

A Message from your Heart; Answers for
Cardiovascular Disease
International College of Integrative Medicine
March 6-10, 2019 Philadelphia.

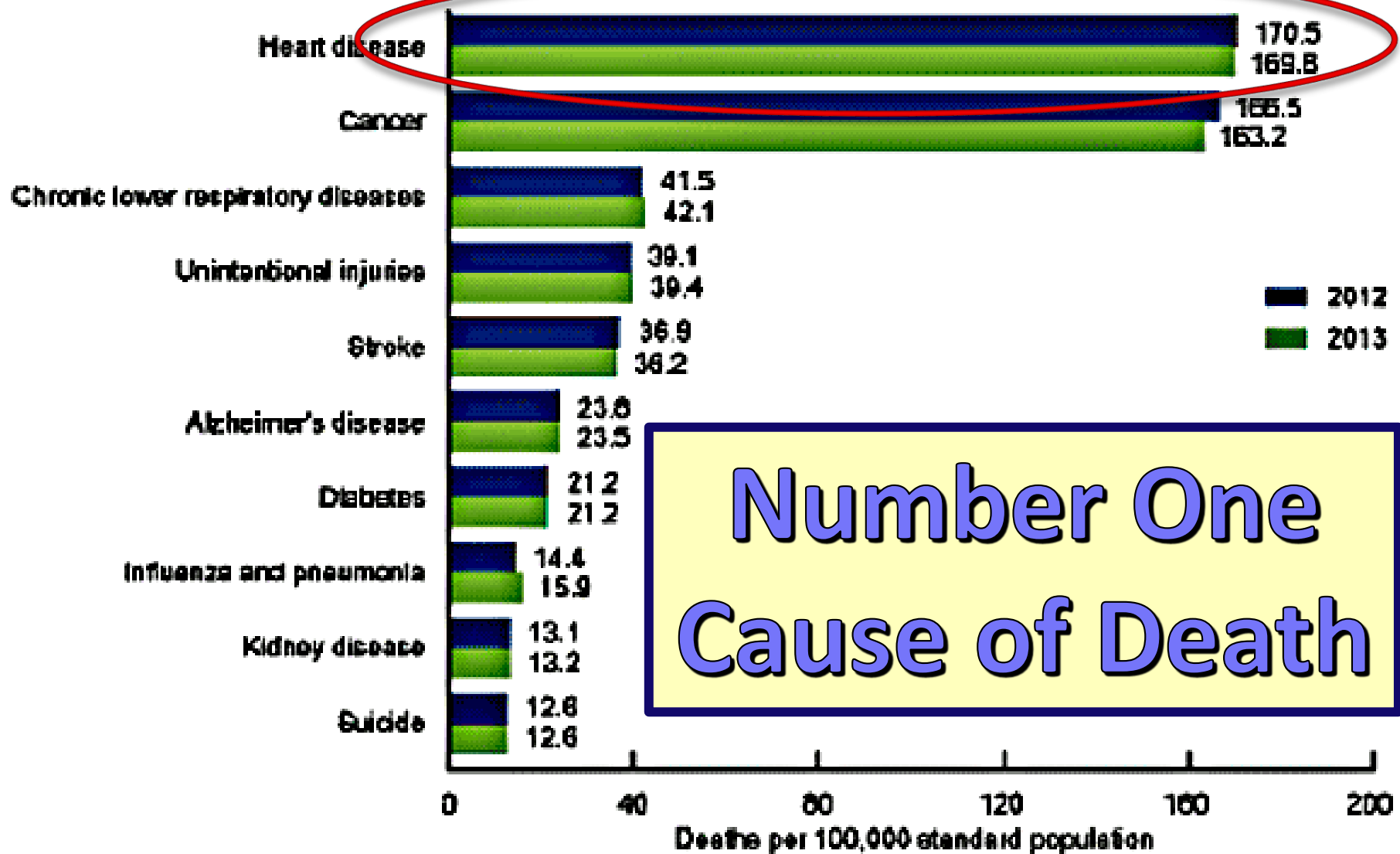
Cardiovascular Disease, Hormones and Coronary Artery Calcium Scores

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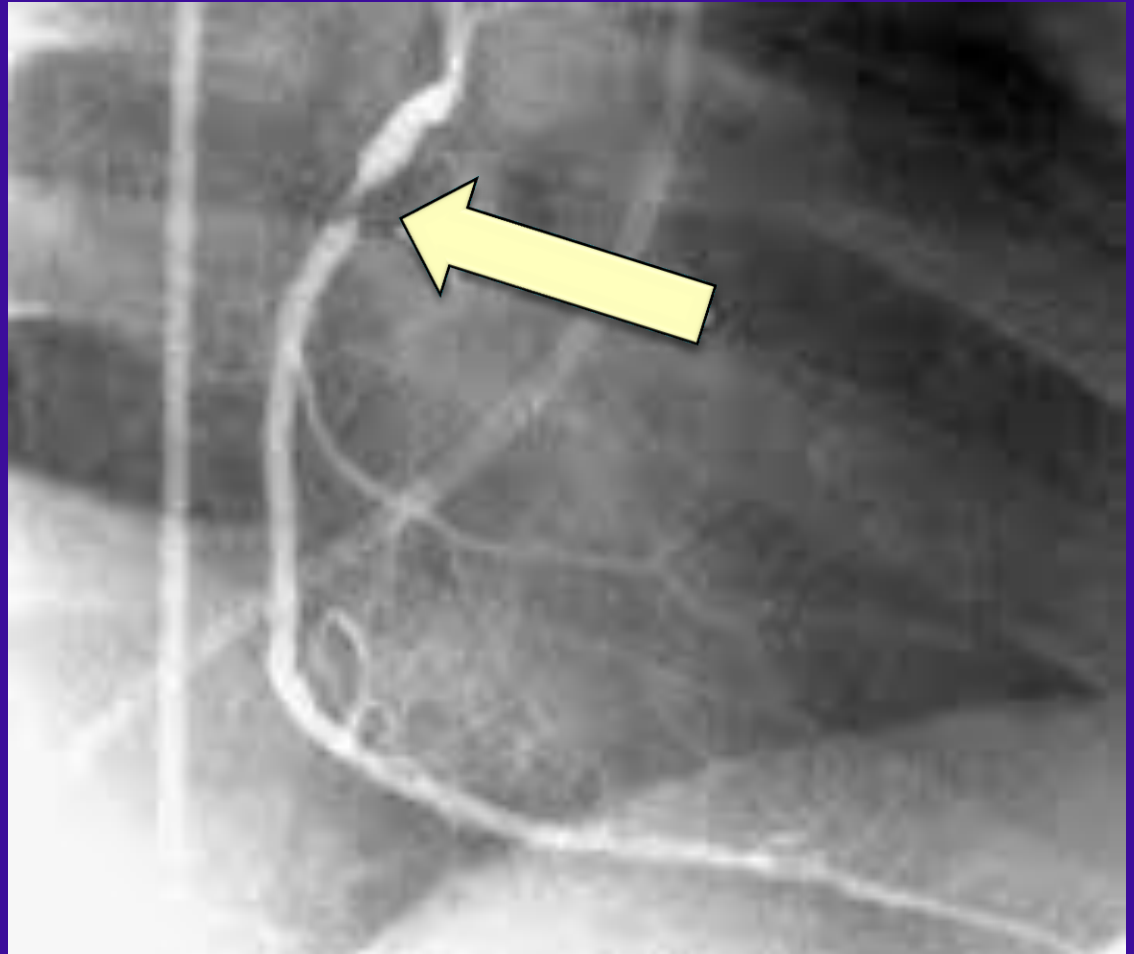
Financial Disclosure : NONE to report

Slides Available At: <https://jeffreydachmd.com>

Coronary Artery Disease

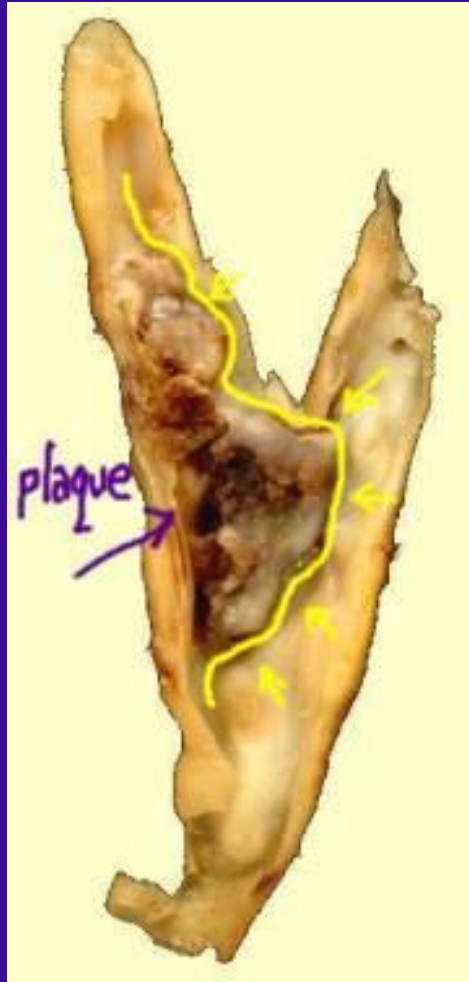


Atherosclerotic Disease



Atherosclerotic Plaque

- Carotid Bifurcation



- Abdominal Aorta

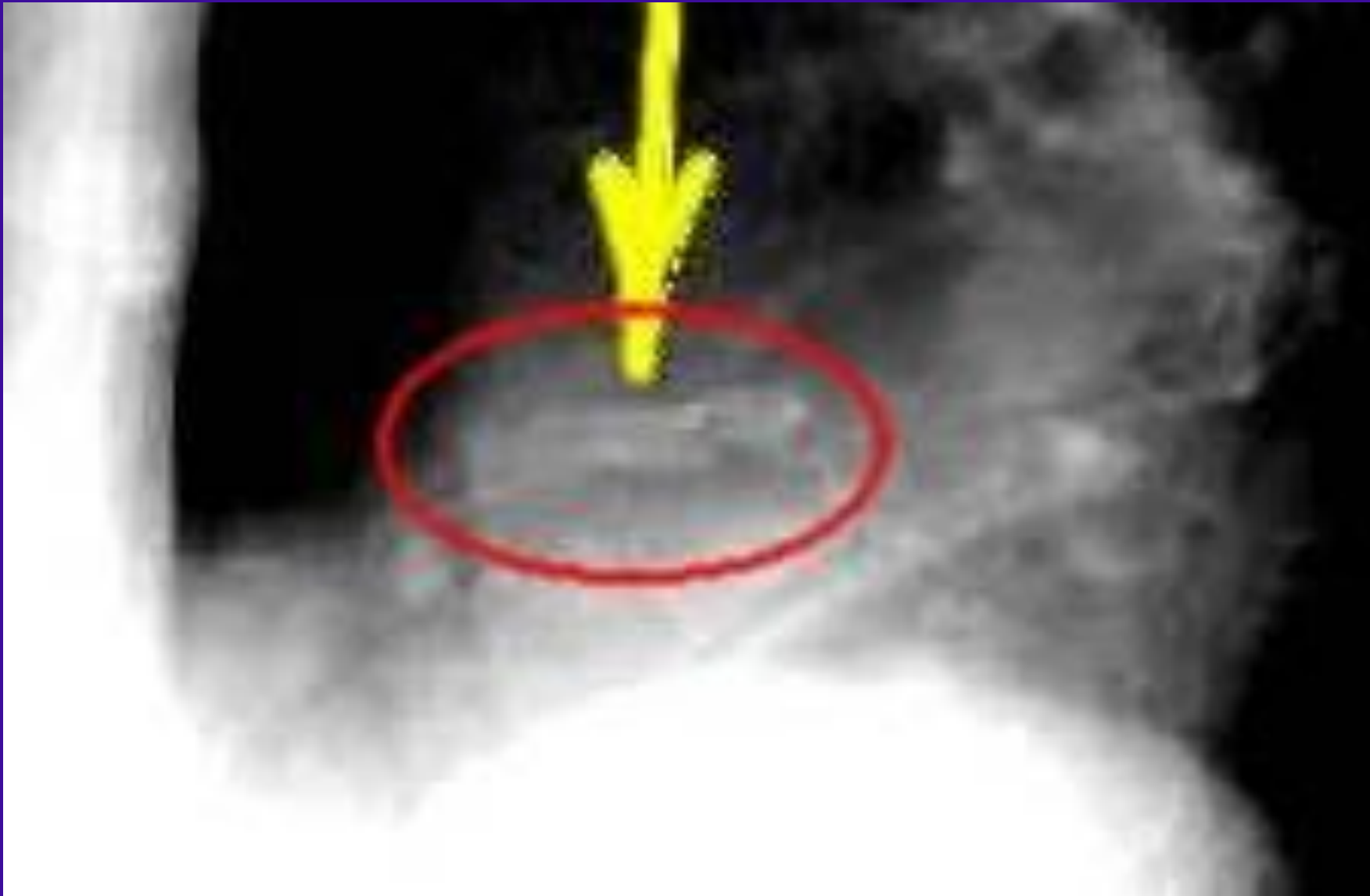


CXR Coronary Artery Calcification



- Calcified LAD on Lateral Chest X Ray
- Difficult to See Finding
- Coronary Artery Calcification X-Ray Marker for CAD.

CXR Coronary Artery Calcification



CAT Scan

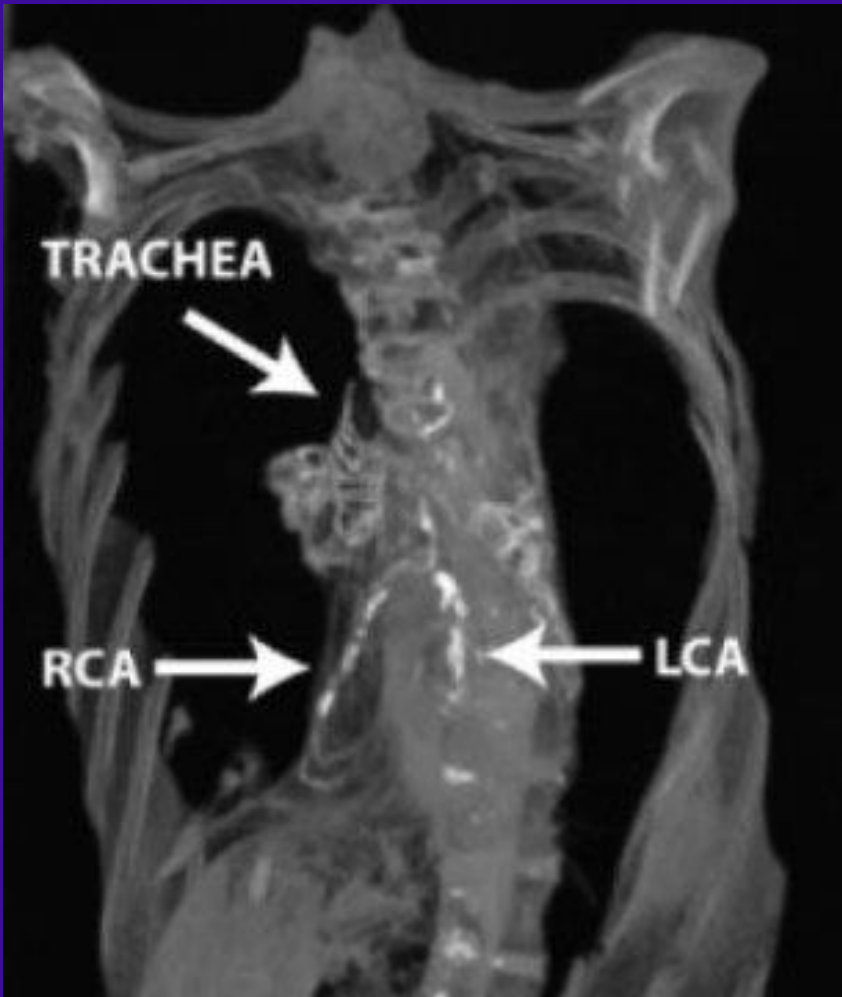
Coronary Artery Calcification



- CAT SCAN Showing Calcified LAD - Left Anterior Descending Artery
- CAT Allows Quantify Amount of Calcium-
- Calcium Score

Orakzai, S. H., et al. "Measurement of coronary artery calcification by electron beam computerized tomography in persons with chronic spinal cord injury: evidence for increased atherosclerotic burden." *Spinal Cord* 45.12 (2007): 775.

Coronal CAT – Three Vessel CAD



- First Person in Human History Diagnosed w/ Coronary Artery Disease.
- Egyptian Princess Ahmose-Meryet-Amon, 1550 BC.
- Wheat Based Diet.

European Society of Cardiology (ESC). "Ancient Egyptian princess now known to be first person in human history with diagnosed coronary artery disease." ScienceDaily. ScienceDaily, 17 May 2011.

The Big Picture - Summary Slide

- 1) Cholesterol Theory Falsified by Modern Imaging Techniques.
- 2) 16s Ribosome: Atherosclerotic Plaque is Infected Bio-Film.
- 3) Arterial Damage at Sites of Shear Stress, associated with underlying Vitamin C Deficiency.
- 4) Leaky Gut and Periodontal Disease Causes Low Level Endotoxemia Which Seeds Atherosclerotic Plaque.
- 5) Soft Tissue Calcification is Inflammatory Response to Infection
- 6) Calcium Score Predicts Future Risk of CAD EVENT
- 7) Annual Progression of Calcium Score Highly Predictive of MI and Failure of Treatment.
- 8) Halting or Slowing Progression of Calcium Score Indicates Good Prognosis and Response to Treatment.
- 9) Statin drugs Benefits Are Due to Pleiotrophic Effects, (anti-inflammatory and antibacterial). Not Cholesterol Lowering.

Interventions for Calcium Score?

- Statin Drugs
- Estrogen
- Testosterone
- Thyroid
- Vitamin C
- Vitamin K2
- Tocotrienol Vit E (Ramanathan,2018)
- Magnesium
- Leaky Gut Protocol
- Blood Sugar Protocol
- Wheat- Gluten Free

Ramanathan

Interventions for Calcium Score?

Botanicals

- Aged Garlic (Hom, Budoff 2015)
- Berberine (Zhang,2016)
- Chinese Skullcap baicalin (Dinda,2017)
- Curcumin (Olszanecki,2005)
- Resveratrol/Pterostilbene (Li 2018)

Zhang, Ming, et al. "Therapeutic Potential and Mechanisms of Berberine in Cardiovascular Disease." *Current Pharmacology Reports* 2.6 (2016): 281-292. and Dinda, Biswanath, et al. "Therapeutic potentials of baicalin and its aglycone, baicalein against inflammatory disorders." *European Journal of Medicinal Chemistry* 131 (2017): 68-80.

