CAN WE ELIMINATE HEART ATTACKS IN OUR LIFETIME?

PAVIA, August 30, 2022

TARGETING PLAQUES, TREATING PATIENTS, OR TWEAKING THE POPULATION?

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NO DISCLOSURES

DOGMA (noun) [ˈdȯg-mə]
- Statement of ideas accepted uncritically.
- A doctrine authoritatively affirmed.
- Doctrines, tenets, or beliefs, collectively.
- Rules that cannot be questioned.

Managing CCS:

CAD is Bad

[It causes hard events]

Progressive Atheroma

↓

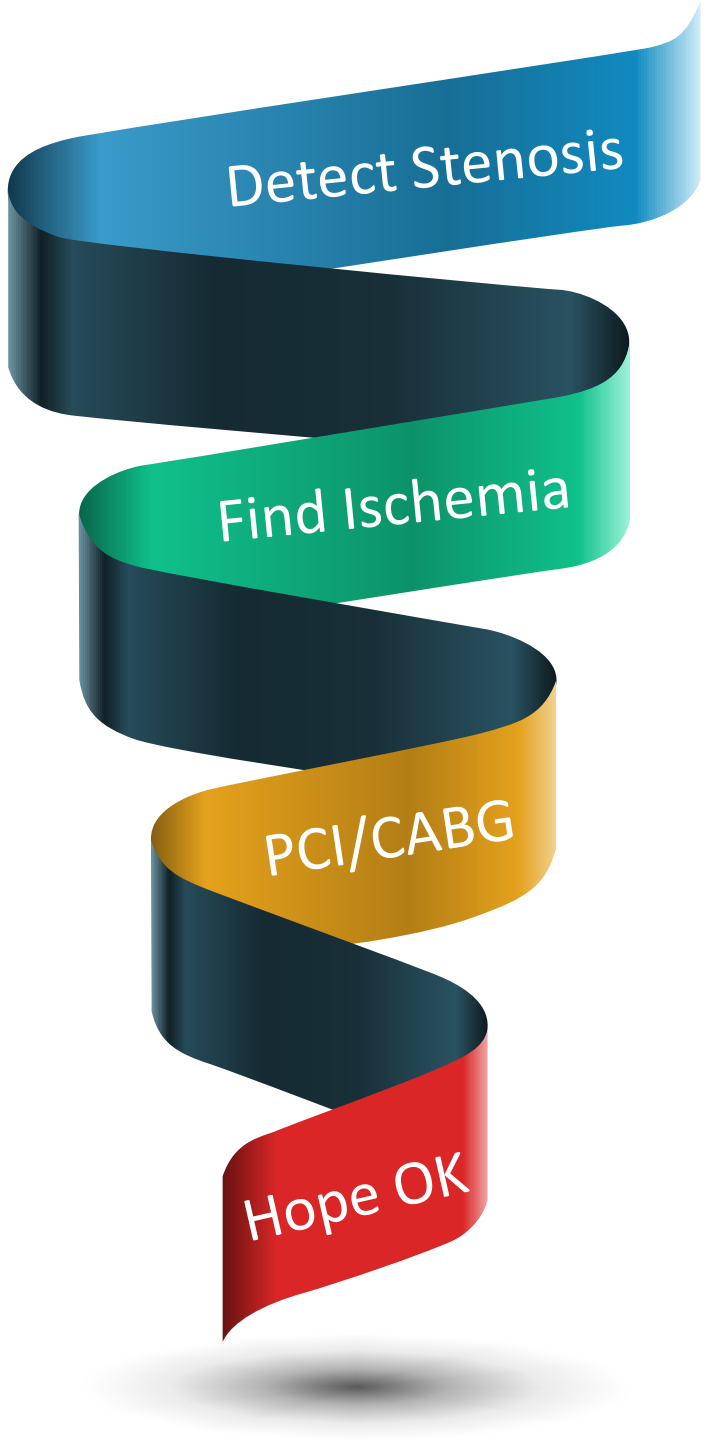
Significant Stenosis

↓

Reduces Flow [so, Ischemia]

↓

Causes Events



Find Coronary Stenosis

Since it Causes Ischemia

Find Ischemia

Since it Causes Events

Treat Stenosis

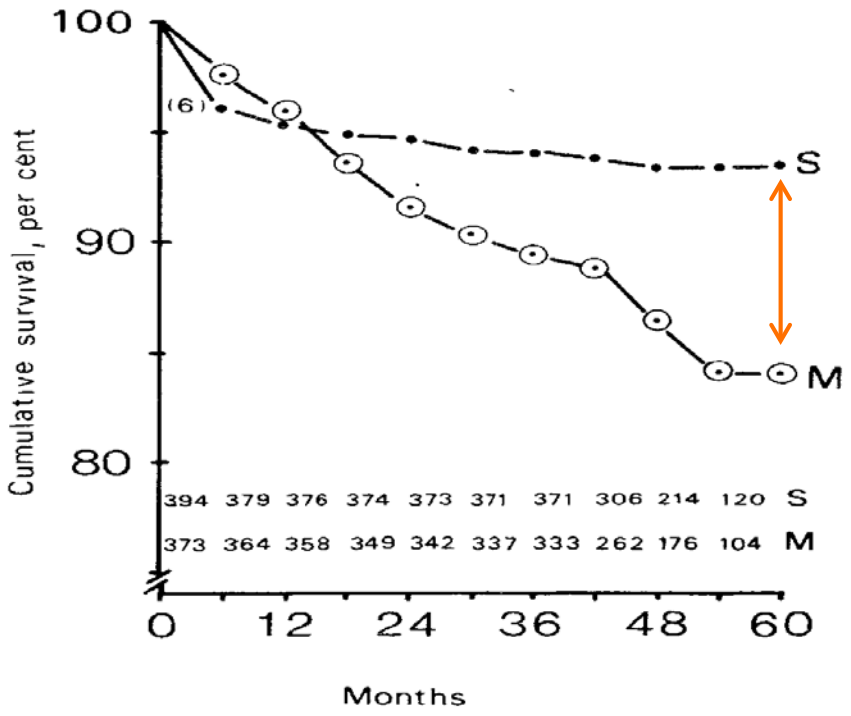
This Will Reduce Ischemia

Improve Outcomes

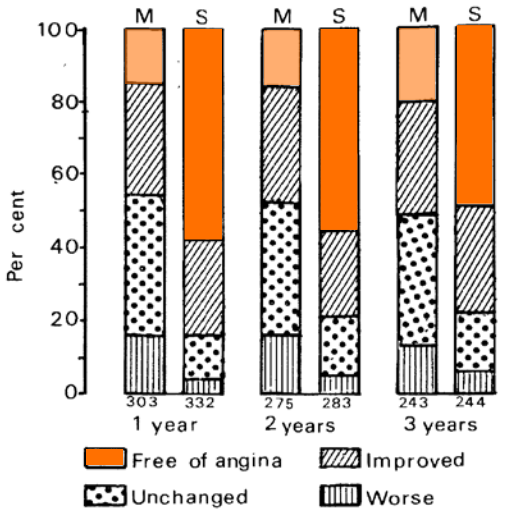
Fixing Stenosis & Reducing Ischemia will automatically mean less MI & Deaths

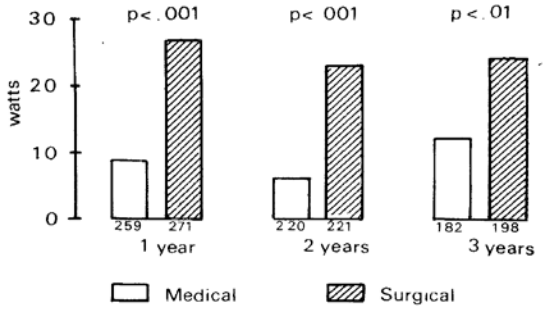
PROSPECTIVE RANDOMISED STUDY OF CABG IN STABLE ANGINA PECTORIS

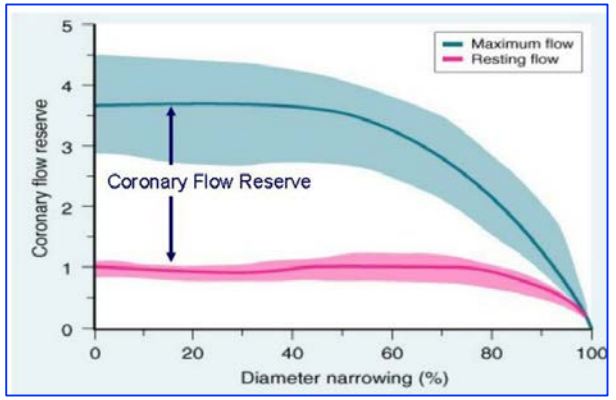
The European Coronary Surgery Study Group



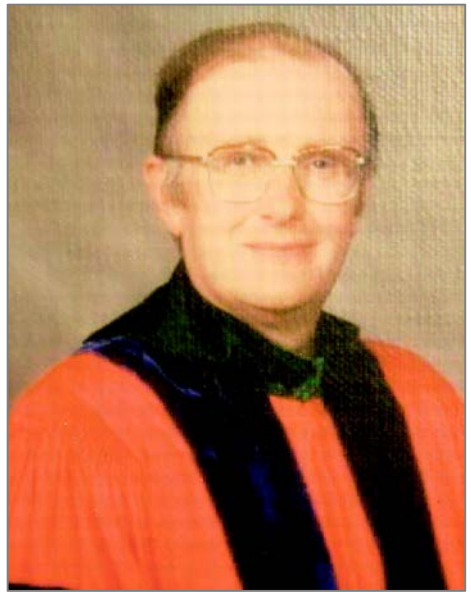
Lancet, 6 Sep.1980







Were the lesions
different in those times?
High-Risk; ready to pop?
And we did not have statins!



Circulation
Volume 94, Issue 8, 15 October 1996; Pages 2013-2020
https://doi.org/10.1161/01.CIR.94.8.2013

American Heart Association.

ARTICLE

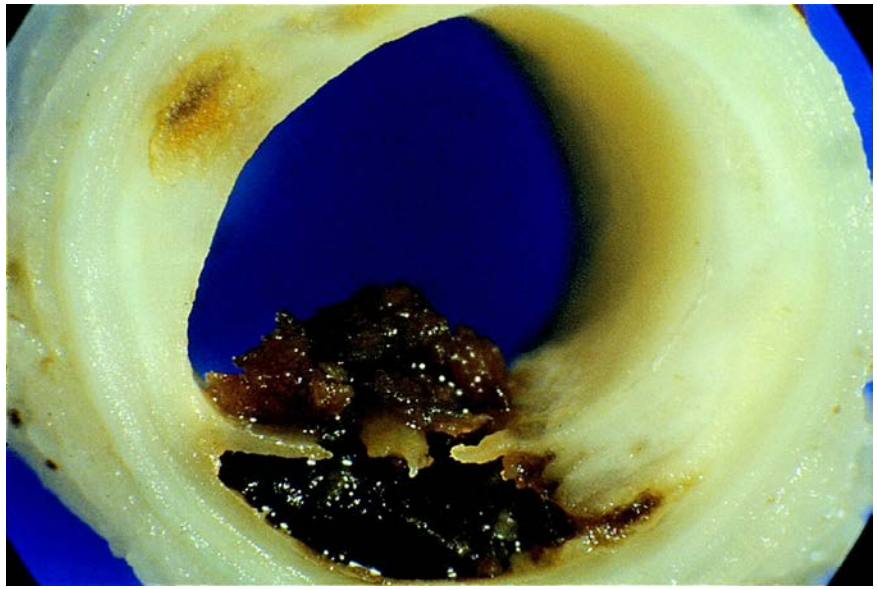
Stability and Instability: Two Faces of Coronary Atherosclerosis

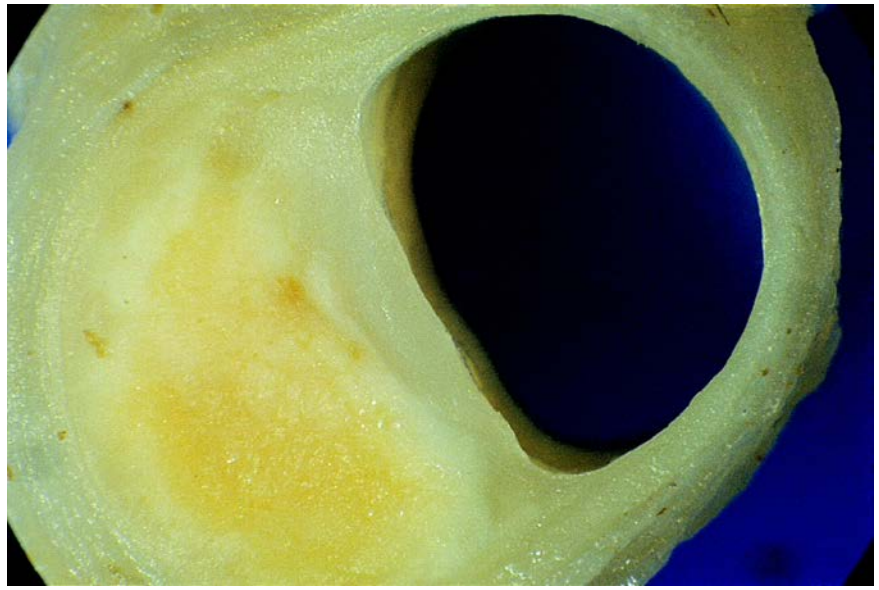
The Paul Dudley White Lecture 1995

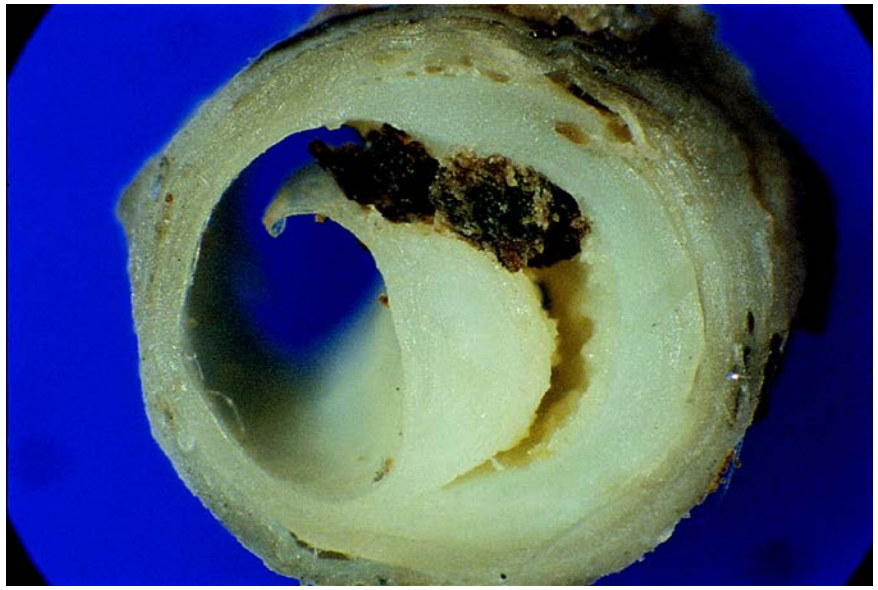
Michael J. Davies

Paul Dudley White was an astute observer of ischemic heart disease who emphasized the unity of acute myocardial infarction and chronic exertional angina as facets of the clinical expression of coronary atherosclerosis. He knew that plaque ulceration was a precipitator of thrombosis, but in the days before angiography was widely used, he reasoned that thrombosis occurred at sites of previous high-grade stenosis. He would be fascinated by the explosion of knowledge concerning the mechanisms of the two major expressions of coronary heart disease that has occurred since his death in 1973.

Any consideration of how symptoms arise in coronary atherosclerosis must begin with plaque. By early adult life, most individuals in developed countries will have some coronary plaques that, in pathological terms, are advanced. This simply means that within the plaque there has been considerable accumulation of extracellular lipid, lipid within foam cells of macrophage origin, and collagen produced by smooth muscle cells.



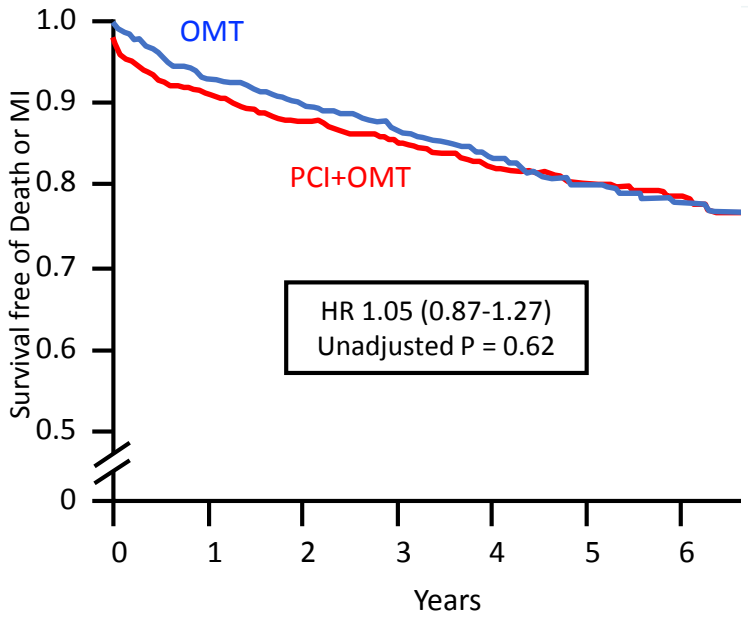


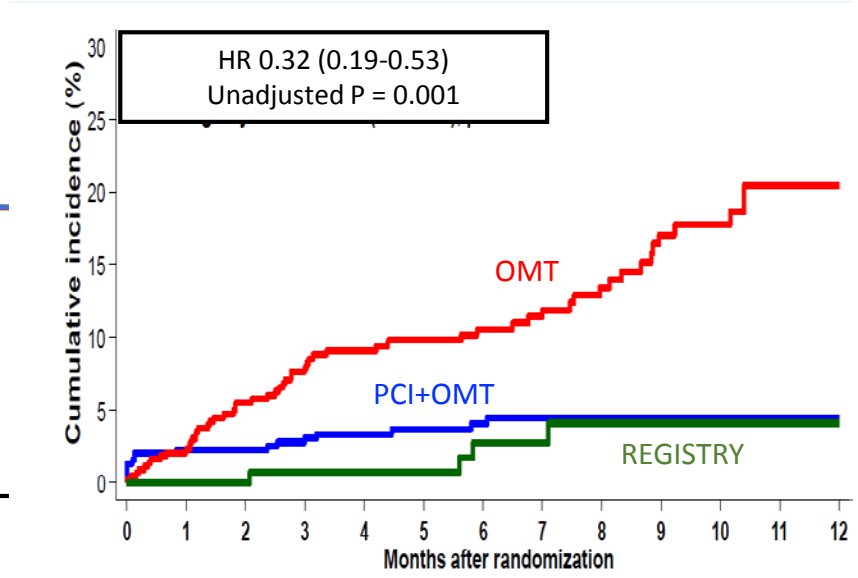


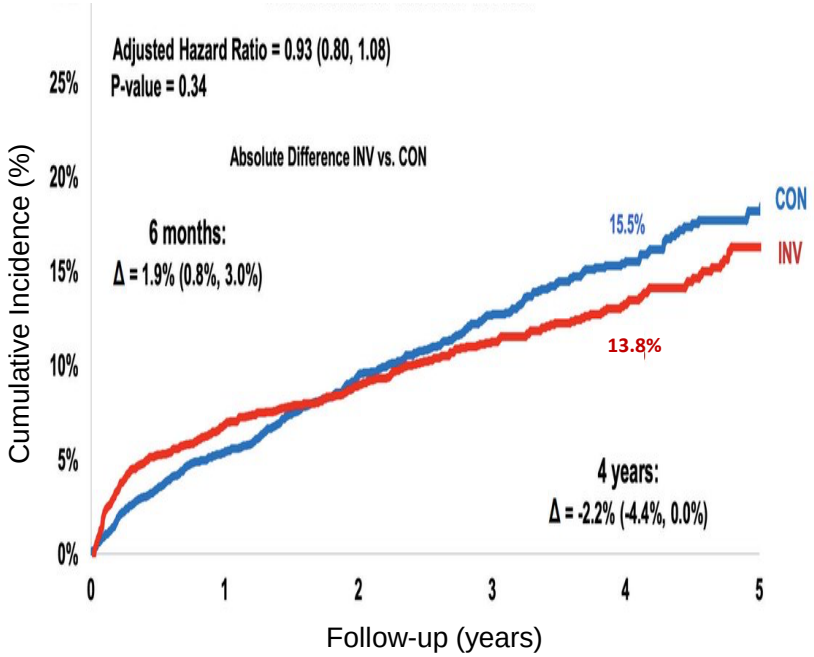
COURAGE: Treatment effect on primary outcome

