Management of Chronic Coronary Syndromes

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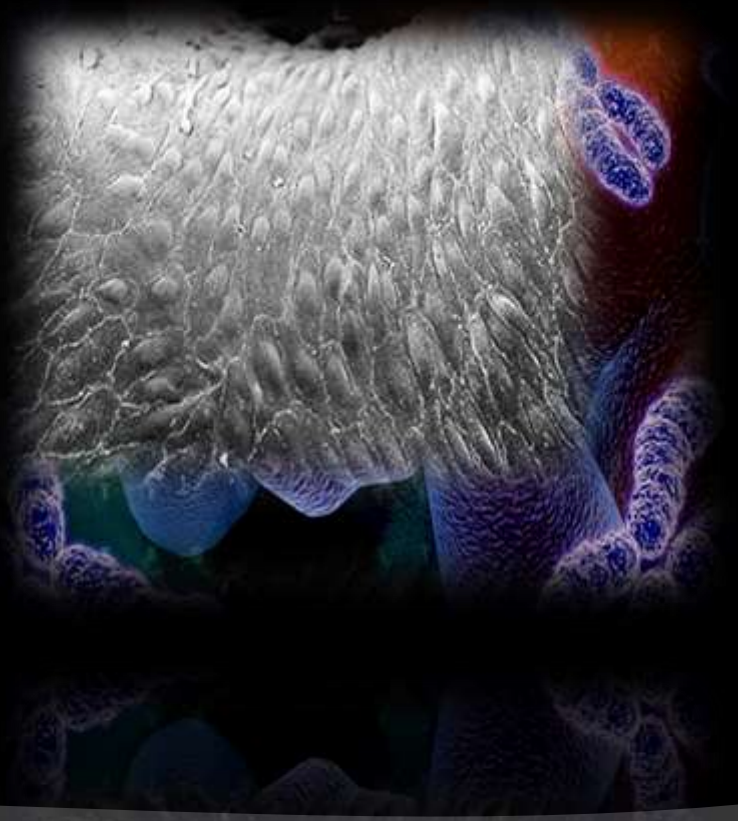
No Disclosures

CHRONIC STABLE ANGINA

BY THE GUIDELINES

Picking Mom and Dad-2016



Global Risk Reduction--WINS

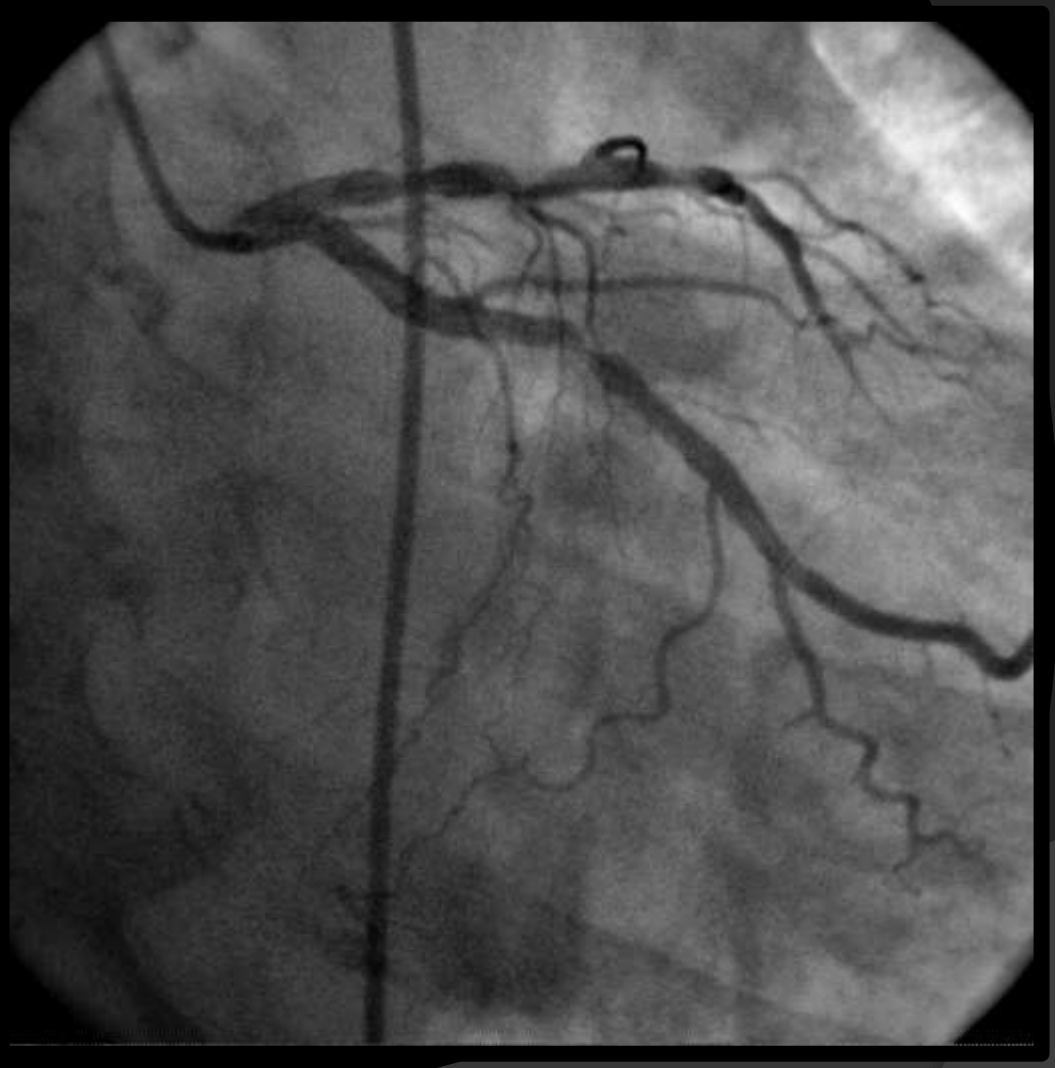
Environmental	Stop smoking-1B Physical activity-1B Weight control-1B Chelation therapy-3C Influenza vaccination-1B
Vascular / Tissue	Blood pressure-1B RAAS blockade-1A Aldosterone blockade-1A/B
Metabolics	Lipids-1B Triglycerides-1B Diabetes-1B Antiplatelets-1A/B

Circulation. 2007;116:2762-2772

AHA 2007 Guidelines for CSA.pdf

50 y/o he presents with increasing fatigue and short of breath on exercise

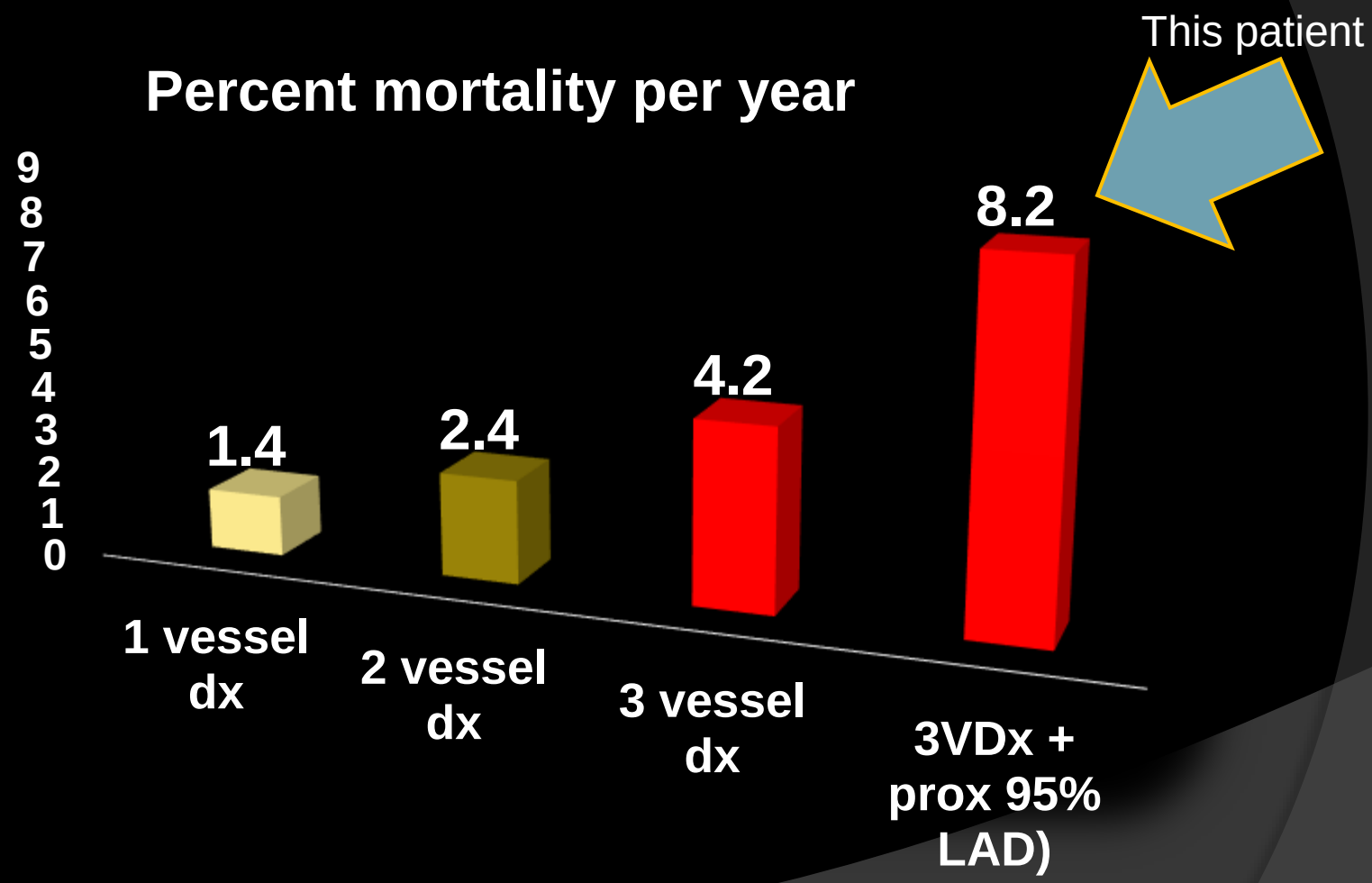
BP 145/90
LDL cholesterol 140 mg/dl
HDL cholesterol 35
Triglycerides 280



Patient from San Antonio

2 over weight dogs

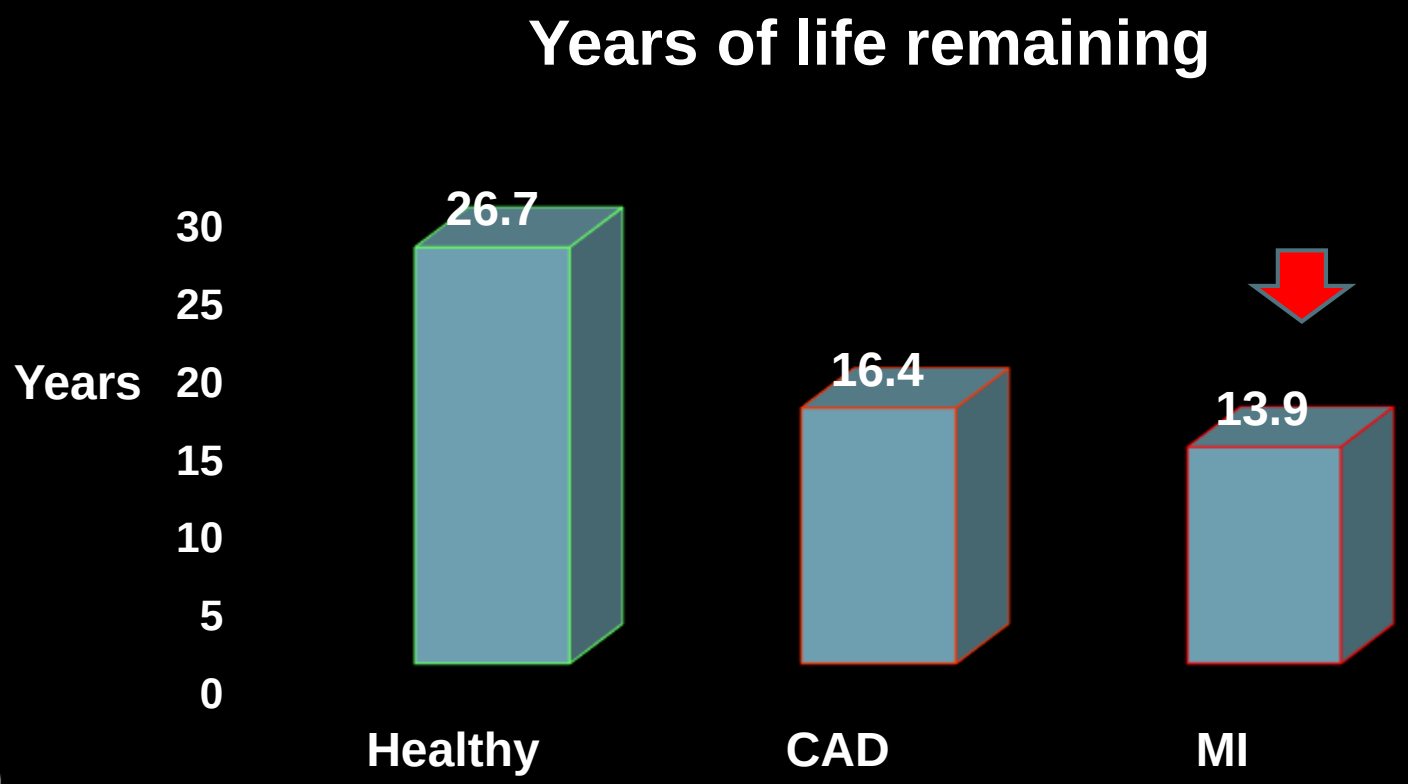
Yearly mortality (death) in medically treated patients by coronary angiogram