Olszanecki, R., et al. "Effect of curcumin on atherosclerosis in apoE/LDLR-double knockout mice." *Journal of physiology and pharmacology*: 56.4 (2005): 627-635.

Hom, Christopher, Matthew Budoff, and Yanting Luo. "The effects of aged garlic extract on coronary artery calcification progression and blood pressure." *Journal of the American College of Cardiology* 65.10 Supplement (2015): A1472.

Cholesterol Theory Falsified

- 1) Calcium Score - No Correlation between Cholesterol level and Calcium Score. (Harvey Hecht, 2001)
- 2) Autopsy Studies show No Correlation between Cholesterol level and Amount of Atherosclerotic Plaque.
- 3) 2004 Raggi Study 495 pts on statins- 41 Heart Attacks Over 6 Years – They had Same Cholesterol and LDL as Heart Attack Free Patients. (Raggi, Paolo,2004)
- 4) CETP Inhibitor Evacetrapib - Lowers LDL - Fails Clinical Trials
- 5) Elderly Patients w/ Familial HyperCholesterolemia- Zero CAC- No CAD-Simon Broome Registry (Neil Andrew,2008)
- Reverse Epidemiology for Dialysis, CHF, RA,COPD, and in elderly High Cholestgerol Improves Survival. (Horwich,2007)

Cholesterol Theory Falsified

- Hecht, Harvey S., et al. "Relation of coronary artery calcium identified by electron beam tomography to serum lipoprotein levels and implications for treatment." *The American journal of cardiology* 87.4 (2001): 406-412.
- Raggi, Paolo, Tracy Q. Callister, and Leslee J. Shaw. "Progression of coronary artery calcium and risk of first myocardial infarction in patients receiving cholesterol-lowering therapy." *Arteriosclerosis, thrombosis, and vascular biology* 24.7 (2004): 1272-1277.
- Neil, Andrew, et al. "Reductions in all-cause, cancer, and coronary mortality in statin-treated patients with heterozygous familial hypercholesterolaemia: a prospective registry study." *European heart journal* 29.21 (2008): 2625-2633
- Horwich, Tamara B., and Gregg C. Fonarow. "Reverse epidemiology beyond dialysis patients: chronic heart failure, geriatrics, rheumatoid arthritis, COPD, and AIDS." *Seminars in dialysis*. Vol. 20. No. 6. 2007.

Cholesterol Theory Falsified

● LDL - Cholesterol Does Not Cause Coronary Artery Disease

Ravnskov, Uffe, et al. "LDL-C does not cause cardiovascular disease: a comprehensive review of the current literature." *Expert review of clinical pharmacology* 11.10 (2018): 959-970.

Cholesterol and CAC –No Correlation

- CAC for 930 Asymptomatic Pts, NOT ON STATINS
- No Significant Differences in the Calcium Scores throughout the entire range of all lipid parameters.
- Calcium Percentiles Were Virtually Identical within Lipid Value Subgroups.
- TC, LDL-C, HDL-C, TC/HDL-C, and triglyceride levels DO **Not Correlate** with either the extent or prematurity of calcified plaque burden.

Hecht, Harvey S., et al. "Relation of coronary artery calcium identified by electron beam tomography to serum lipoprotein levels and implications for treatment." The American journal of cardiology 87.4 (2001): 406-412.

Autopsy Studies –No Correlation Between Cholesterol and Atherosclerosis Severity

- “No relationship was present in any age group. It is concluded that the incidence and severity of atherosclerosis in man is not directly correlated with the blood serum cholesterol content.”-(Lande,1936)
- “No correlation could be observed between the serum cholesterol level and the amount and severity of atherosclerosis in the arteries.”(Mathur,1961)

Landé, K. E., and W. M. Sperry. “Human atherosclerosis in relation to the cholesterol content of the blood serum.” Arch. Pathol. 22 (1936): 301-312.

Mathur, K. S., et al. “Serum cholesterol and atherosclerosis in man.” Circulation 23.6 (1961): 847-852.

Non-Statin Lipid Lowering Drug Fails

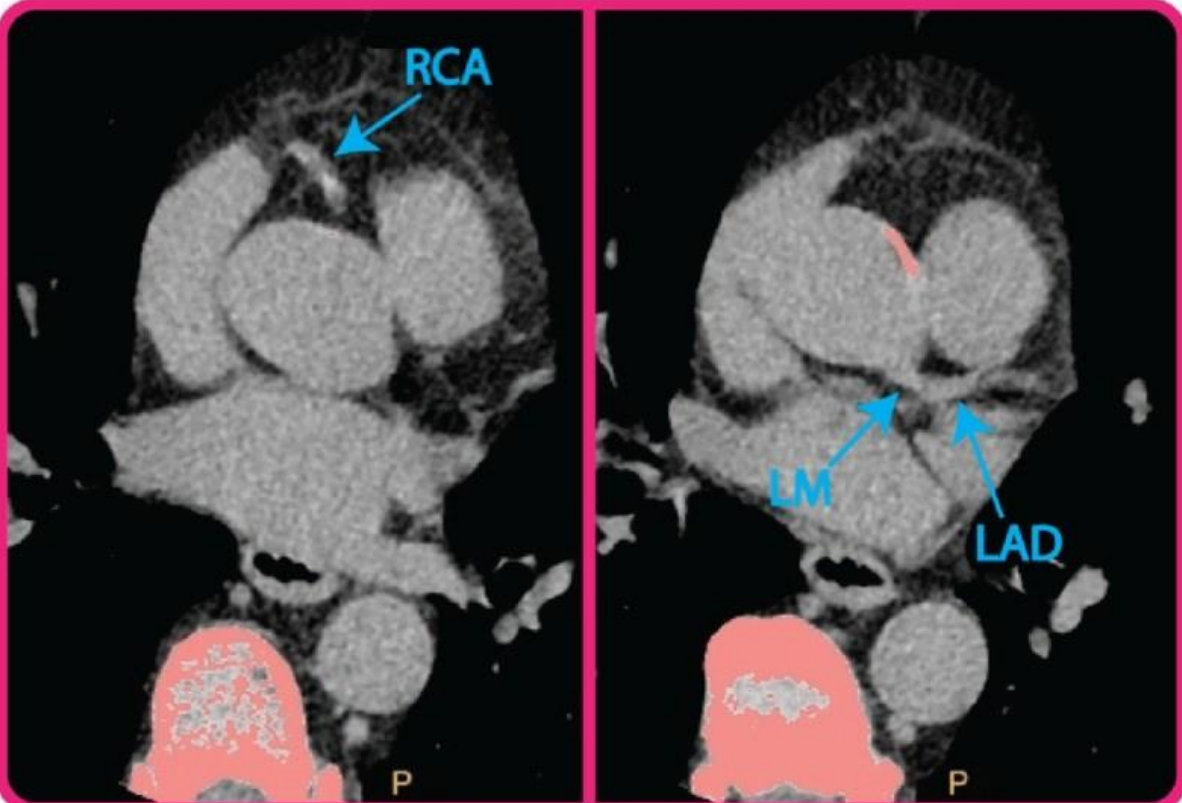
Evacetrapib - CETP

- Cholesteryl Ester Transfer Protein Inhibitor
- Multicenter, randomized, double-blind, placebo-controlled phase 3 trial,
- 12,092 patients w/CAD. Over 26 months.
- Reduced LDL 31%, Increased HDL 131%
- Evacetrapib Did Not Result in a Lower Rate of Cardiovascular Events than Placebo among Patients with High-Risk Vascular Disease.
- Statin Benefits are Due to Pleiotropic effects, NOT Cholesterol Lowering.

Lincoff, A. Michael, et al. "Evacetrapib and cardiovascular outcomes in high-risk vascular disease." *New England Journal of Medicine* 376.20 (2017): 1933-1942.

Falsifying the Cholesterol Theory

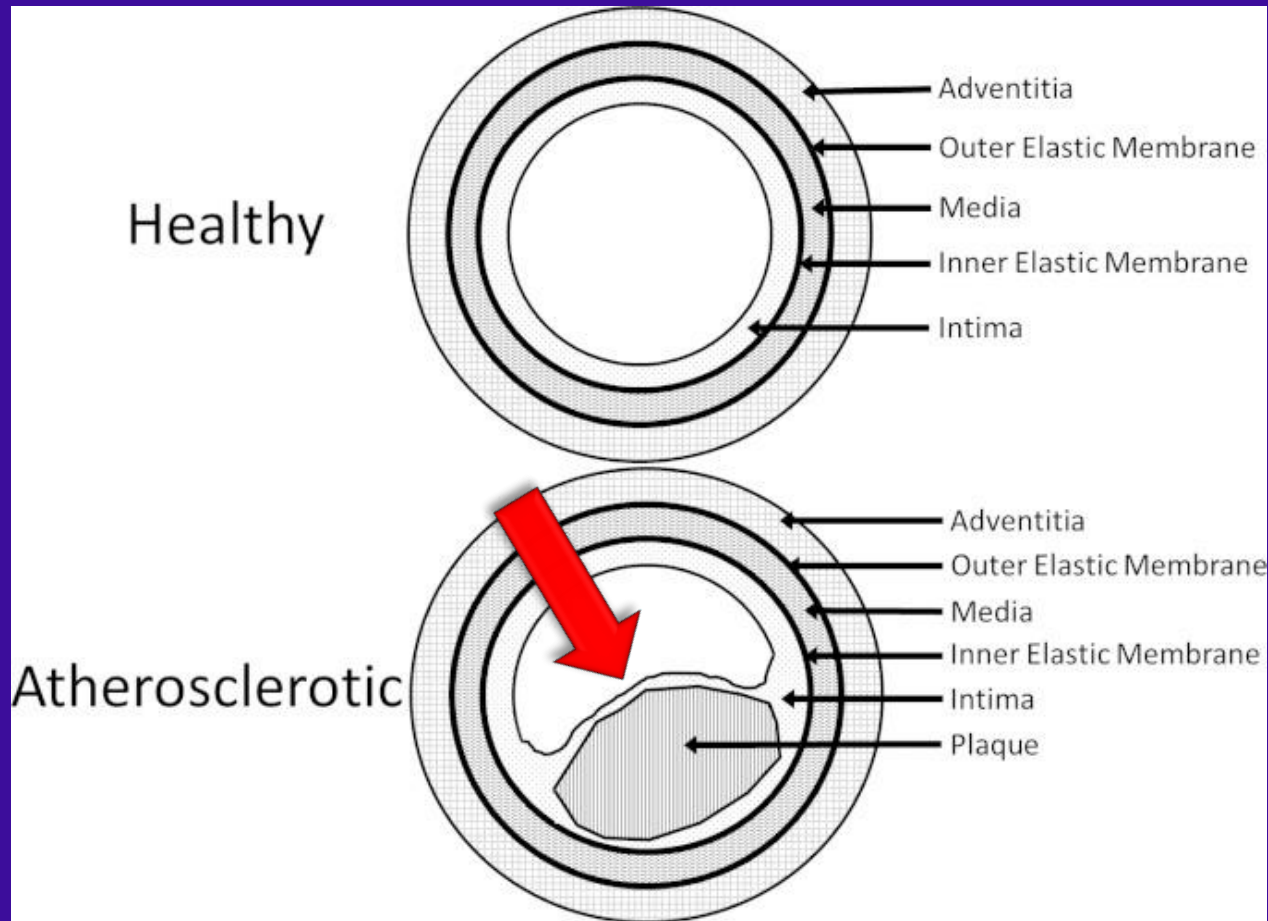
Zero CAC – Lifelong Cholesterol 580



- 72 year old male with untreated familial hypercholesterolemia with cholesterol level 580 and LDL-C 480 mg/dl.
- Calcium Score of Zero

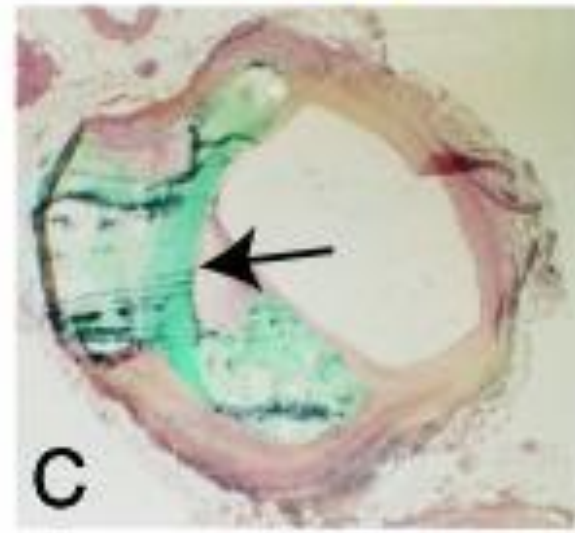
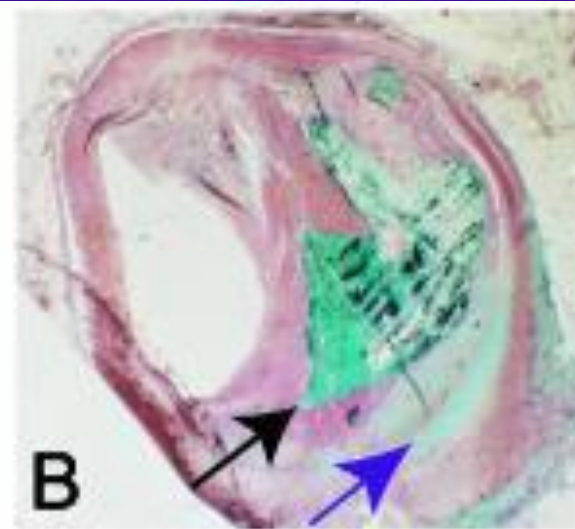
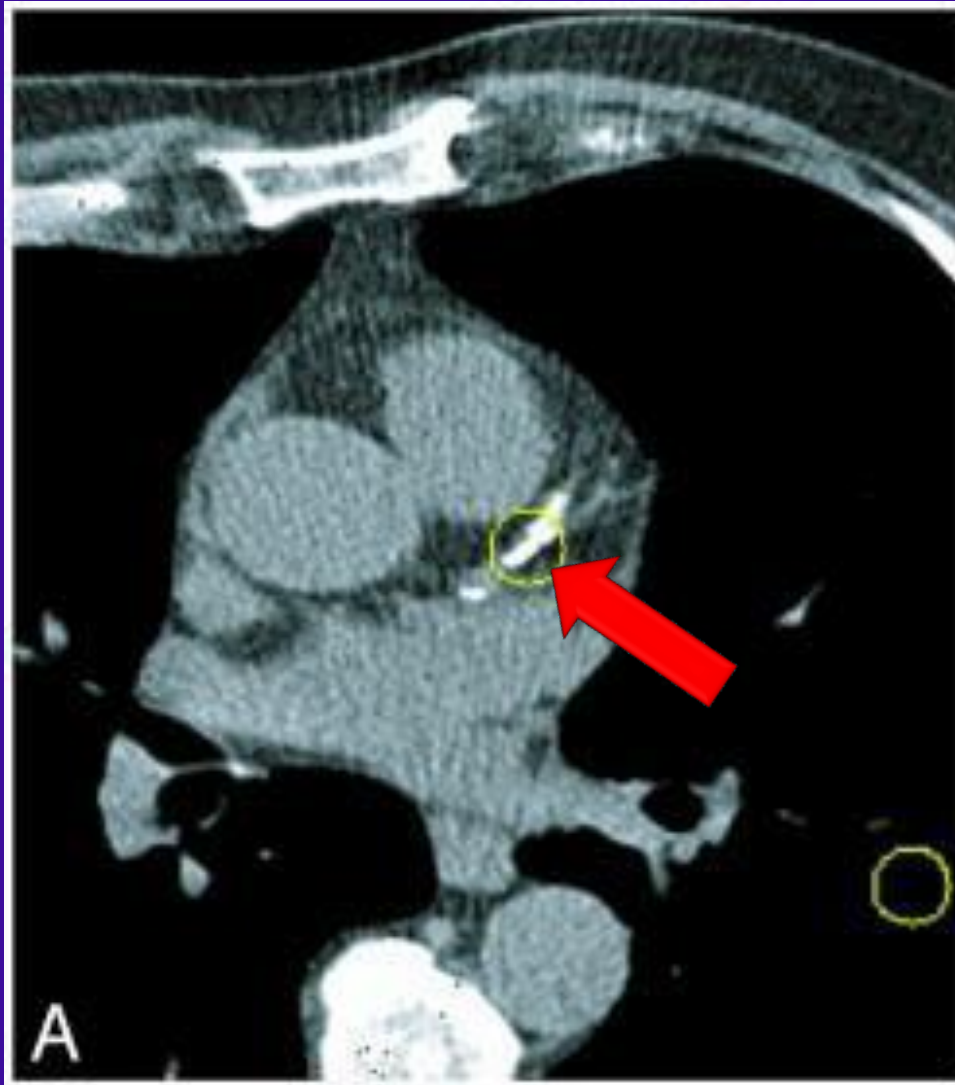
Johnson, Kipp W., Joel T. Dudley, and Jason R. Bobe. "A 72-Year-Old Patient with Longstanding, Untreated Familial Hypercholesterolemia but no Coronary Artery Calcification: A Case Report." *Cureus* 10.4 (2018).

Atherosclerotic Plaque



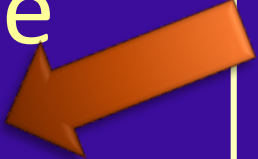
Lanter, B. B., and D. G. Davies. "Propionibacterium acnes Recovered from Atherosclerotic Human Carotid Arteries Undergoes Biofilm Dispersion and Releases Lipolytic and Proteolytic Enzymes in Response to Norepinephrine Challenge In Vitro." *Infection and immunity* 83.10 (2015): 3960-3971.

