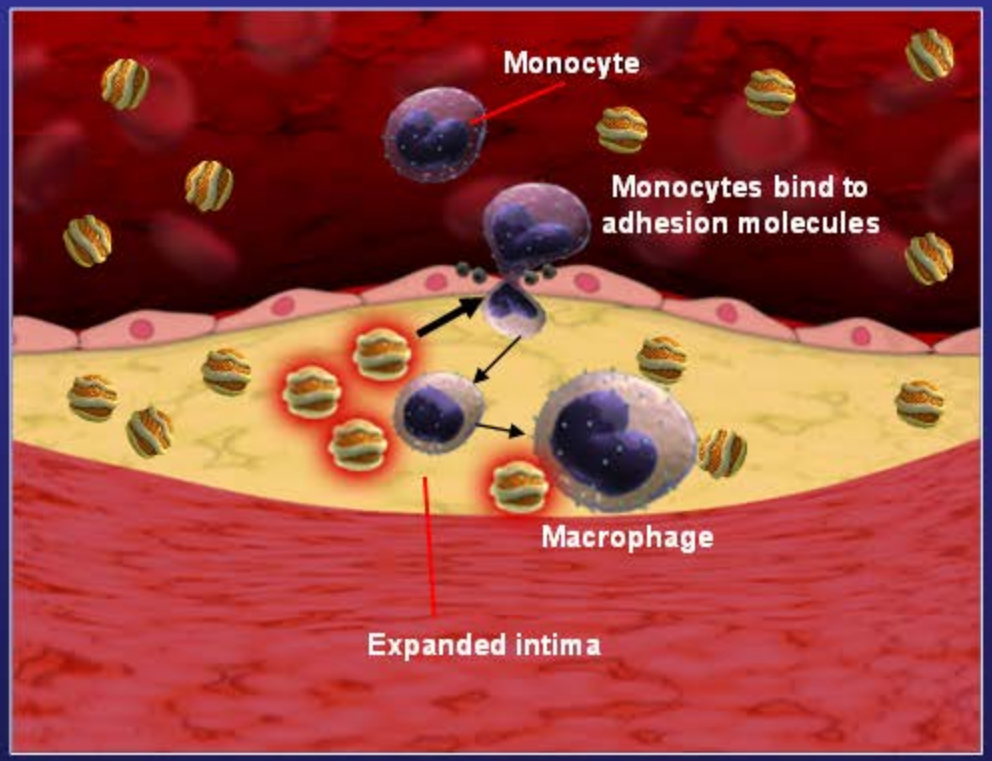
ApoB = apolipoprotein; VSMC = vascular smooth muscle cell.

1. Tabas I et al. *Circulation*. 2007;116:1832–1844.

Lipoprotein Modification Triggers Maladaptive Inflammatory Response[1-3]: Response-to-Retention Model

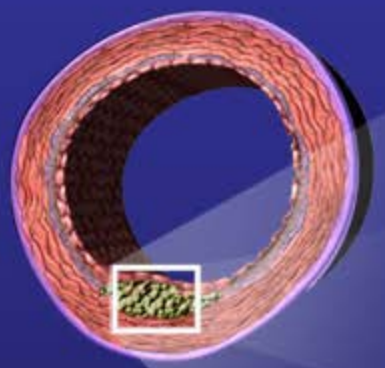


- Attracts circulating monocytes, which differentiate into macrophages
- Inhibits macrophage egress and enhances macrophage uptake of ApoB lipoproteins
- Causes endothelial activation

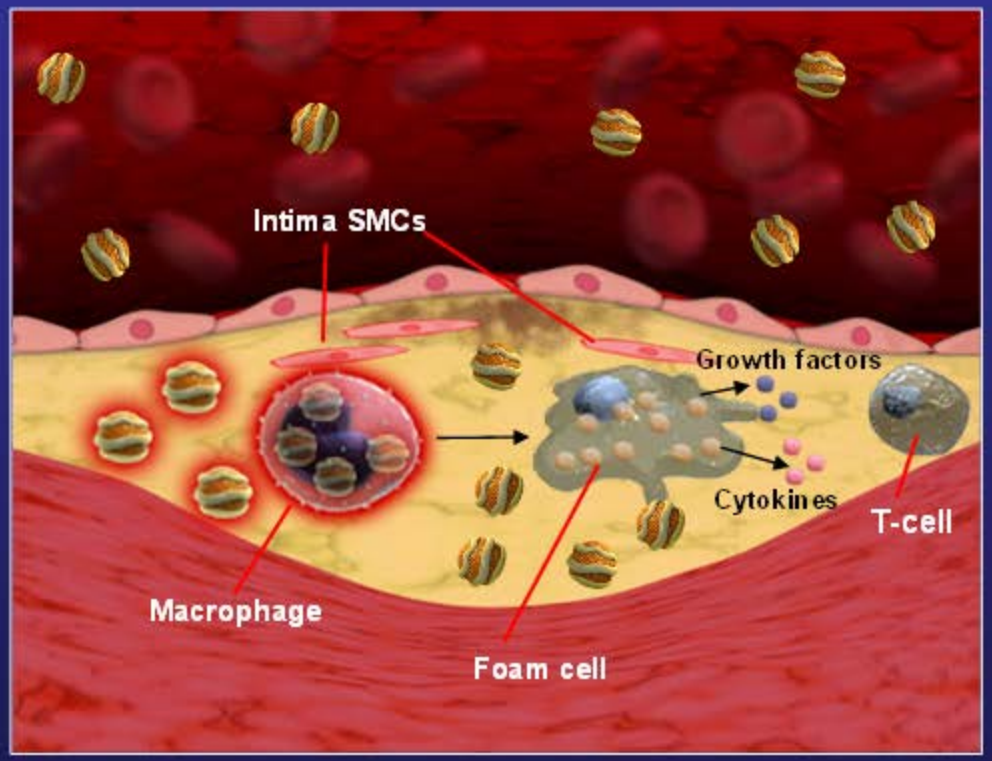


1. Tabas I et al. *Circulation.* 2007;116:1832–1844. **2.** Steinberg D et al. *N Engl J Med.* 1989;320:915–924; **3.** Hansson GK. *J Thromb Haemost.* 2009;7(Suppl 1):328-331.

Lipoprotein Retention Accelerates: Response-to-Retention Model



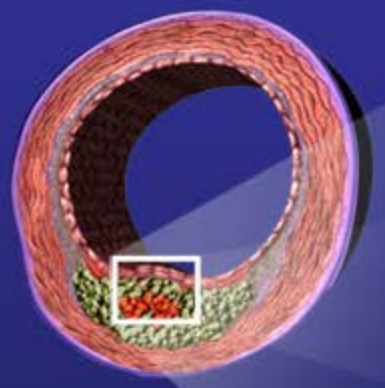
- Macrophages ingesting modified lipoproteins and forming foam cells[1]
- Other immune cells entering lesion[1]
- Release of growth factors and cytokines from foam cells[2]



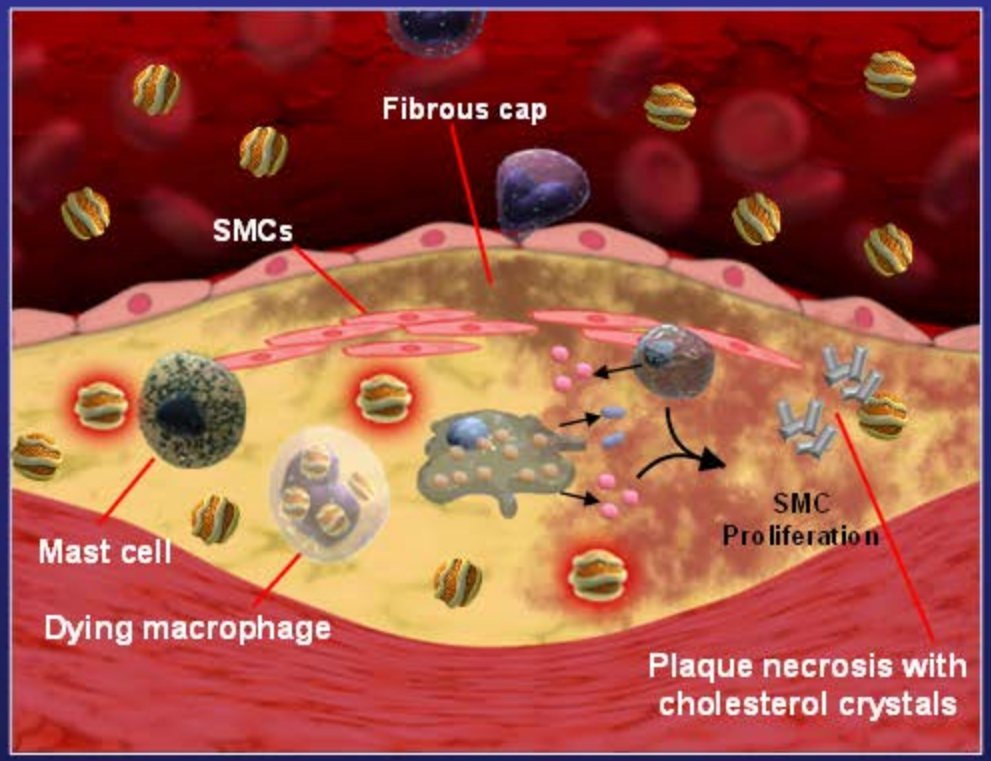
SMC = smooth muscle cell.

1. Tabas I et al. *Circulation.* 2007;116:1832–1844. **2.** Sherer Y et al. *Nat Clin Pract Rheumatol.* 2006;2:99–106.

Advanced Plaque: Response-to-Retention Model[1]



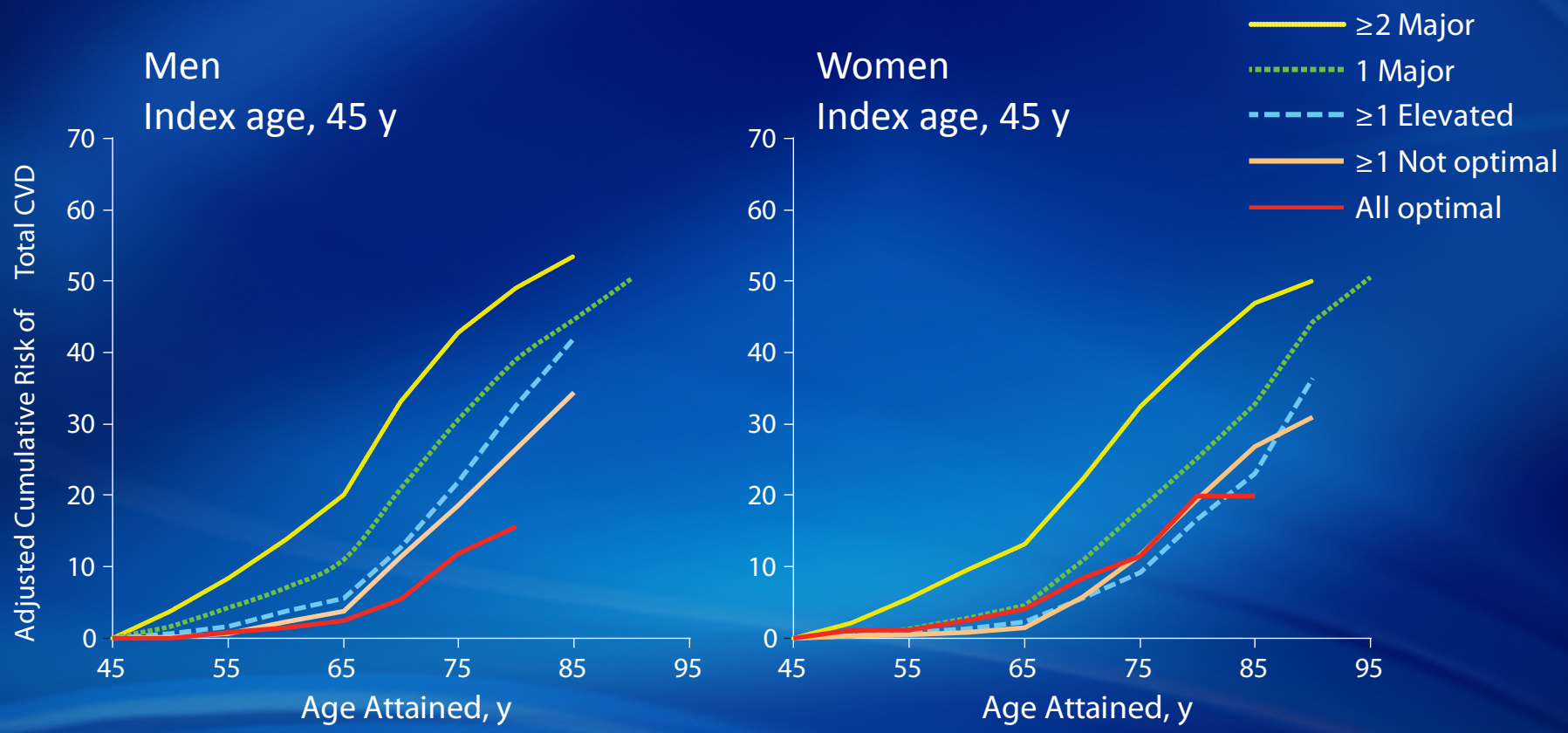
- Immune cells further contribute to inflammatory response
- SMCs migrate into intima
- Fibrous cap forms
- Macrophages begin to die and give rise to necrotic areas



SMC = smooth muscle cell.

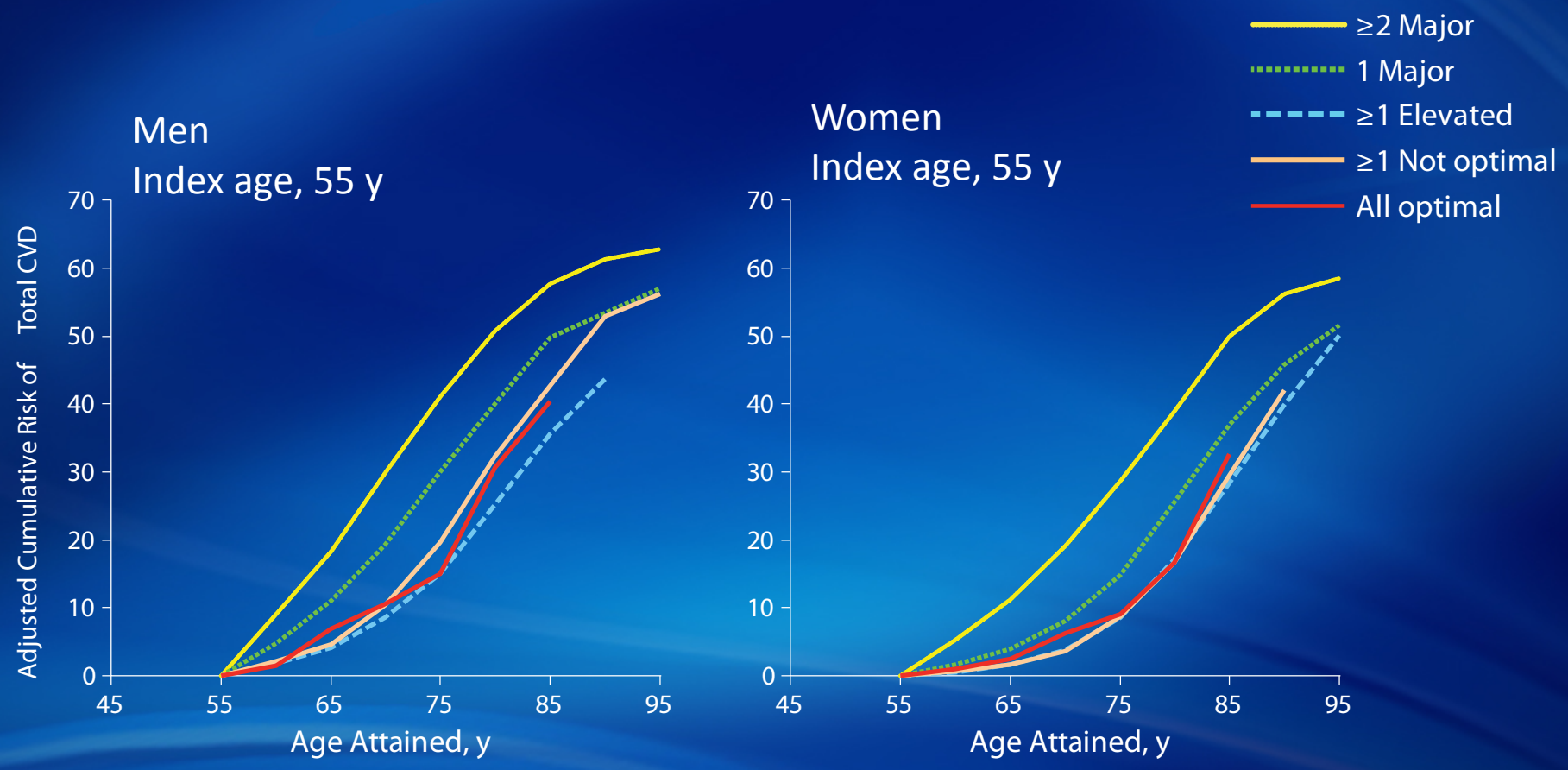
1. Tabas I et al. *Circulation*. 2007;116:1832–1844.