J Am Coll Cardiol. 1996;27:964–1047

Adapted from al Patel et al

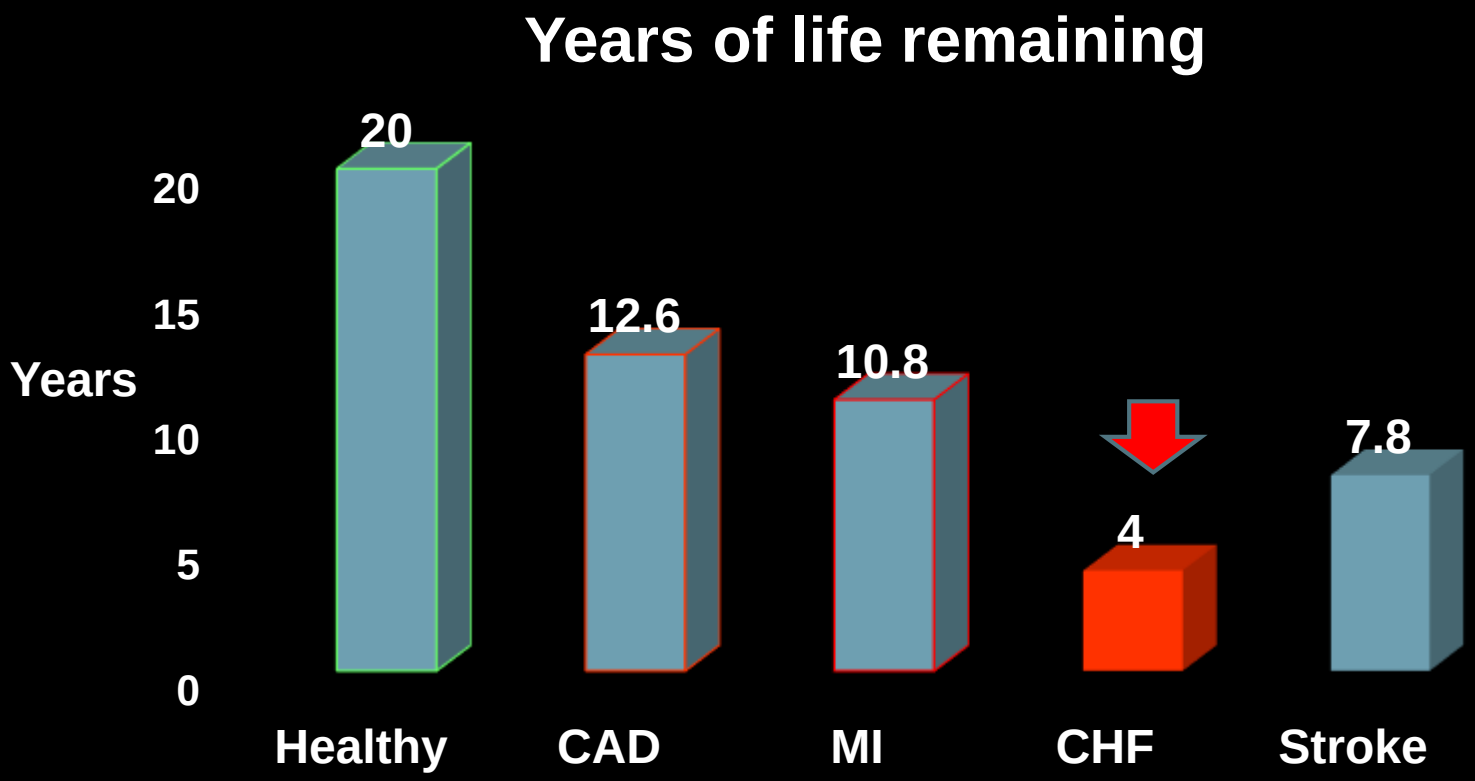
50 year old male



Eur Heart J 2002; 23: 458–466

Framingham 40 year follow up
N=5070

60 year old male



Eur Heart J 2002; 23: 458–466

Framingham 40 year follow up
N=5070

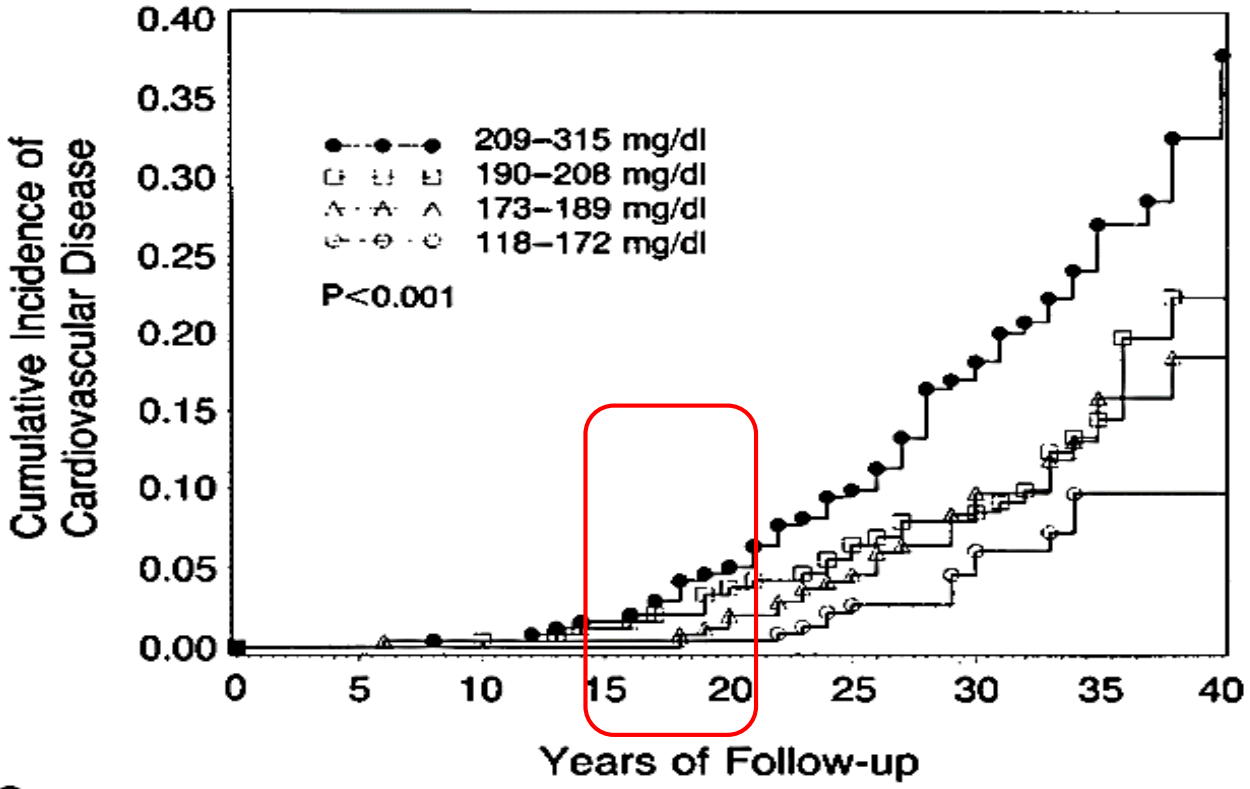
Johns Hopkins: medical students cholesterol and risk of CV disease

- Prospective study
- N=1017 young men
- Mean age 22
- 27-42 years follow up
  - Median 30.5 years
- Endpoint: risk of CV disease and total mortality associated with cholesterol

Variable	All Subjects	Quartile of Cholesterol Level				P Value†
		118–172 mg/dl	173–189 mg/dl	190–208 mg/dl	209–315 mg/dl	
No. of subjects	1017	250	258	254	255	
Age (yr)	22.0±2.3	21.6±1.9	21.8±2.0	21.8±2.0	22.7±3.1	0.001
Coffee intake (cups/day)‡	2.3±1.8	3.1±1.9	2.2±1.8	2.3±1.7	2.4±1.9	0.2
Body-mass index	23.2±2.6	22.5±2.4	22.8±2.2	23.4±2.6	24.0±2.9	0.001
Systolic blood pressure (mm Hg)	125±14	124±14	126±15	125±14	126±14	0.3
Diastolic blood pressure (mm Hg)	75±9	74±9	75±10	75±9	76±10	0.2
Serum cholesterol (mg/dl)	192±29	158±11	181±5	199±6	231±20	—

NEJM 1993;328:313

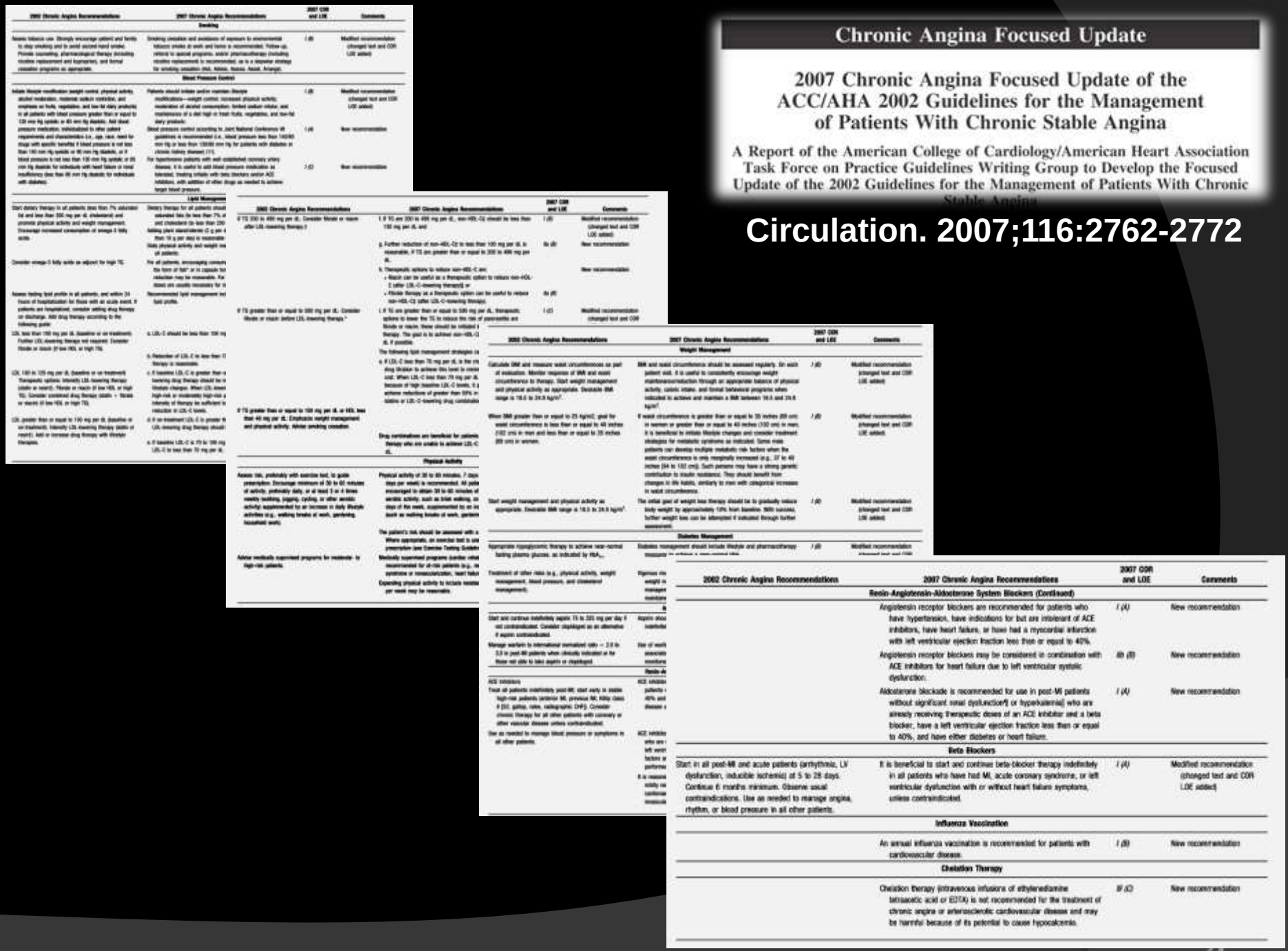
Note: it starts mainly after 15-20yrs



Quartile (mg/dl)									
118–172	250	248	245	240	234	217	128	61	7
173–189	258	256	254	250	243	216	131	62	15
190–208	254	251	248	240	228	208	155	75	12
209–315	255	251	243	235	222	196	140	78	13
Total	1017	1006	990	965	927	837	554	276	47

NEJM 1993;328:313

“The guidelines”



Chronic Angina Focused Update

2007 Chronic Angina Focused Update of the ACC/AHA 2002 Guidelines for the Management of Patients With Chronic Stable Angina

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines Writing Group to Develop the Focused Update of the 2002 Guidelines for the Management of Patients With Chronic Stable Angina

Circulation. 2007;116:2762-2772

2002 Chronic Angina Recommendations	2007 Chronic Angina Recommendations	2007 COR and LOE	Comments
	Renin-Angiotensin-Aldosterone System Blockers (Continued)		
	Angiotensin receptor blockers are recommended for patients who have hypertension, have indications for but are intolerant of ACE inhibitors, have heart failure, or have had a myocardial infarction with left ventricular ejection fraction less than or equal to 40%.	*I (A)*	New recommendation
	Angiotensin receptor blockers may be considered in combination with ACE inhibitors for heart failure due to left ventricular systolic dysfunction.	*IIb (B)*	New recommendation
	Aldosterone blockade is recommended for use in post-MI patients without significant renal dysfunction[*] or hyperkalemia[†] who are already receiving therapeutic doses of an ACE inhibitor and a beta blocker, have a left ventricular ejection fraction less than or equal to 40%, and have either diabetes or heart failure.	*I (A)*	New recommendation
	Beta Blockers		
Start in all post-MI and acute patients (arrhythmia, LV dysfunction, inducible ischemia) at 5 to 28 days. Continue 6 months minimum. Observe usual contraindications. Use as needed to manage angina, rhythm, or blood pressure in all other patients.	It is beneficial to start and continue beta-blocker therapy indefinitely in all patients who have had MI, acute coronary syndrome, or left ventricular dysfunction with or without heart failure symptoms, unless contraindicated.	*I (A)*	Modified recommendation (changed text and COR LOE added)
	Influenza Vaccination		
	An annual influenza vaccination is recommended for patients with cardiovascular disease.	*I (B)*	New recommendation
	Chelation Therapy		
	Chelation therapy (intravenous infusions of ethylenediamine tetraacetic acid or EDTA) is not recommended for the treatment of chronic angina or arteriosclerotic cardiovascular disease and may be harmful because of its potential to cause hypocalcemia.	*III (C)*	New recommendation

Pharmacotherapy for Chronic Stable Angina (class I)

- 1. Aspirin in the absence of contraindications A
- 2. Beta-blockers as initial therapy in the absence of contraindications in patients with prior myocardial infarction or without prior myocardial infarction A,B
- 3. ACE inhibitor in all patients with CAD who also have diabetes and/or LV systolic dysfunction A
- 4. LDL-lowering therapy in patients with documented or suspected CAD and LDL cholesterol >130 mg/dl, with a target LDL of <100 mg/dl A
- 5. Sublingual nitroglycerin or nitroglycerin spray for the immediate relief of angina B
- 6. Calcium antagonists † or long-acting nitrates as initial therapy for reduction of symptoms when beta blockers are contraindicated B