FAME 2: FFR-Guided PCI vs. OMT in Stable CAD

ISCHEMIA: PRIMARY OUTCOME: CV DEATH, MI, hUA, hHF or rCA

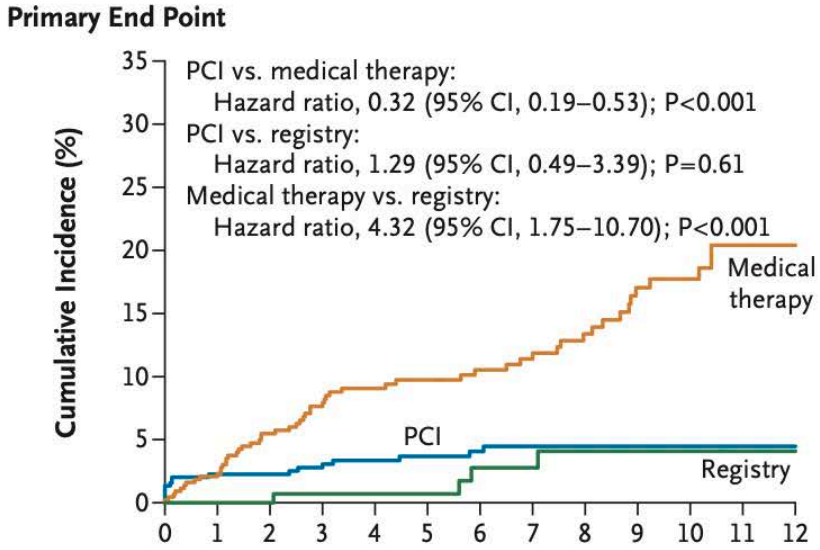


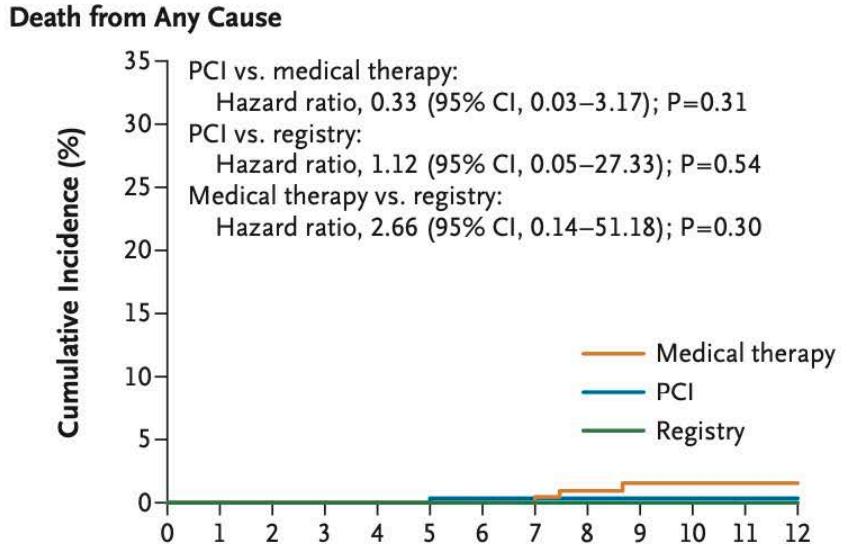


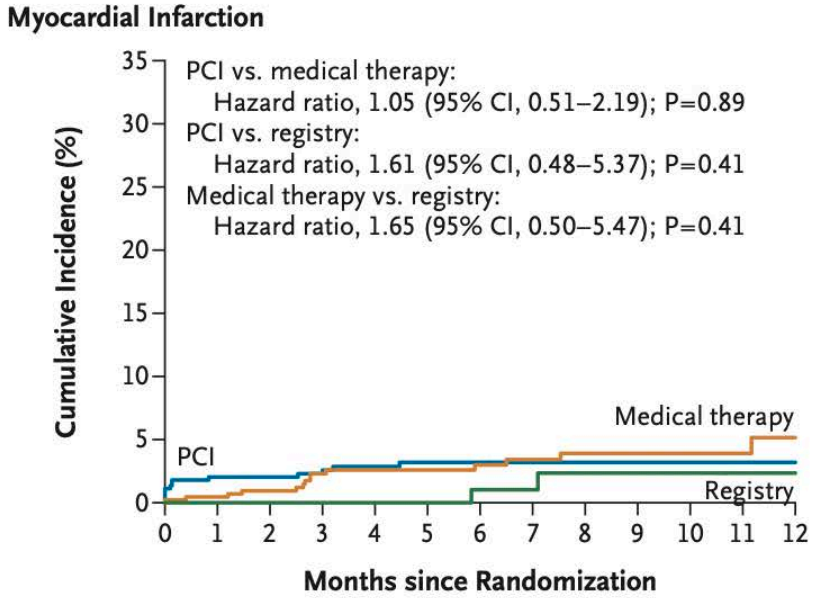


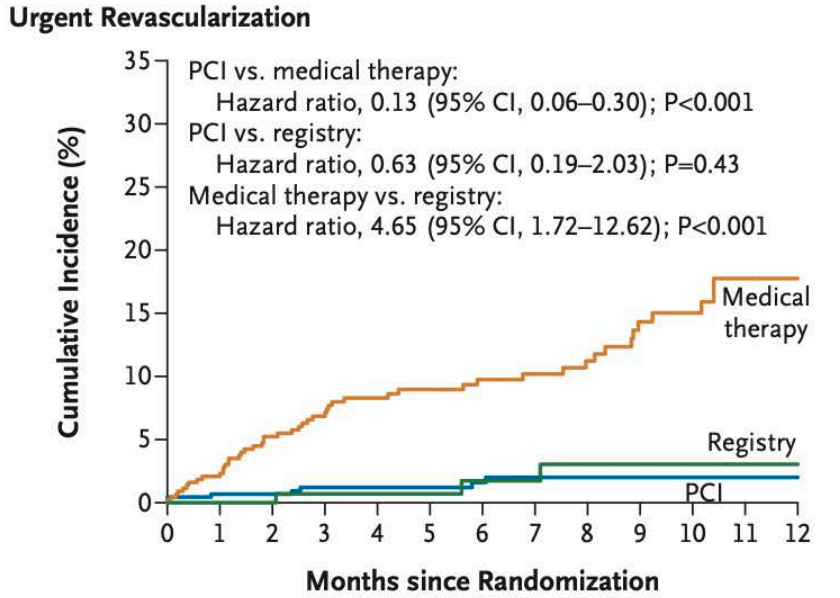
Boden WE et al. *NEJM.* 2007;356:1503-16.
Bruyne et al. NEJM 2012;367:991-1001
Maron et al. NEJM 2020; 382:1395-1407

FAME 2:
FFR-Guided PCI vs OMT in CAD





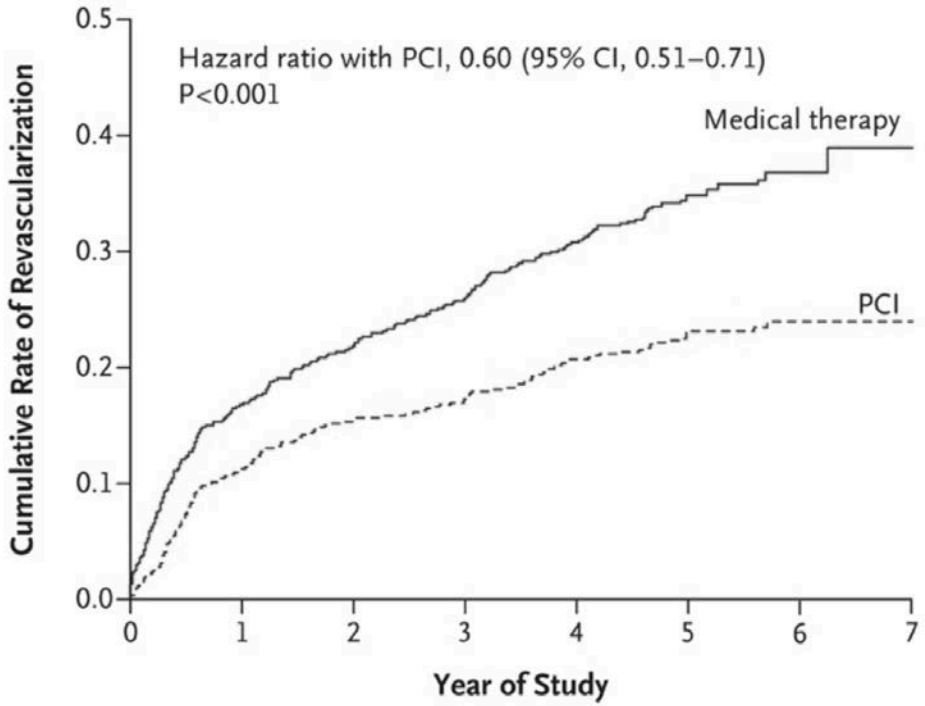


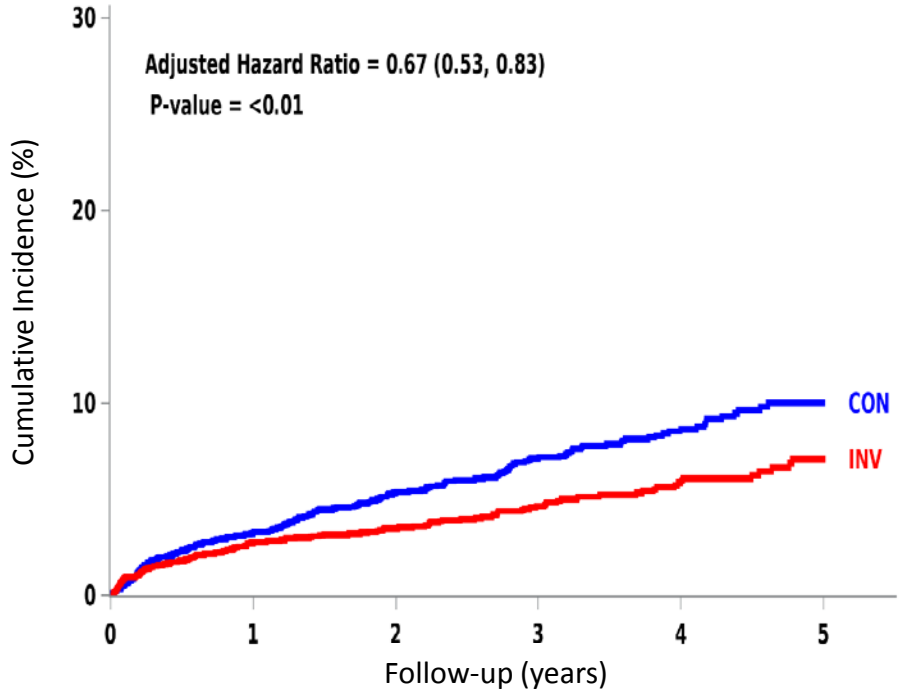


Do we need ischemia producing lesions to succeed with revascularization?

Bruyne et al. NEJM 2012;367:991-1001

COURAGE vs. ISCHEMIA

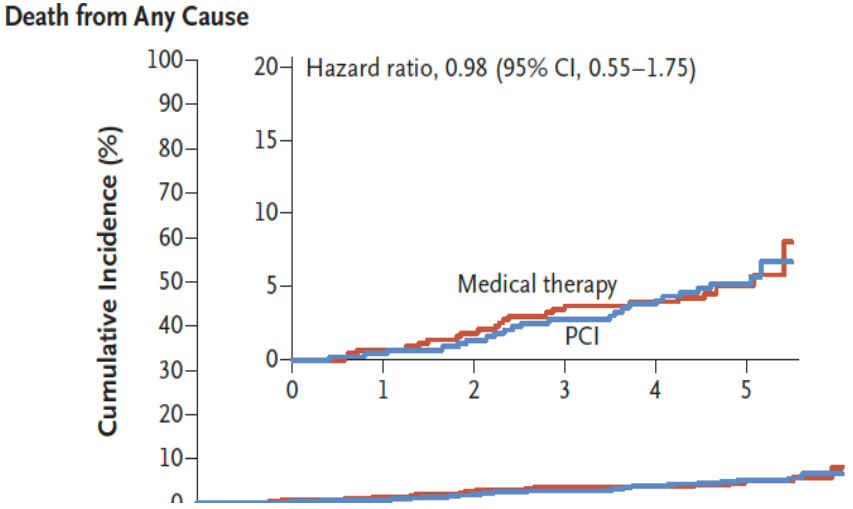


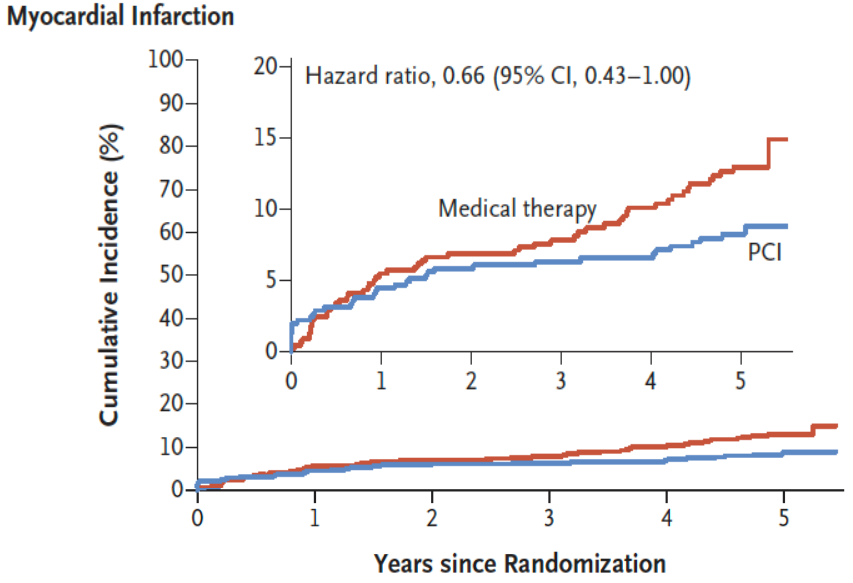


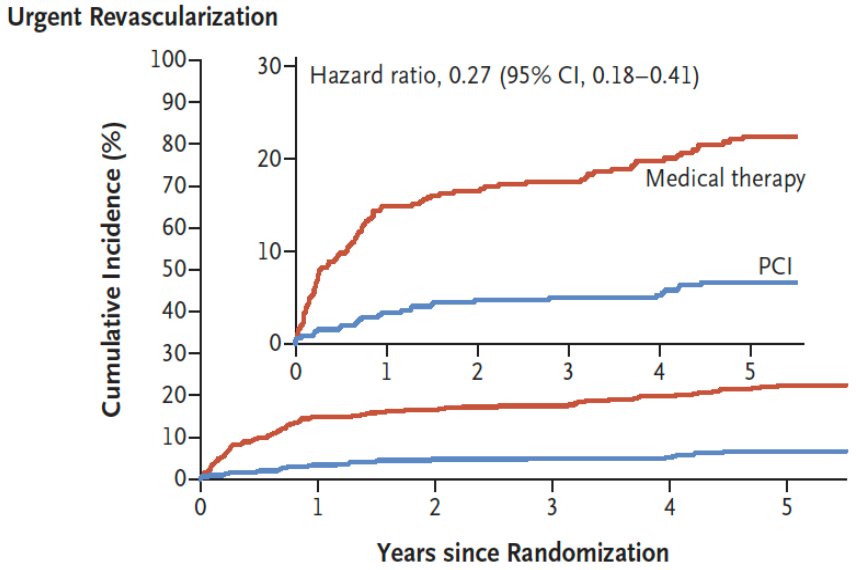
Spontaneous MI rate: Conservative (5.8%); Invasive (2.8%); ARR (3%), RRR (52%)

DID ISCHEMIA DEMONSTRATE FAILURE OF REVASCULARIZATION TO REDOCE MI, OR FAILURE OF ISCHEMIA TESTING TO GUIDE REVASCULARIZATION

5 Year, PCI is Superior to OMT for FFR+ Lesions





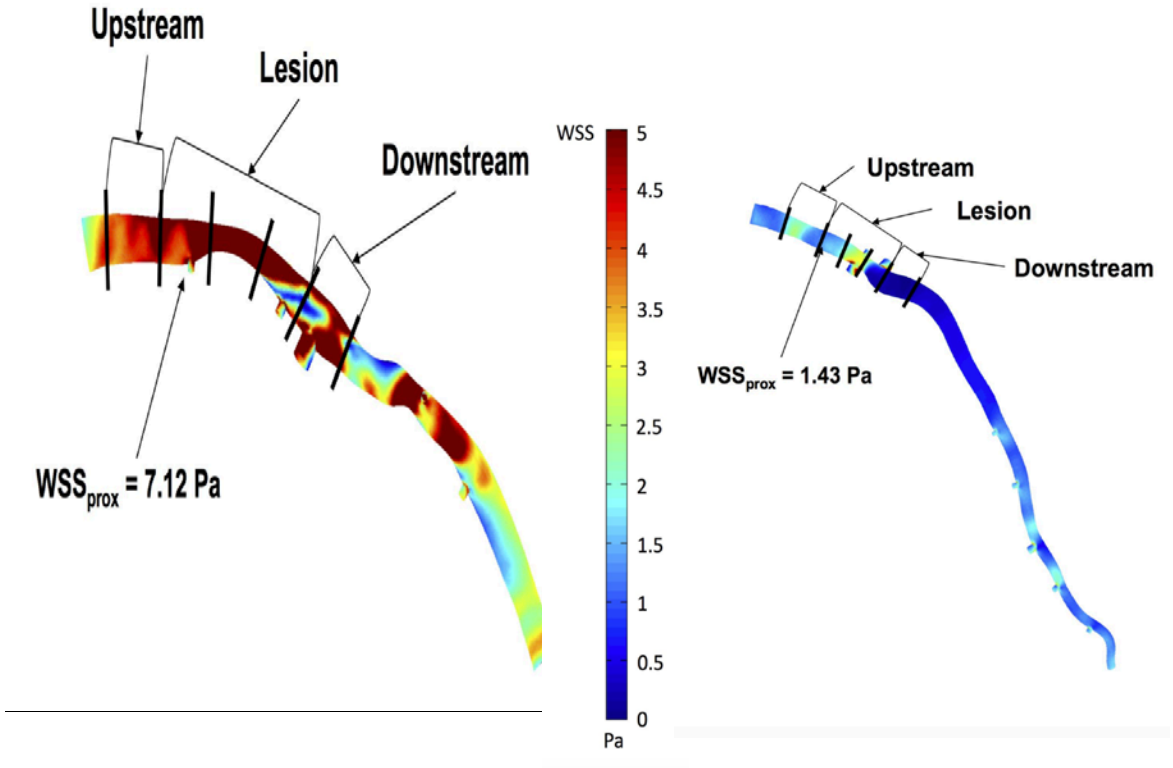


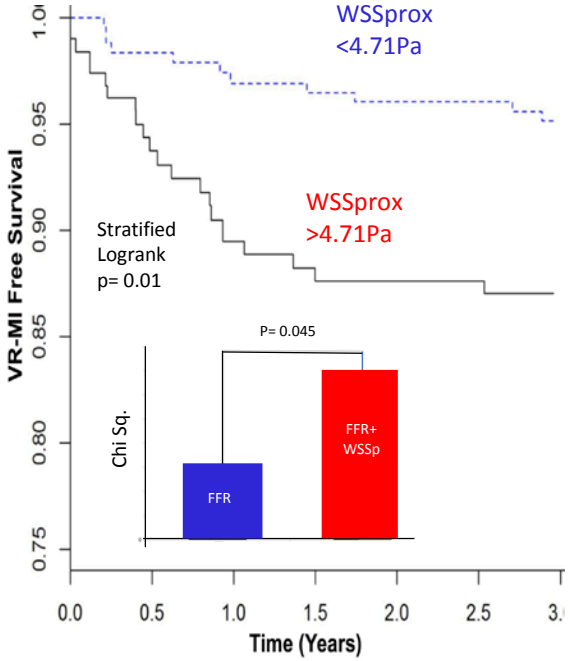
All ischemic lesions may not require revascularization. So, how can we identify ischemic or FFR+ lesions that are safe to defer to OMT?

Xaplanteris et al. NEJM 2018;379:250-259

High Coronary WSS in Patients with Stable CAD Predicts MI

A FAME-2 Sub-Study

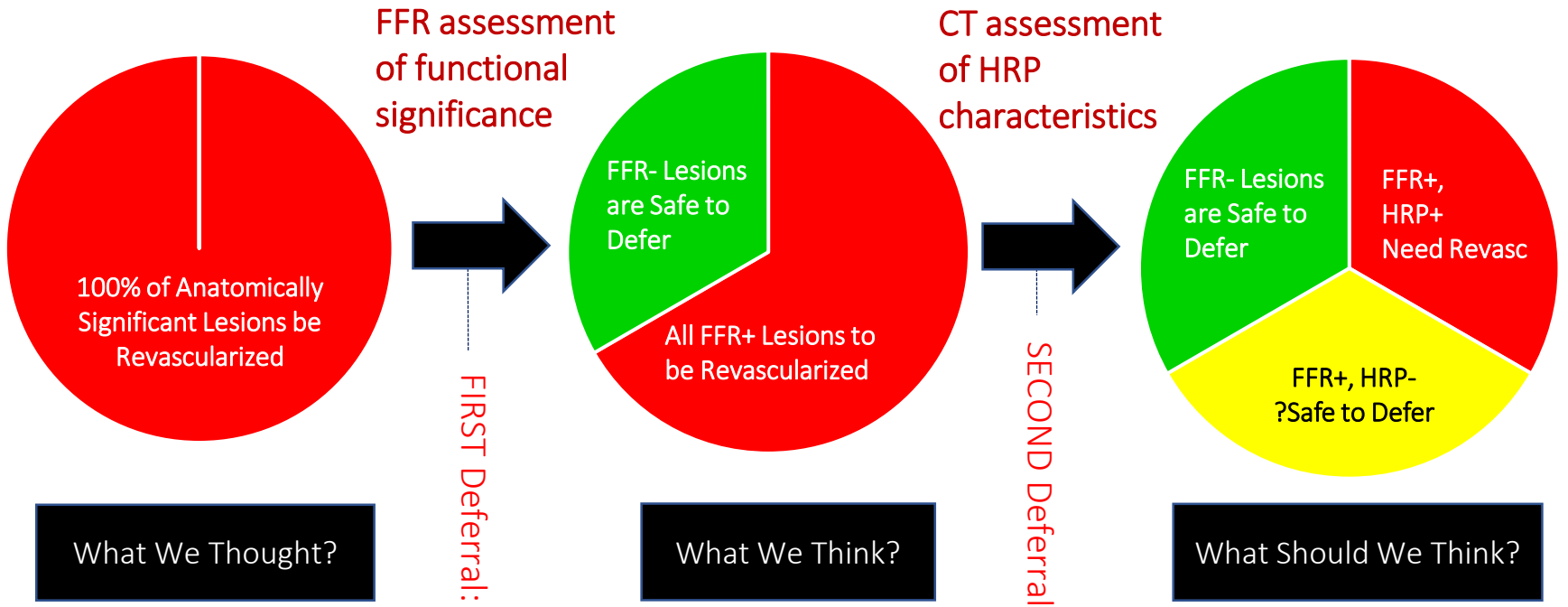




In significantly ischemic lesions, lack of plaque vulnerability probably predicts safe deferral!

Kumar, Bruyne, Samady et al. JACC 2018

EVOLVING PARADIGMS



Should the algorithm change?

