The Advancing Role of Artificial Intelligence in Cardiology

Joel Kahn, MD, FACC

Founder, Kahn Center for Cardiac Longevity

Clinical Professor of Medicine
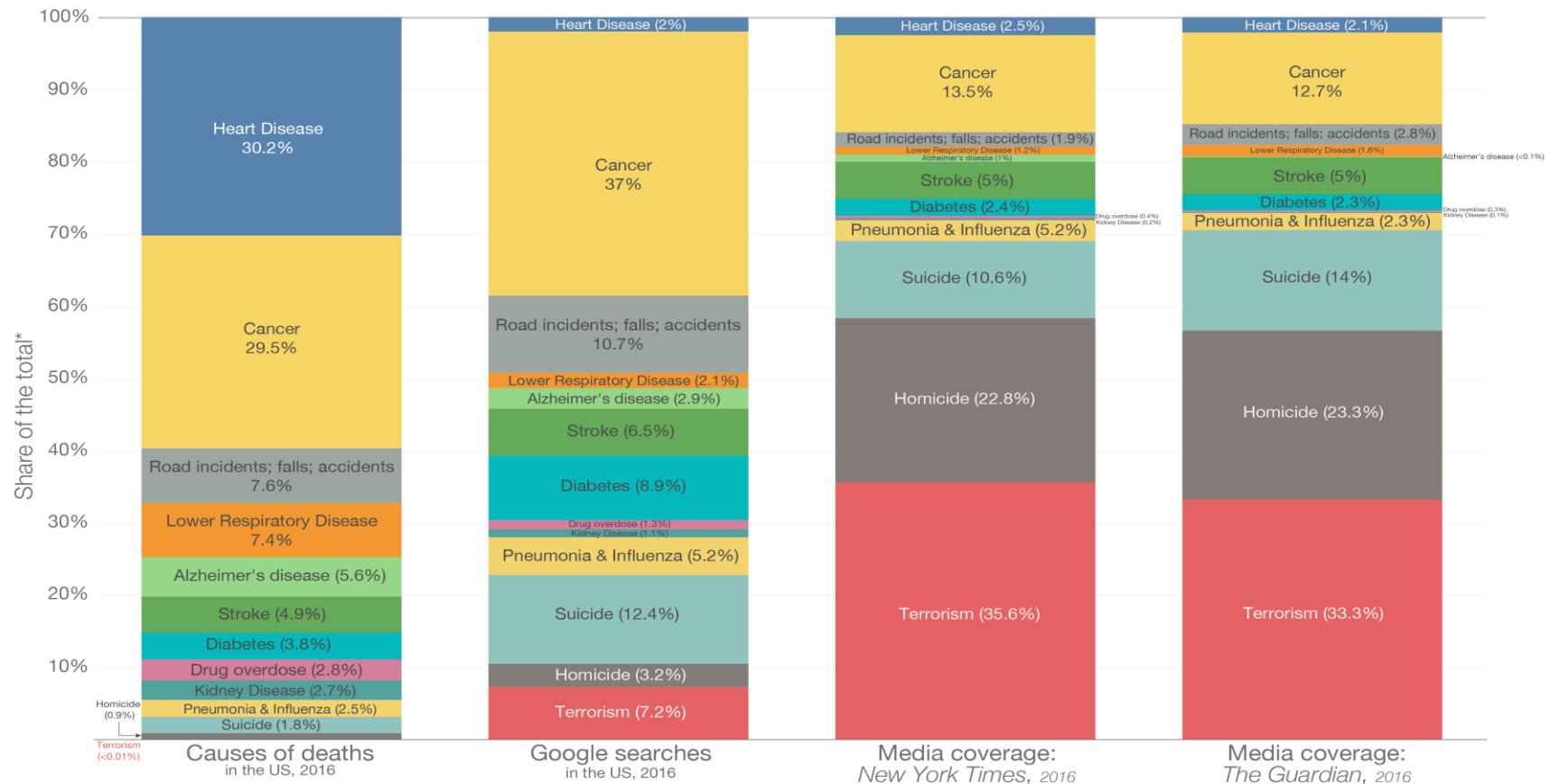
Wayne State University, Detroit, MI

No conflicts

Heart Disease is Still #1

Causes of death in the US
What Americans die from, what they search on Google, and what the media reports on

Our World in Data

Share of the total*

Causes of deaths in the US, 2016:
- Heart Disease 30.2%
- Cancer 29.5%
- Road incidents; falls; accidents 7.6%
- Lower Respiratory Disease 7.4%
- Alzheimer's disease (5.6%)
- Stroke (4.9%)
- Diabetes (3.8%)
- Drug overdose (2.8%)
- Kidney Disease (2.7%)
- Pneumonia & Influenza (2.5%)
- Suicide (1.8%)
- Homicide (0.9%)
- Terrorism (<0.01%)

Google searches in the US, 2016:
- Heart Disease (2%)
- Cancer 37%
- Road incidents; falls; accidents 10.7%
- Lower Respiratory Disease (2.1%)
- Alzheimer's disease (2.9%)
- Stroke (6.5%)
- Diabetes (8.9%)
- Drug overdose (1.3%)
- Kidney Disease (1.1%)
- Pneumonia & Influenza (5.2%)
- Suicide (12.4%)
- Homicide (3.2%)
- Terrorism (7.2%)

Media coverage: New York Times, 2016:
- Heart Disease (2.5%)
- Cancer 13.5%
- Road incidents; falls; accidents (1.9%)
- Lower Respiratory Disease (1.2%)
- Alzheimer's disease (1%)
- Stroke (5%)
- Diabetes (2.4%)
- Drug overdose (0.4%)
- Kidney Disease (0.2%)
- Pneumonia & Influenza (5.2%)
- Suicide (10.6%)
- Homicide (22.8%)
- Terrorism (35.6%)

Media coverage: The Guardian, 2016:
- Heart Disease (2.1%)
- Cancer 12.7%
- Road incidents; falls; accidents (2.8%)
- Lower Respiratory Disease (1.6%)
- Alzheimer's disease (<0.1%)
- Stroke (5%)
- Diabetes (2.3%)
- Drug overdose (0.3%)
- Kidney Disease (0.1%)
- Pneumonia & Influenza (2.3%)
- Suicide (14%)
- Homicide (23.3%)
- Terrorism (33.3%)

*This represents each causes's share of the top ten causes of death in the US plus homicides, drug overdoses and terrorism. Collectively these 13 causes accounted for approximately 88% of deaths in the US in 2016. Full breakdown of causes of death can be found at the CDC's WONDER public health database: https://wonder.cdc.gov/

Based on data from Shen et al (2018) – Death: reality vs. reported. *All data available at: https://owenshen24.github.io/charting-death*
All data refers to 2016.
Not all causes of death are shown: Shown is the data on the ten leading causes of death in the United States plus drug overdoses, homicides and terrorism.
All values are normalized to 100% so they represent their relative share of the top causes, rather than absolute counts (e.g. 'deaths' represents each causes' share of deaths within the 13 categories shown rather than total deaths). The causes of death shown here account for approximately 88% of total deaths in the United States in 2016.
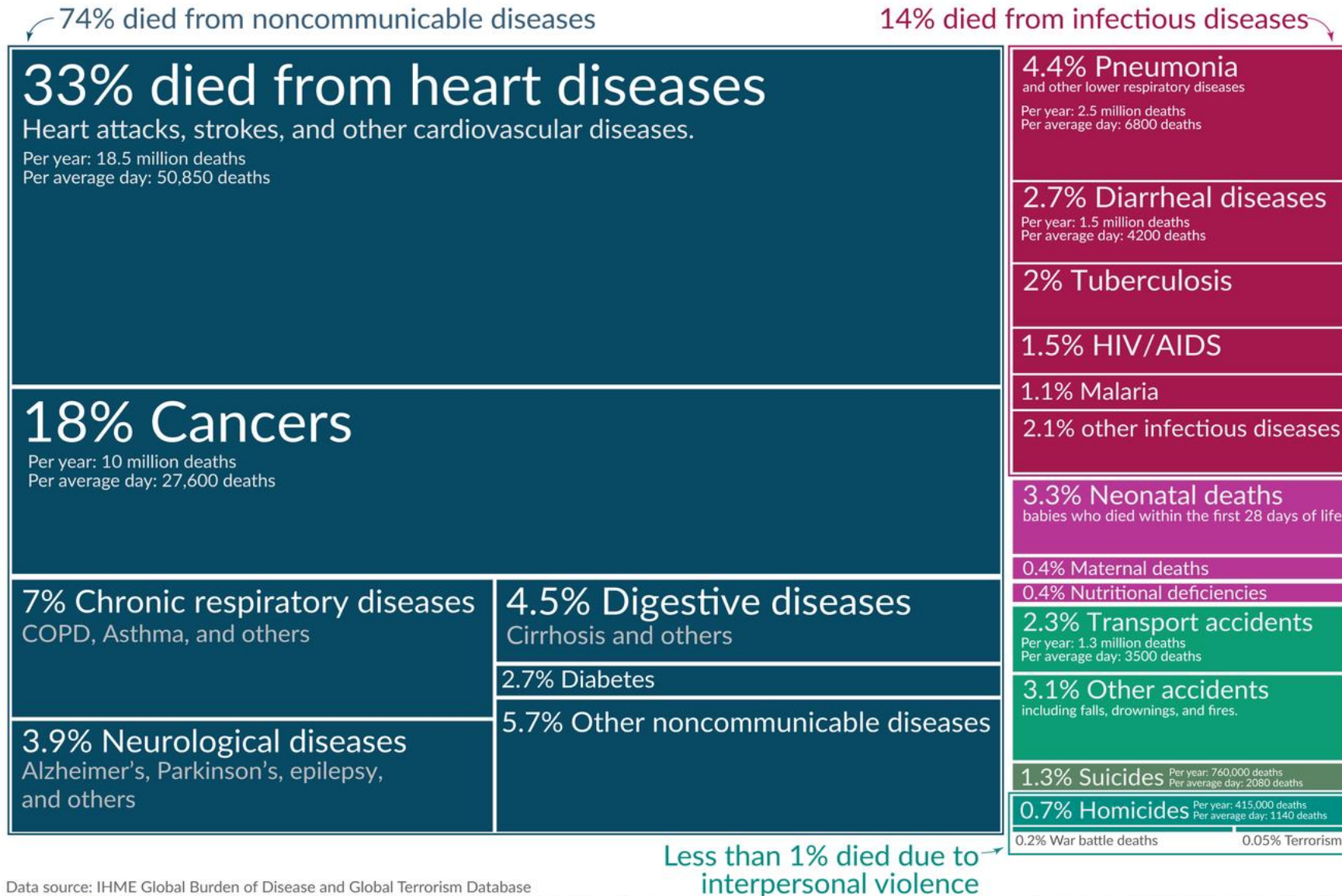This is a visualization from OurWorldinData.org, where you find data and research on how the world is changing. Licensed under CC-BY by the authors Hannah Ritchie and Max Roser.

What do people die from? Causes of death globally in 2019

The size of the entire visualization represents the total number of deaths in 2019: 55 million.
Each rectangle within it is proportional to the share of deaths due to a particular cause.

74% died from noncommunicable diseases

14% died from infectious diseases

33% died from heart diseases
Heart attacks, strokes, and other cardiovascular diseases.

Per year: 18.5 million deaths
Per average day: 50,850 deaths

18% Cancers

Per year: 10 million deaths
Per average day: 27,600 deaths

7% Chronic respiratory diseases
COPD, Asthma, and others

4.5% Digestive diseases
Cirrhosis and others

2.7% Diabetes

5.7% Other noncommunicable diseases

3.9% Neurological diseases
Alzheimer's, Parkinson's, epilepsy, and others

4.4% Pneumonia
and other lower respiratory diseases

Per year: 2.5 million deaths
Per average day: 6800 deaths

2.7% Diarrheal diseases
Per year: 1.5 million deaths
Per average day: 4200 deaths

2% Tuberculosis

1.5% HIV/AIDS

1.1% Malaria

2.1% other infectious diseases

3.3% Neonatal deaths
babies who died within the first 28 days of life

0.4% Maternal deaths

0.4% Nutritional deficiencies

2.3% Transport accidents
Per year: 1.3 million deaths
Per average day: 3500 deaths

3.1% Other accidents
including falls, drownings, and fires.

1.3% Suicides — Per year: 760,000 deaths — Per average day: 2080 deaths

0.7% Homicides — Per year: 415,000 deaths — Per average day: 1140 deaths

0.2% War battle deaths

0.05% Terrorism

Less than 1% died due to interpersonal violence

Heart Disease deaths:
USA 2021

60,000 more people died of COVID-19 during 2021 compared with 2020; COVID-19 remained the 3rd leading cause of death

PROVISIONAL 2021 DEATHS

1 Heart Disease
693K

2 All Cancers
Cancer
605K

3 COVID-19
415K

* Provisional National Vital Statistics System (NVSS) death certificate data on underlying cause of death among U.S. residents in the United States during January–December 2021

bit.ly/MMWR7117

APRIL 22, 2022

MMWR

Why We Need Better Tools

EVERY
40 SECONDS
someone in the US has a **heart attack**.

