Cardiovascular Risk Assessment and Treatment Options

July 30, 2026

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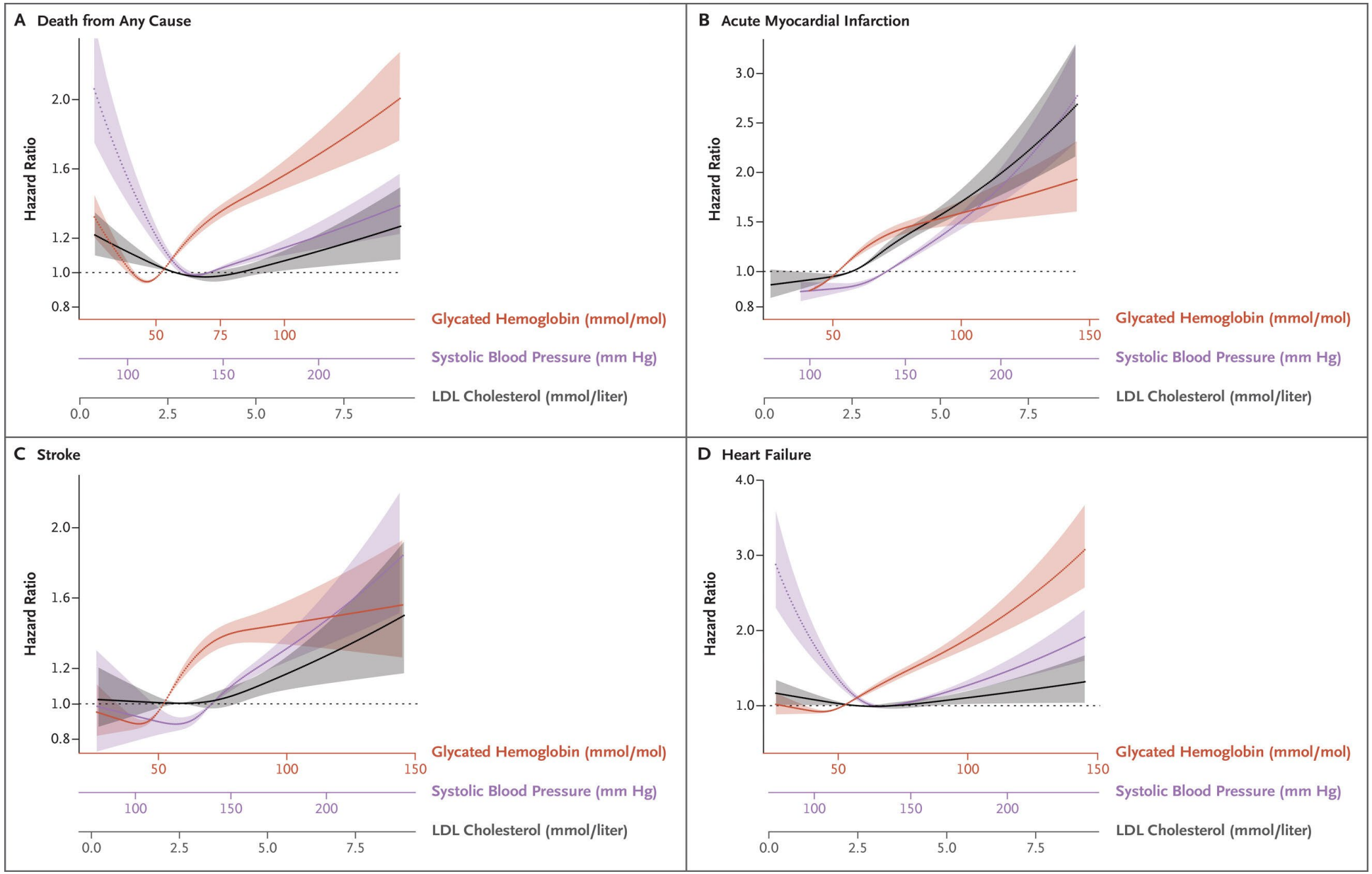
LOUISIANA DEPARTMENT OF HEALTH

Disclosures

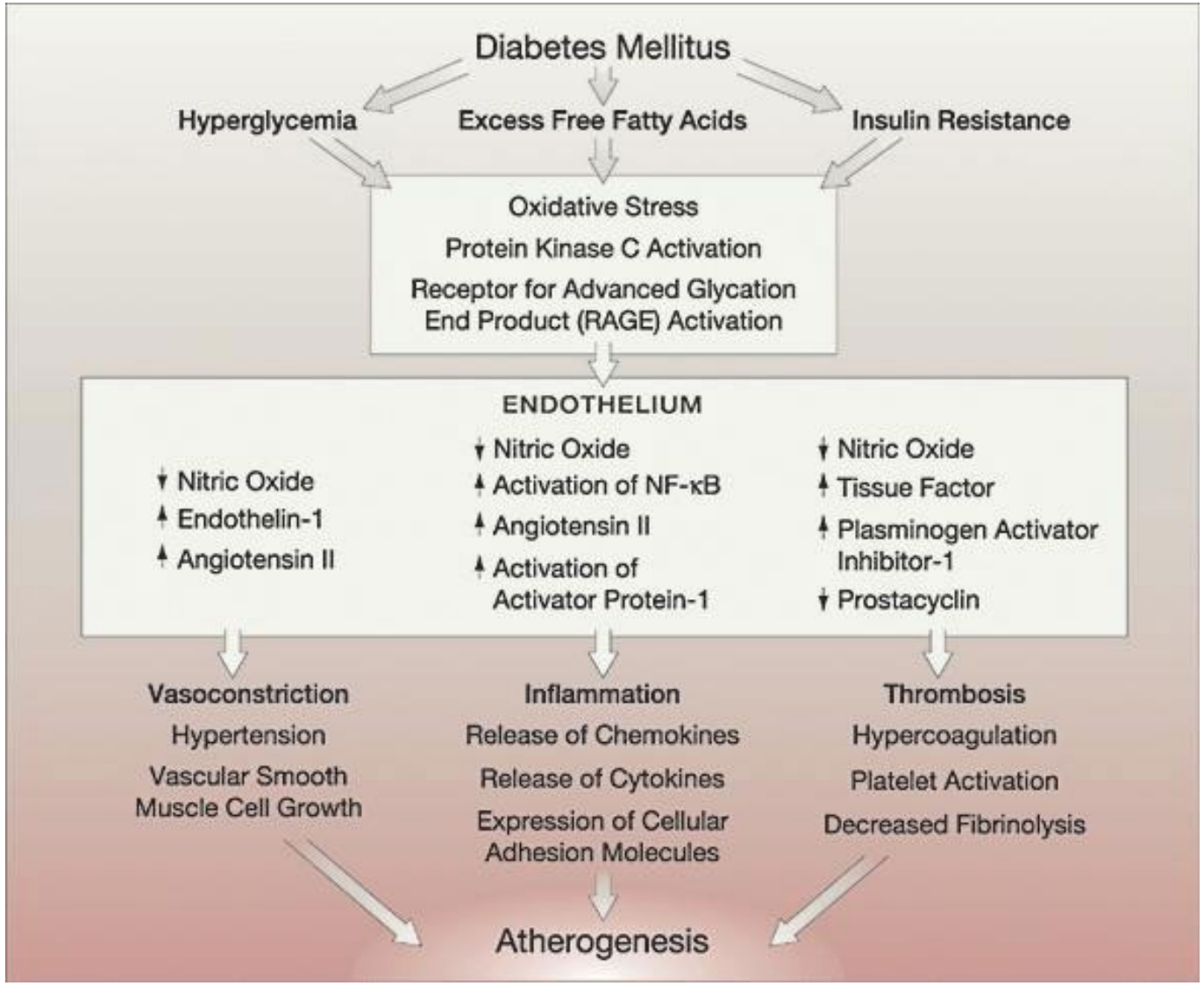
Speaker – Astrazeneca, Amgen
Faculty – Angiodynamics Inc.
Consultant – Ironrod Health