But COURAGE suggested revascularization based on anatomical stenosis alone is not indicated

FAME Trial demonstrated safety of deferral of FFR- lesion, regardless of the degree of luminal stenosis

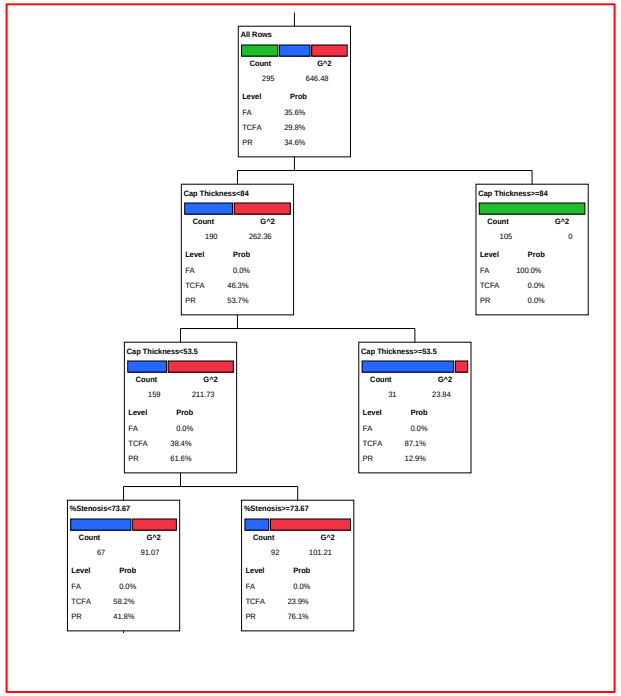
FAME-2: 50% of FFR+ on OMT remain event-free with no difference in rate of death and MI, revascularization, angina

Ahmadi, Narula. JACC 2019

The Plaques that Matter…

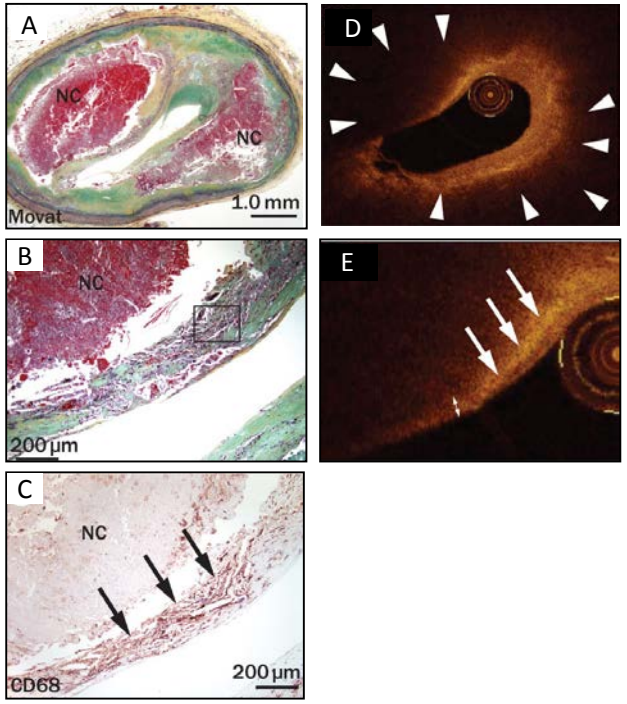
FCT is the most effective determinant of vulnerability

Recursive Partitioning Analyses

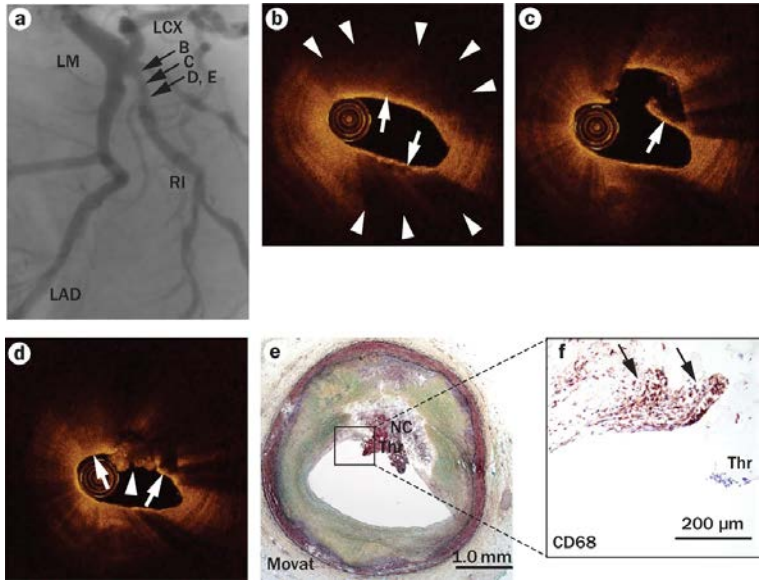


Narula et al. JACC 2013

Post-mortem



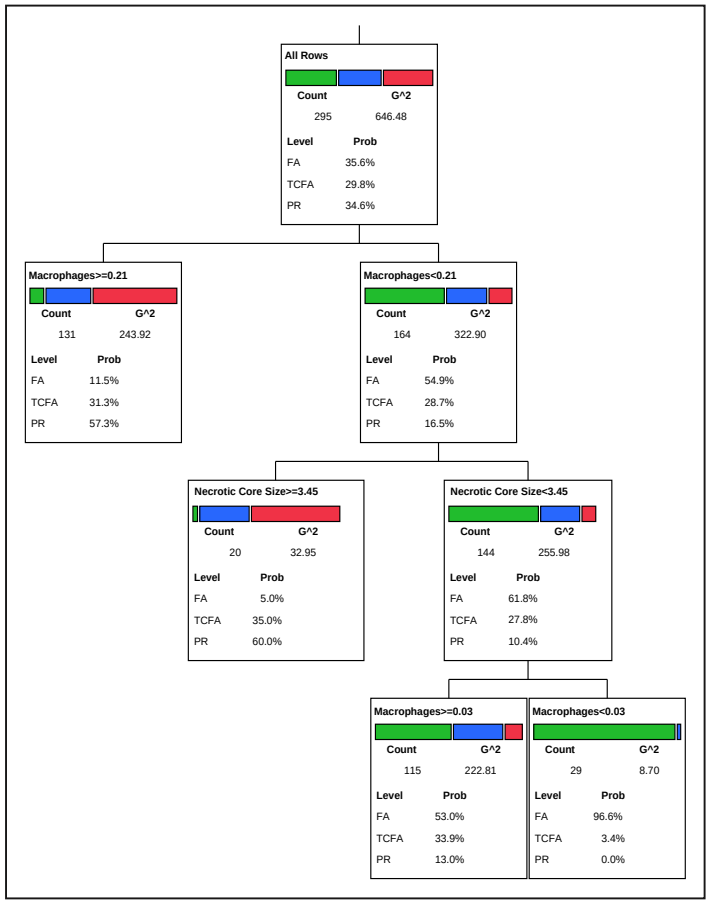
STEMI



Narula et al. Nature Rev Cardiol 2015

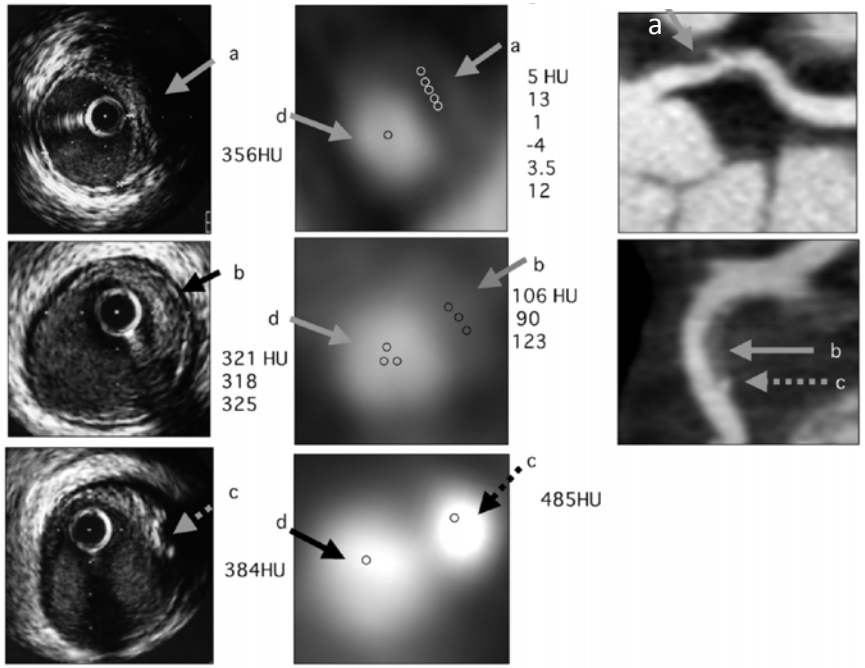
CT Angiography & Plaque Characterization

Recursive Partitioning Analyses



Narula et al. JACC 2013

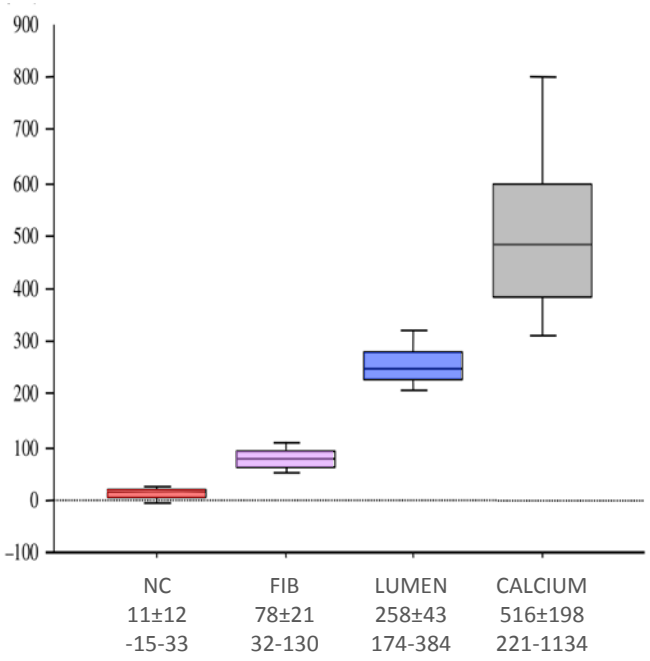
IVUS CT: X-sectional CT: Curved MPR



Motoyama, Narula et al. Circulation J 2007

CT Angiographic Characteristics, and Intravascular Ultrasound

CTA [HU]

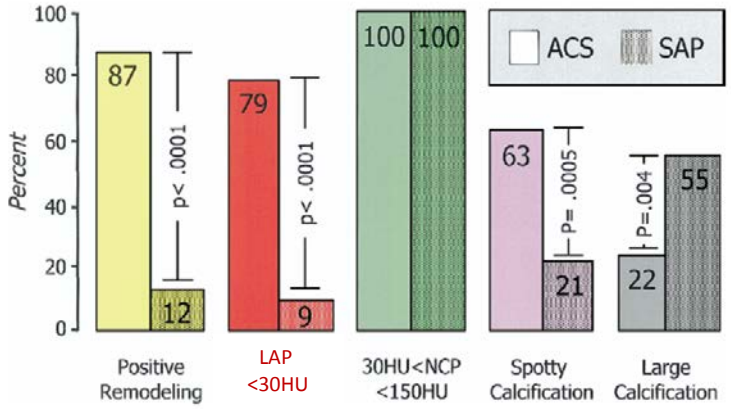


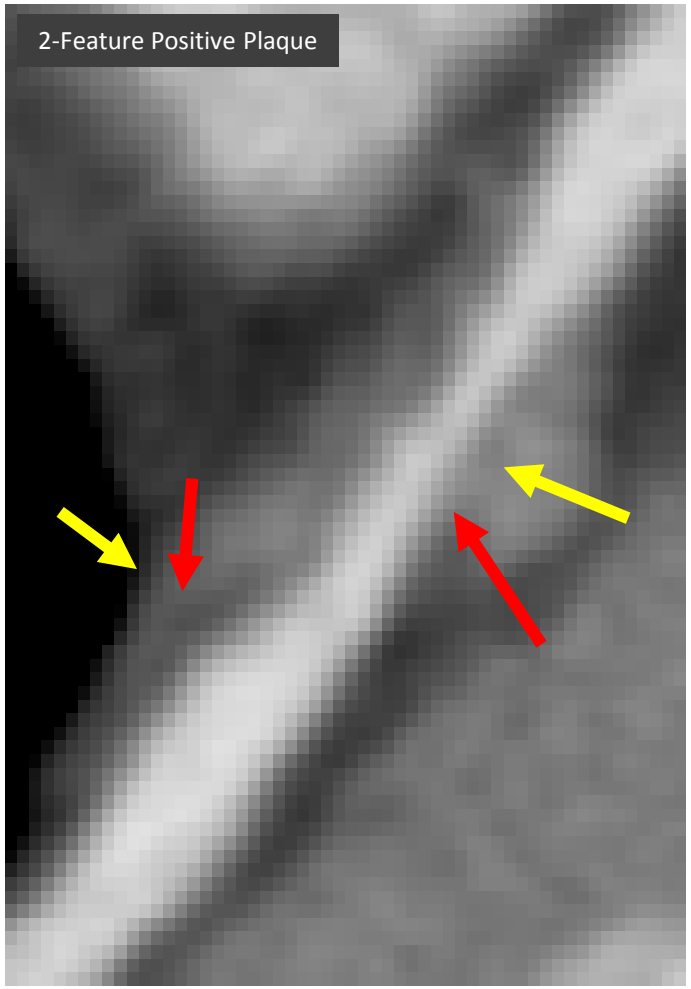
<0.0001, Nonparametric Kruskal-Wallis Tests

Motoyama, Narula et al. JACC 2007

ACS & PLAQUE MORPHOLOGY

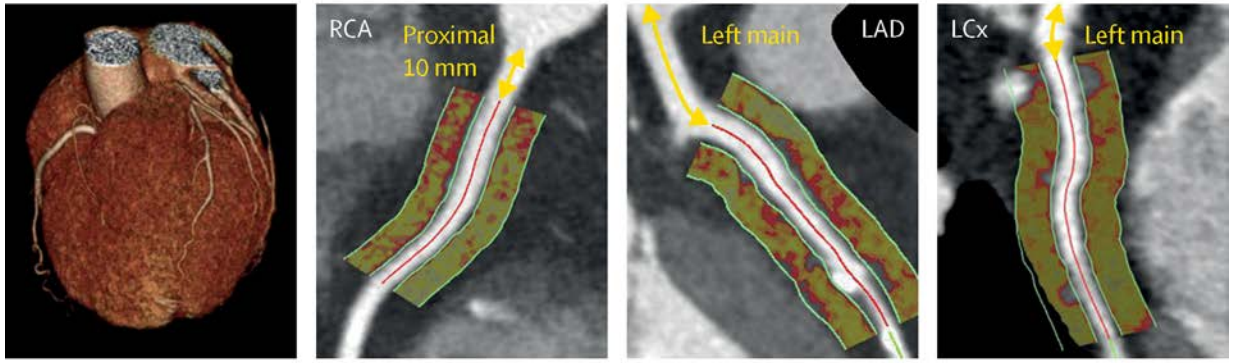
Observational study
ACS 38
Stable CAD 33

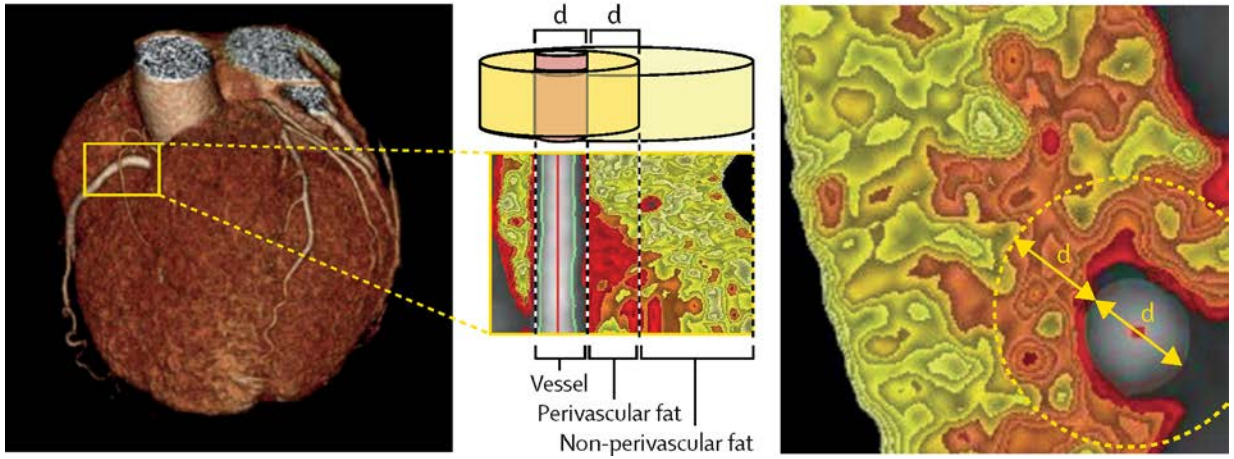




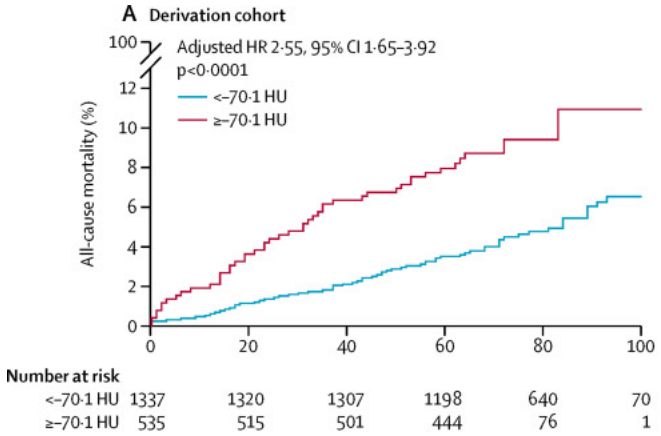
Motoyama, Narula et al. JACC 2007

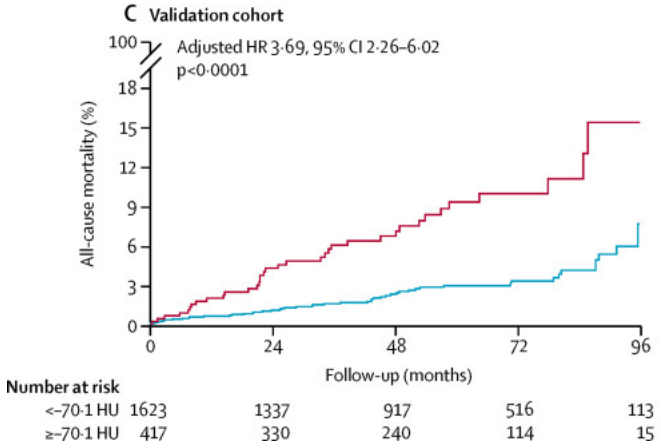
CT-Verified Coronary Inflammation and Prediction of Residual CV Risk (CRISP-CT Study)





Oikonomou, Achenbach, Antonides et al. Lancet 2018; 392: 929-39



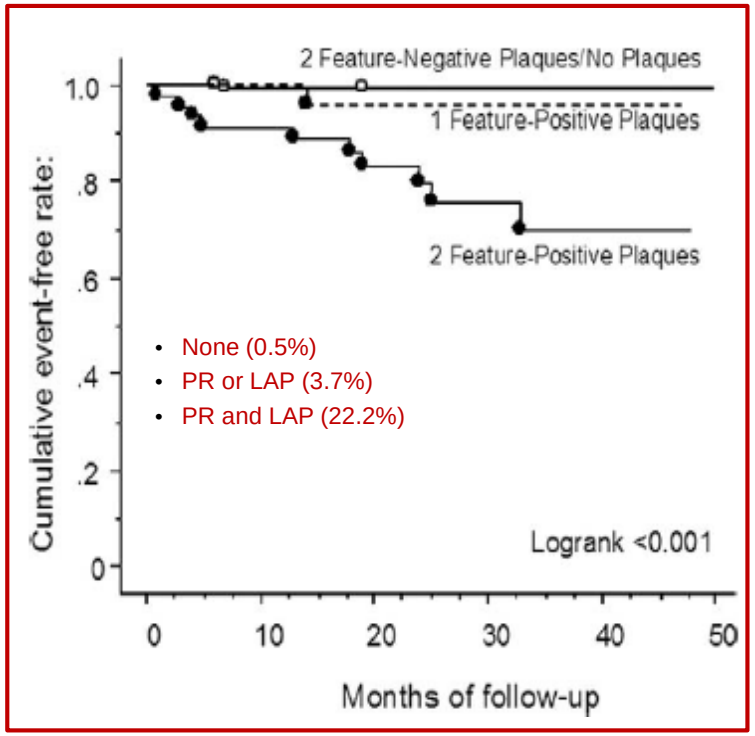


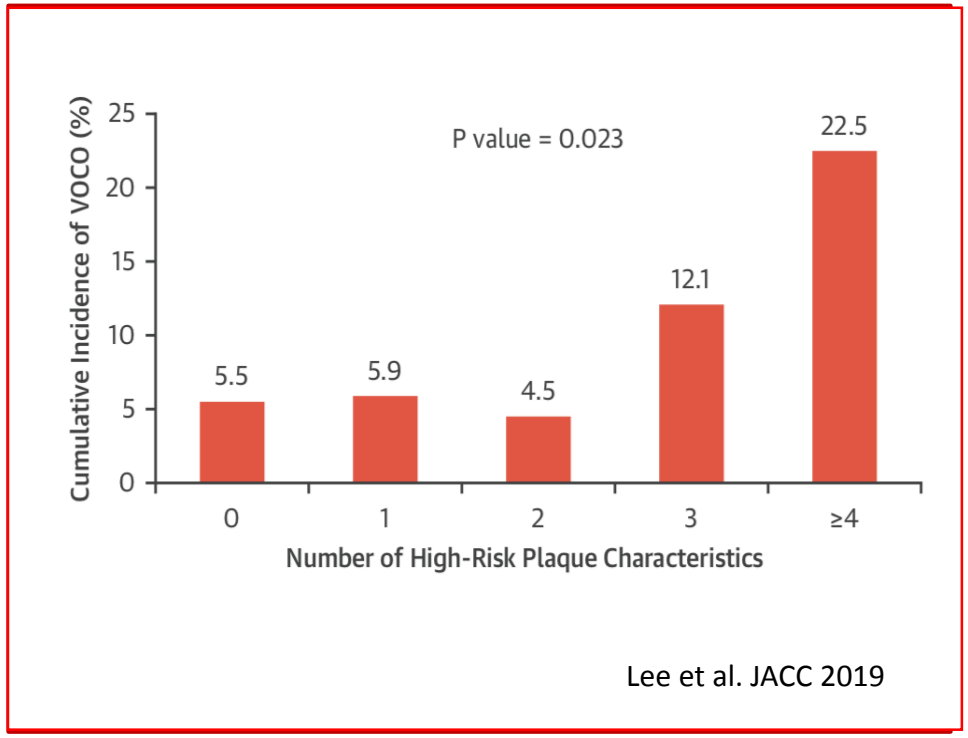
Fluidity of perivascular fat determines the extent of intra-plaque inflammation.

Recognition of HRP and Adverse Outcome?

Longitudinal Follow up; N=1059, 27 mos; Endpoint: MACE

Number of APCs?