Thomas Sydenham, MD 1624-1689

Action step 1: Focus on heart disease
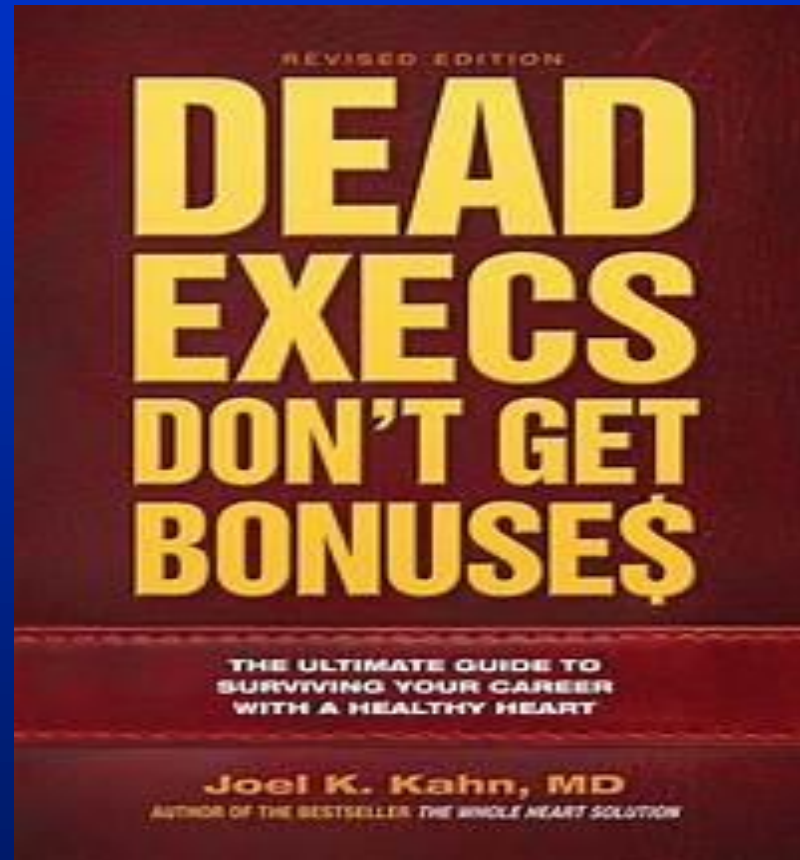
Heart disease starts young, so start early

Coronary Atherosclerosis in American Casualties in Three Wars
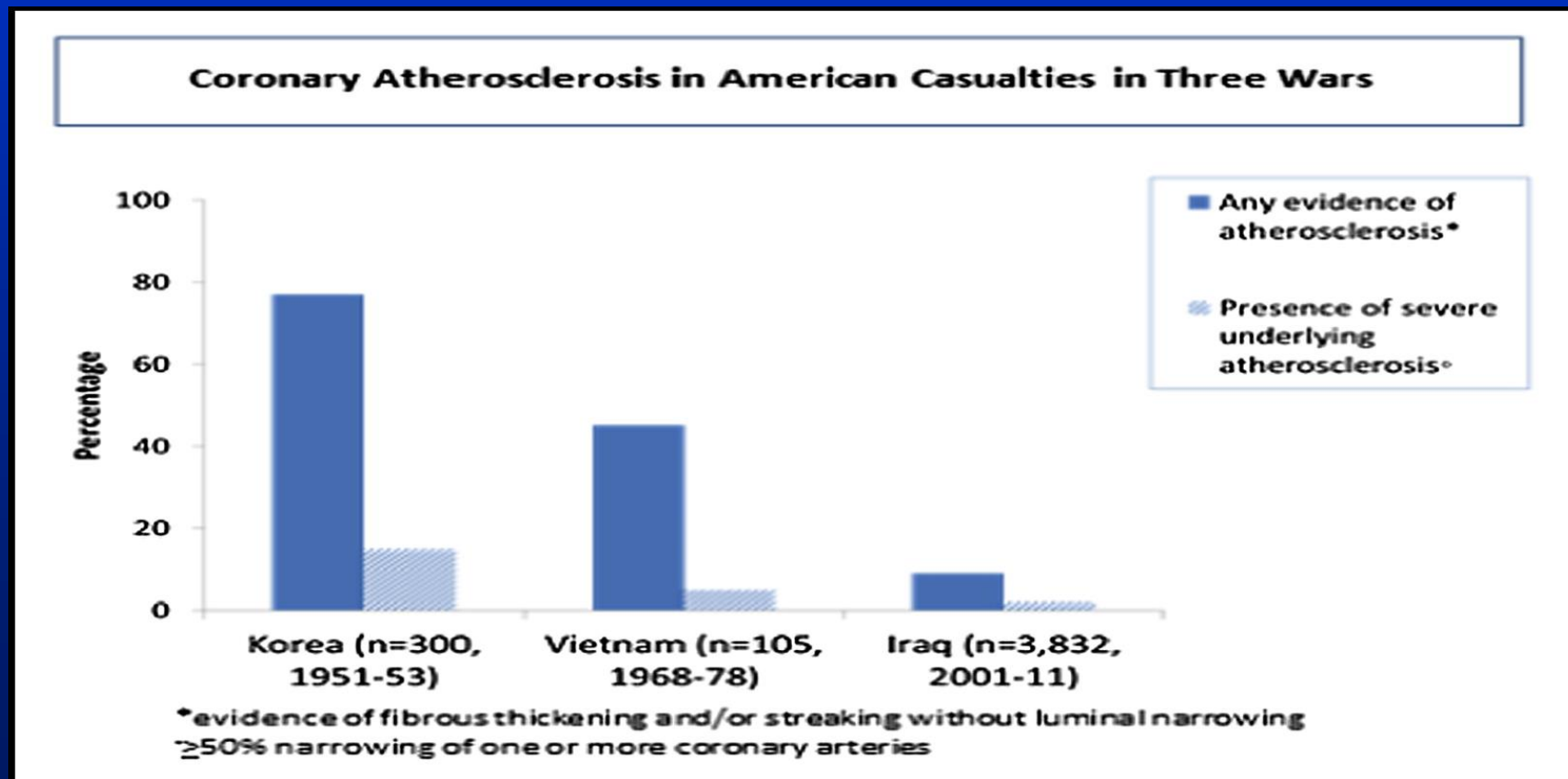
Early Appearance of Atherosclerosis: Bogalusa Heart Study

Prevalence of Fibrous Plaque Lesions

Berenson et al, NEJM, 1998

$p = 0.001$ for trend

We know why

Leading Causes of Death*
United States, 2000

- Heart Disease
- Cancer
- Stroke
- Chronic lower respiratory disease
- Unintentional injuries
- Diabetes
- Pneumonia/influenza
- Alzheimer's disease
- Kidney disease

Percentage (of all deaths)

Actual Causes of Death†
United States, 2000

- Tobacco
- Poor diet/Physical inactivity
- Alcohol consumption
- Microbial agents (e.g., influenza, pneumonia)
- Toxic agents (e.g., pollutants, asbestos)
- Motor vehicles
- Firearms
- Sexual behavior
- Illicit drug use

Percentage (of all deaths)
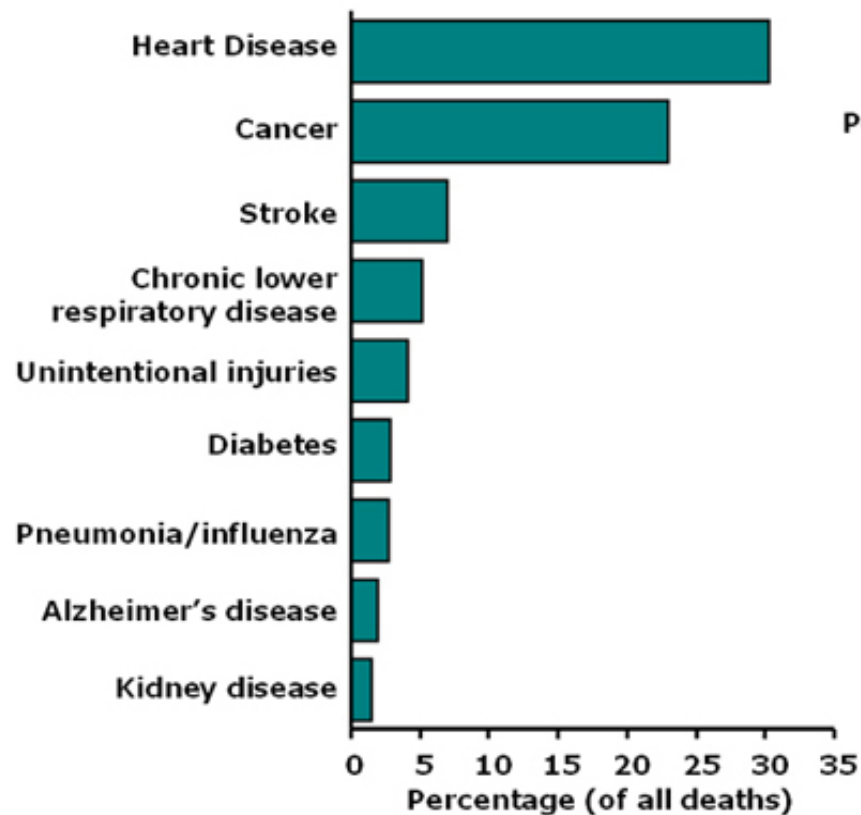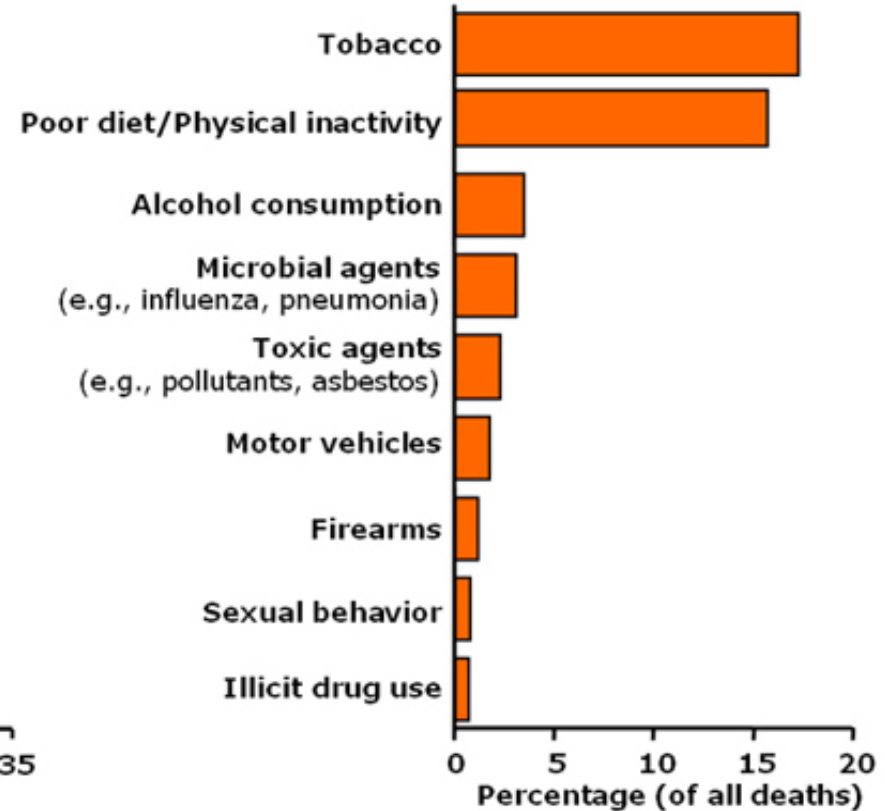
* Miniño AM, Arias E, Kochanek KD, Murphy SL, Smith BL. Deaths: final data for 2000. National Vital Statistics Reports 2002; 50(15):1-120.
† Mokdad AH, Marks JS, Stroup DF, Gerberding JL. Actual causes of death in the United States, 2000. JAMA. 2004;291(10):1238-1246.