Objectives

- Understand Cardiovascular Risk in Diabetes
- Estimating Cardiovascular Risk in Diabetes
- Leveraging AI in Risk Estimation
- Risk Reduction Strategies – BP targets, Lipid targets



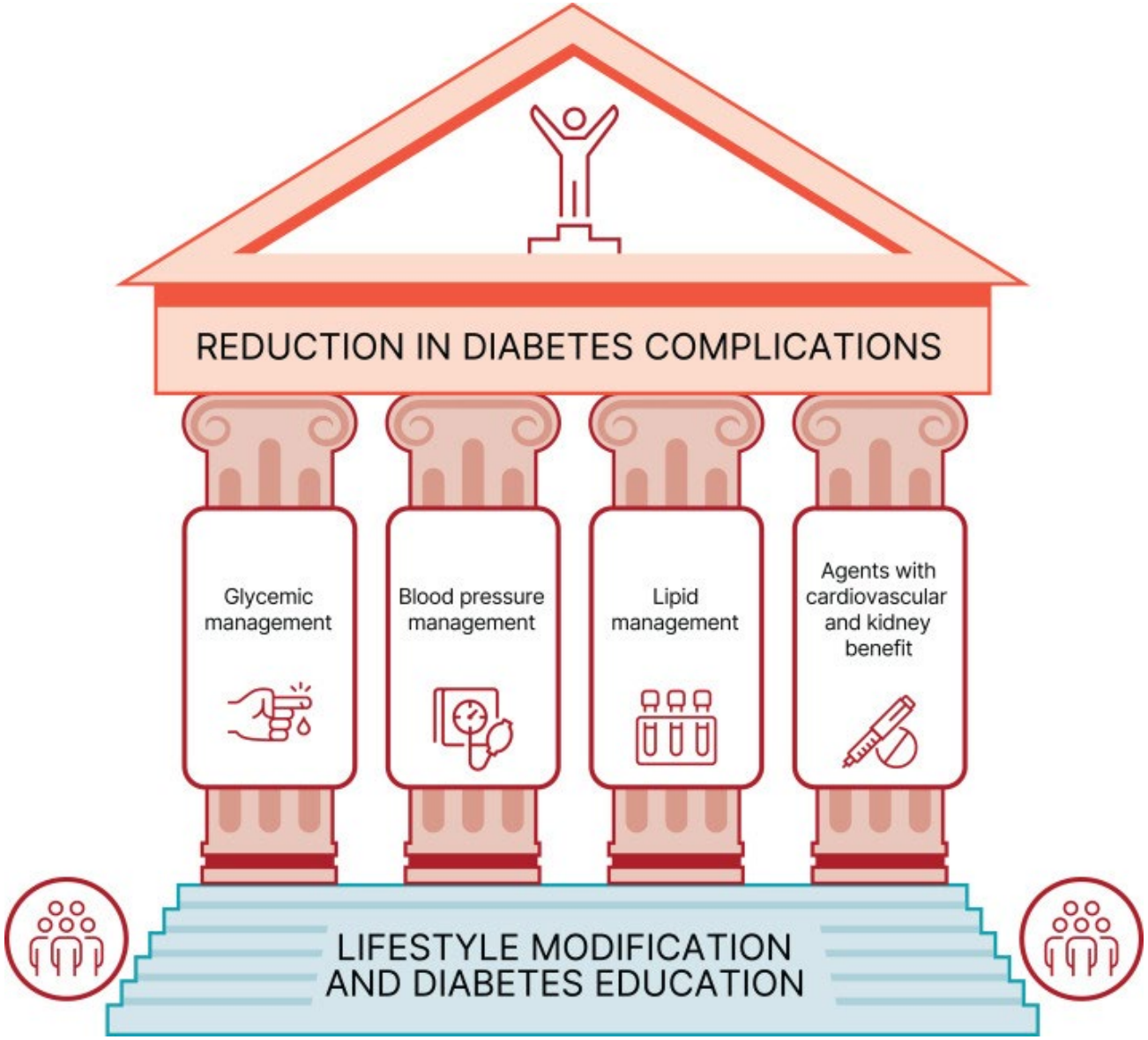
N Engl J Med. August 15, 2018



Diabetes and Atherosclerosis: Epidemiology, Pathophysiology, and Management. JAMA. May 14, 2002

