Contemporary Prevention of Major Cardiovascular Events. An Existential Crisis

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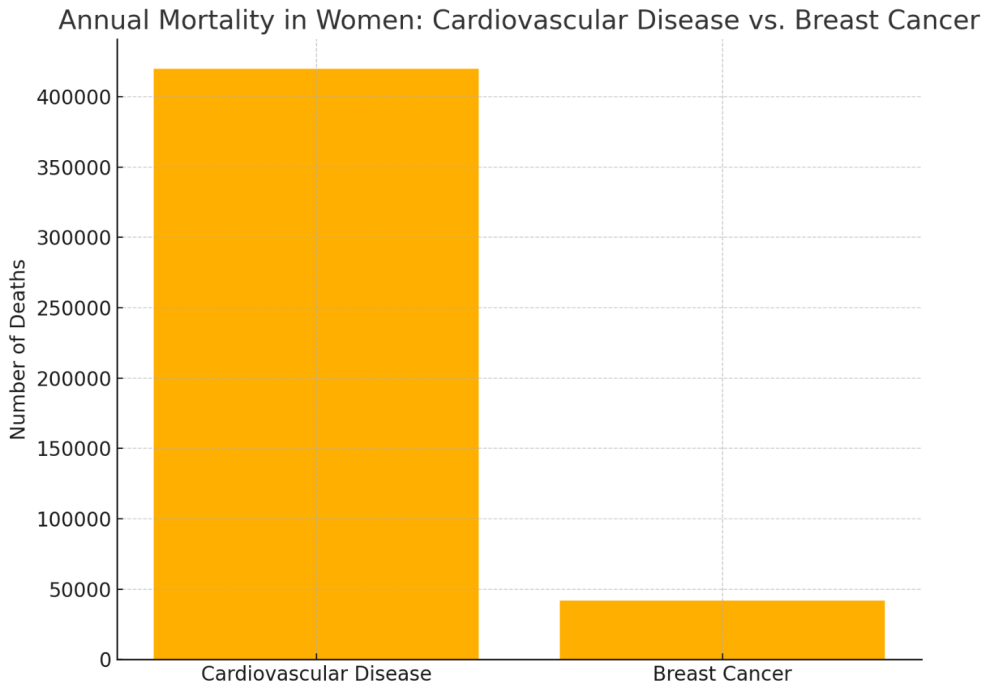
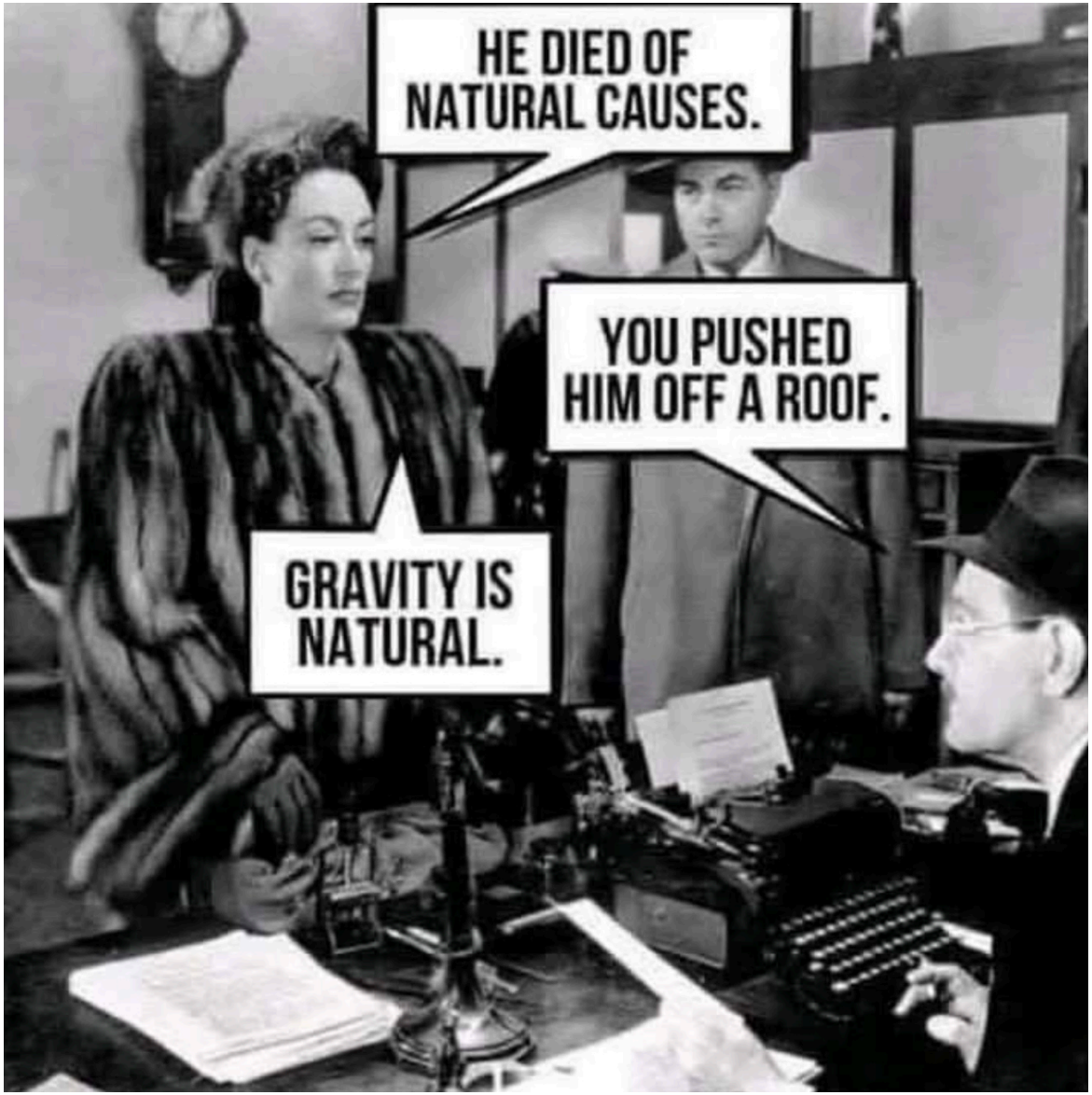
Boulder Heart
May 15, 2025

18,000,000 Deaths World Wide
1 every 40 seconds

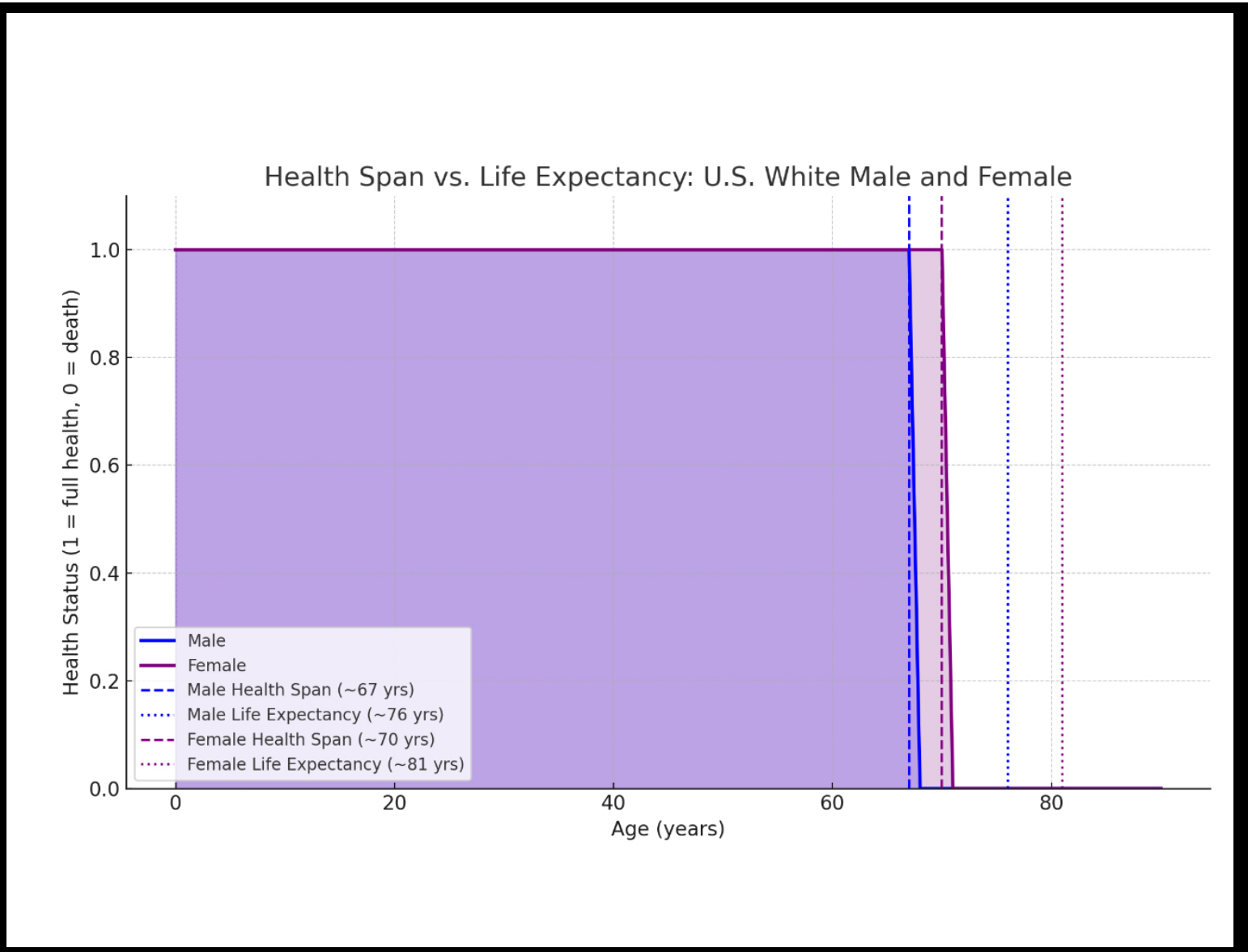
Annual Mortality in Women: Cardiovascular Disease vs. Breast Cancer

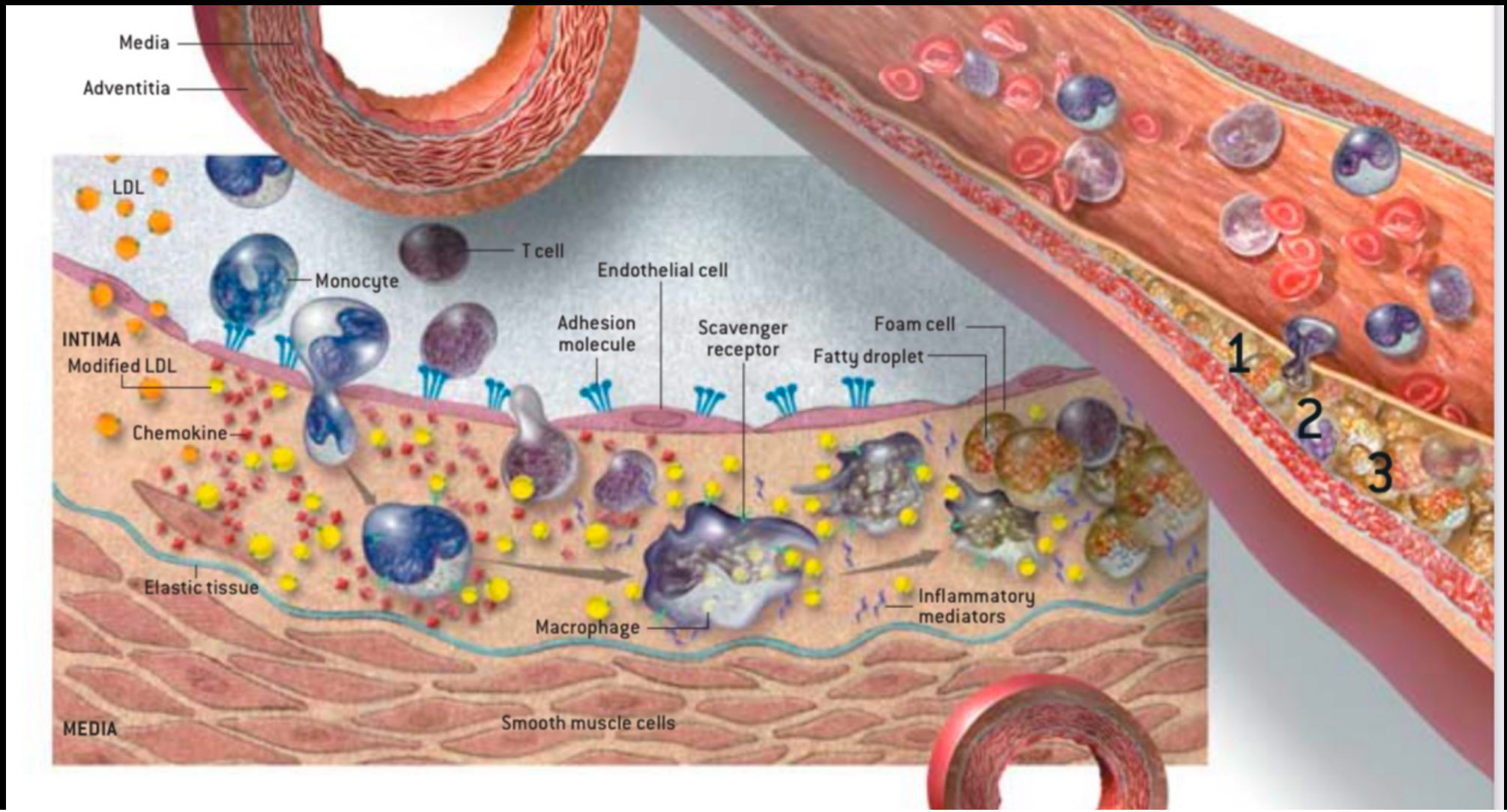



HE DIED OF NATURAL CAUSES.
YOU PUSHED HIM OFF A ROOF.
GRAVITY IS NATURAL.

A reconstruction of Ötzi the Iceman, who lived and died in the European Alps some 5,200 years ago. His naturally mummified remains were discovered by German hikers on September 19, 1991.