Lifetime risk estimates for total CVD by risk factor burden – 45y



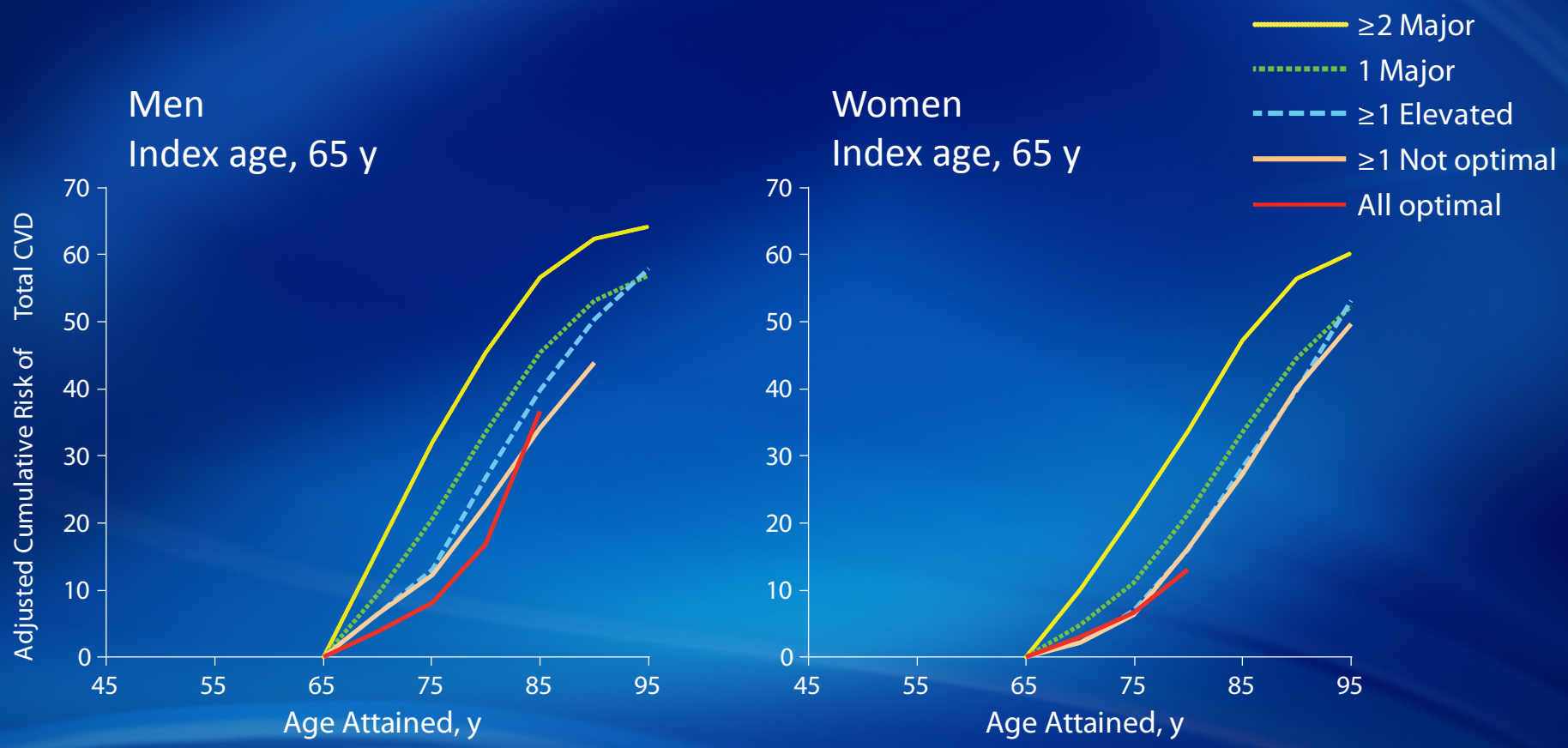
Wilkins JT et al JAMA. 2012;308(17):1795-1801

Lifetime risk estimates for total CVD by risk factor burden – 55y



Wilkins JT et al JAMA. 2012;308(17):1795-1801

Lifetime risk estimates for total CVD by risk factor burden – 65y

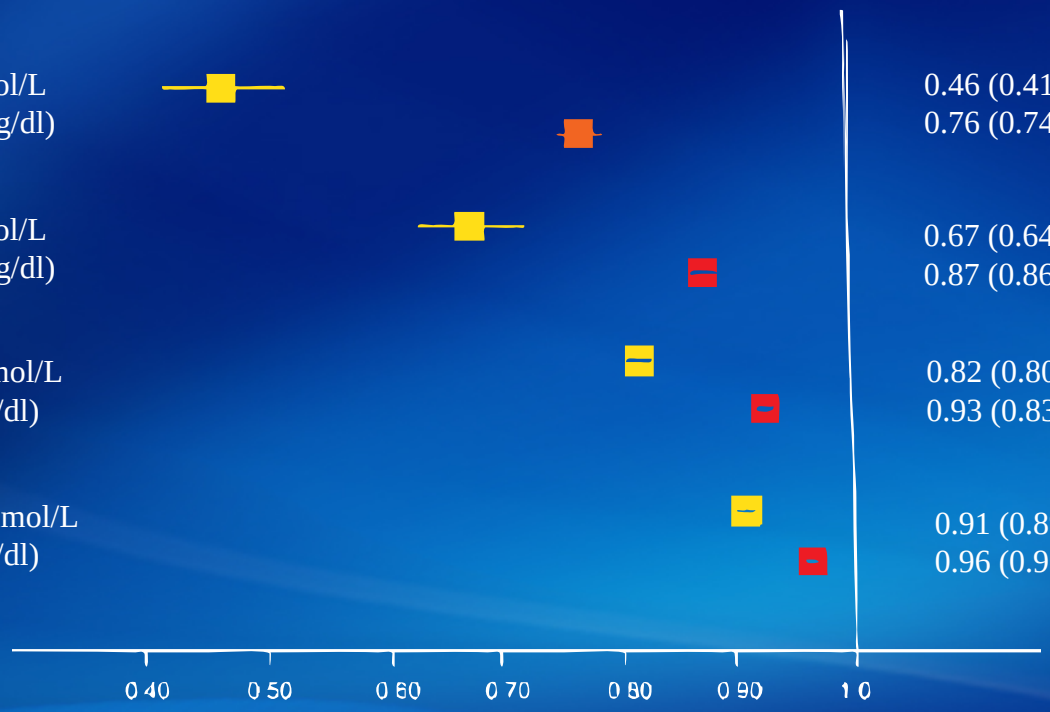


Wilkins JT et al JAMA. 2012;308(17):1795-1801

How confident are you that you can hit the target?

Comparative CHD risk reduction of earlier and later LDL-C lowering

Lower LDL-c	OR (95%CI)	P (difference)
1.0 mmol/L (38.7 mg/dl)	0.46 (0.41- 0.51) 0.76 (0.74- 0.78)	8.4×10^{-19}
0.5 mmol/L (19.3 mg/dl)	0.67 (0.64-0.72) 0.87 (0.86-0.88)	8.4×10^{-19}
0.25 mmol/L (9.7 mg/dl)	0.82 (0.80-0.85) 0.93 (0.83-0.94)	8.4×10^{-19}
0.125 mmol/L (4,8 mg/dl)	0.91 (0.89-0.92) 0.96 (0.96-0.97)	8.4×10^{-19}



Sample Size (N)

Genetic studies 312,321

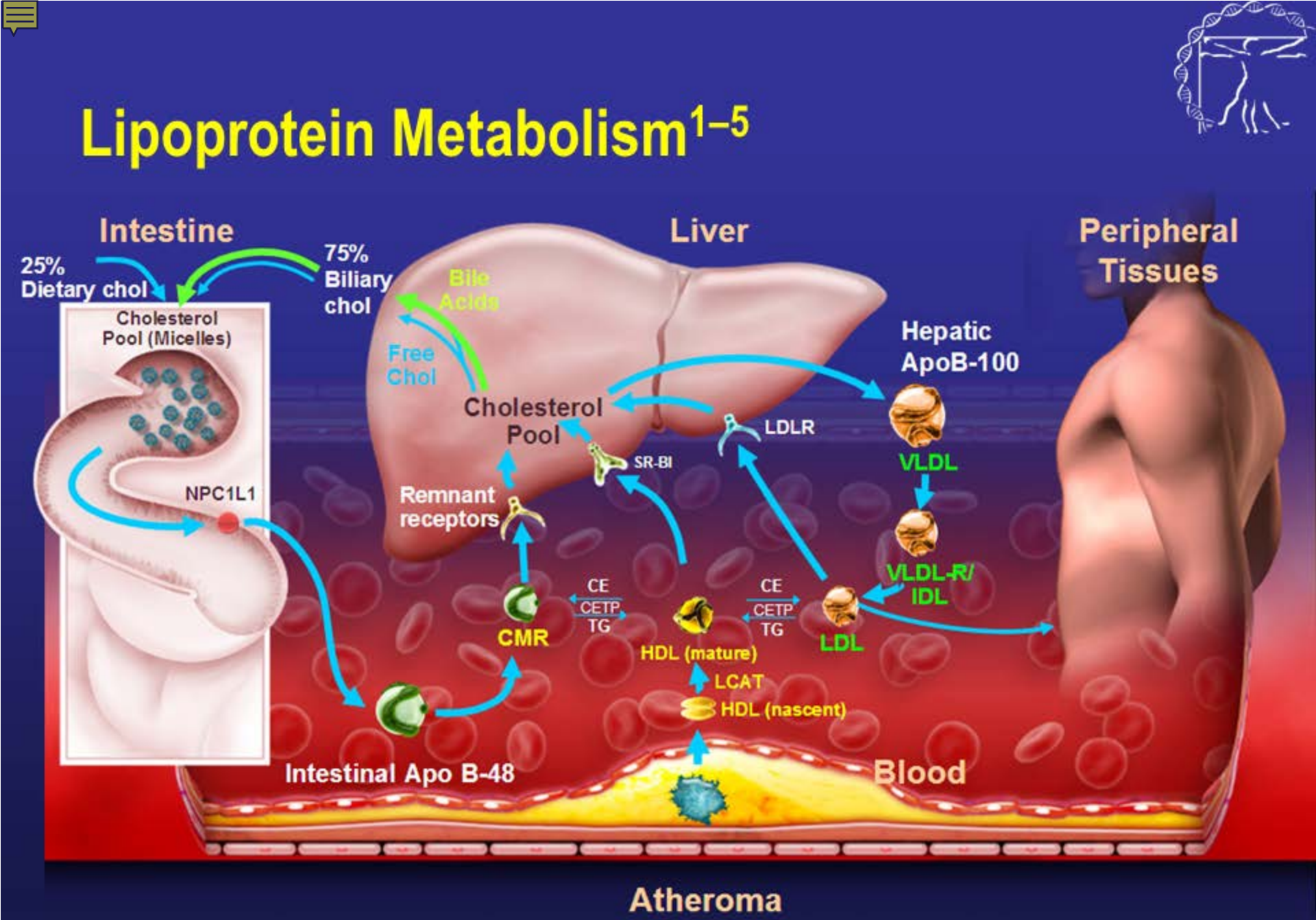
Statin Trials 169,138

Ference BA et al, J Am Coll Cardiol. 2012 doi: 10.1016

The Coolest, Cheapest, Most Useful Lipid Measurement since Sliced-Spam.

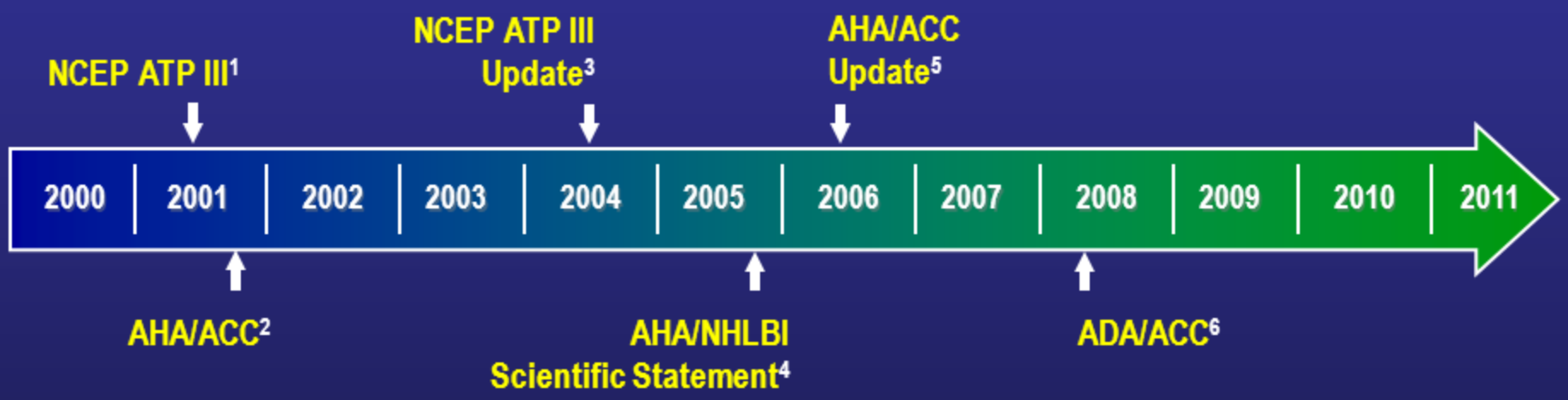
Non–HDL-C as a Predictor of Cardiovascular Risk

Lipoprotein Metabolism[1–5]



1. Goldstein JL et al. *Science*. 2001;292:1310–1312. **2.** Shepherd J. *Eur Heart J*. 2001;3(suppl E):E2–E5. **3.** Turley SD, et al. *Prev Cardiol*. 2003;6:29–33, 64. **4.** Mudd JO et al. *J Am Coll Cardiol*. 2007;50:1735–1741. **5.** Altmann SW et al. *Science*. 2004;303:1201–1204.

History of Non–HDL-C as a Treatment Target



1. NCEP ATP III. *JAMA*. 2001;285:2486–2497. **2.** Smith SC Jr et al. *Circulation*. 2001;104:1577–1579. **3.** Grundy SM et al. *Circulation*. 2004;110:227–239. **4.** Grundy SM et al. *Circulation*. 2005;112:2735–2752. **5.** Smith SC Jr et al. *Circulation*. 2006;113:2363–2372. **6.** Brunzell JD et al. *J Am Coll Cardiol*. 2008;51:1512–1524.

Rationale for Non–HDL-C Assessment

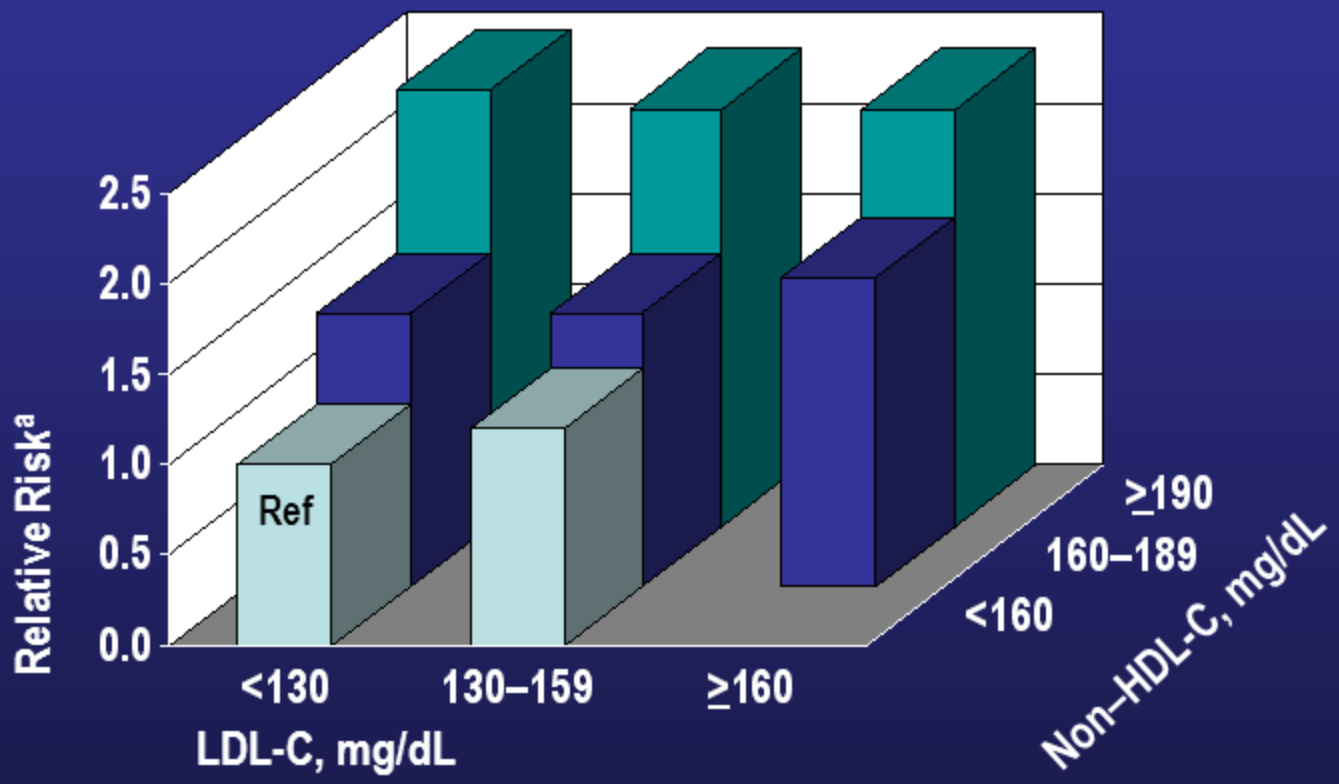
- In the presence of high serum TG, non–HDL-C may better represent the concentration of all apoB-containing lipoproteins than does LDL-C.[1]
- Unlike calculated LDL-C, non–HDL-C can be accurately measured in nonfasting patients.[2,3]
- Non–HDL-C is highly correlated with total apoB.[1]
  - Serum total apoB has been shown to have a strong predictive power for severity of coronary atherosclerosis and CHD events.[1]
- Non–HDL-C is calculated using subtraction of 2 values provided in a standard lipid panel (ie, TC – HDL-C) and therefore incurs no additional cost.[1,4]

TC = total cholesterol

1. NCEP ATP III. *Circulation*. 2002;106:3143–3421. **2.** Miller M et al. *Circulation*. 2011;123:2292–2333.
3. Brunzell JD et al. *J Am Coll Cardiol*. 2008;51:1512–1524. **4.** Mora S et al. *Circulation*. 2009;119:2396–2404.