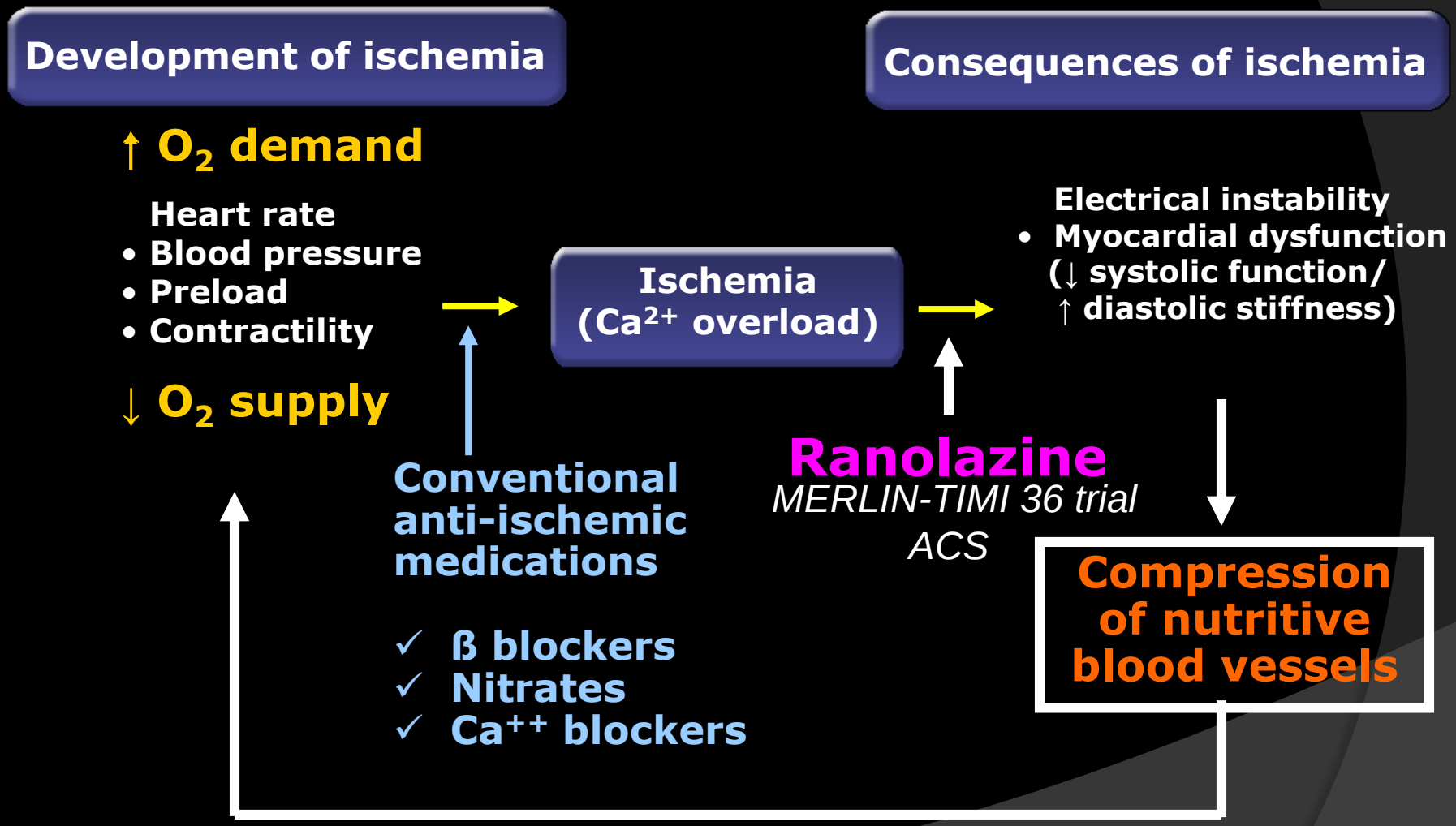
Pharmacotherapy for Chronic Stable Angina (class IIa)

- 1. Clopidogrel when aspirin is absolutely contraindicated
- 2. Long-acting non-dihydropyridine calcium antagonists ‡ instead of beta blockers as initial therapy B
- 3. In patients with documented or suspected CAD and LDL cholesterol 100–129 mg/dl, several therapeutic options are available: B
  - a. Lifestyle and/or drug therapies to lower LDL to <100 mg/dl
  - b. Weight reduction and increased physical activity in persons with the metabolic syndrome
  - c. Institution of treatment of other lipid or non-lipid risk factors; consider use of nicotinic acid or fibric acid for elevated triglycerides or low HDL cholesterol
- 4. ACE inhibitor in patients with CAD or other vascular disease

Pharmacotherapy for Chronic Stable Angina

- IIb (weak supportive evidence)
  - Low-intensity anticoagulation with warfarin in addition to aspirin B
- III (not indicated)
  - 1. Dipyridamole B
  - 2. Chelation therapy B

Ranolazine- new first line indication for the treatment of chronic angina



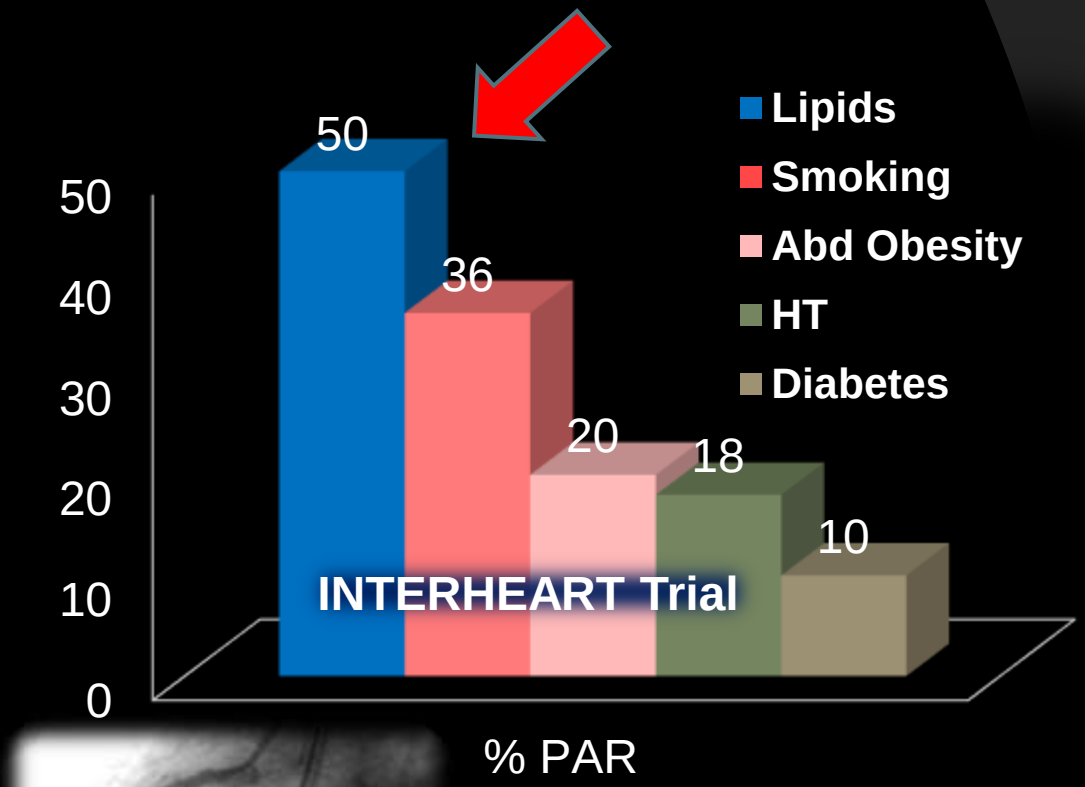
Myocardial ischemia: Sites of action of anti-ischemia medication

Lipids are still # 1 and smoking # 2

- Abnormal lipids
- Smoking
- Hypertension
- Diabetes
- Abdominal obesity

- Psychosocial
- Physical activity
- Alcohol
- Fruits/vegetables

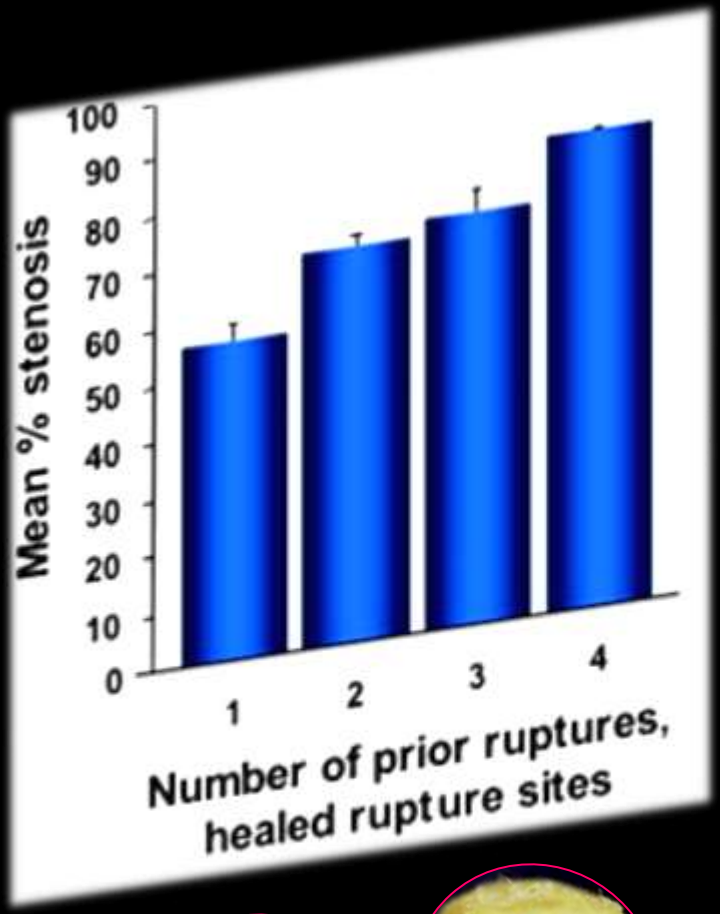
9 Modifiable Factors Account for 90% of First MI

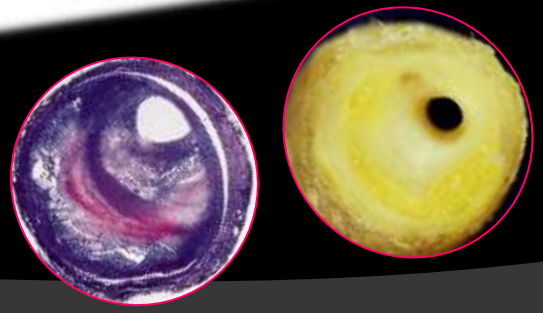


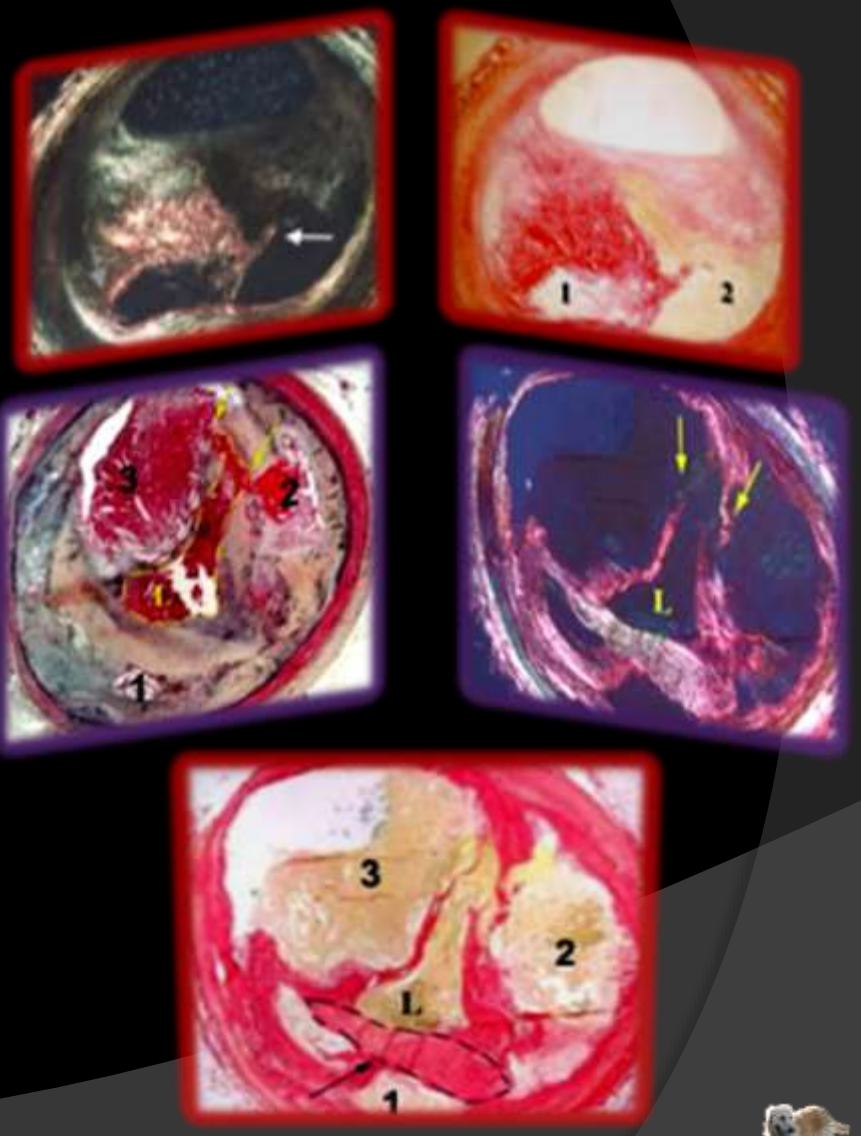
Yusuf S et al. *Lancet*. 2004;364:937-52

PAR = population attributable risk, adjusted for all risk factors

Tight blocks have usually more healed plaque ruptures



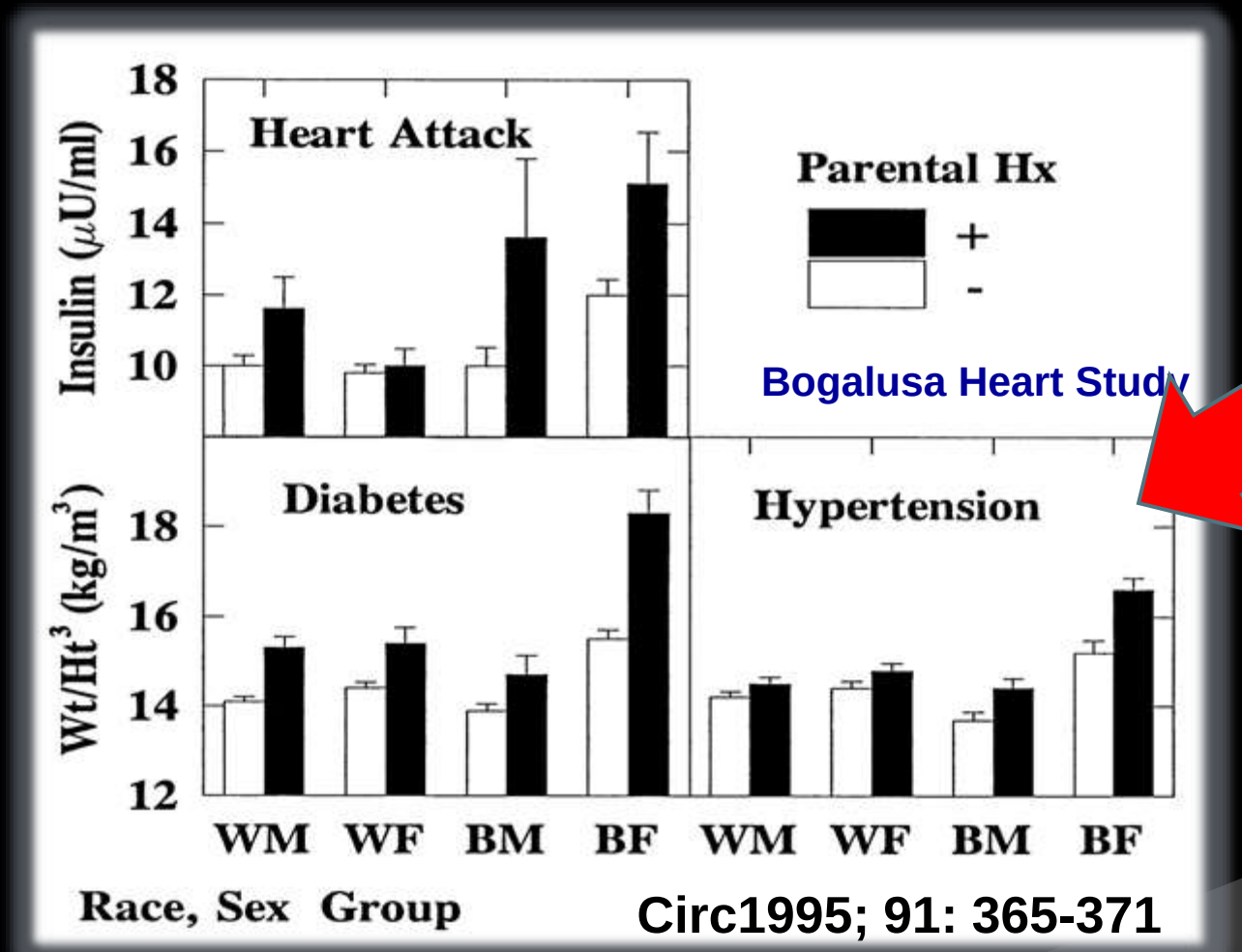




Circ 2001;103:9364

Environmental	Stop smoking-1B Physical activity-1B Weight control-1B Chelation therapy-3C Influenza vaccination-1B
Vascular / Tissue	Blood pressure-1B RAAS blockade-1A Aldosterone blockade-1A/B
Metabolics	Lipids-1B Triglycerides-1B Diabetes-1B Antiplatelets-1A/B