PHOTOGRAPH BY ROBERT CLARK, NAT GEO IMAGE COLLECTION


Health Span vs. Life Expectancy: U.S. White Male and Female
Health Status (1 = full health, 0 = death)
1.0
0.8
0.6
0.4
0.2
0.0
0
20
40
60
80
Age (years)
Male
Female
Male Health Span (~67 yrs)
Male Life Expectancy (~76 yrs)
Female Health Span (~70 yrs)
Female Life Expectancy (~81 yrs)

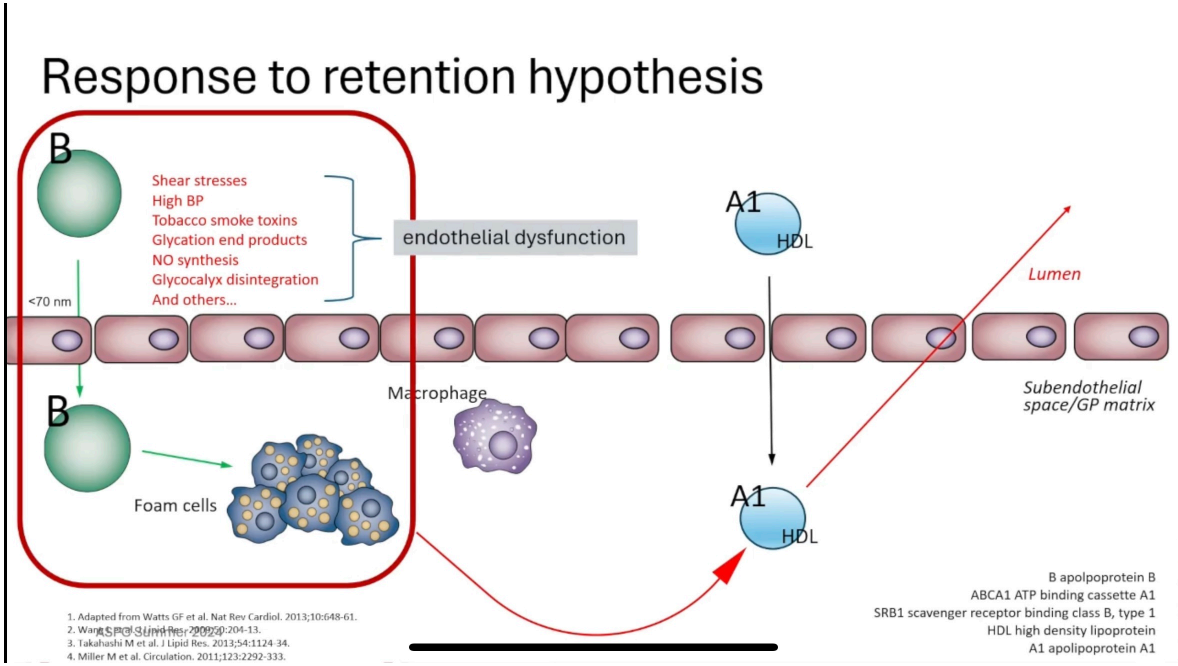

Media
Adventitia
LDL
T cell
Monocyte
Endothelial cell
Adhesion molecule
Scavenger receptor
Foam cell
Fatty droplet
INTIMA
Modified LDL
Chemokine
Elastic tissue
Macrophage
Inflammatory mediators
MEDIA
Smooth muscle cells
1
2
3

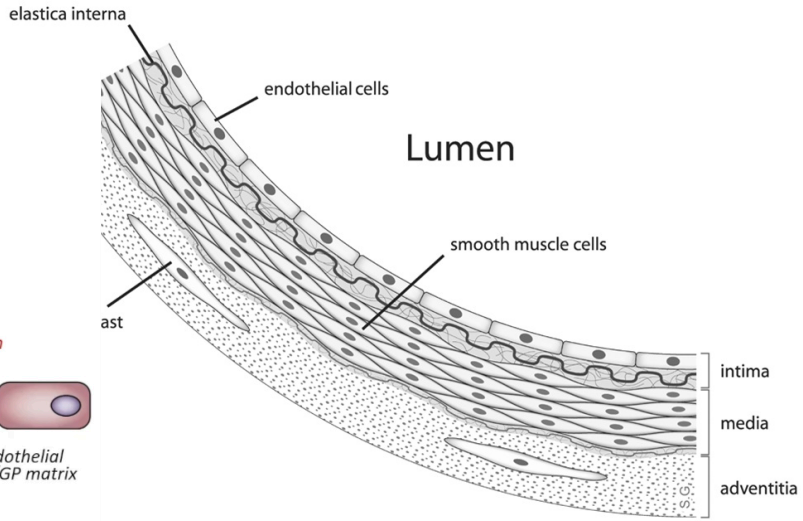
Endothelial Health

Impaired Vasodilation

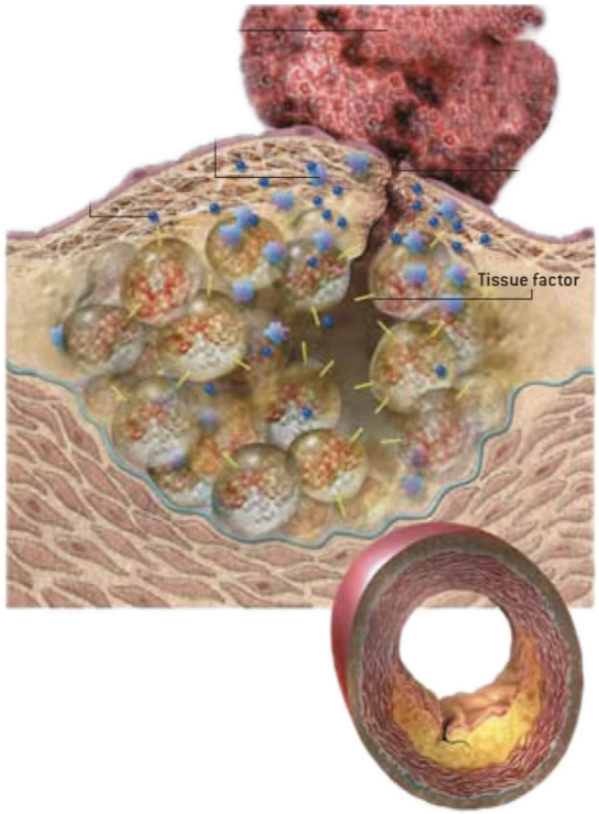
Inflammation

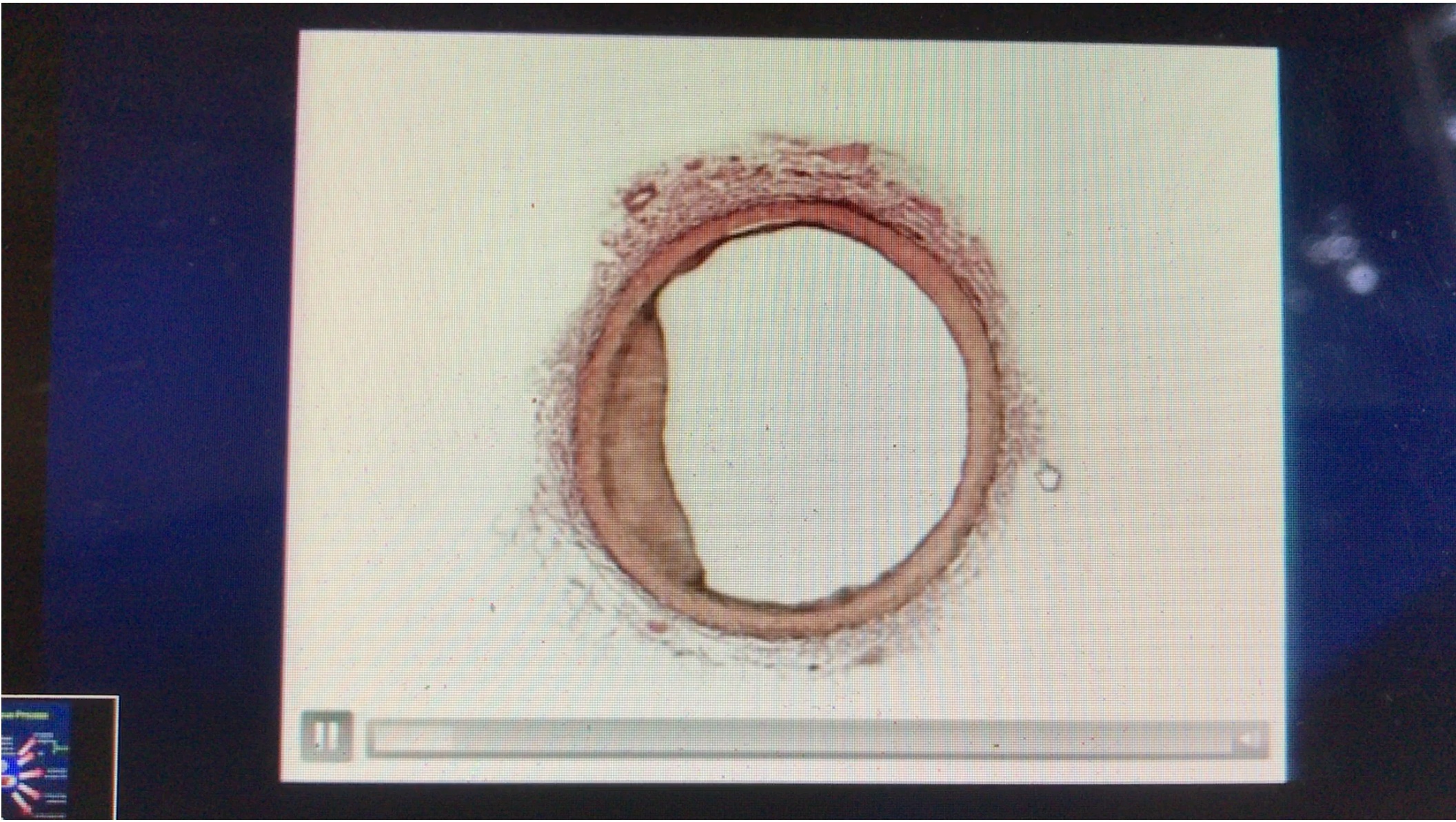
Thrombosis



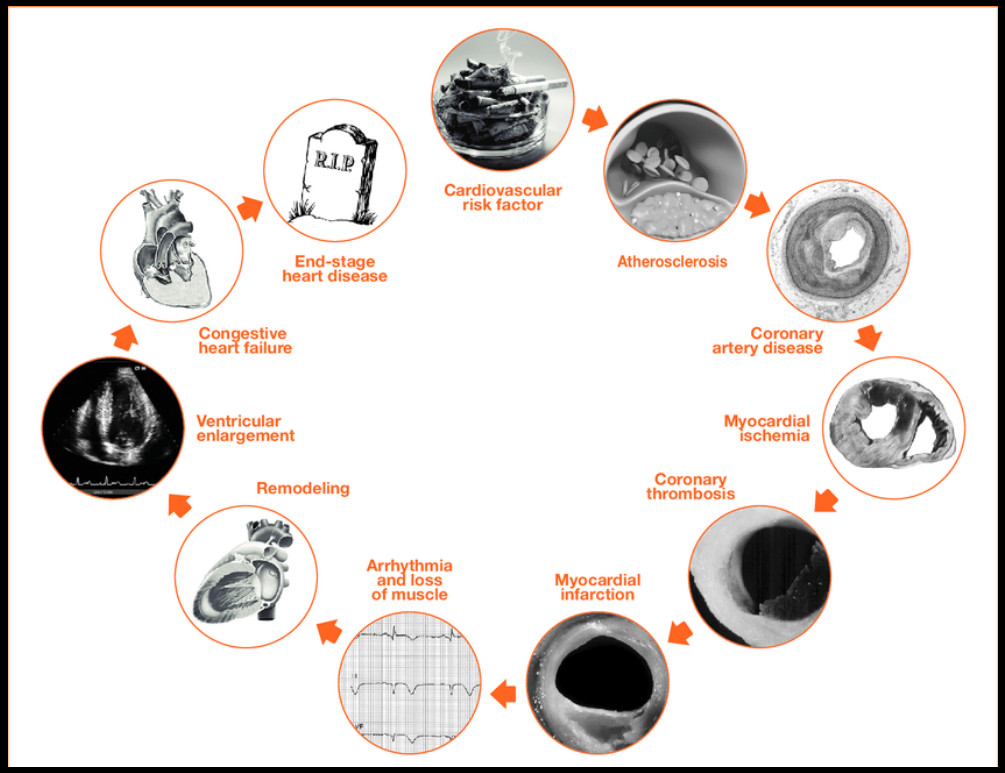



Blood channel
Plaque
4
Thrombus
5

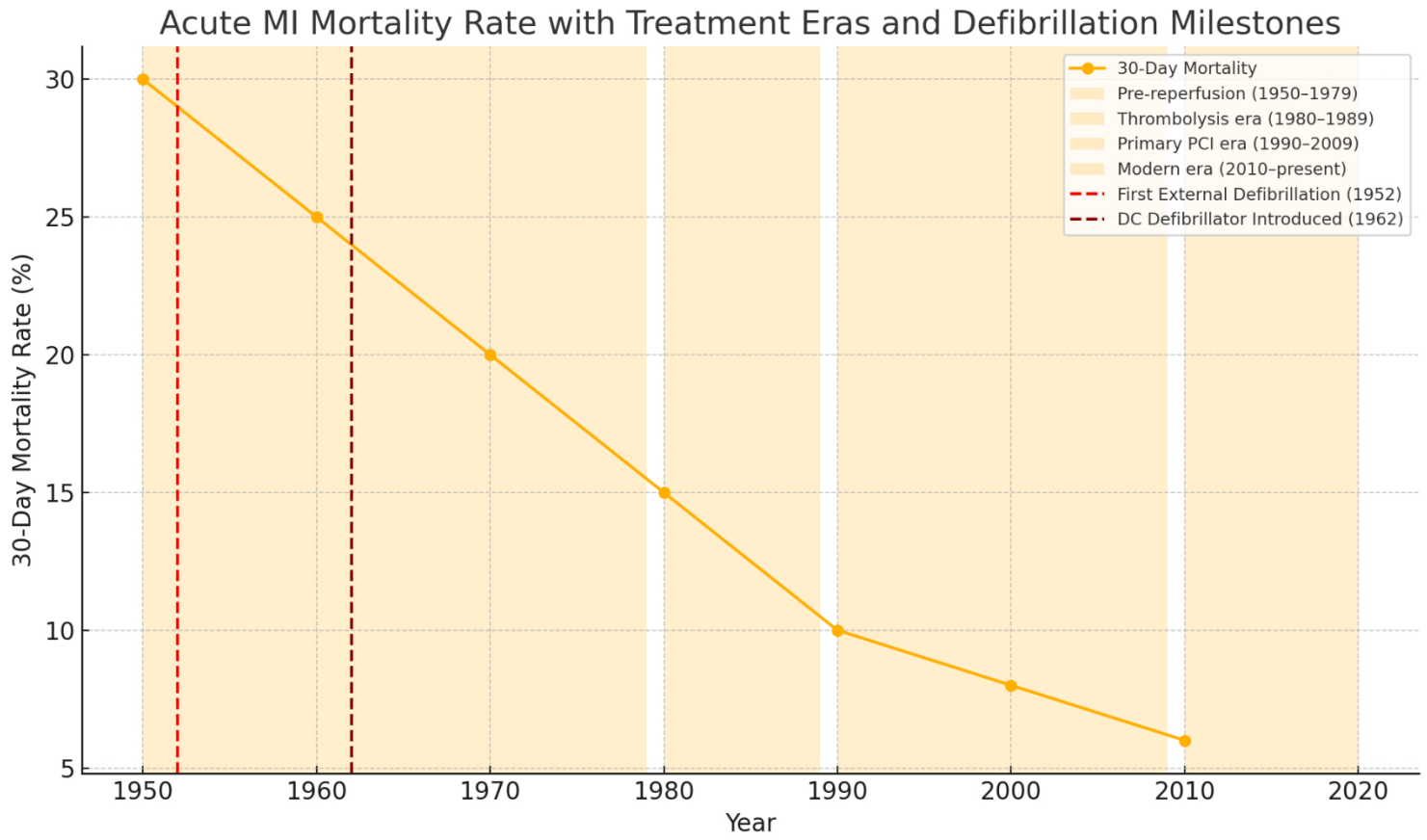

Tissue factor



Cardiovascular Disease is a continuum



Acute MI Mortality Rate with Treatment Eras and Defibrillation Milestones



Focus of an ASCD Risk Reduction Visit

- Life Style and Health Behaviors
- Medical Management
- Shared Decision Making
- Behavioral Counseling
- Medication Reconciliation