Non–HDL-C Was a Better Predictor of CHD Risk Than LDL-C Was: Framingham Heart Study[1]

Risk of CHD for the Distribution of Non–HDL-C and LDL-C



[a]Adjusted for age, gender, study, smoking status, systolic blood pressure, and prevalent diabetes (at baseline).

1. Liu J et al. *Am J Cardiol*. 2006;98:1363–1368.

Treatment Guidelines Address Non–HDL-C

National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III)

- LDL-C is the **primary target** of cholesterol-lowering therapy
- Non–HDL-C is the **secondary target** of therapy when TG levels are 200–499 mg/dL

	1° Target	2° Target
Risk Category	**LDL-C Goal (mg/dL)**	**Non–HDL-C Goal (mg/dL)**
CHD and CHD Risk Equivalent (10-year risk for CHD >20%)	**<100[a]**	**<130[a]**
Multiple (2+) Risk Factors (10-year risk ≤20%)	**<130[b]**	**<160[b]**
0–1 Risk Factor	**<160**	**<190**

Non–HDL-C goal is less than 30 mg/dL above desired LDL-C goals

[a]Optional goals for very high-risk patients are LDL-C <70 mg/dL and Non–HDL-C <100 mg/dL.
[b]Optional goals if risk 10%–20% are LDL-C <100 mg/dL and Non–HDL-C <130 mg/dL.
Executive Summary of the Third Report of NCEP ATP III. *JAMA.* 2001;285:2486–2497. Grundy S, et al. *Circulation.* 2004;110:227-239.

A Sneak Preview of NCEP-ATP IV?

- Calculate Non-HDL on everyone, regardless of triglycerides.

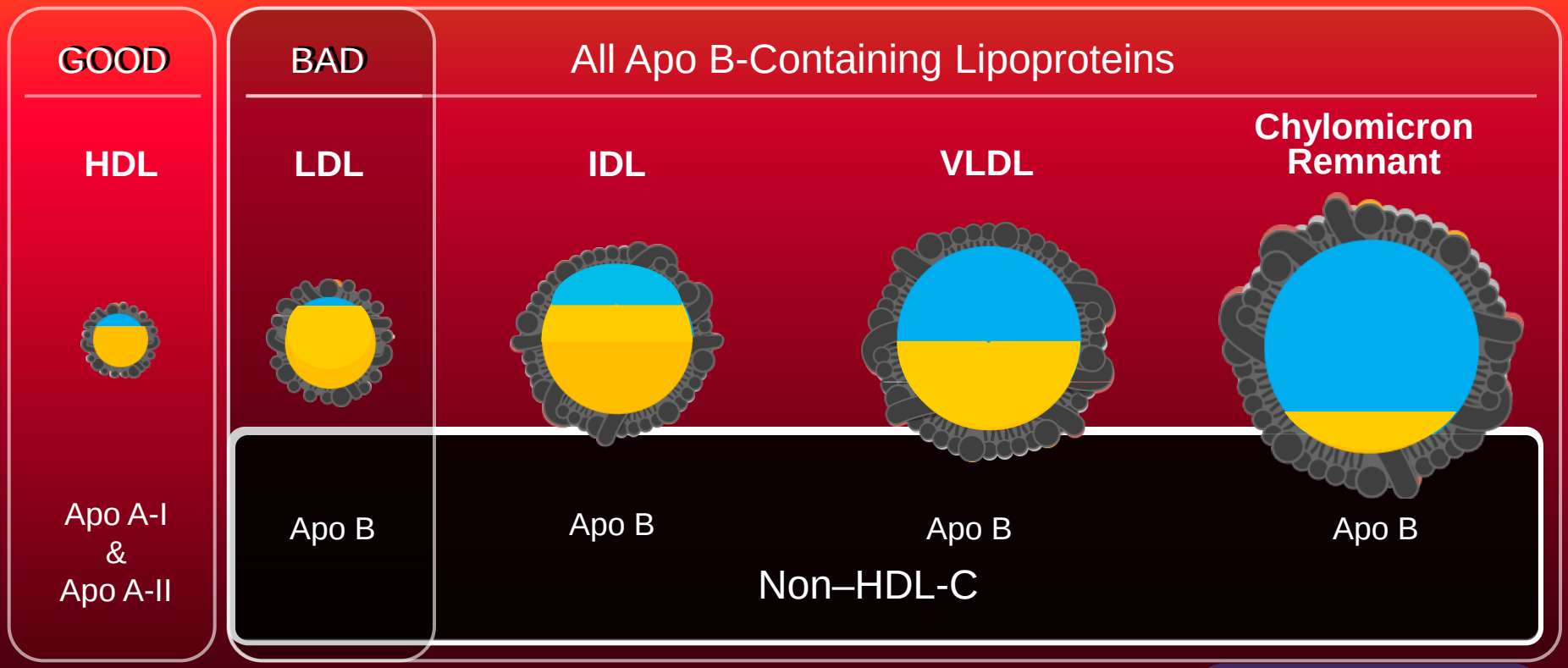
	1° Target	2° Target
Risk Category	**LDL-C Goal (mg/dL)**	**Non–HDL-C Goal (mg/dL)**
CHD and CHD Risk Equivalent (10-year risk for CHD >20%)	**<70**	**<100[a]**
Multiple (2+) Risk Factors (10-year risk ≤20%)	**<100[b]**	**<130[b]**
0–1 Risk Factor	**<130**	**<160**

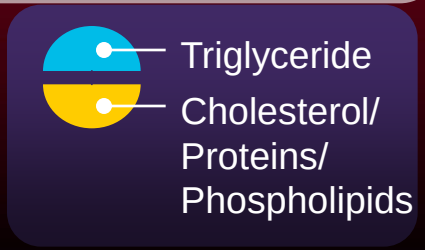
Non–HDL-C goal is less than 30 mg/dL above desired LDL-C goals

What is Non–HDL-C and How Is It Calculated

Non–HDL-C is a Measure of All Atherogenic Particles

Non–HDL-C = Total cholesterol − HDL-C





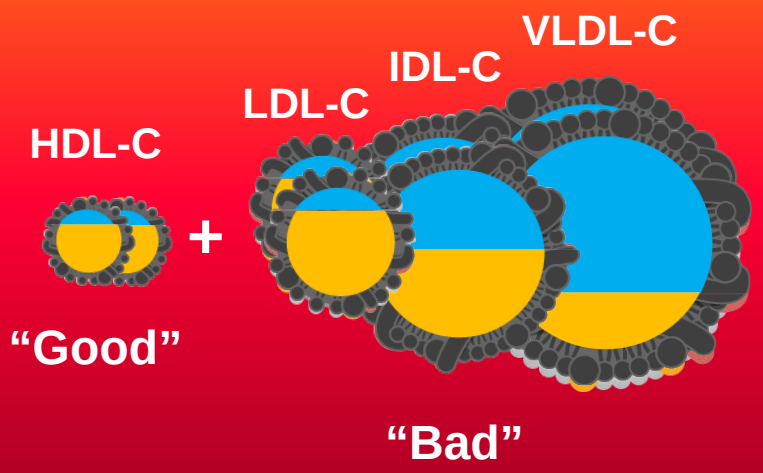
Executive Summary of the Third Report of NCEP ATP III. *JAMA.* 2001;285:2486–2497.
Blaha MJ, et al. *J Clin Lipidol.* 2008;2:267–273.
Ballantyne CM, *Clinical Lipidology: A companion of Braunwald's Heart Disease.* Philadelphia, PA: Saunder Elsevier; 2009

How To Calculate Non–HDL-C

Total Cholesterol

– HDL-C

Non–HDL-C



Clinical Perspective on Using Non–HDL-C in Practice

Practical Aspects of Measuring Non–HDL-C

1. No fasting needed
2. No additional cost
3. Quick calculation (TC – HDL-C)
4. Established cut points based on LDL-C levels
5. Existence within our current “cholesterol-oriented” conceptual framework established in current guidelines

Ramjee V, et al. *J Am Coll Cardiol.* 2011;58:457–463.
Robinson J, et al. *J Am Coll Cardiol.* 2009;53:316–322.

Challenges to Implementing the Use of Non–HDL-C in Current Clinical Practice

- Although Non–HDL-C is called out in the National Guidelines, it is usually not part of standard office protocol or group practice guidelines
- Non–HDL-C is not automatically provided on most standard lab reports
  - Physicians will need to specifically request Non–HDL-C as part of the lab report for their patients
- Physicians too busy to calculate it
  - Can request their labs to provide as an EMR “pop-up” for all patients

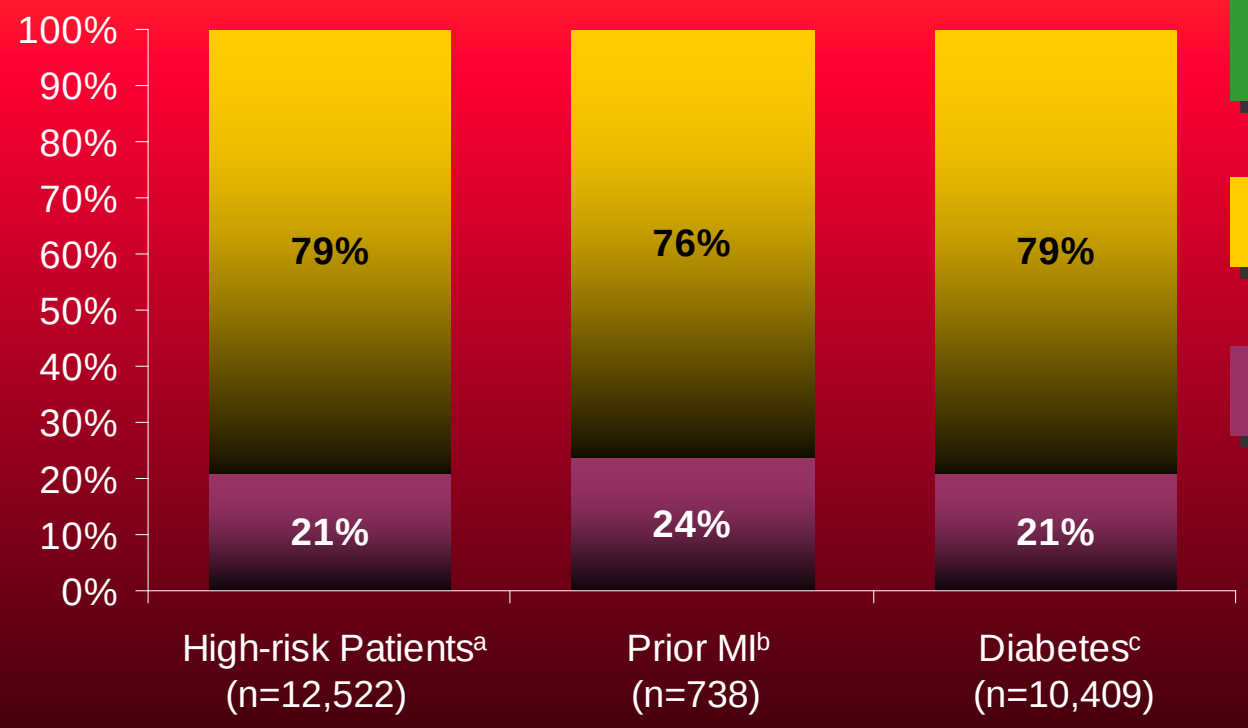
Strategies to Make the Use of Non–HDL-C Part of Clinical Practice

- Educate entire staff on importance of Non–HDL-C
- Where in-office labs are available, have Non–HDL-C print on lab reports
- Establish standard office protocol and provide training to understand:
  - How to calculate Non–HDL-C for all patients. Print the formula Non–HDL-C = TC–HDL-C on all patient charts
  - That the Non–HDL-C value can often be added to the lab report at no additional cost
  - If their lab or other labs in the area provide Non–HDL-C on their reports and how to request it

Real World Data on Reaching Non–HDL-C Goals

Majority of High-Risk Patients on Statin Monotherapy Reaching Optional LDL-C Goal (<70 mg/dL) are not achieving their Non–HDL-C Goal (<100 mg/dL)

Retrospective analysis of the 359,681 high-risk patients on lipid therapy from the GE Healthcare Medical Quality Improvement Consortium database



All patients were on statin monotherapy for >90 days and had TG ≥200 mg/dL

NOT AT GOAL: Not at optional Non–HDL-C (<100 mg/dL) goal

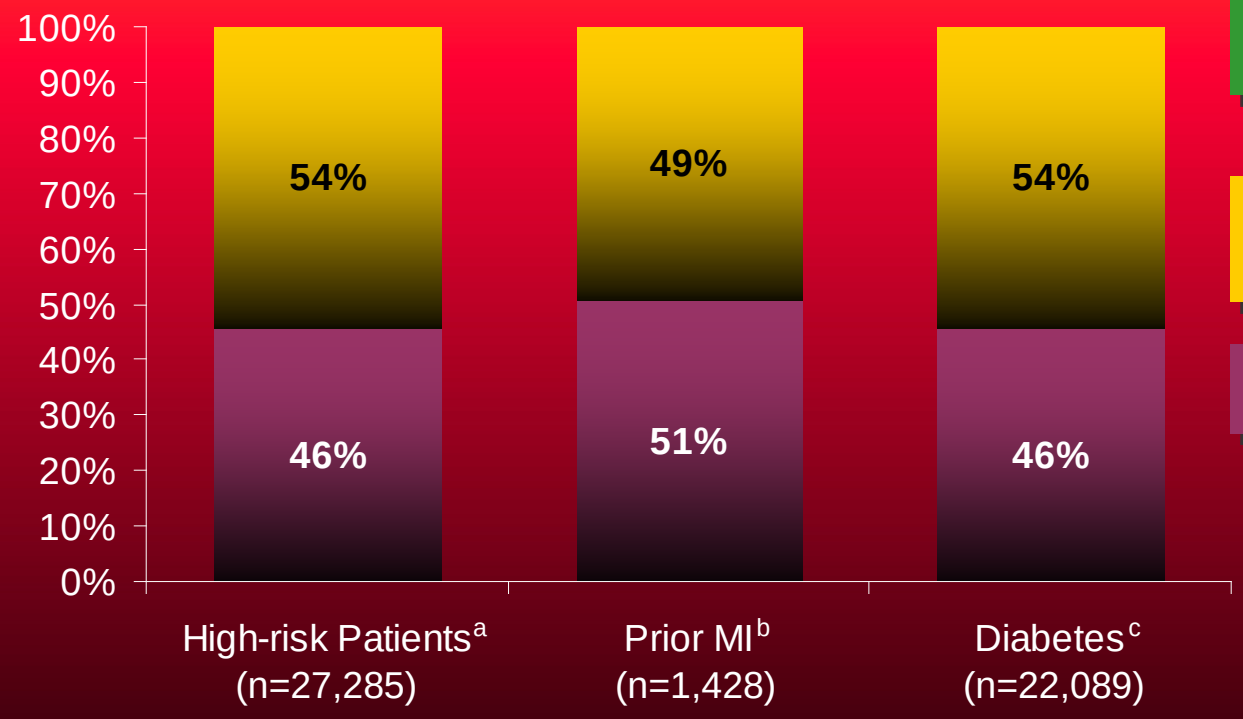
AT GOAL: At optional Non–HDL-C (<100 mg/dL) goal

[a]High-risk patients are those with CHD or a CHD risk equivalent (peripheral artery disease, symptomatic carotid artery disease, abdominal aortic aneurysm, or diabetes).
[b]High-risk patients with prior MI are those with a history of MI (ICD codes 410.XX and 412.XX).
[c]High-risk patients with diabetes are those with a history of diabetes (ICD code 250.XX) or who were prescribed an anti-diabetic therapy.

Data on file, Abbott Laboratories.