Motoyama, Narula et al. JACC 2009

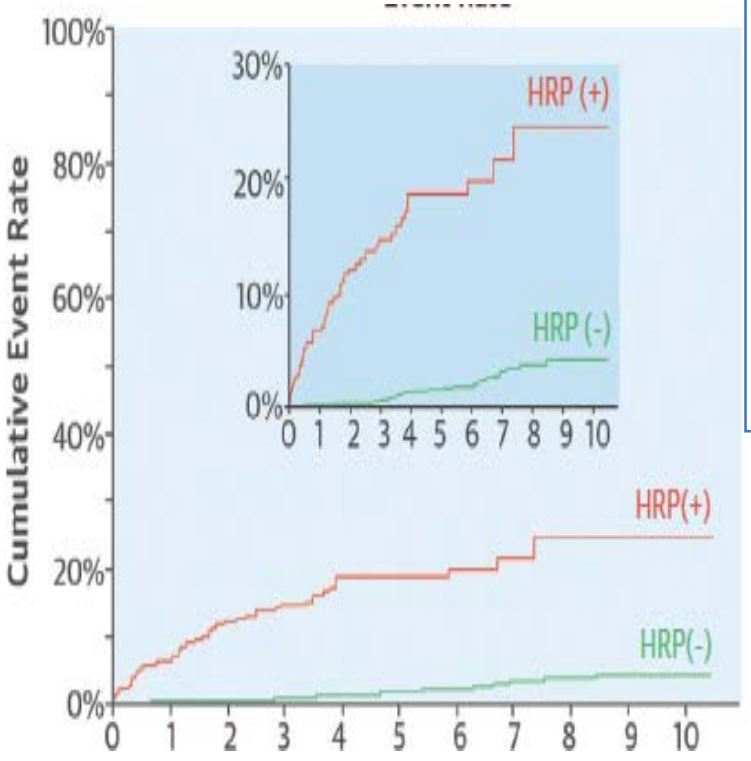
High-risk lesions can be noninvasively recognized;
morphology determines likelihood, time to event!

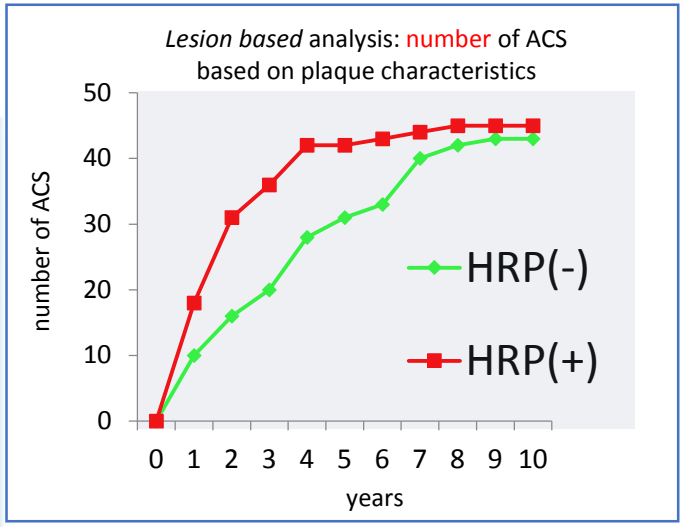
ACS, PLAQUE MORPHOLOGY & APC

Prospective Single Center; N=3000+, up to 10 years; Endpoint: MACE

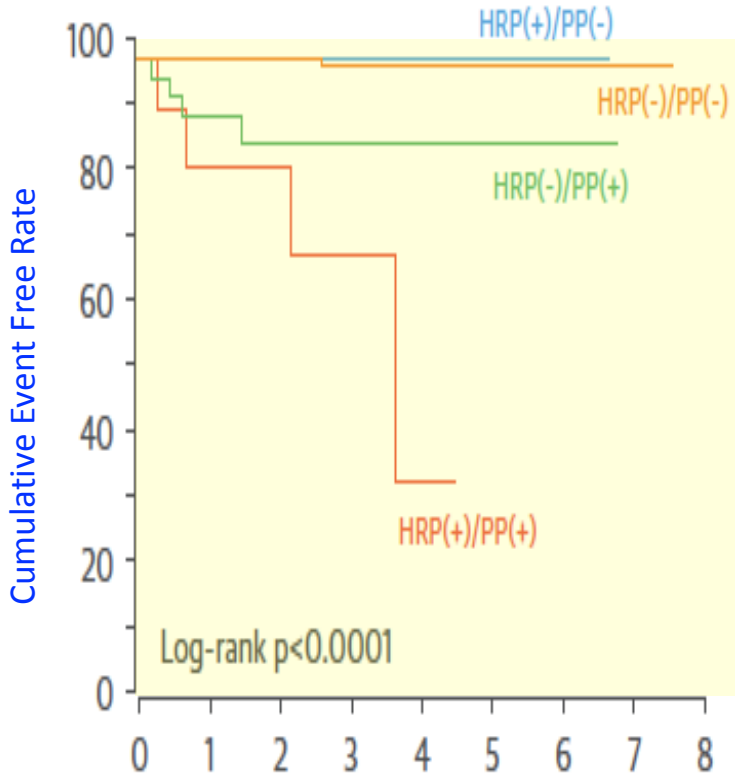
Plaque progression is a prelude to spontaneous MI!

HRP



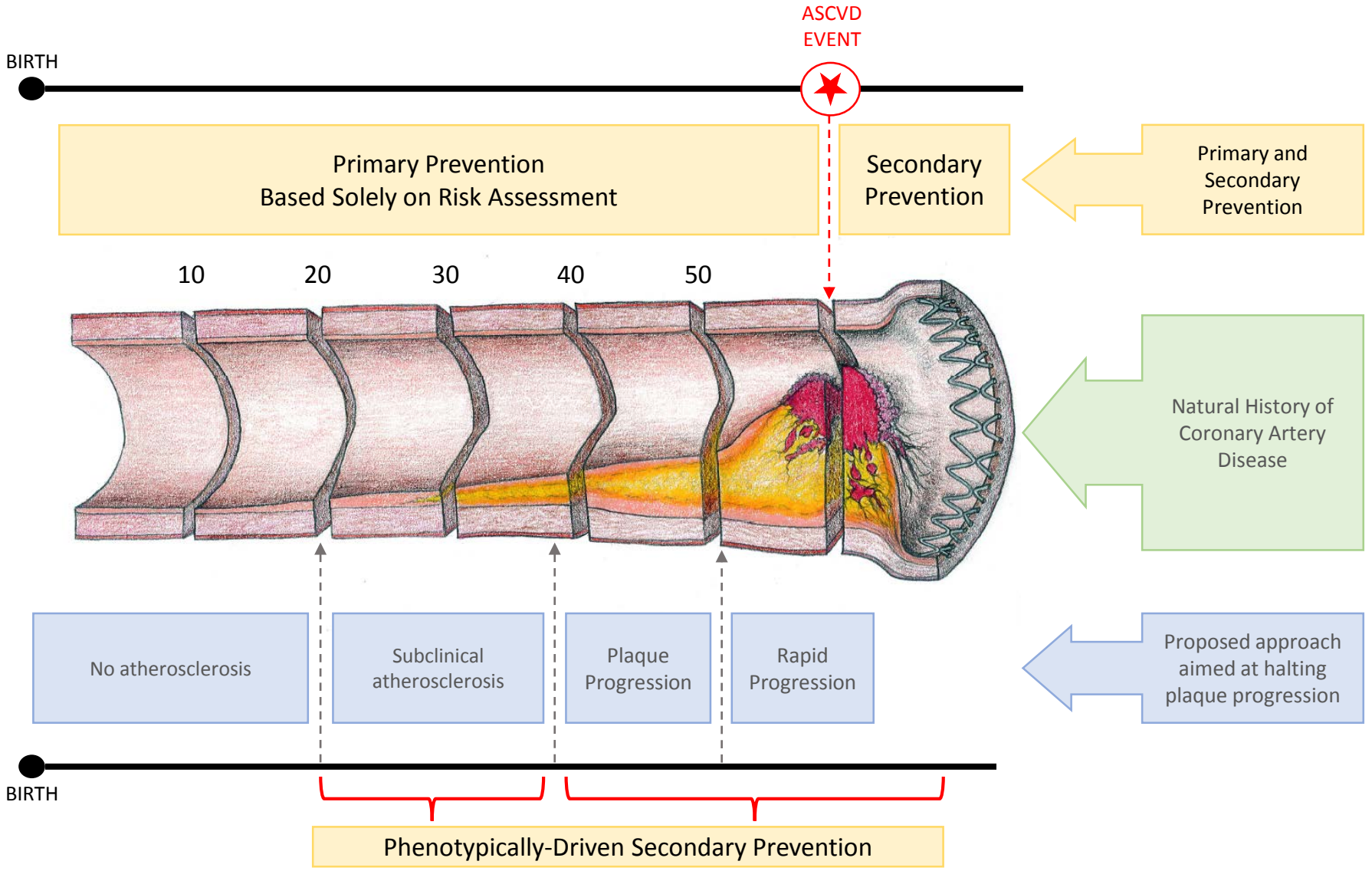


PROGRESSION



Motoyama, Narula JACC 2015

Plaque progression is an essential step?



Ahmadi, Narula et al. JACC 2019

Glagovian hypothesis, positive remodeling, and deceptive lack of luminal encroachment…

COMPENSATORY ENLARGEMENT OF HUMAN ATHEROSCLEROTIC CORONARY ARTERIES

Seymour Glagov, M.D., Elliot Weisenberg, B.A., Christopher K. Zarins, M.D., Regina Stankunavicius, M.P.H., and George J. Kolettis, B.A.

Abstract Whether human coronary arteries undergo compensatory enlargement in the presence of coronary disease has not been clarified. We studied histologic sections of the left main coronary artery in 136 hearts obtained at autopsy to determine whether atherosclerotic human coronary arteries enlarge in relation to plaque (lesion) area and to assess whether such enlargement preserves the cross-sectional area of the lumen. The area circumscribed by the internal elastic lamina (internal elastic lamina area) was taken as a measure of the area of the arterial lumen if no plaque had been present. The internal elastic lamina area correlated directly with the area of the lesion ($r = 0.44$, $P<0.001$), suggesting that coronary arteries enlarge as lesion area increases. Regression analysis yielded the following equation: Internal elastic lamina area = 9.26 + 0.88 (lesion area) + 0.026 (age) + 0.005 (heart weight). The correlation coefficient for the lesion area was significant ($P<0.001$), whereas the correlation coefficients for age and heart weight were not. The lumen area did not decrease in relation to the percentage of stenosis (lesion area/internal elastic lamina area × 100) for values between zero and 40 percent but did diminish markedly and in close relation to the percentage of stenosis for values above 40 percent ($r = -0.73$, $P<0.001$).

We conclude that human coronary arteries enlarge in relation to plaque area and that functionally important lumen stenosis may be delayed until the lesion occupies 40 percent of the internal elastic lamina area. The preservation of a nearly normal lumen cross-sectional area despite the presence of a large plaque should be taken into account in evaluating atherosclerotic disease with use of coronary angiography. (N Engl J Med 1987; 316: 1371-5.)

CORONARY arteries and hind-limb arteries of cynomolgus monkeys[1,2] have been shown to enlarge as intimal plaques form in response to an atherogenic diet. A nearly normal lumen cross-sectional area was maintained in the hind-limb arteries up to 6.5 years after the atherogenic diet was begun, and the hemodynamic responses of these vessels to vasoactive agents were only mildly affected.[2] If arteries enlarge as a consequence of plaque formation, several important questions arise. Does this phenomenon occur in human arteries? Is it independent of the arterial enlargement that commonly occurs with increasing age? To what extent does the arterial enlargement keep pace with the growth of the plaque, and under what conditions is the response arrested, allowing stenosis to progress? To determine whether such an adaptive response is associated with plaque formation in humans and to characterize the transition from an adequate to a functionally stenotic lumen, we studied cross sections of the left main coronary artery in human hearts obtained at autopsy. We report that arterial enlargement does occur, principally in relation to the area of the plaque, and that lumen stenosis is delayed until the lesion occupies approximately 40 percent of the potential lumen area.

Methods

Adult hearts obtained at autopsy 2 to 12 hours after death were stored unopened in normal saline solution at 4°C for 2 to 12 hours until processed. Except for hearts from persons with aortic-valve regurgitation or evidence of communicable disease, specimens were included in the study without regard to sex, premortem diagnosis, or cause of death. This report is based on studies of the first 136 hearts entered into the series between December 1, 1983, and December 28, 1984. The ages of the subjects ranged from 18 to 98 years (mean ±SD, 63±16). Eighty-three were men and 53 were women. The heart weights before fixation were available for 109 hearts and ranged from 200 to 850 g (mean, 446±148).

Each heart was brought to room temperature (approximately 20°C) before fixation by controlled-pressure perfusion of the coronary-artery tree with 10 percent formalin by means of a self-regulating system described previously.[3] In brief, a cannula is tied into the aorta distal to the left subclavian artery and the innominate artery, and both the carotid and left subclavian arteries are clamped. A pressure of 100 mm Hg is applied to the fixative reservoir, and the perfusion pressure is monitored by means of a manometer at the level of the heart during a fixation period of 90 minutes. This procedure results in closure of the aortic valve and continuous perfusion of fixative through the coronary tree at the predetermined pressure. Distention of the coronary tree with fixative under these conditions results in a rigid specimen with both ventricles in a diastolic configuration.[4] Fixative is then flushed out of the arterial tree by perfusion with normal saline solution, the aorta is transected approximately 2.0 cm above the aortic valve, and a warmed mixture (37°C) of barium sulfate and gelatin is injected into each coronary orifice under controlled pressure. Pressure is maintained while the heart is immersed in cold formalin (4°C) to solidify the injection mixture. Radiographs are then made in orthogonal anteroposterior and lateral projections. These preparations are being used to characterize the state of the coronary arteries in an ongoing comprehensive study of the configuration and composition of atherosclerotic plaques in relation to angiographic appearances and clinical consequences.

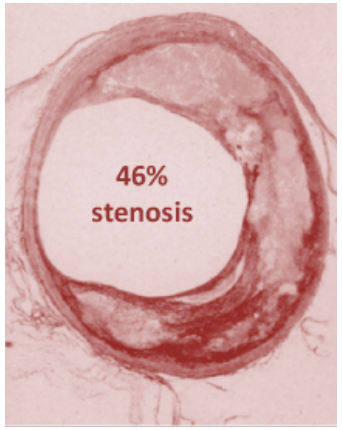
We selected the left main coronary artery for study because it is frequently diseased and is similar in length and diameter in most adult hearts. In order to obtain samples that were not biased with respect to lesion severity, transverse blocks were removed at a standard location midway between the orifice of the left coronary artery and the origin of its left circumflex branch. The samples were embedded in paraffin and sectioned at 5 μm. Adjacent sections were stained with hematoxylin and eosin and with the Gomori trichrome–aldehyde fuchsin procedure, for differentiation of connective tissue.

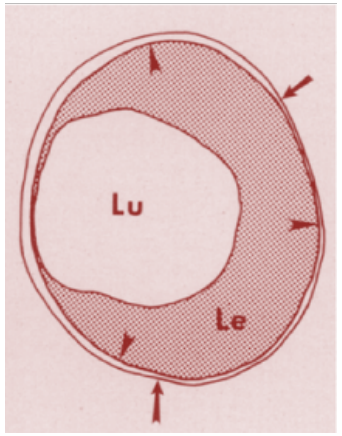
By means of a previously described contour-tracing system consisting of a projecting microscope, a digitizing plate, and a suitably programmed computer,[5] we traced the lumen, the internal elastic lamina, and the outer limit of the media (Fig. 1). The boundaries of the lumen and of the outer media were always distinct. In the presence of advanced disease, however, the internal elastic lamina was often discontinuous, fragmented, or absent beneath the thickest

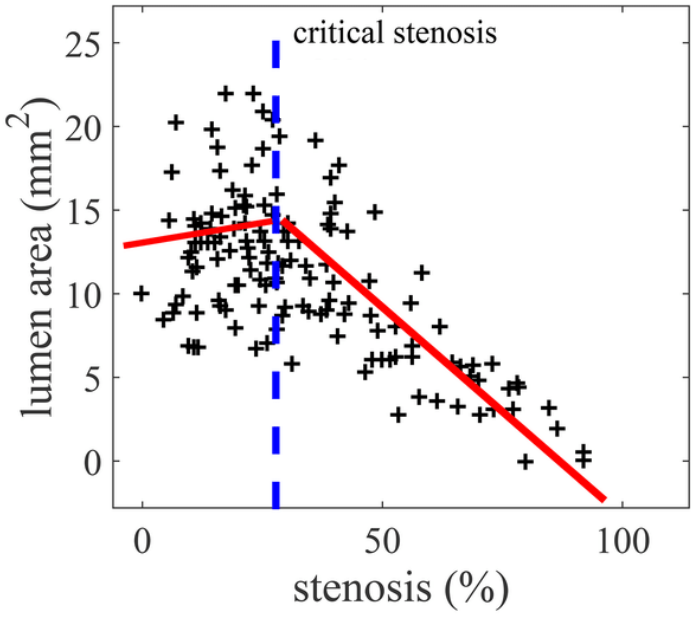
From the Departments of Pathology and Surgery, University of Chicago. Address reprint requests to Dr. Glagov at the Department of Pathology, University of Chicago, 5841 S. Maryland Ave., Chicago, IL 60637.

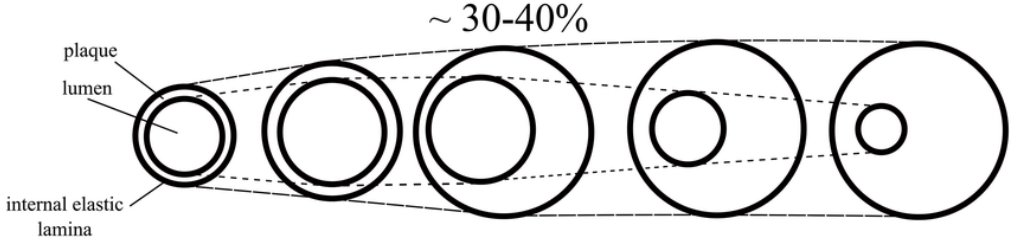
Supported by a grant (15062) from the National Heart, Lung, and Blood Institute (Atherosclerosis Specialized Centers of Research).

Presented in part at the meeting of the Federation of American Societies for Experimental Biology, April 1986, and published in abstract form in *Federation Proceedings* (1986; 45(3):583).



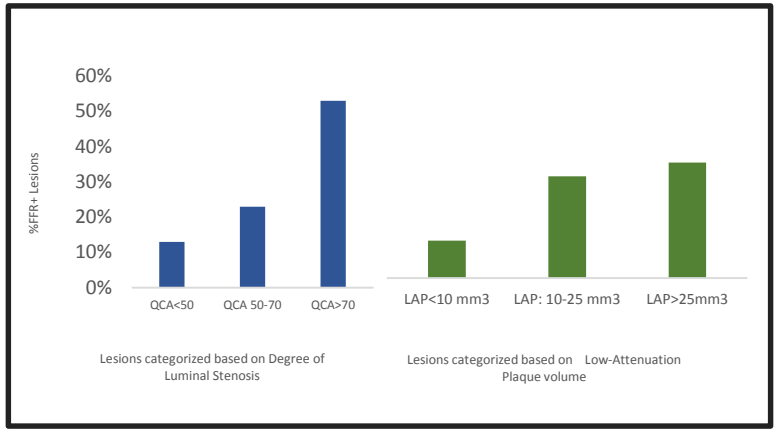


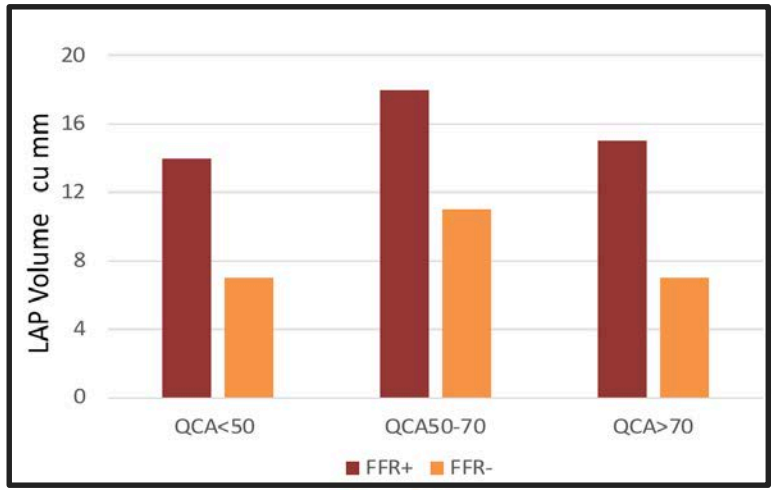




FFR:
Lesion-Specific and Vessel-Related Determinants

Effect	Model: All Vessels		
	Estimate	SE	P
Intercept	1.044	0.020	<0.0001
QCA	-0.002	0.0002	<0.0001
LAP Volume	-0.001	0.0003	0.0006
Vessel Territory (LAD vs. RCA/LCX)	-0.065	0.011	<0.0001
Lesion Location (Proximal vs. Mid/Distal)	-0.024	0.010	0.0174
Number of segments	-0.019	0.006	0.0020
Lesion Length (mm)	0.0002	0.001	<0.7762



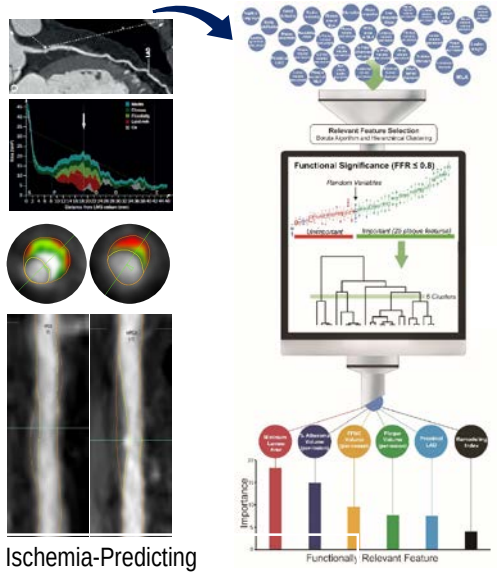


In addition to luminal stenosis, FFR is also attributed to positively-remodeled, lipid-rich plaques.