Screening Guidelines

- - ACC/AHA: Screen adults 20-49 years, repeat every 4–6 years. Emphasis on life style choices and estimating lifetime risk.
- Adults 40-75 Routine Assessment of traditional risk factors using Cohort Equations
- Adults > 75 Individualized approach in the setting of life expectancy and overall health status
- - Lipid panel includes LDL-C, HDL-C, triglycerides,non-HDL-C

Risk Assessment

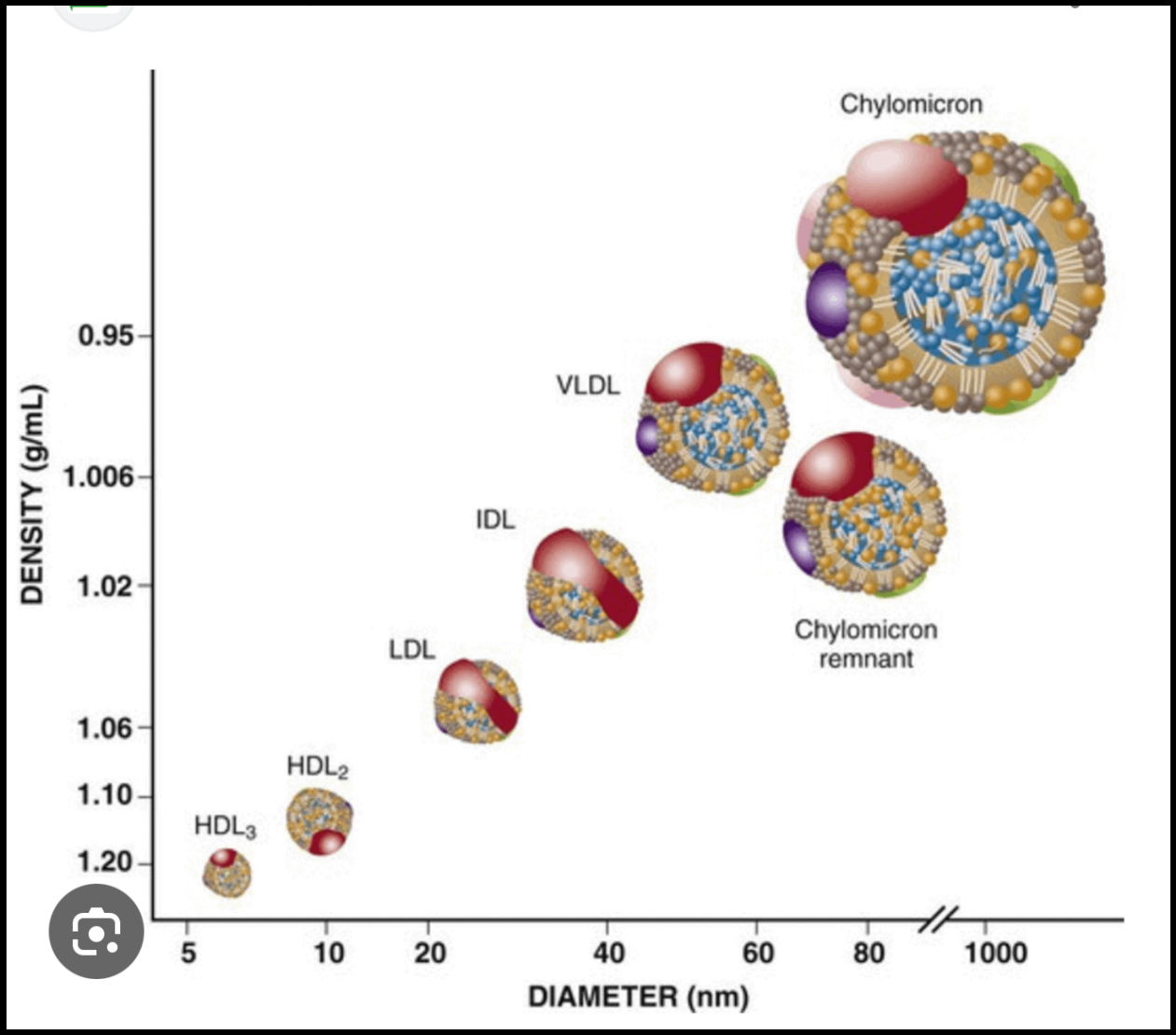
- Primary prevention in ASCVD refers to preventing the initial occurrence of an ASCVD event in individuals who have not yet developed clinical manifestations of the disease.
- Secondary prevention refers to a comprehensive set of measures to prevent recurrent ASCVD events and improve long term prognosis.

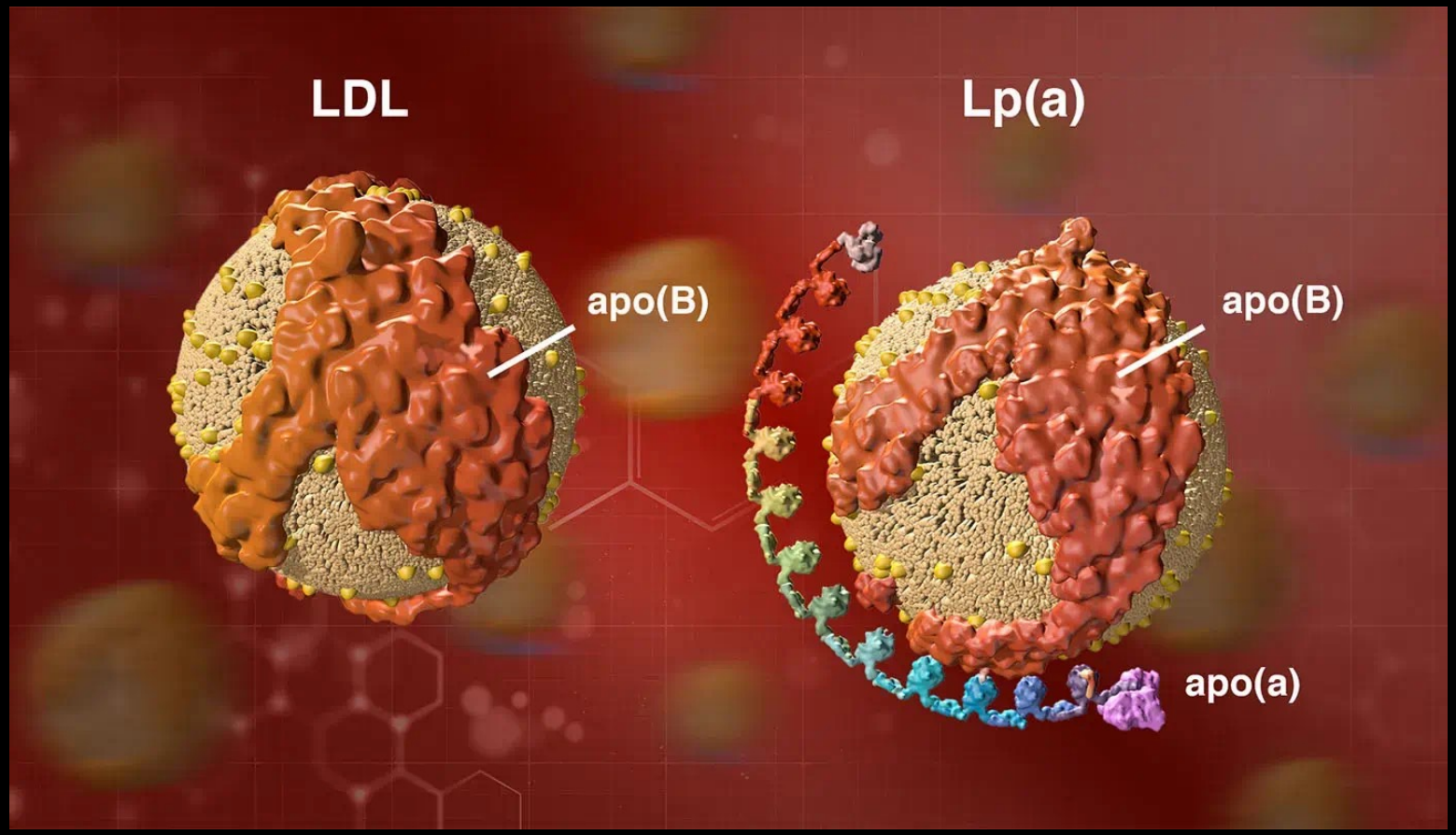
Risk Stratification

- - ASCVD risk calculator: categorizes risk as low, borderline, intermediate, high.
- PREVENT
- MESA
- QRISK3
- SCORE2
- INTERHEART

Attributable Risk
InterHeart Trial

- Abnormal lipids (PAR 49.2%)
- Smoking (PAR 35.7%)
- Psychosocial factors (PAR32.5%)
- Abdominal Obesity (PAR 20.1%)
- Hypertension (PAR 17.9%)
- Lack of Daily Consumption Fruits and Vegetables (PAR 13.7%)
- Lack of Regular Physical Activity (PAR12.2%)
- Diabetes (PAR 9.9%)
- Alcohol (PAR 6.7%)


Chylomicron
VLDL
IDL
LDL
HDL2
HDL3
Chylomicron remnant
DENSITY (g/mL)
0.95
1.006
1.02
1.06
1.10
1.20
5
10
20
40
60
80
1000
DIAMETER (nm)


LDL
apo(B)
Lp(a)
apo(B)
apo(a)

Cardiovascular Risk

- Majority of ASCVD risk attributable to:
  - Smoking
  - Poor Diet
  - Obesity
  - Sedentary Lifestyle
  - hypertension
  - Hyperlipidemia
  - Diabetes

  Ideal cardiovascular health defined as having all 7 factors at goal is very rare among US adults. It is estimated that 87% of middle-aged US adults and 95% of individuals ≥60 years old meet ≤4 of these health metrics.1

  CIRCULATION 2019 GUIDLINES

Risk-enhancing Factors for Clinician-Patient Risk Discussion

- **Family history of premature ASCVD;** (males <55 years; females <65 years)
- **Primary hypercholesterolemia** (LDL-C 160-189 mg/dL (4.1- 4.8 mmol/L); non-HDL-C 190-219 mg/dL (4.9-5.6 mmol/L).
- **Metabolic syndrome** (increased waist circumference, elevated TG (>150 mg/dL, elevated BP, elevated glucose, low HDL-C (<40 mg/dL in men, <50 mg/dL in women) are factors; tally of 3 makes the diagnosis)
- **Chronic kidney disease** (eGFR 15- 59 ml/min per 1.73 m^2 with or without albuminuria; not treated with dialysis or kidney transplantation)
- **Chronic inflammatory conditions** such as psoriasis, rheumatoid arthritis (RA) or human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS)
- **History of premature menopause (before age 40) and history of pregnancy-associated conditions that increase later ASCVD risk such as pre-eclampsia**
- **High-risk ethnicities** (e.g. South Asian ancestry)
- **Lipid/Biomarkers:** Associated with increased ASCVD risk

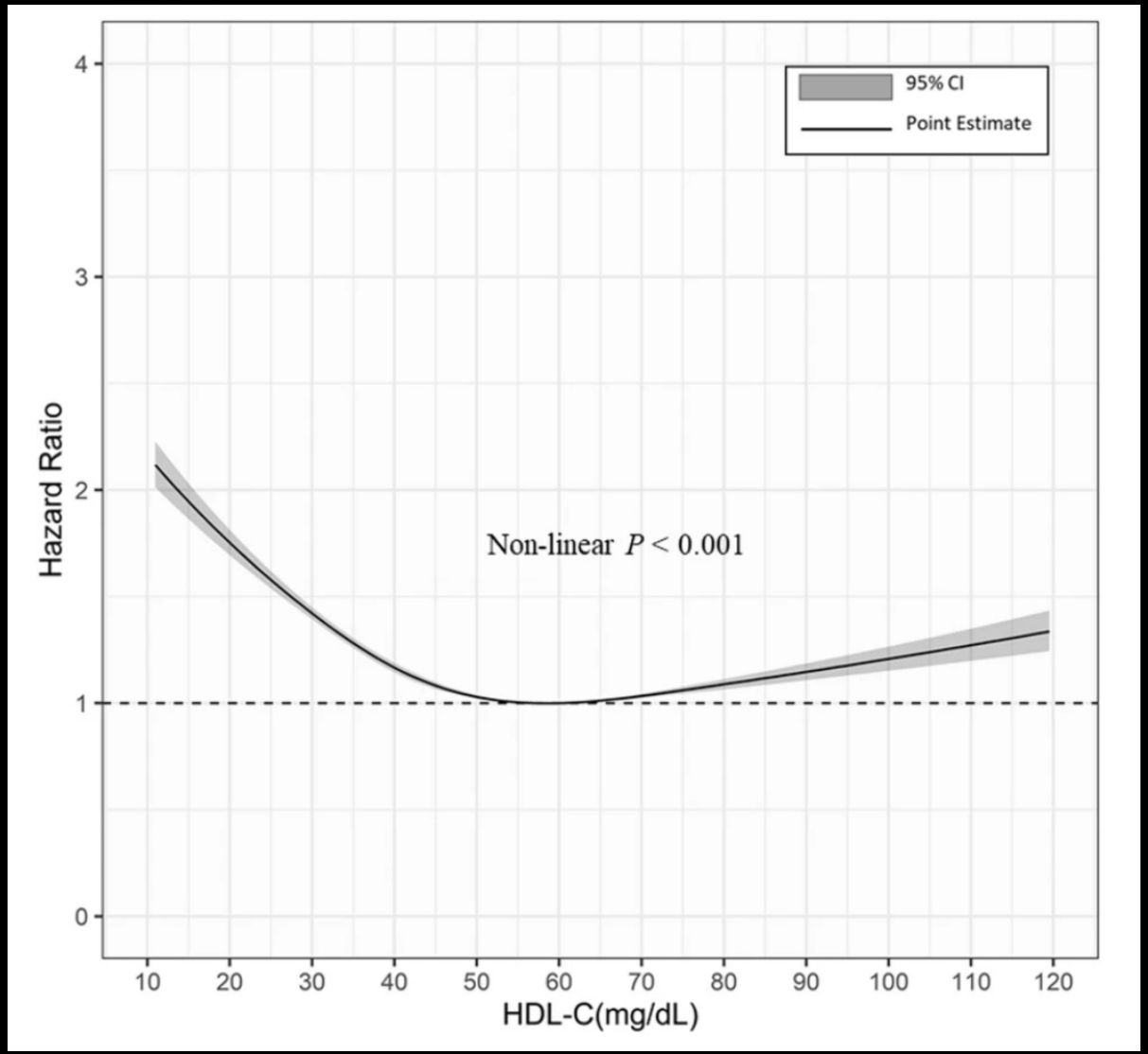
  -Persistently* elevated, primary hypertriglyceridemia (≥175 mg/dl);

  -If measured:

  - **High-sensitivity C-reactive protein** - (≥2.0 mg/L)
  - **Elevated lipoprotein (a)** - A relative indication for its measurement is family history of premature ASCVD. An Lp(a) ≥ 50 mg/dL or ≥125 nmol/L constitutes a risk enhancing factor especially at higher levels of Lp(a).
  - **Elevated apo B ≥130 mg/dL** - A relative indication for its measurement would be triglyceride ≥ 200 mg/dL. A level ≥ 130 mg/dL corresponds to an LDL-C ≥160 mg/dL and constitutes a risk enhancing factor.
  - **ABI <0.9**

AIDS indicates acquired immunodeficiency syndrome; ABI, ankle-brachial index; apoB, apolipoprotein B; ASCVD, atherosclerotic cardiovascular disease; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; HIV, human immunodeficiency virus; LDL-C, low-density lipoprotein cholesterol; Lp(a), lipoprotein (a); and RA, rheumatoid arthritis.