Prevent 85% of heart attacks

- **Don't smoke**
- **Walk 30-40 minutes daily**
- **Eat >5 servings of fruit/veg a day**
- **Sleep 7 hours a night**
- **Enjoy a few alcoholic beverages a week**

- MORGEN STUDY 2013 Netherlands 17,887 men and women
- Karolinska study 2014 Sweden 20,721 men

person

A man is as old as
his arteries.
Thomas Sydenham

QuoteAddicts

Test Not Guess

IF CORONARY ARTERY DISEASE WAS ATTACKING YOUR FACE RATHER THAN YOUR HEART, YOU'D DO SOMETHING ABOUT IT.
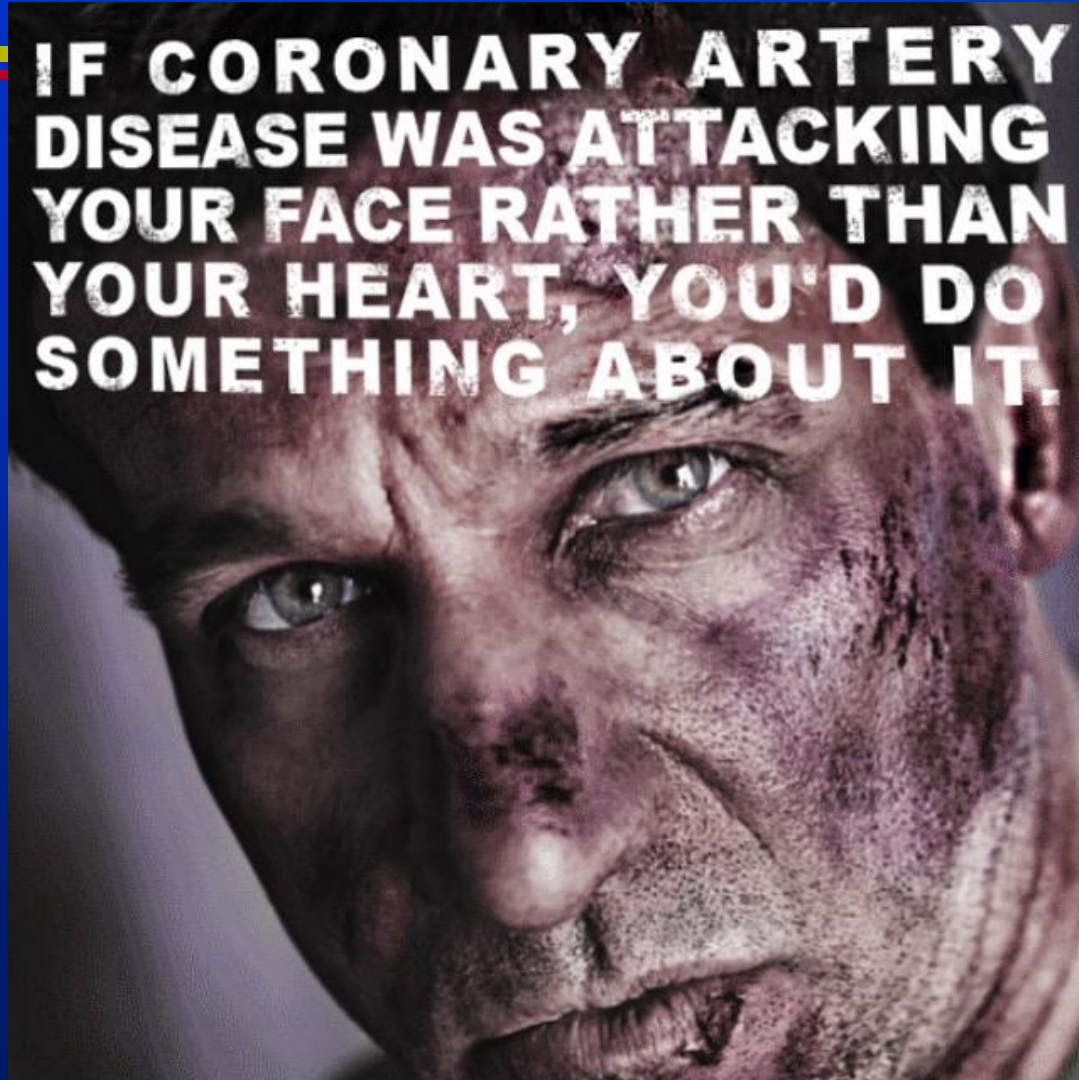
Early detection of America's #1 killer

SHAPE — Society for Heart Attack Prevention and Eradication

Support HEART ATTACK ERADICATION Campaign

Sir Winston Churchill, 91 ✝
- Overweight
- Not Fit
- Heavy Smoker

Jim Fixx, 53 ✝ ♥
- Not Overweight
- Very Fit
- Non-Smoker

Clues to silent heart disease

Signs That May Signal
Heart Attack Risk

Hair Loss (Crown)

Hair Loss (Temples)

Yellow Fatty Deposits
on Eyelid

Earlobe Crease

Source - American Heart Association
Scientific Sessions Abstract 15333

Diagonal EarLobe Crease: DELC

Erectile Dysfunction:
Canary in the Coal Mine

Erectile Dysfunction Is a Warning Sign of Atherosclerosis/Clogged Arteries

Tools of the heart attack prevention specialist

50% Traditional testing only identifies **half** of the people who will have a *heart attack* or *stroke.*

Carotid Intima Media Thickness (CIMT)

Interior of Carotid Artery

Intima Media Layer of Arterial Wall
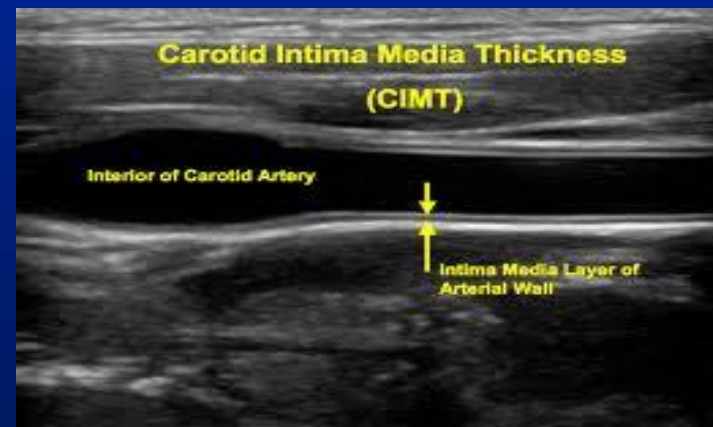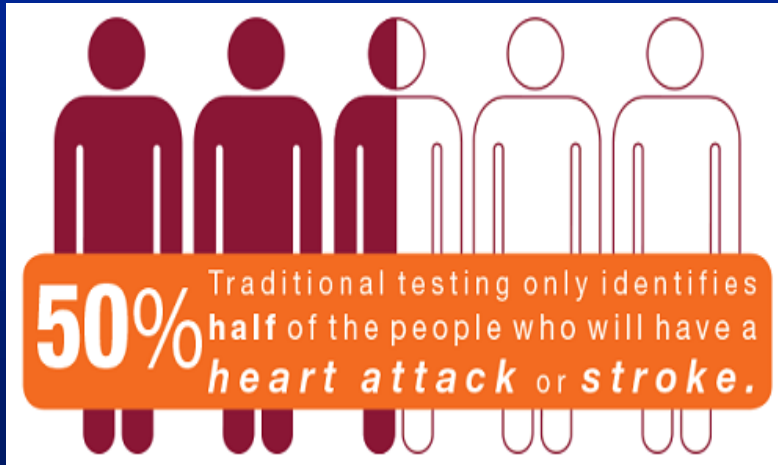
Common Sense

"The best test for prediction of the risk of atherosclerosis is the demonstration of atherosclerosis"

Dr. Ernest Schaeffer, Editor-in-Chief of Atherosclerosis

Screening for Atherosclerosis — Risk Factors vs Disease

Numerous Risk Factors:
- High LDL
- Low HDL
- High BP
- Diabetes
- Smoking
- CRP
- Metabolic Syn
- Lp(a)
- Homocysteine
- Dense LDL
- Lp-PLA2
- ApoB/ApoA
- Family History
- Sedentary Life
- Obesity
- Stress
- ...
- ?

Over 200 risk factors have been reported.
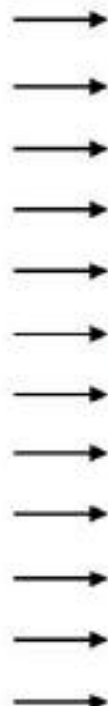
Examples of Arterial Structure Tests:
- Carotid IMT and Plaque Measured by Ultrasound
- Aortic and Carotid Plaque Detected by MRI
- Coronary Calcium Score Measured by CT
- Ankle Brachial Index

Examples of Arterial Function Tests:
- Brachial Vasoreactivity Measured by Ultrasound
- Vascular Compliance Measured by Radial Tonometry
- Microvascular Reactivity Measured by Fingertip Tonometry

Detect Your Plaques Earlier
Comparing Detection by Positive Cardiac CT and Positive Nuclear Stress Test

Stages >>	Early	Moderate	Advanced	Late
Obstruction	none	20%	50%	70%
Symptoms	none	none	none	yes
Stress test	normal	normal	normal	abnormal
Cardiac CT	none	abnormal	abnormal	abnormal

Shapesociety.org

The 1st SHAPE Guidelines
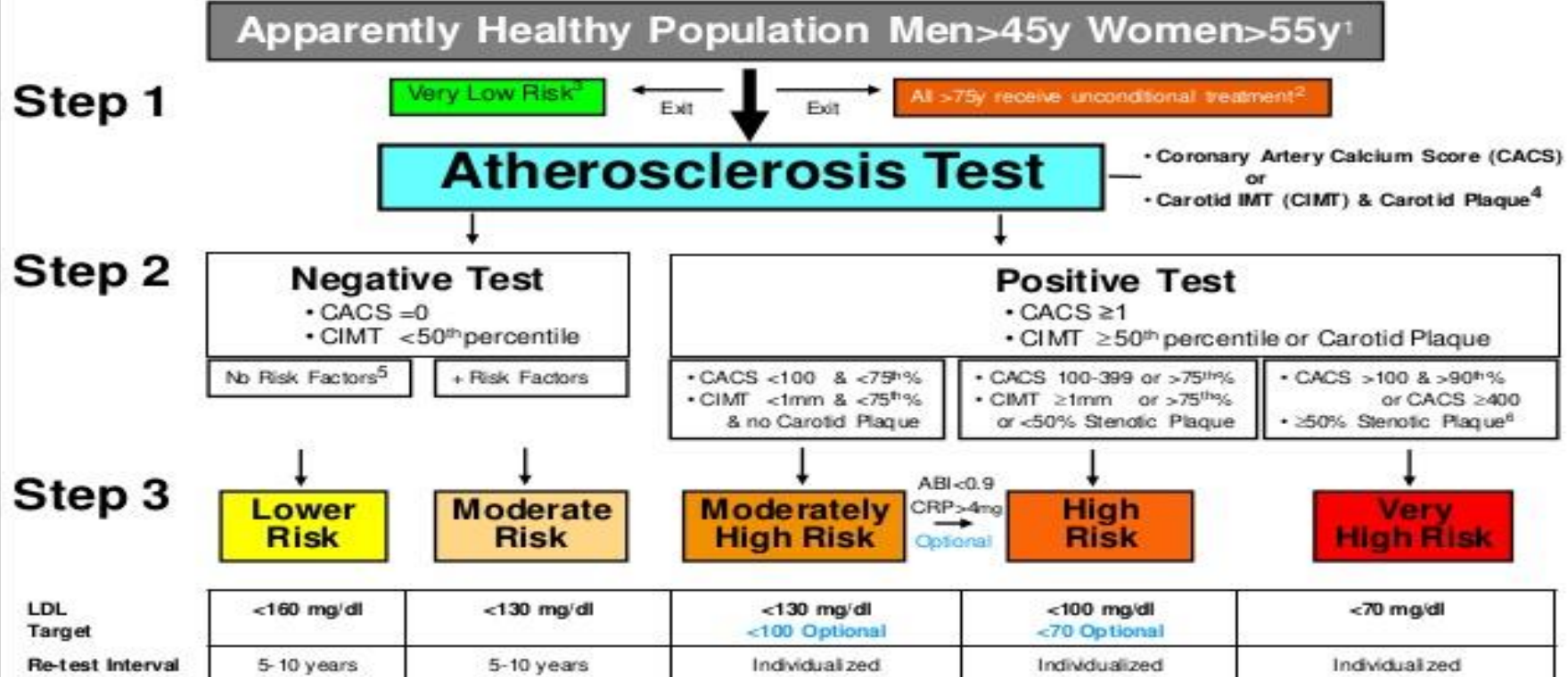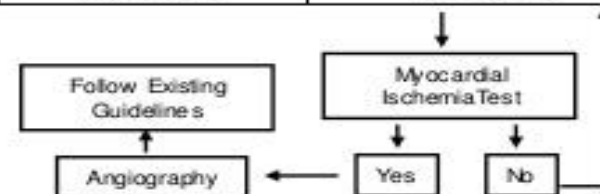
Coronary Artery Calcium Score (CACS)
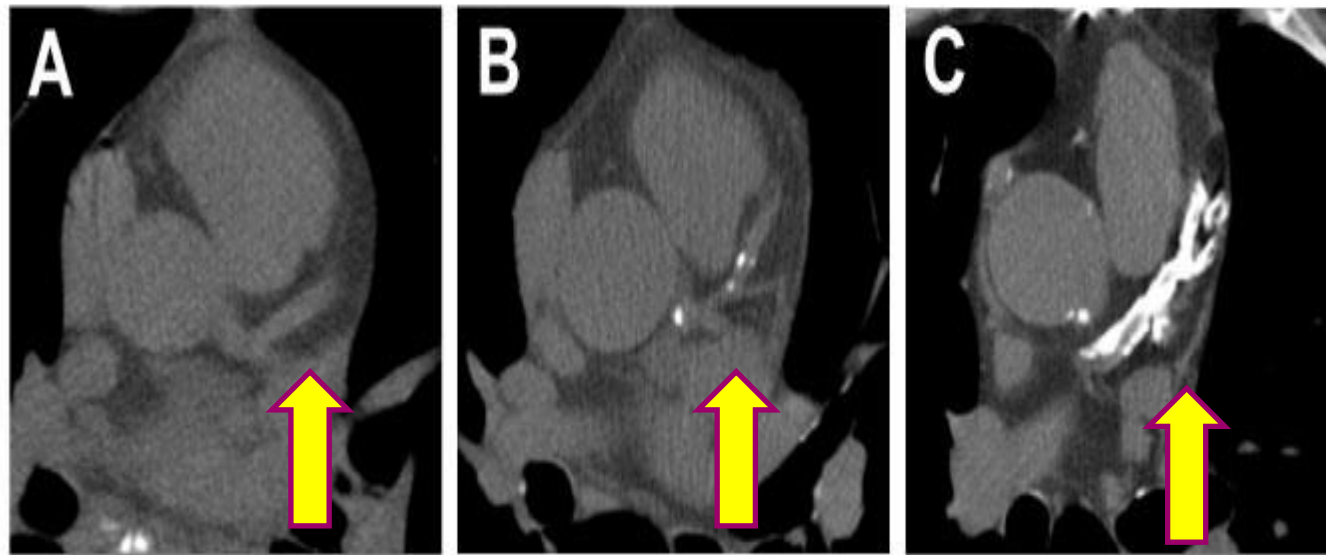
Figure 1 - Images illustrating the coronary artery calcium score of three patients with increasing calcification grades in the territory of the anterior descending artery: A. no calcification; B. mild calcification; C. severe calcification.