Arterial Calcification Stains Green



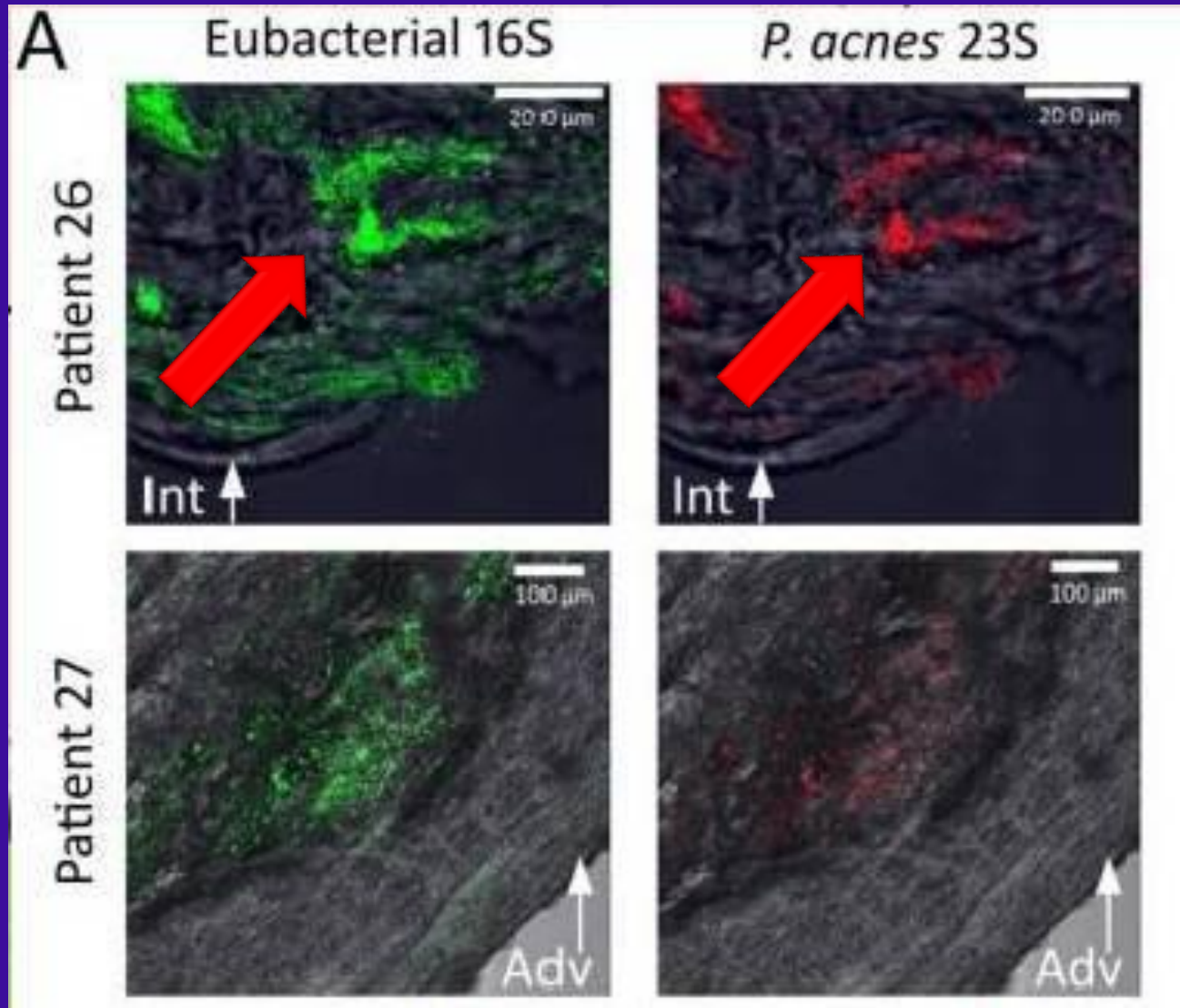
Doherty, Terence M., et al. "Calcification in atherosclerosis: bone biology and chronic inflammation at the arterial crossroads." PNAS (2003)

Soft Tissue Calcification

- “Vascular calcification is a clinical marker for atherosclerosis and may represent a special example of the general phenomenon of soft tissue calcification surrounding chronic inflammatory foci.” (Abedin, 2004)
 - Inflammatory Foci = Infection
- 

Abedin, Moeen, Yin Tintut, and Linda L. Demer. “Vascular calcification: Mechanisms and clinical ramifications.” *Arteriosclerosis, Thrombosis, and Vascular Biology* 24.7 (2004): 1161–1170..

Atherosclerotic Plaque as Poly-Microbial Biofilm



Lanter, B. B., and D. G. Davies. "Propionibacterium acnes Recovered from Atherosclerotic Human Carotid Arteries Undergoes Biofilm Dispersion and Releases Lipolytic and Proteolytic Enzymes in Response to Norepinephrine Challenge In Vitro." *Infection and immunity* 83.10 (2015): 3960-3971.

Plaque is Infected Biofilm

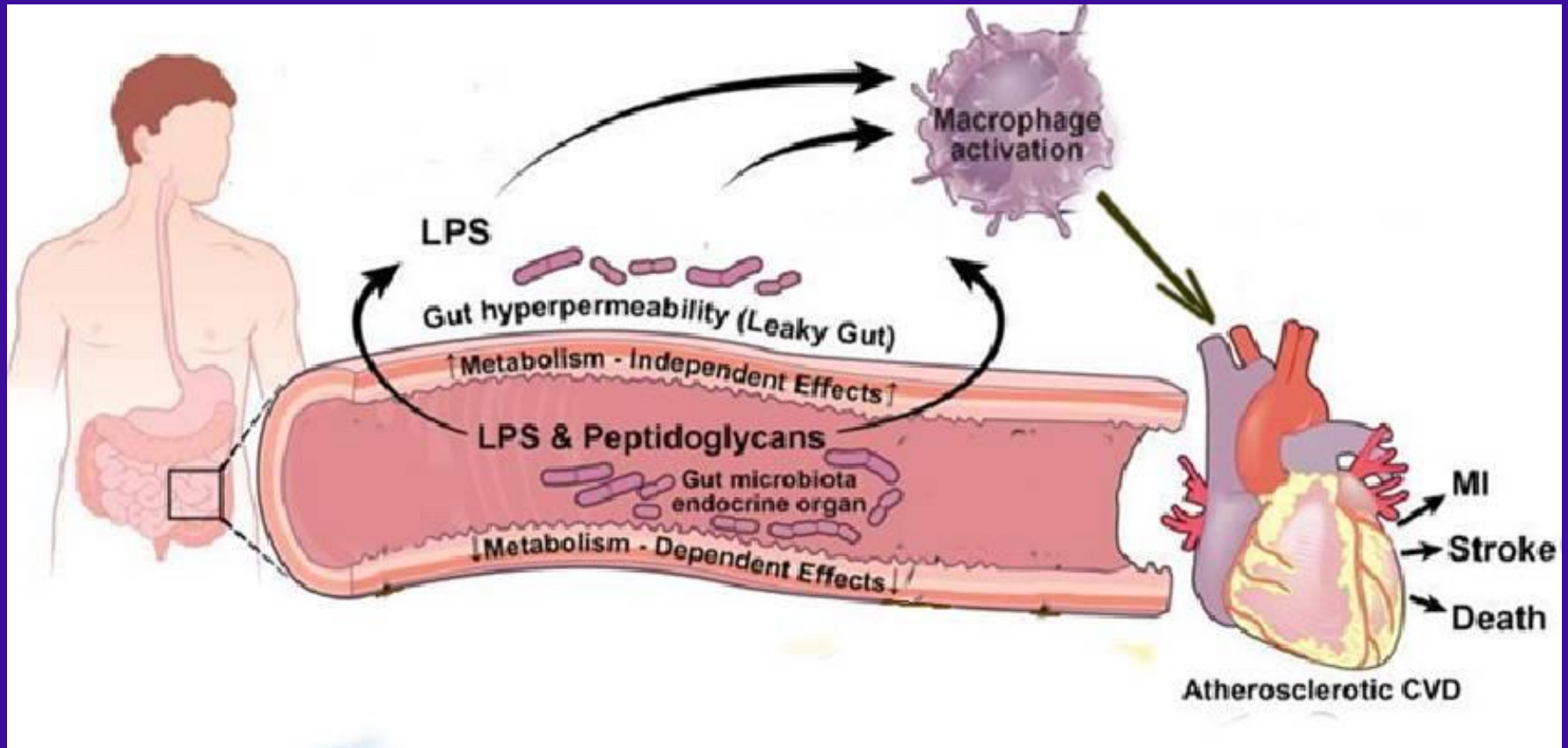
- Atherosclerotic Plaque Samples
- 16s Ribosome Technique
- Atherosclerotic Plaque is Infected Biofilm Colonized by Bacterial, Fungal and Protozoal Organisms.

Lanter, Bernard et al “Bacteria present in carotid arterial plaques are found as biofilm deposits ” MBio 5.3 (2014): e01206-14.

Stephen Fry et al. Putative biofilm-forming organisms in the human vasculature: expanded case reports and review of the literature.. Phlebol Review 2014; 22, 1: 24–37

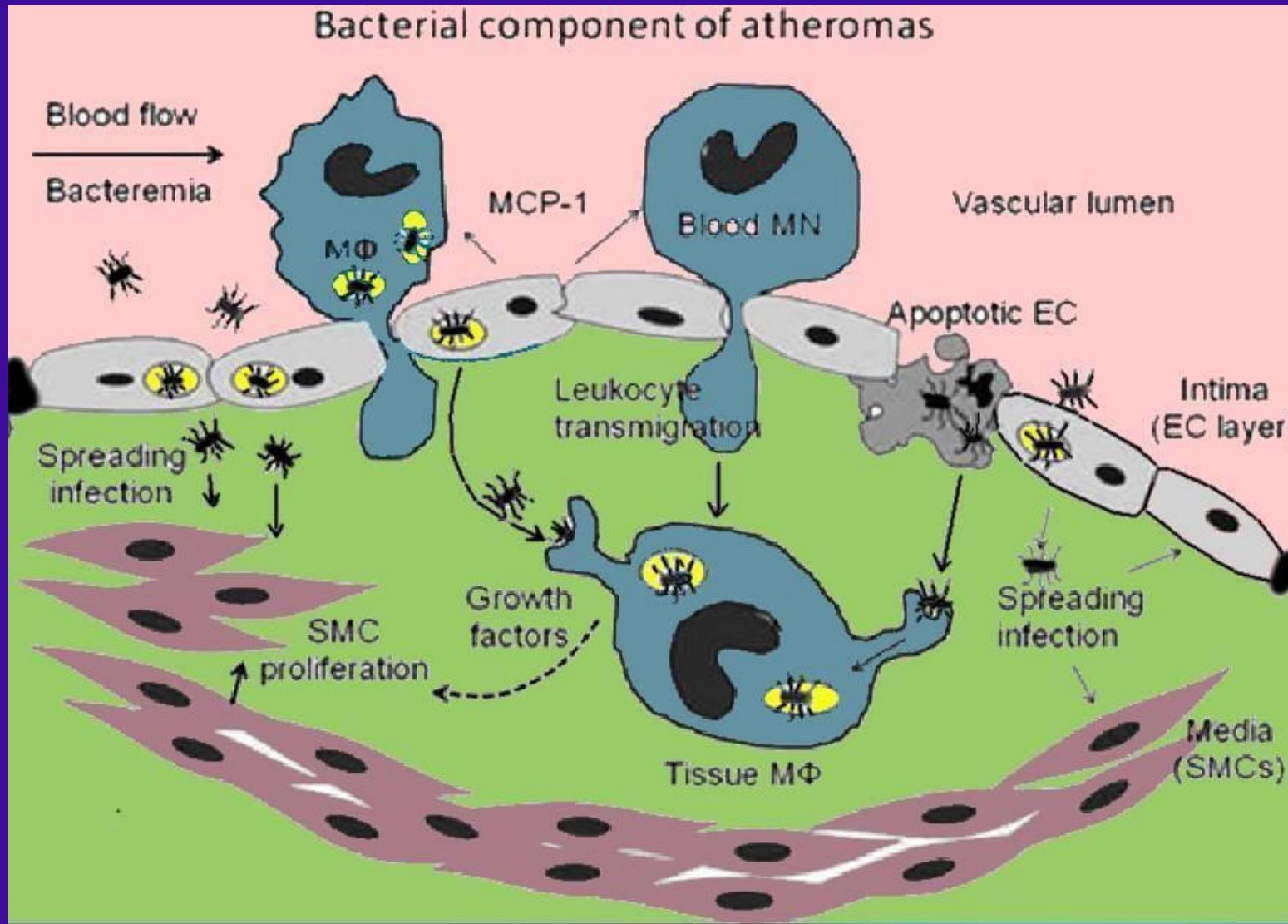
Ott, Stephan J., et al. “Detection of diverse bacterial signatures in atherosclerotic lesions of patients with coronary heart disease.” Circulation 113.7 (2006): 929-937.

LPS From Gut Drives Atherosclerosis



Brown, J. Mark, and Stanley L. Hazen. "The Gut Microbial Endocrine Organ: Bacterially-Derived Signals Driving Cardiometabolic Diseases." *Ann rev med* 66 (2015): 343.

Atherosclerotic Plaque as Poly-Microbial Biofilm



Kozarov, Emil, Teresa Padro, and Lina Badimon. "View of statins as antimicrobials in cardiovascular risk modification." *Cardiovascular research* 102.3 (2014): 362-374.

Atherosclerotic Plaque as Polymicrobial Infected Biofilm

- 63 Studies and 23 Bacteria in Human Atherosclerotic Plaque Samples.

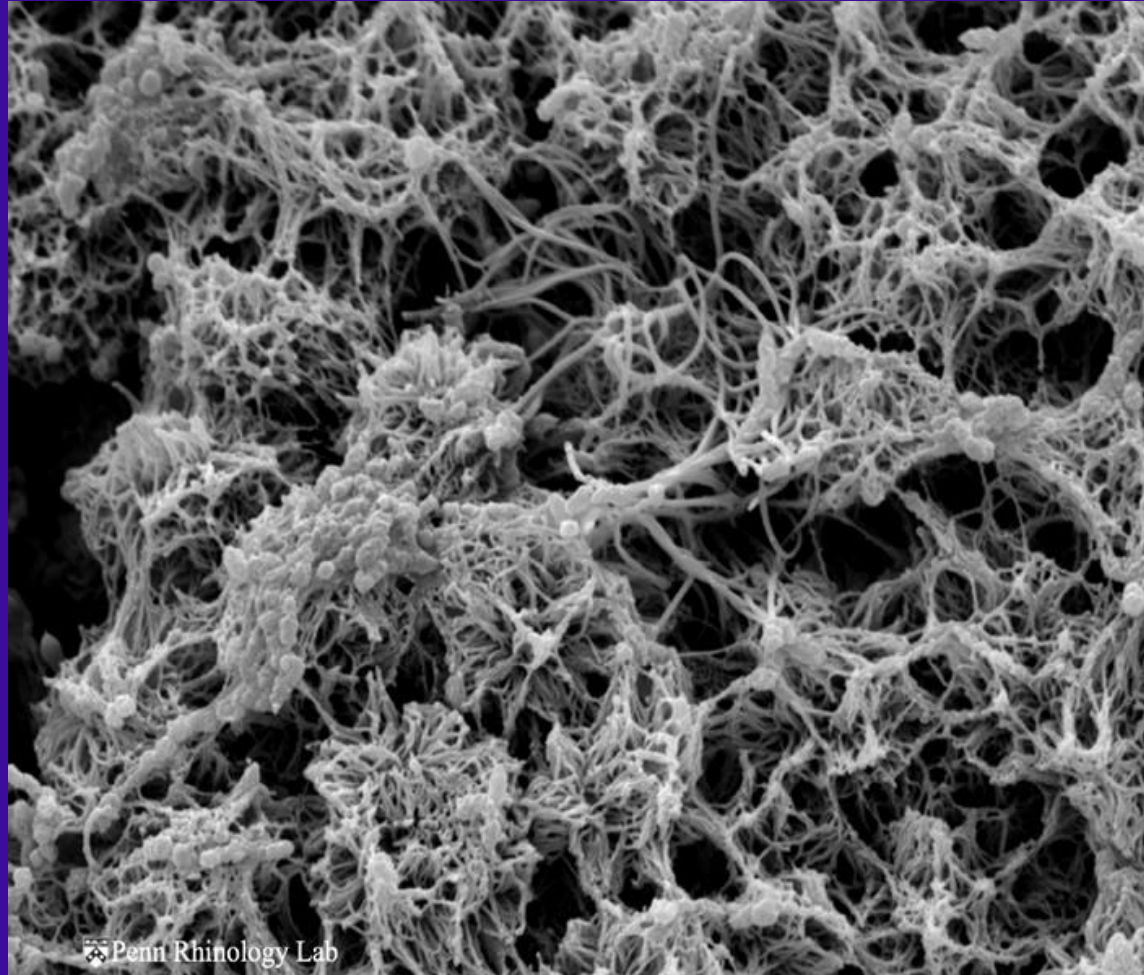
Chhibber-Goel, Jyoti, et al. "Linkages between oral commensal bacteria and atherosclerotic plaques in coronary artery disease patients." NPJ biofilms and microbiomes 2.1 (2016): 7.

Atherosclerotic Plaque as Polymicrobial Infected Biofilm

- Mawhorter SD, Lauer MA. Is atherosclerosis an infectious disease? *Cleve Clin J Med*. 2001;68(5):449-58.
- Kuo CC, Shor A, Campbell LA, et al. Demonstration of *Chlamydia pneumoniae* in atherosclerotic lesions of coronary arteries. *J Infect Dis*. 1993;167(4):841-9.
- Fry SE, et al Putative biofilm-forming organisms in the human vasculature: expanded case reports and review of the literature. *Phlebological Review* 2014; 22(1): 24–37.
- Lanter BB, et al. Bacteria present in carotid arterial plaques are found as biofilm deposits which may contribute to enhanced risk of plaque rupture. *MBio*. 2014;5(3):
- Ott SJ, et al. Detection of diverse bacterial signatures in atherosclerotic lesions of patients with coronary heart disease. *Circulation*. 2006;113(7):929-37.
- Ott SJ, et al. Fungal rDNA signatures in coronary atherosclerotic plaques. *Environ Microbiol*. 2007;9(12):3035-45.
- Koren O, et al. Human oral, gut, and plaque microbiota in patients with atherosclerosis. *Proc Natl Acad Sci U S A*. 2011;108 Suppl 1:4592-8.
- Chakravorty, S et al. "Detailed analysis of 16S ribosomal RNA gene segments for diagnosis of pathogenic bacteria." *Journal of microbiological methods* 69.2 (2007): 330-339.

Infected Biofilms

- Organisms Secrete Matrix
- Cell to Cell communication
- Quorum Sensing
- Resistant to antibiotics



Intestinal Origin of Bacteria in CAD

- Detection of Intestinal Bacterial by 16S rRNA in both the Blood sample and Atherosclerotic plaques. (Li, 2016)
- Intestinal Bacteria in Plaques may Originate from Intestine.



Li, Chuanwei, et al. "Zonulin regulates intestinal permeability and facilitates enteric bacteria permeation in coronary artery disease." Scientific reports 6 (2016): 29142.