	All Participants		Participants with diabetes		
	Glycaemic control (HbA1c <8%)	Glycaemic control (HbA1c ≥8%)	Glycaemic control (HbA1c <8%)	Glycaemic control (HbA1c ≥8%)	
Without diabetes	Ref.	NA			Fatal/nonfatal CVD
Diabetes duration <5 y	1.31 (1.19, 1.44)	1.53 (1.22, 1.91)	Ref.	1.11 (0.87, 1.42)	
Diabetes duration ≥5 to <10 y	1.29 (1.12, 1.48)	2.31 (1.82, 2.95)	1.03 (0.87, 1.22)	1.80 (1.39, 2.33)	
Diabetes duration ≥10 to <15 y	1.61 (1.34, 1.94)	2.82 (2.15, 3.69)	1.31 (1.06, 1.61)	2.22 (1.67, 2.95)	
Diabetes duration ≥15 y	2.32 (1.98, 2.73)	3.94 (3.25, 4.77)	1.86 (1.54, 2.24)	3.12 (2.52, 3.86)	
Without diabetes	Ref.	NA			Fatal CVD
Diabetes duration <5 y	1.65 (1.39, 1.95)	1.97 (1.32, 2.93)	Ref.	1.04 (0.68, 1.60)	
Diabetes duration ≥5 to <10 y	1.09 (0.83, 1.44)	2.48 (1.62, 3.79)	0.73 (0.53, 1.00)	1.50 (0.95, 2.34)	
Diabetes duration ≥10 to <15 y	2.06 (1.54, 2.76)	3.33 (2.11, 5.26)	1.42 (1.02, 1.97)	2.07 (1.28, 3.34)	
Diabetes duration ≥15 y	2.33 (1.75, 3.10)	5.15 (3.77, 7.04)	1.56 (1.13, 2.16)	3.24 (2.29, 4.57)	
Without diabetes	Ref.	NA			All-cause Mortality
Diabetes duration <5 y	1.36 (1.27, 1.46)	1.59 (1.35, 1.88)	Ref.	1.08 (0.91, 1.29)	
Diabetes duration ≥5 to <10 y	1.43 (1.30, 1.57)	2.03 (1.69, 2.44)	1.10 (0.99, 1.23)	1.45 (1.20, 1.76)	
Diabetes duration ≥10 to <15 y	1.59 (1.40, 1.80)	2.49 (2.03, 3.05)	1.24 (1.07, 1.42)	1.82 (1.47, 2.25)	
Diabetes duration ≥15 y	1.82 (1.62, 2.06)	3.30 (2.86, 3.82)	1.42 (1.24, 1.63)	2.48 (2.12, 2.90)	

Cardiovascular disease (CVD) and all-cause mortality risk matrix for the combined effect of diabetes duration and glycaemic control. Diabetes Obes Metab. May 31, 2021.



Multifactorial approach to reduction in risk of diabetes complications. Diabetes Care. 2025 Dec

Traditional Risk Factors

- Age > 65 years
- Male sex
- Family history
- Others

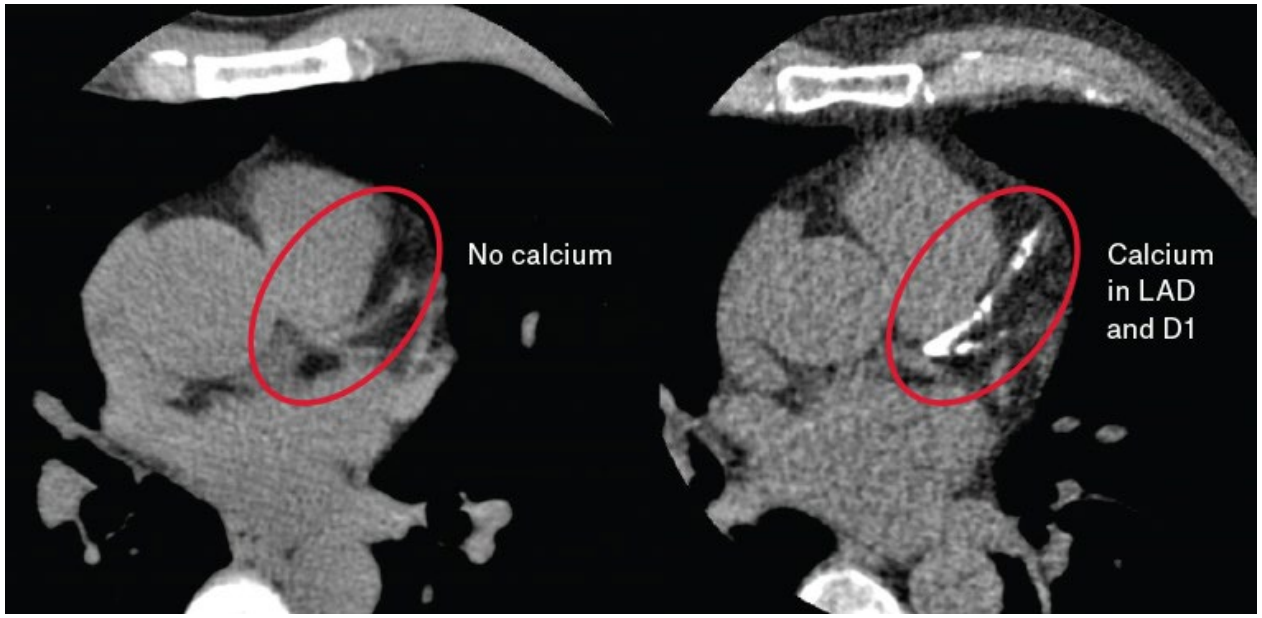
IRREVERSIBLE

- High Blood Pressure
- High Cholesterol
- Smoking
- Physical inactivity
- Diabetes