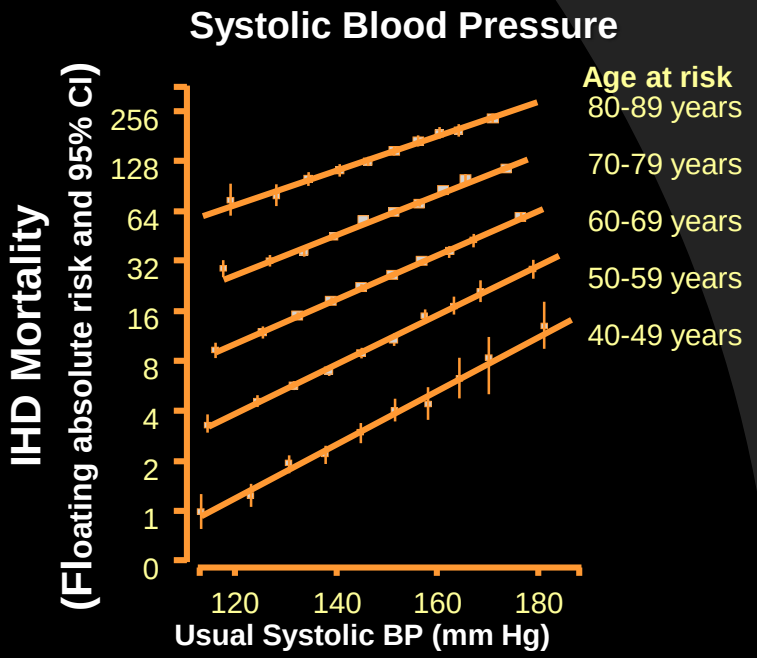
Importance of genetic factors when picking your parents

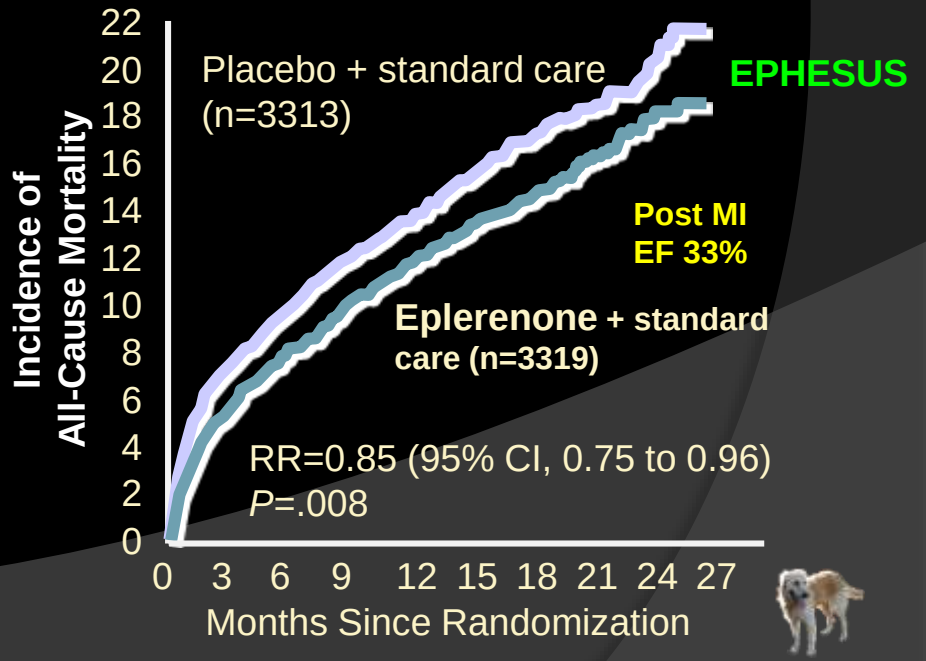


Selected risk factor variables in offspring ages 18 to 31 years by parental history of disease, race, and sex

Vascular / Tissue

- Blood pressure-1B
  - Lifestyle (low salt, weight control and exercise
  - Moderate etoh & vegetables
  - BP <140 / 90 by JNC VII-HCTZ
  - Diabetes & CRDx 130 / 80
  - HT with CAD—BB &/or ACEI
- RAAS blockade-1A
  - EF<40 ACEI
  - Mild/moderate risk & normal EF-2B
- Aldosterone blockade-1A/B
  - After MI (normal kid function & K+)
  - Patients already on BB & ACEI
  - EF<40 with HF or diabetes



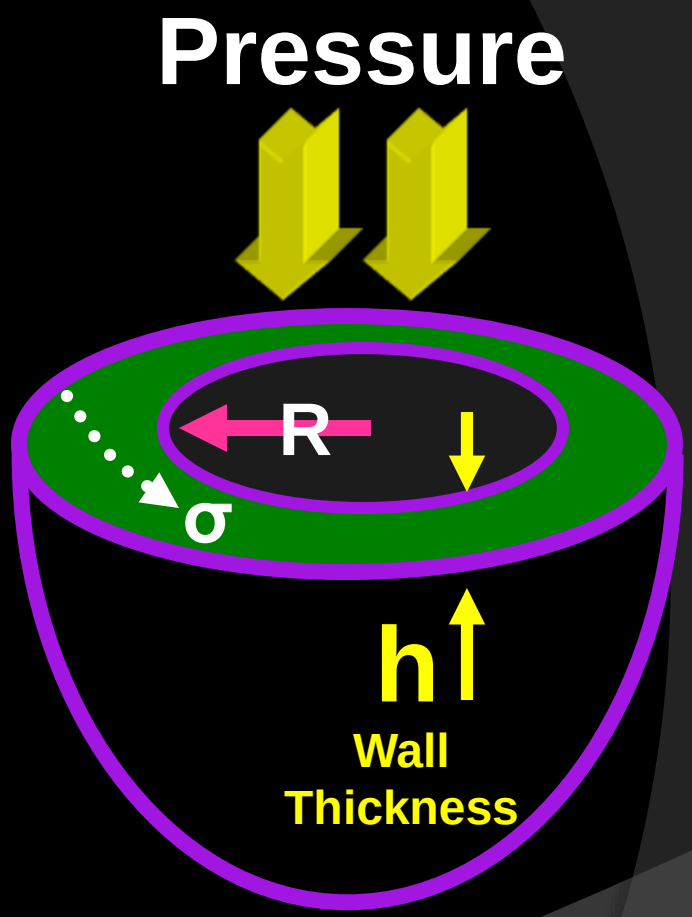


N Engl J Med. 2003;348:1309-1321 EPHESUS

N Engl J Med. 1999;341:709-717 RALES

Myocardial Oxygen Consumption Factors MVO_2

- Heart Rate
  - Most important
- Myocardial wall tension
  - Pressure
  - Volume
  - Thickness
- Contractility



σ=Wall Tension
P=Pressure
R=Radius
h=Wall thickness

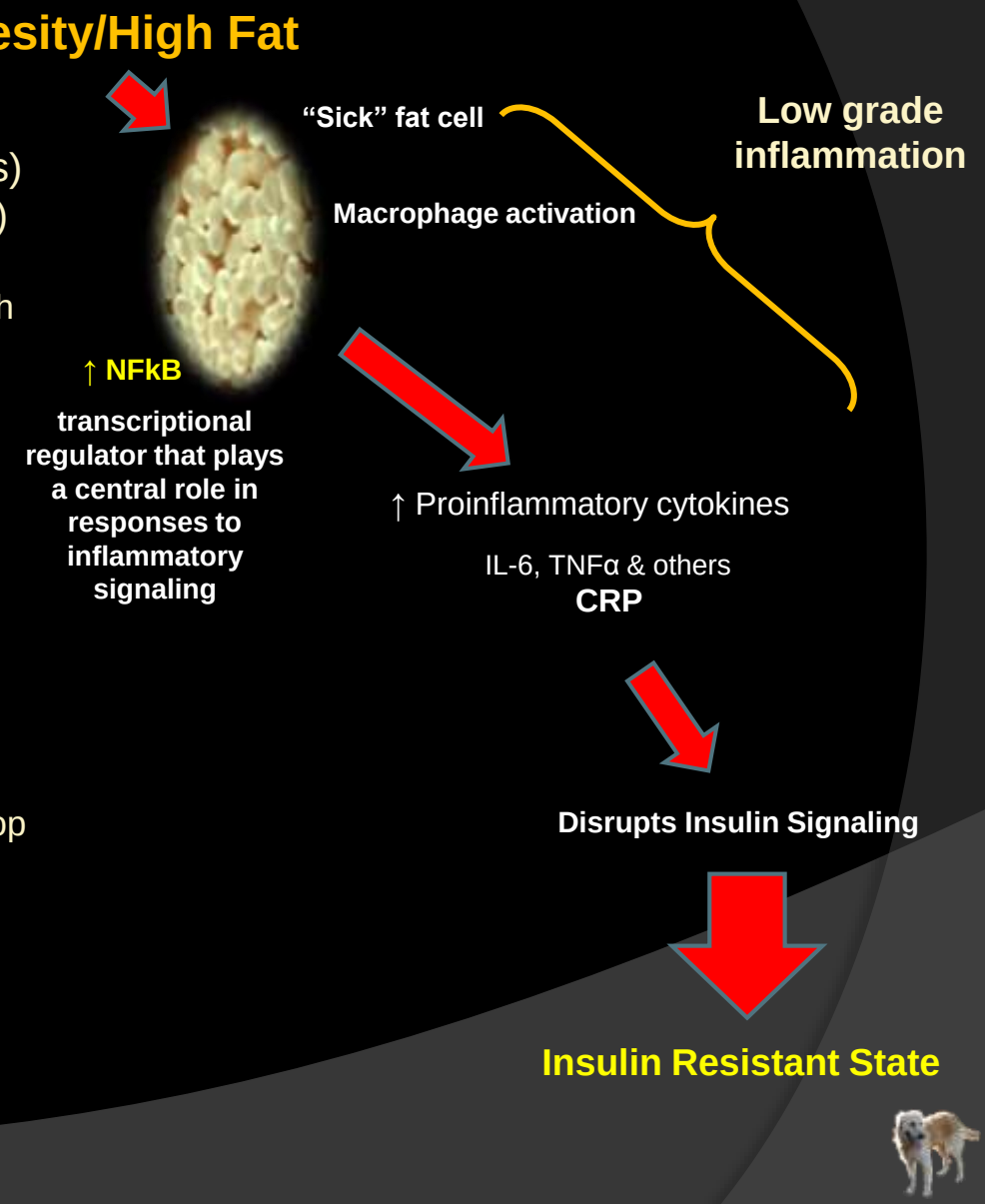
$\sigma = P \times R/2h$

LaPlace's Law

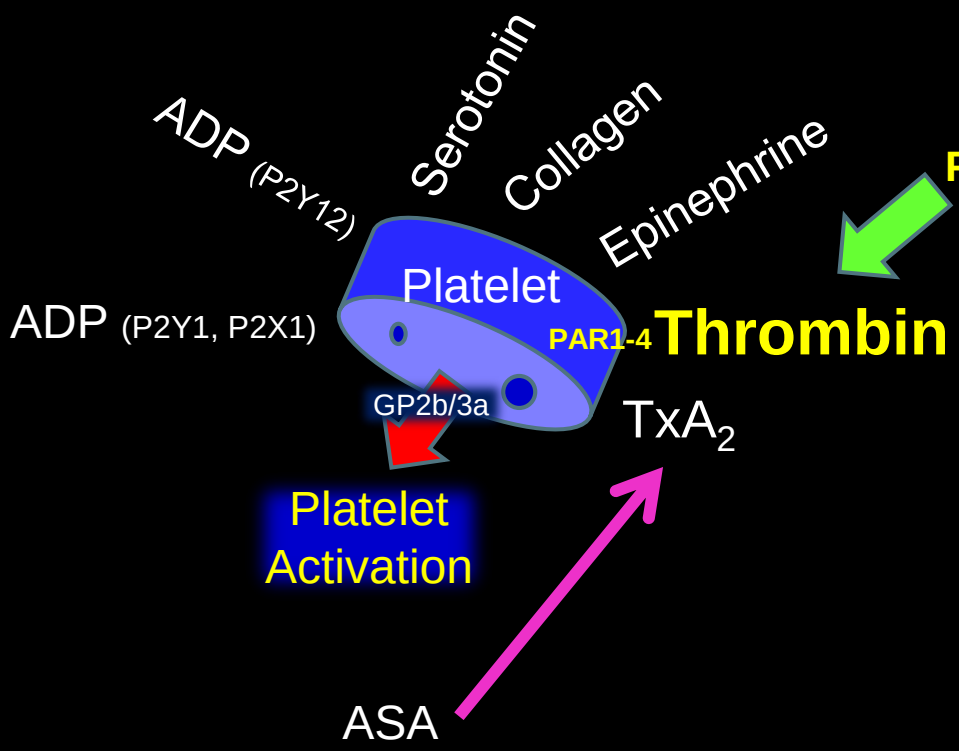
Environmental	Stop smoking-1B Physical activity-1B Weight control-1B Chelation therapy-3C Influenza vaccination-1B
Vascular / Tissue	Blood pressure-1B RAAS blockade-1A Aldosterone blockade-1A/B
Metabolics	Lipids-1B Triglycerides-1B Diabetes-1B Antiplatelets-1A/B

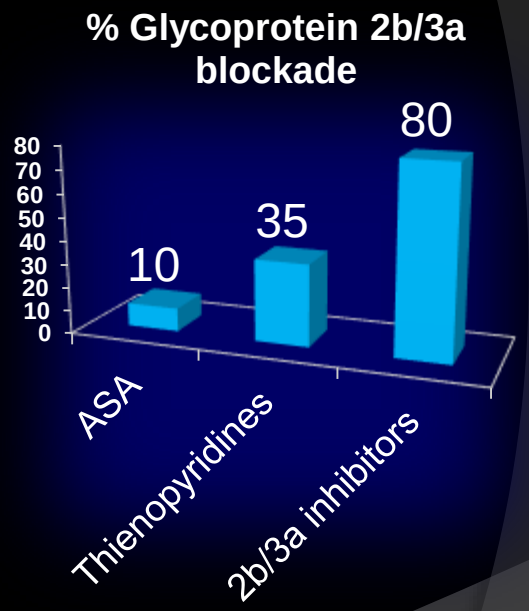
Metabolics & Hematology

- Lipids-1B
  - Fasting lipid profile
  - Lifestyle and high fiber
  - Omega 3 pills/fish (high triglycerides)
  - LDL <100 / 70 (high dose statins ok)
  - Targets
    - 30-40% LDL reduction (moderate-high risk)
    - Higher risk 70-100 LDL
    - Very high risk <70 mg/dl -2A
    - Small dense LDL --KILL
- Triglycerides-1B
  - Triglycerides (200-499)
    - Non HDL <130
    - Niacin / fibrates
  - Triglycerides >500 (pancreatitis)
    - Fibrate / niacin before statin
    - Target <130 trig
    - LDL high -combination to get 50% drop
- Diabetes-1B
  - HbA1c <7.0/6.5%
- Antiplatelets-1A/B
  - 75-162 mg ASA for life
  - Coumadin increases bleeding risk
  - Genetic testing for both agents