LPS Theory Of CAD

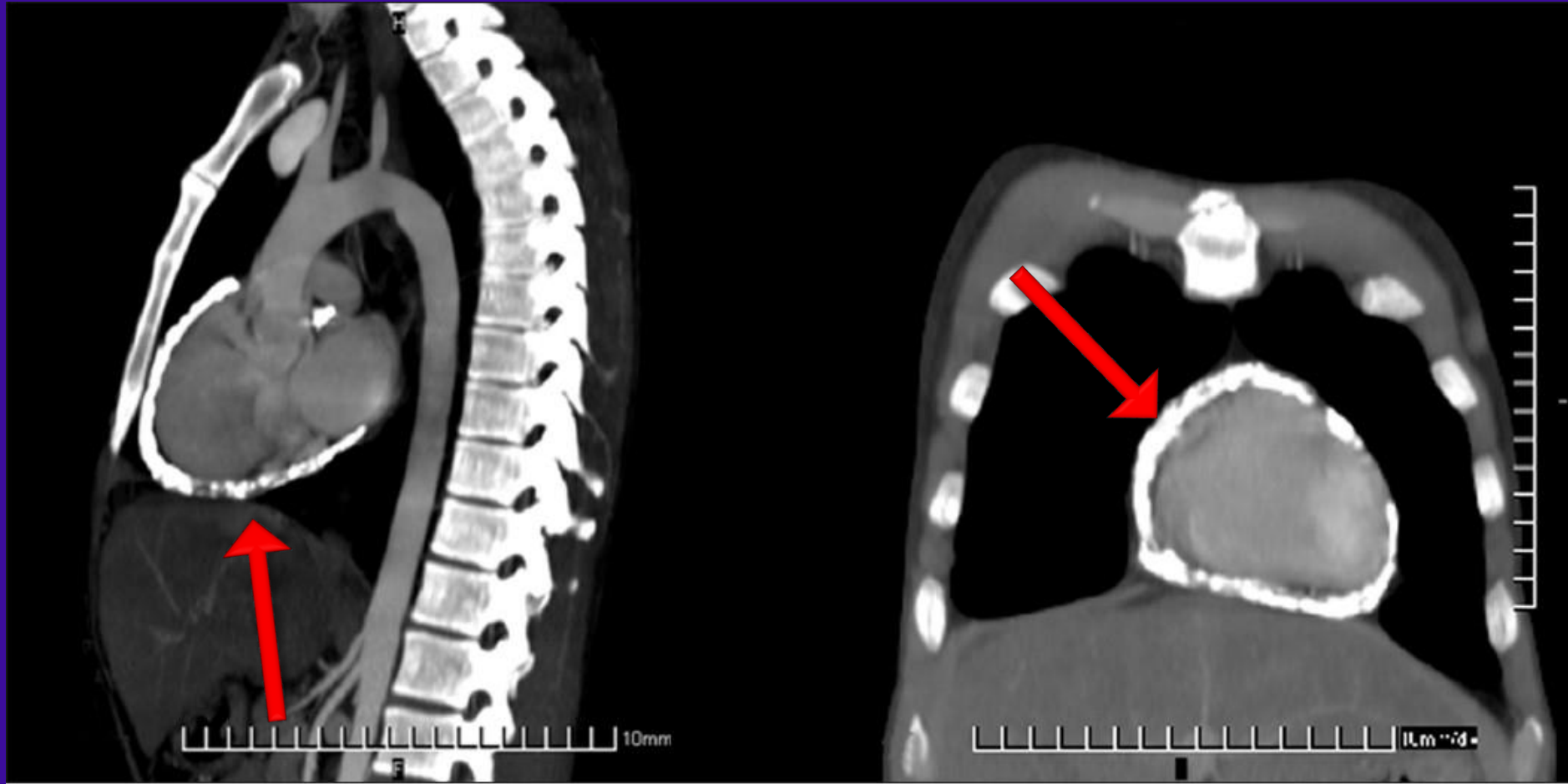
- “Endotoxin-treated Rabbits exhibited significantly Accelerated Atherosclerosis compared with Control Animals” (Lehr et al. 2001).



Lehr, Hans-Anton, et al. “Immunopathogenesis of atherosclerosis Endotoxin accelerates atherosclerosis in rabbits on hypercholesterolemic diet.” *Circulation* 104.8 (2001): 914-920.

Cholesterol or Infection?

TB Pericarditis

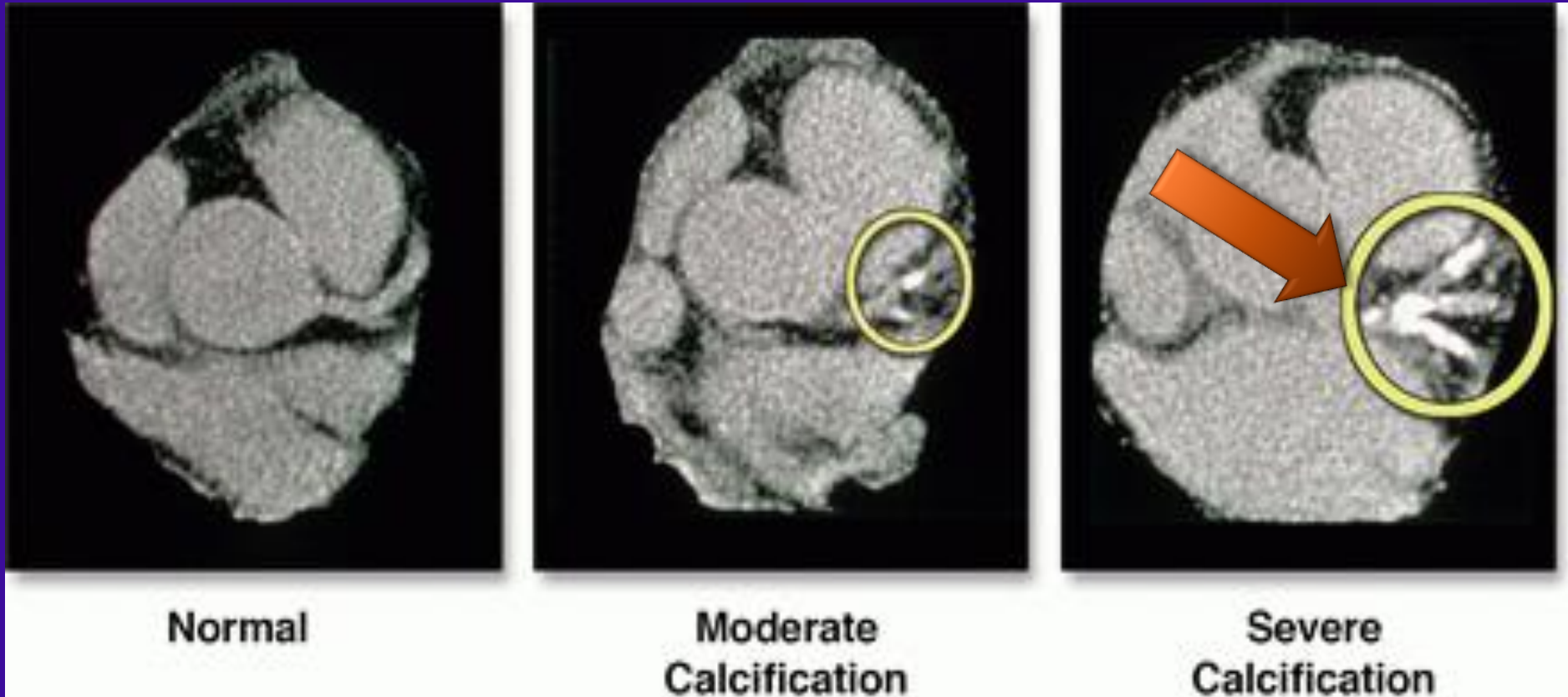


Goel, Pravin K., and Nagaraja Moorthy. "Tubercular chronic calcific constrictive pericarditis." (2011). Heart Views. 2011 Jan-Mar; 12(1): 40–41.

White Cliffs of Dover Microbial Calcification

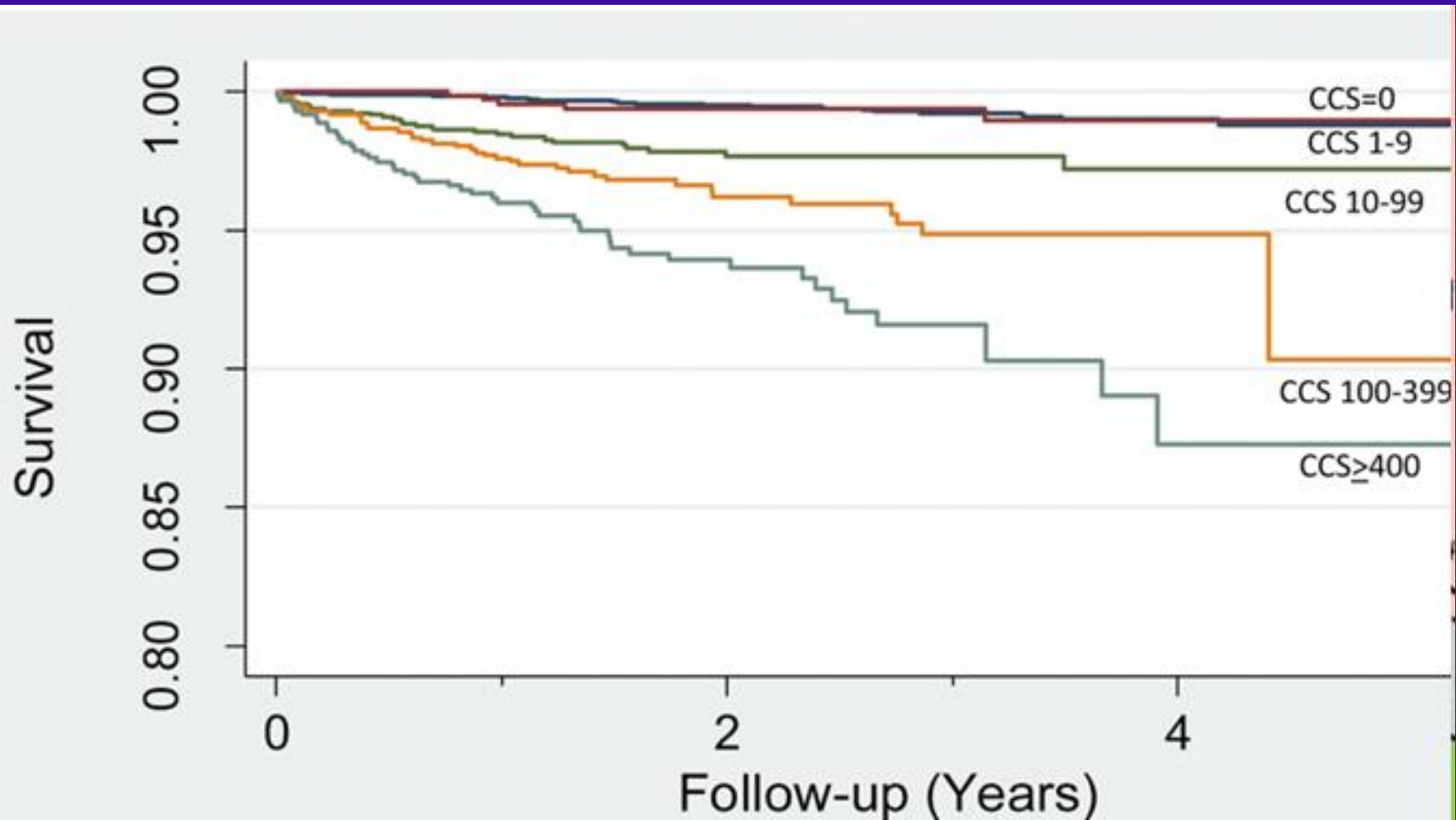


Calcium Score Highly Predictive of Future Event



Hecht, Harvey S. "Coronary artery calcium scanning: past, present, and future." JACC: Cardiovascular Imaging 8.5 (2015): 579-596.

Calcium Score Predicts Survival



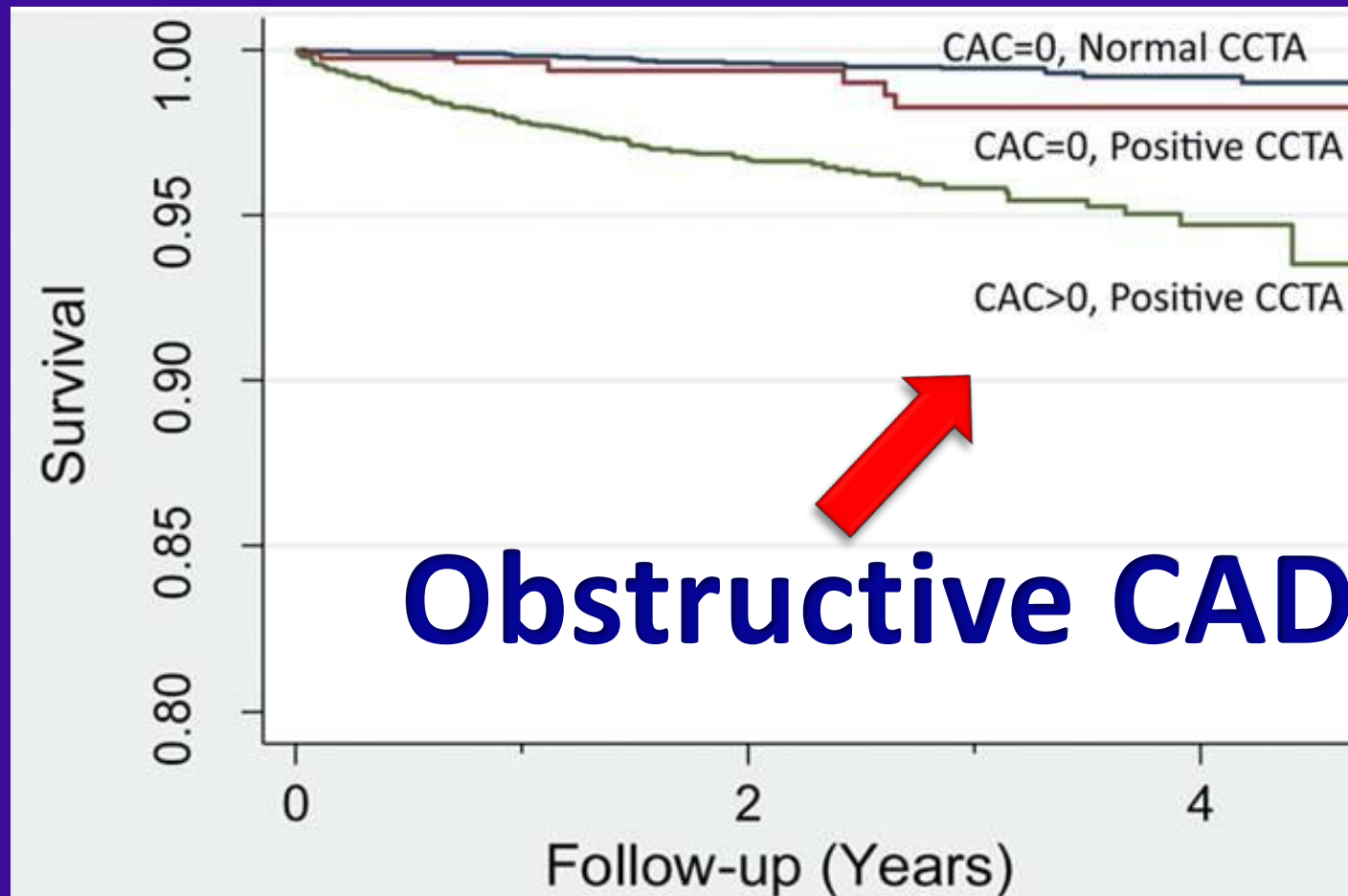
Al-Mallah, Mouaz H., et al. "Does coronary CT angiography improve risk stratification over coronary calcium scoring in symptomatic patients with suspected coronary artery disease?" *European Heart Journal* 15.3 (2013): 267-274.

Calcium Score NOT Perfect

- **Calcium Score Best Use: Asymptomatic Pts.**
- **If Symptomatic Patient w/ Angina, then Proceed to CTA or SPECT Perfusion Scan Regardless of Zero or Low Calcium Score**

Samanta, Anweshan, et al. "SUBTOTAL LEFT MAIN DISEASE IN PATIENT WITH ZERO CALCIUM SCORE: IS IT POSSIBLE?." Journal of the American College of Cardiology 71.11 Supplement (2018): A2197.

Calcium Score – CT Angio Add-On



Aids in
Discrimination

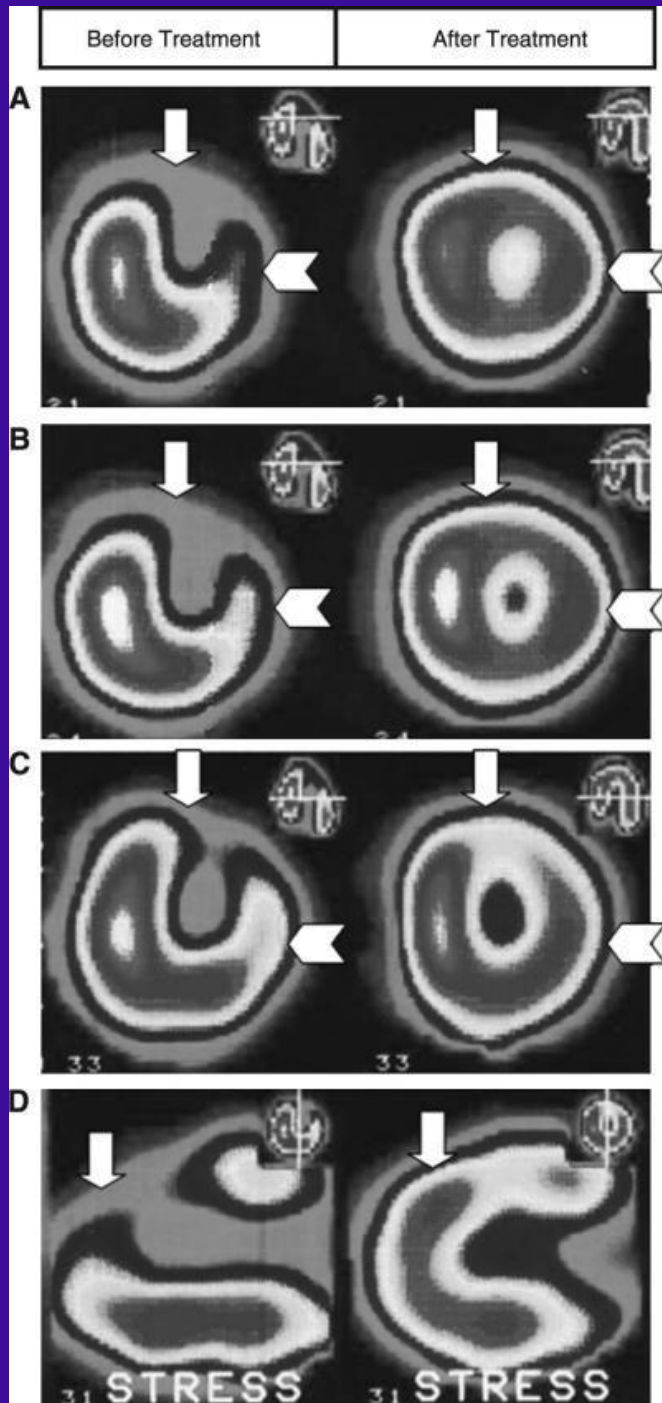
1.36% of
symptomatic
patients w/
CAC=0 had
obstructive
CAD on CTA

Al-Mallah, Mouaz H., et al. "Does coronary CT angiography improve risk stratification over coronary calcium scoring in symptomatic patients with suspected coronary artery disease? Results from the prospective multicenter international CONFIRM registry." *European Heart Journal–Cardiovascular Imaging* 15.3 (2013): 267-274.