Carotid Intima Media Thickness (CIMT)

- Direct *in vivo* measurement of thickness of carotid artery wall by B-mode ultrasound

- Vessel wall thickness correlates with status of atherosclerosis and CV events

- Atherosclerosis is a systemic disorder
  - Atherosclerosis in the carotid artery is predictive of disease in other vascular beds

de Groot E, et al. *Circulation.* (2004) 109[Suppl III]:III-33–III-38.

CIMT: Carotid Intimal Medial Thickness Ultrasound
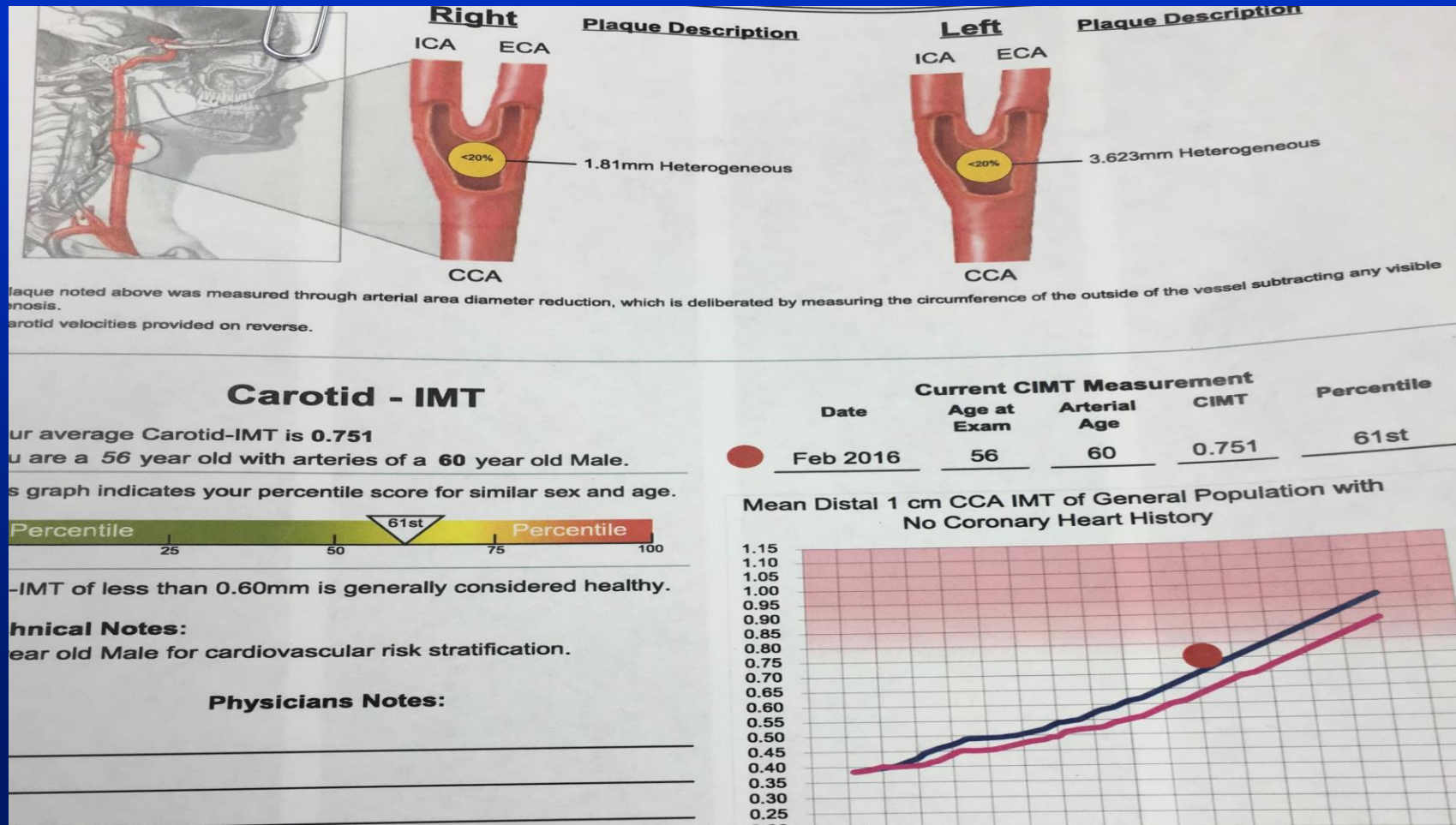
CIMT: A NORMAL

Visualized Plaque and Atherosclerotic Burden Assessment
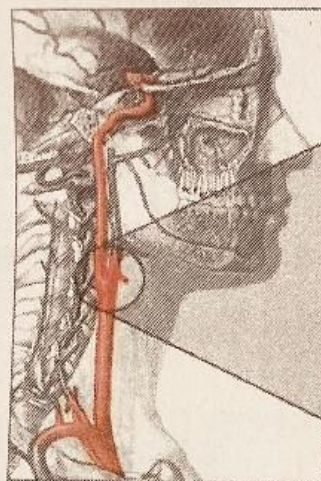
ACTION STEP

PARADIGM SHIFT

A change from one way of thinking to another.
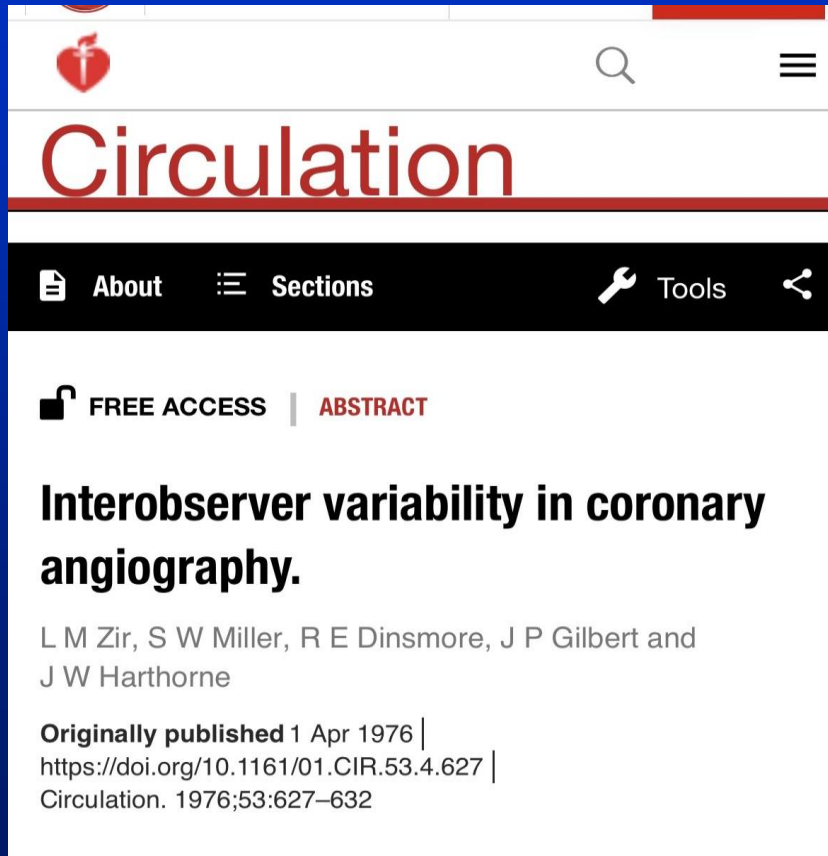
Mason Sones, MD 1958
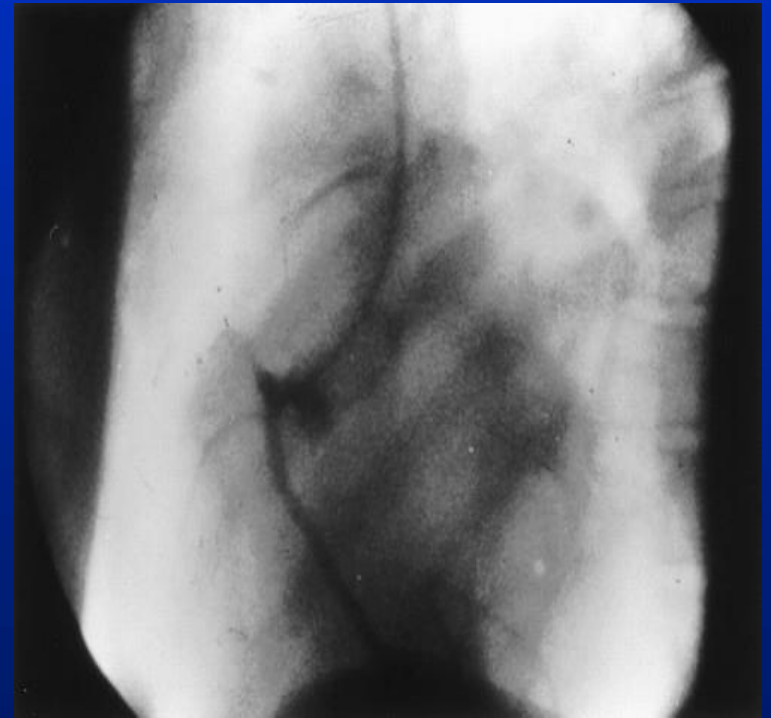
Visual Estimation of Coronary Stenoses

Right Coronary Artery

50% blockage

Moderate Coronary Artery Disease Typically 40-70% blockage
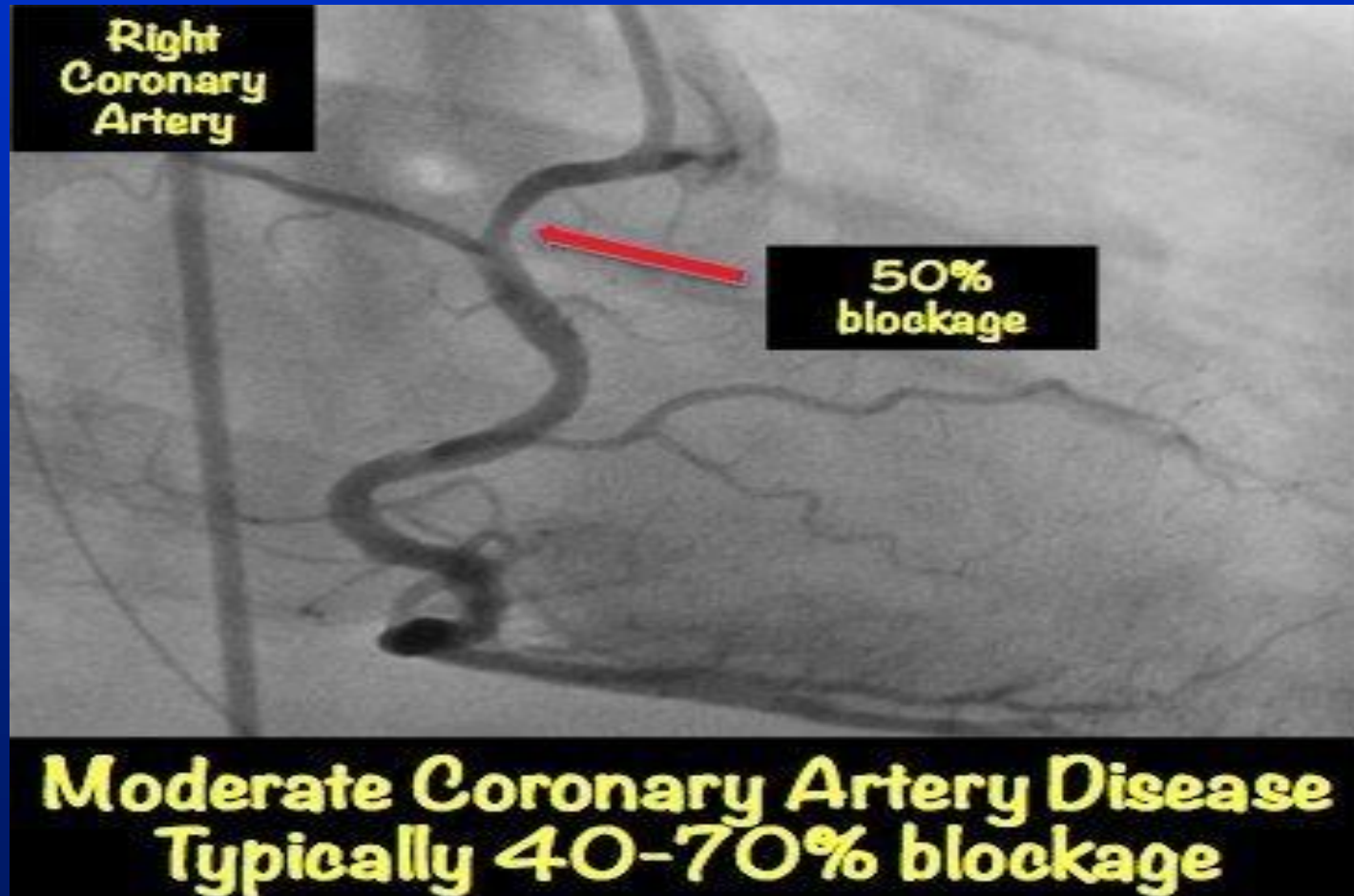
High Interobserver Variability: Coronary Angiography

Circulation

About · Sections · Tools

🔓 FREE ACCESS | ABSTRACT

Interobserver variability in coronary angiography.