*Optimally, 3 determinations


95% CI
Point Estimate
Hazard Ratio
Non-linear $P < 0.001$
HDL-C(mg/dL)
0
1
2
3
4
10
20
30
40
50
60
70
80
90
100
110
120

Novel Risk 2025

Cannabis

Microplastics

Cannabis Use Substantially Increases Risk of Heart Attack

Mar 24, 2025

Save to Library Print

Citation:

Kamel I, Mahmoud A, Twayana A. et al. Myocardial infarction and cardiovascular risks associated with cannabis use: A multicenter retrospective study. *JACC Adv.* Published online March 18, 2025. https://doi.org/10.1016/j.jacadv.2025.101698

Microplastics Possibly Associated With Chronic NCDs

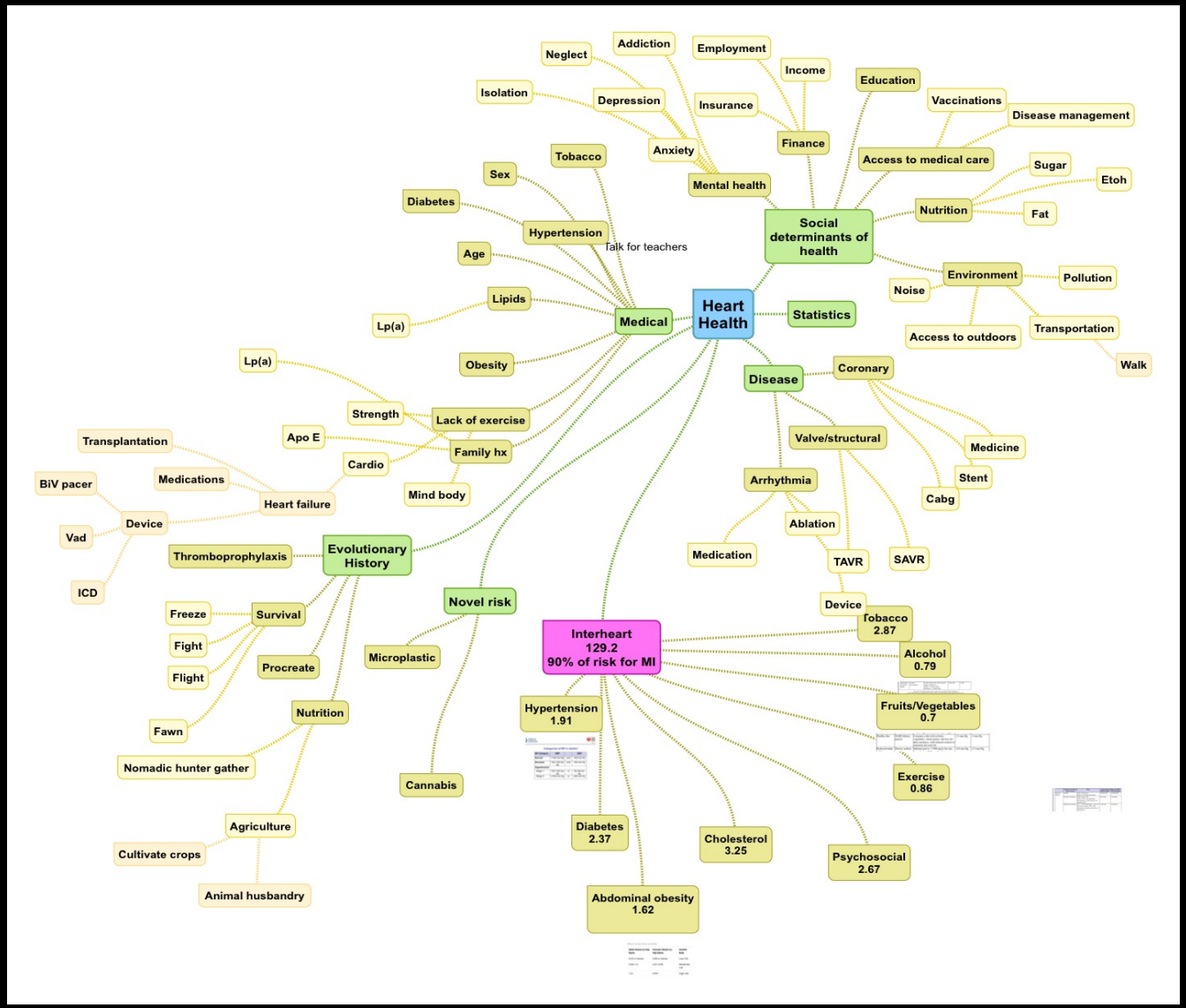
Mar 25, 2025

ACC News Story

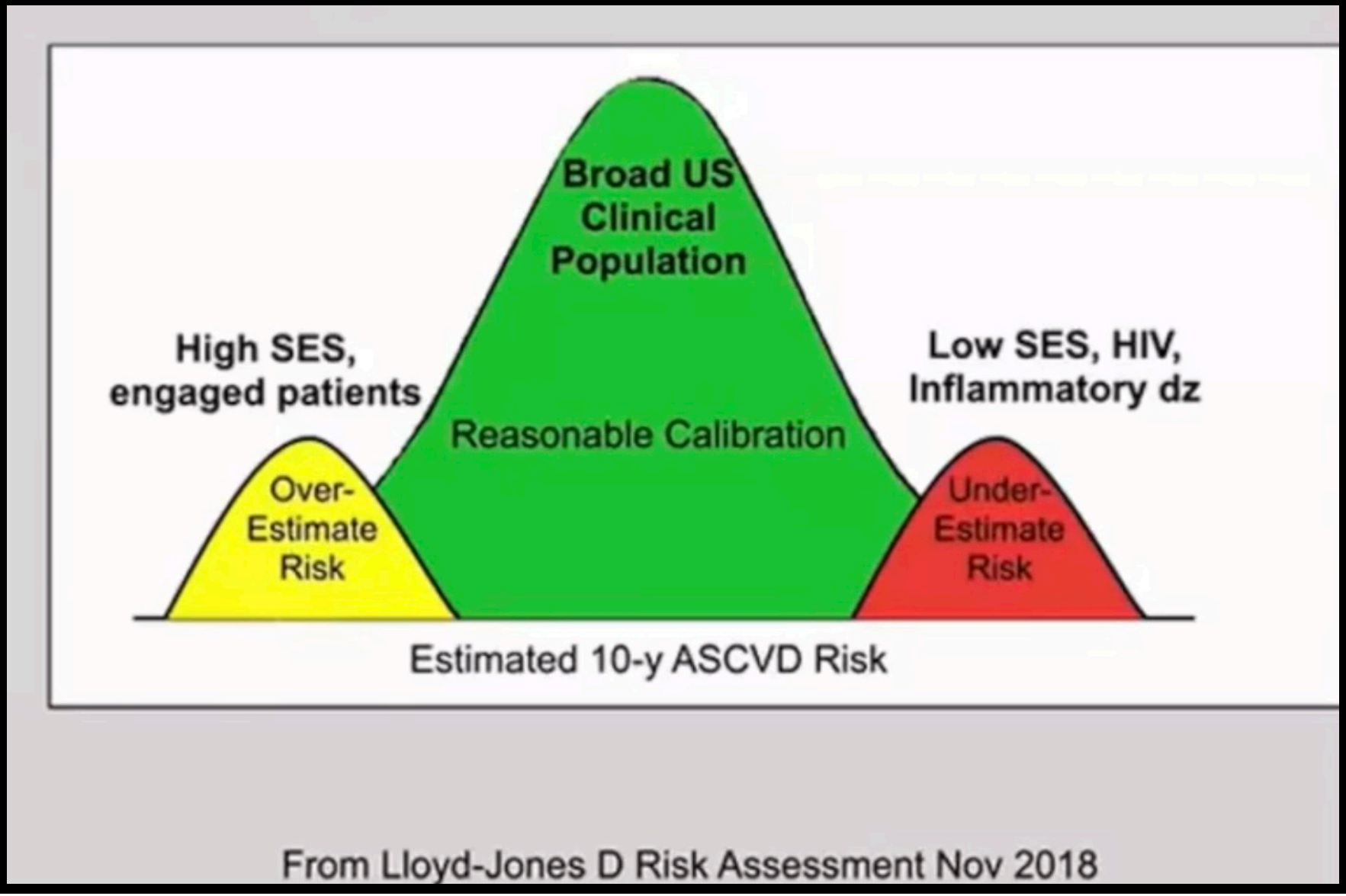
Save to Library Print

On this page: Resources

Microplastic exposure is associated with a higher prevalence of chronic noncommunicable diseases (NCDs) including hypertension, diabetes and stroke, according to a study presented at ACC.25 in Chicago.

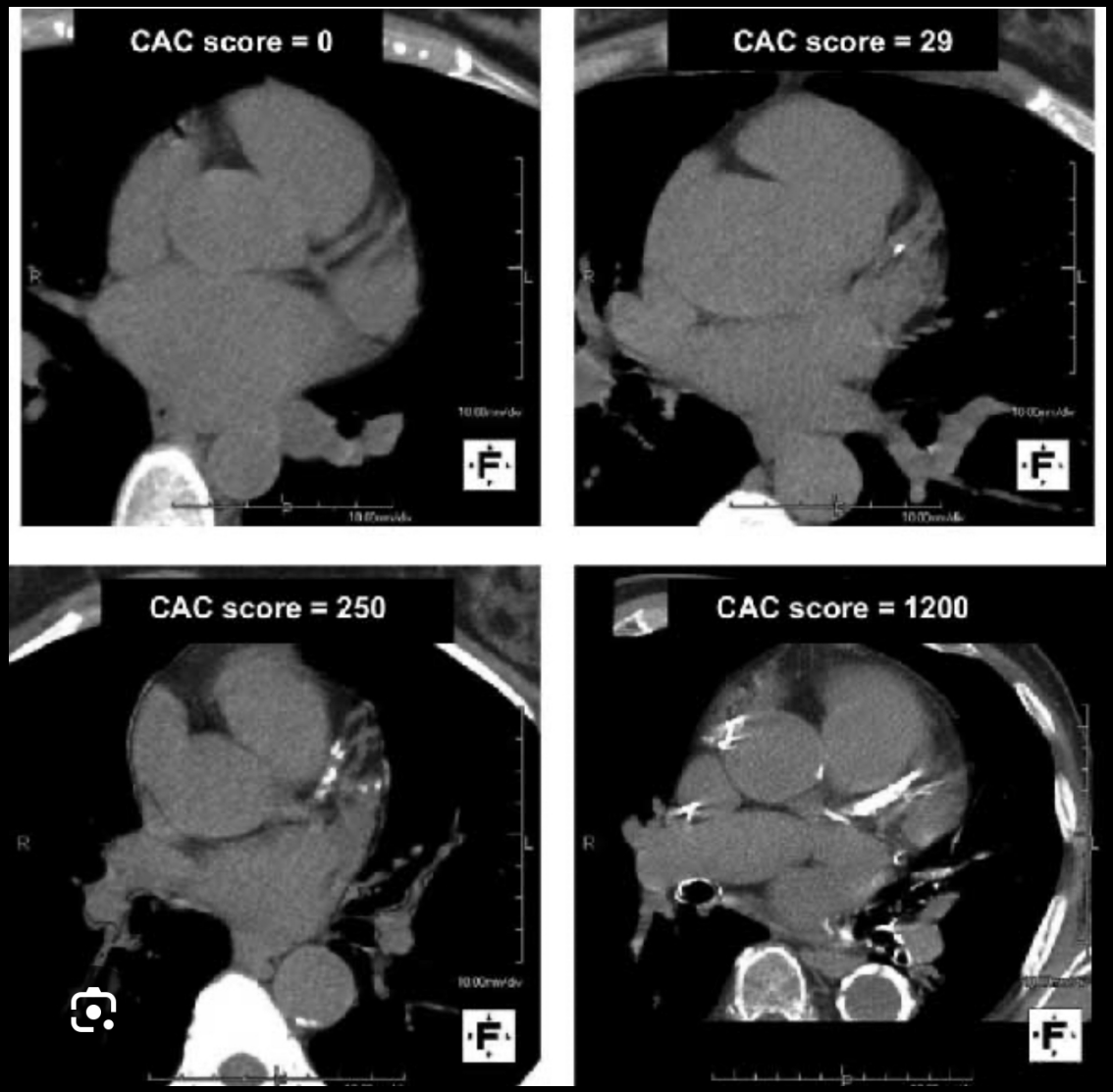

Heart Health
Talk for teachers
Social determinants of health
Addiction
Employment
Income
Neglect
Education
Isolation
Depression
Insurance
Vaccinations
Disease management
Anxiety
Finance
Tobacco
Access to medical care
Sex
Mental health
Sugar
Etoh
Diabetes
Nutrition
Fat
Hypertension
Age
Environment
Pollution
Noise
Lipids
Statistics
Medical
Lp(a)
Access to outdoors
Transportation
Lp(a)
Obesity
Walk
Disease
Coronary
Strength
Lack of exercise
Valve/structural
Transplantation
Apo E
Family hx
Medicine
Cardio
Arrhythmia
Stent
BiV pacer
Medications
Mind body
Cabg
Heart failure
Ablation
Device
Medication
TAVR
SAVR
Vad
Thromboprophylaxis
Evolutionary History
ICD
Device
Novel risk
Freeze
Survival
Tobacco 2.87
Interheart 129.2 90% of risk for MI
Fight
Microplastic
Alcohol 0.79
Procreate
Flight
Hypertension 1.91
Fruits/Vegetables 0.7
Nutrition
Fawn
Exercise 0.86
Nomadic hunter gather
Cannabis
Agriculture
Diabetes 2.37
Cholesterol 3.25
Cultivate crops
Psychosocial 2.67
Animal husbandry
Abdominal obesity 1.62

4-19% of major adverse cardiac events occur in patients with no standard modifiable CV risk factors.