In High-Risk Patients on Statin Monotherapy Reaching Goal for LDL-C (<100 mg/dL), Many are Still Not at Recommended Non–HDL-C Levels

Retrospective analysis of the 359,681 high-risk patients on lipid therapy from the GE Healthcare Medical Quality Improvement Consortium database



All patients were on statin monotherapy for >90 days and had TG ≥200 mg/dL

NOT AT GOAL: Not at recommended Non–HDL-C (<130 mg/dL) goal

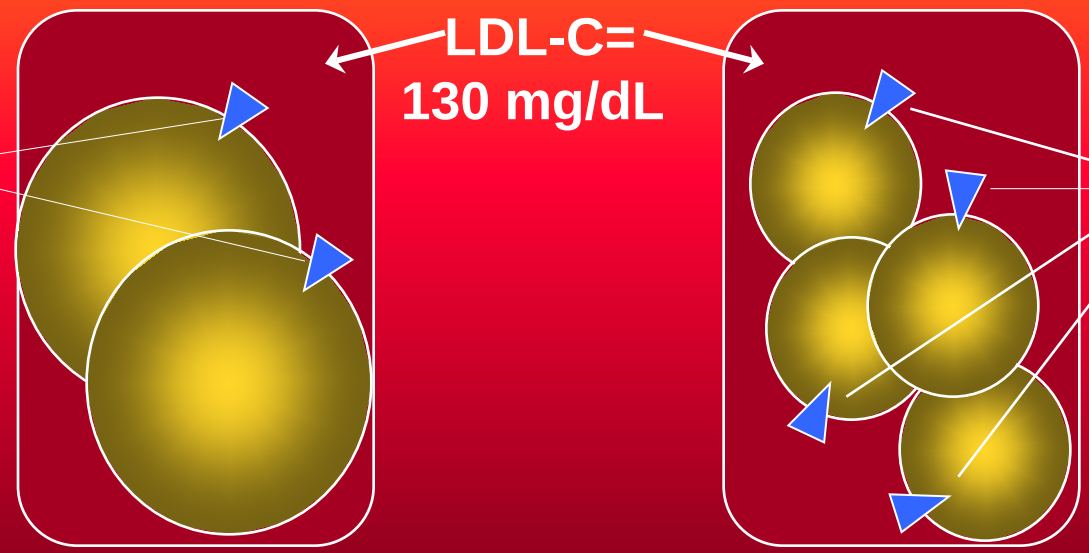
AT GOAL: at recommended Non–HDL-C (<130 mg/dL) goal

[a]High-risk patients are those with CHD or a CHD risk equivalent (peripheral artery disease, symptomatic carotid artery disease, abdominal aortic aneurysm, or diabetes).
[b]High-risk patients with prior MI are those with a history of MI (ICD codes 410.XX and 412.XX).
[c]High-risk patients with diabetes are those with a history of diabetes (ICD code 250.XX) or who were prescribed an anti-diabetic therapy.

Data on file, Abbott Laboratories.

Case Studies:
Role of Non–HDL-C

Differences in Lipoprotein Cholesterol Distribution



TC	198 mg/dL
LDL-C	**130 mg/dL**
TG	90 mg/dL
HDL-C	50 mg/dL
Non–HDL-C	**148 mg/dL**

TC	210 mg/dL
LDL-C	**130 mg/dL**
TG	250 mg/dL
HDL-C	30 mg/dL
Non–HDL-C	**180 mg/dL**

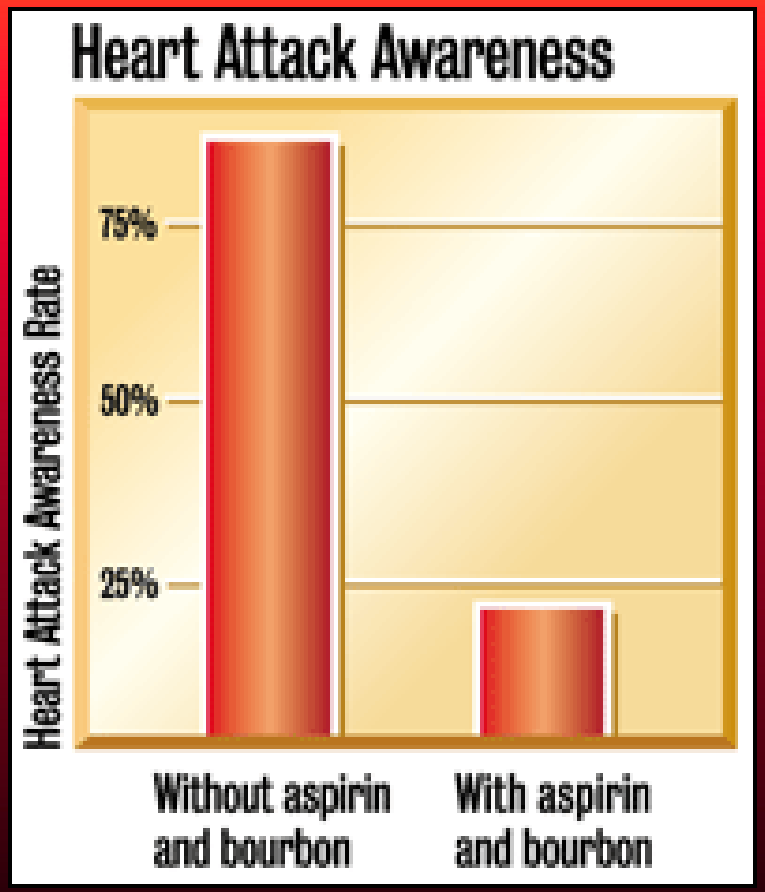
Otvos JD, et al. *Am J Cardiol.* 2002;90:22i–29i.

Reviewing the Practical Aspects of Non–HDL-C

- Non–HDL-C consists of all the “bad” cholesterol
- Non–HDL-C can be easily and accurately calculated on all routine lipid profiles
- Can be obtained from fasting or non-fasting patients
- No additional expense to the patient or third-party payer
- It is treatable
- Targeted in current treatment guidelines

The Role of Alcohol and Heart Disease

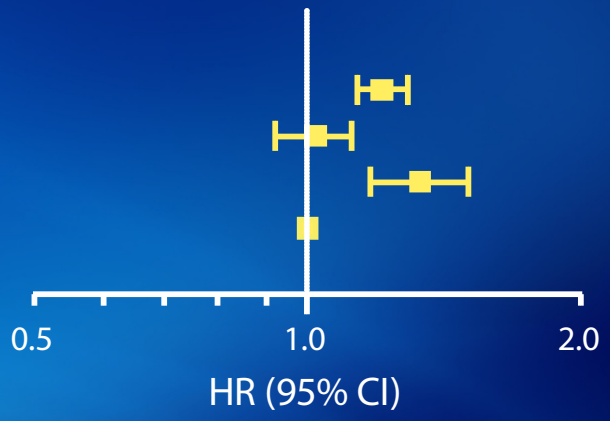
A Fifth of Bourbon and an Aspirin Reduces *Awareness* of Heart Attacks by 85%



Why is my cholesterol so high, Doc?

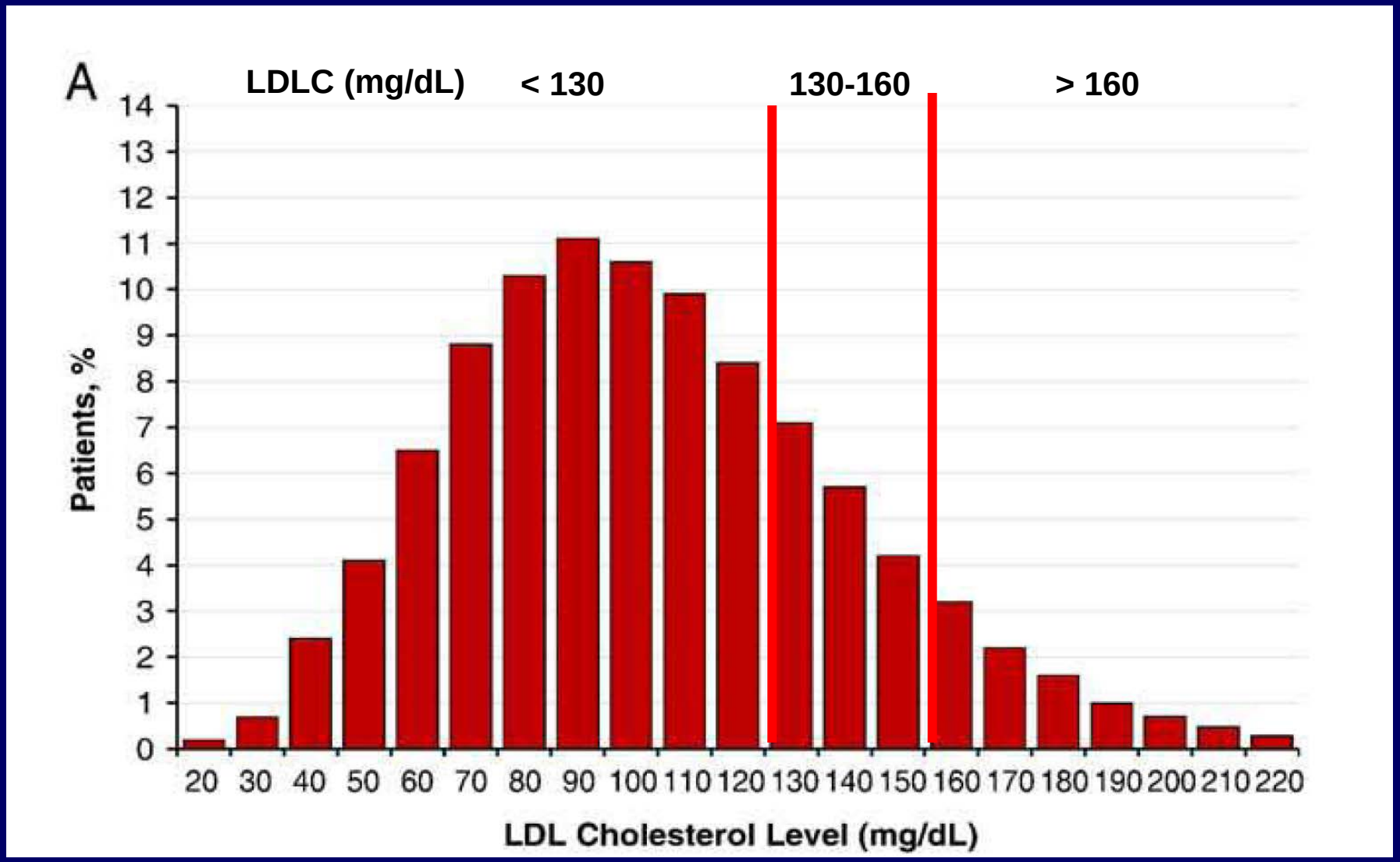
Risk of Major Cardiovascular Events by LDL and non-HDL Cholesterol Categories

Target Level				
LDL-C	Non–HDL-C	No. of Major CV Events	Total No. of Participants	HR (95% CI)
≥ 100 mg/dL	≥ 130 mg/dL	1877	10419	1.21 (1.13-1.29)
≥ 100 mg/dL	< 130 mg/dL	467	2873	1.02 (0.92-1.12)
< 100 mg/dL	≥130 mg/dL	283	1435	1.32 (1.17-1.50)
< 100 mg/dL	< 130 mg/dL	2760	23426	1.00 [Reference]



Boekholdt MSS et al JAMA, March 28, 2012—Vol 307, No. 12

LDLC Levels in 136,905 Patients Hospitalized With CAD: 2000- 2006



Sachdeva et al, Am Heart J 2009;157:111-7.e2.

Improvement in C statistic with apolipoproteins on top of conventional factors

Marker	Improvement in C statistic (95% CI)	Net reclassification improvement, % (95% CI)
ApoB+apoA1	0.0006 (0.0002-0.0009)	-0.10 (-0.49-0.29)
Lp(a)	0.0016 (0.0009-0.0023)	0.05 (-0.59-0.70)
Lp-PLA_2	0.0018 (0.0010-0.0026)	0.81 (-0.15-1.77)

Artery
CLEANERS
1
HOUR

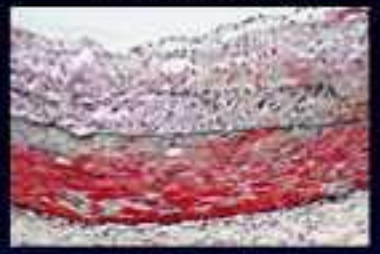
Objectives - Restated

Is there a need for a “Cardiac Colonoscopy”?

Development of Human Coronary Atherosclerosis

Adaptive Intimal thickening

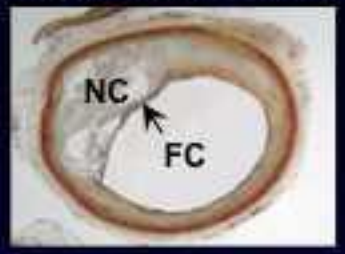
Intimal xanthoma

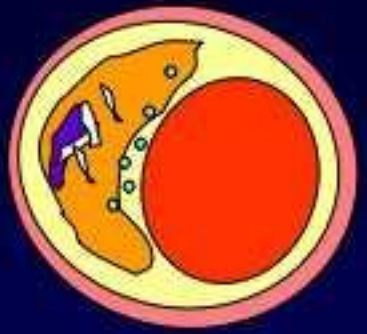


Pathologic intimal thickening

Fibrous cap atheroma

Thin-cap Fibroatheroma

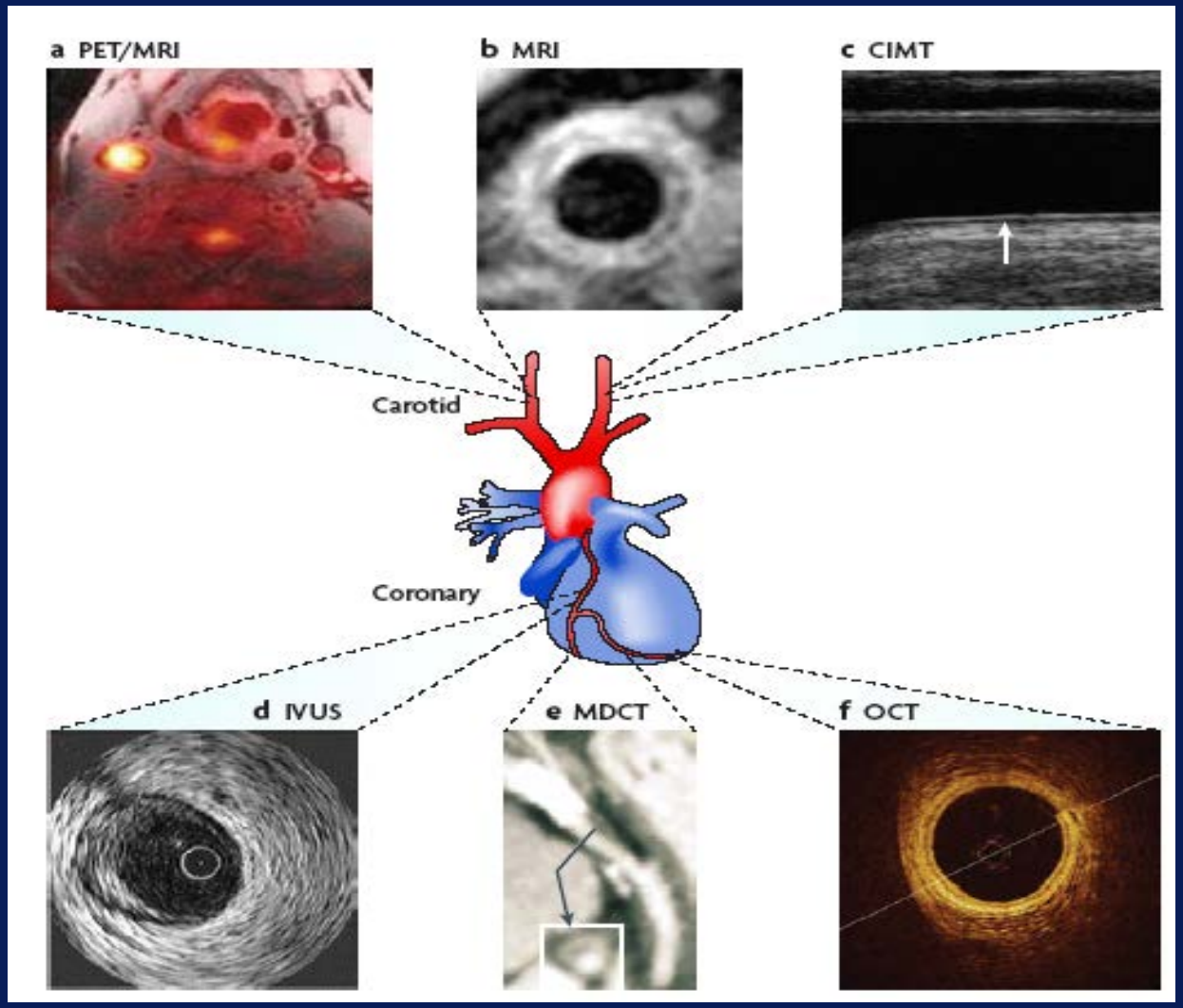




- Smooth muscle cells
- Macrophage foam cells
- Extracellular lipid
- Cholesterol clefts
- Necrotic core
- Calcified plaque
- Hemorrhage
- Thrombus
- Healed thrombus
- Collagen