L M Zir, S W Miller, R E Dinsmore, J P Gilbert and J W Harthorne

Originally published 1 Apr 1976 |
https://doi.org/10.1161/01.CIR.53.4.627 |
Circulation. 1976;53:627–632

NIH National Library of Medicine
National Center for Biotechnology Information

Log in

PubMed®
Advanced User Guide

Comparative Study

Coronary angiogram interpretation. Interobserver variability

J E Galbraith et al. JAMA. 1978.

Show details ⚙

Full text links · Cite · ...

Interobserver Variability 2018: Not Much Has Changed

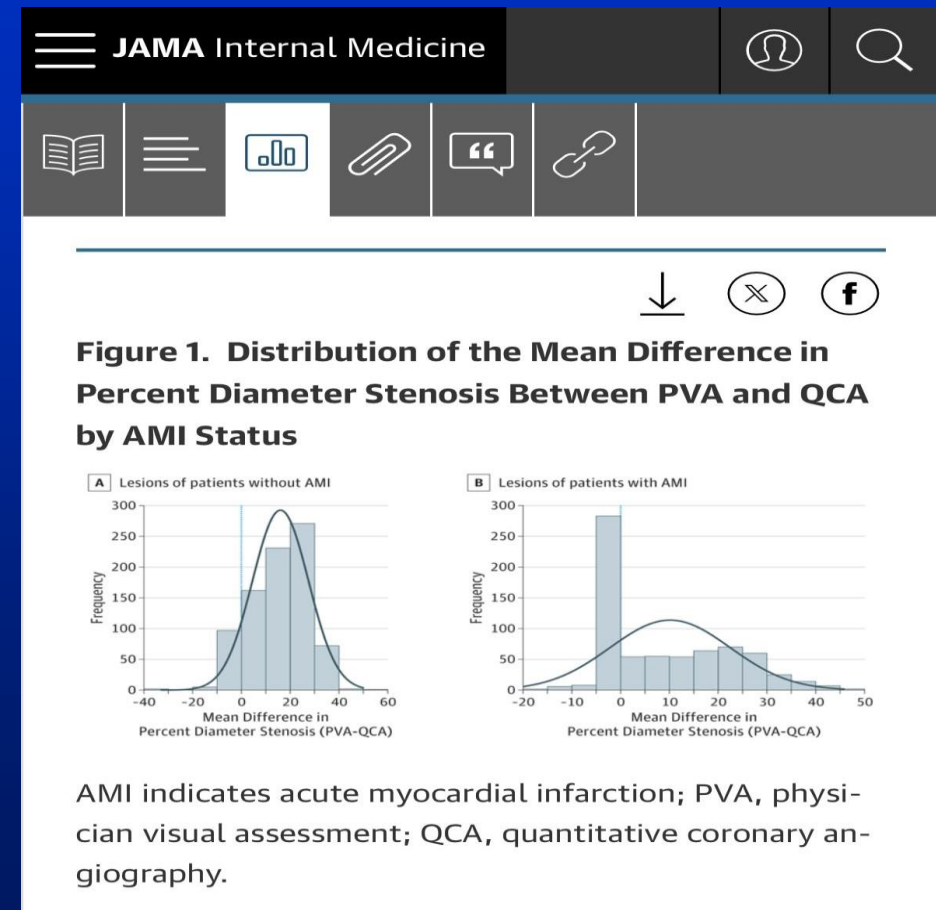JAMA Internal Medicine

FREE

Original Investigation

February 2018

Comparison of Physician Visual Assessment With Quantitative Coronary Angiography in Assessment of Stenosis Severity in China
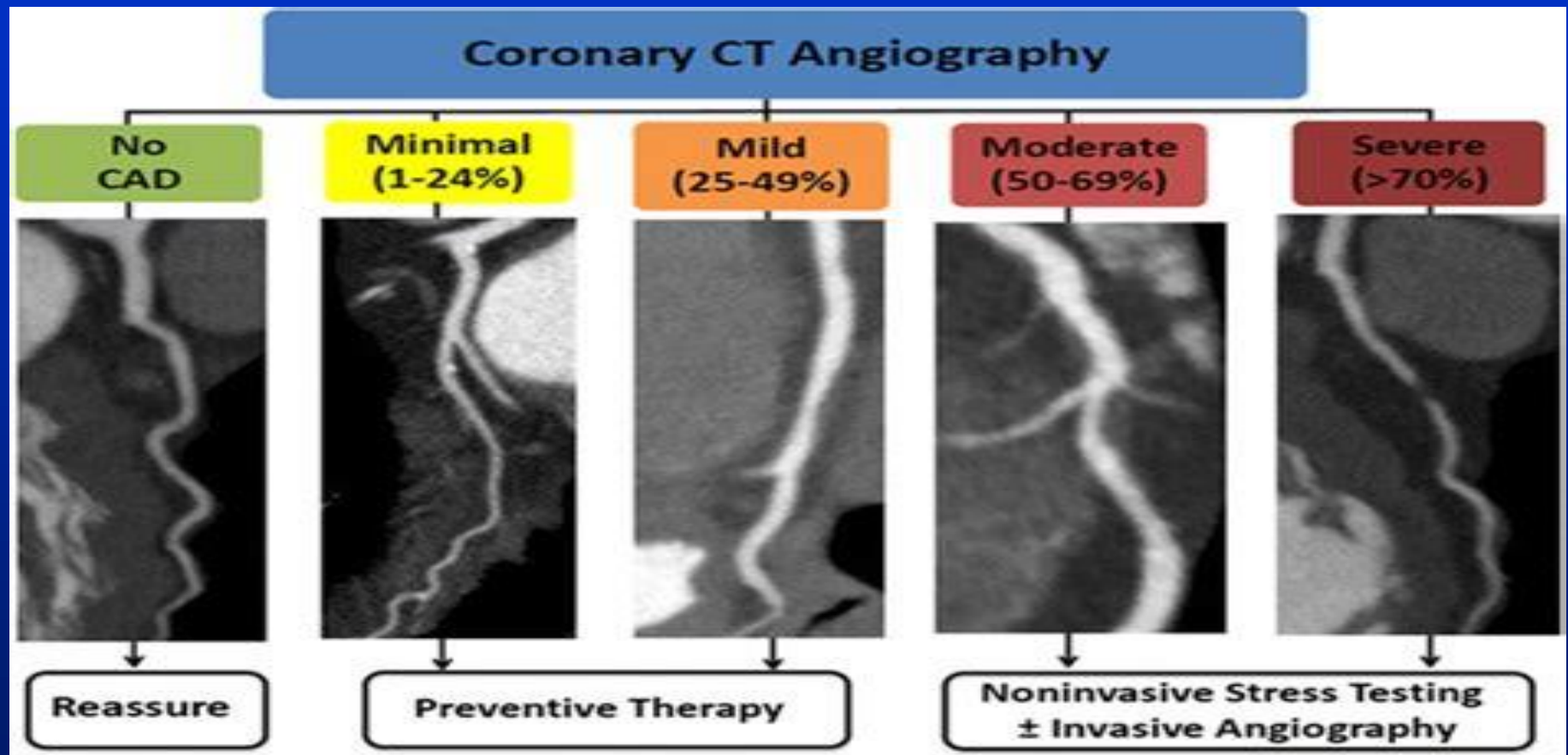
Haibo Zhang, MD[1]; Lin Mu, BS[2,3]; Shuang Hu, PhD[1]; et al

≫ Author Affiliations | Article Information

JAMA Intern Med. 2018;178(2):239-247. doi:10.1001/jamainternmed.2017.7821

JAMA Internal Medicine

Figure 1. Distribution of the Mean Difference in Percent Diameter Stenosis Between PVA and QCA by AMI Status

A Lesions of patients without AMI

B Lesions of patients with AMI

AMI indicates acute myocardial infarction; PVA, physician visual assessment; QCA, quantitative coronary angiography.

Coronary CT Angiography CCTA: 2010
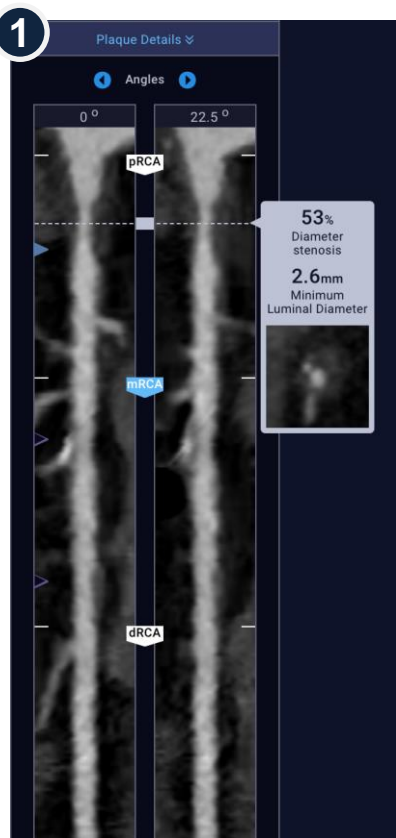
Why Use CCTA vs a Heart Catheterization?