Left Main CAD with Zero CAC (+)SPECT Perfusion Scan

- 61 y/o female ER 18-mo. hx of Angina, AODM, HTN, hypothyroidism. 20-pack year smoker.
- CAC score of ZERO.
- SPECT: Extensive Myocardial Ischemia Anteriorly, Septally, Laterally and Apically.
- Cardiac Cath: 95% Stenosis of Ostium Left Main
- Symptom Free 12 months since 2 vessel CABG.

Samanta, Anweshan, et al. "SUBTOTAL LEFT MAIN DISEASE IN PATIENT WITH ZERO CALCIUM SCORE: IS IT POSSIBLE?." Journal of the American College of Cardiology 71.11 Supplement (2018): A2197.



SPECT Perfusion Scan

- Treatment with Thombolytic Enzymes
- Improvement in Perfusion Scan in Angina Pt w/Lumbrokinase
- Left: Before Perfusion Deficit
- Right: After. NL. Scan

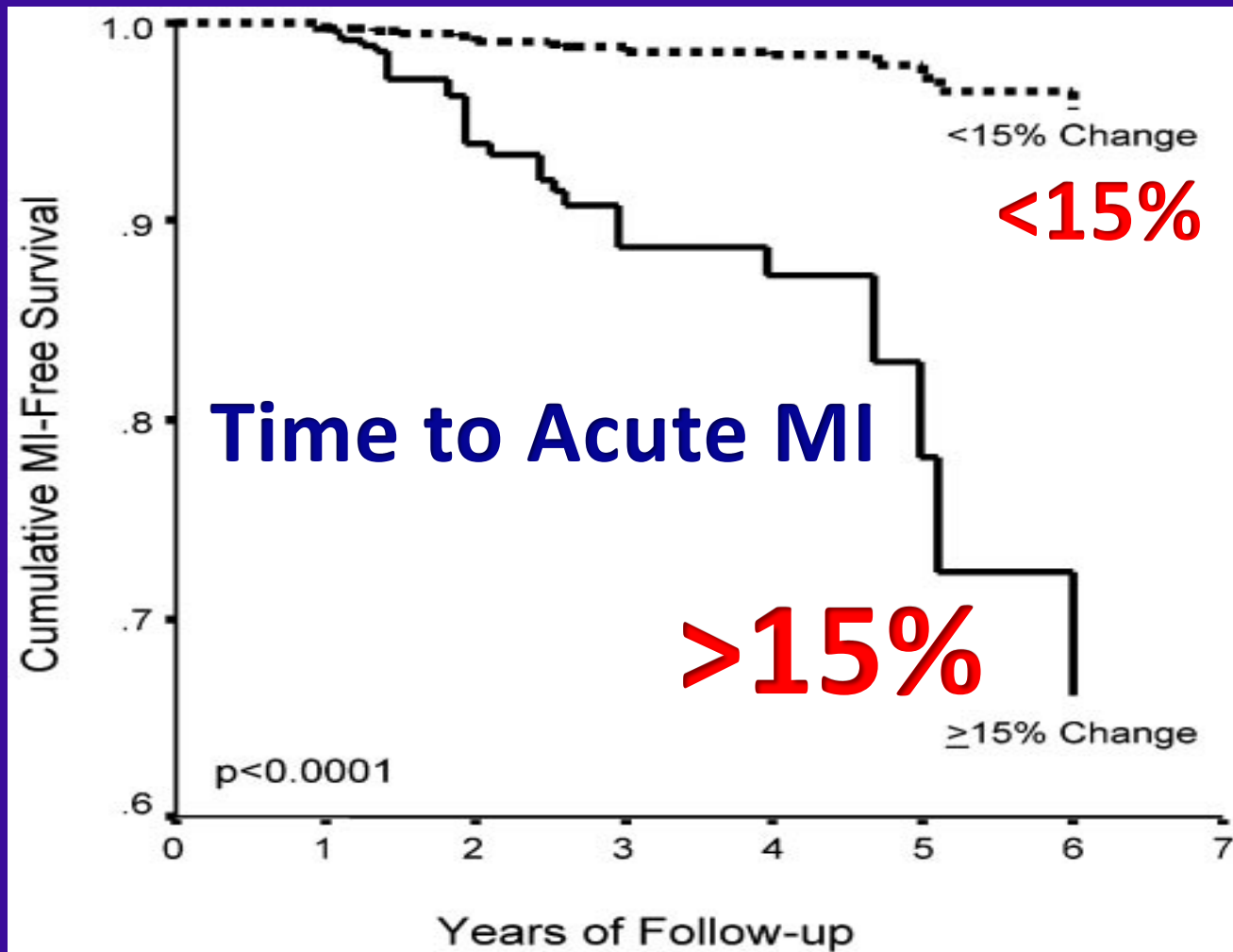
Kasim, Manoefris, et al. "Improved myocardial perfusion in stable angina pectoris by oral lumbrokinase: a pilot study." *The Journal of Alternative and Complementary Medicine* 15.5 (2009): 539-544.

CAC Progression Paradigm Shift - 2004

- 495 Asymptomatic Pts - ALL on Statins.
- No History of Coronary Artery Disease, stent or CABG.
- 42 MI's over 6 years.
- Mean LDL Did Not Differ !!!
- 118 vs. 122 mg/dL, (MI versus NON-MI)

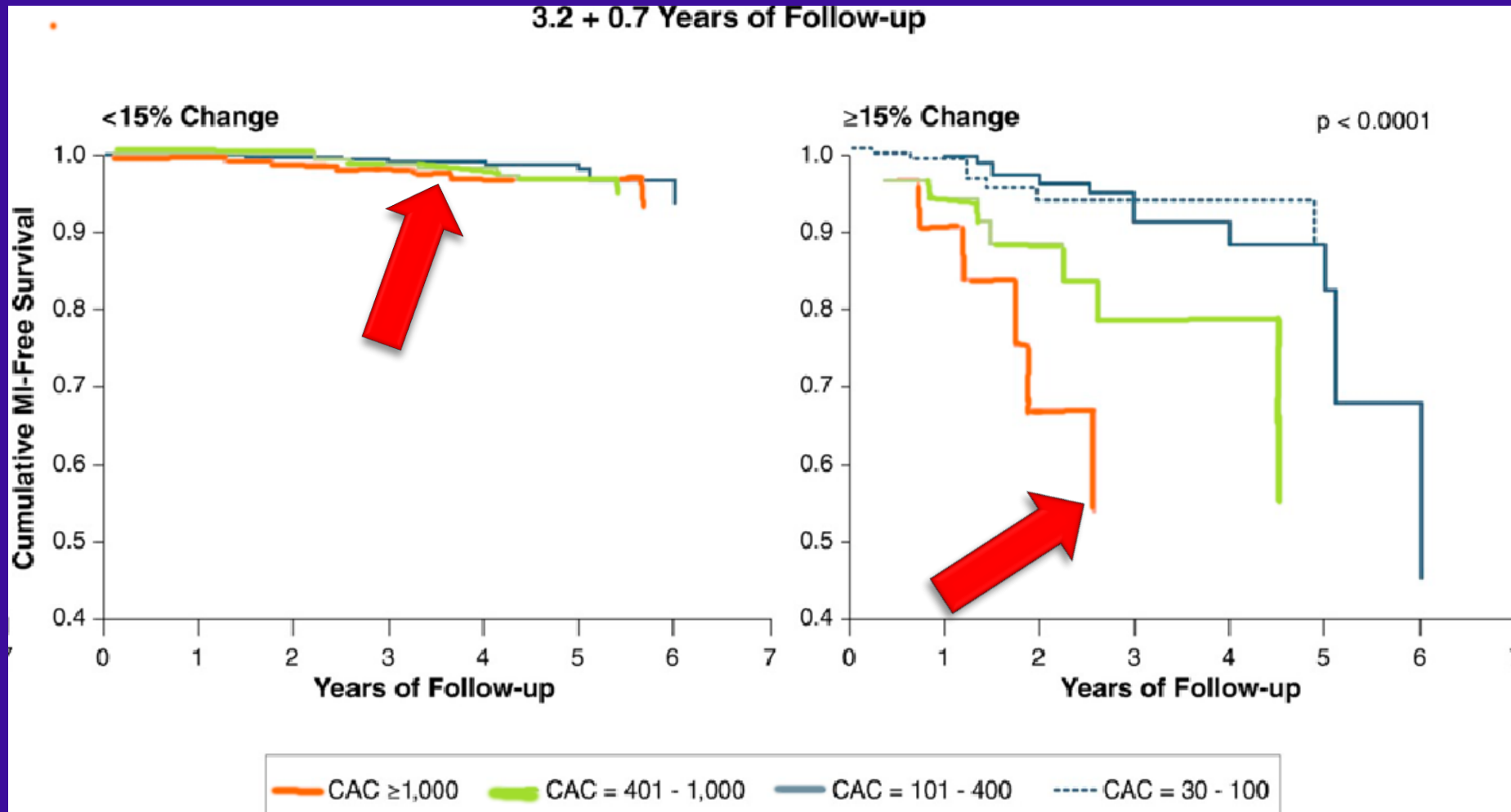
Raggi, Paolo, Tracy Q. Callister, and Leslee J. Shaw. "Progression of coronary artery calcium and risk of first myocardial infarction in patients receiving cholesterol-lowering therapy." *Arteriosclerosis, thrombosis, and vascular biology* 24.7 (2004): 1272-1277.

CAC Progression Paradigm Shift - 2004

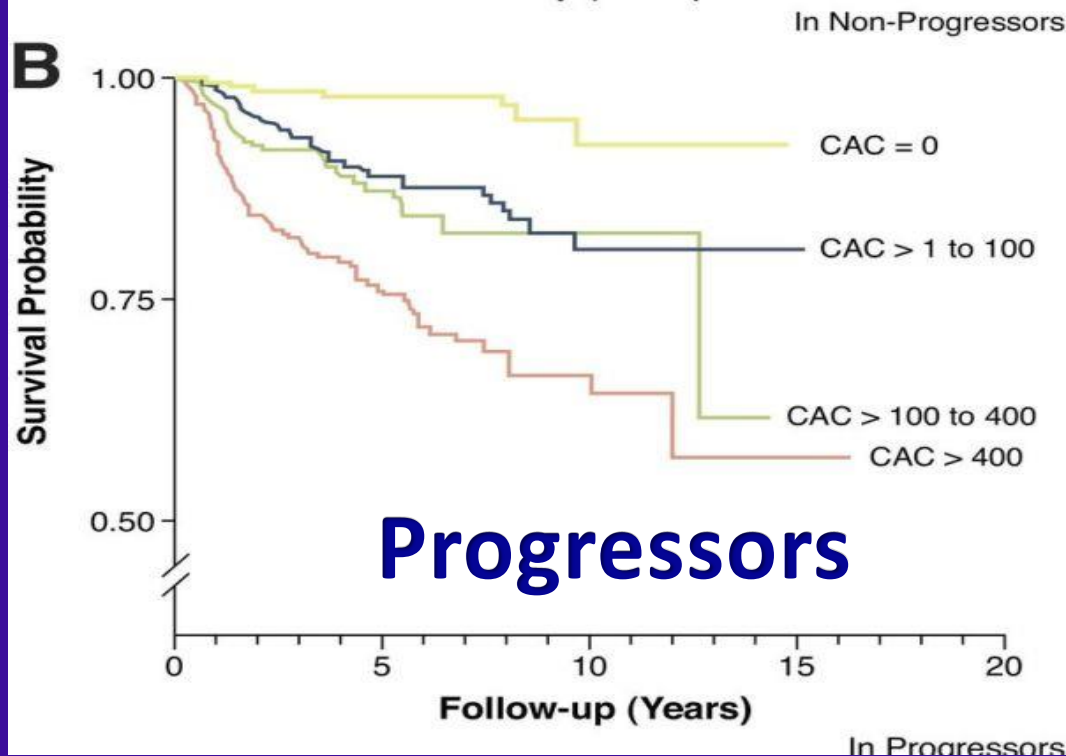
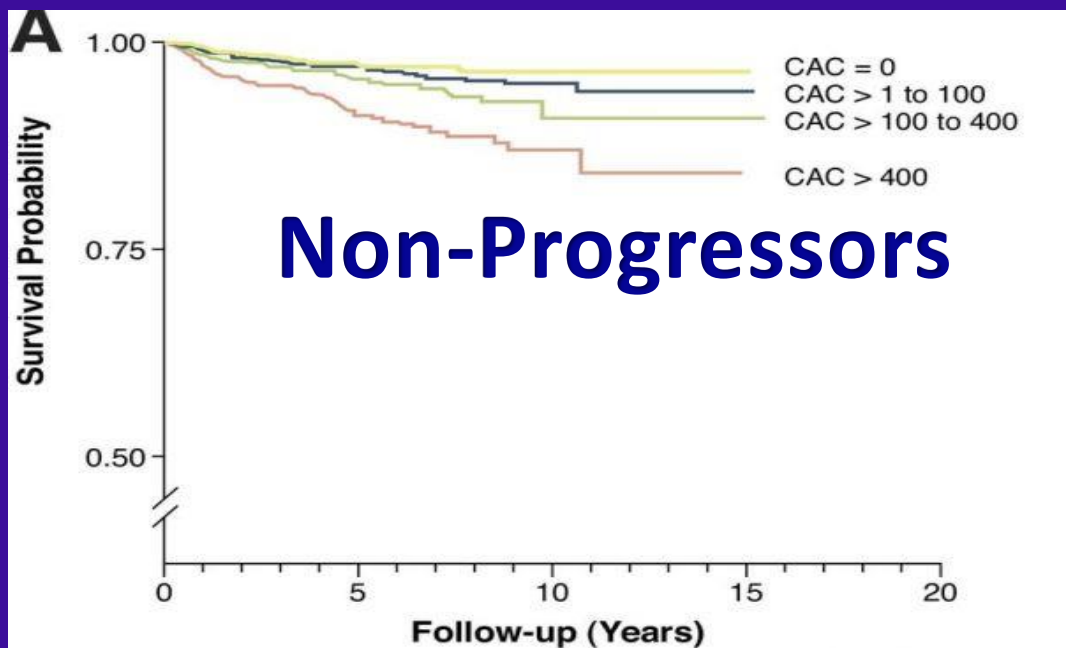


Raggi, Paolo, Tracy Q. Callister, and Leslee J. Shaw. "Progression of coronary artery calcium and risk of first myocardial infarction in patients receiving cholesterol-lowering therapy." *Arteriosclerosis, thrombosis, and vascular biology* 24.7 (2004): 1272-1277.

Annual Calcium Score >15%



CAC progression of <15% per year is associated with a benign prognosis
Harvey S. Hecht JACC: Cardiovascular Imaging Volume 8, Issue 5, May 2015



- 4,609 asymptomatic referred by primary for CAC.
- All cause mortality data.
- Fig 2 Budoff, Matthew "Progression of coronary artery calcium predicts all-cause mortality" JACC: Cardiovascular Imaging 2010

Statin Drugs

- Beneficial in Males w/ Known CAD
 - Not Useful for Primary Prevention, Women, Hemodialysis, COPD, Elderly (reverse epidemiology)
 - Beneficial in Diabetics- 20-30% Reduction Mortality
 - Not Useful for Calcium Score- May Increase Calcification
-
- All Benefits Due to Pleiotrophic Effects – Not Due to Cholesterol Lowering
 - Anti-Inflammatory- Inhibits Activation of Nuclear Factor Kappa Beta
 - Anti-Bacterial Effects

Statins A Failure for Calcium Score

- “As of 2010 there had been five randomized controlled studies showing that statin drug treatment does not reduce coronary calcium score.
- Worse, the statin treatment showed progression of coronary calcium score indistinguishable from the non-treated placebo group.”
- New Studies : Statins Increase Arterial Calcification
- Depletion of Vitamin K2

Quote Edward A. Gill, MD

Gill EA Jr. Does statin therapy affect the progression of atherosclerosis measured by a coronary calcium score? Curr Atheroscler Rep. 2010;12(2):83-7.

Statins Pleiotrophic Effects

Clinical Observations

- Statins While Undergoing CABG: 50-70% reduction in Mortality. (Curtis 2017) (Barakat 2016)
- Statins Improve Survival in Sepsis and Pneumonia. (Hennessy,2016)

Curtis, Michael, et al. "Effect of Dose and Timing of Preoperative Statins on Mortality After Coronary Artery Bypass Surgery." *The Annals of Thoracic Surgery* (2017).

Barakat, Amr F., et al. "Perioperative statin therapy for patients undergoing coronary artery bypass grafting." *The Annals of thoracic surgery* 101.2 (2016): 818-825.

Hennessy, Emma, et al. "Is there potential for repurposing statins as novel antimicrobials?." *Antimicrobial agents and chemotherapy* 60.9 (2016): 5111-5121.