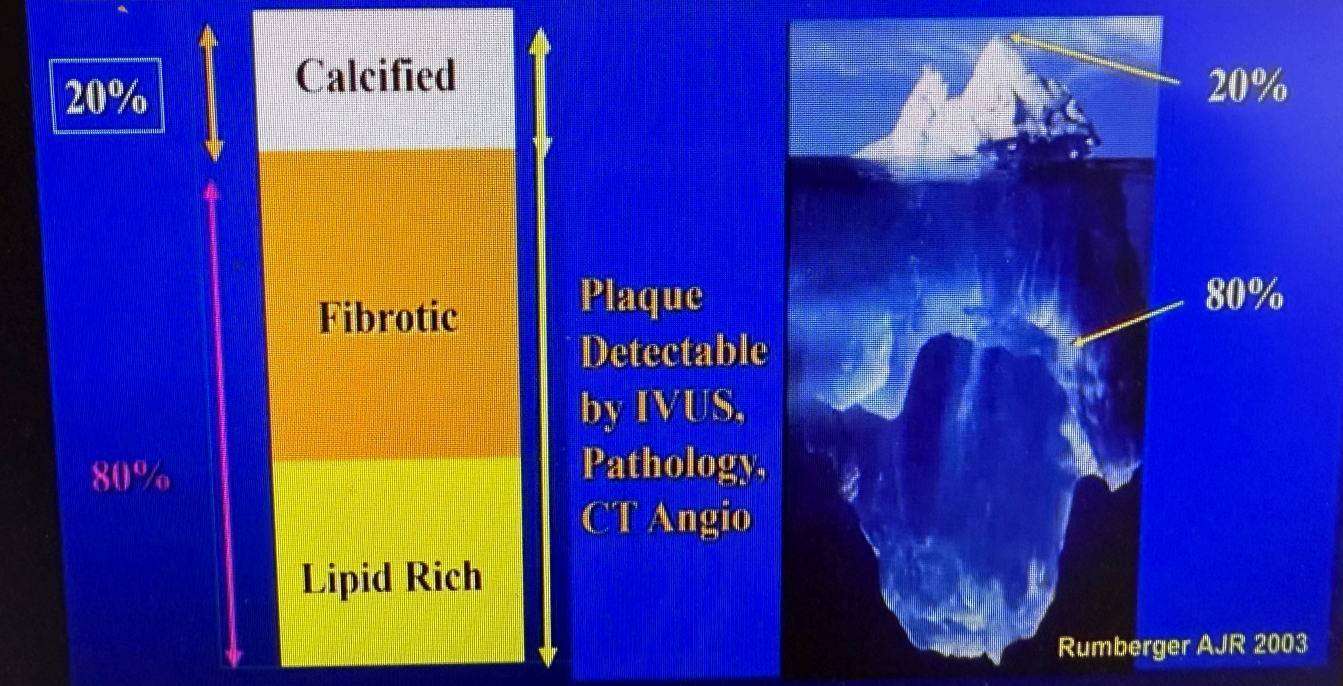


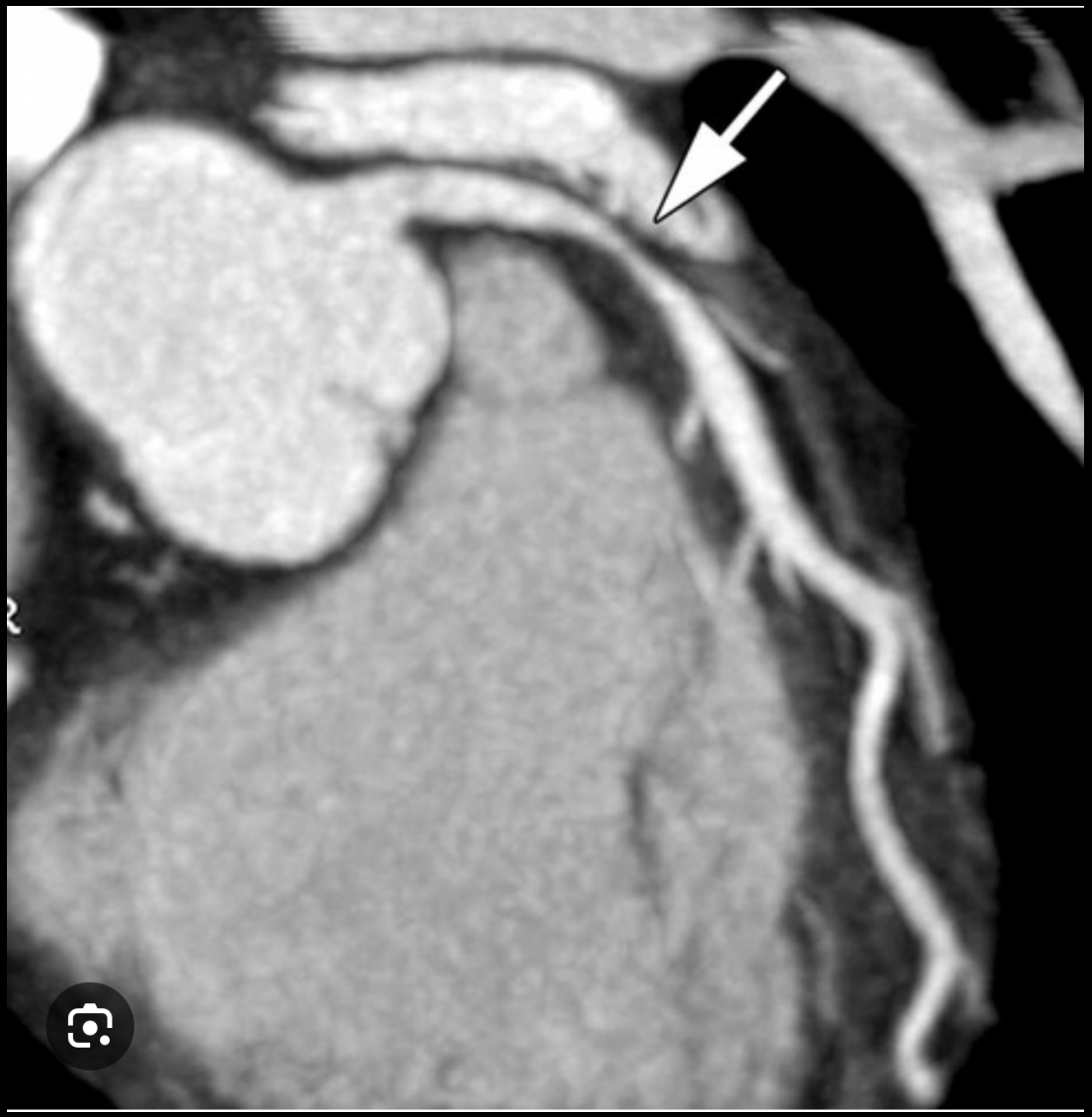
From Lloyd-Jones D Risk Assessment Nov 2018


LESS CHOLESTEROL
REGULAR CHECKUPS
NO NICOTINE
NO ALCOHOL
LOW SODIUM
MODERATE EXERCISE
NO SUGAR


CAC score = 0
CAC score = 29
CAC score = 250
CAC score = 1200

Total Coronary Artery Plaque and EBCT Coronary Calcium

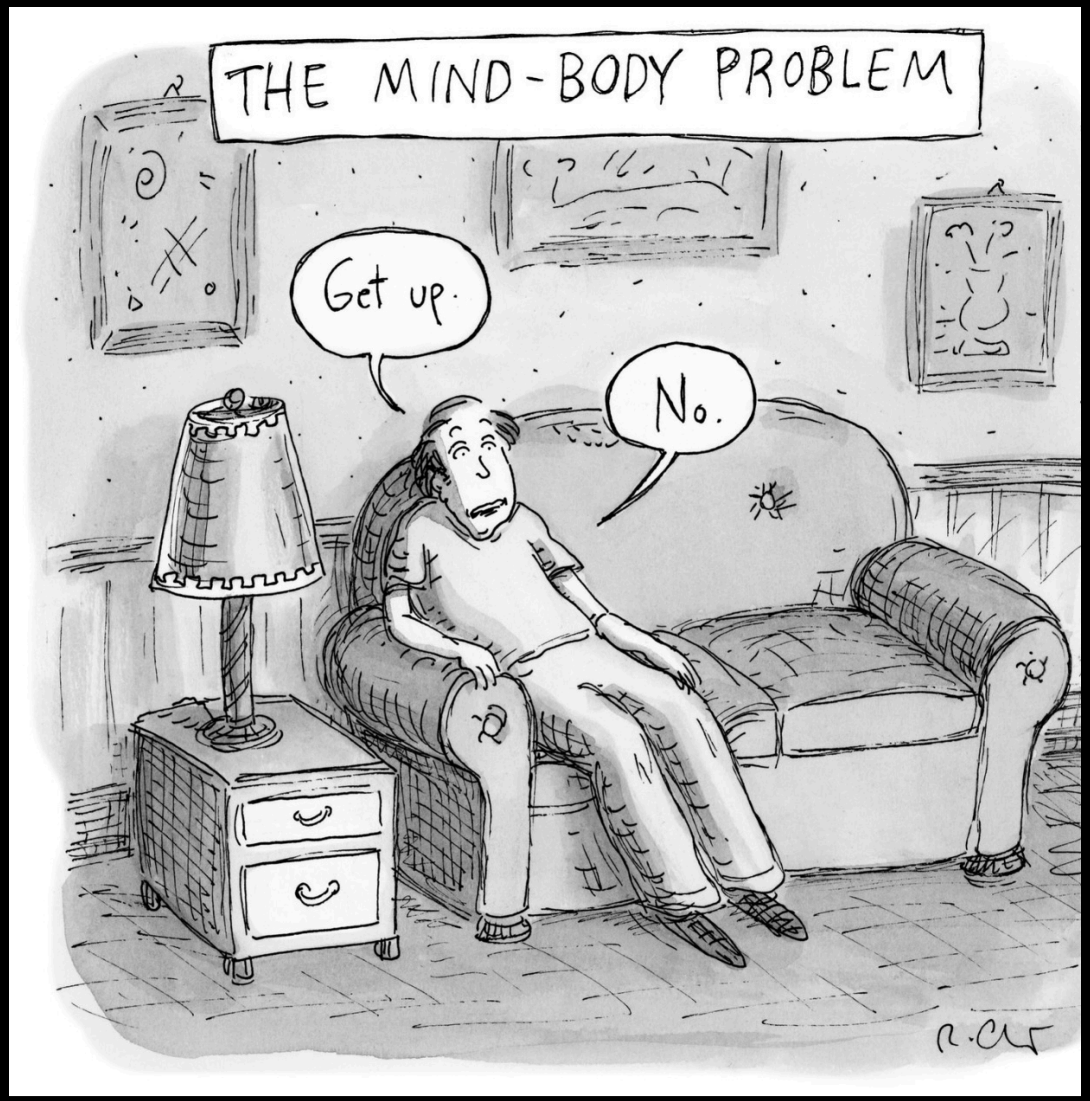





WW/WL 782 / 333
Right-Dominant
No Anomalies
Compare Study
APPROVED
Edit
View Report
Segment
Stenosis
Exclusion
Walls
0°
22.5°
45°
67.5°
Plaque Type
Low-Density
Non-calcified
Calcified
pLAD
359%
159/714
HU
Diameter Stenosis 24%
Remodeling Index 1.1
Ref. Mean Diam. 3.4mm
Lum. Mean Diam. 2.6mm
Labels
Axial
60%
146/169
HU
Path
Coronal
91%
HU
Sagittal
91%
HU
LM+LAD
Vessel
158.3 mm
Vessel Length
795.6 mm³
Total Vessel Volume
736.2 mm³
Total Lumen Volume
Lesion
Lesion is included in RI vessel
Plaque Thresholds
Hounsfield Units
Low-Density - Non-Calcified -189
Non-calcified -189 35
Calcified 351 250
Plaque
7.5 %
Percent Atheroma Volume
59.4 mm³
Total Plaque Volume
0 mm³
Low-Density – Non-Calcified Plaque Volume
42.7 mm³
Total Non-Calcified Plaque Volume
16.7 mm³
Total Calcified Plaque Volume
Stenosis
pLAD 1.1
RI 1.4
Highest Remodeling Index
pLAD 29 %
RI 33 %
Greatest Diameter Stenosis
pLAD 47 %
RI 60 %
Greatest Area Stenosis
Stenosis
1.2
Highest Remodeling Index

Prevention

- Lifestyle (intensive cardiac rehab.)
  - tobacco
  - exercise
  - Whole food plant based/Mediterranean/DASH Diet
  - Stress/Isolation
  - Weight
- Pharmacological
  - ASA/Plavix
  - Statins/PCSK-9
  - Ace/entresto
  - Beta-blockers
  - Aldactone
  - SGLT-2inhibitors/GLP1-agonist


THE MIND-BODY PROBLEM
Get up.
No.

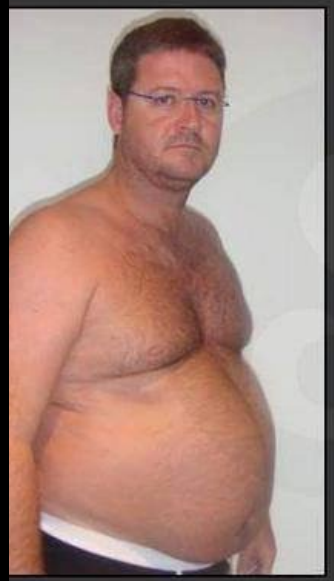
Non-Pharmacologic Management

- - Diet:Whole Food/Plant Based, Mediterranean, DASH, reduced saturated/ trans fats, increased fiber.
- - Exercise: 150 min/week of moderate-vigorous aerobic activity.
- - Weight loss and smoking cessation improve lipid profiles.