REVERSIBLE

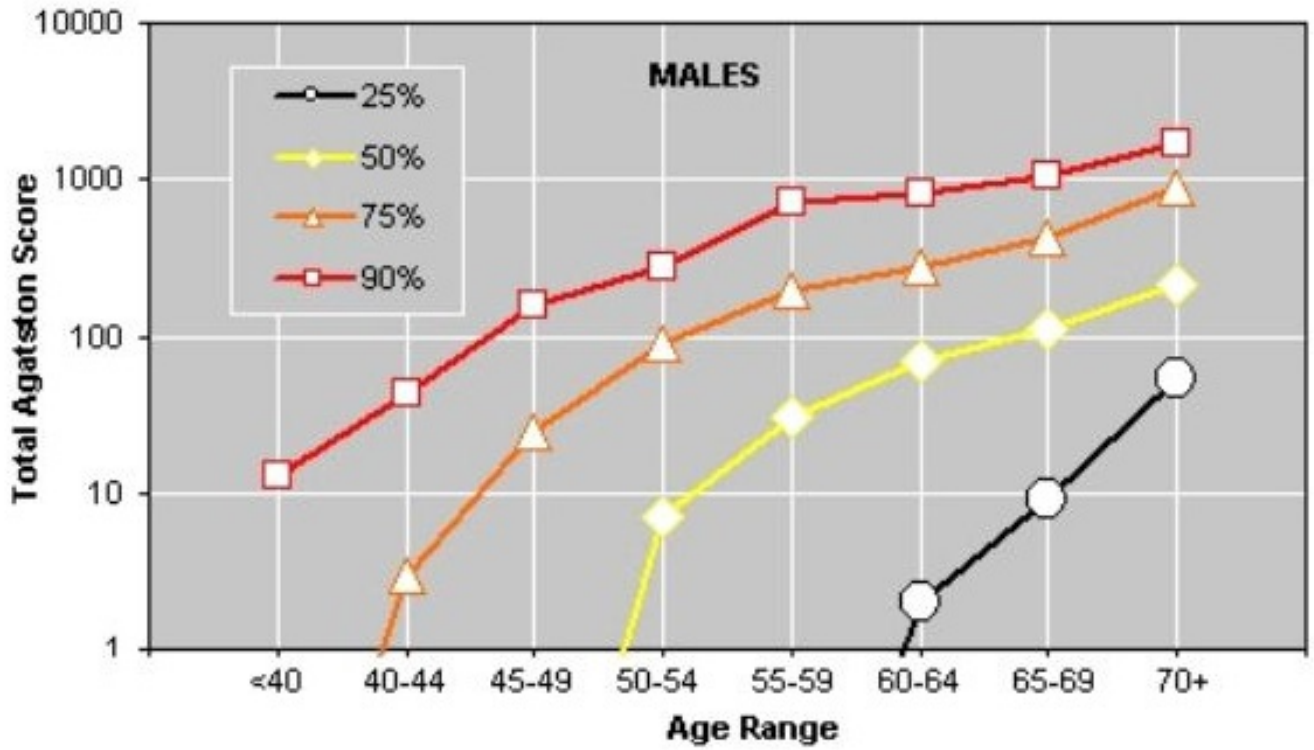
Estimating Individual risk

- ASCVD Risk Estimator (pooled cohort risk estimates)
- Non-traditional risk factors: Ankle-Brachial Index (ABI), Coronary Calcium score, Lp(a), etc.
- AI-based Risk Assessment



Calcium score	Interpretation	Risk of myocardial infarction/stroke at 10 years
0	Very low risk	<1%
1–100	Low risk	<10%
101–400	Moderate risk	10–20%
101–400 and >75th percentile	Moderately high risk	15–20%
>400	High risk	>20%

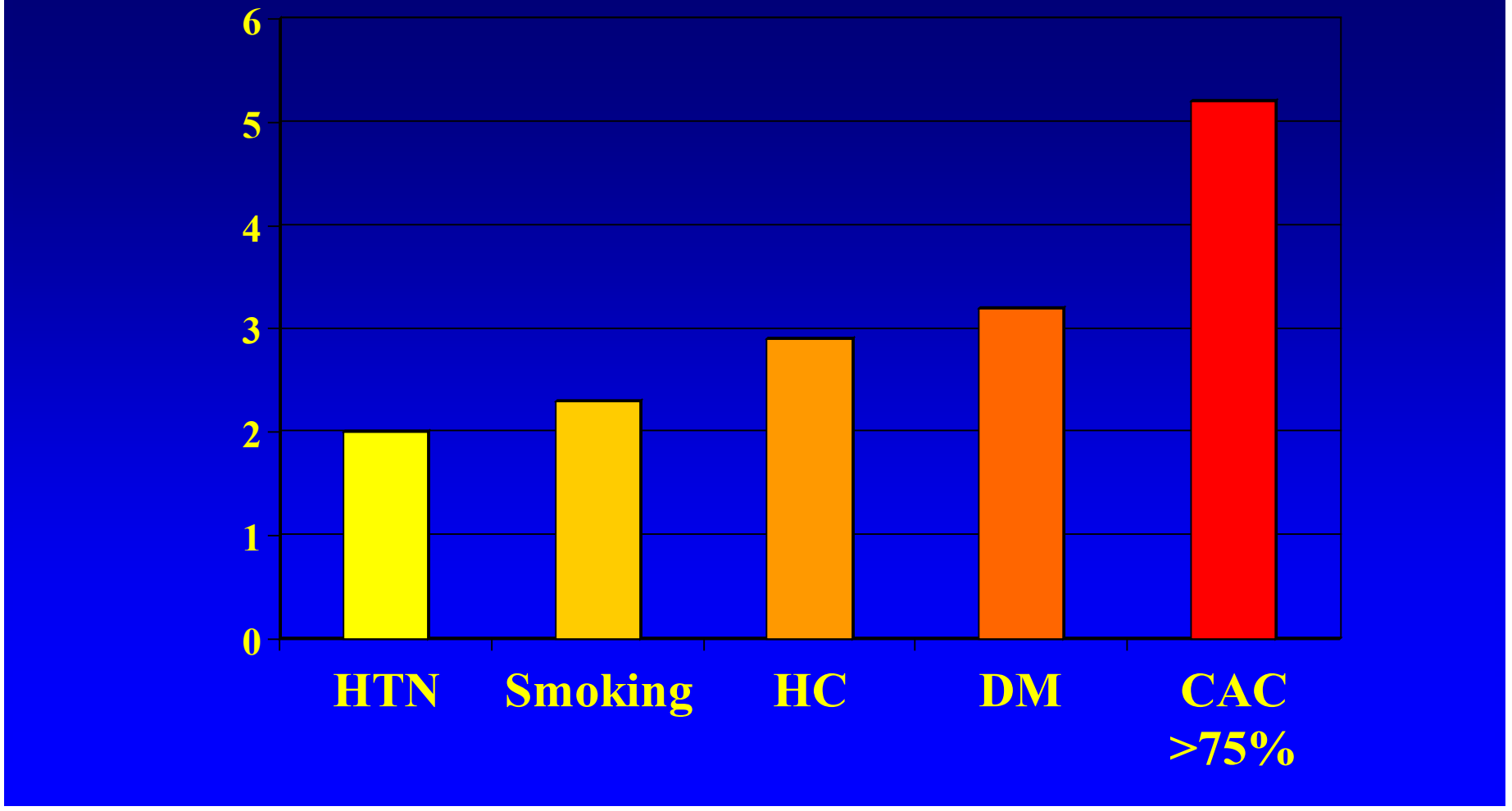
Agatston Calcium Scores in Asymptomatic Males