Aspirin reduced the risk of first myocardial infarction by 44% (p<0.00001) Physicians Health Study





Blocks platelet activation-(8 to 10 days)
Prevents conversion of arachidonic acid to prostaglandin H_2

Thromboxane A_2

Platelets are unable to generate (no nucleus) new cycloxygenase enzyme
Endothelial cells also blocked but recovery quickly cycloxygenase

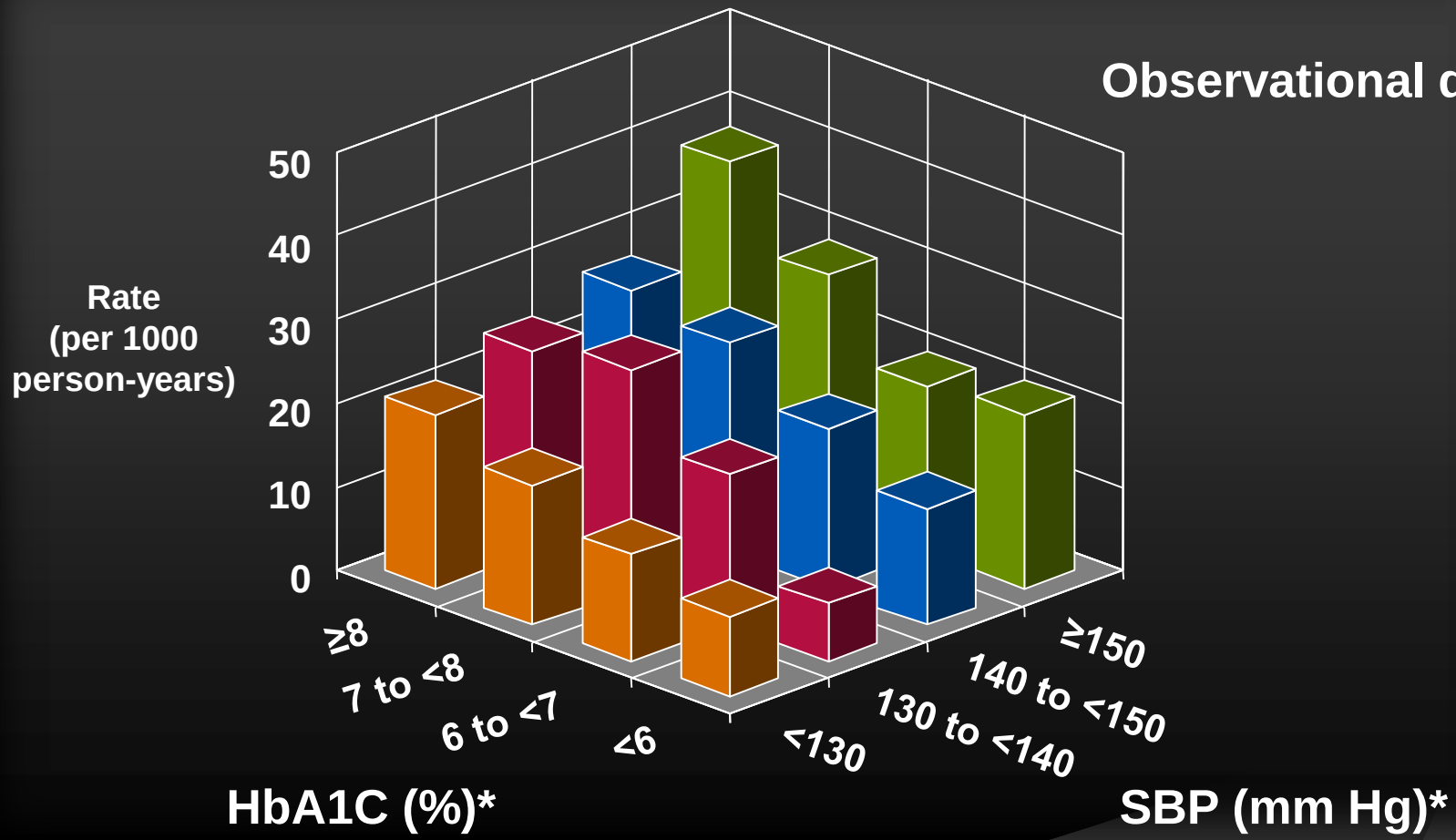
Chilton et al Clinical diabetology March 2011
Mehta et al JACC 2003;41:79s
N Engl J Med. *1989 Jul 20*;321(3):183-5

UKPDS 75: Elevated glucose and BP increase

MI risk

N = 4320 with newly diagnosed diabetes

Observational data



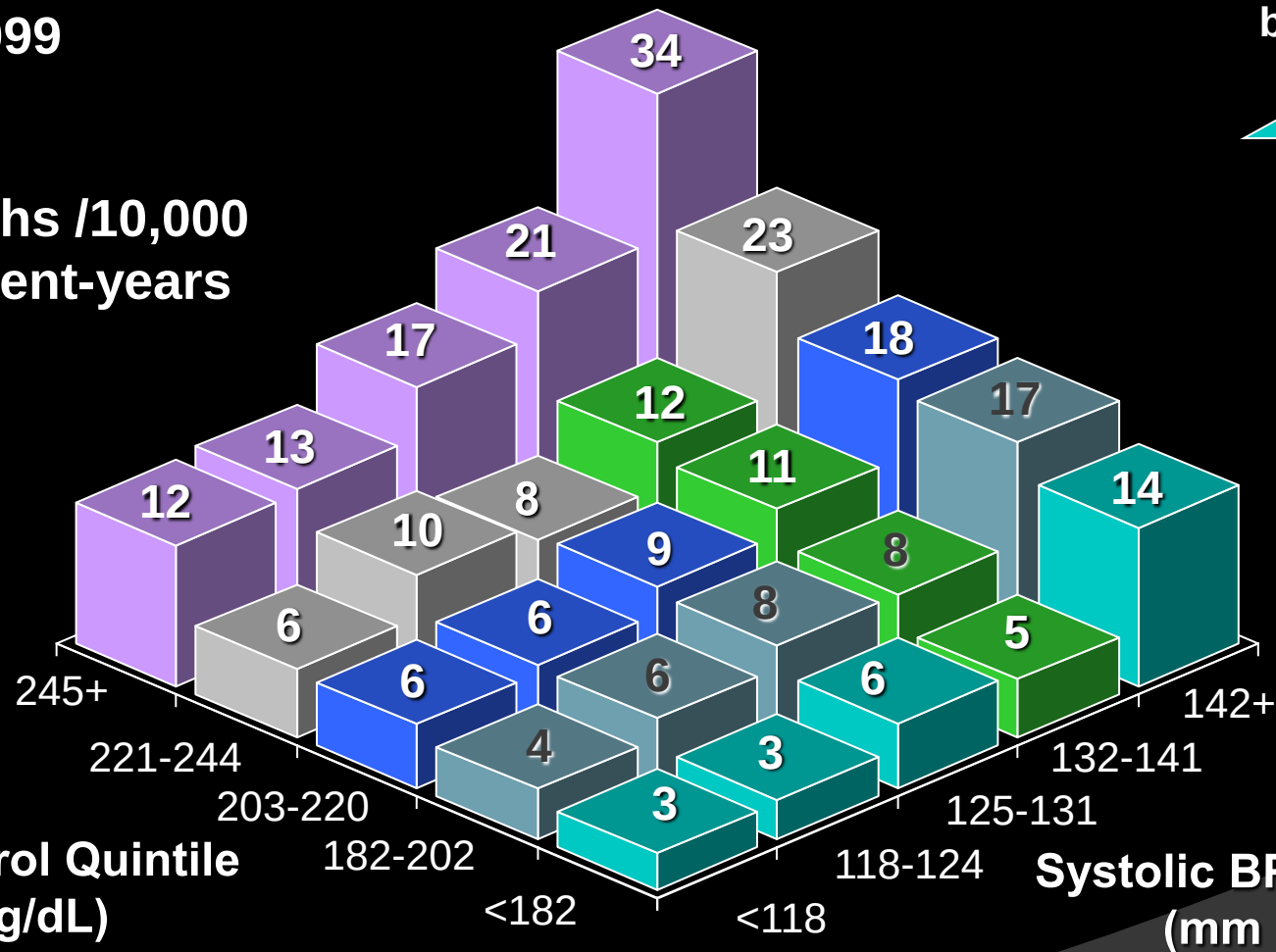
*Updated mean.

Stratton IM et al. *Diabetologia.* 2006;49:1761-9.

Additive Effect of Cholesterol and Systolic BP on Risk of CHD Death

N=316,099

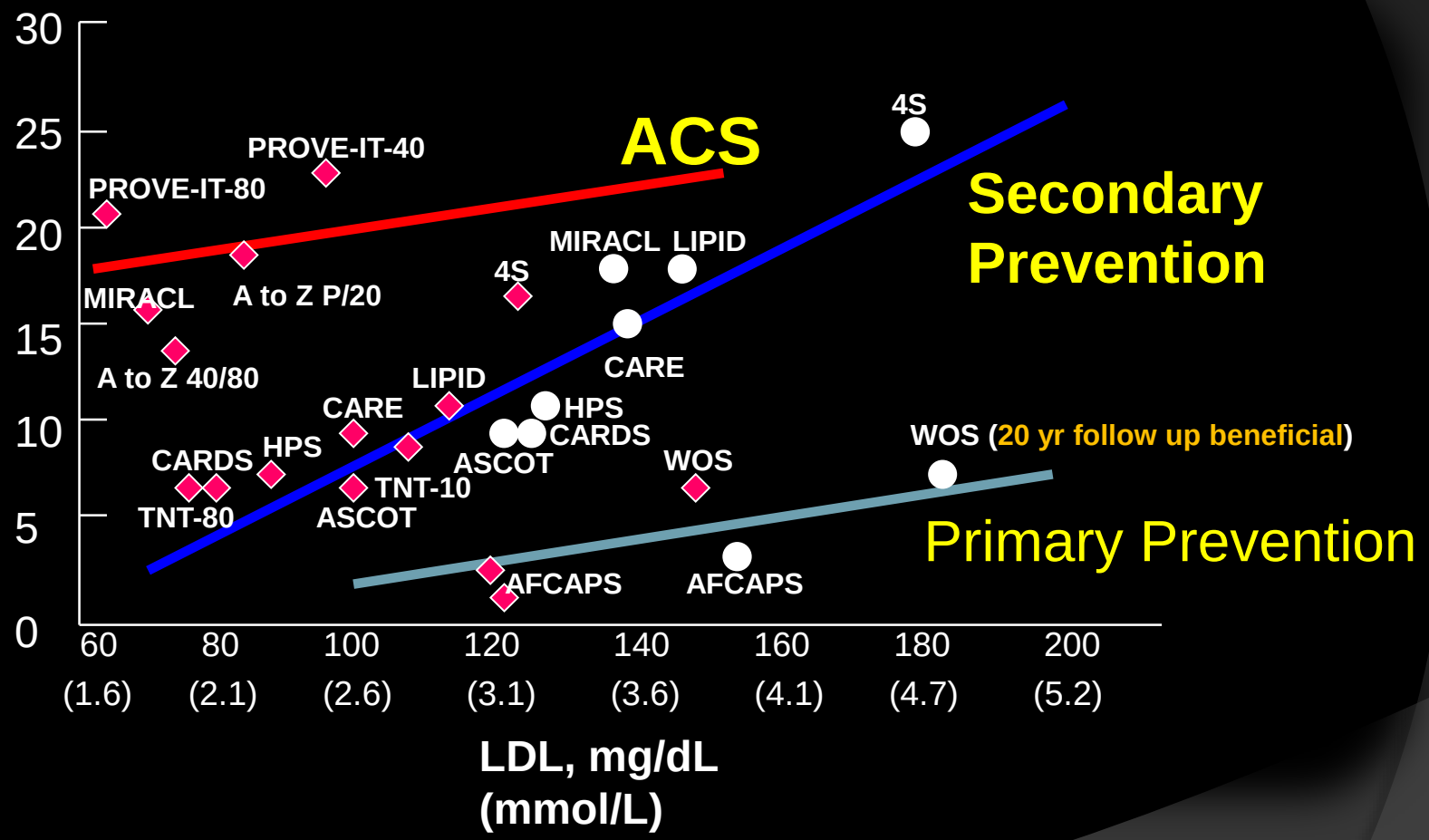
Deaths /10,000 Patient-years



↑ CRP amplifies both CV Risk

Neaton et al. *Arch Intern Med.* 1992;152:56-64

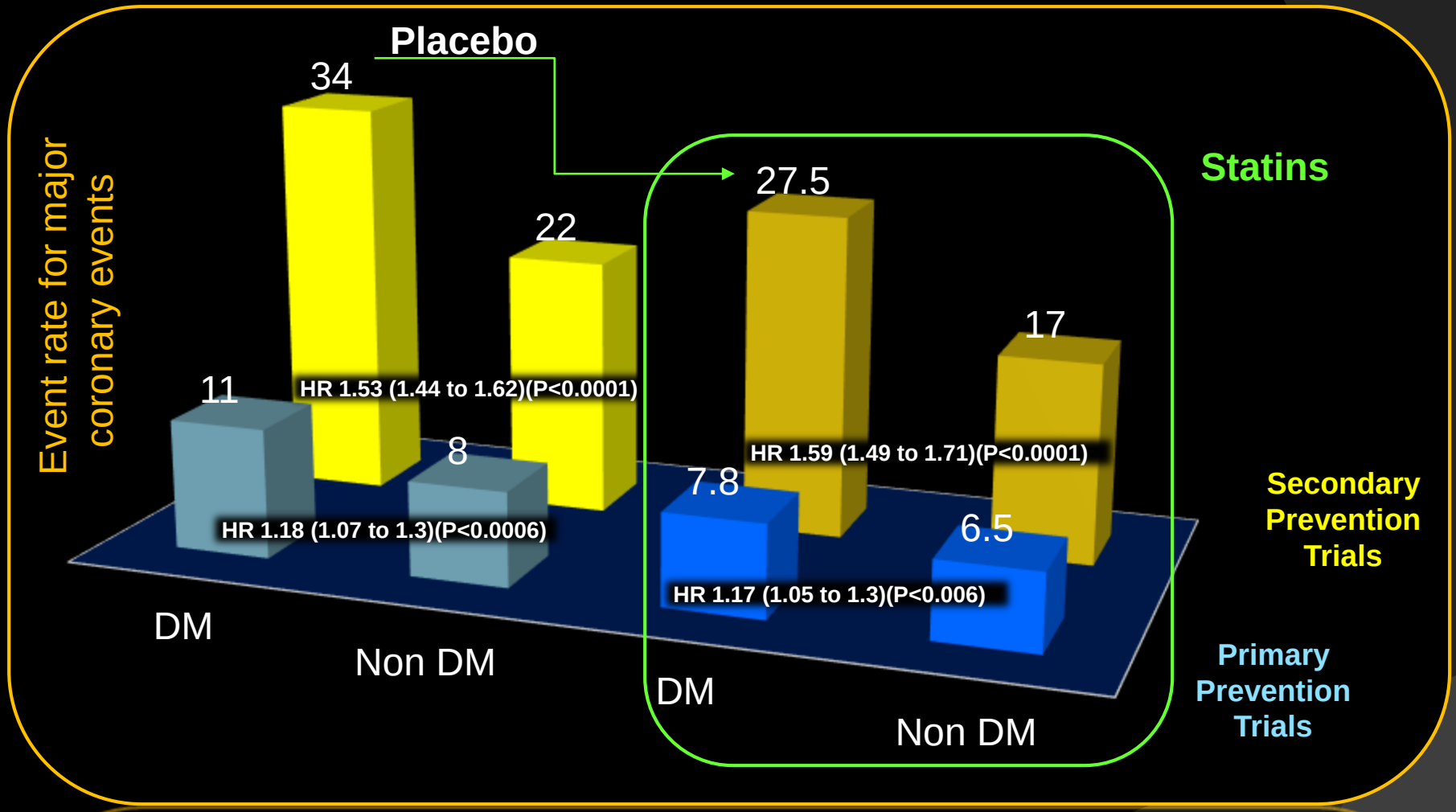
Lowering LDL with statins reduces CV events