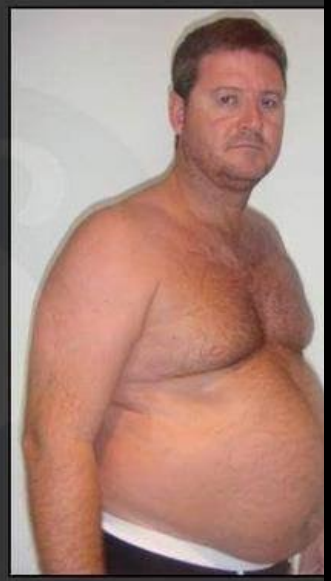
Statue of David returns to Italy after 3 years in the USA

ROBERT

Before



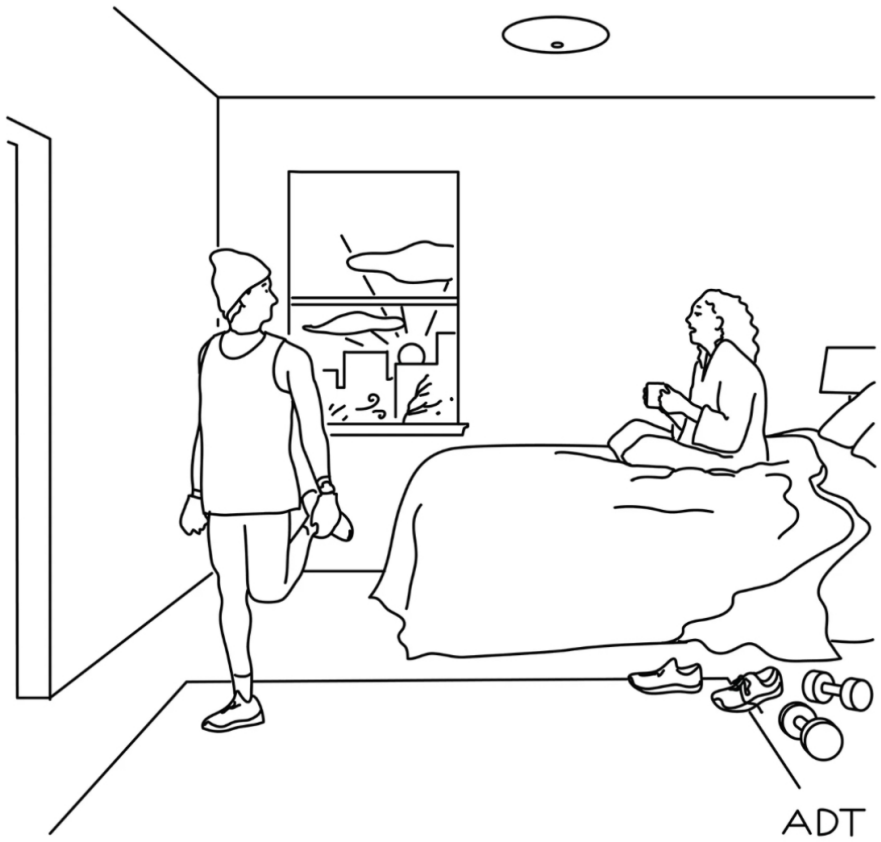
After



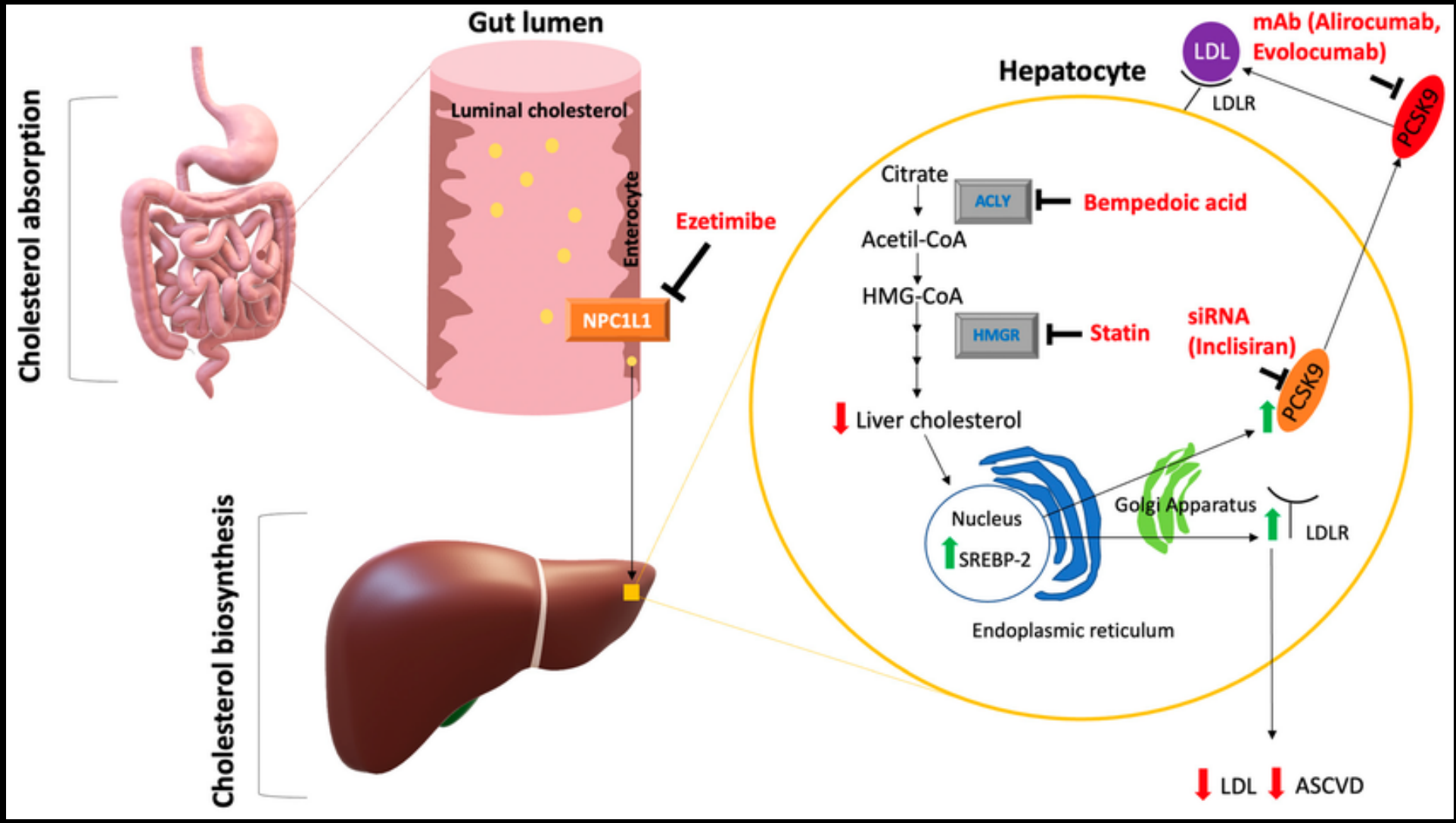
In only 2 weeks
Robert lost his glasses

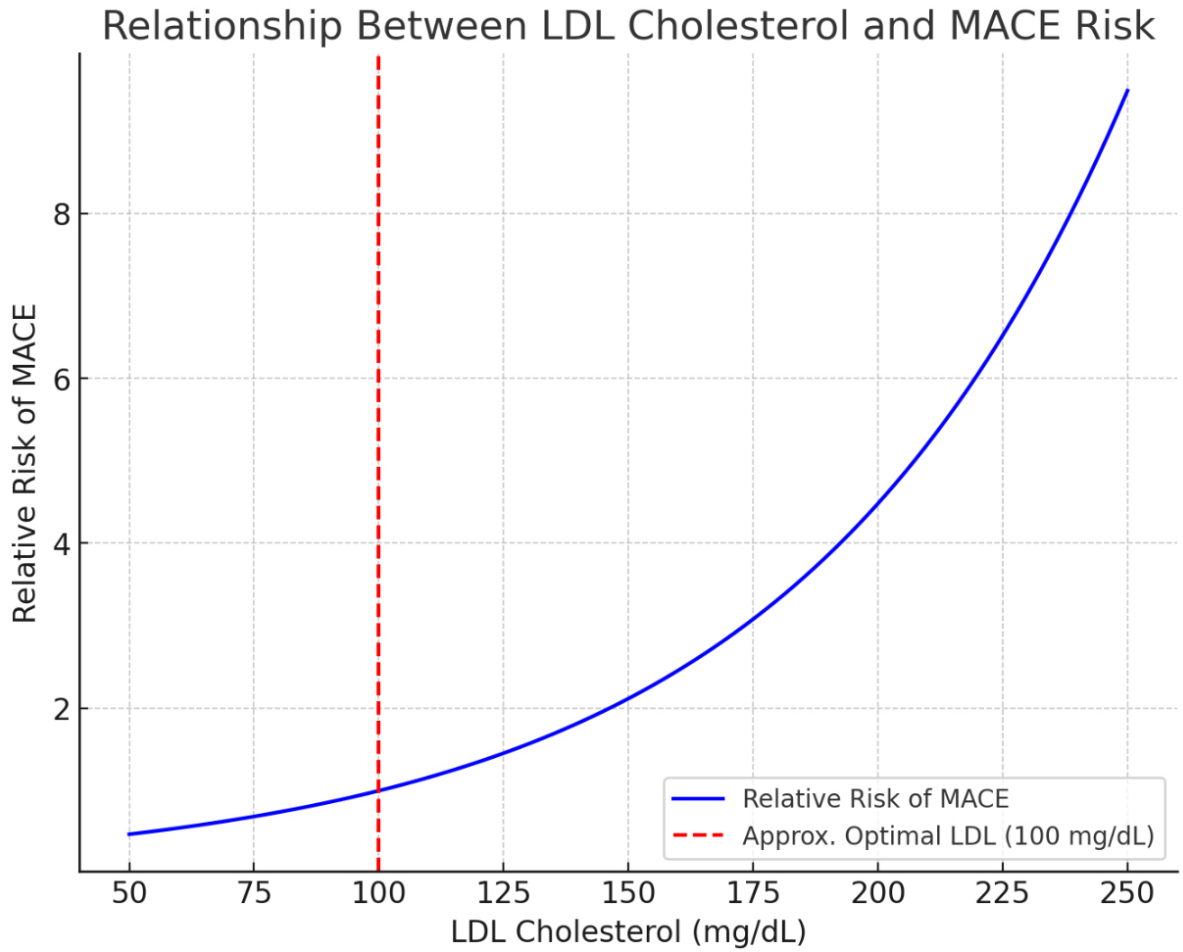

धुम्रपान तथा
फोक्सोको
आन्तरिक राज
CIGARE
70 MM-FI
KHUKURI

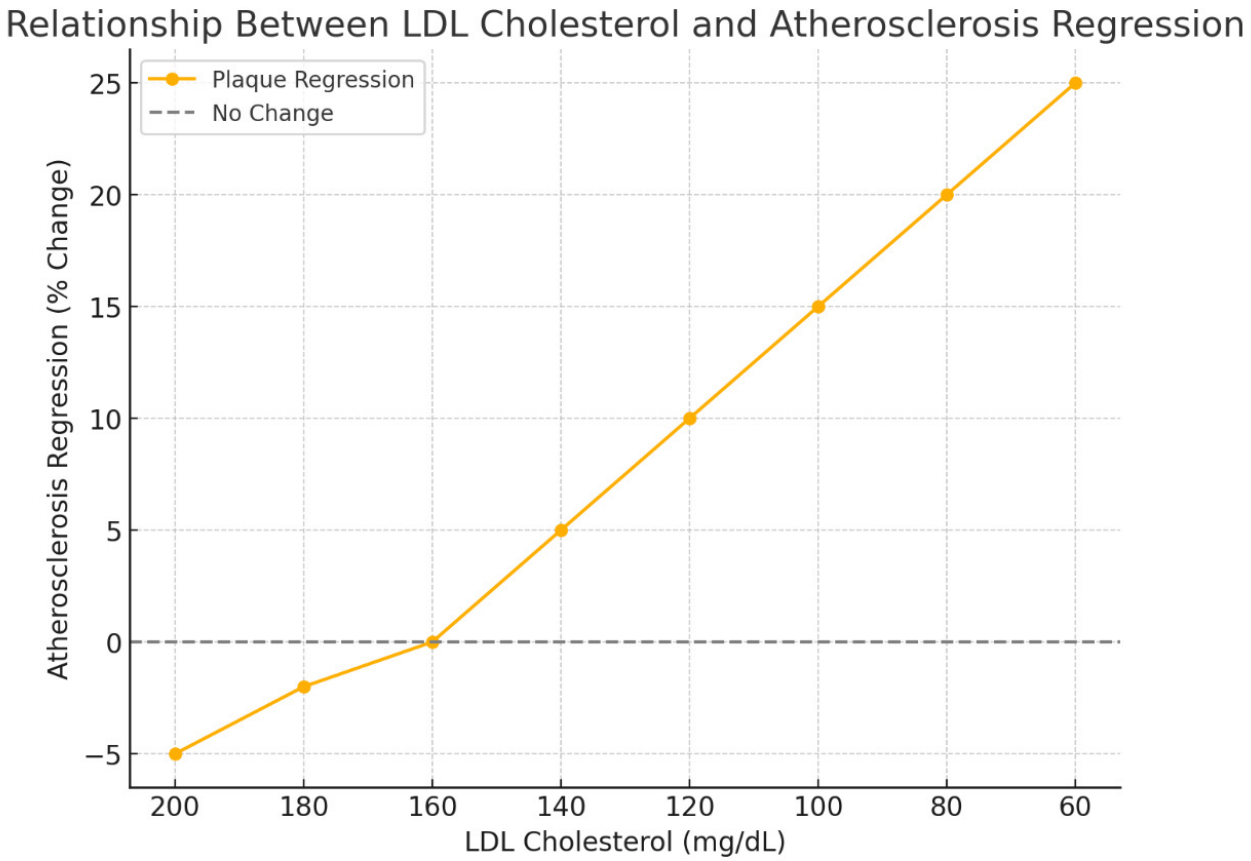

ALO 171
Sigara Bırakma
Danışma Hattı
Sigara içmek
kan akışını yavaşlatır
ve cinsel iktidarsızlığa
neden olur.

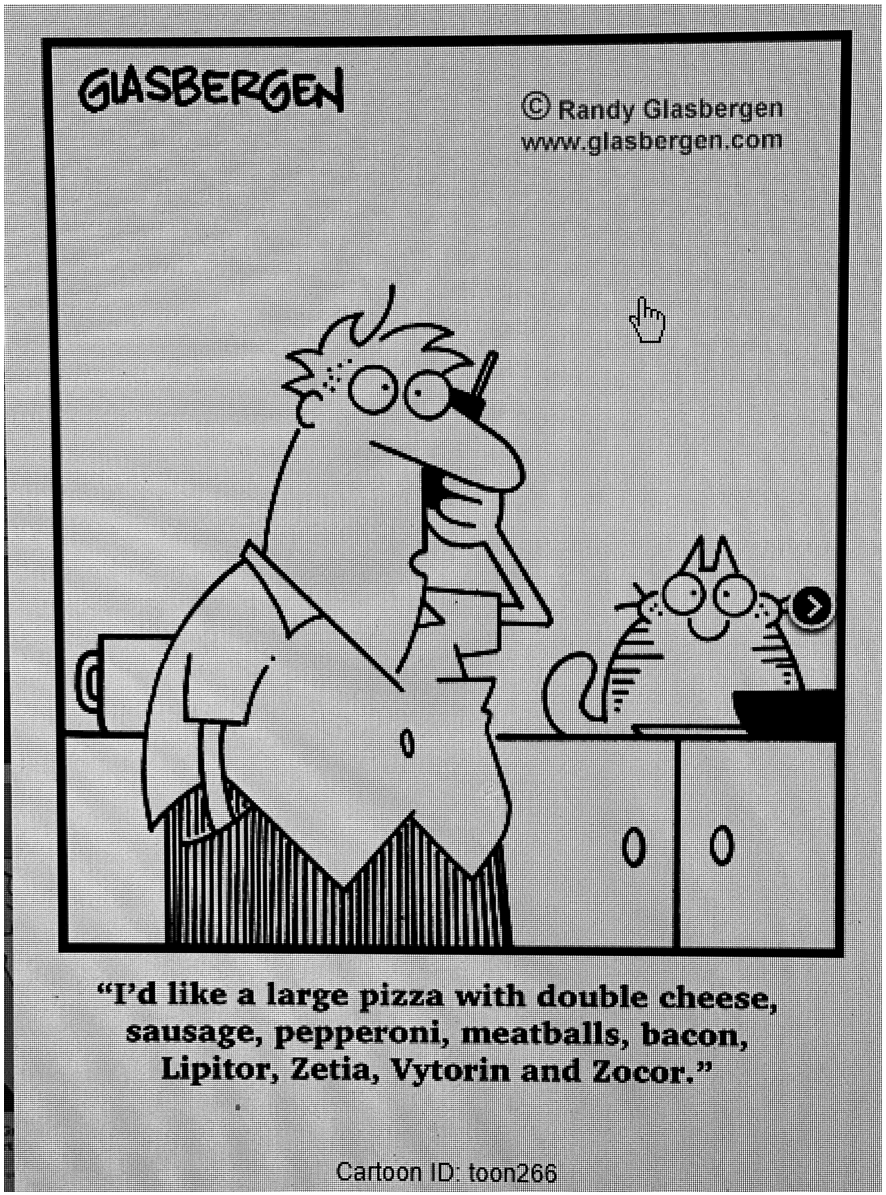


"I've decided to focus less on cardio and more on strength to get out of bed in the morning."