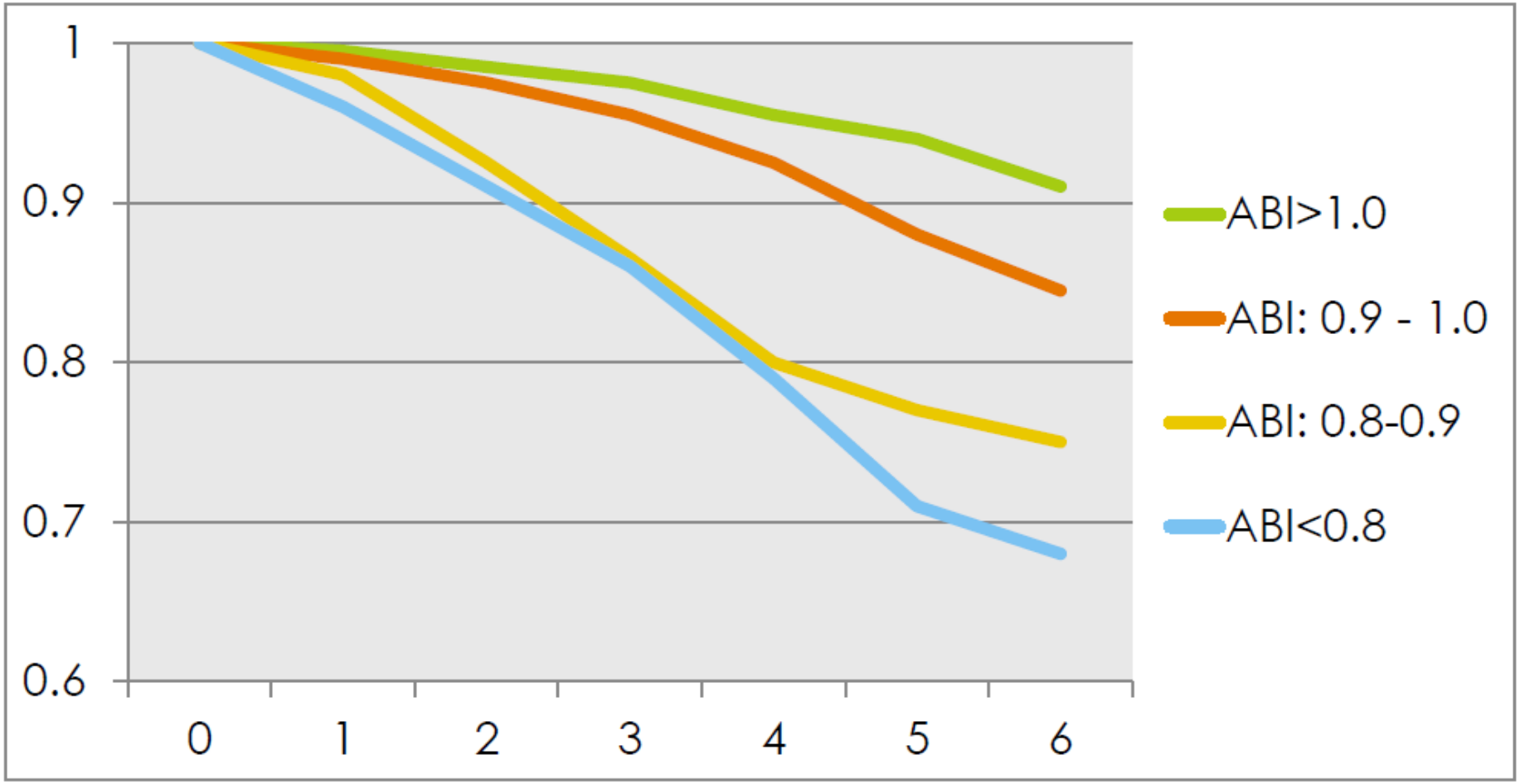
* The graph and percentile ranking used in this report are based on data analysis from 3911 male patients asymptomatic for coronary artery disease. Data was acquired using a Philips Medical Systems 4-slice Computed Tomography (CT) scanner with prospective ECG gating. Additional reference literature regarding risk stratification can be found in: Schmermund A, Silber S, et al, AJC 2002; 90:168-173.

Leber A et al, Am Heart J 2007 (in press)

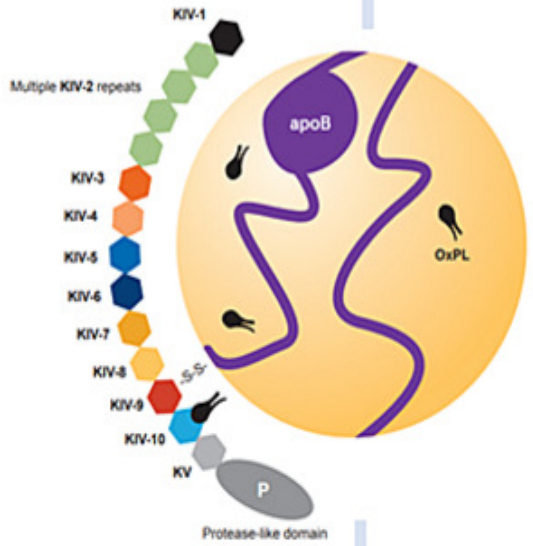
Relative Predictive Value of CAC and Traditional Risk Factors for CHD in 1726 Asymptomatic Subjects over 40 Months: Dichotomous Analysis



Patient survival by ABI in Cardiovascular Health Study…



Newman et al ATVB 1999;19; 538-545



Elevated Lp(a) is an **independent causal risk factor for ASCVD**

Patients with elevated Lp(a) may have **residual ASCVD risk while on statins**

Practical points for Lp(a) testing

Lp(a) testing requires a standard, **non-fasting blood draw**

Lp(a) concentration may be reported as **nmol/L or mg/dL***

Lp(a) testing may only be required **once in an individual's lifetime†**

Plasma Lp(a) concentration is **predominantly genetically determined**

Elevated Lp(a) affects approximately **1.4 billion people globally**

Elevated Lp(a) is associated with **atherogenesis, inflammation,** and **anti-fibrinolytic activity**

Key benefits of Lp(a) testing

Lp(a) testing can help to **predict** and/or **reclassify** patients' **risk of CVD**

Lp(a) testing can identify patients **potentially less likely to respond to statins**

Lp(a) testing may lead to healthcare system **savings**

Timely identification of elevated Lp(a) allows **intensive management of CVD risk factors**

Lp(a) testing may identify potential candidates for **Lp(a)-lowering therapy** in the future