Patients with CHD events (%)

…….Statins work

Statins Reduce Major Coronary Events



4 to 5.1 years Cochrane
Meta-analysis of randomized controlled trials

BMJ, doi:10.1136/bmj.38793.468449.AE
published 3 April 2006

>2% per yr-Primary Prevention-Cochrine 2011

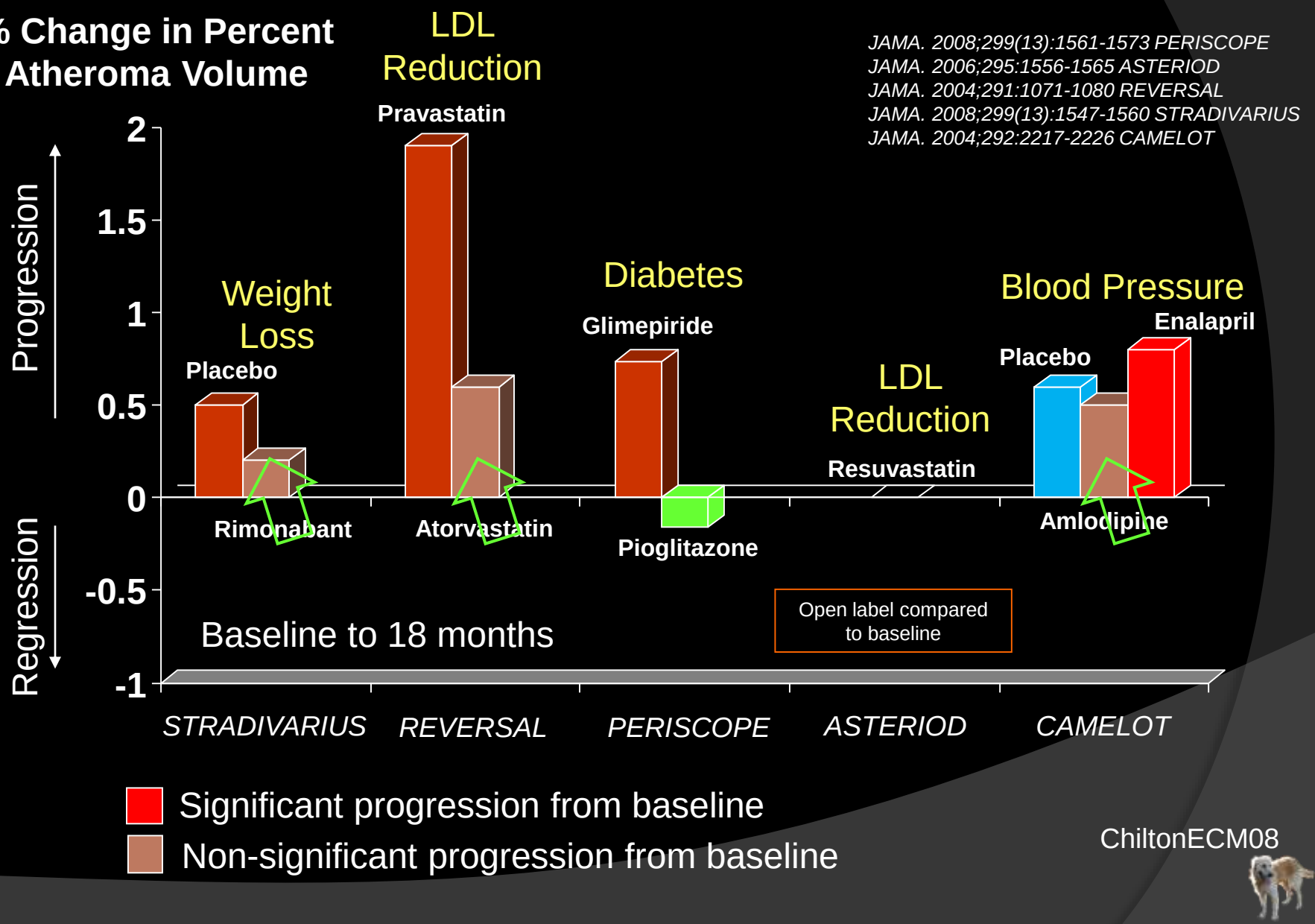
Limitations of Statin Monotherapy on CHD Events

Trial	Drug	N	Events,* n		Risk Reduction, %†	Events not Avoided, %
			Control Group	Statin Group		
4S WOSCOPS CARE AFCAPS LIPID TNT	Simvastatin Pravastatin Pravastatin Lovastatin Pravastatin Atorvastatin	>30,817	2,042	1,490	26	74
HPS	Simvastatin	20,586	1,212	898	26	74
PROSPER	Pravastatin	5,804	356	292	19	81
ASCOT-LLA	Atorvastatin	10,305	154	100	36	64
Total		**67,462**	**3,764**	**2,780**	**27**	**73**

* Nonfatal MI and CHD death; AFCAPS also included unstable angina
† Weighted average

Adapted from Bays H. *Expert Rev Cardiovasc Ther* 2004;2:89-105.

IVUS and Cardiometabolic Drug Trials

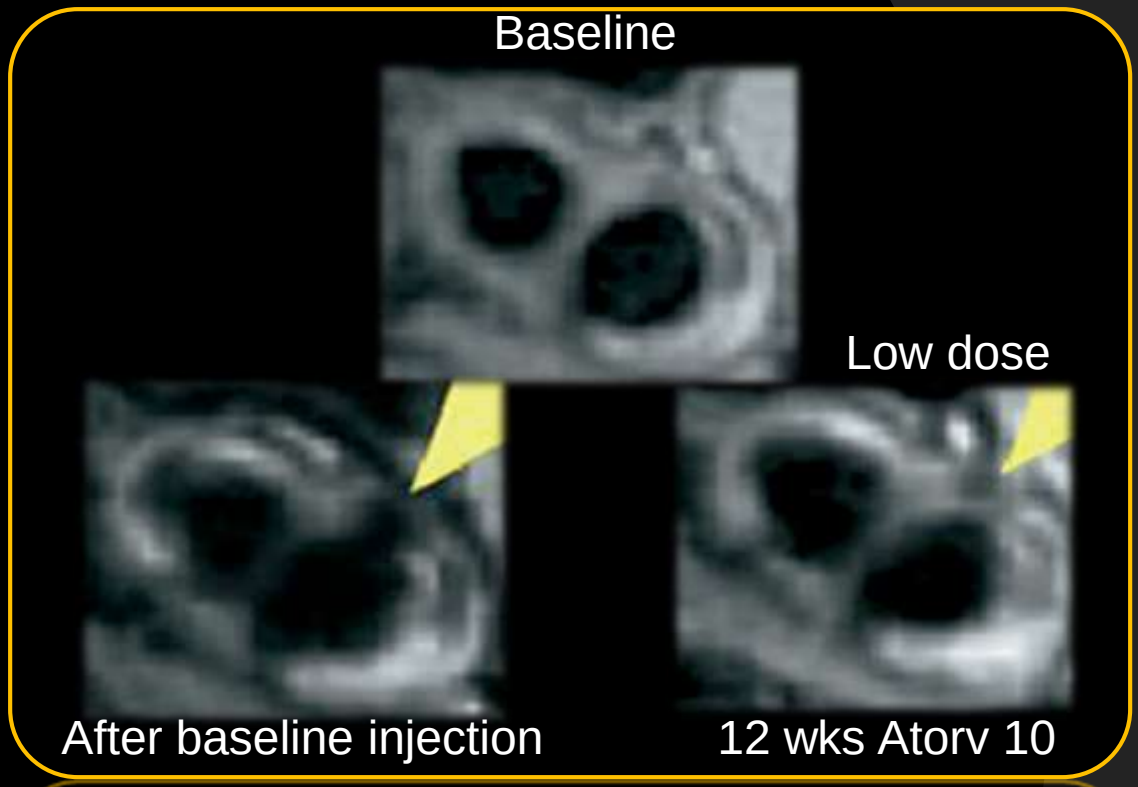


JAMA. 2008;299(13):1561-1573 PERISCOPE
JAMA. 2006;295:1556-1565 ASTERIOD
JAMA. 2004;291:1071-1080 REVERSAL
JAMA. 2008;299(13):1547-1560 STRADIVARIUS
JAMA. 2004;292:2217-2226 CAMELOT

ChiltonECM08

ATHEROMA Trial

- The ATHEROMA (Atorvastatin Therapy: Effects on Reduction of Macrophage Activity) Study
- Forty-seven patients with carotid stenosis >40% on duplex ultrasonography and who demonstrated intraplaque accumulation of **IRON oxide** USPIO on MRI at baseline
- Double blind
  - A-80 mg
  - A-10 mg
- 12 week follow up
- Change from baseline in signal intensity on USPIO-enhanced MRI in carotid plaque at 6 and 12 weeks



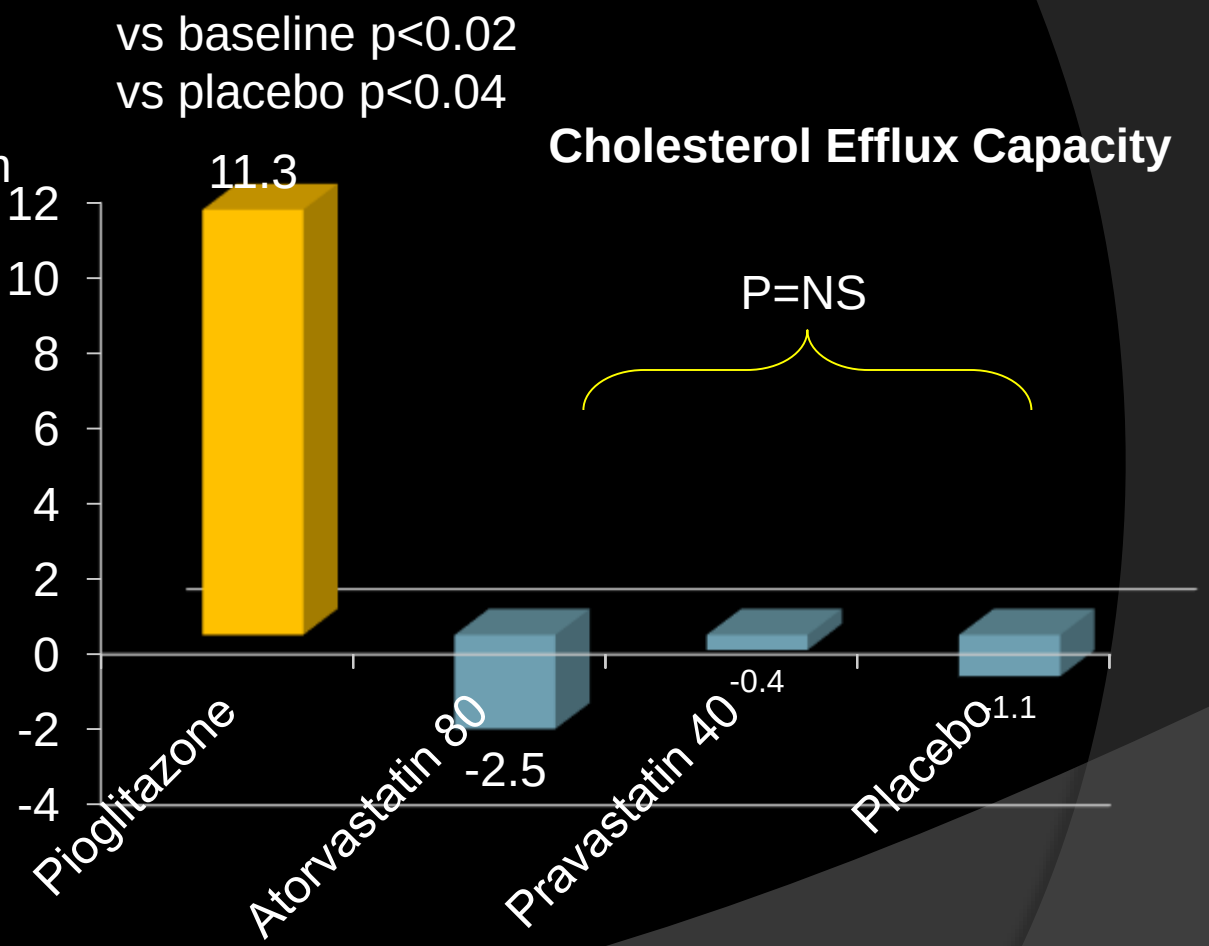
Iron is located in macrophages (black)

Ultrasmall superparamagnetic iron oxide (USPIO)-enhanced carotid magnetic resonance imaging (MRI)

J Am Coll Cardiol 2009;53:2039–50

Metabolic Syndrome patients with low HDL showed enhanced efflux capacity with pioglitazone…not with statins