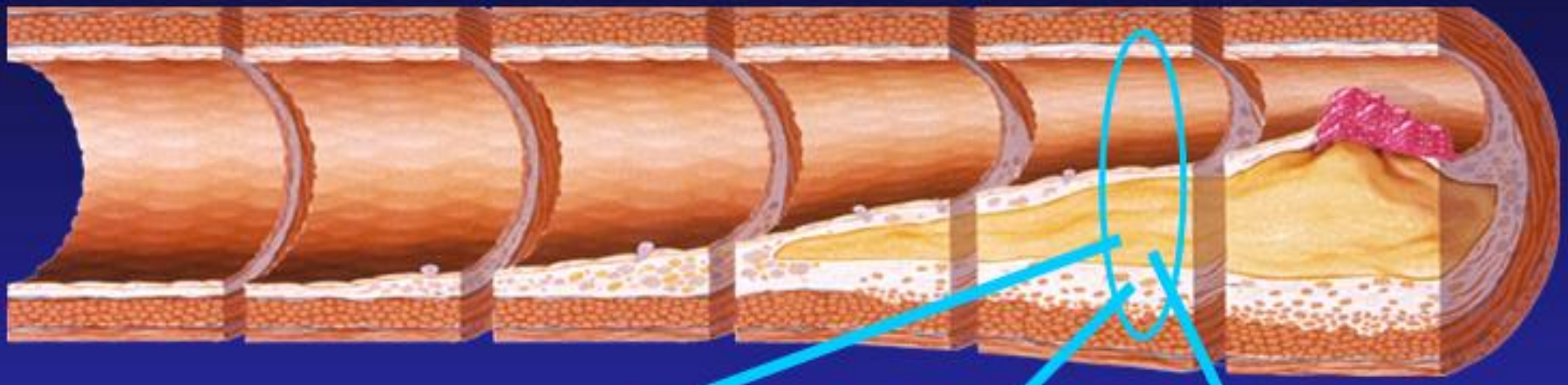
FC = fibrous cap
LP = lipid pool
NC = necrotic core

Imaging the vessel in atherosclerosis



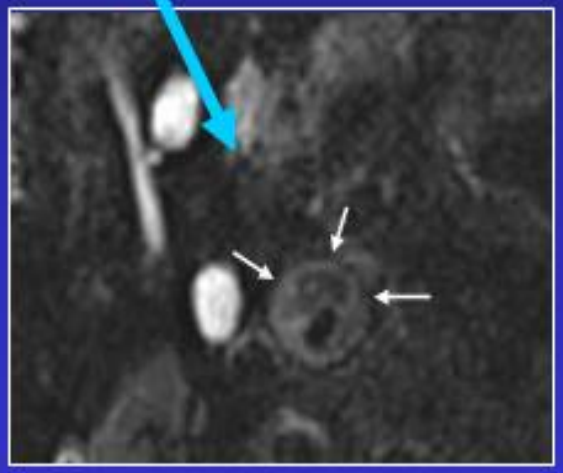
Lindsay and Choudhury, *Nature Reviews: Drug Discovery 2008, 7: 517-29*

Atheroma plaque: hallmark of atherosclerosis
Noninvasive imaging



Carotid US

MDCT - CAC

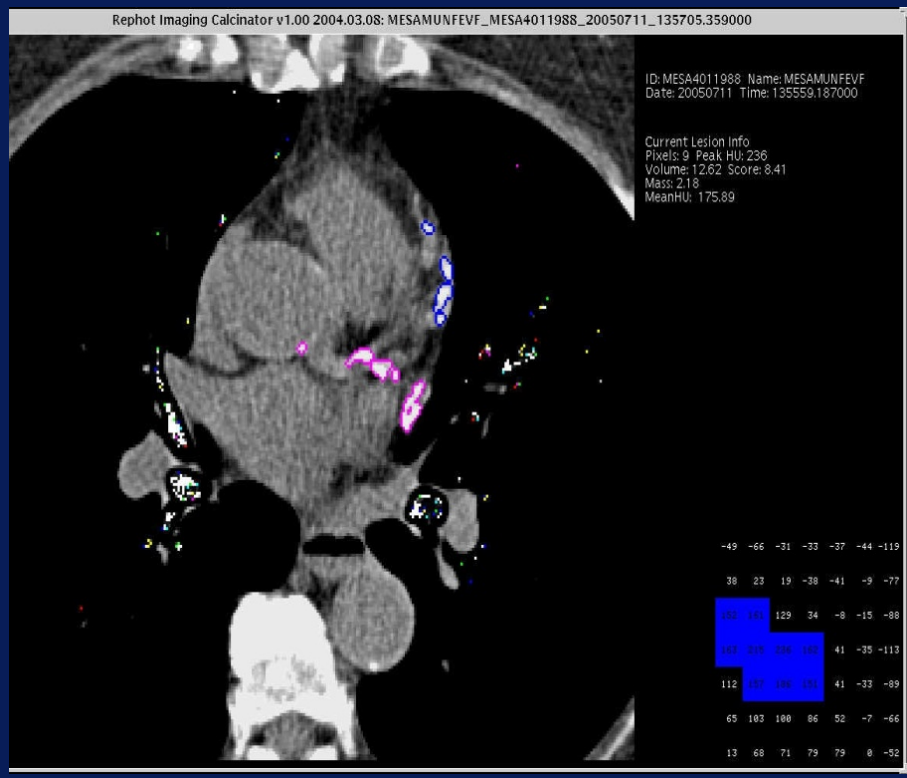


MRI

New techniques: Proton MR spectroscopy, PET, PET/CT

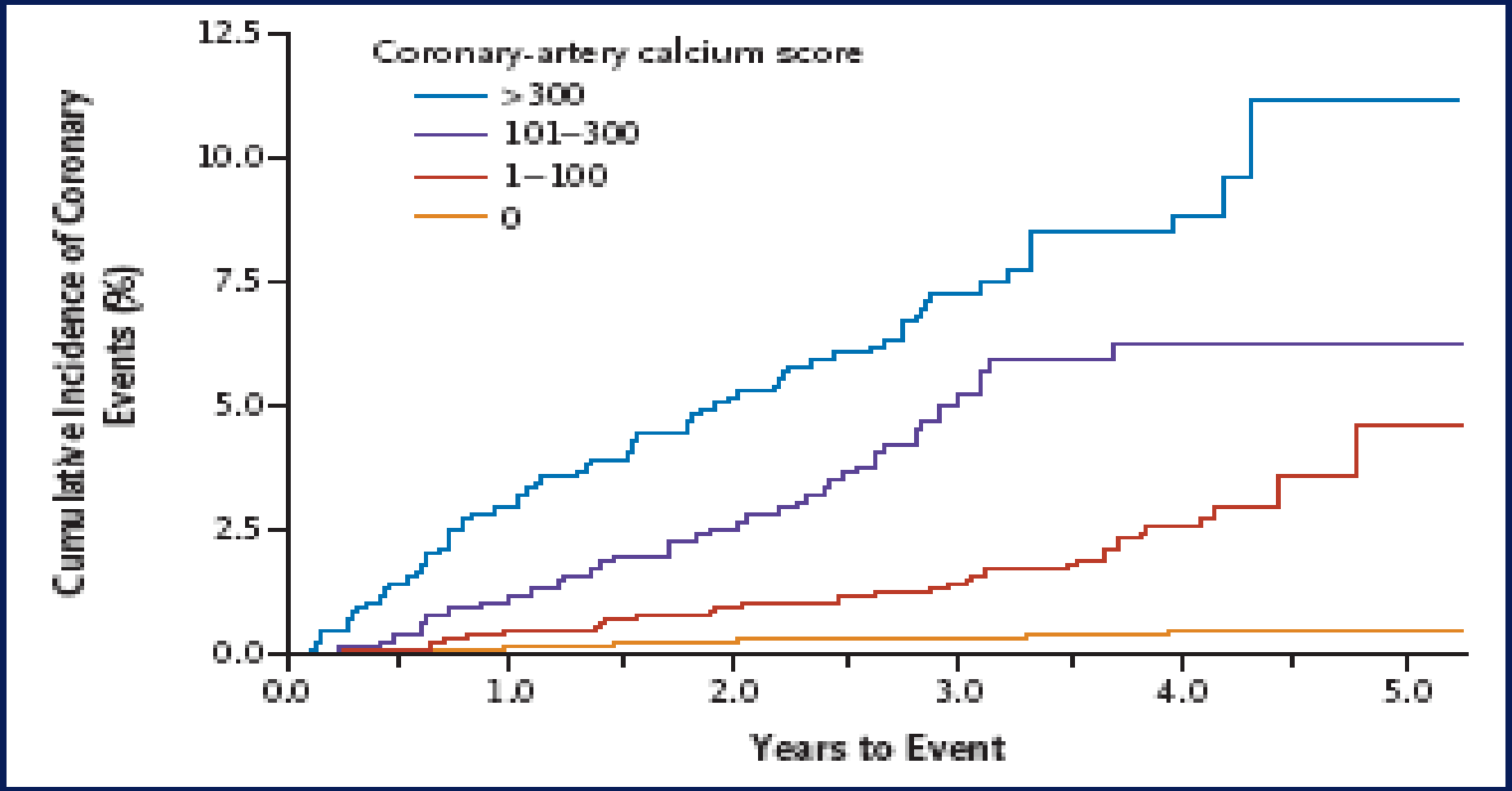
Coronary Calcium and Atherosclerosis: Pathology Evidence

- Coronary calcium invariably indicates the presence of atherosclerosis, but atherosclerotic lesions do not always contain calcium (1-3).
- Calcium deposition may occur early in life, as early as the second decade, and in lesions that are not advanced (4-5).
- Correlates with plaque burden; highly sensitive for angiographic disease



1) Wexler et al., Circ 1996; 94: 1175-92, 2) Blankenhorn and Stern, Am J Roentgenol 1959; 81: 772-7, 3) Blankenhorn and Stern, Am J Med Sci 1961; 42: 1-49, 4) Stary, Eur Heart J 1990; 11(suppl E): 3-19, 5) Stary, Arteriosclerosis 1989; 9 (suppl I): 19-32.

Cumulative Incidence of Any Coronary Event: MESA Study (Detrano et al., NEJM 2008)



Risk Factor-Adjusted Hazard Ratios by Coronary Calcium Score: MESA Study (Detrano et al., NEJM 2008)

Table 3. Risk of Coronary Events Associated with Increasing Coronary-Artery Calcium Score after Adjustment for Standard Risk Factors.*

Coronary-Artery Calcium Score	Major Coronary Event†			Any Coronary Event		
	No./No. at Risk	Hazard Ratio (95% CI)	P Value	No./No. at Risk	Hazard Ratio (95% CI)	P Value
0	8/3409	1.00		15/3409	1.00	
1–100	25/1728	3.89 (1.72–8.79)	<0.001	39/1728	3.61 (1.96–6.65)	<0.001
101–300	24/752	7.08 (3.05–16.47)	<0.001	41/752	7.73 (4.13–14.47)	<0.001
>300	32/833	6.84 (2.93–15.99)	<0.001	67/833	9.67 (5.20–17.98)	<0.001
Log_2(CAC+1)†		1.20 (1.12–1.29)	<0.001		1.26 (1.19–1.33)	<0.001

* CAC denotes coronary-artery calcium score, and CI confidence interval.

† Major coronary events were myocardial infarction and death from coronary heart disease.

† Each unit increase in log_2(CAC+1) represents a doubling of the coronary-artery calcium score.

Area Under Curve for Risk Factors Alone and Risk Factors Plus CAC by Ethnic Group: MESA Study (Detrano et al., NEJM 2008)

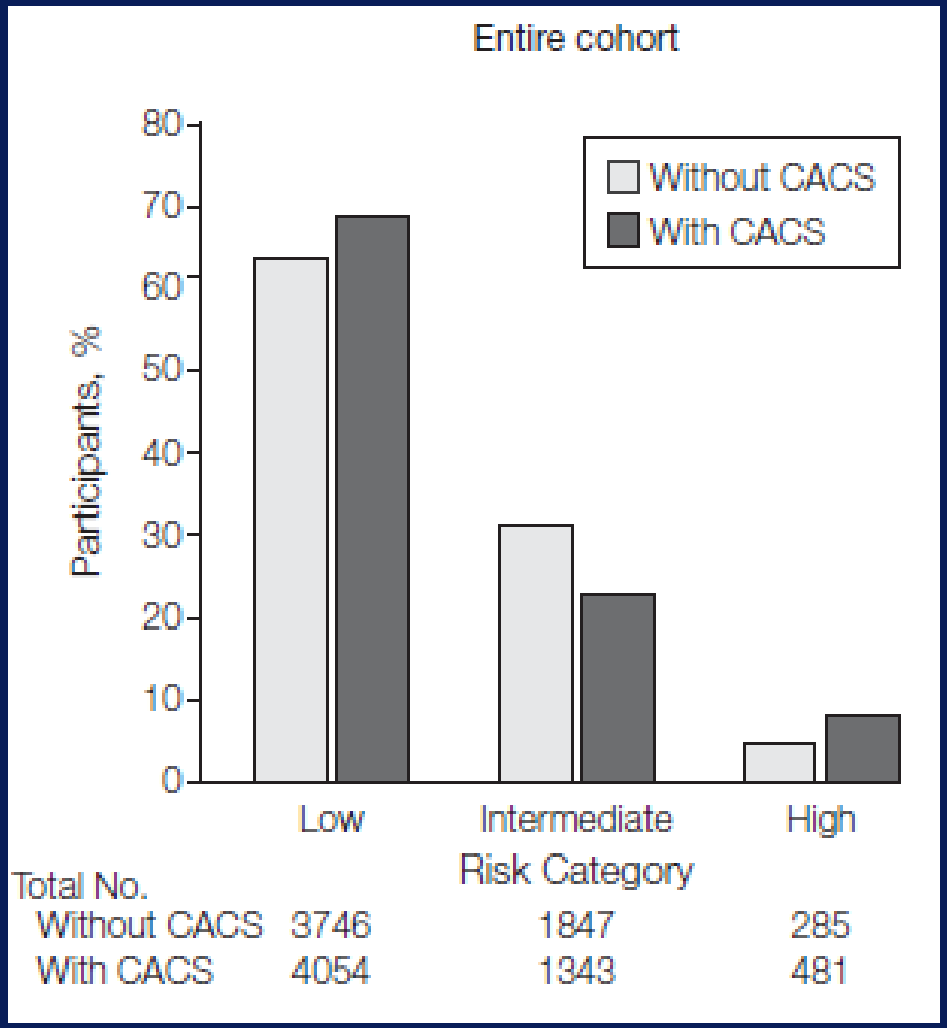
Table 5. Use of Area under the Curve for Risk Factors Alone and for Risk Factors plus Coronary-Artery Calcium Score to Predict Major Coronary Events and Any Coronary Event, According to Racial or Ethnic Group.*

Racial or Ethnic Group	Major Coronary Event†			Any Coronary Event		
	AUC for Risk Factors Alone	AUC for Risk Factors plus Coronary-Artery Calcium Score	P Value	AUC for Risk Factors Alone	AUC for Risk Factors plus Coronary-Artery Calcium Score	P Value
White	0.76	0.79	0.10	0.75	0.79	0.02
Chinese	0.83	0.88	0.05	0.74	0.85	<0.001
Black	0.79	0.87	0.04	0.81	0.87	0.005
Hispanic	0.84	0.86	0.11	0.80	0.84	0.10
Total	0.79	0.83	0.006	0.77	0.82	<0.001

* Separate models are fitted for each racial or ethnic group. AUC denotes area under the receiver-operating-characteristic curve. P values are for the comparison between AUC without and AUC with the coronary-artery calcium score.

† Major coronary events were myocardial infarction and death from coronary heart disease.

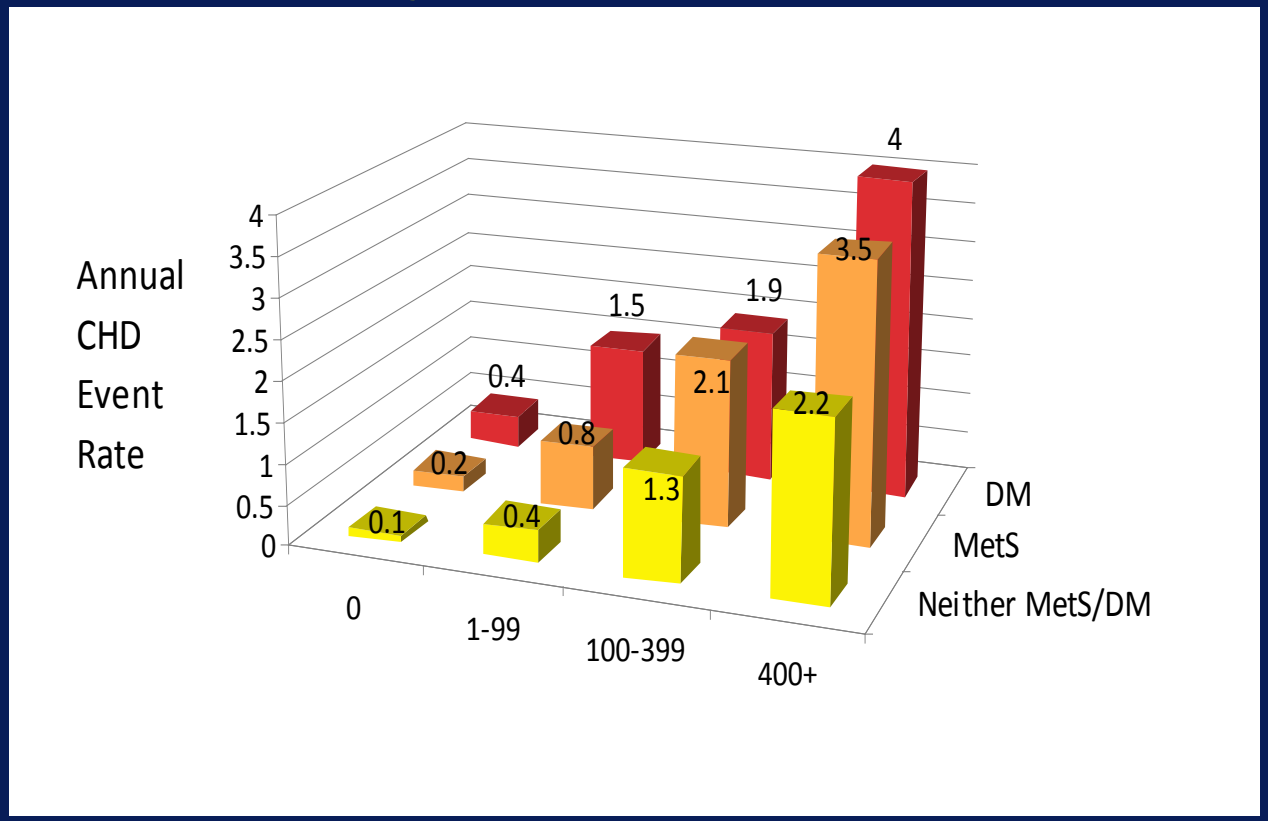
Net Reclassification of CHD Risk by Coronary Calcium: MESA Study (Polonsky et al., JAMA 2010)



The addition of CAC to models with age, gender, ethnicity and risk factors alone resulted in net reclassification of 0.25 ($p<0.001$); 23% of those with events were reclassified as high risk and 13% without events were reclassified as low risk.