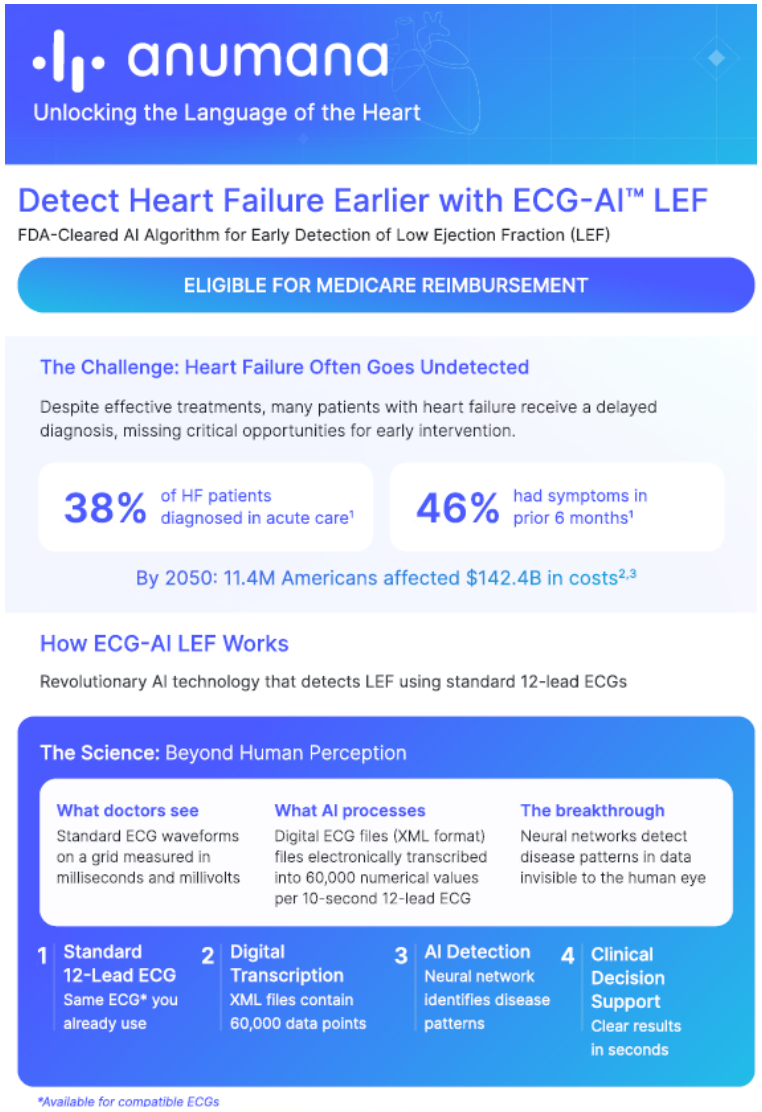
Lp(a) testing may help patients and physicians to understand the basis of **familial risk**

Lp(a) testing may influence an individual's decision to **adhere to risk mitigation strategies**

*Clinical assays that report Lp(a) concentrations in nmol/L are preferred over those that report in mg/dL. Due to substantial variation in assays, it is not recommended to directly convert between nmol/L and mg/dL; a conversion factor of 2.5 from mg/dL to nmol/L provides an approximation only (2); †Non-genetic factors such as kidney disease may affect Lp(a) measurement and may necessitate repeat testing in select patients. Repeat testing may also be beneficial in post-menopausal women. In addition, repeat testing may be required if/when Lp(a)-lowering therapies become available in order to assess treatment response.

AI vs Traditional Risk Models: Current Performance

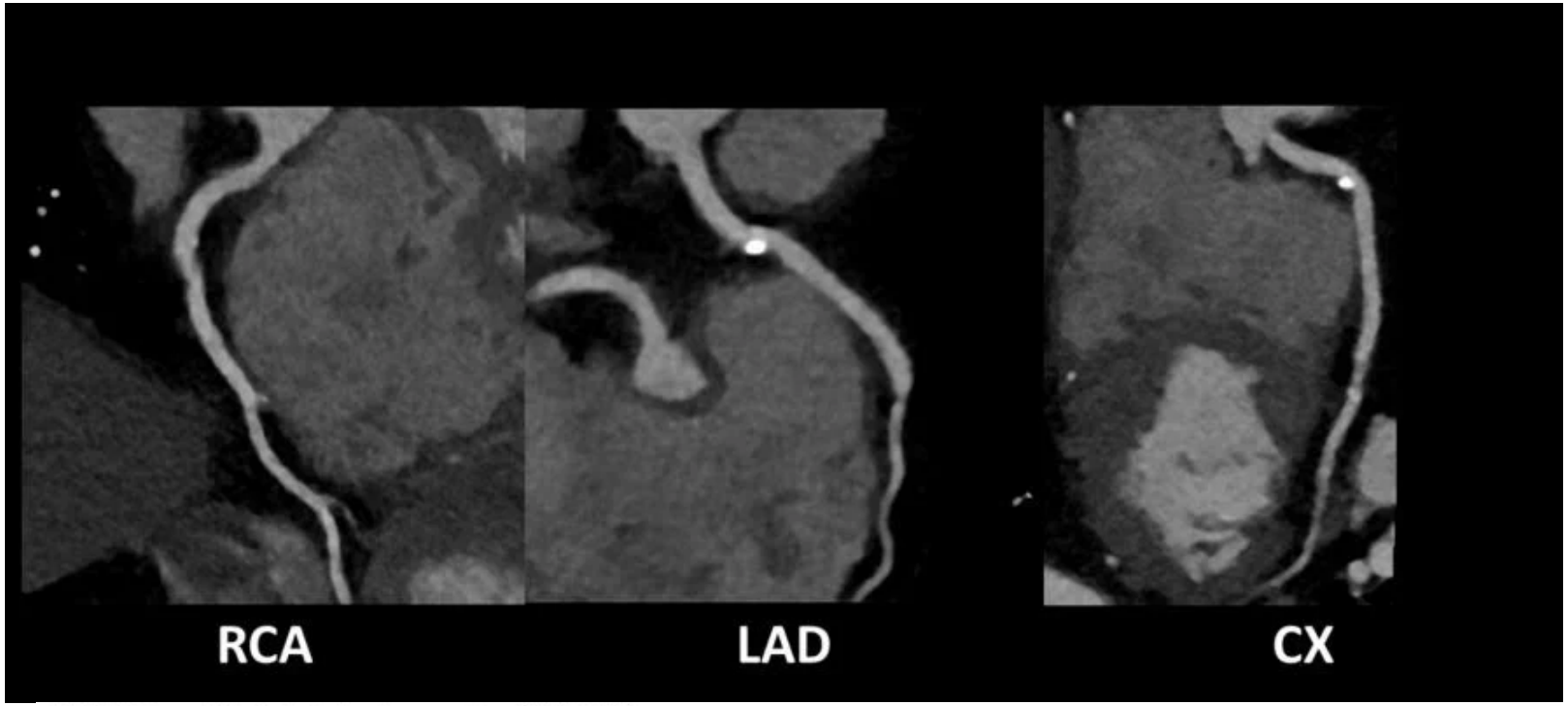
- When ML models use the same established risk factors as traditional tools (age, sex, blood pressure, cholesterol, diabetes, smoking), head-to-head comparisons generally show similar or only modestly superior discrimination compared to the Pooled Cohort Equations (PCE) or SCORE2 [Comparison of State-of-the-Art Neural Network Survival Models With the Pooled Cohort Equations for Cardiovascular Disease Risk Prediction. BMC Medical Research Methodology. 2023.]
- However, when ML models incorporate high-dimensional or longitudinal data, performance improves meaningfully. A deep learning model incorporating 8 years of longitudinal risk factor trajectories improved AUROC from 0.792 (PCE) to 0.815, with a net reclassification index of 0.385. [Incorporating Longitudinal History of Risk Factors Into Atherosclerotic Cardiovascular Disease Risk Prediction Using Deep Learning. Scientific Reports. 2024. Yu J, Yang X, Deng Y, et al.]