Ahmadi, Narula et al. JACC Imaging 2018

Prognostic Implications of Selected Plaque Features

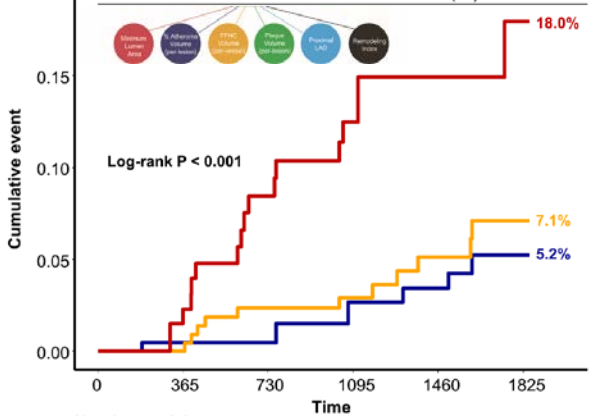
MLA, PAV, NCV, PV, pLAD, RI



Ischemia-Predicting Plaque Features

OMT GROUP

# Ischemia-Predicting Features	HR (95% CI)	P-value
≥ 4	4.1 (1.5-11.0)	0.01
2 or 3	1.4 (0.5-3.7)	0.52
0 or 1	1 (ref)	NA



ORIGINAL RESEARCH

CT Angiographic and Plaque Predictors of Functionally Significant Coronary Disease and Outcome Using Machine Learning

Yang, Koo, Narula et al. JACC Imaging 2021

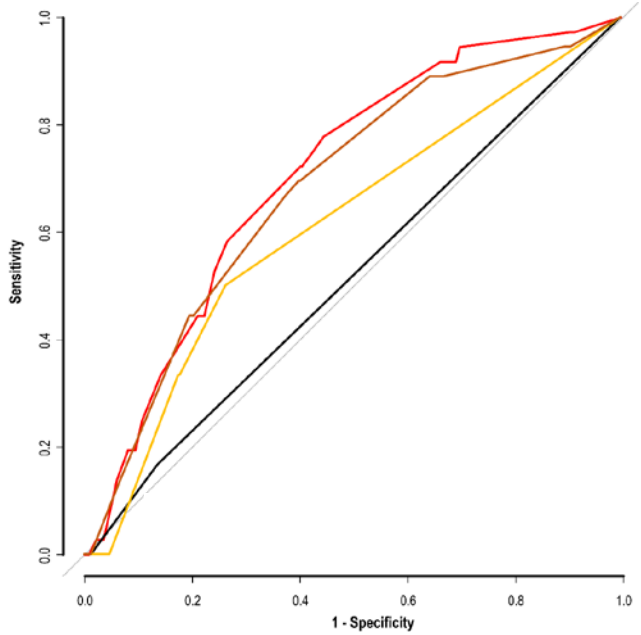
NEW RESEARCH PAPER

High-Risk Morphological and Physiological Coronary Disease Attributes as Outcome Markers After Medical Treatment and Revascularization

Yang, Koo, Narula et al. JACC Imaging 2021

Automated, quantitative assessment of plaque morphology is possible!

Model	AUC	P-value
Model 1: % Diameter stenosis	0.515	0.030
Model 2: % Diameter stenosis + FFR ≤ 0.80	0.611	0.226
Model 3: % Diameter stenosis + No. of six features	0.681	0.202
Model 4: % Diameter stenosis + FFR ≤ 0.80 + No. of six features	0.706	0.031, <0.001



DISCOVER-FLOW 10Y F-U

136 lesions from 78 deferred vessels

Lesion and hemodynamic characterization

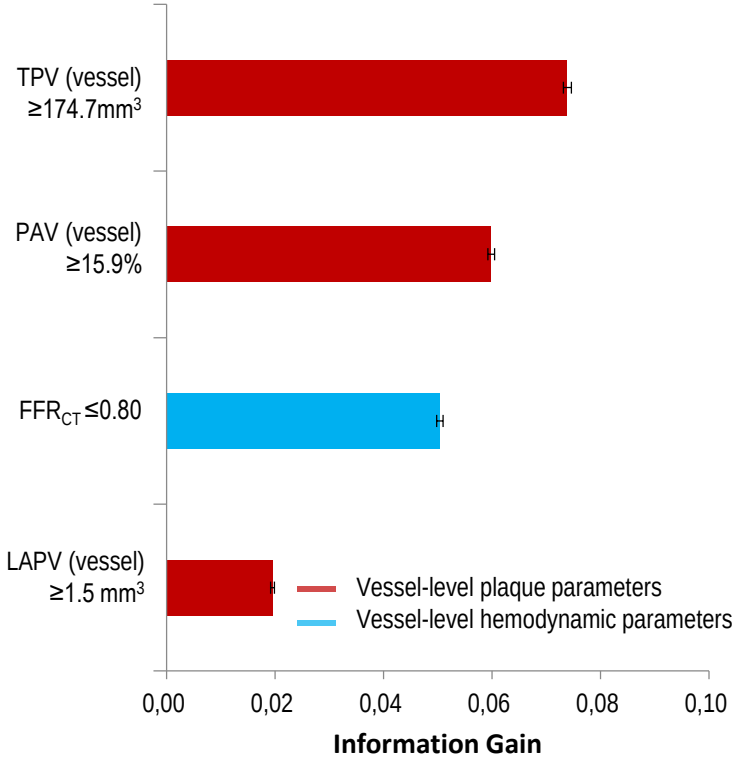
745 patients, CTA ☞ ICA ☞ Rx

Post-hoc HRP and FFR characterization

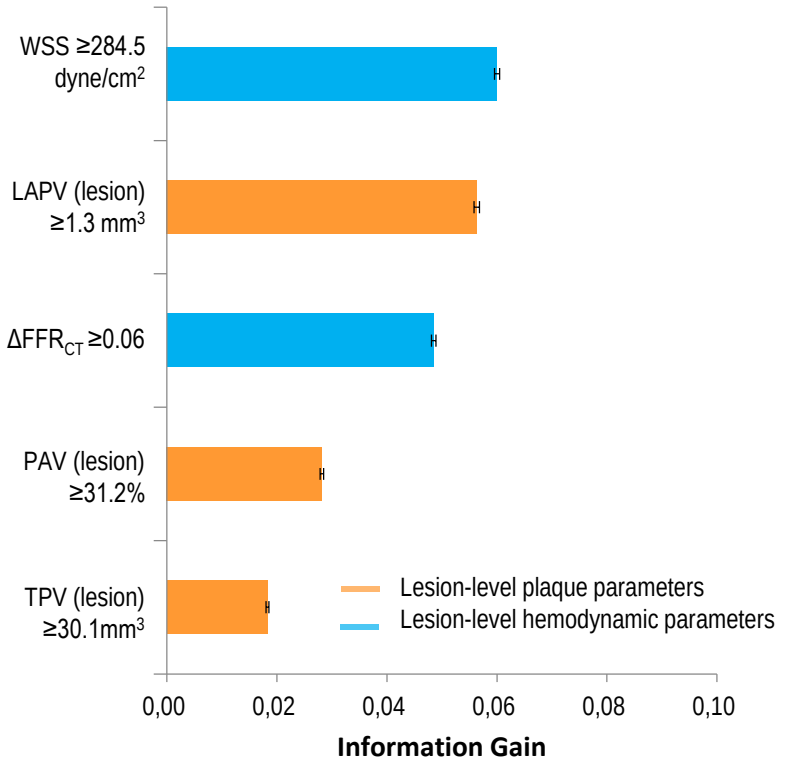
	FFR+	FFR-
HRP+	CR>>OMT [I]	CR>OMT NS [IIA]
HRP-	CR=OMT [IIB]	CR<OMT [III]

Motoyama, Ahmadi, Narula et al.
JACC Imaging 2022 (in press)

10-year Target Vessel Failure

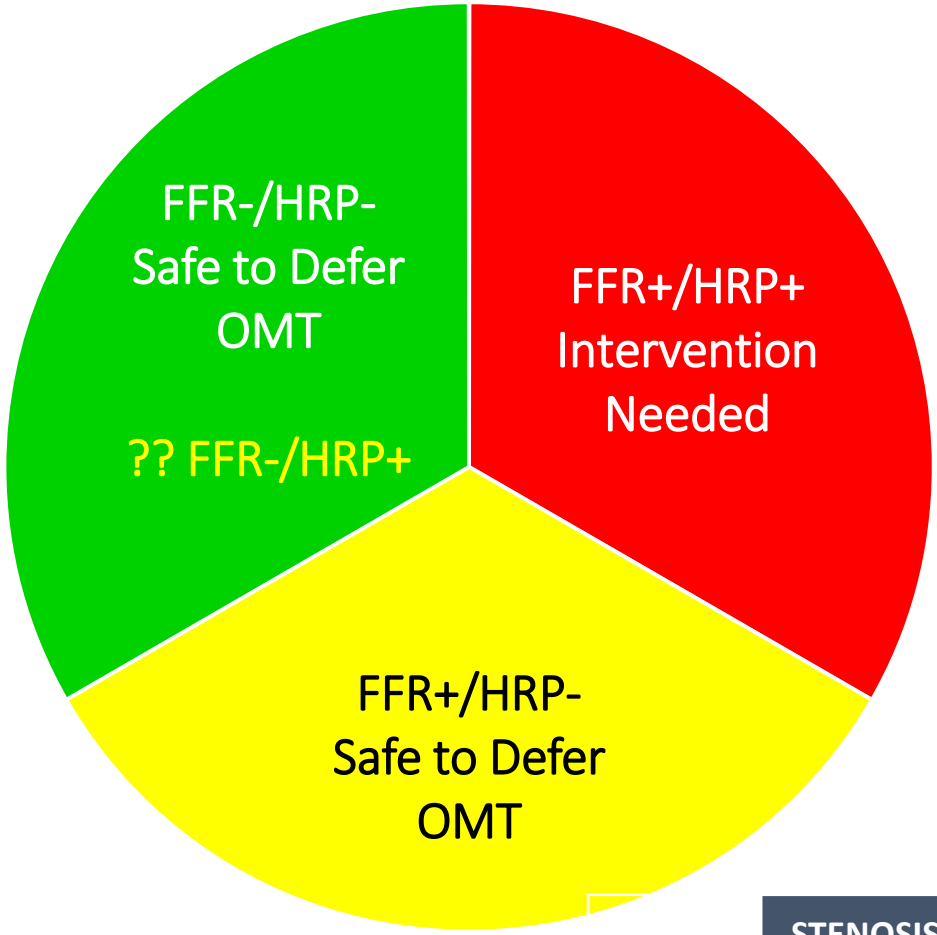


10-year Target Lesion Failure



Yang, Naula, Koo et al.
JACC Imaging 2022 (in press)

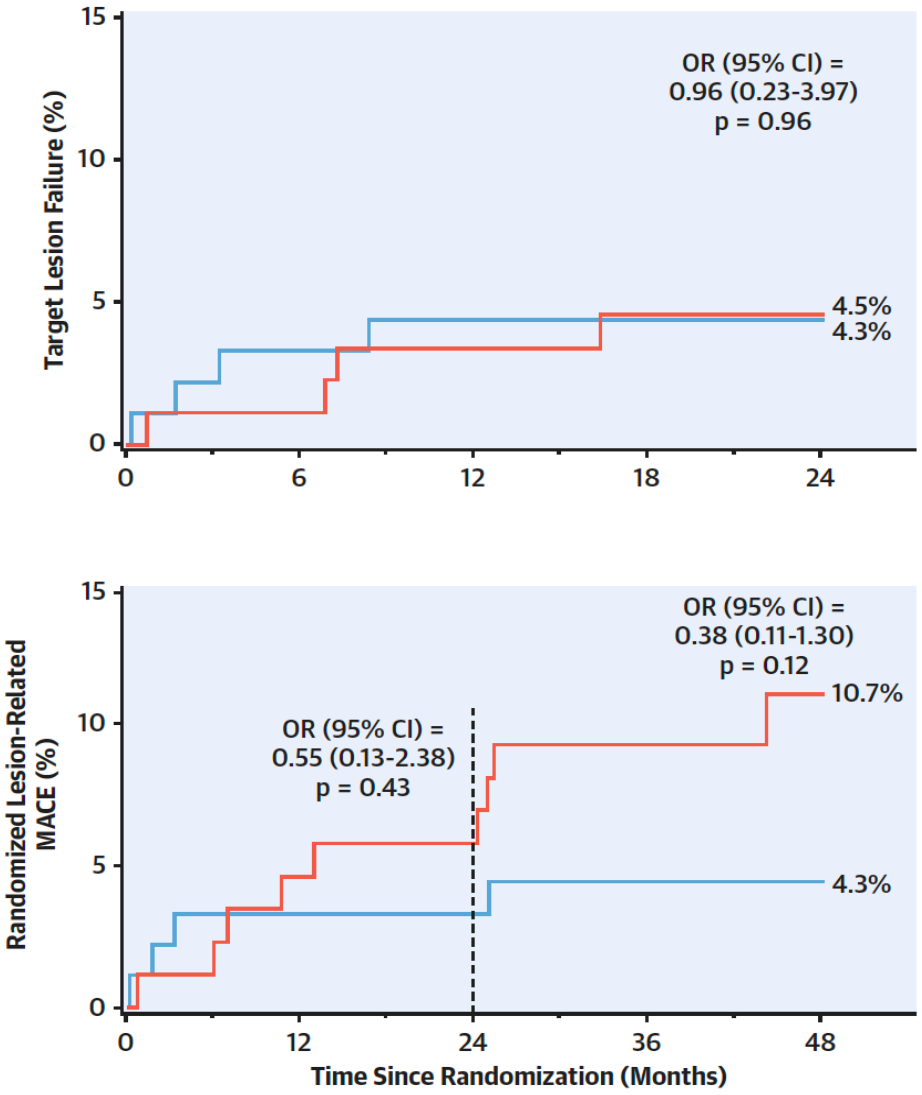
Forget Anatomy?
Forget Physiology??