Annual CHD Event Rates (in %) by Calcium Score Events by CAC Categories in Subjects with DM, MetS, or Neither Disease (Malik and Wong et al., Diabetes Care 2011)

Coronary Heart Disease

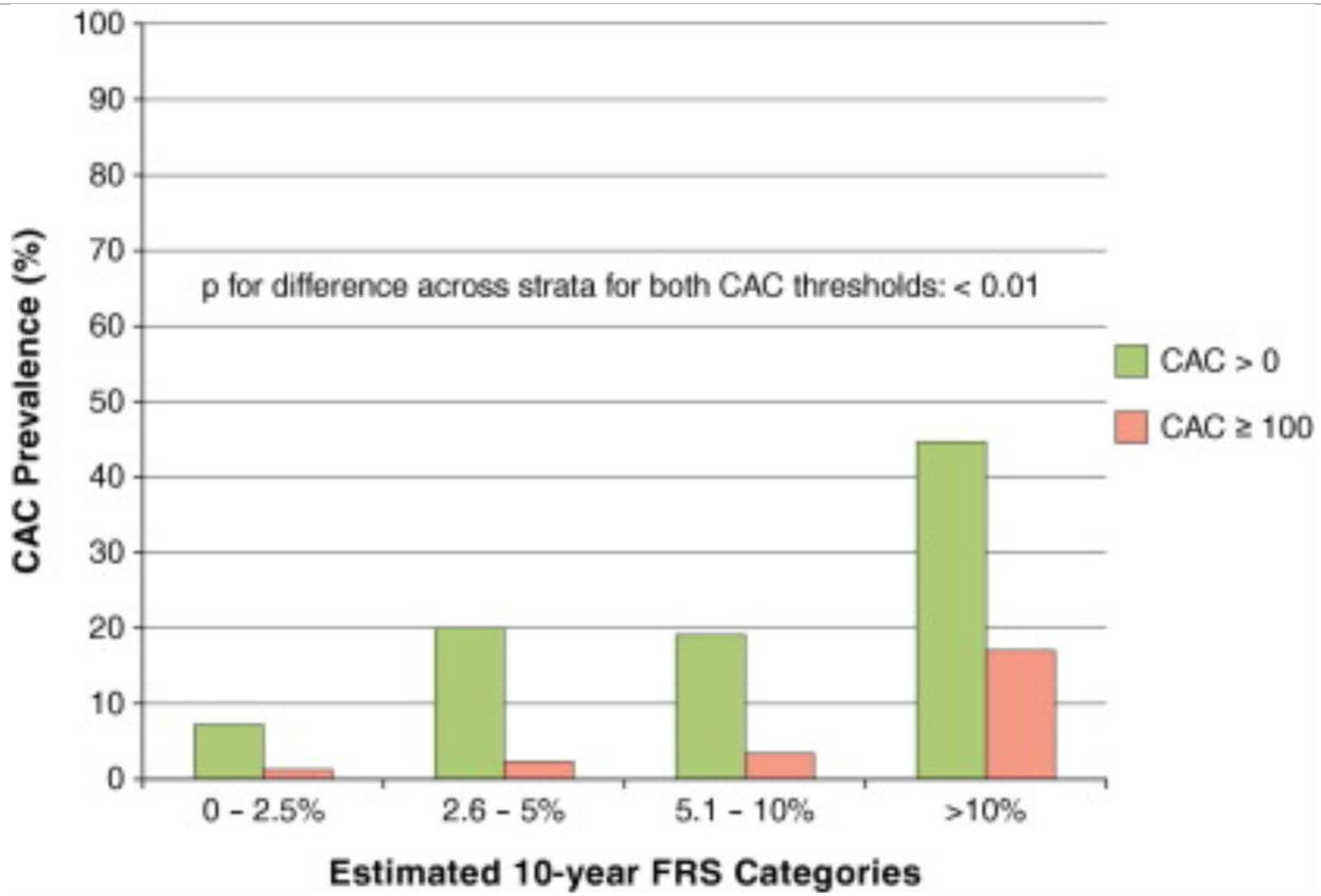


Coronary Artery Calcium Score

ACCF/AHA 2010 Guideline: CAC Scoring for CV risk assessment in asymptomatic adults aged 40 and over with diabetes (Class IIa-B)

From: Yield of Screening for Coronary Artery Calcium in Early Middle-Age Adults Based on the 10-Year Framingham Risk Score: The CARDIA Study

J Am Coll Cardiol Img. 2012;5(9):923-930. doi:10.1016/j.jcmg.2012.01.022



CAC Score Compared With FRS

Prevalence of coronary artery calcium (CAC) scores >0 and ≥100 compared across 10-year Framingham Risk Score (FRS) strata in the CARDIA study. There was significant concordance between CAC prevalence/amount and FRS such that prevalence of CAC scores >0 and ≥100 were low in the lower FRS strata and increased with higher FRSs.

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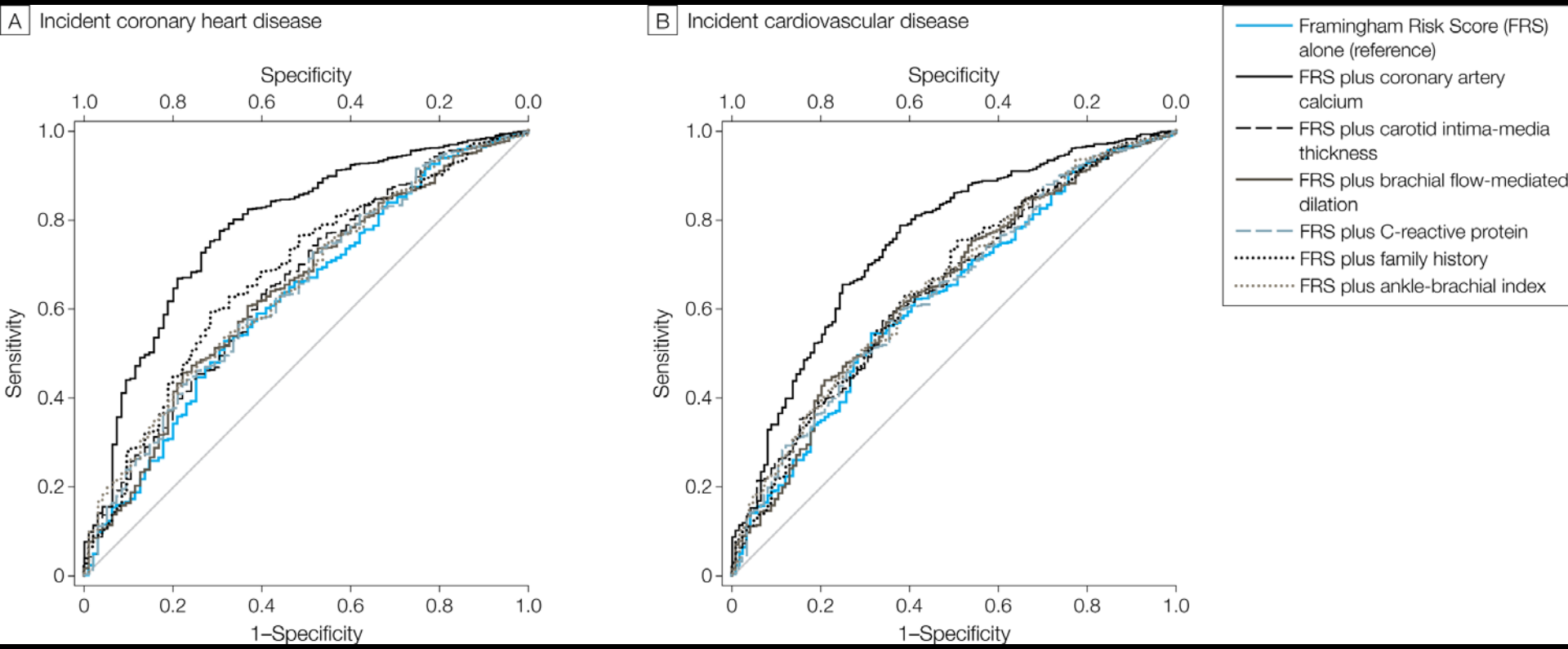
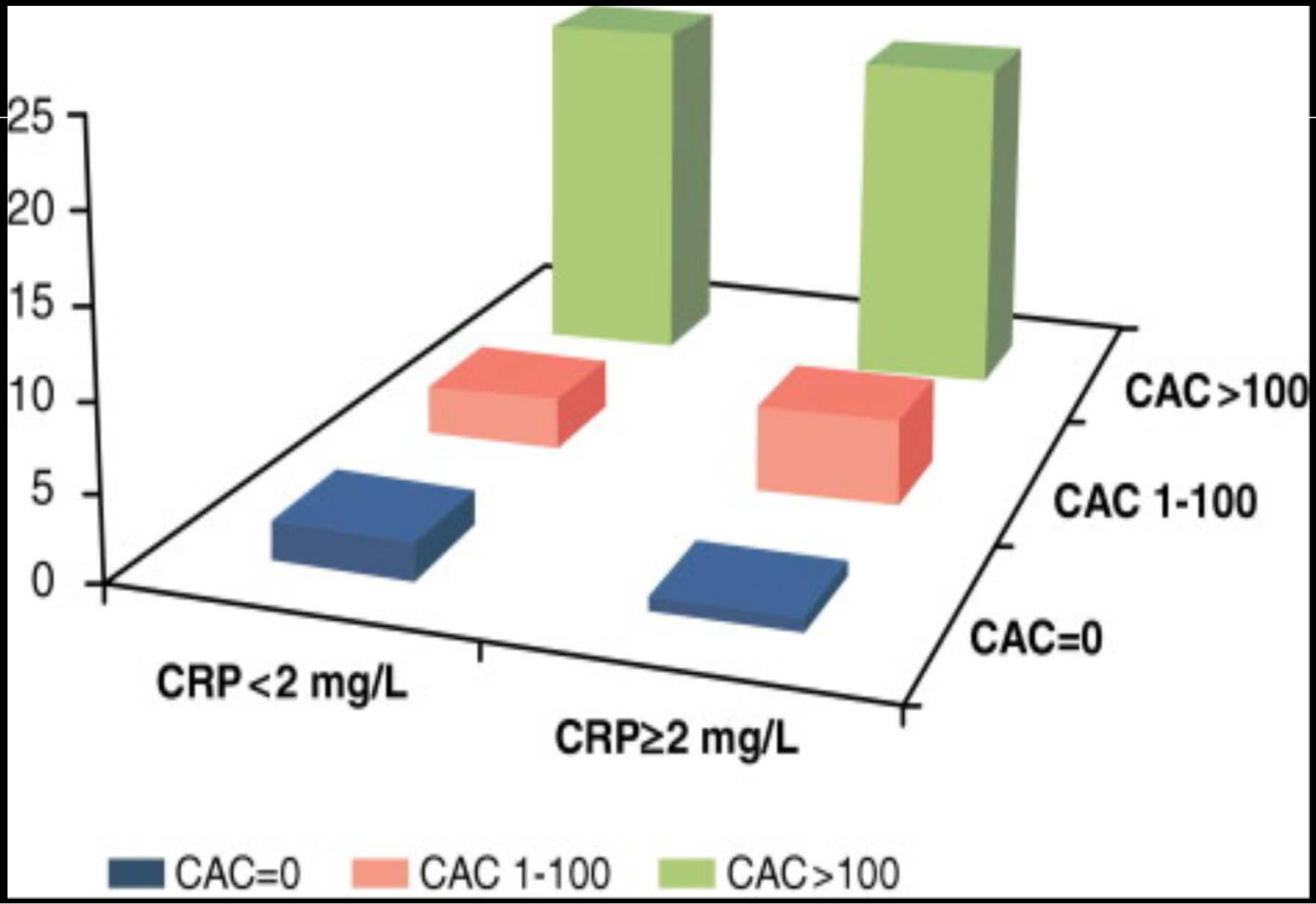
Indications for CAC Assessment

(Greenland et al., ACCF/AHA Guideline for Assessment of Cardiovascular Risk in Asymptomatic Adults (Circulation, 2010)

- CV risk assessment in asymptomatic adults at intermediate risk (10-20% 10-year risk) (Class IIa, Level of Evidence B)
- CV risk assessment in persons at low to intermediate risk (6-10% 10-year risk) (Class IIb, Level of Evidence B)
- CV risk assessment in asymptomatic adults with diabetes (Class IIa-B)
- Persons at low risk (<6% 10-year risk) should not undergo CAC measurement for CV risk assessment (Class III, Level of Evidence B)


A
Incident coronary heart disease
Specificity
1.0
0.8
0.6
0.4
0.2
0.0
Sensitivity
1.0
0.8
0.6
0.4
0.2
0
0
0.2
0.4
0.6
0.8
1.0
1–Specificity
B
Incident cardiovascular disease
Specificity
1.0
0.8
0.6
0.4
0.2
0.0
Sensitivity
1.0
0.8
0.6
0.4
0.2
0
0
0.2
0.4
0.6
0.8
1.0
1–Specificity
Framingham Risk Score (FRS) alone (reference)
FRS plus coronary artery calcium
FRS plus carotid intima-media thickness
FRS plus brachial flow-mediated dilation
FRS plus C-reactive protein
FRS plus family history
FRS plus ankle-brachial index



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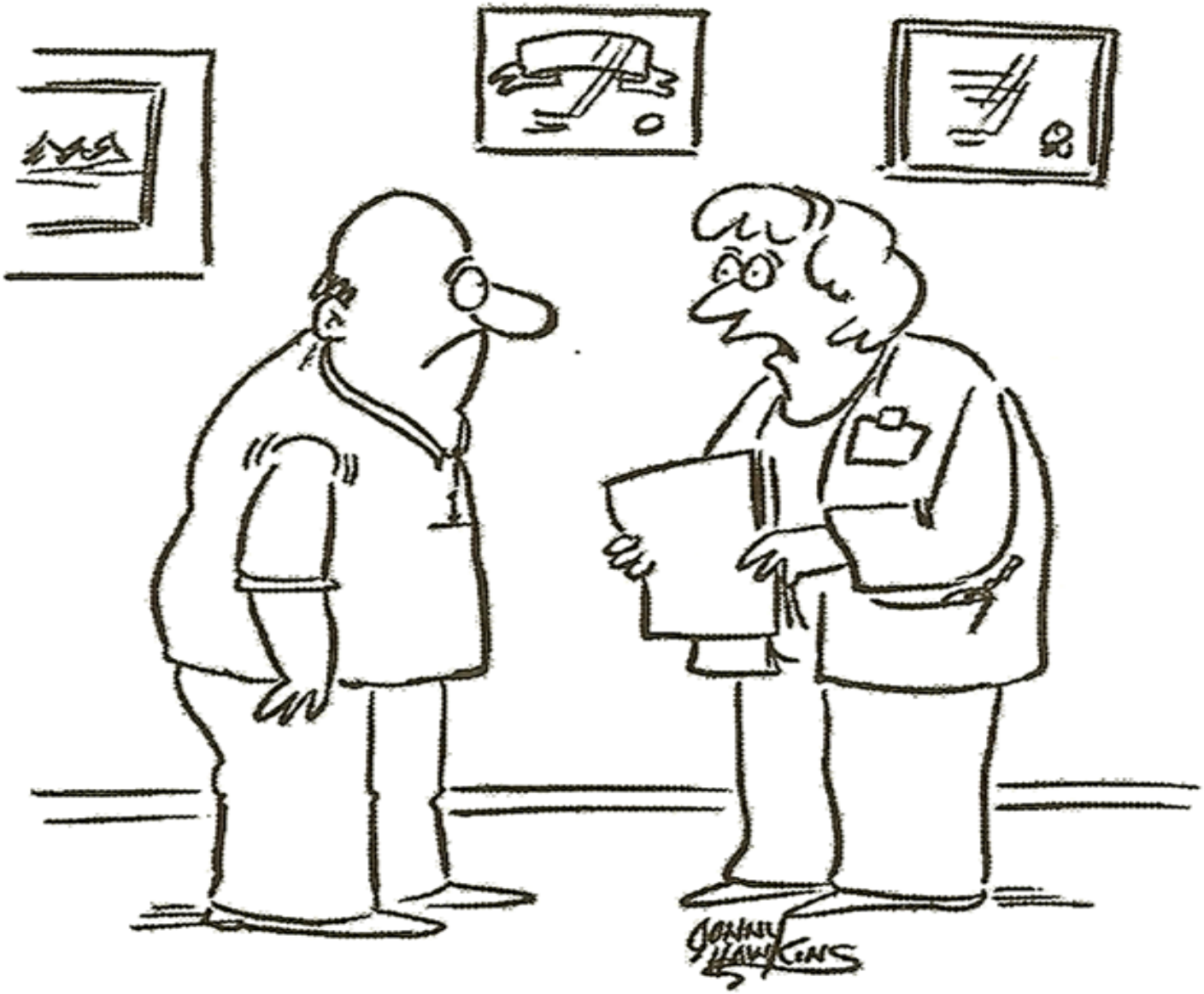


"I think Dr. Lugendorf recommended a *biopsy*—
I'm sure 'autopsy' was a slip of the tongue."