Statins Pleiotrophic Effects

Anti-Inflammatory Mechanisms

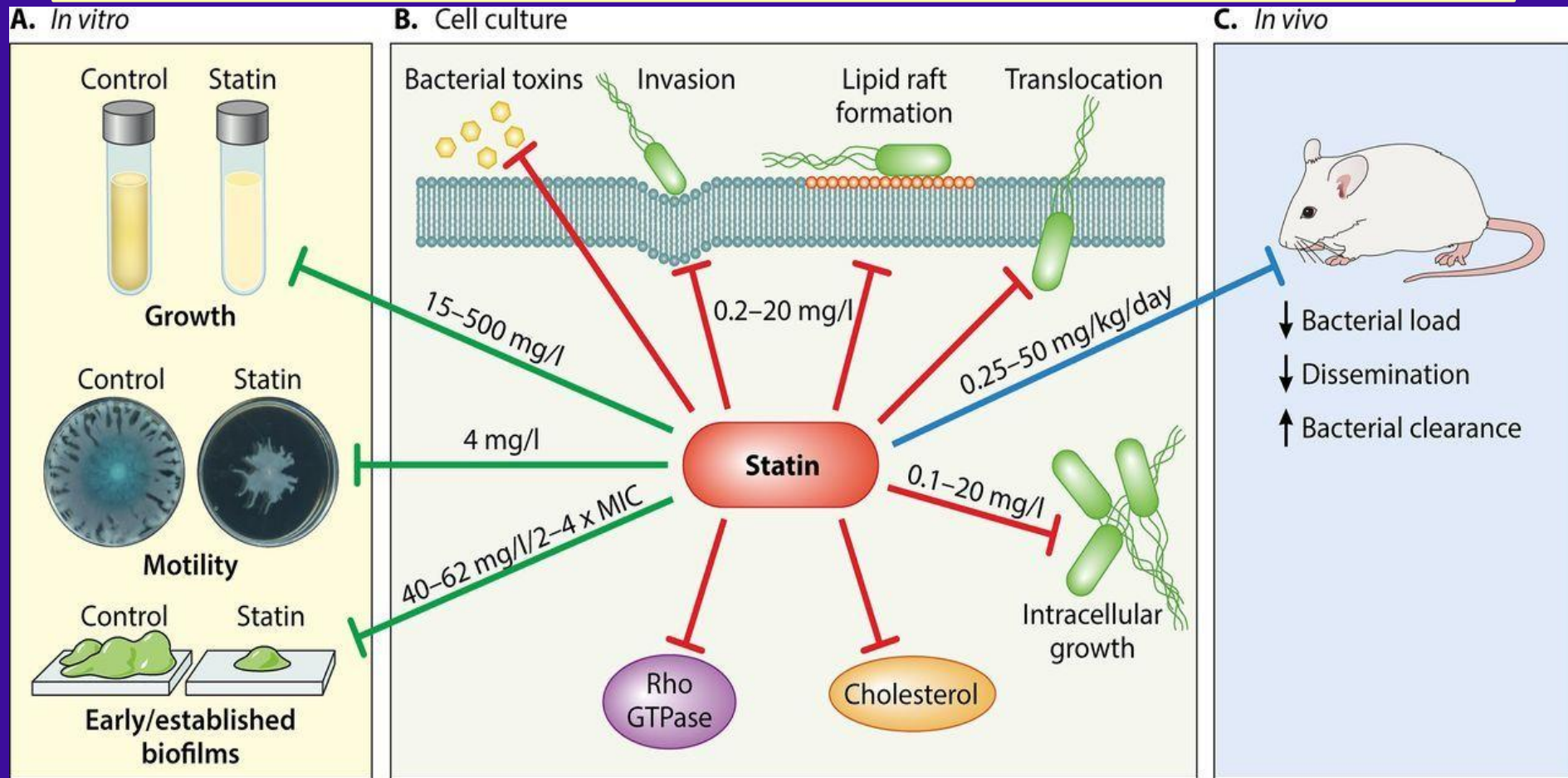
- Suppresses LPS Signaling in Monocytes (Patel,2004)
- Blocks LPS -release of IL-6 and TNF-alpha. Decreases Nuclear factor-kappaB - direct anti-inflammatory effect. (Devaraj,2006)
- Prevents TNF-alpha-induced NF-kappaB activation and gene transcription in cultured EC.(Hölschermann, 2006)

Patel, Tushar R., and Siobhan A. Corbett. "Simvastatin suppresses LPS-induced Akt phosphorylation in the human monocyte cell line THP-1." *Journal of Surgical Research* 116.1 (2004): 116-120.

Devaraj, Sridevi, Emily Chan, and Ishwarlal Jialal. "Direct demonstration of an antiinflammatory effect of simvastatin in subjects with the metabolic syndrome." *The Journal of Clinical Endocrinology & Metabolism* 91.11 (2006): 4489-4496.

Hölschermann, Hans, et al. "Statins prevent NF-κB transactivation independently of the IKK-pathway in human endothelial cells." *Atherosclerosis* 185.2 (2006): 240-245.

Statins Pleiotrophic Effects Anti-Bacterial Drug



Hennessey, Emma, et al. "Is there potential for repurposing statins as novel antimicrobials?." *Antimicrobial agents and chemotherapy* 60.9 (2016): 5111-5121.

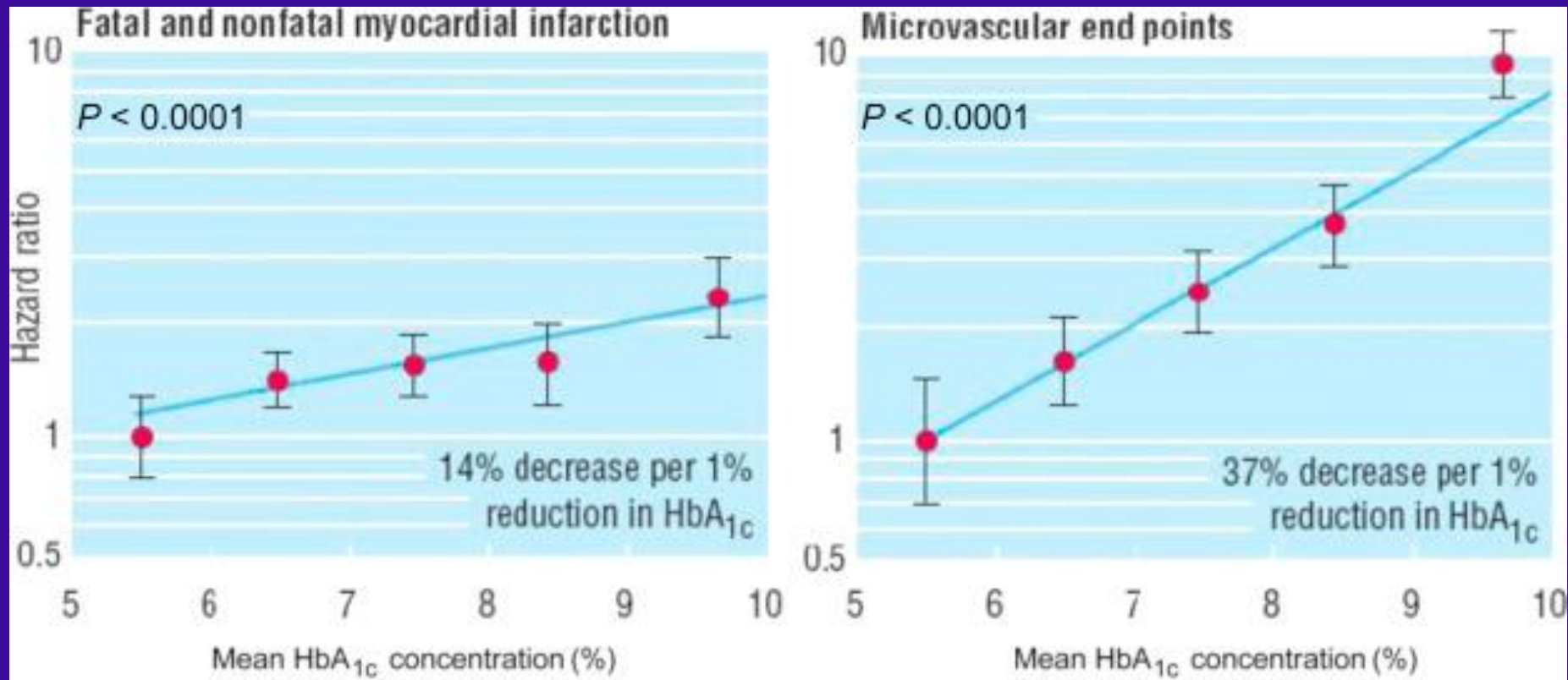
Diabetics Accelerated CAD

HyperGlycemia Drives Intestinal Barrier Dysfunction

- Elevated Blood Sugar is a “A Driver of Intestinal Barrier Dysfunction”.
- “Glucose as an Orchestrator of Intestinal Barrier Function.”

- Thaiss, Christoph A., et al. “Hyperglycemia drives intestinal barrier dysfunction and risk for enteric infection.” Science (2018):

HgbA1c and MI



- Feinman, Richard D., et al. "Dietary carbohydrate restriction as the first approach in diabetes management: critical review and evidence base." Nutrition 31.1 (2015): 1-13.

Diabetics Have Leaky Gut and Low Level Endotoxemia

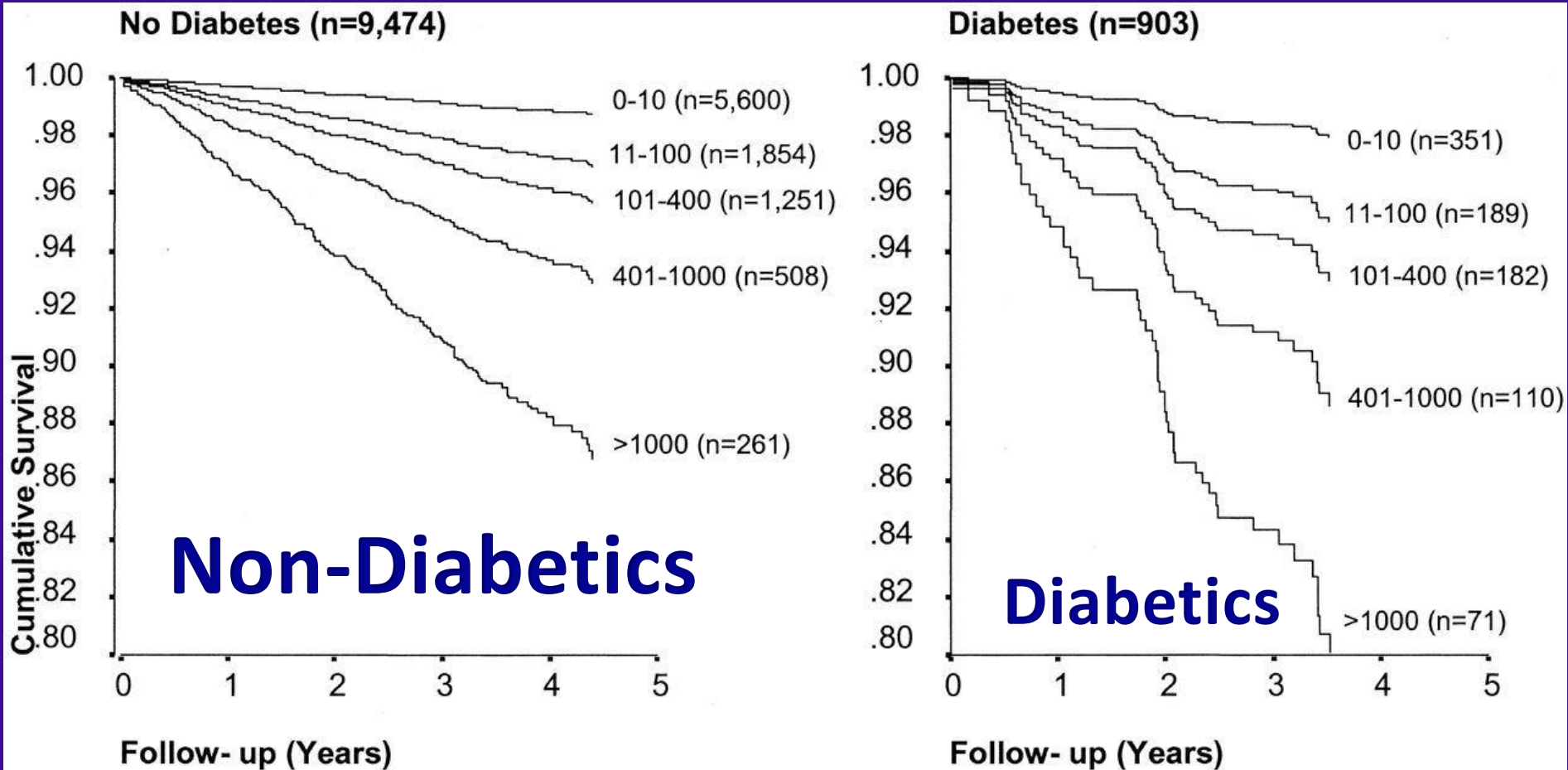
- Patients with elevated fasting blood sugar had significantly higher levels of LPS, zonulin and oxLDL compared to control subjects.
 - Diabetics had significantly higher serum LPS, and higher inflammatory cytokines IL-6 and TNF-alpha.
-
- Carnevale, R., et al. "Low-grade endotoxemia, gut permeability and platelet activation in patients with impaired fasting glucose." *Nutrition, Metabolism and Cardiovascular Diseases* 27.10 (2017): 890-895.
 - Aravindhan, Vivekanandhan, et al. "Chronic endotoxemia in subjects with type-1 diabetes is seen much before the onset of microvascular complications." *PloS one* 10.9 (2015): e0137618.

Diabetics – Benefits of Statins

- Diabetics Have Accelerated Coronary Artery Disease
- Elevated Glucose Induces Leaky Gut
- Statins Reduce Mortality by 20-30% in early Diabetic
- Statins Ineffective for End Stage Diabetics on Hemodialysis.
- Statin Benefits NOT DUE to Cholesterol Lowering
- All of Statin Benefits Due to Pleiotrophic Effects (anti-inflammatory, antibacterial)

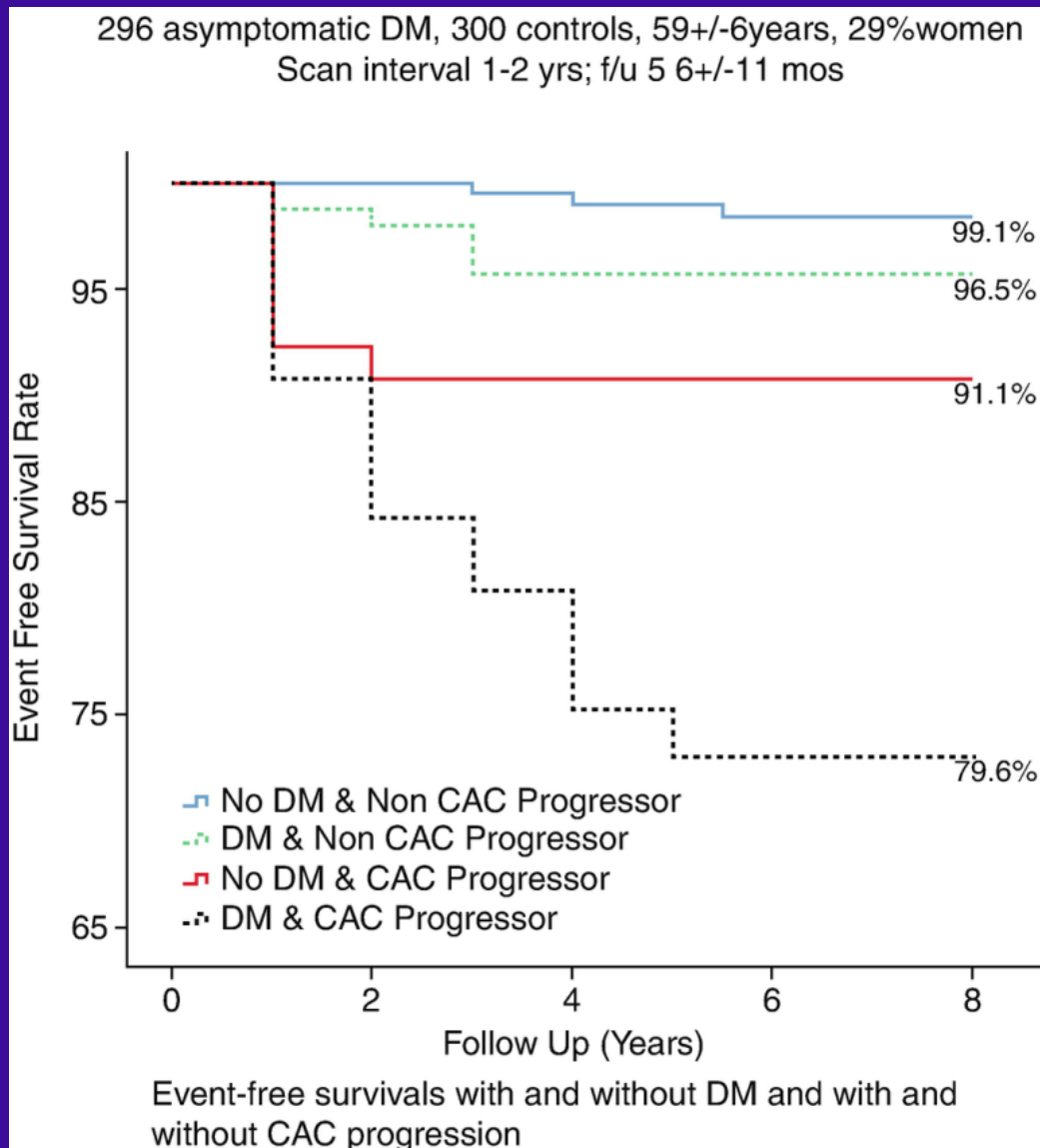
Raggi et al. (22) Prognostic value of coronary artery calcium screening in subjects with and without diabetes. Journal of the American College of Cardiology 2004;43(9):1663-1669.