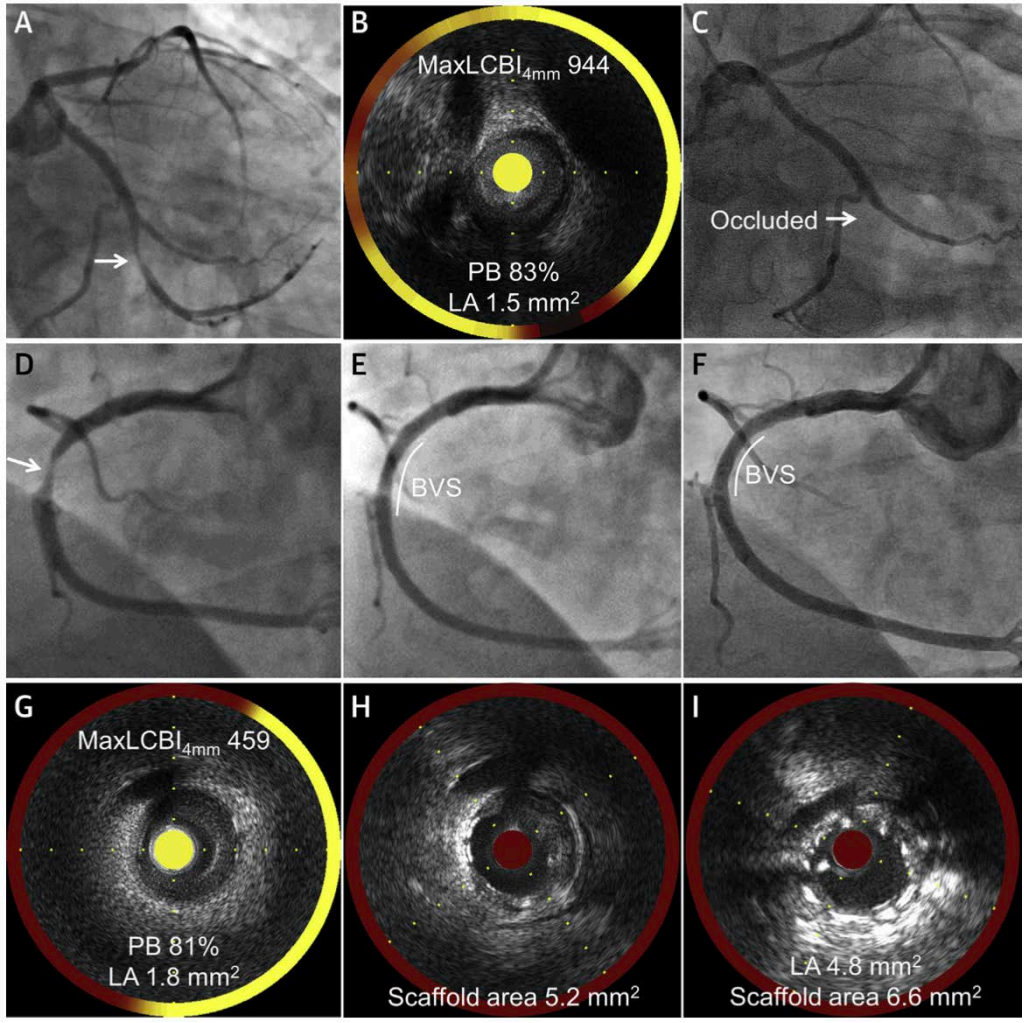


	STENOSIS+	STENOSIS-
HRP+	S+HRP+	S-HRP+
HRP-	S+HRP-	S-HRP-

FORECAST-FLOWER MI-FUTURE-RIPCORD-2

PROSPECT II Study: PROSPECT ABSORB RCT

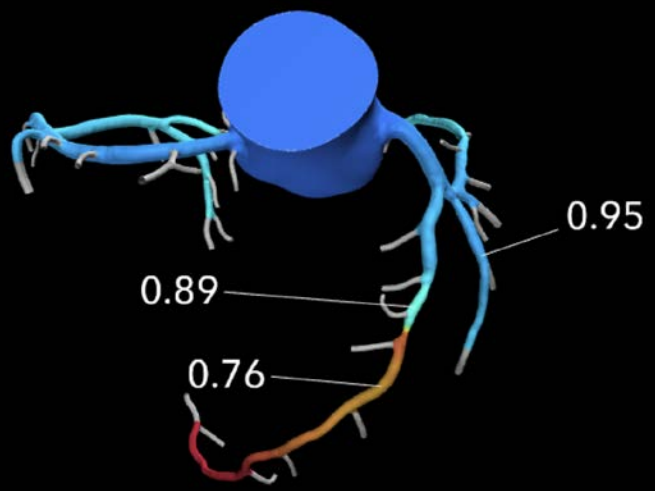




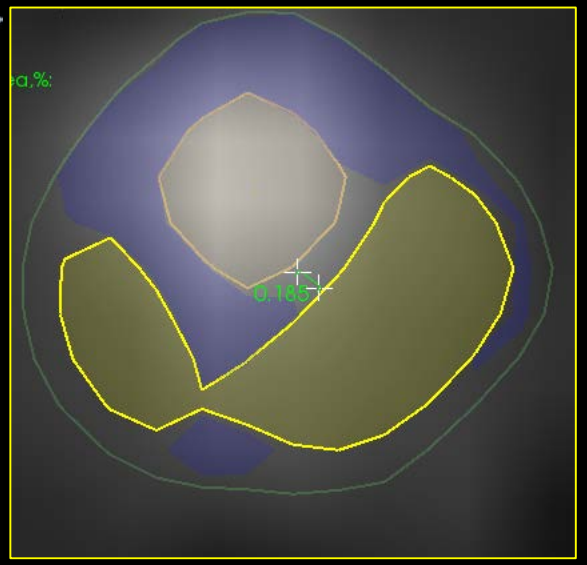
Stone et al. JACC 2020

PLAQUE PROGRESSION IS A MODIFIABLE STEP

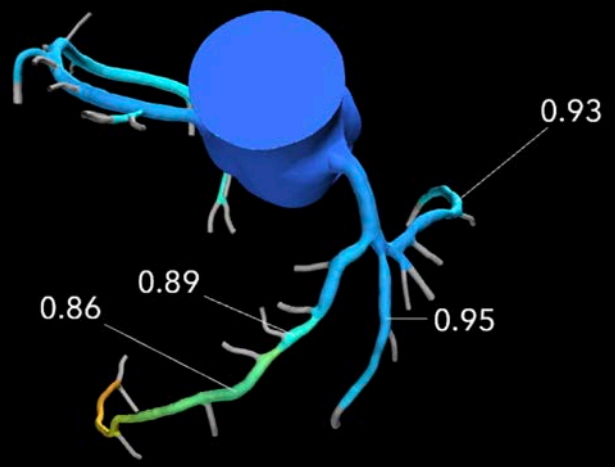
CT-FFR

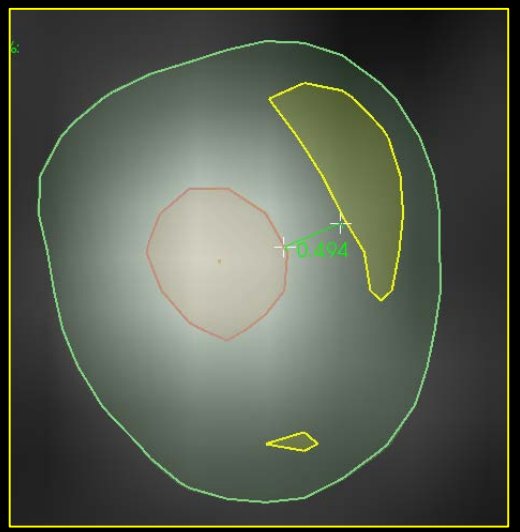


Q-PLAQUE CHARACTERISTICS



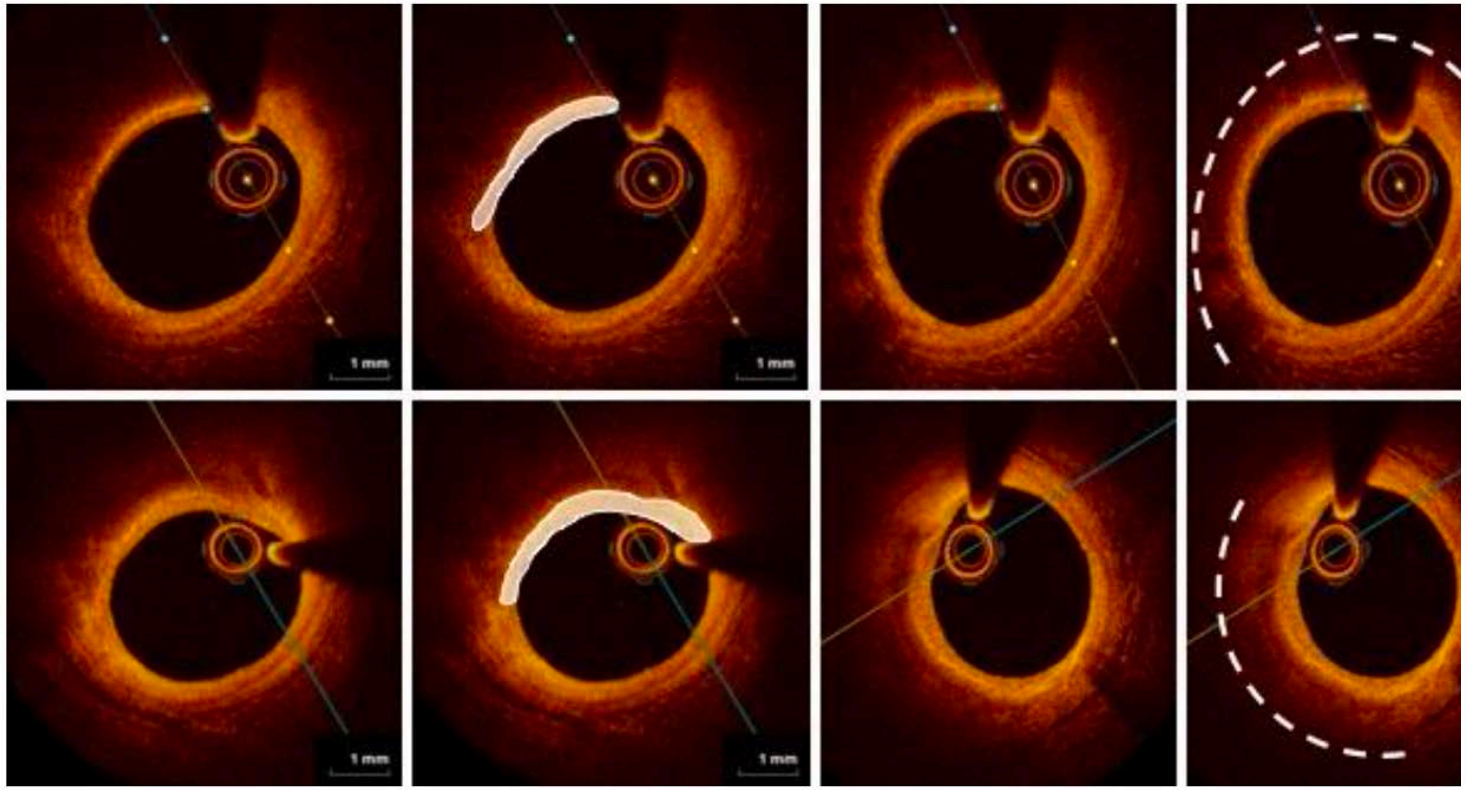
6 mo. Follow Up

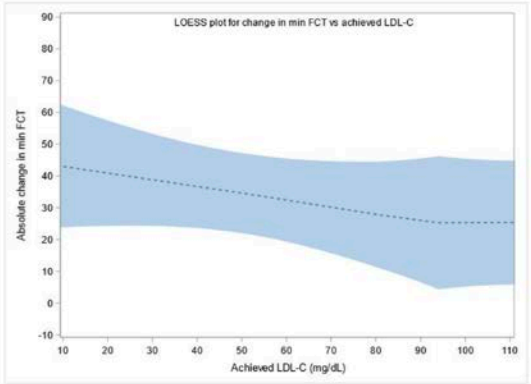


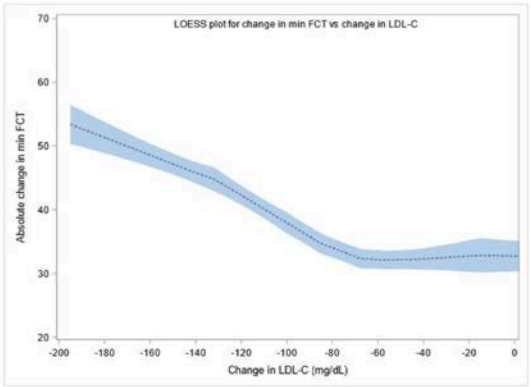


Ahmadi, Leipsic, Narula et al.
JACC Imaging [in press]

HUYGENS STUDY
AT ESC 2021



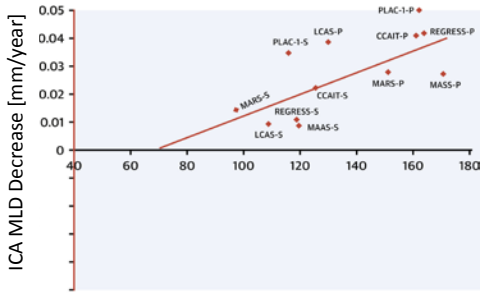


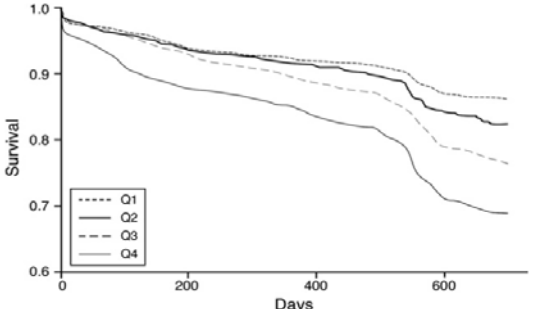


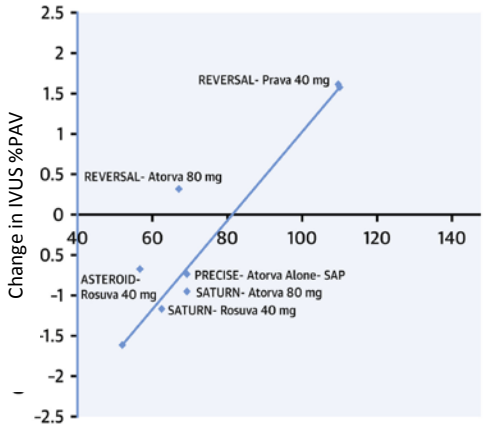
LDL lowering also helps increase FCT!

Nicholls et al. JACC 2010;55:2399-2407

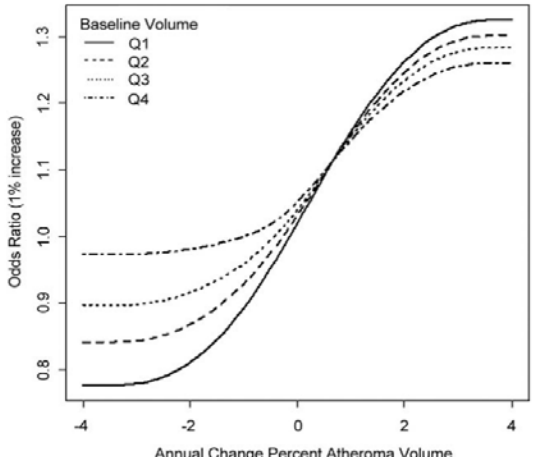
Plaque Progression is Modifiable?



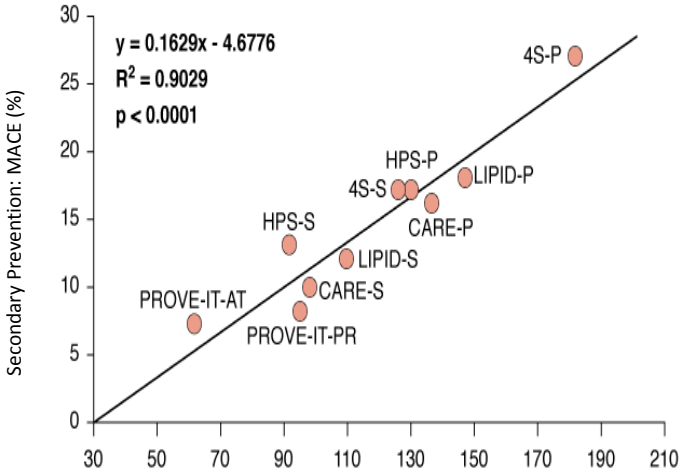


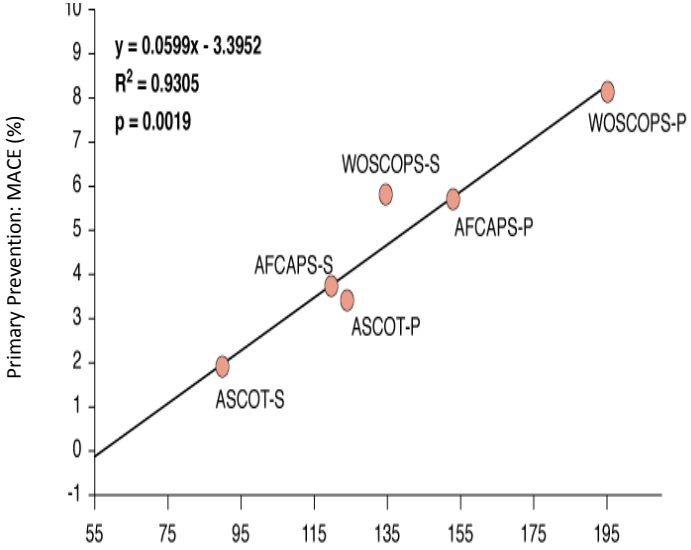


Achieved LDL Cholesterol (mg/dL)



Annual Change in PAV





Achieved LDL Cholesterol (mg/dL)

LLRx halts progression
and even allow regression!

Ahmadi & Narula, JACC 2019; Puri et al. JACC 2015;65:1273-1282; Nicholls et al. JACC 2010;55:2399-2407

2019 ESC/EAS risk-based LDL-C goals have became more aggressive

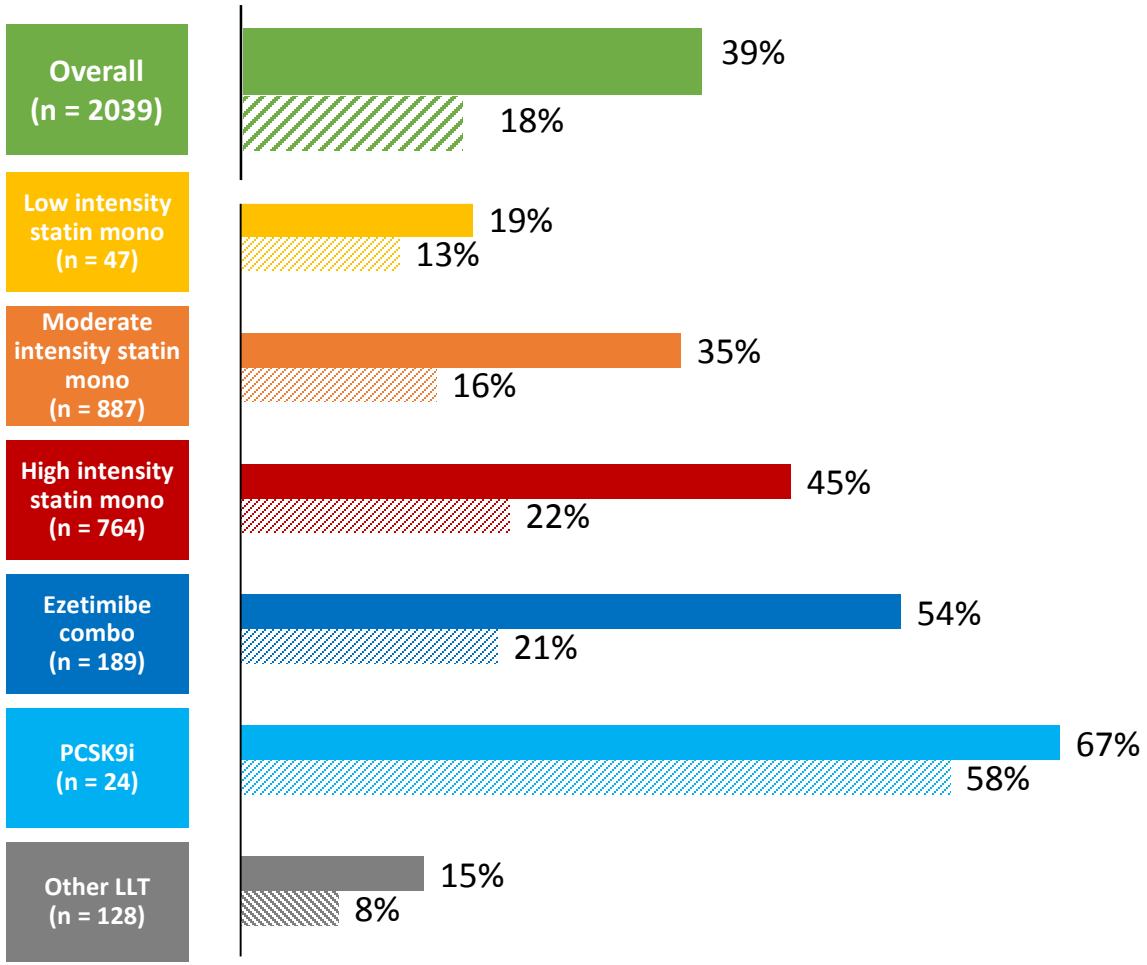
	2016 LDL-C goals	2019 LDL-C goals
Low risk	**<115 mg/dL**	
Moderate risk	**<115 mg/dL**	**<100 mg/dL**
High risk	**50% reduction OR <100 mg/dL**	**50% reduction AND <70 mg/dL**
Very high risk	**50% reduction OR <70 mg/dL**	**50% reduction AND <55 mg/dL**
Second CV event within 2 yrs	**NA***	**50% reduction AND <40 mg/dL**

*Not applicable, extreme high risk patients did not have a specific LDL-C goal in the 2016 guidelines

CV, cardiovascular; EAS, European Atherosclerosis Society; ESC, European Society of Cardiology; LDL-C, low-density lipoprotein cholesterol; NA, not applicable. 1. Catapano AL, et al. *Eur Heart J* 2016;37:2999–3058. 2. Mach F, et al. *Eur Heart J* 2019;41:111–88.

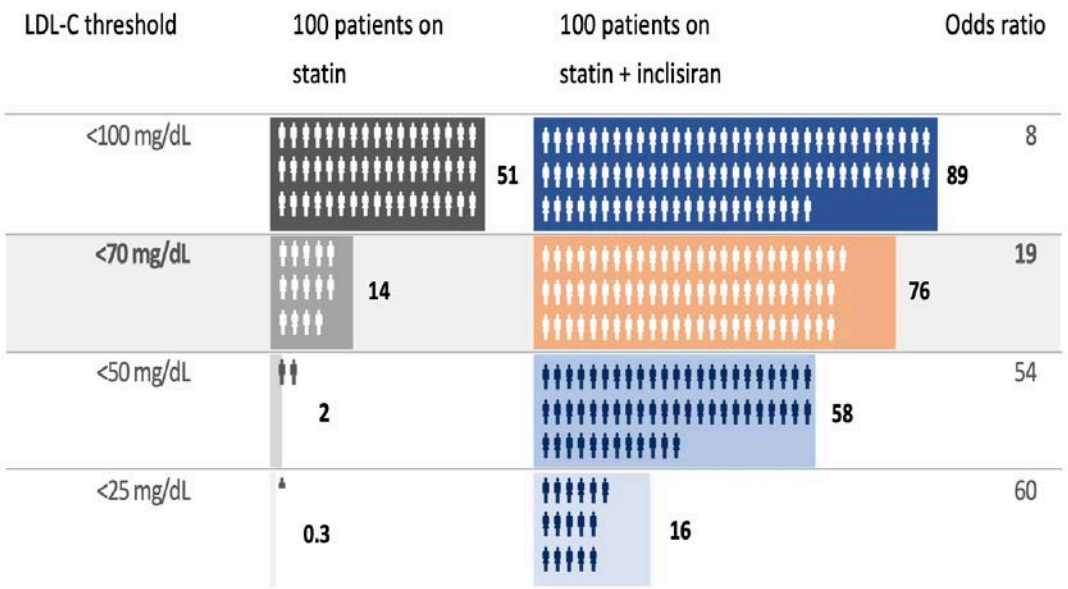
LDL-C goal attainment by LLT in patients with established ASCVD

2016/2019 goal attainment in ASCVD patients



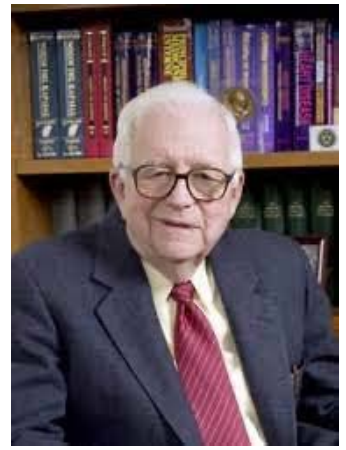
% patients achieving 2016 (solid) and 2019 (hashed) LDL-C goals
Ray K- Da Vinci Registry.

Likelihood of achieving specific LDL-C thresholds with Inclisiran



Likelihood of reaching LDL-C thresholds at Day 510 with Inclisiran
Ray K, Orion-13

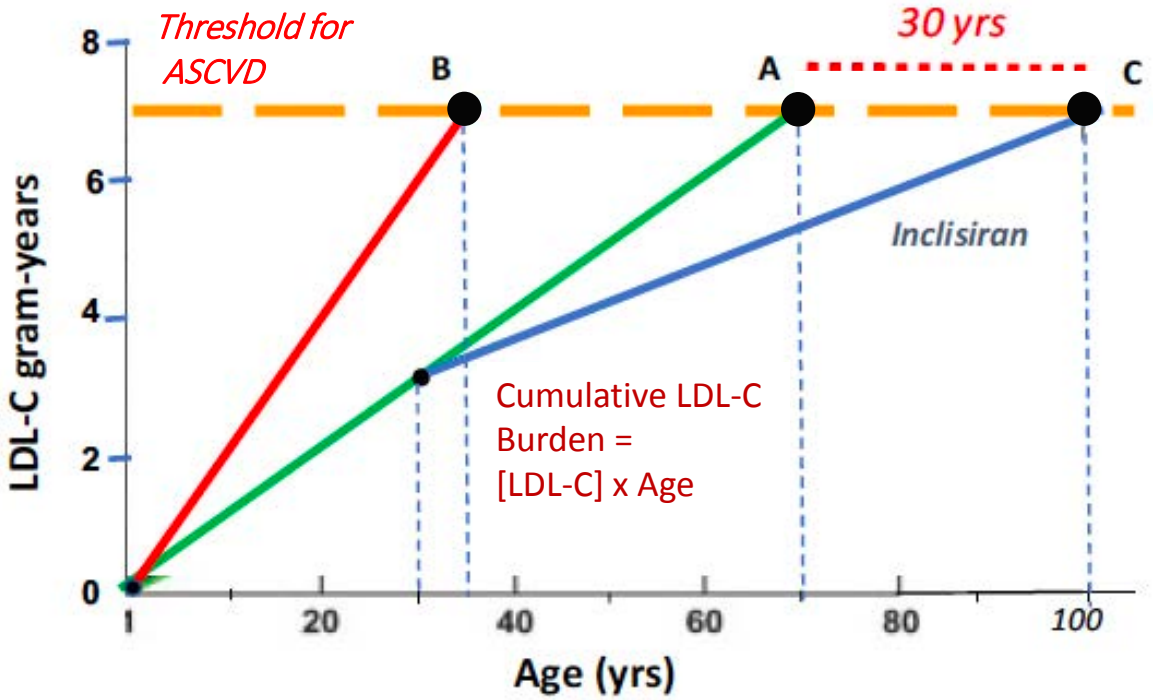
ESC European Society of Cardiology
European Heart Journal (2021)
doi:10.1093/eurheartj/ehab532



Braunwald's Corner

How to live to 100 before developing clinical coronary artery disease: a suggestion

Eugene Braunwald



>51% reduction in LDL cholesterol over 24 weeks by PCSK9 antisense- inclisiran, ie. equivalent to antibody-based inhibition with evolocumab, or alirocumab.