Top five causes of global DALY

1990	2010
Lower respiratory infections	Ischaemic heart disease
Diarrhoea	Lower respiratory infections
Preterm birth complications	Stroke
Ischaemic heart disease	Diarrhoea
Stroke	HIV/AIDS

Communicable, maternal, neonatal, and nutritional disorders

Non-communicable disease

DALY = Disability-Adjusted Life Years

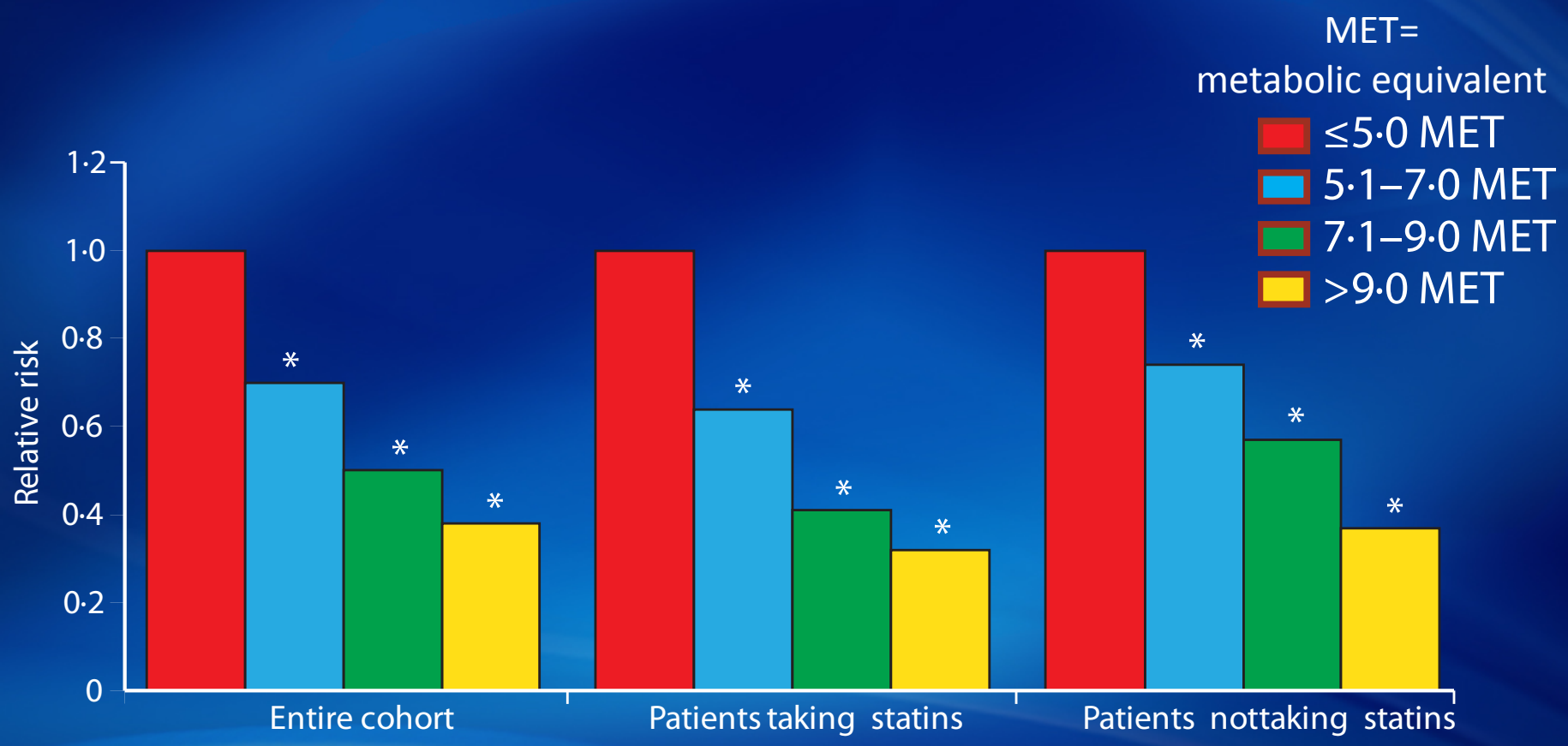
The Lancet, Vol 380 December 15/22/29, 2012

"Give it to me straight, Doc.
How long do I have to ignore your advice?"

Conclusions

- We need to make the diagnosis and treatment more closely resemble the natural history of the disease of atherosclerosis.
- Novel approaches include changing the time-scale of assessment and treatment, particularly as medical therapy becomes cheaper via cheaper proven, time-tested pharmacotherapy

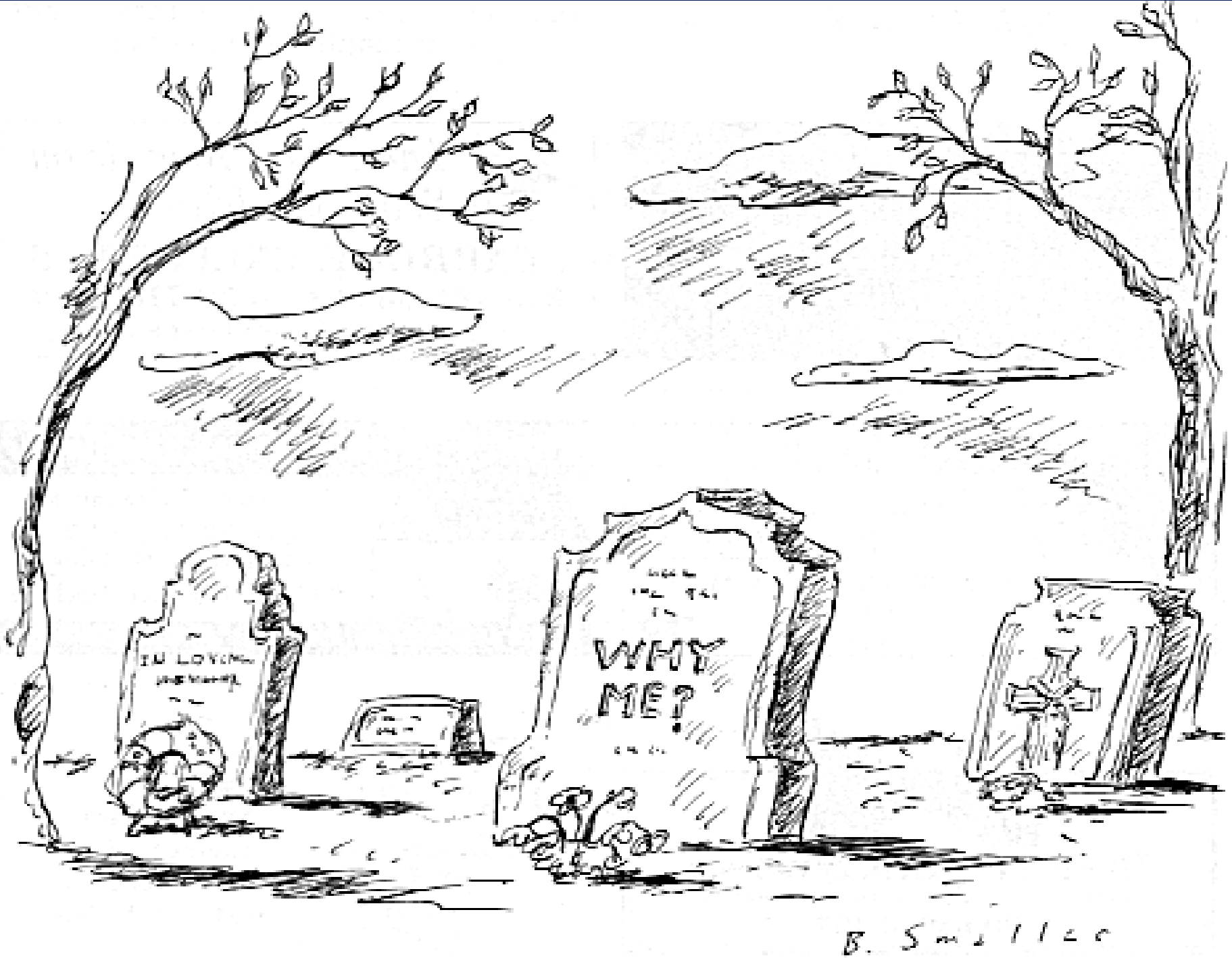
Interactive effects of fitness and statin treatment on relative mortality risk

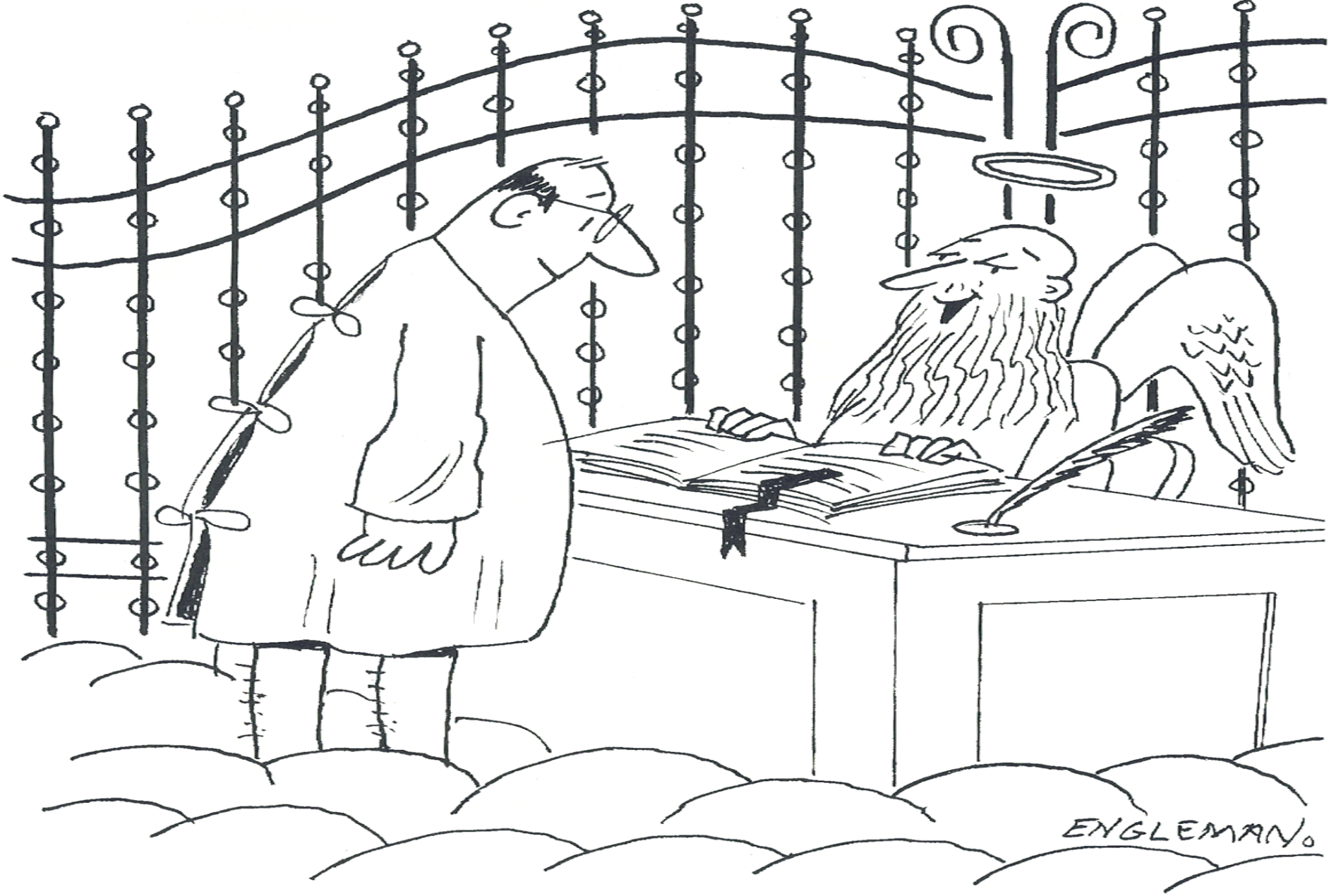


Kokkinos PF, et al.The Lancet (online)
dx.doi.org/10.1016/S0140-6736(12)61426-3

Conclusions - Continued

- A growing awareness that atherosclerosis is a medical condition and but unfortunately largely treated as a surgical emergency.
- Non-HDL and Coronary Artery Calcium Scoring are very promising tools that may allow us to better understand who has early, preclinical atherosclerosis.
- These efforts will ultimately require a team-based approach with all stakeholders involved and invested in these strategies.


WHY ME?
B. Smallec

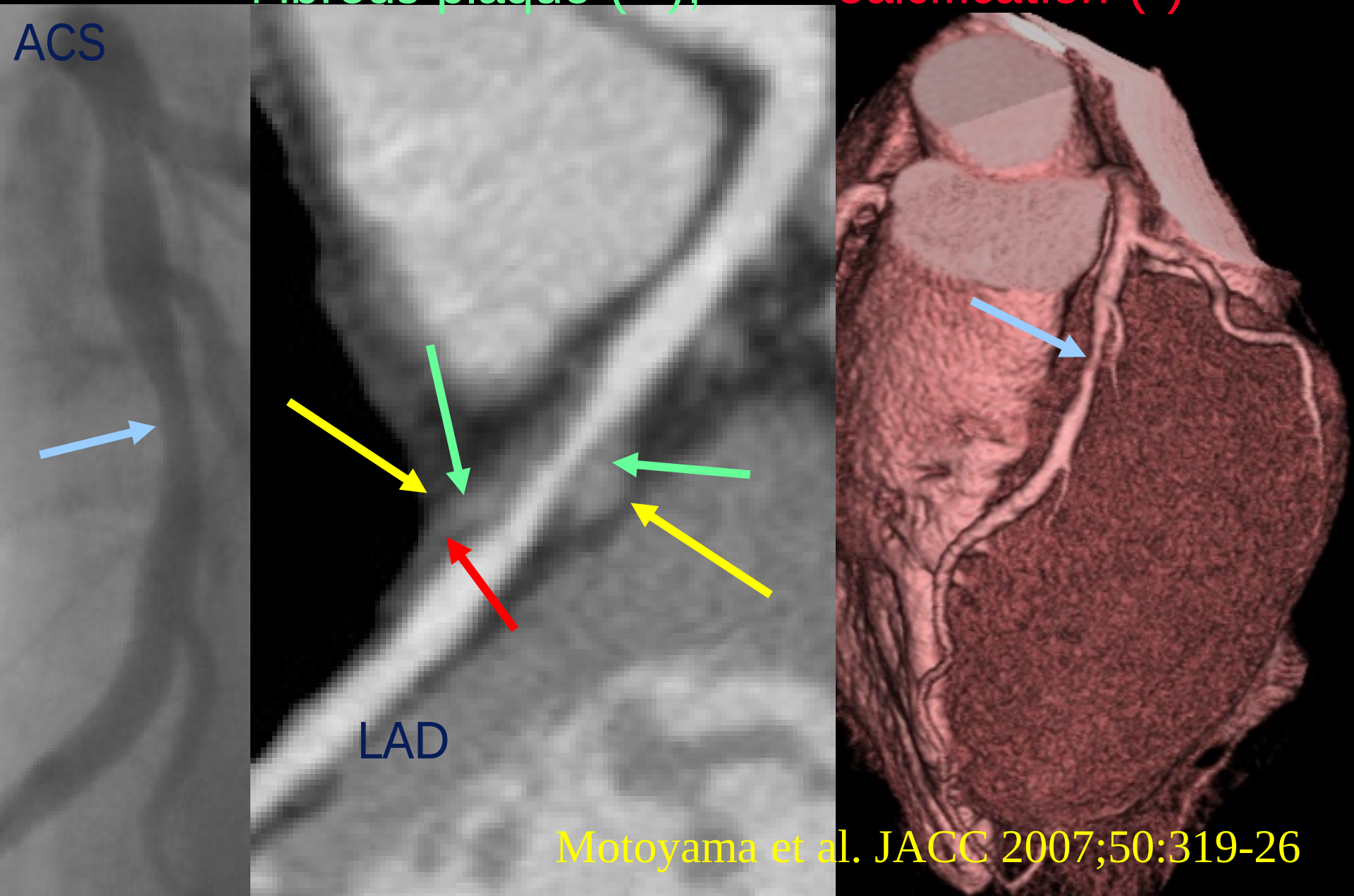


Your time on earth has been extended
go back and thank your Doctor

"It takes a Village - to Eradicate Heart Disease"