- Non-invasive Imaging of Atherosclerosis
  - Allows for serial imaging of changes in coronary atherosclerosis
  - Less expensive and minimally invasive
  - Less radiation exposure
  - 3-dimensional
- Assessment of the Entire Coronary Tree
  - Allows imaging in the culprit and non-culprit vessel
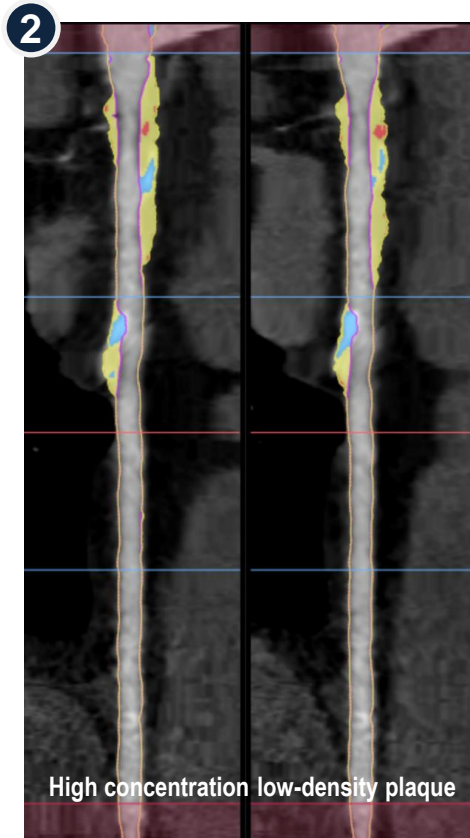
Welcome AI to Cardiology
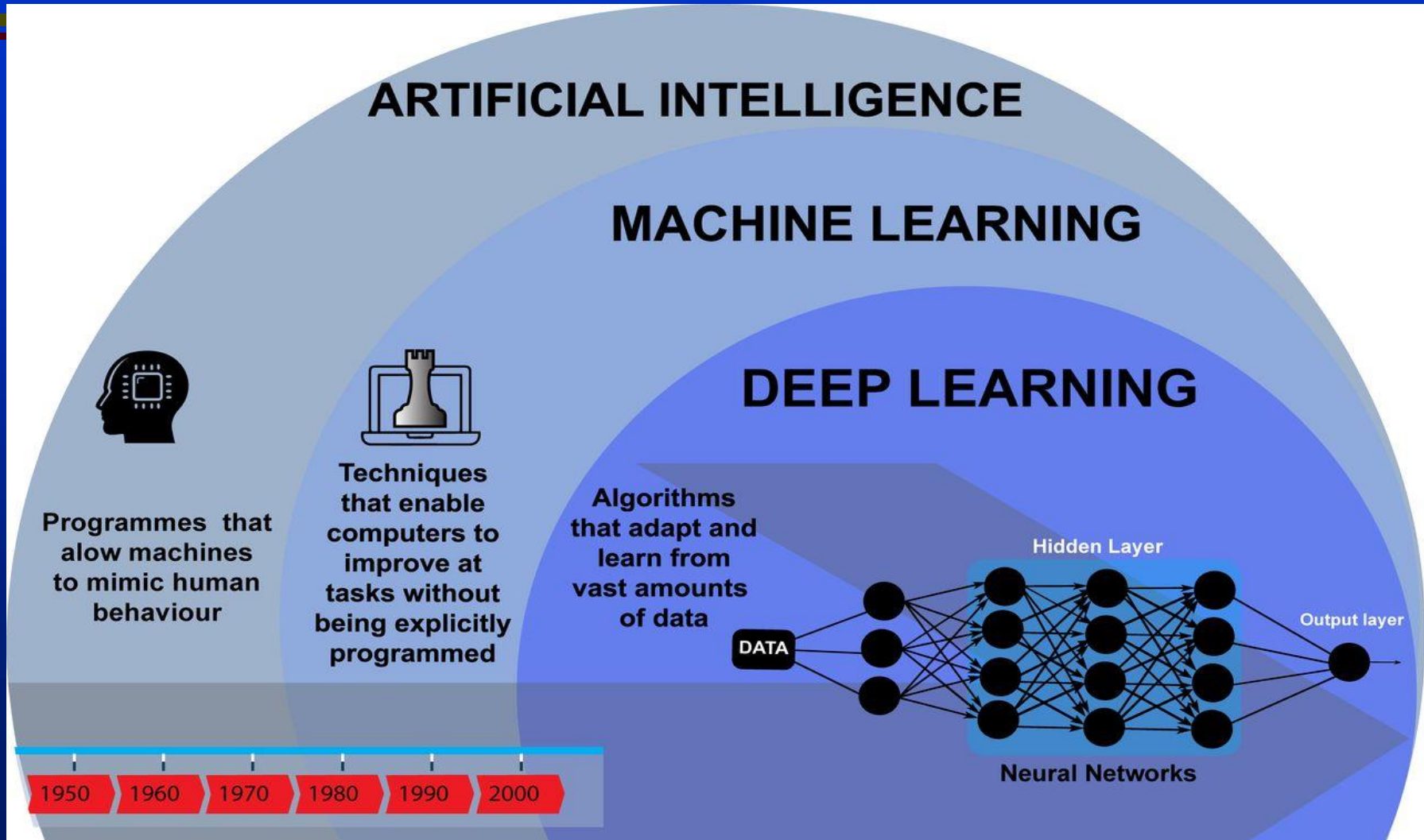
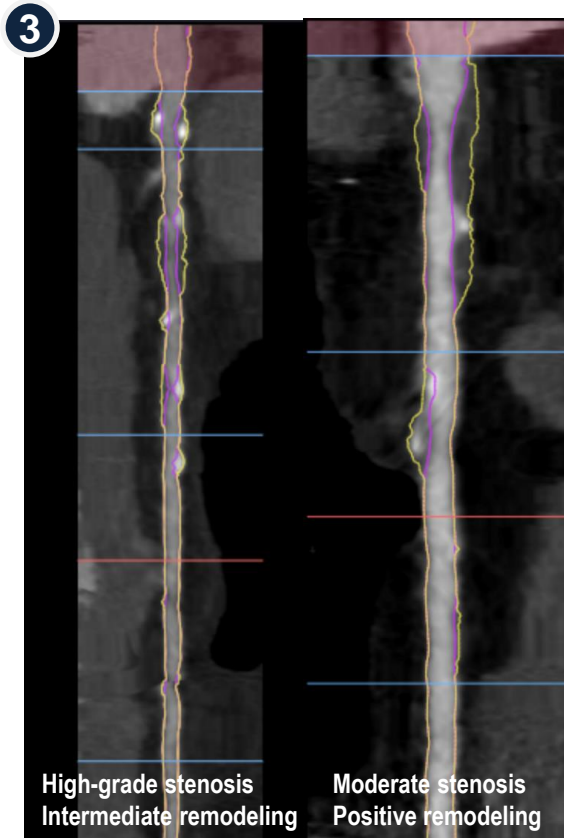# Coronary CCTA With AI Enables Comprehensive Evaluation of Individual Risk

The four (4) most important features of risk: CONFIRM, ICONIC, PARADIGM, PROMISE, SCOT-HEART, ISCHEMIA, PROSPECT, etc.
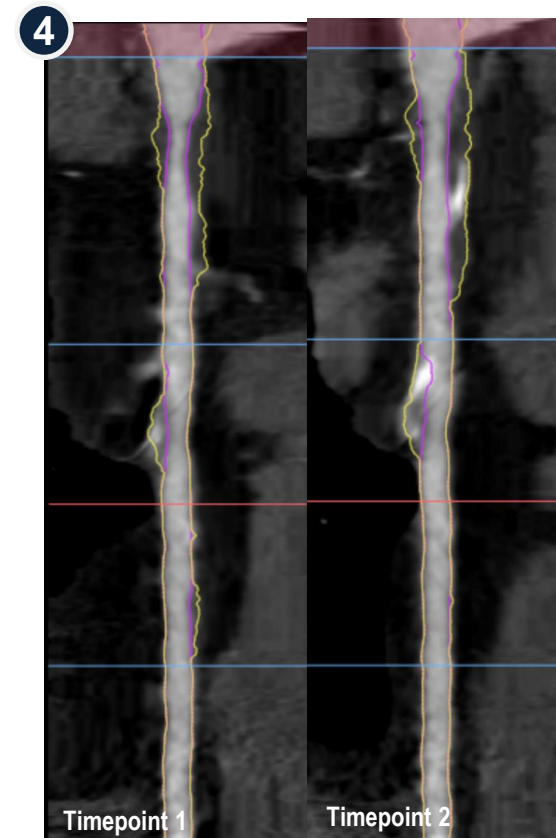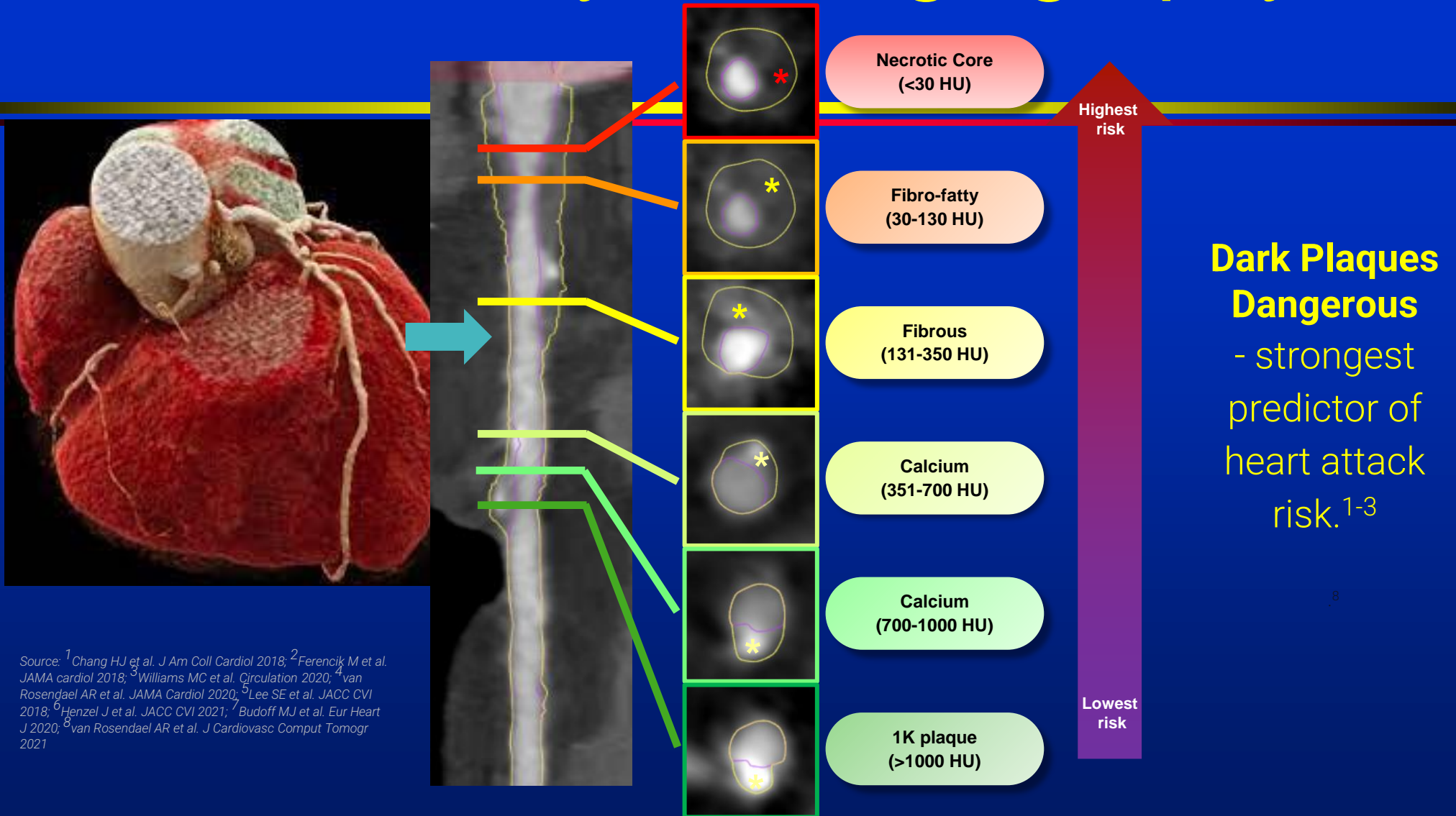

① Plaque Burden

② Plaque Composition

High concentration low-density plaque

③ Vascular Morphology (Stenosis / Remodeling)

High-grade stenosis Intermediate remodeling

Moderate stenosis Positive remodeling

④ Plaque Progression

Timepoint 1

Timepoint 2

AI-Coronary CT Angiography

Necrotic Core (<30 HU)

Fibro-fatty (30-130 HU)

Fibrous (131-350 HU)

Calcium (351-700 HU)

Calcium (700-1000 HU)

1K plaque (>1000 HU)

Highest risk

Lowest risk

Dark Plaques Dangerous - strongest predictor of heart attack risk.[1-3]

Source: [1] Chang HJ et al. J Am Coll Cardiol 2018; [2] Ferencik M et al. JAMA cardiol 2018; [3] Williams MC et al. Circulation 2020; [4] van Rosendael AR et al. JAMA Cardiol 2020; [5] Lee SE et al. JACC CVI 2018; [6] Henzel J et al. JACC CVI 2021; [7] Budoff MJ et al. Eur Heart J 2020; [8] van Rosendael AR et al. J Cardiovasc Comput Tomogr 2021

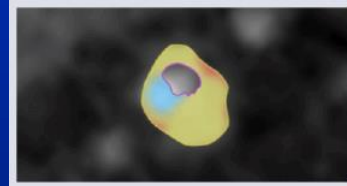# Not All Plaque Is the Same.
The FUTURE IS NOW
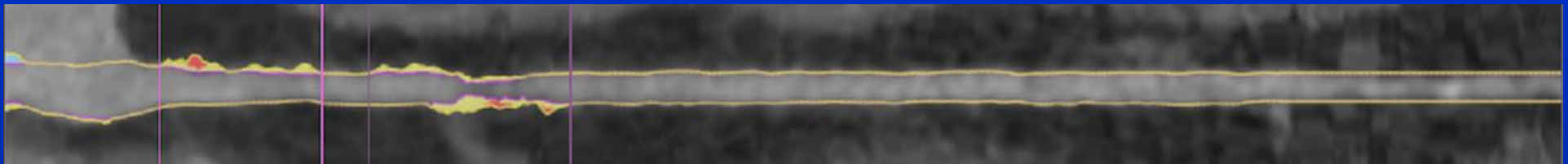
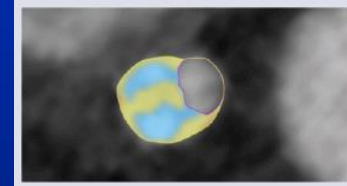**PLAQUES THAT LOOK DIFFERENT BEHAVE DIFFERENTLY.**
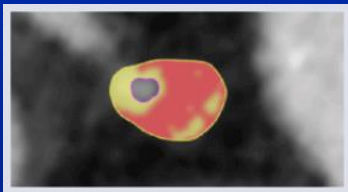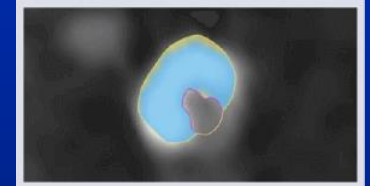
| LOW-DENSITY-NON-CALCIFIED PLAQUE (RED) | NON-CALCIFIED PLAQUE (YELLOW) | ALL PLAQUE TYPES | NON-CALCIFIED (YELLOW) AND CALCIFIED PLAQUE (BLUE) | CALCIFIED PLAQUE (BLUE) |