NOVARTIS

Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland

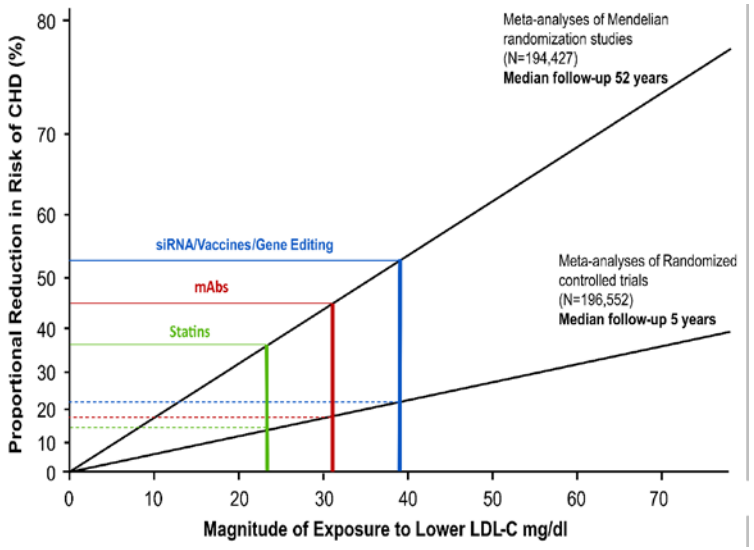
https://www.novartis.com
https://twitter.com/novartisnews

MEDIA & INVESTOR RELEASE

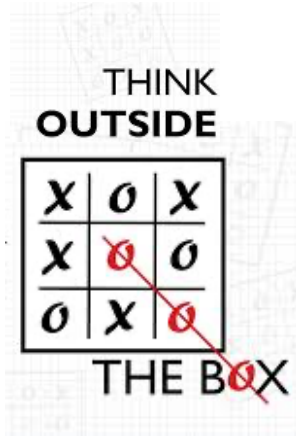
World-first agreement between Novartis and the NHS enables broad and rapid access to first-in-class cholesterol-lowering medicine - INCLISIRAN

- *Agreement follows positive NICE recommendation and commits to deliver Leqvio® (inclisiran) access via a population health management approach identifying eligible patients across England[1]*
- *Over three years ~300,000 patients at high risk of a second cardiovascular event are expected to be treated with inclisiran, a small interfering RNA therapy administered as a 6-monthly maintenance dose‡, in the community setting*
- *Long-term elevated LDL cholesterol (LDL-C) is a known cause of atherosclerotic cardiovascular disease (ASCVD) and a key modifiable risk factor in the prevention of cardiovascular disease[2]*
- *Cardiovascular disease, which can lead to heart attack and stroke, causes more than 1 in 4 deaths across the UK and places a considerable financial burden on the NHS and wider society[3,4]. It is estimated that there are over 3.5 million people living with ASCVD in the UK[5]*
- *NHS agreement is a strong demonstration of Novartis' commitment to increasing access to innovative medicines through pioneering partnerships with health systems*

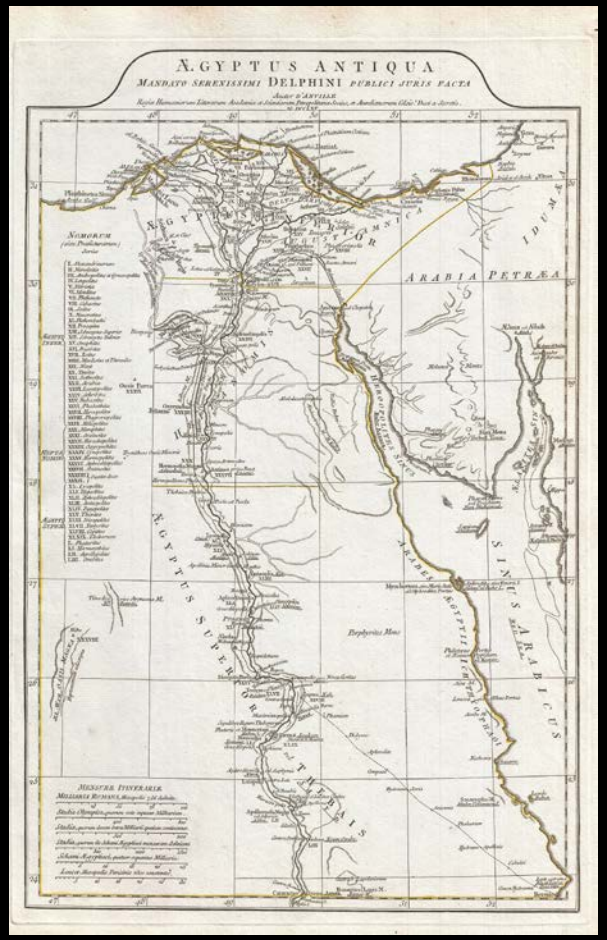
Basel, September 01, 2021

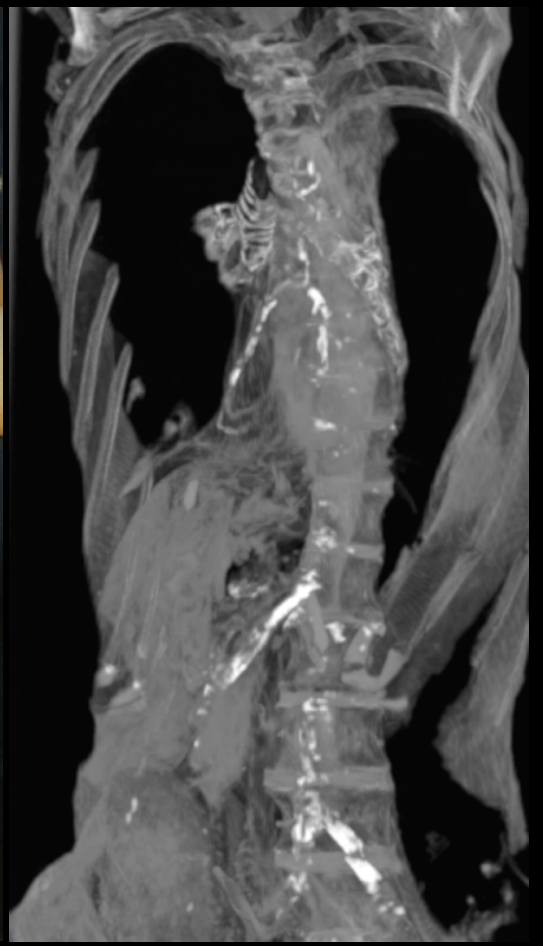


Brandts & Ray. Circ 2020



Hatiay, male scribe, died 45-50 yrs.
New Kingdom, 1570–1293 BCE

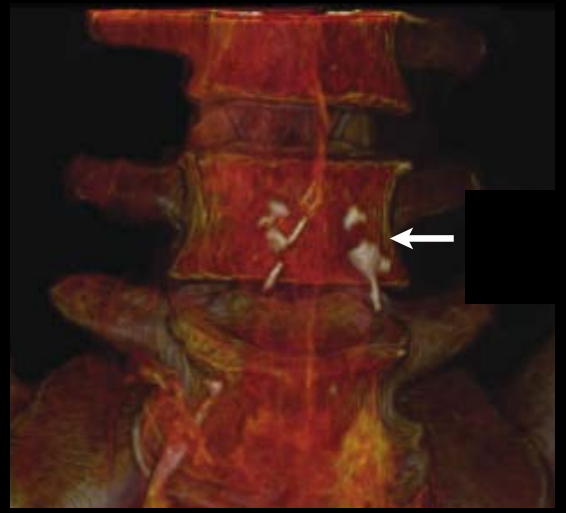




*Beef, wildfowl-goose, bread, fruit, vegetables, cake, wine, beer

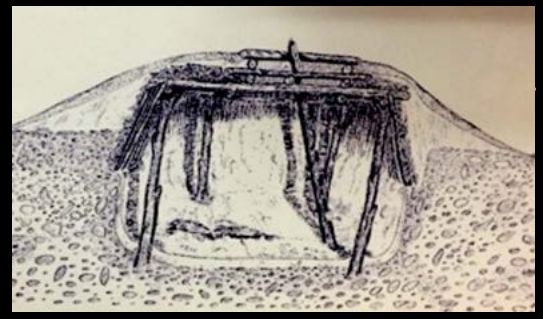
Allam et al. JAMA 2009;302:2091-2094
Thomas, Narula, Wann et al. Glob. Heart 2014

Vascular Calcification and Atherosclerosis, PERU 1000 AD



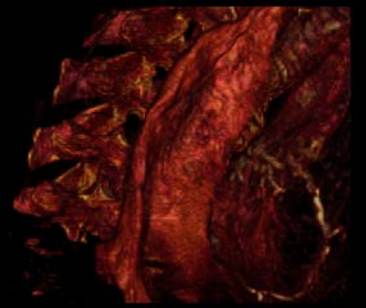
Lima, Peru, May 2012

Thompson, Narula, Thomas et al. Lancet 2013



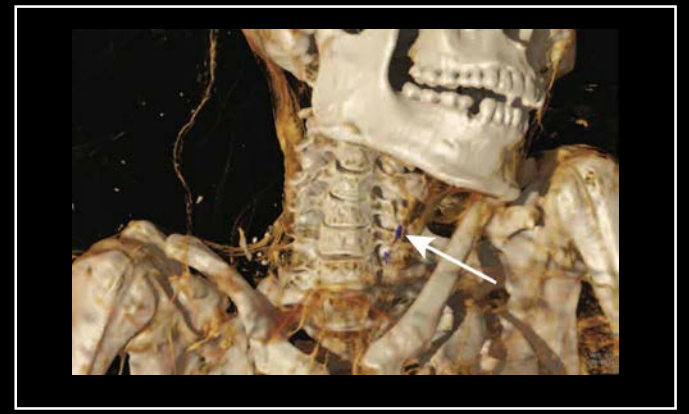
The Unangan Hunter Gatherers

Aleutian Island, 1756-1930 CE

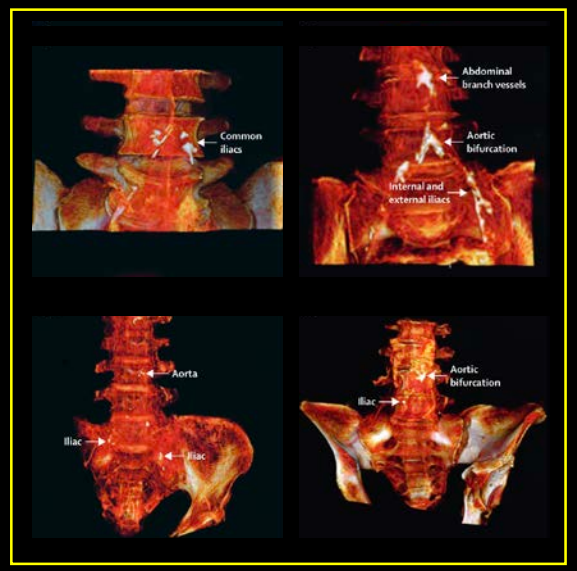


Thompson, Narula, Thomas et al. Lancet 2013

Greenlandic Inuit Mummies, 16th Century



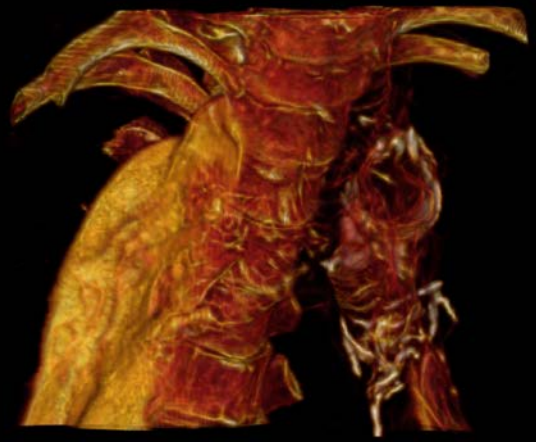
Wann, Narula, Thomas et al. JAMA 2019



Thompson, Narula, Thomas et al.
Lancet 2013

Anasazi Puebloans

SE Utah, NE Arizona, NW New Mexico and SW Colorado



F, 47-51 Yeras

Ötzi the Iceman's Last Meal Included Goat Bacon

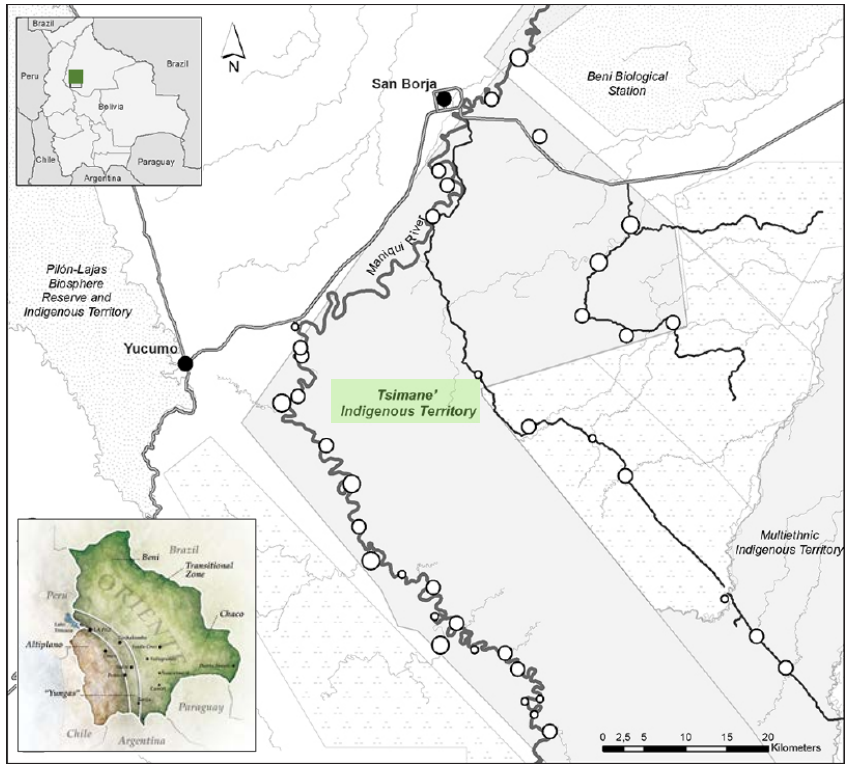
5,300-year-old mummy's stomach contents shows he ate dry-cured meat from a mountain ibex

https://www.smithsonianmag.com/smart-news/otzi-

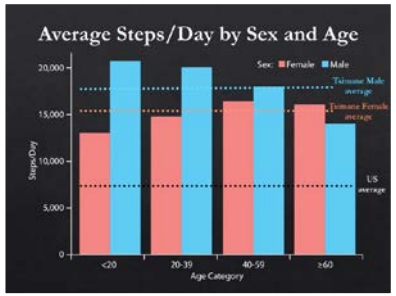
Courtesy: Albert Zink

Murphy WA, et al. Radiology 2003;226:614-629

Seeking Living Population with Low Atherosclerotic Burden Bolivian Amazon…



CAN CORONARY ARTERY DISEASE BE ELIMINATED IN OUR LIFETIME?

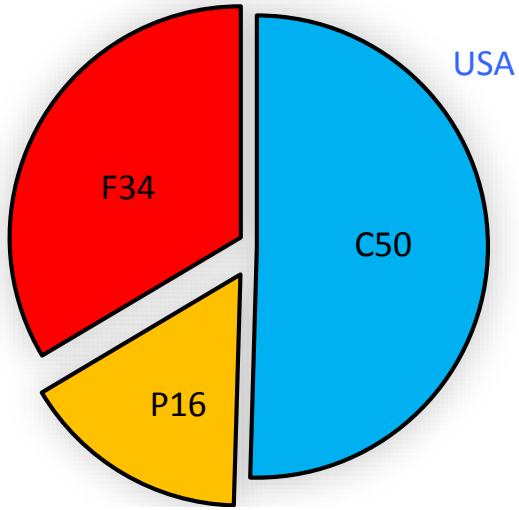


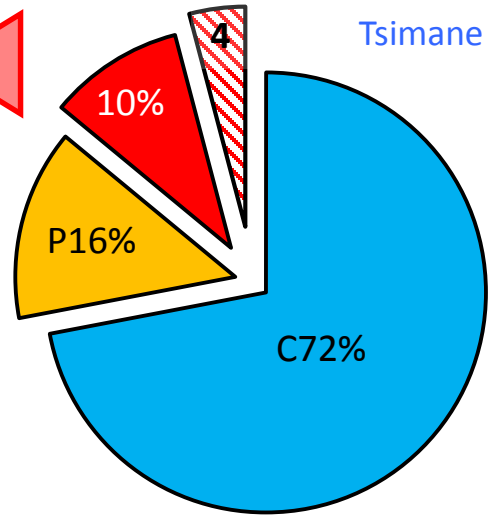
15,000 steps/day
<10% sedentary time

No air pollution

LDL 70
BP 116/73
FBS ≈79, BMI 24

No or minimal CAC throughout life





Very low sat fat, No trans fats
Minimal added sugar

However, they do know how to live better than us!

Kaplan et al. Lancet 2017

Heart Healthy in the Amazon

Leer en español

By GRETCHEN REYNOLDS APRIL 6, 2017

How to maintain a healthy heart is a surprisingly contentious question. Diet and exercise are crucial, everyone agrees — but the ideal specifics and the relationships among them remain mysterious. Some experts recommend avoiding dietary fats; others endorse fat and low carbohydrates. The impact of the high levels of inflammation on heart disease is disputed. And almost no one can agree about how much or what type of exercise is optimal.

But a study published last month in The Lancet points the way to resolving some of these issues by focusing on the Tsimane, a group of subsistence farmers and hunters living in Bolivia along a tributary of the Amazon River.

HOME SEARCH

The New York Times

WELL | LIVE

Learning From Our Parents' Heart Health Mistakes

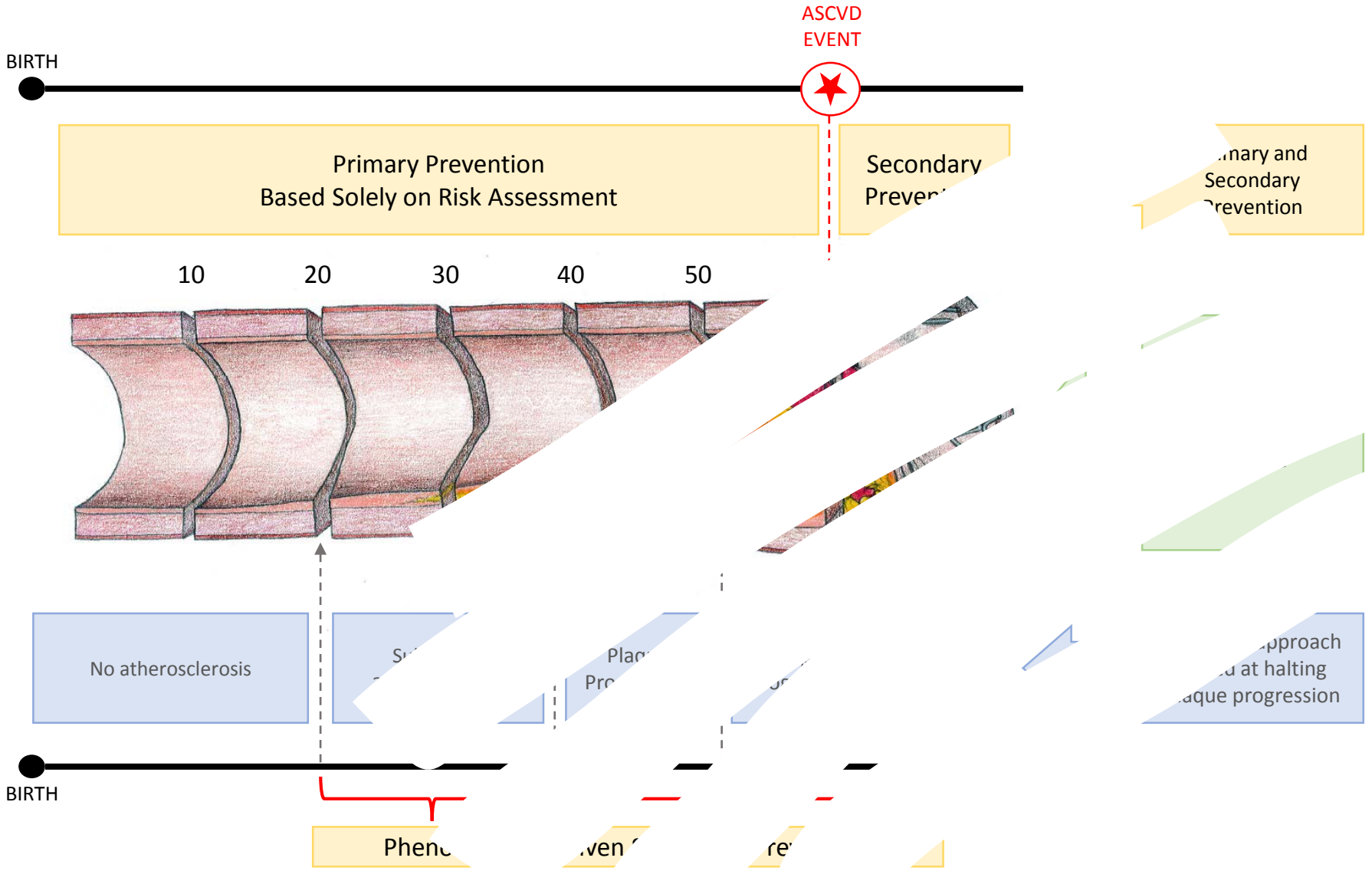
Personal Health

By JANE E. BRODY APRIL 10, 2017

Paul Rogers

Narrowed, aging blood vessels, which put most older American adults at risk for heart disease and strokes, are not inevitable. This fact was underscored by a newly published study of a population in the Bolivian Amazon. Among these indigenous South Americans, known as the Tsimane (pronounced chee-MAH-nay), coronary atherosclerosis was found to be one-fifth as common than in the United States. CT scans of the hearts of 705 Tsimane adults aged 40 to 94 revealed that nearly nine in 10 had clean coronary arteries and faced no risk of heart disease. The research team estimated that an 80-year-old in the Tsimane group has the same vascular age as an American in his mid-50s.

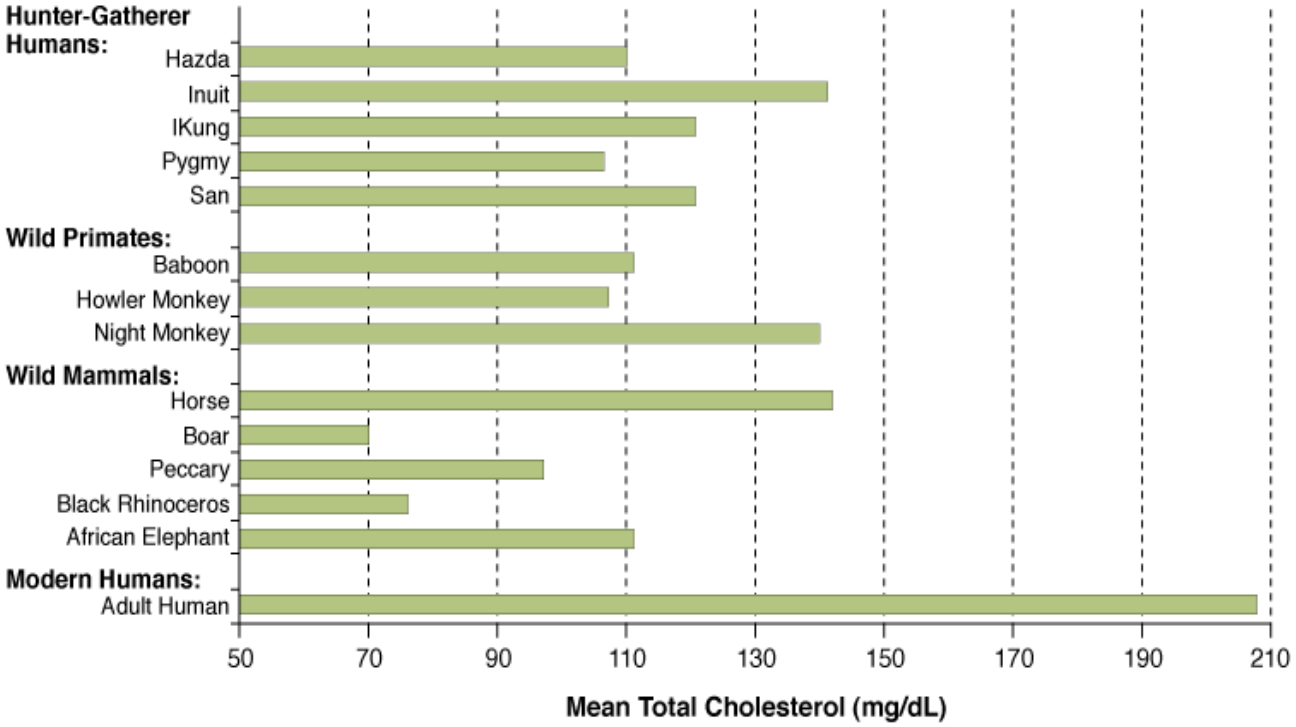
Is plaque progression an essential step?



Wiping our sins away!