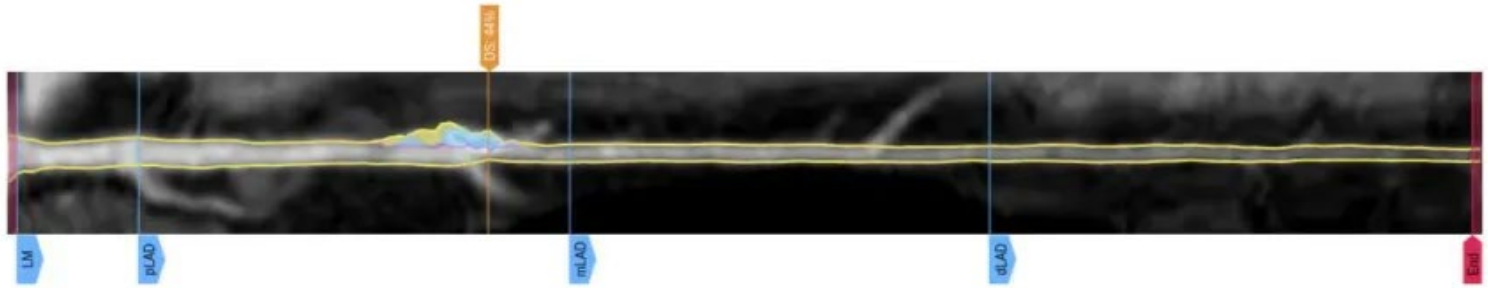
- Deep learning models applied to 12-lead ECGs can detect occult left ventricular dysfunction (AUC 0.92 in a prospective trial of >20,000 patients), screen for paroxysmal atrial fibrillation in sinus rhythm (AUC 0.87), and identify subclinical coronary artery disease. [Use of Artificial Intelligence in Improving Outcomes in Heart Disease: A Scientific Statement From the American Heart Association. Circulation. 2024. Armoundas AA, Narayan SM, Arnett DK, et al.]

AI-Retinal Imaging

- In patients with T2DM, a deep learning model using routine retinal screening photographs predicted 10-year MACE with performance comparable to the PCE (both AUC 0.697). When combined with clinical and polygenic risk scores, AUC improved to 0.728. This raises the possibility of a one-stop CVD risk assessment at routine diabetic retinal screening. [Deep-Learning Prediction of Cardiovascular Outcomes From Routine Retinal Images in Individuals With Type 2 Diabetes. Cardiovascular Diabetology. 2025. Syed MG, Trucco E, Mookiah MRK, et al.]



Left Main and Left Anterior Descending (LM+LAD)



47.9 mm^3 12% PAV
Total Plaque Volume

0 mm^3 0% PAV
Low-Density - Non-Calcified Plaque Volume

24.2 mm^3 6% PAV
Total Non-Calcified Plaque Volume

23.7 mm^3 5.9% PAV
Total Calcified Plaque Volume

44% Greatest Diameter Stenosis

1.8 Highest Remodeling Index

CLEERLY (Cleerly Labs, Cleerly Inc.)

- **CLEERLY is an FDA-cleared, AI-enabled software platform** that performs automated quantitative coronary plaque analysis (QCPA) from coronary CT angiography (CCTA)
- Volumetric assessment of plaque burden, plaque composition, etc.
- Plaque detection and characterization based on Hounsfield unit (HU) attenuation:
  - **Low-attenuation plaque (LAP)**: <30 HU — a marker of lipid-rich necrotic core
  - **Noncalcified plaque**: 30–350 HU
  - **Calcified plaque**: >350 HU

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2026 Diabetes ECHO

Summary

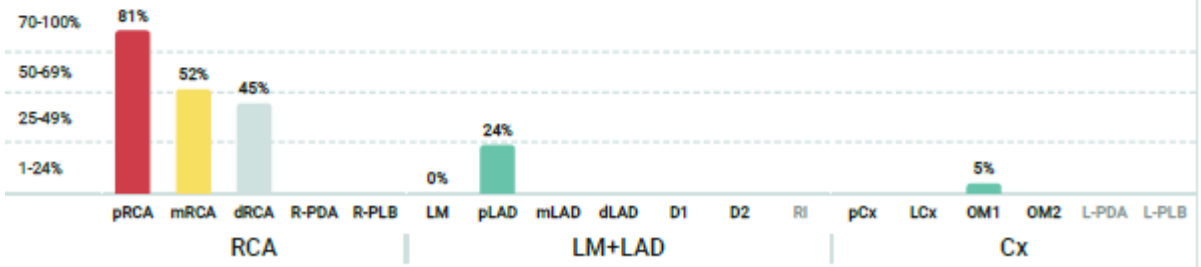
Atherosclerosis	**158 mm³ Total Plaque** (84 mm³ Low-Density - Non-Calcified, 21.9 mm³ Non-Calcified, 52.1 mm³ Calcified)
Stenosis	**1 Severe** (pRCA); **1 Moderate** (mRCA); **1 Mild** (dRCA); **4 Minimal** (pRCA, mRCA, pLAD, OM1)
Ischemia	**Likely Present** (RCA, R-PDA, R-PLB)
Dominance	**Right-Dominant**
CAD-RADS	**4A/P4/I+**
Exclusions*	**2% of coronary length was excluded. Non-Evaluable portion(s) in pCx, LCx, D1, D2.**

Atherosclerosis

Territory	Plaque Volume (mm³) TOTAL	Low-Density - Non-Calcified	Non-Calcified	Calcified	Percent Atheroma Volume
RCA	129.1	71	19.3	38.8	16.4%
LM+LAD	10.9	3.6	0.9	6.4	1%
Cx	18	9.4	1.7	6.9	3.6%
TOTAL	158	84	21.9	52.1	6.6%