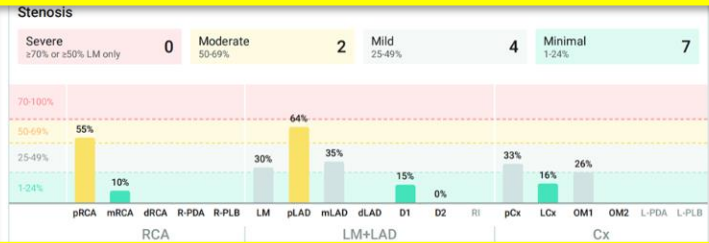HIGH RISK   INTERMEDIATE RISK   LOW RISK

Provider Report

Summary

Plaque Detail and Stage

Stenosis Summary and Detail

Vessels with plaque color overlay

AI-CCTA: Improved CV Risk Assessment

MACE Prediction:

- **CCTA Plaque Stage is a better predictor of short- and long-term MACE events than:**
  - **Risk Score (ASCVD etc.).**
  - **Agatston Score.**
  - **Stenosis presence**

Novel AI-QCT Plaque Staging

CAD Stage 0	
PAV	0%
10y CVD risk	0%

CAD Stage 1	
PAV	>0-5%
10y CVD risk	≤10.0%

CAD Stage 2	
PAV	≥5-15%
10y CVD risk	≥10.1%-15.3%

CAD Stage 3	
PAV	≥15%
10y CVD risk	≥15.4%

Plaque Stages Provide 10-Year Prognostic Value

$P < 0.0001$
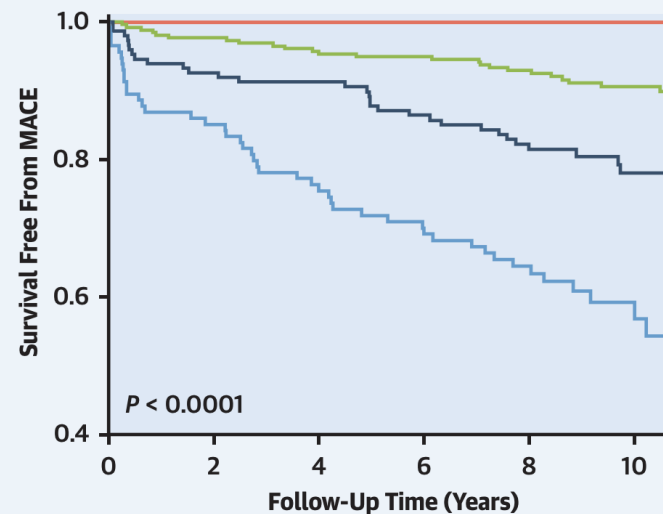
N = 539   FU = 10.3 years

AI-QCT Improves 10y CVD Risk Stratification

AUC 0.73
Clinical risk + CACS

NRI 0.21

AUC 0.82
Clinical risk + AI-QCT

Nurmohamed et al JACC Imag 2023

Therapy Based on Plaque Stage

Stage	Stenoses	Action	Rescan (until stable):
Stage 0: No Plaque	0	• GDMT / Consider de-escalation	4 years
Stage 1: Mild	<50%	• Statin, Ezetimibe	3 years
Stage 2: Moderate	<50%	Stage 1 Plus • Aspirin, Rivaroxaban • GLP1 if diabetic	2 years
Stage 3: Severe	<50%	Stage 2 plus • Consider PCSK9, Icosapent ethyl, Inclisirin, Bempedoic acid, Colchicine • GLP1 and SGLT2 if diabetic	1 year

The American Journal of Medicine
Available online 10 December 2022
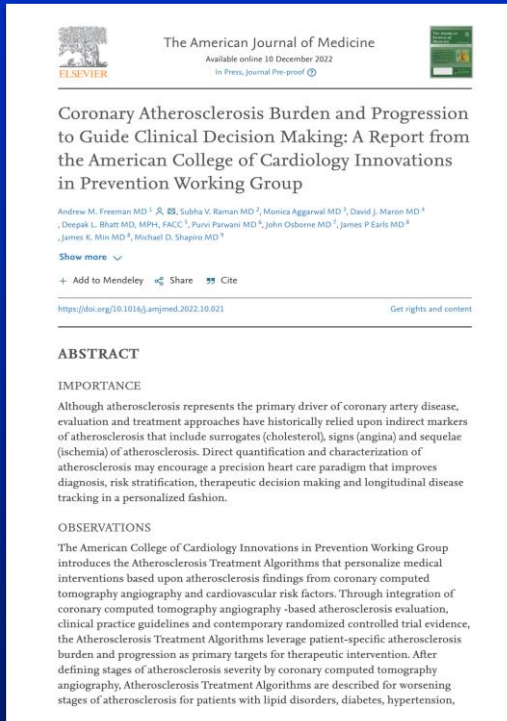In Press, Journal Pre-proof

Coronary Atherosclerosis Burden and Progression to Guide Clinical Decision Making: A Report from the American College of Cardiology Innovations in Prevention Working Group

Andrew M. Freeman MD ¹, Subha V. Raman MD ², Monica Aggarwal MD ³, David J. Maron MD ⁴, Deepak L. Bhatt MD, MPH, FACC ⁵, Purvi Parwani MD ⁶, John Osborne MD ⁷, James P Earls MD ⁸, James K. Min MD ⁸, Michael D. Shapiro MD ⁹

ABSTRACT

IMPORTANCE

Although atherosclerosis represents the primary driver of coronary artery disease, evaluation and treatment approaches have historically relied upon indirect markers of atherosclerosis that include surrogates (cholesterol), signs (angina) and sequelae (ischemia) of atherosclerosis. Direct quantification and characterization of atherosclerosis may encourage a precision heart care paradigm that improves diagnosis, risk stratification, therapeutic decision making and longitudinal disease tracking in a personalized fashion.

OBSERVATIONS

The American College of Cardiology Innovations in Prevention Working Group introduces the Atherosclerosis Treatment Algorithms that personalize medical interventions based upon atherosclerosis findings from coronary computed tomography angiography and cardiovascular risk factors. Through integration of coronary computed tomography angiography -based atherosclerosis evaluation, clinical practice guidelines and contemporary randomized controlled trial evidence, the Atherosclerosis Treatment Algorithms leverage patient-specific atherosclerosis burden and progression as primary targets for therapeutic intervention. After defining stages of atherosclerosis severity by coronary computed tomography angiography, Atherosclerosis Treatment Algorithms are described for worsening stages of atherosclerosis for patients with lipid disorders, diabetes, hypertension,

Freeman, A et al Am J Med 2022

Coronary Imaging and CV Outcome Trials

Drug	CTA Progression	CVOT
Statin	+++ (Regression)	+++
Estrogen	Neutral	Neutral
Xarelto vs Warfarin	+ (slowed progression)	+
Fish Oil (EPA)	++ (slowed progression)	+++
Testosterone	Progression	Harmful
Eliquis vs Warfarin	+ (slowed progression)	+
Atorvastatin	+++ (regression)	+++
Colchicine	++ (mild regression)	++

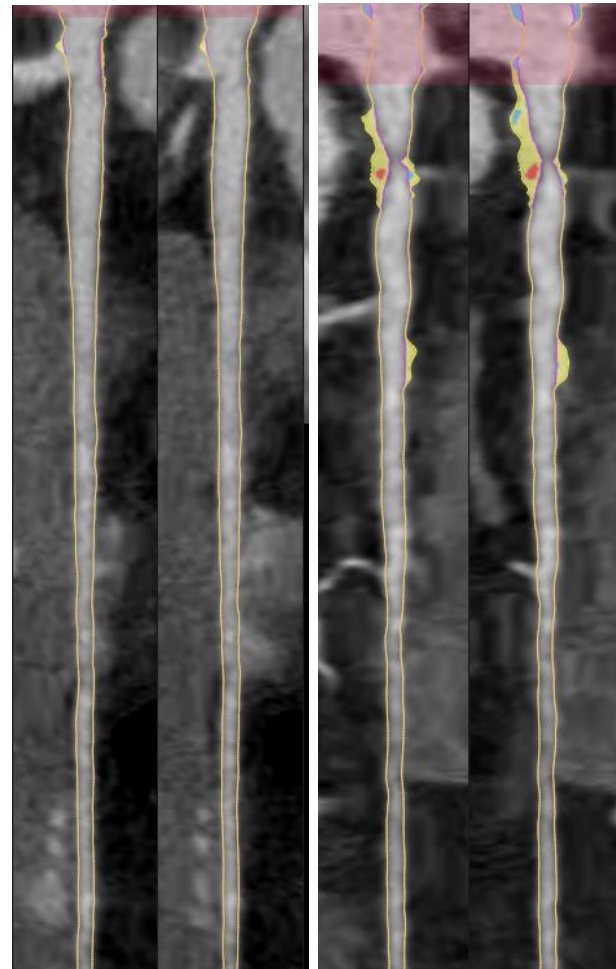# Aged Garlic Extract
Matsumoto 2016
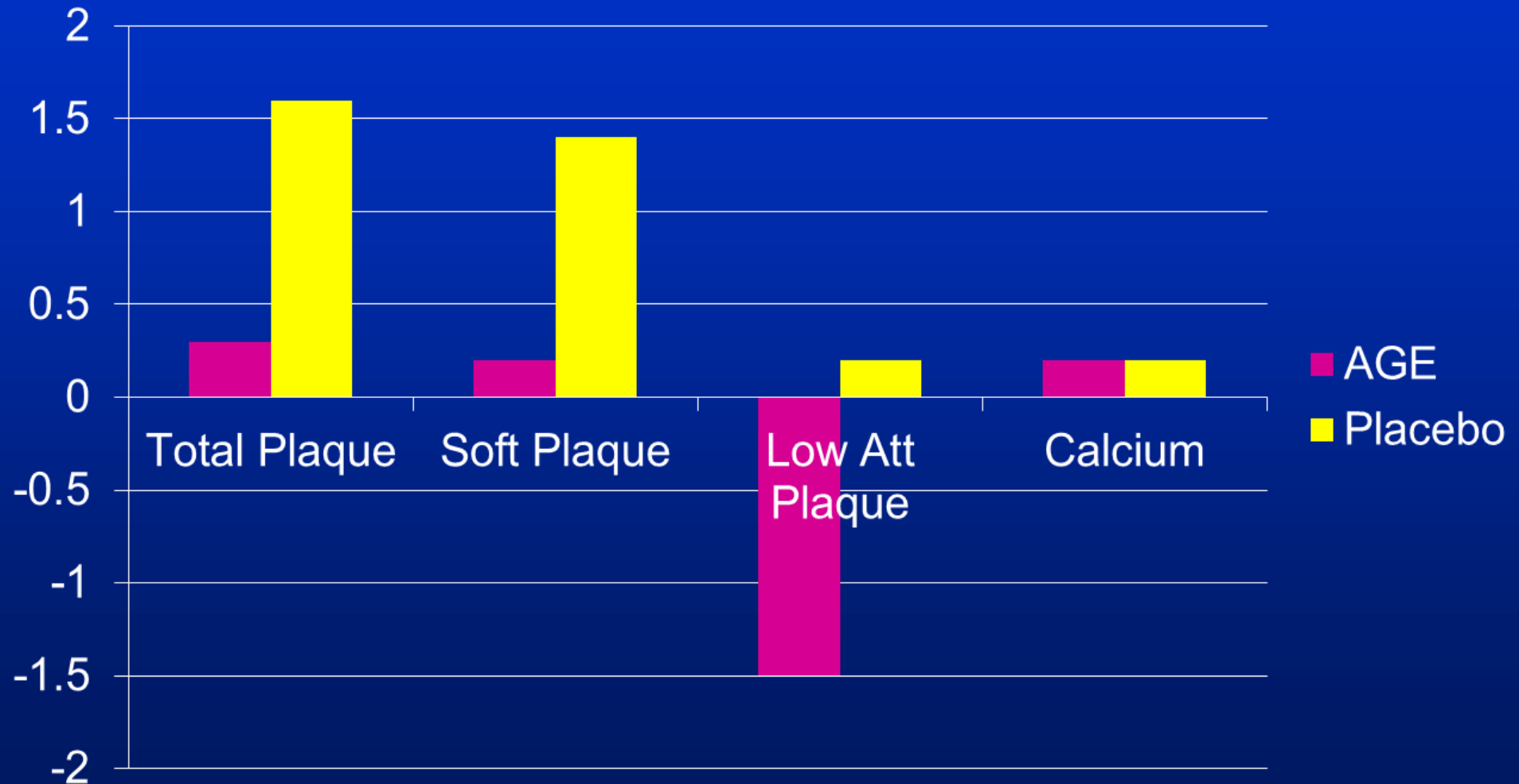
Plaque Progression.

60-year-old female not on medical therapy.