Calcium Score in Diabetics



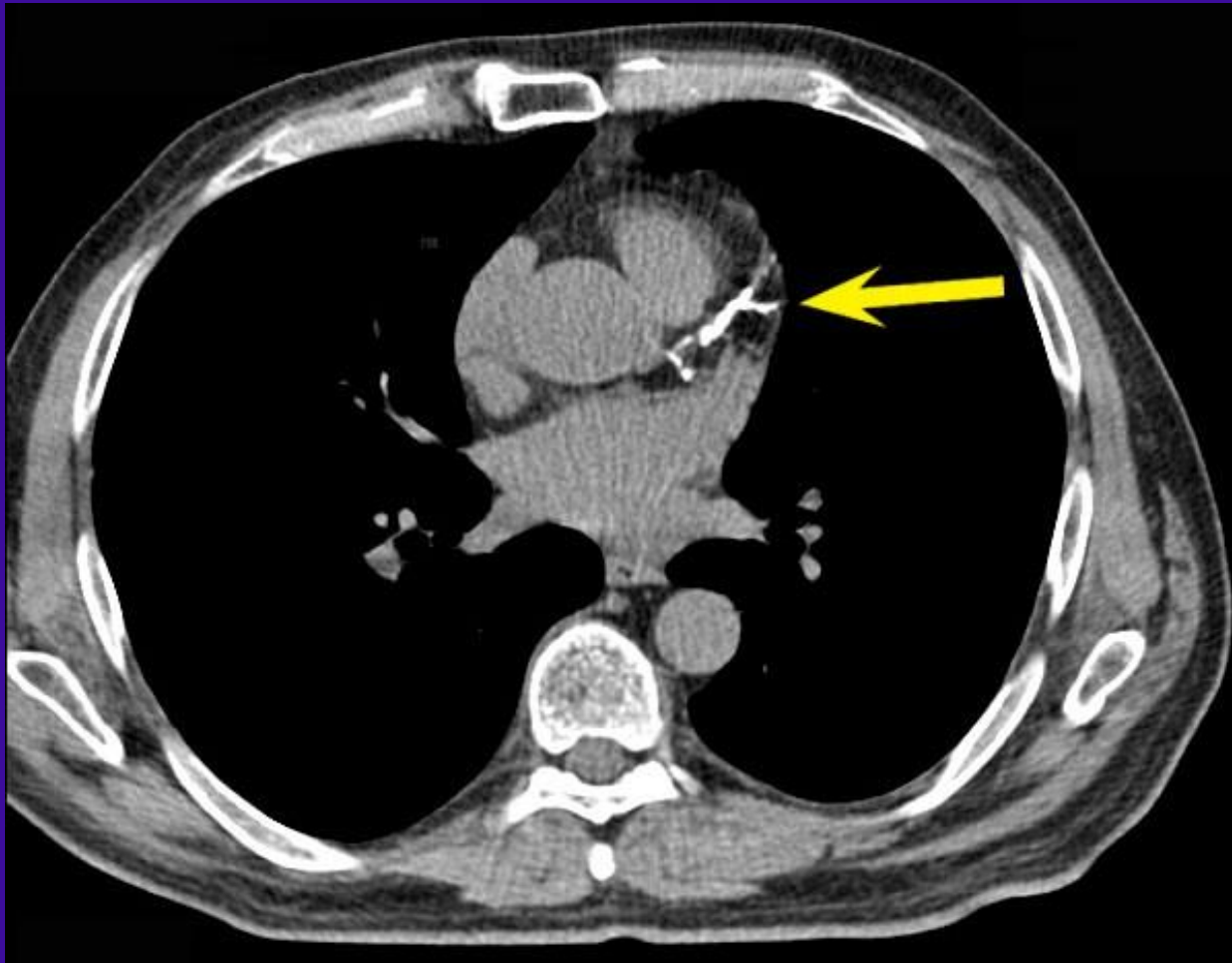
Raggi et al. (22) Prognostic value of coronary artery calcium screening in subjects with and without diabetes. Journal of the American College of Cardiology 2004;43(9):1663-1669.

Progression of Calcium Score in Diabetics



Kiramijyan, Sarkis, et al. "Impact of coronary artery calcium progression and statin therapy on clinical outcome in subjects with and without diabetes mellitus." AmJ Card cardiology (2013): 356-361.

Estrogen Prevents Coronary Artery Disease –Calcium Score



Estrogen Prevents Heart Disease

- Martha is Asymptomatic 56 year old Nurse
CAC = 101 (94th Percentile)
- Rx: Bioidentical Hormone Program
- Rx: Aged Garlic, Vit C, Toco Vit E, Vit K2 (MK-7),
Gluten Free Diet
- One Year Later CAC =109, 9% annual increase
- (22% increase expected, Budoff 2005 Manson 2007)


Budoff, Matthew J., et al. "Effects of hormone replacement on progression of coronary calcium as measured by electron beam tomography." *Journal of women's health* 14.5 (2005): 410-417. (177 women 9% E2 vs 22% control Annual Progression)

Estrogen Slows Calcium Progression

- 7.4 Year Follow Up of WHI
- (50-60 yrs) Premarin-Alone
- 32% Less Calcium in the Estrogen Treated Arm of the Women's Health Initiative.

Manson, JoAnn E., et al. "Estrogen therapy and coronary-artery calcification." New England Journal of Medicine 356.25 (2007): 2591-2602.

Estrogen Prevents Heart Disease

- 11 Year Follow Up of WHI
 - “Younger” age group (age 50-60 yrs),
 - HRT with Premarin-Alone
 - 41% Reduction in Coronary Artery Disease.
 - 46% Reduction in Myocardial Infarctions.
 - 27 % Reduction in All Cause Mortality.
 - 20-30% Reduction in Invasive Breast Cancer.
- 

JAMA. 2011;305(13):1305-1314. Health Outcomes After Stopping Conjugated Equine Estrogens Among Postmenopausal Women With Prior Hysterectomy A Randomized Controlled Trial –Andrea Z. LaCroix, PhD; Rowan T. Chlebowski, MD, PhD; JoAnn E. Manson, MD, DrPH; for the WHI Investigators

What Works for Calcium Score ?

- Estrogen HRT
- Aged Garlic
- Vit C, Lysine (Linus Pauling)
- Tocotrienol Vit E
- MK7- Vit K2
- Gluten Free Diet
- ? MTHFR – Methyl-folate
- ? Homocysteine – B6,B12, Methylfolate

Budoff, Matthew. "Aged garlic extract retards progression of coronary artery calcification." The Journal of nutrition 136.3 (2006): 741S-744S

Gonen, Ayelet et al. "The antiatherogenic effect of allicin: possible mode of action." Pathobiology 72.6 (2005): 325-334.

Miskovic, Daniel J., et al. "Clonidine citrate is safe and effective for long-term management of hypogonadism." Endo international 110.10 (2012): 1524-1526

Testosterone for Males

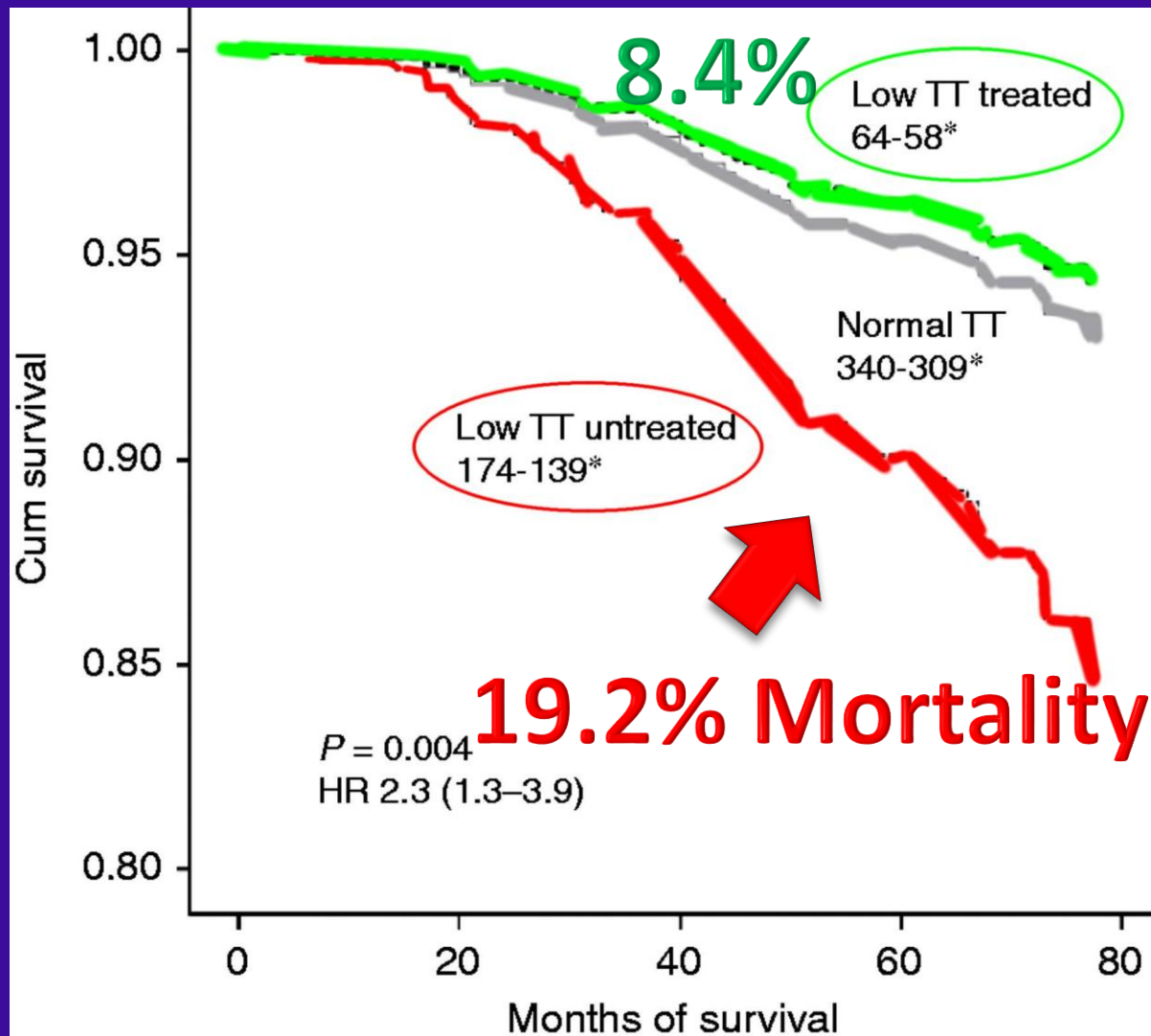


Testosterone Improves Survival in AODM

- JIM, 46 y/o Stockbroker with Chronic Fatigue, AODM.
- Testosterone 290
- FBS =120 HgbA1c =6.2
- LH,FSH Low Normal
- Rx: Testosterone Cyp Injections 100 mg weekly, Metformin, Gluten Free Low Carb Diet.
- One Year Later: More Energy, Lost 20 LBS Weight.
- Testosterone = 650
- FBS = 98
- HgbA1c = 5.8

Muraleedharan, Vakkat, et al. "Testosterone deficiency is associated with increased risk of mortality and testosterone replacement improves survival in men with type 2 diabetes." European Journal of Endocrinology 169.6 (2013): 725-733.

Testosterone Improves Survival in AODM



- U of Sheffield
- 581 males
AODM
6 year F/U
- Red Line
Low T
Untreated
- Green Line
Low T
Treated
- Grey-High T
Untreated

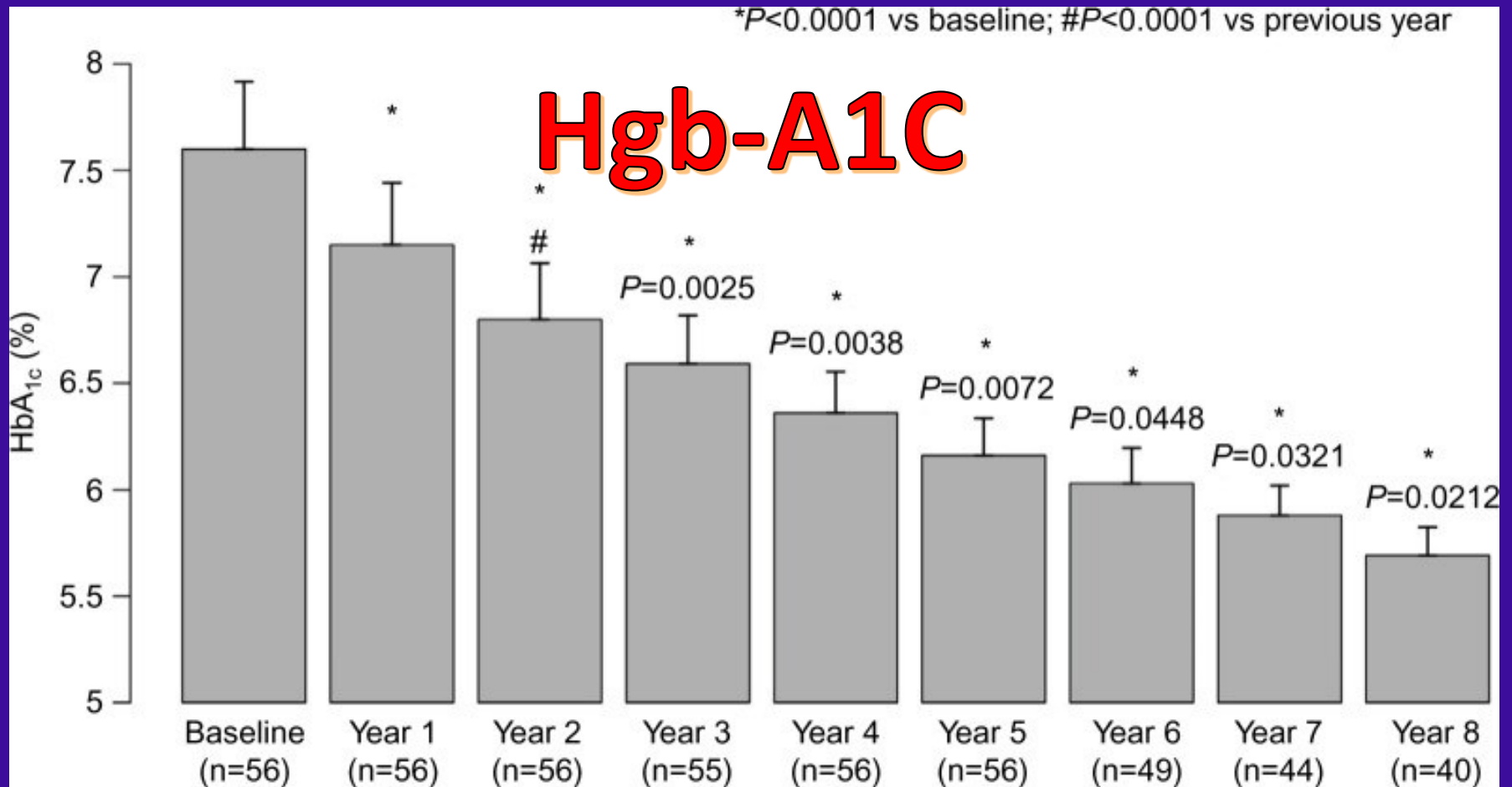
Muraleedharan, Vakkat, et al. "Testosterone deficiency is associated with increased risk of mortality and testosterone replacement improves survival in men with type 2 diabetes." European Journal of Endocrinology 169.6 (2013): 725-733.

Testosterone for Males w/ CVD

- Testosterone RX for 77 males w/ CVD Over 8 Yrs.
- Improved Glycemic Control, FBS, HgbA1c
- Decrease Weight
- Decrease in Waist Circumference
- Decrease in BMI.
- Improved BP
- No Calcium Score Data ? Would be Nice.

Haider, Ahmad, et al. "Men with testosterone deficiency and a history of cardiovascular diseases benefit from long-term testosterone therapy: observational, real-life data from a registry study." *Vascular health and risk management* 12 (2016): 251. (Germany)

Testosterone Reduces HgbA1C



Haider, Ahmad, et al. "Men with testosterone deficiency and a history of cardiovascular diseases benefit from long-term testosterone therapy: observational, real-life data from a registry study." *Vascular health and risk management* 12 (2016): 251.

Testosterone for Males w/ CVD

- “No Patient Suffered Major Adverse Cardiovascular Event “
- “Sustained Improvements in All Cardiometabolic Risk Factors “
- “May be Effective in Secondary Prevention CV Events in Hypogonadal Men with CVD.”

Haider, Ahmad, et al. “Men with testosterone deficiency and a history of cardiovascular diseases benefit from long-term testosterone therapy: observational, real-life data from a registry study.” Vascular health and risk management 12 (2016): 251.

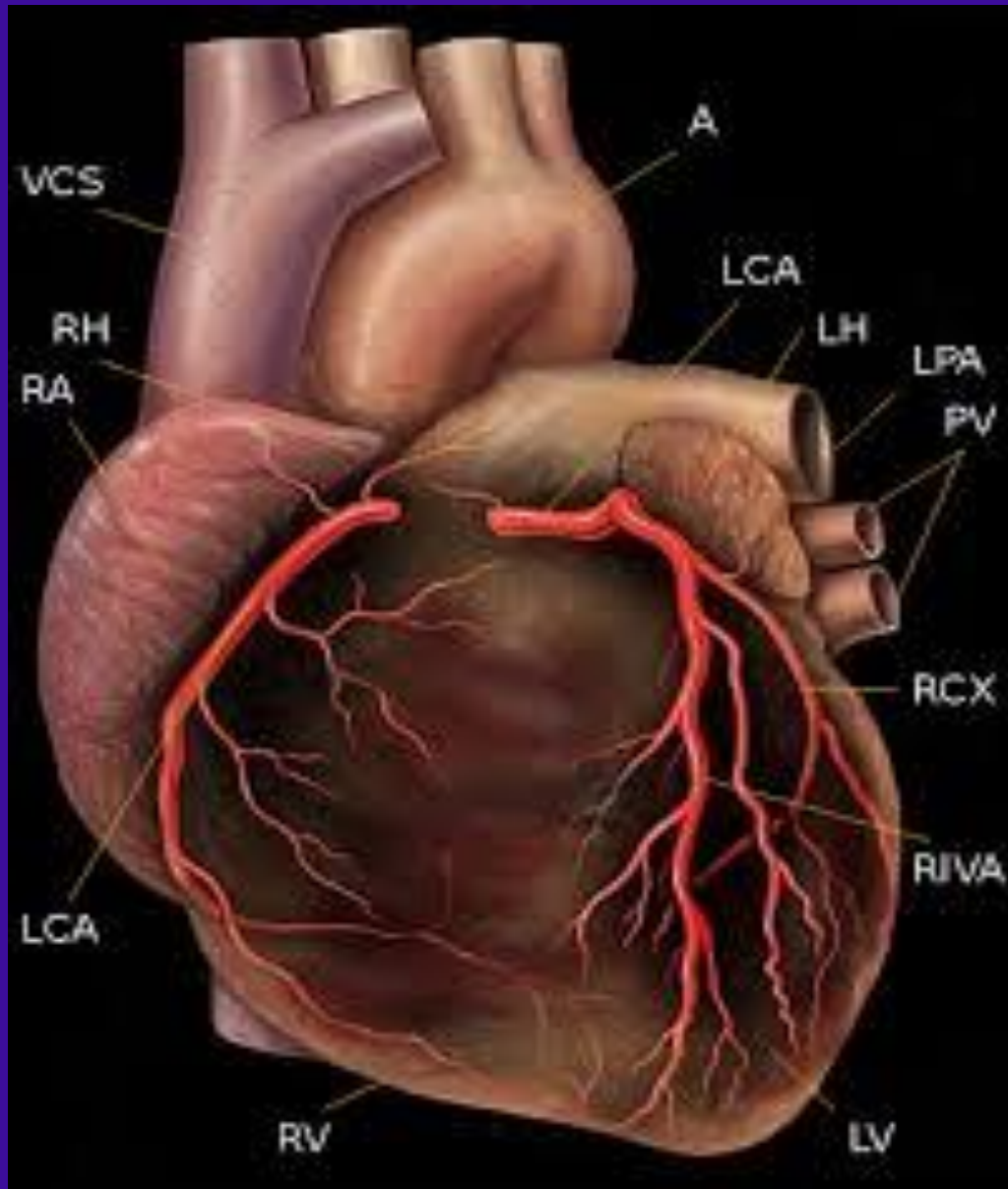
Final Word from the Mayo Clinic

- “Testosterone levels may directly cause (or prevent) CAD and CVD events, or testosterone levels may simply be a **MARKER** of overall quality of health and have no direct effect on CAD and CVD events at all”. Quote : Dr Andrew Elagizi Mayo Clinic 2018

- **Leaky Gut ?** Low FSH, Low LH
 - Low Level Endotoxemia LPS Causes CAD
- 

Elagizi, Andrew, Tobias S. Köhler, and Carl J. Lavie. “Testosterone and Cardiovascular Health.” Mayo Clinic Proceedings. Vol. 93. No. 1. Elsevier, 2018.