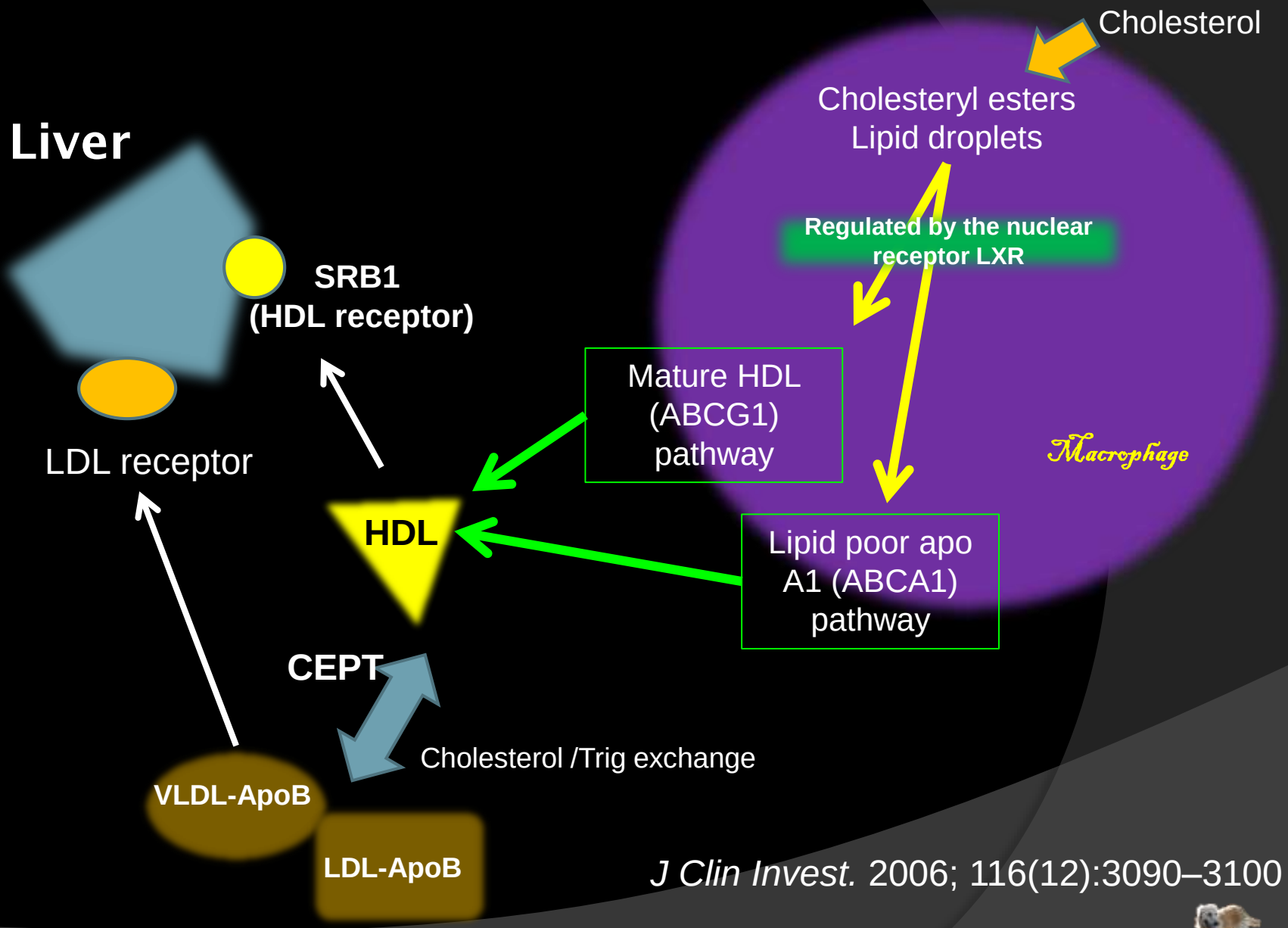
- Hypothesis
  - Capacity of HDL to accept cholesterol from macrophages…predict or of atherosclerosis
- N=203 healthy
  - CIMT
- N=442 CAD cath proven
- N=351 w/o cath
- Methods
  - Incubation of macrophages with apo B deleted serum from patients



Khera et al N Engl J Med 2011;364:127-35

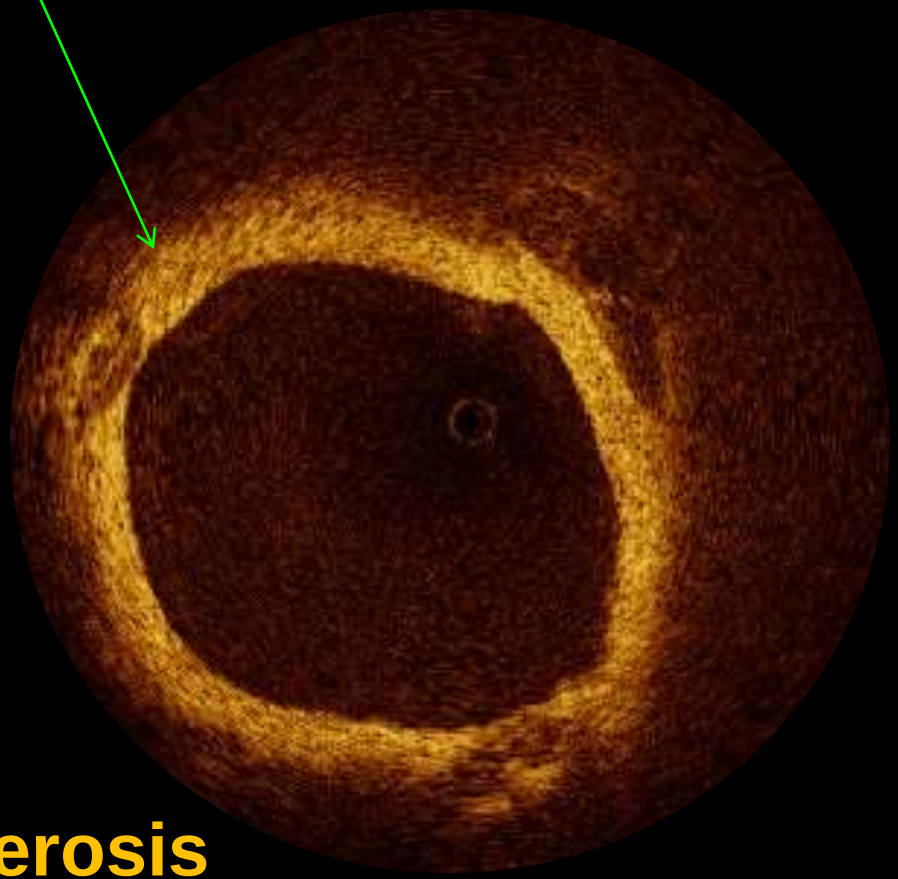
Rader NEJM Jan 2011 early HDL chol rever PIO.pdf

HDL key player in cellular cholesterol efflux



J Clin Invest. 2006; 116(12):3090–3100

Risk of soft lipid cores



Children-PDAY

↑ BMI more CAD

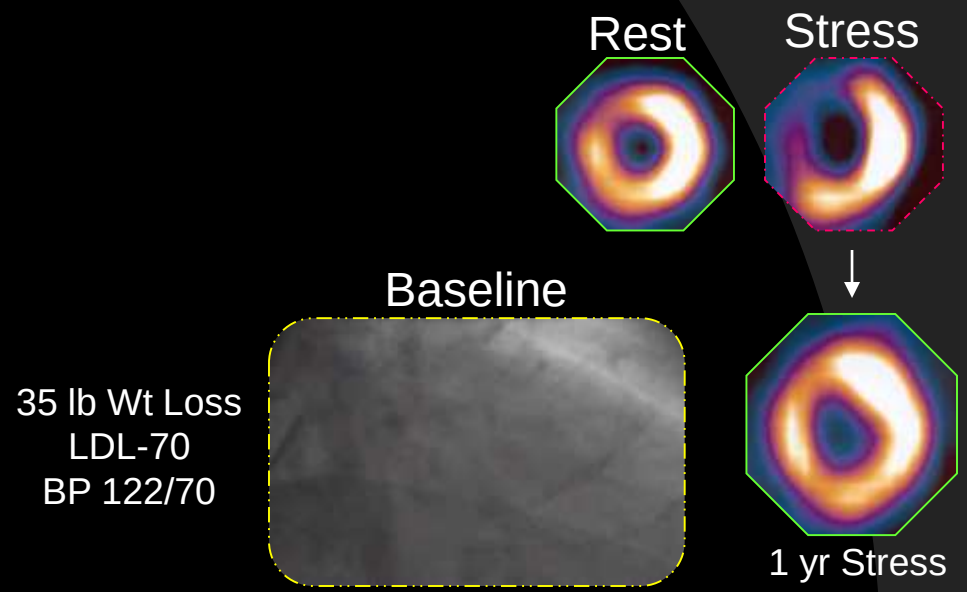
Atherosclerosis

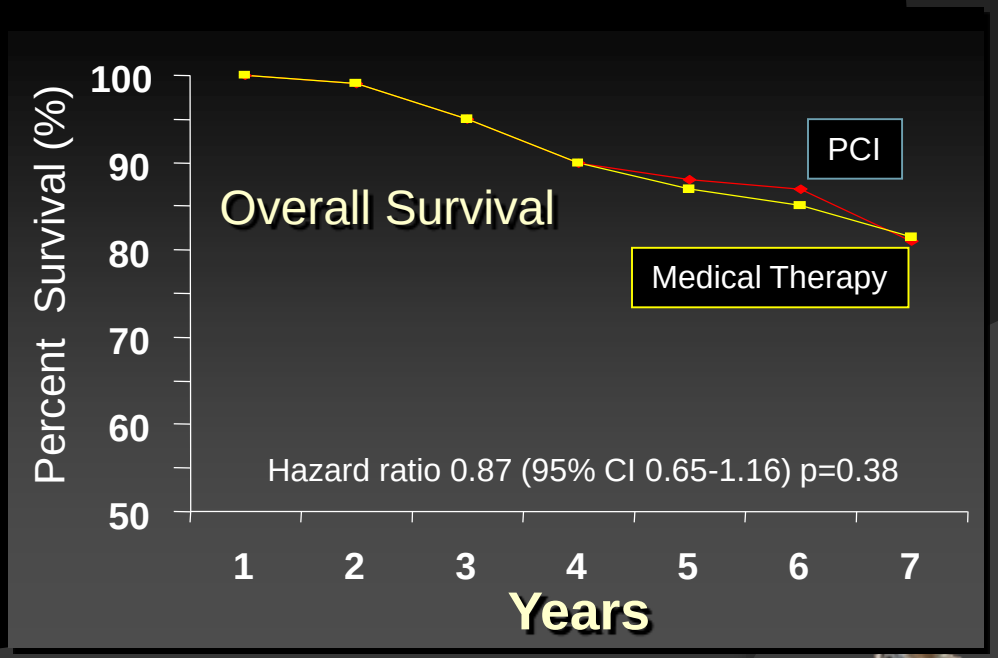
Normal “looking coronary artery”

Optimal Medical Therapy with or without PCI for Stable Coronary Disease

COURAGE

- Stable coronary artery disease with stenosis of at least 70% in at least one proximal epicardial coronary artery and objective evidence of myocardial ischemia
- N=1149 PCI + optimal medical therapy
- N=1138 optimal medical therapy alone
- F/U 2.5 to 7.0 years (median, 4.6)
- Primary outcome (NS)
  - Death from any cause and nonfatal MI
  - 19.0% - PCI group
  - 18.5% - Medical only
    - Hazard ratio1.05; 95% confidence interval [CI], 0.87 to 1.27; P = 0.62)
- **33% crossed over** to PCI
- Levels at end of study
  - LDL-70
  - HDL-42
  - TRG-125
  - BP 122/70