2010

2017

ALL	mm³ PAV	Current Cleerly ID: 2600EFC9 8/12/2010	# %	Compared Cleerly ID: 393D4BD4 6/19/2017
Total Plaque Volume (mm³)		64.4	▲ +203%	195.1
▶ Total Non-Calcified Plaque Volume (mm³)		64.3	▲ +177.6%	178.5
Low-Density - Non-Calcified Plaque Volume (mm³)		0	▲ N/A	3.8
Total Calcified Plaque Volume (mm³)		0.1	▲ +16500%	16.6
# of Severe Stenosis		0	▲ N/A	1
# of Moderate Stenosis		0	=	0
Highest Remodeling Index		1.2	▲ +8.3%	1.3
Greatest Diameter Stenosis (%)		12	▲ +508.3%	73
Greatest Area Stenosis (%)		24	▲ +287.5%	93
Length (mm)		694	▼ -6.5%	649

Per-Patient analysis:
- **230% TPV increase**
- **3.8 mm3 new LD-NCP**
- **180% NCP increase**
- **New severe LAD stenosis**

SMPRs

| Current Cleerly ID: 2600EFC9 8/12/2010	Compared Cleerly ID: 393D4BD4 6/19/2017
◀ Lesion 1 ▶ ↺ 0° ↻	↺ 0° ↻ ◀ Lesion 1 ▶
44.7 mm³	**128.3** mm³
Total Plaque Volume	Total Plaque Volume
● Low-Density - Non-Calcified 0	● Low-Density - Non-Calcified 3.7
● Non-Calcified 44.6	● Non-Calcified 109.1
● Calcified 0.1	● Calcified 15.5

Per-Plaque (pLAD) analysis:
- 190% TPV increase
- 3.7 mm3 new LD-NCP
- 240% NCP 1

Plaque Stabilization.

56-year-old man on high intensity statin.
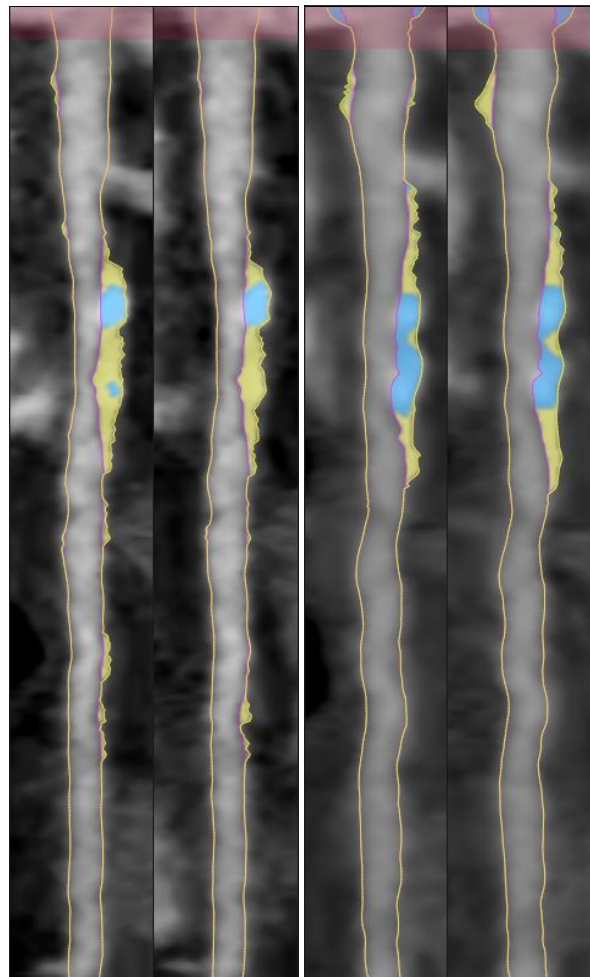
2018 **2021**

ALL	mm³ PAV	Current Cleerly ID: 960D53B4 4/23/2018	# %	Compared Cleerly ID: E554BB57 8/3/2021
Total Plaque Volume (mm³)		313	▲ +1.2%	316.7
▶ Total Non-Calcified Plaque Volume (mm³)		289.8	▼ -17.1%	240.2
Low-Density - Non-Calcified Plaque Volume (mm³)		0	▲ N/A	0.2
Total Calcified Plaque Volume (mm³)		23.2	▲ +229.7%	76.5
# of Severe Stenosis		1	=	1
# of Moderate Stenosis		1	▼ -100%	0
Highest Remodeling Index		1.3	▲ +7.7%	1.4
Greatest Diameter Stenosis (%)		71	▲ +2.8%	73
Greatest Area Stenosis (%)		91	▲ +2.2%	93
Length (mm)		645.5	▲ +6.2%	685.8

Per-Patient analysis:
- 1% TPV change/3.4 years
- 17% decrease in non-calcified plaque
- 230% increase in CP

| Current Cleerly ID: 960D53B4 4/23/2018	Compared Cleerly ID: E554BB57 8/3/2021
Lesion 1	Lesion 1
148 mm³ Total Plaque Volume	132.2 mm³ Total Plaque Volume
Low-Density - Non-Calcified 0.8 Non-Calcified 135.6 Calcified 11.6	Low-Density - Non-Calcified 0 Non-Calcified 90.4 Calcified 41.8

Per-Plaque (pLAD) analysis:
- 10% TPV reduction
- 100% Low Density NCP reduction
- 33% Non-calcified plaque reduction
- 260% increase in CP

Plaque Regression.

## 55-year-old man taking a PCSK9 inhibitor.
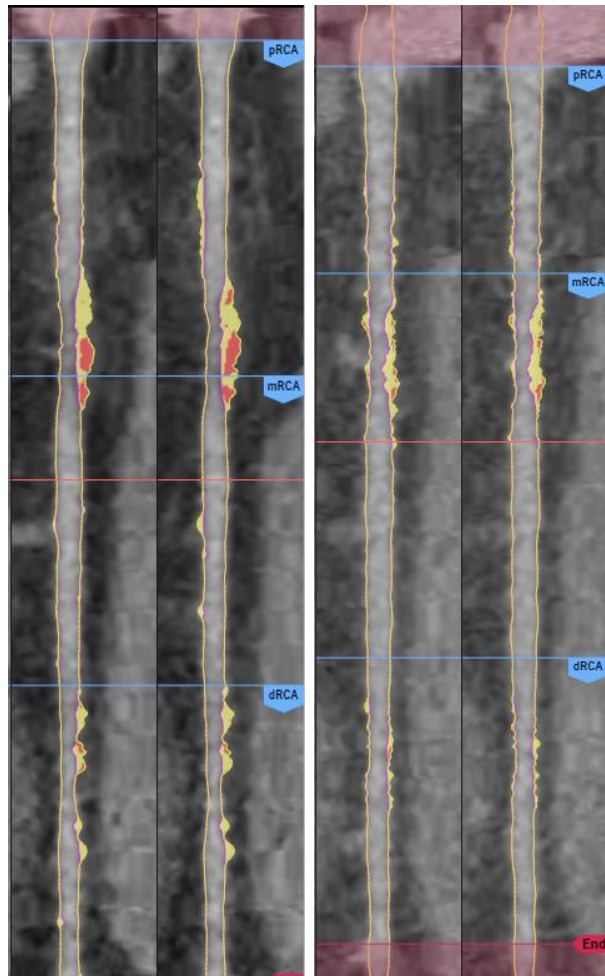
2017 **2018**

ALL	mm² PAV	Current	# %	Compared
		Cleerly ID: F9F050BC 3/1/2017		Cleerly ID: 5D3467A0 10/31/2018
Total Plaque Volume (mm³)		444.5	▼ -133	311.5
▶ Total Non-Calcified Plaque Volume (mm³)		442.3	▼ -144	298.3
Low-Density - Non-Calcified Plaque Volume (mm³)		67.8	▼ -35.3	32.5
Total Calcified Plaque Volume (mm³)		2.2	▲ +11	13.2
# of Severe Stenosis		0	=	0
# of Moderate Stenosis		1	▼ -1	0
Highest Remodeling Index		1.7	▼ -0.4	1.3
Greatest Diameter Stenosis (%)		53	▼ -5	48
Greatest Area Stenosis (%)		78	▼ -5	73
Length (mm)		634.3	▲ +94.7	729

Per-Patient analysis:
- 34% total regression
- 33% regression of NCP
- 52% regression of Low density NCP
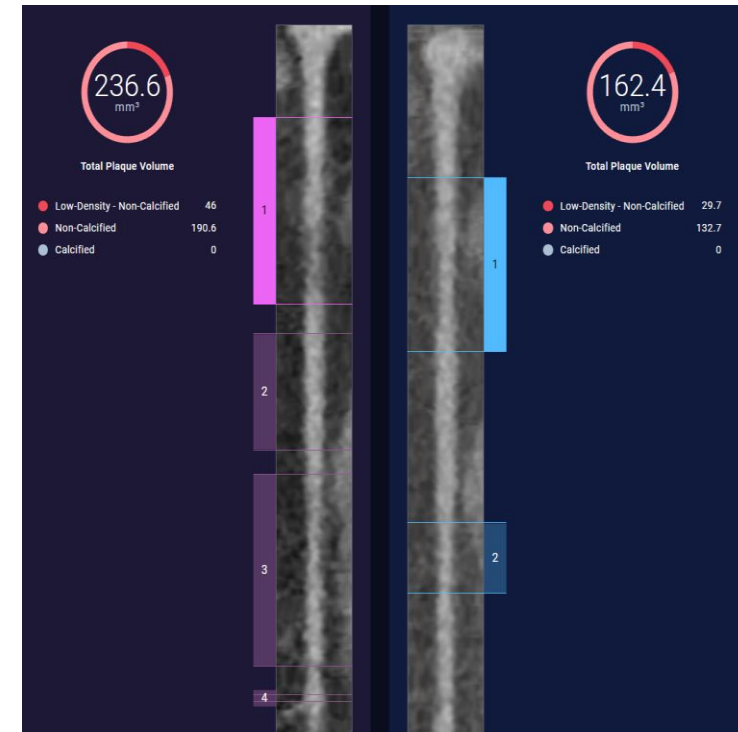
Per-Plaque analysis:
- 31% regression of pRCA plaque
- 39% regression of LD-NCP content

What I'm seeing - CCTA Testing with AI Read - Reveals (n=3,256)

Patients classified with stage 2 or 3 CAD
14.6%

Patients classified with stage 1 CAD
76.3%

Stage 2 or 3 CAD (2424)

Stage 1 CAD (477)

Healthy (295)
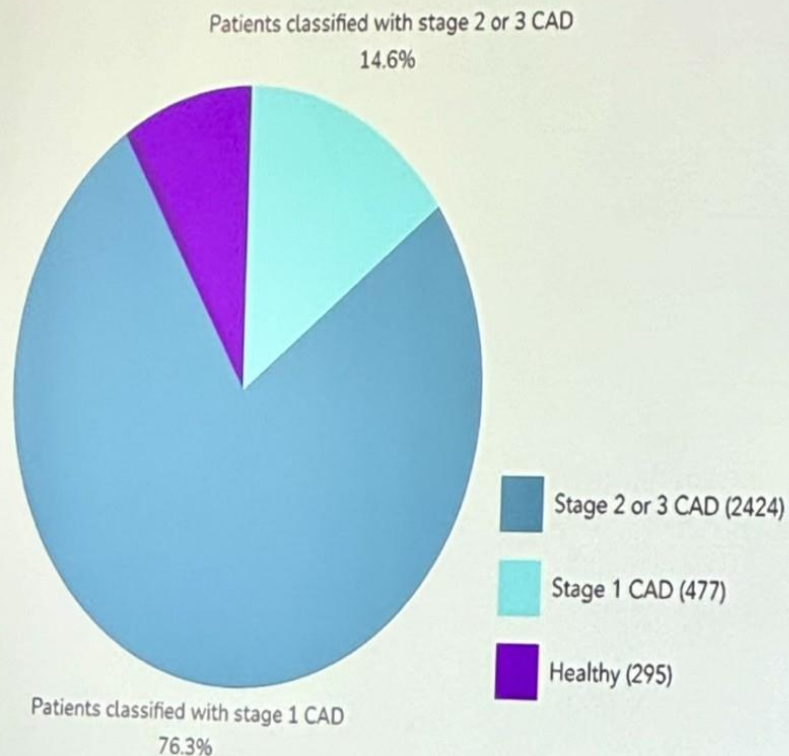
- Asymptomatic "healthy" population

- 15% (477) of people classified with stage 2 or 3 CAD

- 76% (2484) of patients classified with stage 1 CAD

  - 36% (889/2484) of stage 1 disease patients had **no calcified plaque** and **would be missed** by conventional methods

    - These are high risk for CAD event

  - 9% (295/3256) of patients had moderate and/or severe stenoses detected at their first study

Conclusions

- CCTA-AI can be used as a non-invasive imaging modality with low cost and low risk

- CCTA-AI may allow more wide use to assess drug efficacy on atherosclerosis progression in primary and secondary prevention populations

- Precision tracking with CCTA-AI will allow individual assessment of efficacy of treatments

Widespread Uses of AI

May 2024

The Future is AI

Conclusions

"All truth passes through three stages.
First, it is ridiculed.
Second, it is violently opposed.
Third, it is accepted as
being self-evident."
-Arthur Schopenhauer