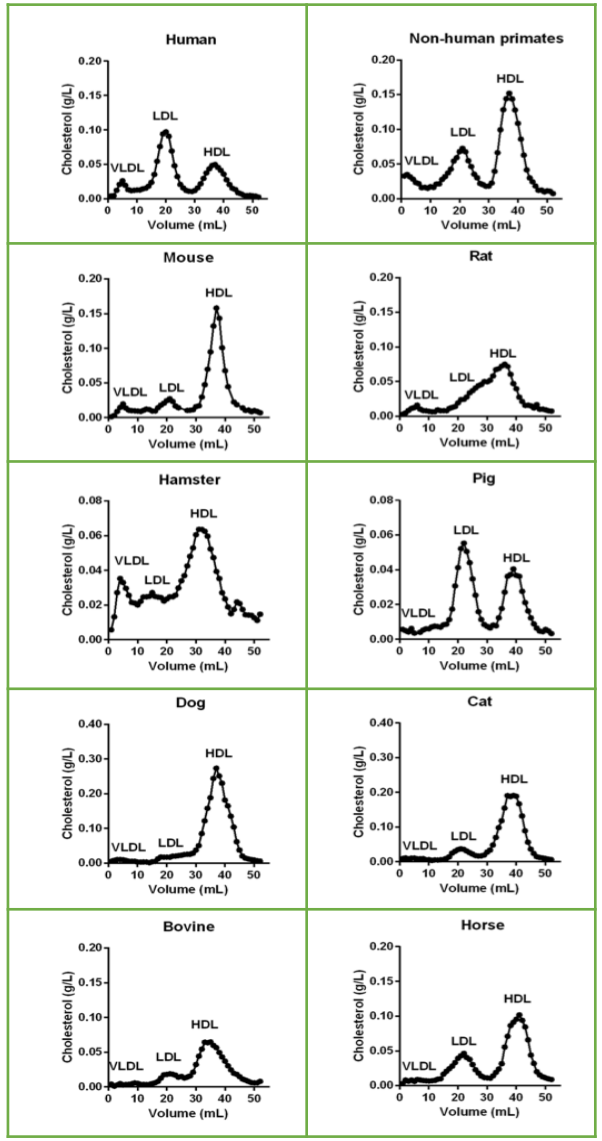
Ahmadi, Narula et al. JACC 2019

WHAT IS THE IDEAL CHOLESTEROL LEVEL?



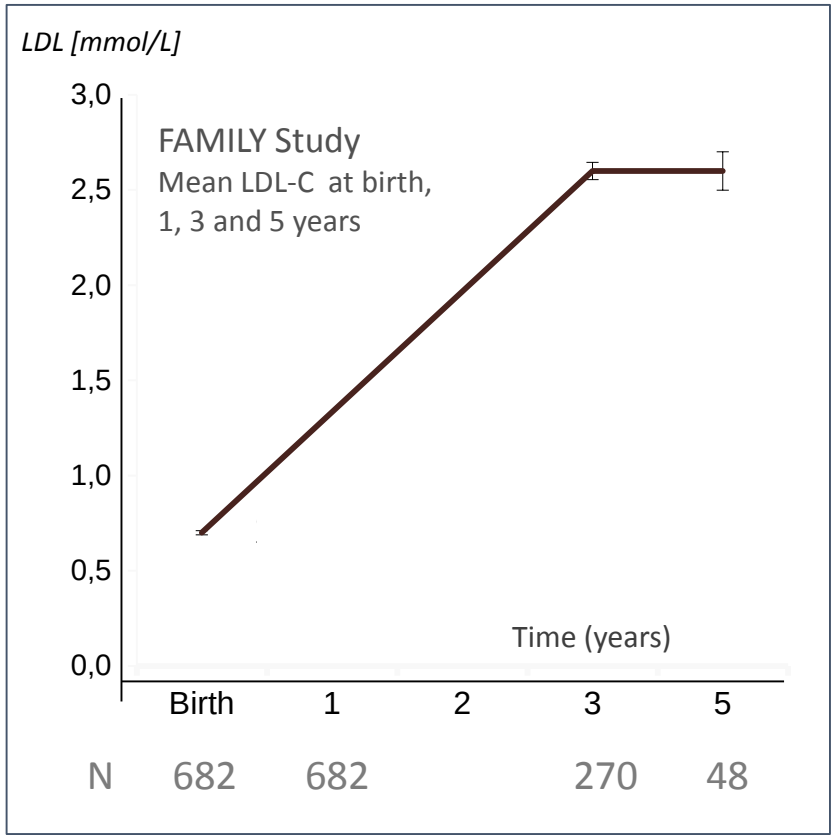
James H. O'Keefe Jr, Robert Vogel et al. JACC 2004;43:2142-2146

Lipoprotein profile of Humans and selected animals by FPLC

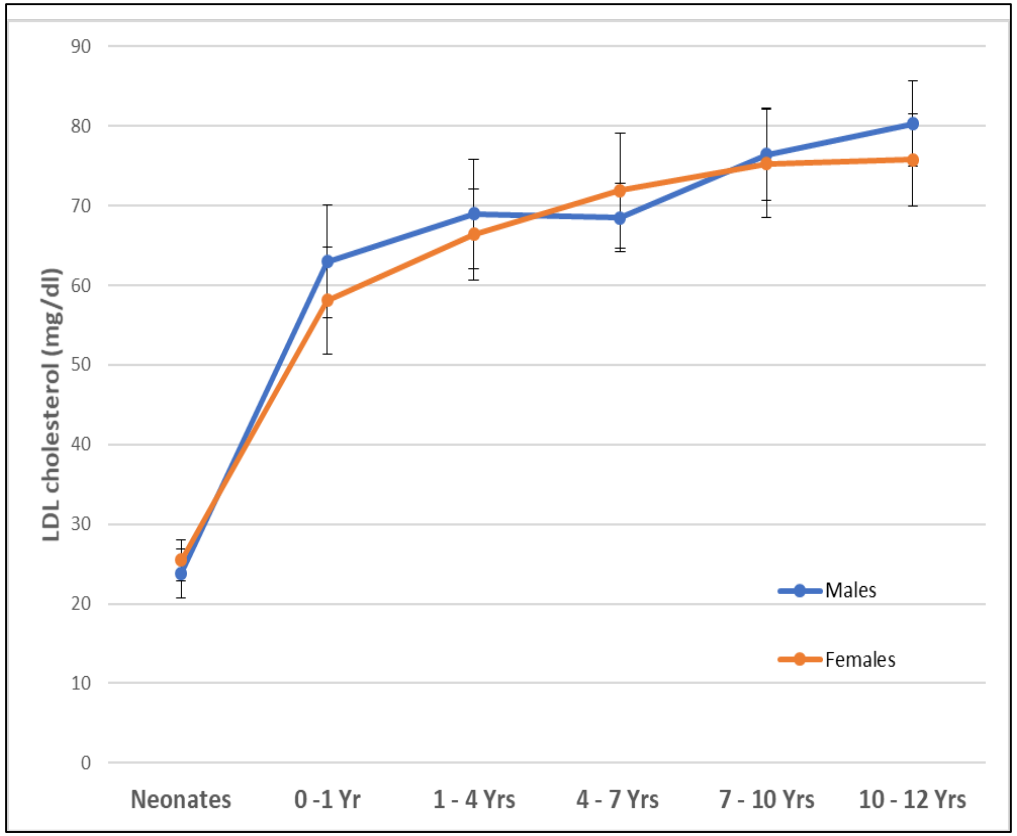


Kaabia Z et al. *Sci Rep* 2018;8:15893

Evolution of LDL Cholesterol Levels

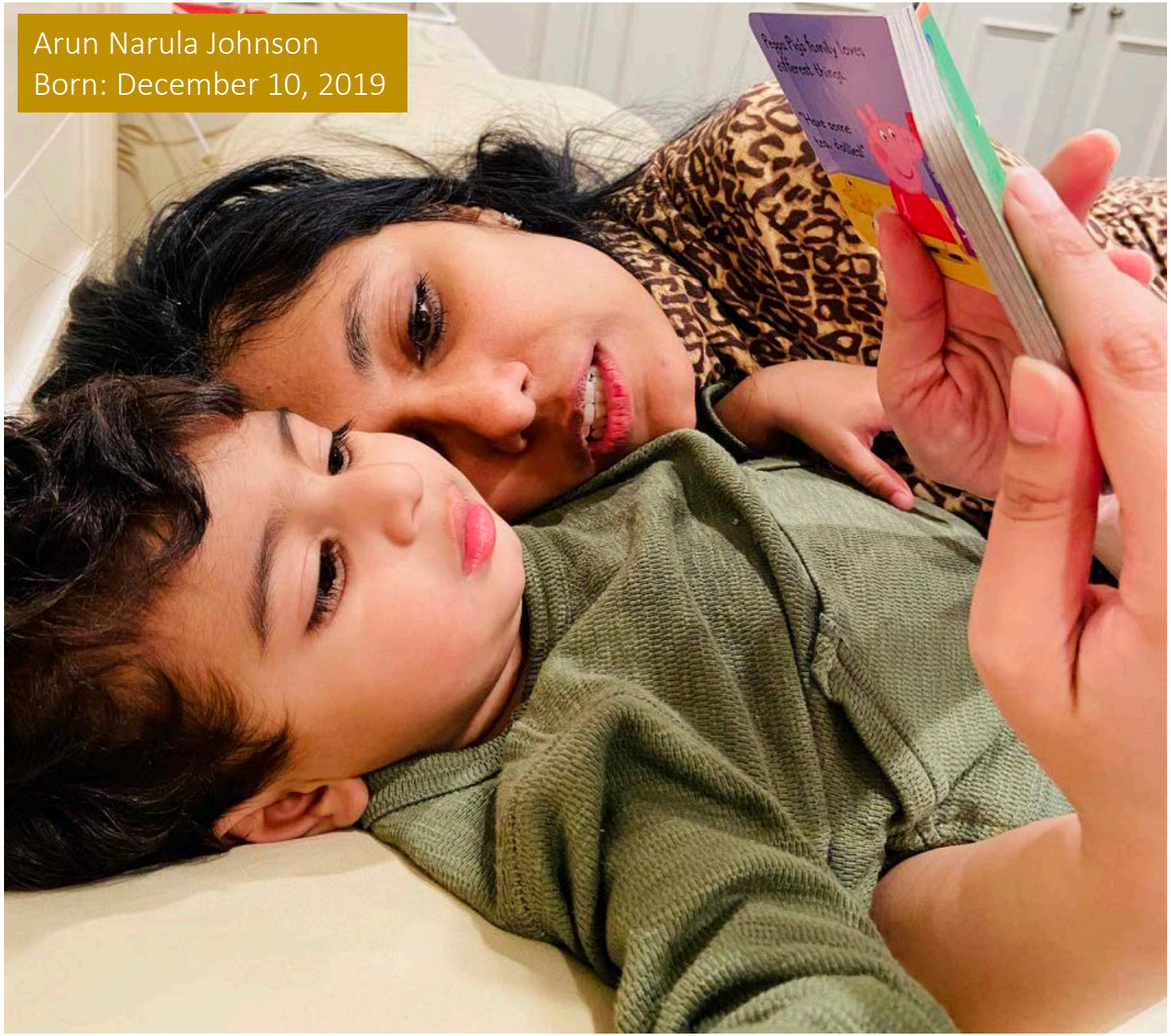


Courtesy: S. Anand & S. Yusuf, PHRI, Canada



Zubin, Hill, Luscher, Narula, EHJ 2021

What LDL did God give us!



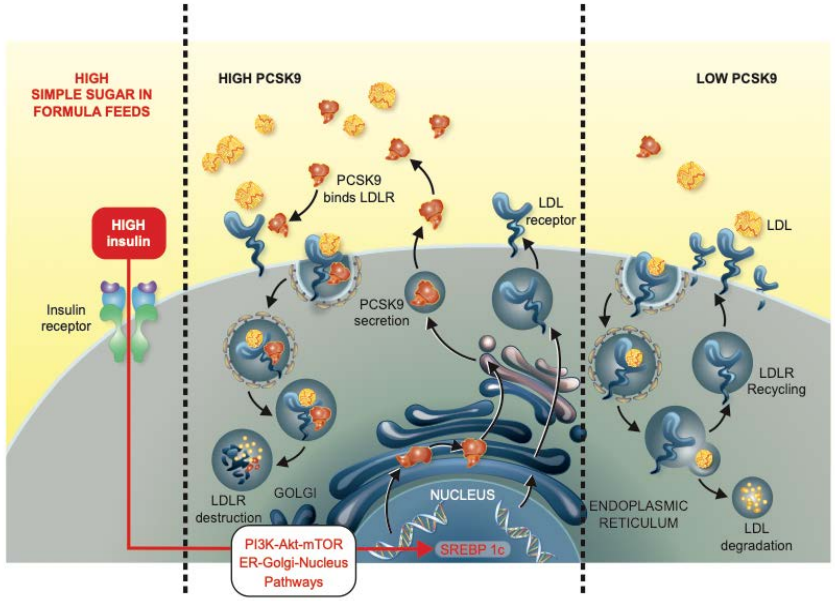
ESC European Society of Cardiology
European Heart Journal (2020) 00, 1–4
doi:10.1093/eurheartj/ehaa868

VIEWPOINT
Epidemiology

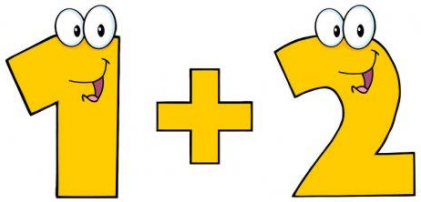
High-sugar feeding and increasing cholesterol levels in infants

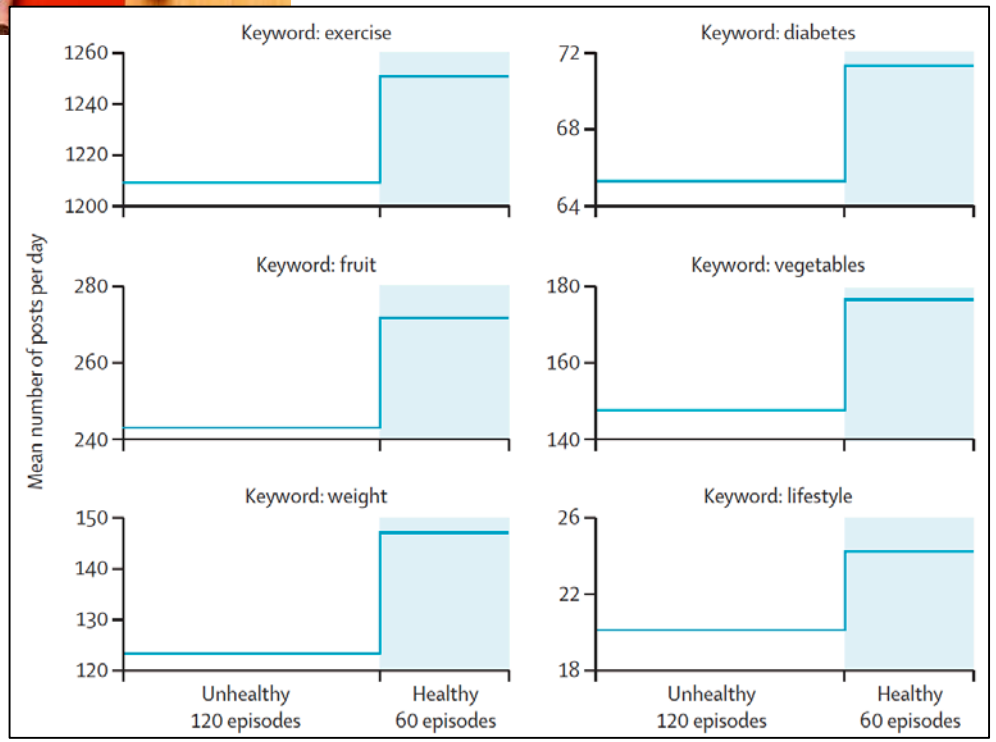
Petra Zubin Maslov[1], Joseph A. Hill[2], Thomas F. Lüscher[3,4], and Jagat Narula[1]*

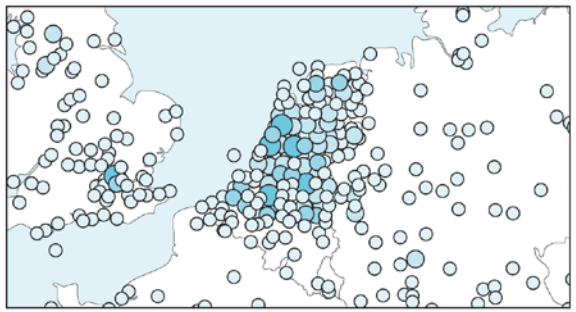
Hypercholesterolaemia is an important risk factor for cardiovascular disease. Both total and LDL cholesterol levels are three-fold higher at the end of the first year of life and about four-fold higher in adulthood compared with the neonatal period. In the USA, only 25% of infants are exclusively breastfed and simple carbohydrate-rich formulas are preferentially consumed. Spikes in fasting glucose and insulin have been reported in formula-fed infants and are associated with higher levels of proprotein convertase subtilisin/kexin type 9, suggesting a potential link between high simple sugar intake and consequent increase in LDL cholesterol in early childhood.

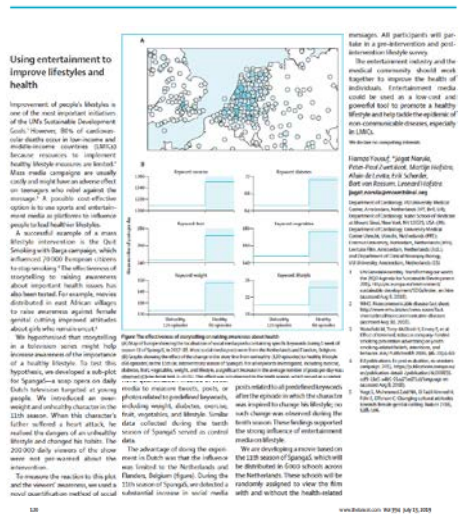


National Dutch Television; Alain deLevita









Hofstra & Narula, Lancet 2021

He says to Brutus:
“Men at sometime were masters of their fates. The fault, dear Brutus, is not in our stars, but in ourselves…”

(I. ii. 140–142)

The Death of Diseases

That our grand children will not know what CVD is and ask us … **“Granpa or Granma… it must have been a terrible time when there were all those nasty diseases….plague, smallpox, polio and heart disease…Why did those diseases die?”**

- Salim Yusuf 2012

…eliminate, eradicate, rule out, annihilate, exclude, wipe out, remove, liquidate, get rid of, reject, do away with…

The Journey of 30 Years in Cardiovascular Research




Does Endomyocardial Biopsy Aid in the Diagnosis of Active Rheumatic Carditis?

Jagat Narula, MD; Prem Chopra, MD; Kewal K. Talwar, MD; K. Srinath Reddy, MD; Ramachandran S. Vasan, MD; Rajendra Tandon, MD; Madan L. Bhatia, MD; James F. Southern, MD, PhD

Circulation
Volume 94, Issue 1, 1 July 1996; Pages 73-82
https://doi.org/10.1161/01.CIR.94.1.73

ARTICLE

Echocardiographic Evaluation of Patients With Acute Rheumatic Fever and Rheumatic Carditis

Ramachandran S. Vasan, Savitri Shrivastava, Manam Vijayakumar, Rajiv Narang, Bradford C. Lister, and Jagat Narula

Circulation
Volume 100, Issue 14, 5 October 1999; Pages 1576-1581
https://doi.org/10.1161/01.CIR.100.14.1576

CURRENT PERSPECTIVE

Diagnosis of Active Rheumatic Carditis

The Echoes of Change

Jagat Narula, Y. Chandrasekhar, and Shahbudin Rahimtoola

The New England Journal of Medicine

APOPTOSIS IN MYOCYTES IN END-STAGE HEART FAILURE

Jagat Narula, M.D., Ph.D., Nezam Haider, Ph.D., Renu Virmani, M.D., Thomas G. DiSalvo, M.D., Frank D. Kolodgie, Ph.D., Roger J. Hajjar, M.D., Ulrich Schmidt, M.D., Marc J. Semigran, M.D., G. William Dec, M.D., and Ban-An Khaw, Ph.D.

nature medicine

01 December 2001

Annexin-V imaging for noninvasive detection of cardiac allograft rejection

Jagat Narula, Elmo R. Acio, Navneet Narula, Louis E. Samuels, Billy Fyfe, Diana Wood, Jane M. Fitzpatrick, P.N. Raghunath, John E. Tomaszewski, Christine Kelly, Neil Steinmetz, Allan Green, John F. Tait, Jeffrey Leppo, Francis G. Blankenberg, Diwakar Jain & H. William Strauss

ORIGINAL INVESTIGATIONS

Plaque Characterization by Coronary Computed Tomography Angiography and the Likelihood of Acute Coronary Events in Mid-Term Follow-Up

Sadako Motoyama, MD, PhD,*† Hajime Ito, MD, PhD,* Masayoshi Sarai, MD, PhD,* Takeshi Kondo, MD, PhD,* Hideki Kawai, MD, PhD,* Yasuomi Nagahara, MD,* Hiroto Harigaya, MD, PhD,*† Shino Kan, MD,*† Hirofumi Anno, MD, PhD,† Hiroshi Takahashi, BSc,‖ Hiroyuki Naruse, MD, PhD,* Junichi Ishii, MD, PhD,* Harvey Hecht, MD,† Leslee J. Shaw, PhD,¶ Yukio Ozaki, MD, PhD,* Jagat Narula, MD, PhD†

EDITORIAL COMMENT

Noninvasive Detection of Vulnerable Coronary Plaques

Locking the Barn Door Before the Horse Is Stolen*

Eugene Braunwald, MD

Boston, Massachusetts

Coronary atherosclerosis in indigenous South American Tsimane: a cross-sectional cohort study

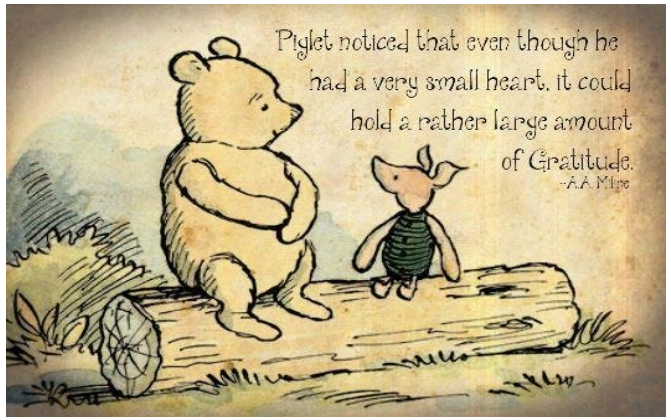
Atherosclerosis across 4000 years of human history: the Horus study of four ancient populations

JAMA Cardiology | Special Communication

Time to Add a Fifth Pillar to Bedside Physical Examination

Inspection, Palpation, Percussion, Auscultation, and Insonation

Jagat Narula, MD, PhD; Y. Chandrashekhar, MD; Eugene Braunwald, MD



Pathology



CT Angiography




Mummies +




Media, Entertainment