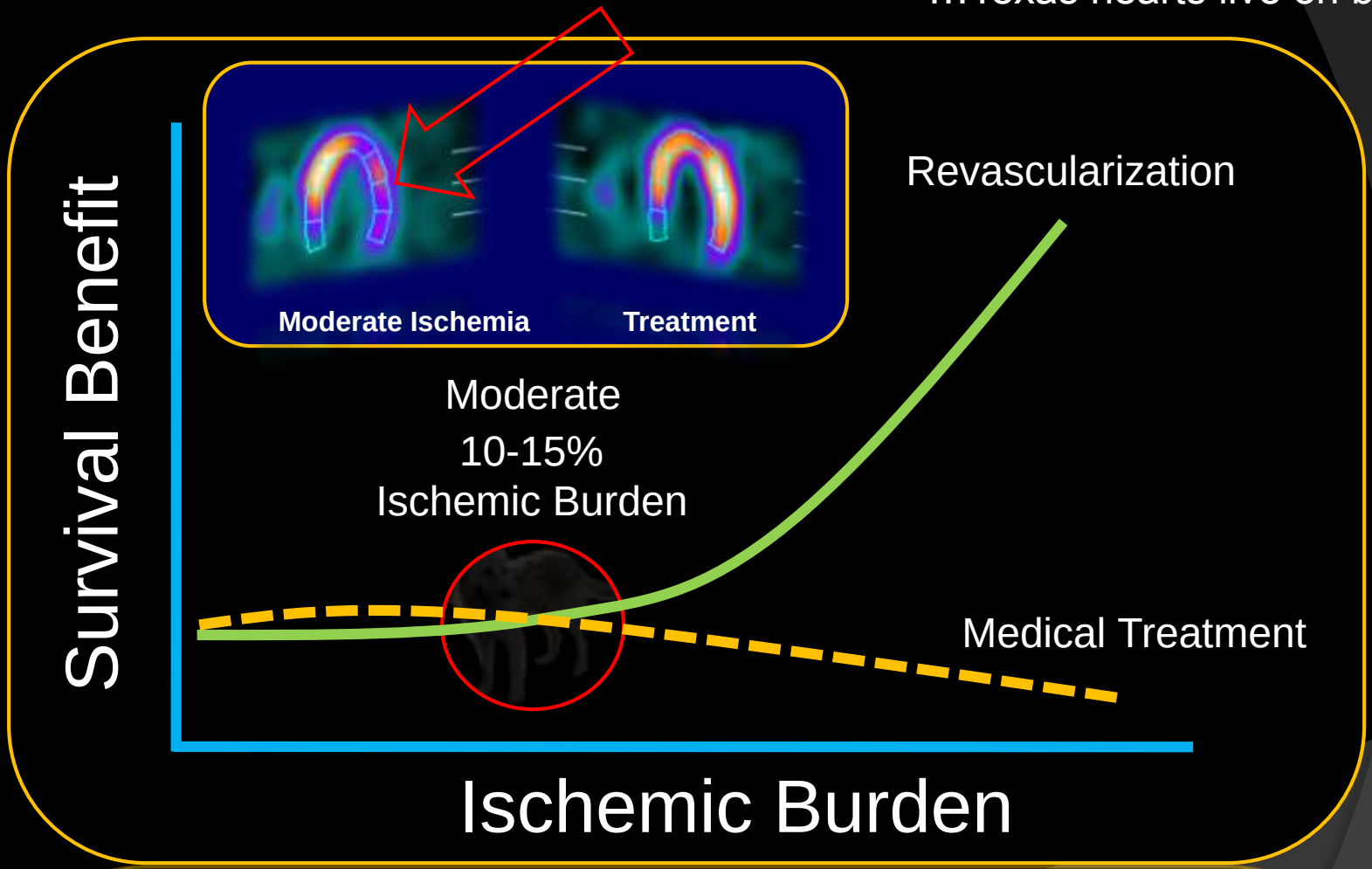




N Engl J Med March 27, 2007;356:000

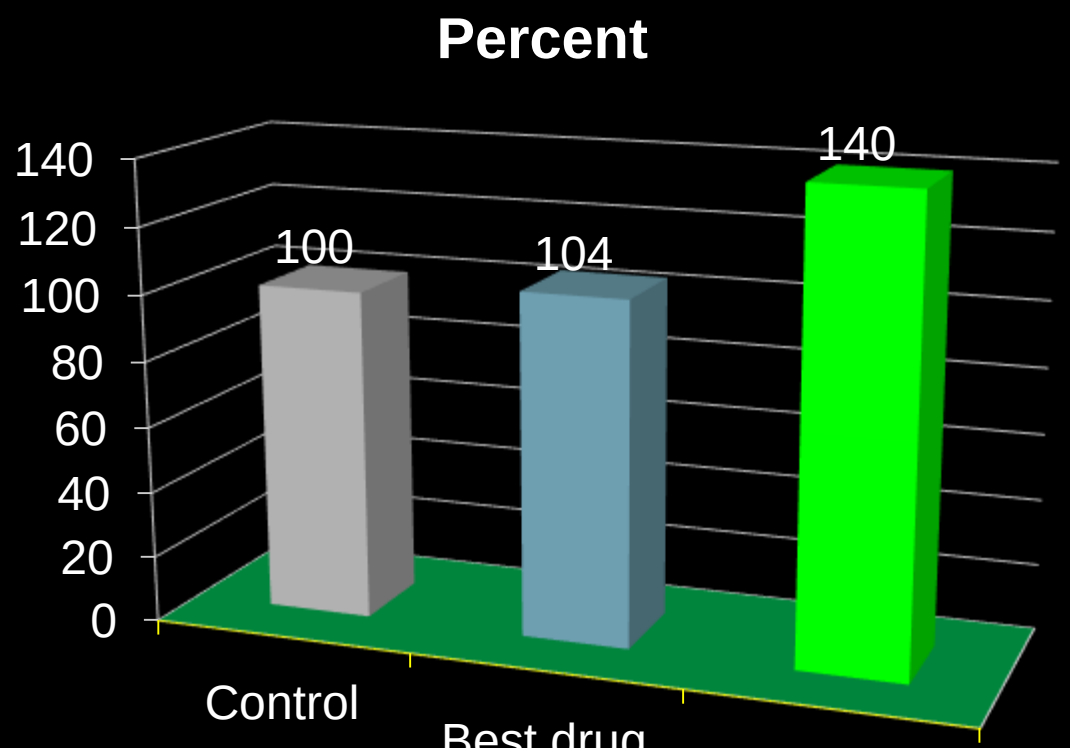
Moderate-severe ischemia needs blood

…Texas hearts live on blood



COURAGE
BARI-2D
ISCHEMIA pending

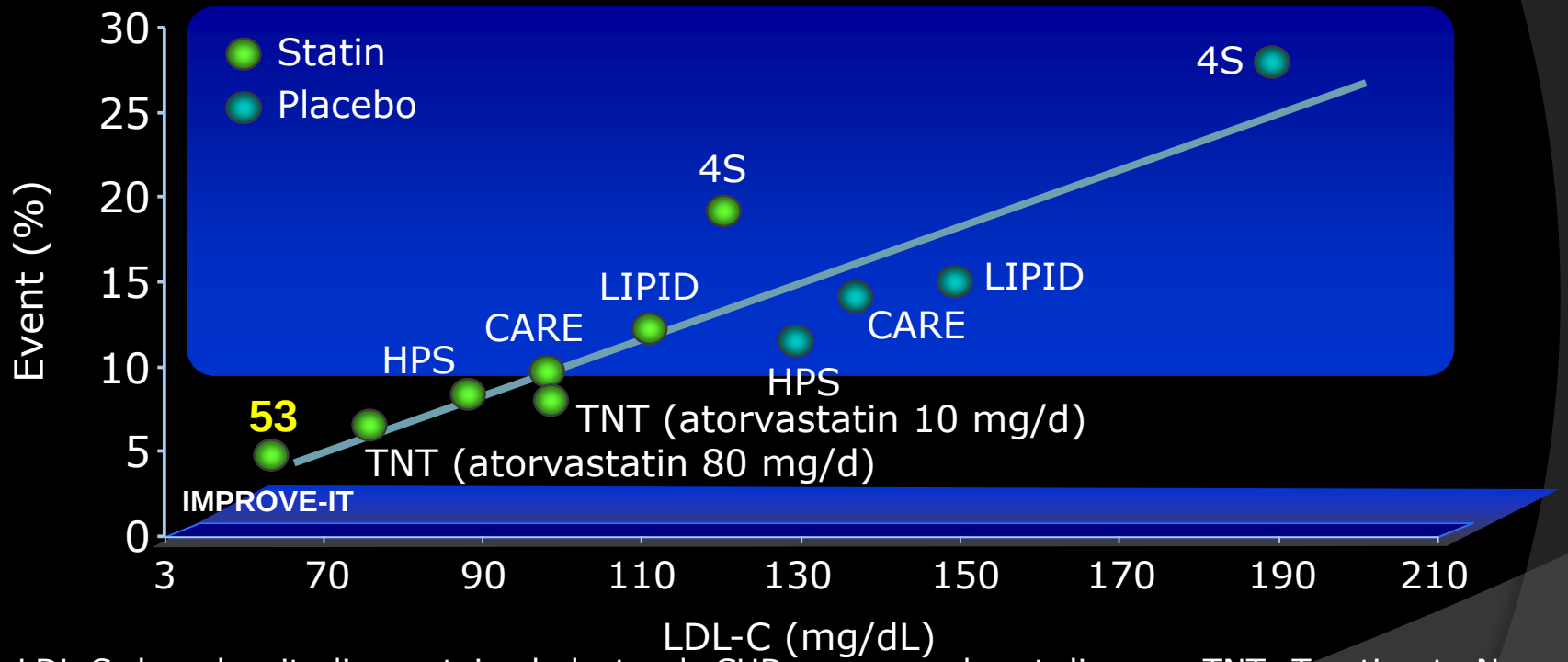
Reduction Vascular Events-2011



Environmental choices

HMG-CoA Reductase Inhibitor: Secondary Prevention

Relationship between LDL-C Levels and Event Rates in Secondary Prevention Trials of Patients with Stable CHD



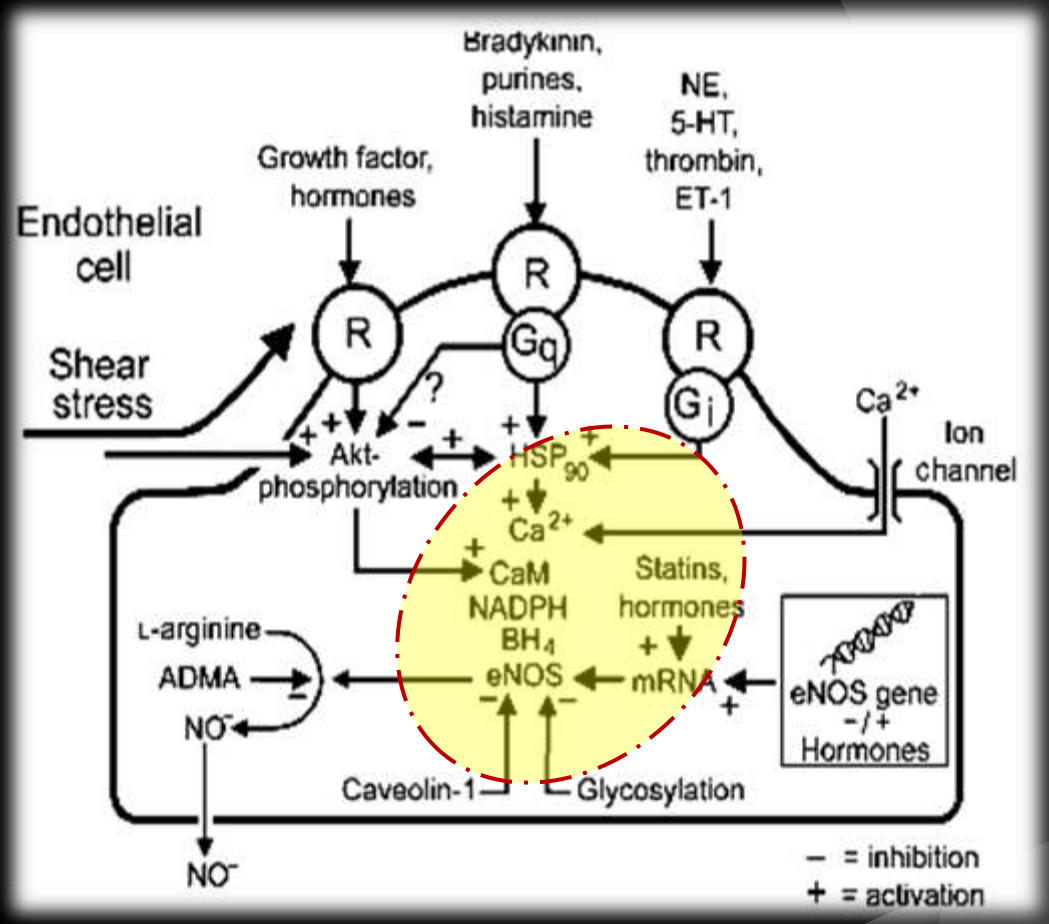
LDL-C=low-density lipoprotein cholesterol; CHD=coronary heart disease; TNT=Treating to New Targets; HPS=Heart Protection Study; CARE=Cholesterol and Recurrent Events Trial; LIPID=Long-term Intervention with Pravastatin in Ischaemic Disease; 4S=Scandinavian Simvastatin Survival Study.

LaRosa et al. *N Engl J Med* 2005;352:1425–1435.

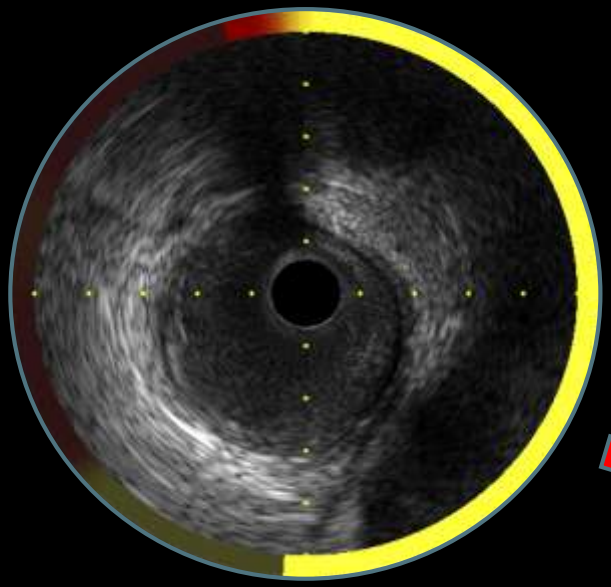
4 take home messages

- Pick your parents carefully
- Control you environment …drugs / surgery are not match for uncontrolled environment
- Vascular / tissue – blood pressure very important..wall stress
- Metabolics – nutrients of vascular life…needs clean fuel for healthy endothelium

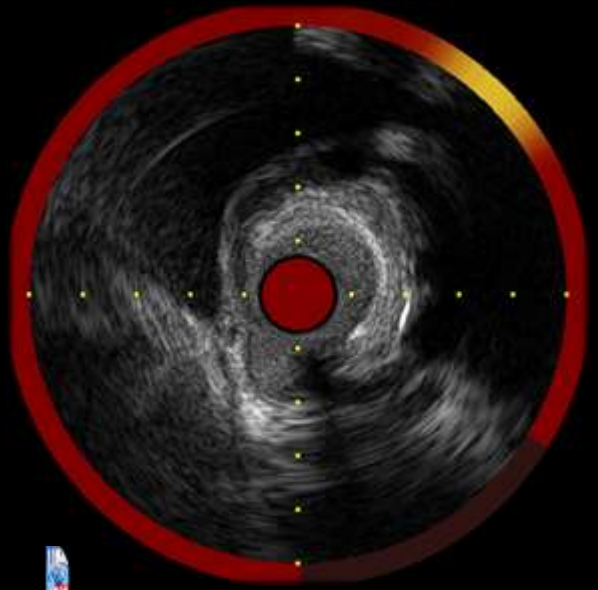
Nitric oxide is life

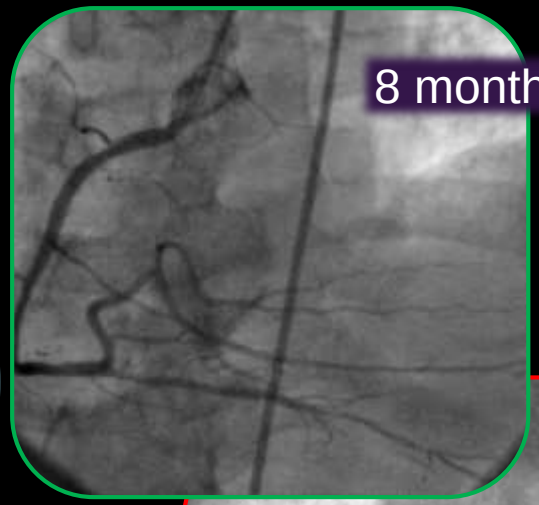


Acta Physiol 2009, 196, 193–222

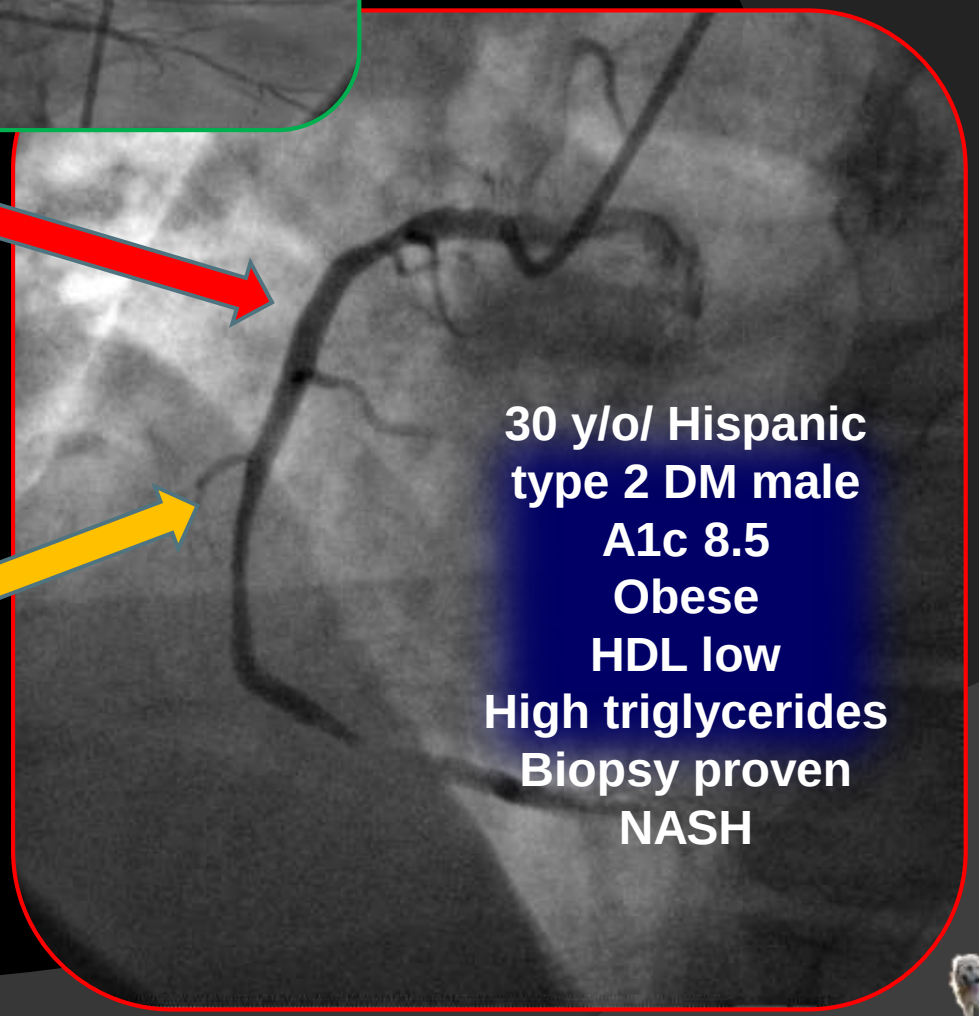


NIRS-IVUS





8 months before



30 y/o/ Hispanic
type 2 DM male
A1c 8.5
Obese
HDL low
High triglycerides
Biopsy proven
NASH

Thank you