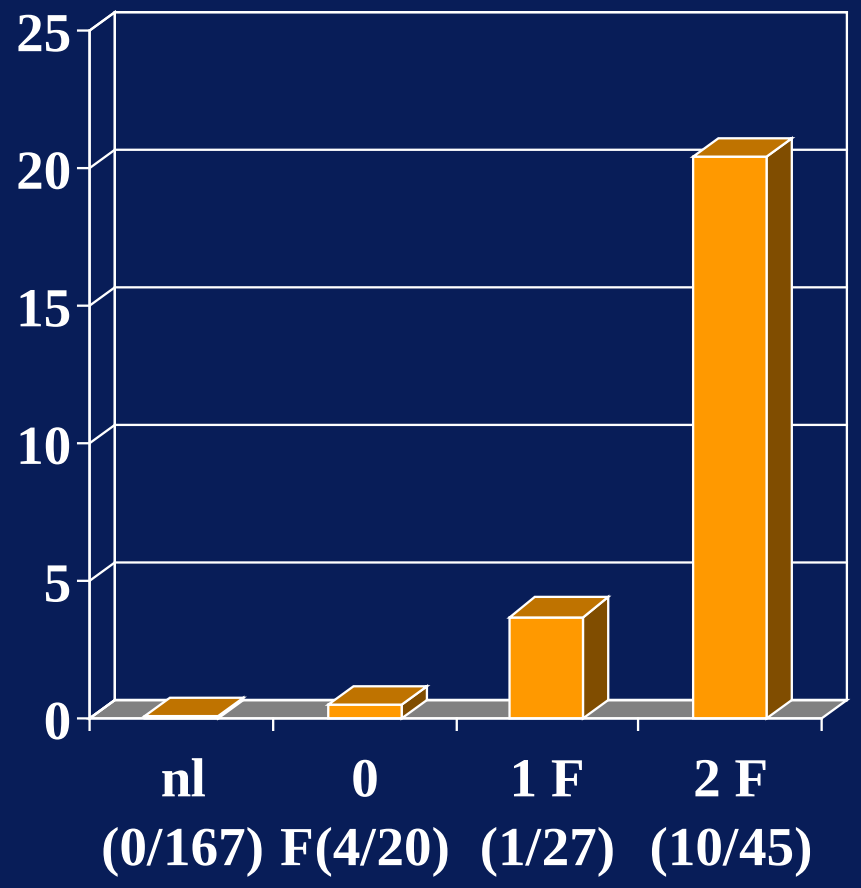
John A Osborne, MD, PhD, FACC
State of the Heart Cardiology
Director and Founder

Positive remodeling (+), Soft plaque (+),
Fibrous plaque (+), Calcification (-)



Motoyama et al. JACC 2007;50:319-26

% of Patients Subsequently Resulting in ACS by CCTA Plaque Features (F)



Adverse features (F):
positive remodeling
low-attenuation plaques

% with events

1,059 pts with CCTA followed up for 27 ± 10 mo
ACS developed in 15 patients.
None had >75% stenosis in the culprit lesion at time of CCTA

Motoyama et al. *JACC* 2009;54:49-57

All-Cause Mortality from CCTA Findings in the CONFIRM Registry (Min et al., JACC 2011)

- 24,775 pts underwent >=64 detector CCTA
- After 2.3 years follow-up 404 deaths occurred
- HR for death was 2.6 for obstructive and 1.6 for nonobstructive (both $p<0.01$)
- HR by no of obstructive vessels was 1.6 for nonobstructive, 2.0 for 1 vessel, 2.9 for 2 vessels, and 3.7 for 3+ vessels (all $p<0.01$)
- Absence of CAD by CCTA was associated with low incident death rates (0.28%).
- Hazards for death from multiple vessel CAD were higher for younger persons and women.

From: Prognostic Value of Coronary CT Angiography and Calcium Score for Major Adverse Cardiac Events in Outpatients

J Am Coll Cardiol Img. 2012;5(10):990-999. doi:10.1016/j.jcmg.2012.06.006

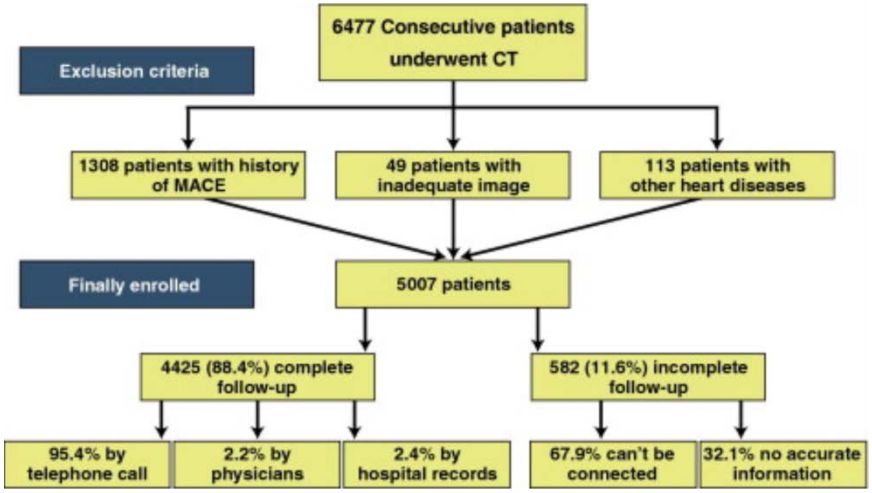


Figure Legend:

Flow Chart of the Follow-Up

In all, 6,477 consecutive patients who underwent cardiac computed tomography between January 2007 and August 2008 in Fu Wai Hospital were evaluated. For the present study, 5,007 patients were finally enrolled, and 4,425 patients were finally analyzed. CT = computed tomography; MACE = major adverse cardiac events.

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From: Prognostic Value of Coronary CT Angiography and Calcium Score for Major Adverse Cardiac Events in Outpatients

J Am Coll Cardiol Img. 2012;5(10):990-999. doi:10.1016/j.jcmg.2012.06.006

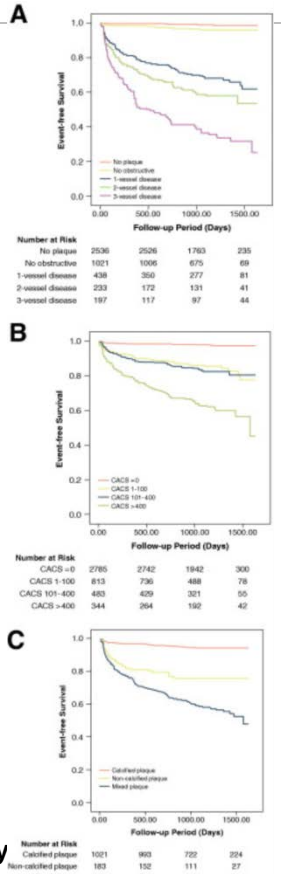

Figure Legend:

Kaplan-Meier Curves of MACE as Stratified by Coronary

(A) Coronary computed tomography angiography (CTA) categories stratified into no plaque (red line), no obstructive (yellow line), 1-vessel disease (blue line), 2-vessel disease (green line), and 3-vessel disease (purple line). (B) Coronary artery calcium score (CACS) categories stratified into CACS = 0 (red line), CACS 1 to 100 (yellow line), CACS 101 to 400 (blue line), and CACS >400 (green line). (C) The characteristics of the plaques categories stratified into calcified plaque (red line), noncalcified plaque (yellow line), and mixed plaque (blue line). The cohort was followed up for a median of 1,081 days (quartile 1 = 960 days, quartile 3 = 1,192 days). MACE = major adverse cardiac events.

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From: Prognostic Value of Coronary CT Angiography and Calcium Score for Major Adverse Cardiac Events in Outpatients

J Am Coll Cardiol Img. 2012;5(10):990-999. doi:10.1016/j.jcmg.2012.06.006

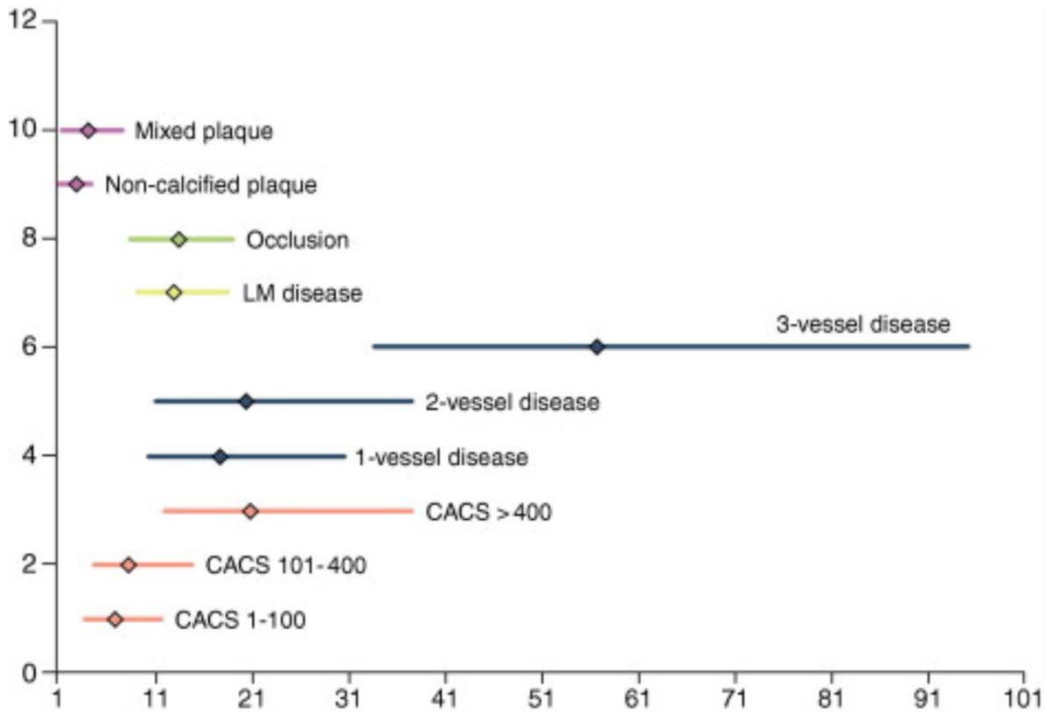

Figure Legend:

Unadjusted Cardiac CT Findings for Predicting MACE

Computed tomography (CT) strata for coronary artery calcium score (CACS) and several coronary computed tomography angiography (CTA) findings demonstrated significant associations with major adverse cardiac events (MACE). LM = left main.

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From: Prognostic Value of Coronary CT Angiography and Calcium Score for Major Adverse Cardiac Events in Outpatients

J Am Coll Cardiol Img. 2012;5(10):990-999. doi:10.1016/j.jcmg.2012.06.006

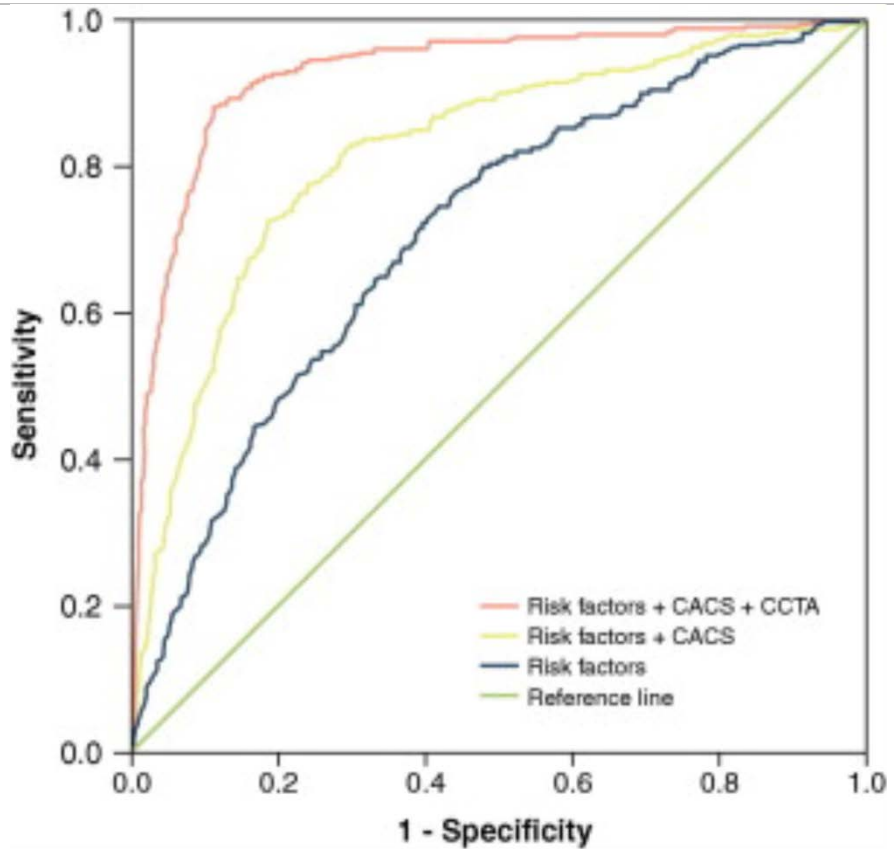

Figure Legend:

ROC Curves of 3 Models

Receiver-operating characteristic (ROC) curves show the incremental value of coronary artery calcium score (CACS) and coronary computed tomography angiography (CTA): risk factors only (area under the curve [AUC] 0.71; 95% confidence interval [CI]: 0.68 to 0.74, p < 0.001 [blue line]). Risk factors plus CACS (AUC 0.82; 95% CI: 0.80 to 0.85, p < 0.001 [yellow line]), and risk factors plus CACS plus coronary CTA (AUC 0.93; 95% CI: 0.92 to 0.95, p < 0.001 [red line]). Green line indicates reference line.

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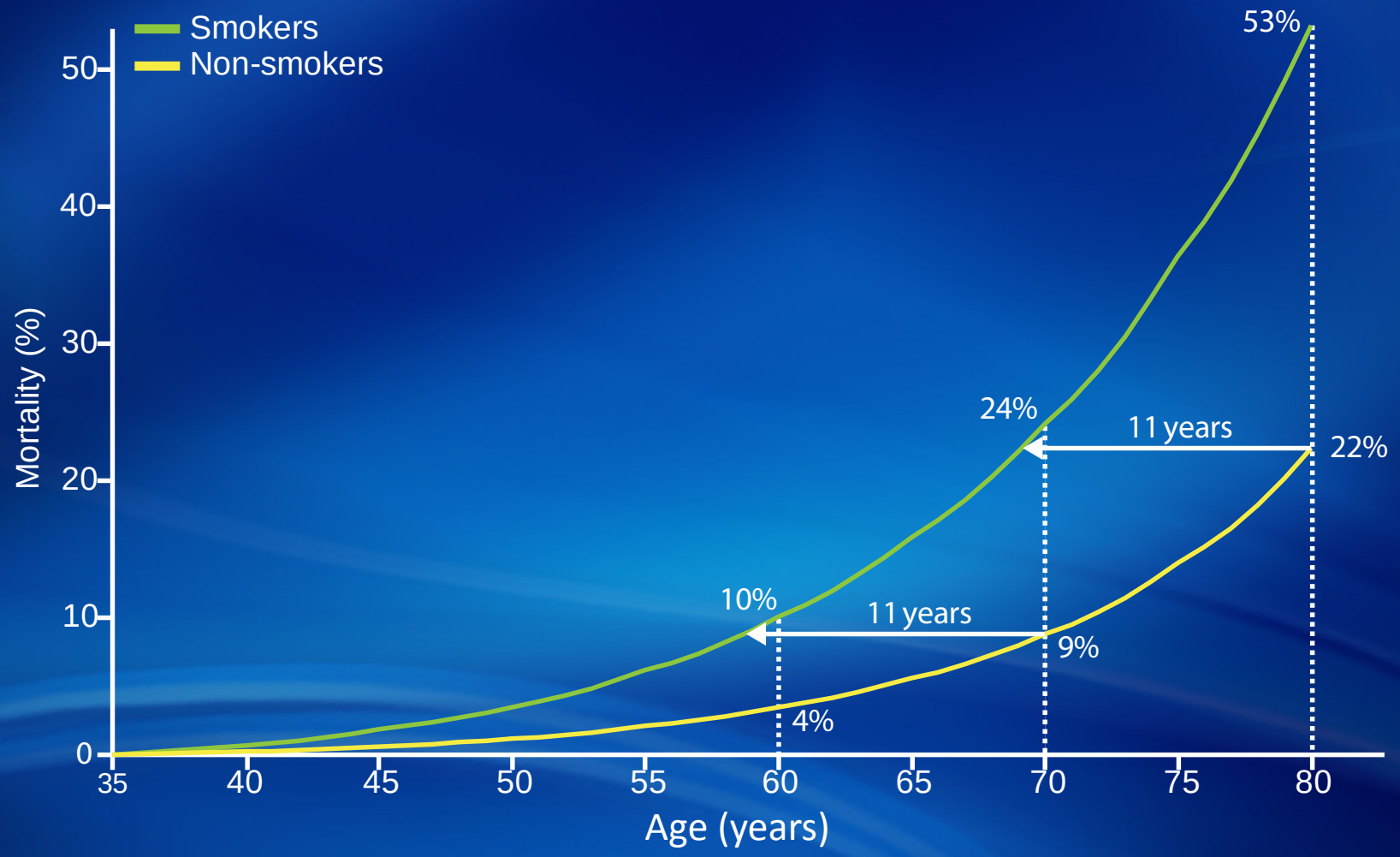
Smokers – Non Smokers

3-fold difference in annual death rates on mortality from age 35 years to age 80 years



Kirstin Pirie et al, Lancet, October 2012