Gut lumen
Cholesterol absorption
Luminal cholesterol
Enterocyte
Ezetimibe
NPC1L1
Cholesterol biosynthesis
Hepatocyte
LDL
LDLR
mAb (Alirocumab, Evolocumab)
PCSK9
Citrate
ACLY
Bempedoic acid
Acetil-CoA
HMG-CoA
HMGR
Statin
siRNA (Inclisiran)
PCSK9
Liver cholesterol
Nucleus
SREBP-2
Golgi Apparatus
LDLR
Endoplasmic reticulum
LDL
ASCVD


Relationship Between LDL Cholesterol and MACE Risk
Relative Risk of MACE
2
4
6
8
50
75
100
125
150
175
200
225
250
LDL Cholesterol (mg/dL)
Relative Risk of MACE
Approx. Optimal LDL (100 mg/dL)


Relationship Between LDL Cholesterol and Atherosclerosis Regression
Plaque Regression
No Change
Atherosclerosis Regression (% Change)
25
20
15
10
5
0
−5
200
180
160
140
120
100
80
60
LDL Cholesterol (mg/dL)


GLASBERGEN
© Randy Glasbergen
www.glasbergen.com
"I'd like a large pizza with double cheese, sausage, pepperoni, meatballs, bacon, Lipitor, Zetia, Vytorin and Zocor."
Cartoon ID: toon266

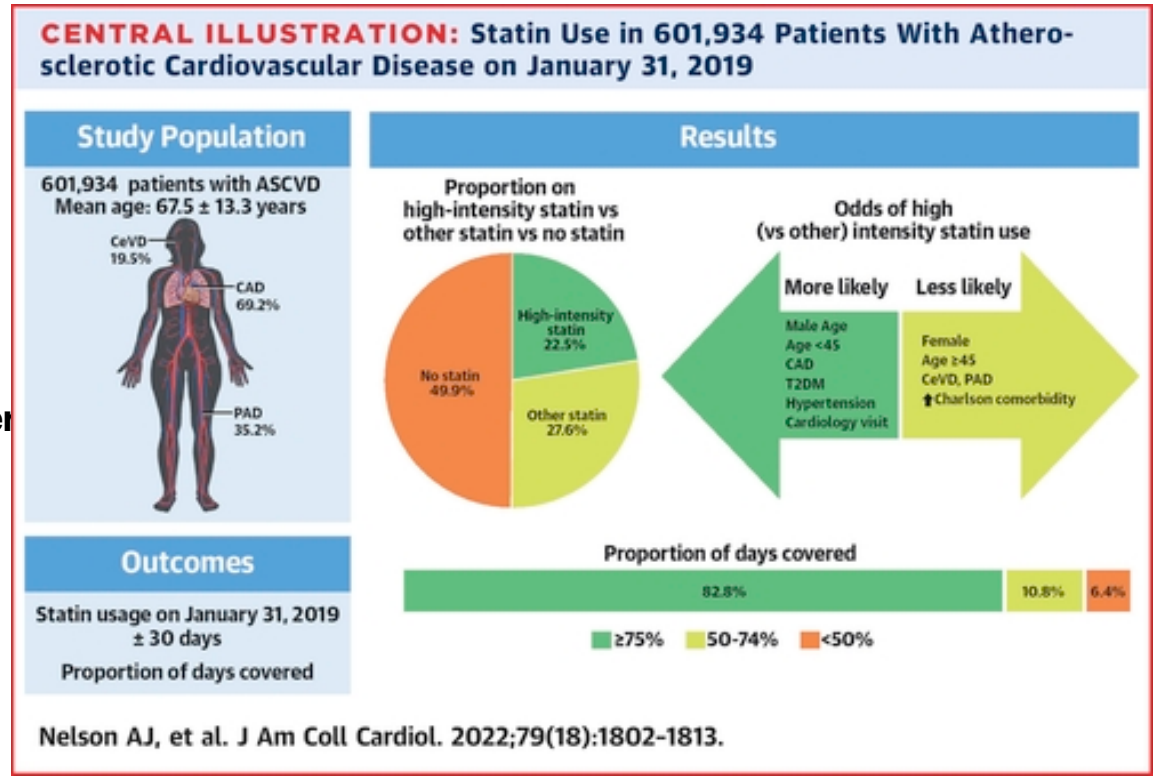
10,249

"How much longer do I have before I have to change to a healthy lifestyle?"

How good are we?

Non adherence
Side Effects
Worsening Co-morbidities
Provider Directions
Genetic differences
Therapeutic inertia

Hazard Ratio of 3.45 all cause mortality over years



UUUUUUGH!

Dinner with Larry

Development and Validation of a Protein-Based Risk Score for Cardiovascular Outcomes Among Patients With Stable Coronary Heart Disease

Peter Ganz [1], Bettina Heidecker [2], Kristian Hveem [3], Christian Jonasson [3], Shintaro Kato [4], Mark R Segal [5], David G Sterling [6], Stephen A Williams [6]

Affiliations + expand

PMID: 27327800 DOI: 10.1001/jama.2016.5951

Abstract

Importance: Precise stratification of cardiovascular risk in patients with coronary heart disease (CHD) is needed to inform treatment decisions.

Objective: To derive and validate a score to predict risk of cardiovascular outcomes among patients with CHD, using large-scale analysis of circulating proteins.

Design, setting, and participants: Prospective cohort study of participants with stable CHD. For the derivation cohort (Heart and Soul study), outpatients from San Francisco were enrolled from 2000 through 2002 and followed up through November 2011 (≤11.1 years). For the validation cohort (HUNT3, a Norwegian population-based study), participants were enrolled from 2006 through 2008 and followed up through April 2012 (5.6 years).

Exposures: Using modified aptamers, 1130 proteins were measured in plasma samples.

Main outcomes and measures: A 9-protein risk score was derived and validated for 4-year probability of myocardial infarction, stroke, heart failure, and all-cause death. Tests, including the C statistic, were used to assess performance of the 9-protein risk score, which was compared with the Framingham secondary event model, refit to the cohorts in this study. Within-person change in the 9-protein risk score was evaluated in the Heart and Soul study from paired samples collected 4.8 years apart.

Results: From the derivation cohort, 938 samples were analyzed, participants' median age at enrollment was 67.0 years, and 82% were men. From the validation cohort, 971 samples were analyzed, participants' median age at enrollment was 70.2 years, and 72% were men. In the derivation cohort, C statistics were 0.66 for refit Framingham, 0.74 for 9-protein, and 0.75 for refit

Purpose of the CVD Secondary Panel Study

- Collect real-world feedback about the test
- Obtain opinions from physicians about clinical utility
- Understand actions taken by individuals based upon results
- Determine if there are changes in risk scores from baseline to a 2nd test
- 200 participants to be enrolled at Boulder Heart

SomaLogic's first prospective study using an insight

The CVD Secondary Panel

- Test performed in the CLIA lab
- Measures 7 analytes
  - Growth and Remodeling: ANGPT2, GDF11/8, MMP-12
  - Inflammation: C7 and CCL18/PARC
  - Proteases: SERPINA3 and SERPINF2
- Test predicts the likelihood of a CVD event in the next 5 years
  - CVD event is defined as a heart attack, stroke, hospitalization for heart failure, or all-cause death

CVD Secondary Risk Categories

Circulation

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ABSTRACT | Originally Published 18 May 2021 |

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Abstract P027: Individualized Protein Based Cardiovascular Risk Stratification: Impact On Patient And Physician Decision Making In Patients With Real World Cardiovascular Disease

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Abstract

There is a growing population of patients with established cardiovascular disease and residual cardiovascular risk. Identification of patients who would benefit most from more advanced risk reduction strategies would be ideal.

Hypothesis: Identification of secondary risk of MACE may change both physician recommendations and patient choices regarding goal directed therapy (GDT).

Methods: Retrospective review of 244 patients with established CAD with traditional assessment of secondary cardiovascular risk and SomaScan proteomic risk assessment followed over 3 years. Patients were evaluated for GDT and standard measurements were made at baseline. SomaScan protein risk score was obtained. Patients received advice regarding risk and offered GDT with established secondary prevention goals. Willingness to change, physician recommendations to change therapy and therapy changes were recorded. Patients were followed over three years

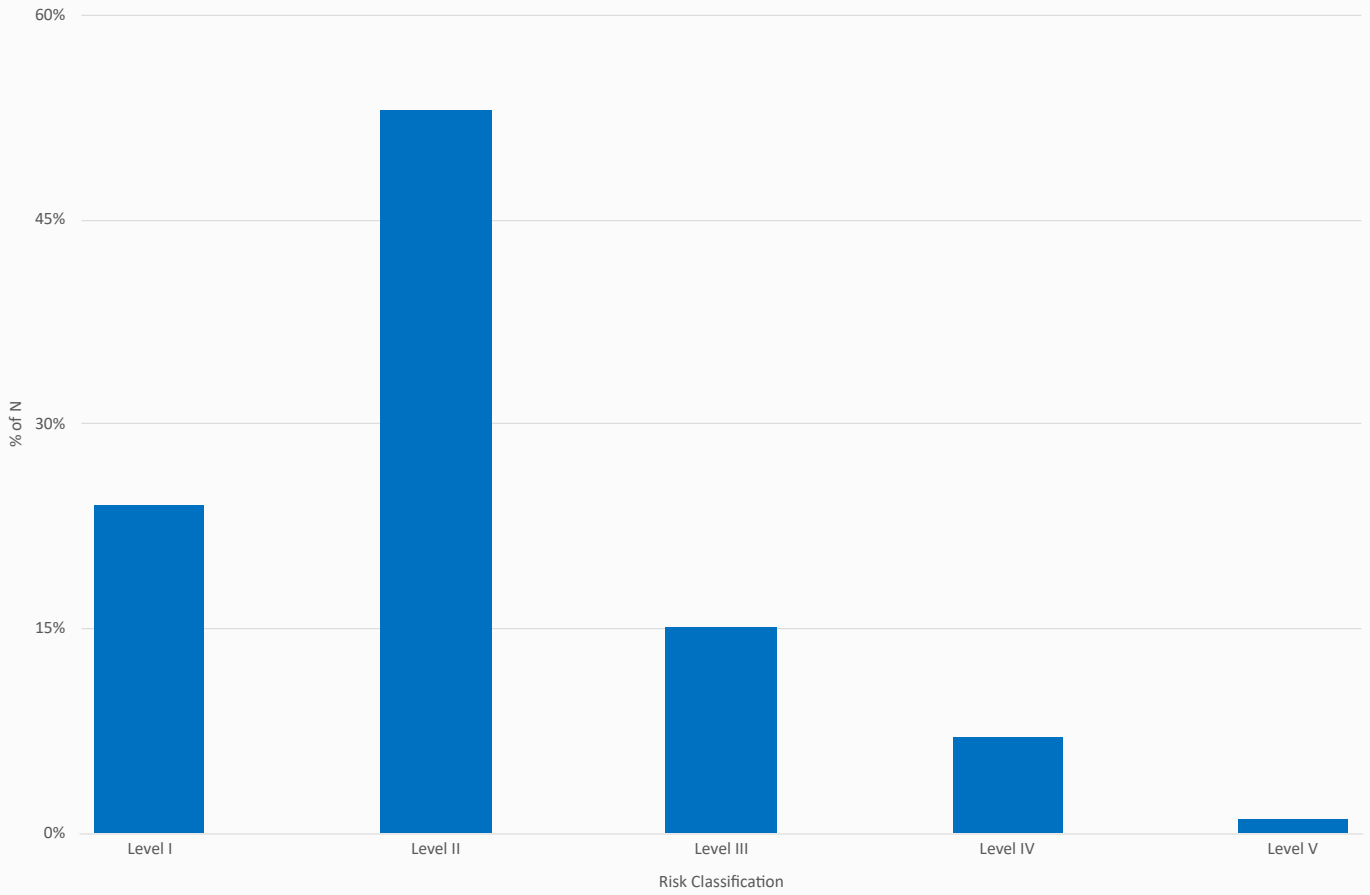
Individualized Protein Based Cardiovascular Risk Stratification

- 244 Patients
  - Male 76% (186)
  - Female 24%(58
- Mean age 66 (32-84)
- Diagnosis
  - 49%(121) Imaging
  - 51%(123) Clinical Events: CABG,MI,PCI

Individualized Protein Based Cardiovascular Risk Stratification

- 58% (n=143) of patients were on guideline directed therapy (statin,asa,ace)
- 42% (n=101) of patients were sub-optimally managed.

Risk Profile of Study Population (n=244)

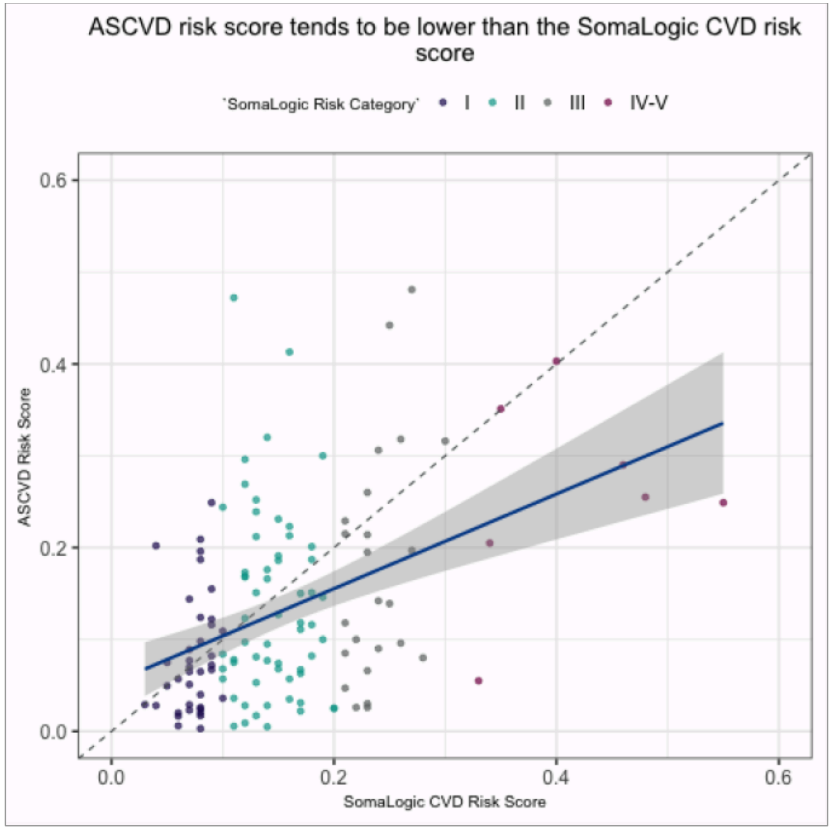


Boulder Cohort
244 patients

Re-classification of patients.