Thyroid and the Heart



HUNT Study

- TSH in 17,000 women, no thyroid or heart disease.
- All patients had “normal TSH” 0.5 to 3.5
- Lower TSH, Intermediate and Upper TSH levels
- Mortality from heart disease over an 8 years.

	TSH	Death from Heart Disease
● Group 1	0.50-1.4	baseline risk
● Group 2	1.5-2.4	40% higher than baseline
● Group 3	2.5-3.5	70% higher than baseline

Åsvold, Bjørn O., et al. “Thyrotropin levels and risk of fatal coronary heart disease: the HUNT study.” Archives of internal medicine 168.8 (2008): 855-860.

Sub-Clinical Hypothyroidism

- Elevated Serum TSH 5 -10 mIU/L
- Normal Thyroid Hormone Levels (Free T3, Free T4)

Razvi, Salman, et al. 2012. Arch Int Med) Levothyroxine treatment of subclinical hypothyroidism, fatal and nonfatal cardiovascular events, and mortality

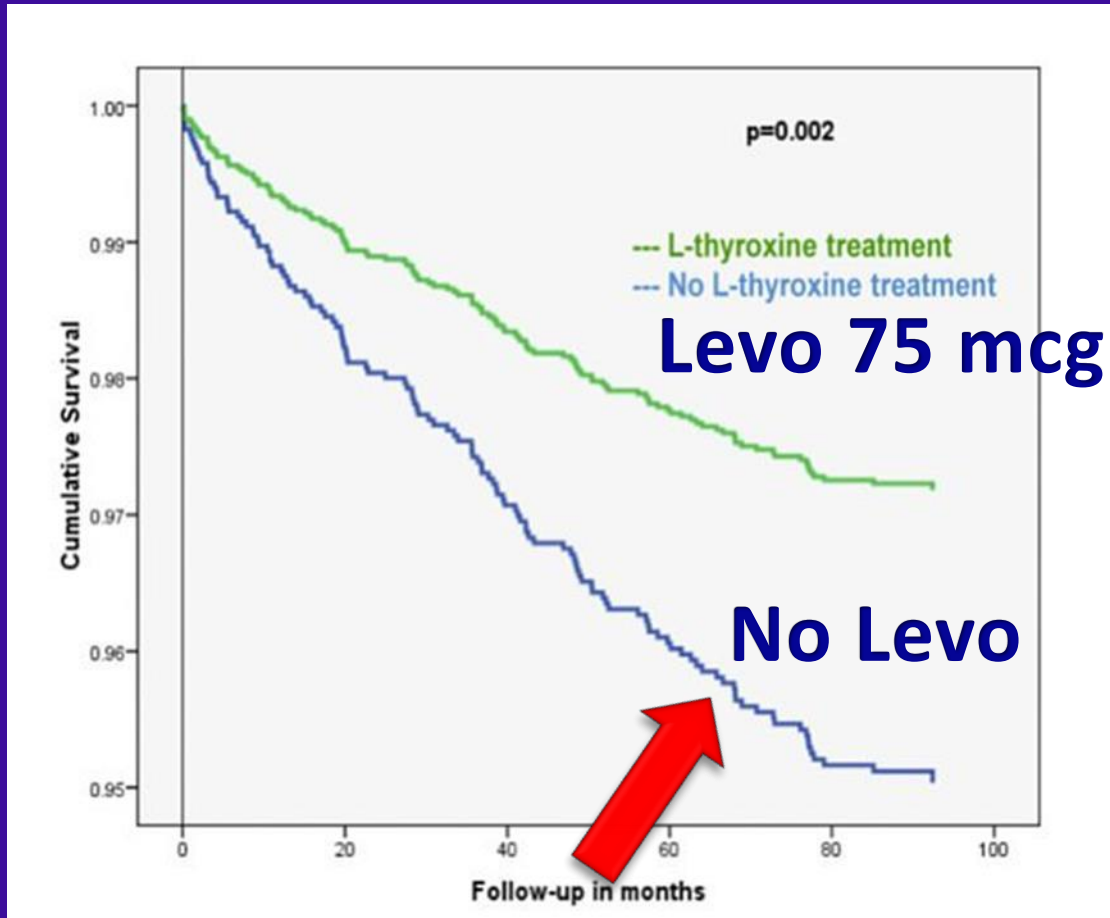
Sub-Clinical Hypothyroidism

- 3040 pts, 40-70 yrs. Randomized to Levo 75 or Placebo, Followed 8 yrs.
- Levo Treated: Fewer Ischemic Heart Disease Events, Reduced All-Cause Mortality

Razvi, Salman, et al. 2012. Arch Int Med) Levothyroxine treatment of subclinical hypothyroidism, fatal and nonfatal cardiovascular events, and mortality

Sub-Clinical Hypothyroidism

Levo Improves Survival



Razvi, Salman, et al. 2012. Arch Int Med) Levothyroxine treatment of subclinical hypothyroidism, fatal and nonfatal cardiovascular events, and mortality

Thyroid Enhances Immune System



- Mouse Model of Endotoxemia
IP INJ LPS.
- 70% survival in T3 -Treated Mice.
- 10 % Survival in Hypothyroid Mice.
- T3 Significantly Protected Mice Against LPS Endotoxemia.

- Perrotta, Cristiana, et al. "The thyroid hormone triiodothyronine controls macrophage maturation and functions: protective role during inflammation." The American journal of pathology 184.1 (2014): 230-247.

Hypothyroidism and CAC

- Low FT3 Level is Important Risk Factor of High Calcification Scores and MACE (Major Adverse Cardiac Event)."

Zhu, Lijie, et al. "Relationship of serum free T3 with the coronary artery calcification and major adverse cardiac events in patients with suspected coronary artery disease."
Zhonghua xin xue guan bing za zhi 42.12 (2014): 1017-1021.

References SCH and Heart Disease

- Razvi, Salman, et al. "Levothyroxine treatment of subclinical hypothyroidism, fatal and nonfatal cardiovascular events, and mortality." *Archives of internal medicine* 172.10 (2012): 811-817.
- Kvetny, J., et al. "Subclinical hypothyroidism is associated with a low-grade inflammation, increased triglyceride levels and predicts cardiovascular disease in males below 50 years." *Clinical endocrinology* 61.2 (2004): 232.
- Hak, A. Elisabeth, et al. "Subclinical Hypothyroidism Is an Independent Risk Factor for Atherosclerosis and Myocardial Infarction in Elderly Women: The Rotterdam Study." *Ann Intern Med* 132 (2000): 270-278
- Imaizumi, Misa, et al. "Risk for ischemic heart disease and all-cause mortality in subclinical hypothyroidism." *The Journal of Clinical Endocrinology & Metabolism* 89.7 (2004): 3365-3370.
- Tseng, Fen-Yu, et al. "Subclinical hypothyroidism is associated with increased risk for all-cause and cardiovascular mortality in adults." *Journal of the American College of Cardiology* 60.8 (2012): 730-737.
- RAZVI, Salman, et al. "The Incidence of Ischemic Heart Disease and Mortality in People with Subclinical Hypothyroidism: Reanalysis of the Whickham Survey Cohort." *The Journal of clinical endocrinology and metabolism* 95.4 (2010): 1734-1740.
- Rodondi, Nicolas, et al. "Subclinical Hypothyroidism and the Risk of Coronary Heart Disease and Mortality." *JAMA: the journal of the American Medical Association* 304.12 (2010): 1365.

Linus Pauling Protocol

High Dose Vitamin C Slows Progression of CAC

- 55 patients treated with High Dose Vitamin C, (and other nutrients)
- Subset of 21 patients with CAC <100
- Serial EBT (Electron Beam CAT Calcium Score
- Treated Patients had significant slowing of progression of CAC
- Untreated pts 34% annual progression
- Treated pts 6% annual progression.(Fig 3b. Niedzwiecki, 1996)

Niedzwiecki, Aleksandra, and Matthias Rath. "Nutritional supplement program halts progression of early coronary atherosclerosis documented by ultrafast computed tomography." *Journal of Applied Nutrition* 48 (1996): 68–78.

Aged Garlic for Calcium Score



- Reduces Progression of Calcium Score by 60-70% compared to controls.

Budoff M. Aged garlic extract retards progression of coronary artery calcification. J Nutr. 2006;136(3 Suppl):741S-744S.

Budoff MJ, Ahmadi N, Gul KM, et al. Aged garlic extract supplemented with B vitamins, folic acid and L-arginine retards the progression of subclinical atherosclerosis: a randomized clinical trial. Prev Med. 2009;49(2-3):101-7.

Zeb I, Ahmadi N, Nasir K, et al. Aged garlic extract and coenzyme Q10 have favorable effect on inflammatory markers and coronary atherosclerosis progression: A randomized clinical trial. J Cardiovasc Dis Res. 2012;3(3):185-90.

Aged Garlic

Mechanism for Prevention in Apo-E Mouse

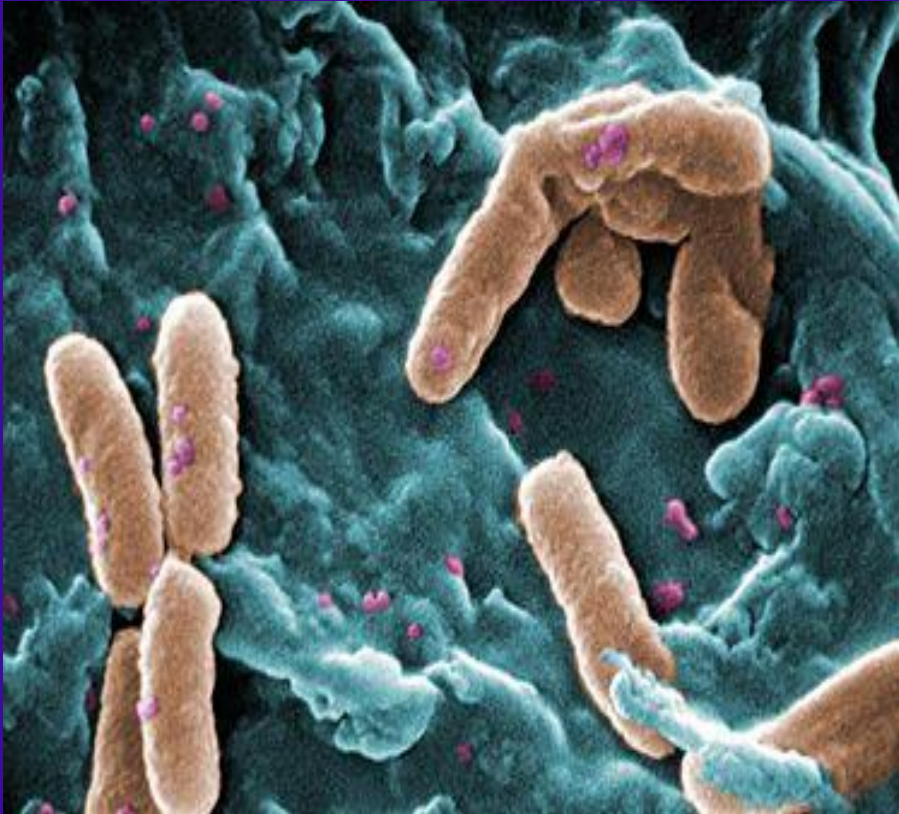
- Daily Garlic (Allicin) Reduced Plaque Area 70% in ApoE-Deficient Mice, and 60% in LDL receptor knockout mice.
- Garlic (Allicin) : NO Effect on Lipid Levels.

Gonen A, Harats D, Rabinkov A, et al. The antiatherogenic effect of allicin: possible mode of action. Pathobiology. 2005;72(6):325-34. Ayelet Gonen, Aviv Shaish, and Dror Harats, Institute of Lipid and Atherosclerosis.

Allicin Reduces Plaque in Apo-E Mice



Pseudomonas Infected Biofilm

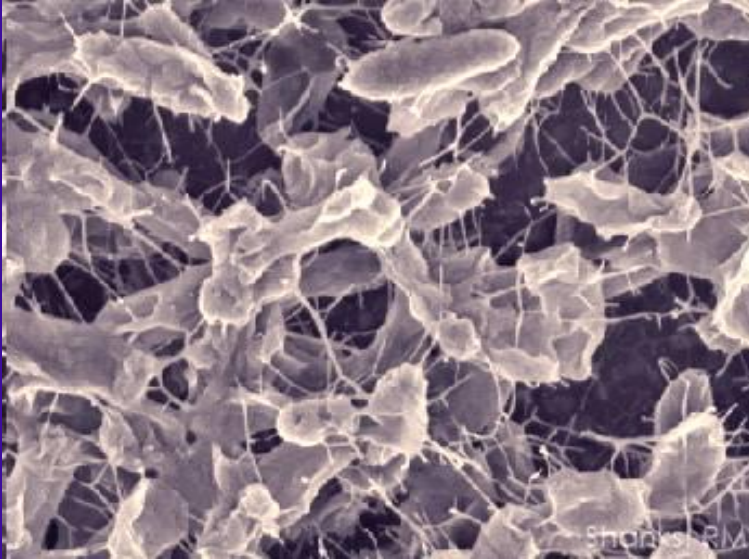


- Pseudomonas in 6 of 15 atherosclerotic plaques. (Bernard Lanter, 2014)
- Pseudomonas (Chryseomonas) in all (100%) plaque specimens (Omry Koren 2011)

Lanter BB, Sauer K, Davies DG. Bacteria present in carotid arterial plaques are found as biofilm deposits which may contribute to enhanced risk of plaque rupture. MBio. 2014;5(3):e01206-14.

Koren O, Spor A, Felin J, et al. Human oral, gut, and plaque microbiota in patients with atherosclerosis. Proc Natl Acad Sci U S A. 2011;108 Suppl 1:4592-8.

Garlic (Allicin) Effective For Pseudomonas Biofilm



- Garlic is Anti-Microbial.
- Garlic Effective Against Pseudomonas Biofilm.
- Inhibits Quorum Sensing and Virulence. (66-67)

Bjarnsholt T, Givskov M. The role of quorum sensing in the pathogenicity of the cunning aggressor *Pseudomonas aeruginosa*. *Anal Bioanal Chem*. 2007;387(2):409-14.

Harjai K, Kumar R, Singh S. Garlic blocks quorum sensing and attenuates the virulence of *Pseudomonas aeruginosa*. *FEMS Immunol Med Microbiol*. 2010;58(2):161-8.

Lihua L, Jianhuit W, Jialini Y, Yayin L, Guanxin L. Effects of allicin on the formation of *Pseudomonas aeruginosa* biofilm and the production of quorum-sensing controlled virulence factors. *Pol J Microbiol*. 2013;62(3):243-51.

Leaky Gut, Gluten Sensitivity, Early Auto-Immune Disease

- Lab Pattern- Low B12, Low Fe, Low Se, Low Triglycerides, Hair Loss, Muscle Cramping.
- Elevated Anti-Gliadin Antibodies (blood or stool)
- Chronic Low Grade Endotoxemia – Coronary Artery Calcium Score
- Food Sensitivity Testing
- Gluten Free Diet- Wheat, Dairy, Egg, Soy etc.
- Hypochlorhydria? –Betaine HCL

Leaky Gut and Coronary Artery Disease

- Leaky Gut Causes Metabolic Endotoxemia
- Elevated Cytokines (IL-6, CRP)
- Activation of Nuclear Factor Kappa Beta (NFKB)
- Linked to Metabolic Syndrome, AODM, Obesity, Atherosclerosis, Parkinson's

Brown, J. Mark et al. "The Gut Microbial Endocrine Organ: Bacterially-Derived Signals Driving Cardiometabolic Diseases." Annual review of medicine 66 (2015): 343.

Rice, James B., et al. "Low-level endotoxin induces potent inflammatory activation of human blood vessels inhibition by statins." Arteriosclerosis, thrombosis, and vascular biology 23.9 (2003): 1576-1582.

Treatment For Leaky Gut

Eliminate

- NSAIDS
- PPI's
- Alcohol
- Wheat Gluten
- Reactive Foods
- Glyphosate
- GMO Food
- Pesticides

Give

- Berberine
- Probiotics
- Digestive Enzymes
- Fiber
- Glutamine
- Colostrum
- Zinc (Resnick, 2010)

Summary/Conclusion

Low Level Endotoxemia/ Leaky Gut



**Depression
Chronic
Fatigue**



**Hypothalamic
Dysfunction**



**Coronary
Artery Disease**



- Endocrinopathy
- Central Hypothyroid
- HypoGonadism
- Hypertension

- Garlic (Allicin)
- Berberine

Calcium Score Progression Indicates Treatment Failure

- “If someone is on a statin or not and they are progressing (meaning the calcium score is progressing), They Are Failing their current therapy.” (Matthew Budoff, 2017)

- Matthew Budoff, SCCT 2017 coronary calcium scores in 2017: Useful, yes, but hard outcomes data still lacking.” Society of Cardiovascular Computed Tomography (SCCT) 2017 Annual Scientific Meeting.

Calcium Score

Look at Actual Disease

- “It’s time that we should let traditional risk scores and risk factor-based management rest in peace.... . They have served their “purpose” for the last 50 years and now in 2017, we have the ability to look at the actual disease with calcium testing.....CAC (Calcium Score) testing provides the most precise insight of what your actual risk is so you can tailor the treatment. (Nasir 2017)

- Khurram Nasir, MD, MPH, of Baptist Health South Florida, Miami. Dr. Nasir stated in a session of the 2017 annual meeting of the Society of Cardiovascular Computed Tomography

Calcium Score

My Treatment Protocol

- Vitamin C
- Vitamin K2
- Tocotrienol Vitamin E
- Berberine
- Fibrinolytic Enzymes
- Diet Lifestyle- Eliminate Wheat, Sugar, Low Carb Diet, WeightLoss
- Control Diabetes

Thank You – Any Questions?



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