Motivates patients to make changes.

Risk appropriate pharmacological therapy.

- 

This figure plots the concordance between the ASCVD and SomaLogic CVD Risk scores. The dots are colored by SomaLogic Risk Category. The grey, dashed line represents perfect concordance between the two risk scores. The solid, blue line is the linear fit between the two and shows that the ASCVD calculation tends to produce a lower risk score than the SomaLogic algorithm, particularly at increasing levels of risk. The grey shading around the line represents the 95% confidence interval.

Individualized Protein Based Cardiovascular Risk Stratification

Study results identified 111 (45%) patients where the clinician advised alteration in therapy; initiation of GDT in 20 patients and increase in GDT for 52 patients (65%).

The majority of patients offered more intensive therapy were in the higher study classifications. (PCSK-9 inhibitors, ACE, etc..)

These higher classifications were not associated and would not have been identified with traditional risk factors suggesting incremental benefit to the study results.

17 patients would not consider initiation of medical therapies

Individualized Protein Based Cardiovascular Risk Stratification

- Use of Somascan results in conjunction with standard assessment allowed an additional 30% of patients to change therapy including starting GDY and or intensification of GDT.

Clinical Utility

Clinical utility of a novel test for assessing cardiovascular disease risk in type 2 diabetes: a randomized controlled trial

John W. Peabody, David Paculdo, Enrico de Belen, Divya Ganesan, Isabella Cooney & Nelson Trujillo

Diabetology & Metabolic Syndrome **15**, Article number: 155 (2023) | Cite this article

Abstract

Background

The risk for and treatment of cardiovascular disease (CVD) in type 2 diabetes (T2DM) is often incorrect and delayed. We wished to determine if a novel test improved physicians' ability to risk stratify, diagnose, and treat patients with T2DM.

Methods

In a 2-phase randomized controlled trial comparing the clinical workup, diagnosis, and management of online, simulated patients with T2DM in a nationwide sample of cardiologists and primary care physicians, participants were randomly assigned to control or one of two intervention groups. Intervention participants had access to standard of care diagnostic tools plus a novel diagnostic CVD risk stratification test.

Results

In control, there was no change in CV risk stratification of simulated patients between baseline and round 2 (37.1 to 38.3%, p = 0.778). Pre-post analysis showed significant improvements in risk stratification in both Intervention 1 (38.7 to 65.3%) and Intervention 2 (41.9 to 65.8%) (p < 0.01) compared to controls. Both intervention groups significantly increased prescribing SGLT2 inhibitors/GLP1 receptor agonists versus control, + 18.9% for Intervention 1 (p = 0.020) and 1 + 9.4% for Intervention 2 (p = 0.014). Non-pharmacologic treatment improved significantly compared to control (+ 30.0% in Intervention 1 (p < 0.001) and + 22.8% in Intervention 2 (p = 0.001). Finally, monitoring HgbA1C, blood pressure, and follow-up visit frequency improved by + 20.3% (p = 0.004) in Intervention 1 and + 29.8% (p < 0.001) in

Individualized Protein Based Cardiovascular Risk Stratification

Does this change outcomes?

Lesson's

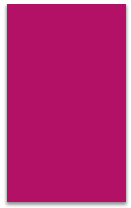
1 High risk is high risk.

2. Low risk can become high risk.

3. Low risk maybe high risk.

4. High risk maybe low risk.

5. Low risk is low risk.



High Risk is high risk.

#42
77 yo s/p CABG and PCI
LDL 107 mg/dl
Calculated risk:29%
Measured Risk: 64%

VF with rescue

Add Zetia.

Low risk becomes high risk.

66 yo male known 70% stenosis of the LAD

LDL:60 mg/dl
Calculated risk:15%
Measured risk: 12%

Normal exercise test with normal myocardial perfusion.

Elective PCI . Complications. Emergency CABG leading to stroke and death.

Low risk is high risk.

60 yo with CAD
LDL:127 mg/dl
Calculated risk: 20%
Measured risk: 58%

More aggressive secondary prevention.

High risk is low risk.

61 yo s/p CABG for critical left main disease

LDL:149 mg/dl
Calculated risk: 47%
Measured risk: 11%

Re-assurance.
Continued aggressive secondary prevention.

Low Risk is low risk.

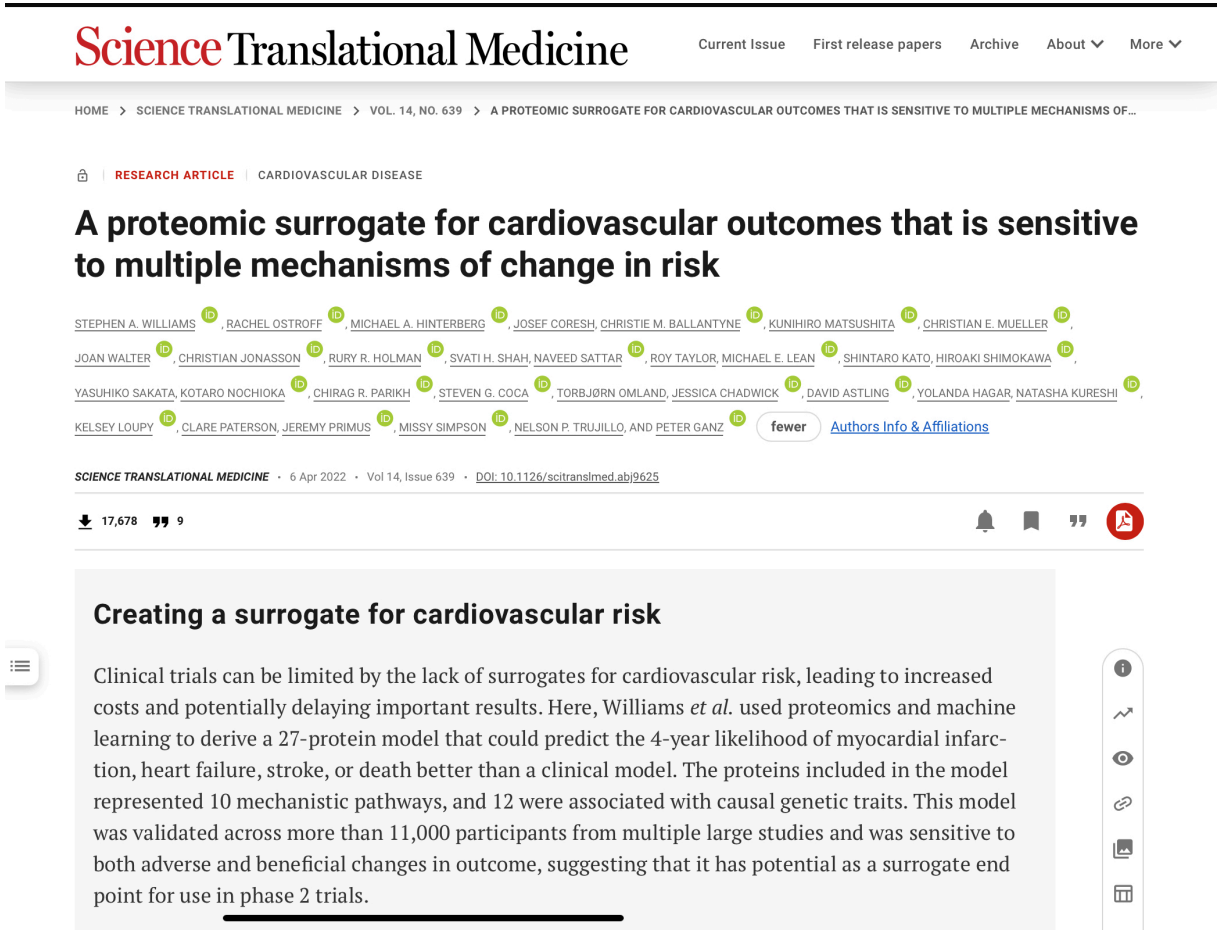
56 yo s/p CABG

Ldl: 69 mg/dl

Calculated risk: 2.9%
Measured risk: 3%

Re-assurance

SomaLogic

- 
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RESEARCH ARTICLE | CARDIOVASCULAR DISEASE
A proteomic surrogate for cardiovascular outcomes that is sensitive to multiple mechanisms of change in risk
STEPHEN A. WILLIAMS, RACHEL OSTROFF, MICHAEL A. HINTERBERG, JOSEF CORESH, CHRISTIE M. BALLANTYNE, KUNIHIRO MATSUSHITA, CHRISTIAN E. MUELLER, JOAN WALTER, CHRISTIAN JONASSON, RURY R. HOLMAN, SVATI H. SHAH, NAVEED SATTAR, ROY TAYLOR, MICHAEL E. LEAN, SHINTARO KATO, HIROAKI SHIMOKAWA, YASUHIKO SAKATA, KOTARO NOCHIOKA, CHIRAG R. PARIKH, STEVEN G. COCA, TORBJØRN OMLAND, JESSICA CHADWICK, DAVID ASTLING, YOLANDA HAGAR, NATASHA KURESHI, KELSEY LOUPY, CLARE PATERSON, JEREMY PRIMUS, MISSY SIMPSON, NELSON P. TRUJILLO, AND PETER GANZ
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SCIENCE TRANSLATIONAL MEDICINE • 6 Apr 2022 • Vol 14, Issue 639 • DOI: 10.1126/scitranslmed.abj9625
17,678
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Creating a surrogate for cardiovascular risk
Clinical trials can be limited by the lack of surrogates for cardiovascular risk, leading to increased costs and potentially delaying important results. Here, Williams et al. used proteomics and machine learning to derive a 27-protein model that could predict the 4-year likelihood of myocardial infarction, heart failure, stroke, or death better than a clinical model. The proteins included in the model represented 10 mechanistic pathways, and 12 were associated with causal genetic traits. This model was validated across more than 11,000 participants from multiple large studies and was sensitive to both adverse and beneficial changes in outcome, suggesting that it has potential as a surrogate end point for use in phase 2 trials.

"I'm sorry, we did everything we could before Elon cut our funding."

Cartoon by Brendan Loper

Future Work

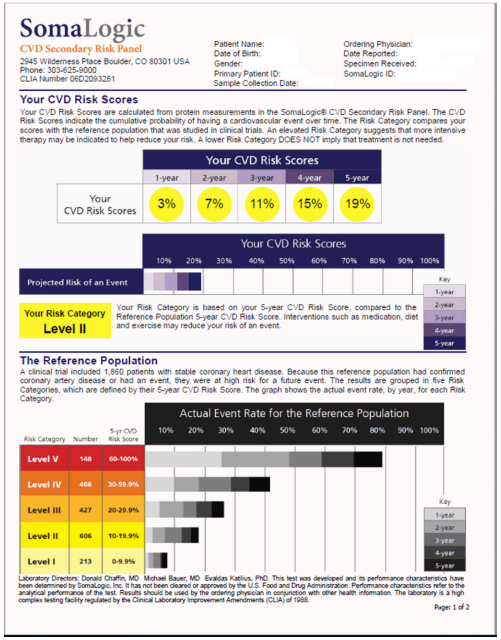

COLS
Colorado Longitudinal Study
Building the world's most comprehensive longitudinal repository of biological samples and sociological health data.

SomaLogic

27 proteins

Thematic grouping of at least 10 different biological processes represented in the model:

- blood volume and natriuresis [NTproBNP, ANP],
- vesicle biogenesis [ARL11],
- matrix/tissue modeling, growth, angiogenesis or adhesion [ANTR2, CILP-2, CA125*, GOLM1, spondin-1*, SVEP1*, PTRPJ, ITI heavy-chain 2*, NELL1, GDF11/8*],
- cellular immunity [MMP12*, ERBB3, NCAM-120*],
- calcium channel modulation [CA2D3*],
- glomerular filtration rate [TFF3],
- immunoglobulins [IGDC4, JAM-B, sTREM1*],
- metabolism & lipids [SIRT2, PPR1A, LRP11*],
- inflammation [suPAR*, NDST1]
- coagulation [ATS13*].


SomaLogic

CVD Secondary Risk Panel

2945 Wilderness Place Boulder, CO 80301 USA
Phone: 303-625-9000
CLIA Number 06D2093281

Patient Name:
Date of Birth:
Gender:
Primary Patient ID:
Sample Collection Date:

Ordering Physician:
Date Reported:
Specimen Received:
SomaLogic ID:

Your CVD Risk Scores

Your CVD Risk Scores are calculated from protein measurements in the SomaLogic® CVD Secondary Risk Panel. The CVD Risk Scores indicate the cumulative probability of having a cardiovascular event over time. The Risk Category compares your scores with the reference population that was studied in clinical trials. An elevated Risk Category suggests that more intensive therapy may be indicated to help reduce your risk. A lower Risk Category DOES NOT imply that treatment is not needed.

Your CVD Risk Scores

	1-year	2-year	3-year	4-year	5-year
Your CVD Risk Scores	3%	7%	11%	15%	19%

Your CVD Risk Scores

10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

Projected Risk of an Event

Key: 1-year, 2-year, 3-year, 4-year, 5-year

Your Risk Category: Level II

Your Risk Category is based on your 5-year CVD Risk Score, compared to the Reference Population 5-year CVD Risk Score. Interventions such as medication, diet and exercise may reduce your risk of an event.

The Reference Population

A clinical trial included 1,860 patients with stable coronary heart disease. Because this reference population had confirmed coronary artery disease or had an event, they were at high risk for a future event. The results are grouped in five Risk Categories, which are defined by their 5-year CVD Risk Score. The graph shows the actual event rate, by year, for each Risk Category.

Actual Event Rate for the Reference Population

10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

Risk Category	Number	5-yr CVD Risk Score
Level V	148	60-100%
Level IV	466	30-59.9%
Level III	427	20-29.9%
Level II	606	10-19.9%
Level I	213	0-9.9%

Key: 1-year, 2-year, 3-year, 4-year, 5-year

Laboratory Directors: Donald Chaffin, MD Michael Bauer, MD Evaldas Katilius, PhD. This test was developed and its performance characteristics have been determined by SomaLogic, Inc. It has not been cleared or approved by the U.S. Food and Drug Administration. Performance characteristics refer to the analytical performance of the test. Results should be used by the ordering physician in conjunction with other health information. The laboratory is a high complex testing facility regulated by the Clinical Laboratory Improvement Amendments (CLIA) of 1988.

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1. J. Zheng et al., Phenome-wide Mendelian randomization mapping the influence of the plasma proteome on complex diseases. Nature genetics 52, 1122-1131 (2020).

Biologic plausibility of 27 proteins

The Laughing Heart

Your life is your life
Don't let it be clubbed into dank submission.
Be on the watch.
There are ways out.
There is a light somewhere.
It may not be much light but
It beats the darkness.
Be on the watch.
The gods will offer you chances.
Know them.
Take them.
You can't beat death but
You can beat death in life, sometimes.
And the more often you learn to do it,
The more light there will be.
Your life is your life.
Know it while you have it.
You are marvelous
The gods wait to delight
In you.