Stenosis

Severe	Moderate	Mild	Minimal
≥70% or ≥50% LM only	50-69%	25-49%	1-24%
1	1	1	4



Ischemia

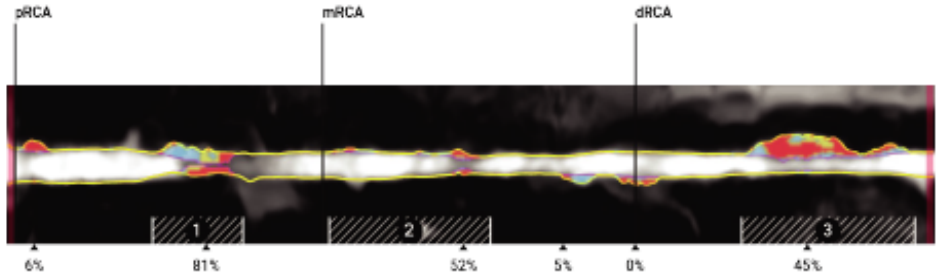
Likely present in: RCA R-PDA R-PLB

Right Coronary Artery (RCA) ISCHEMIA LIKELY

129.1 mm³ 24.1% PAV	71 mm³ 13.2% PAV	90.3 mm³ 16.8% PAV	38.8 mm³ 7.2% PAV
Total Plaque Volume	Low-Density - Non-Calcified Plaque Volume	Total Non-Calcified Plaque Volume	Total Calcified Plaque Volume

81% Greatest Diameter Stenosis

1.5 Highest Remodeling Index



❶ Lesion

81% pRCA
Greatest Diameter Stenosis

9.8 mm	0.5 mm	2.6 mm
Plaque Length	Minimum Luminal Diameter	Reference Diameter Before Stenosis

Plaque Volume 39.3 mm³ (0 / 100 / 200)

Low-Density - Non-Calcified (mm³)	20.2
Non-Calcified (mm³)	6.3
Calcified (mm³)	12.8

❷ Lesion

52% mRCA
Greatest Diameter Stenosis

17 mm	1 mm	2.7 mm
Plaque Length	Minimum Luminal Diameter	Reference Diameter Before Stenosis

Plaque Volume 27.2 mm³ (0 / 100 / 200)

Low-Density - Non-Calcified (mm³)	17.4
Non-Calcified (mm³)	2.2
Calcified (mm³)	7.6

❸ Lesion

45% dRCA
Greatest Diameter Stenosis

18.3 mm	1.2 mm	2.1 mm
Plaque Length	Minimum Luminal Diameter	Reference Diameter Before Stenosis

Plaque Volume 52.1 mm³ (0 / 100 / 200)

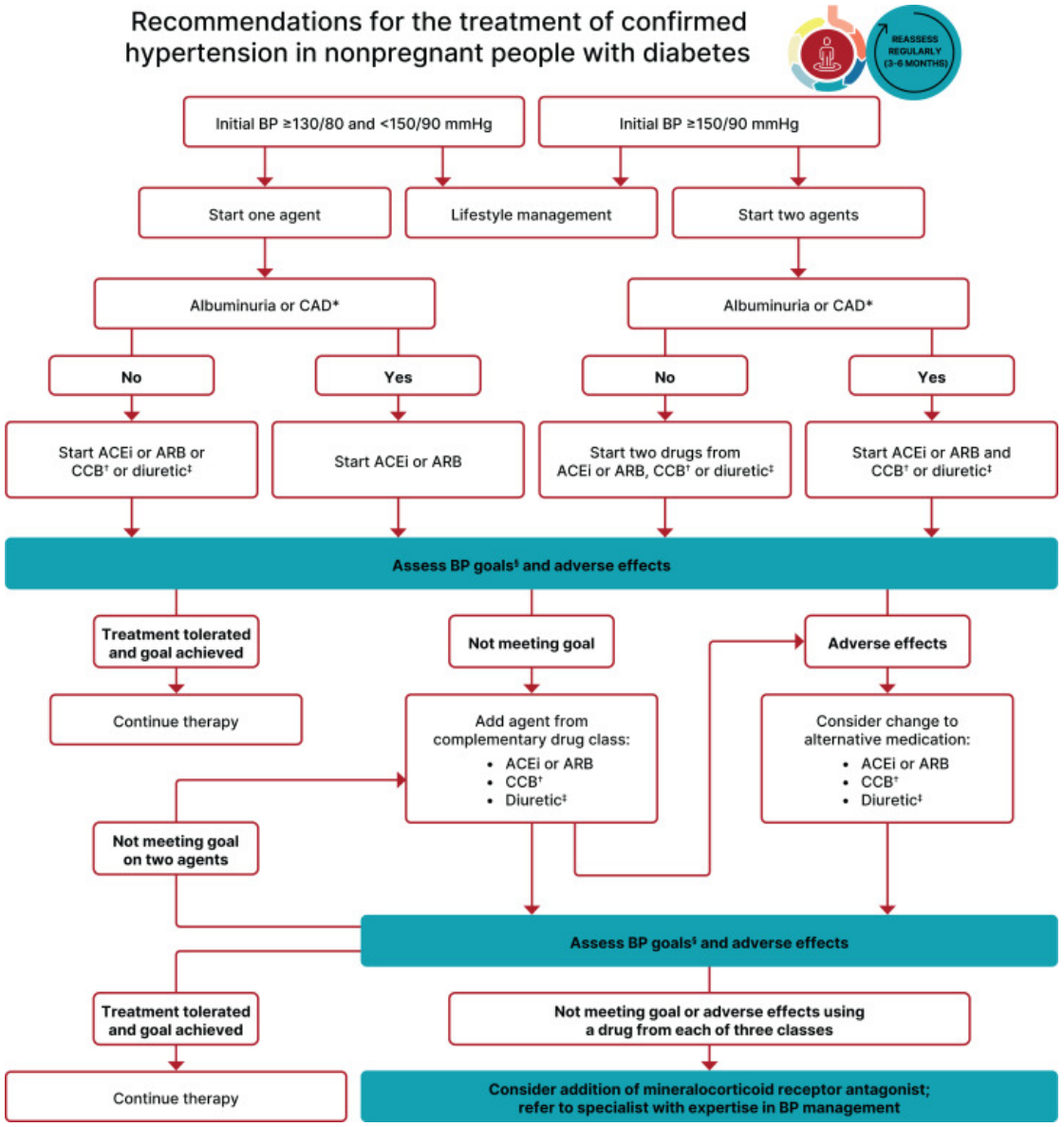
Low-Density - Non-Calcified (mm³)	27.6
Non-Calcified (mm³)	9.8
Calcified (mm³)	14.7

ⓘ A lesion spans the mRCA and dRCA with 5% in mRCA and 0% in dRCA.

Prognostic Evidence

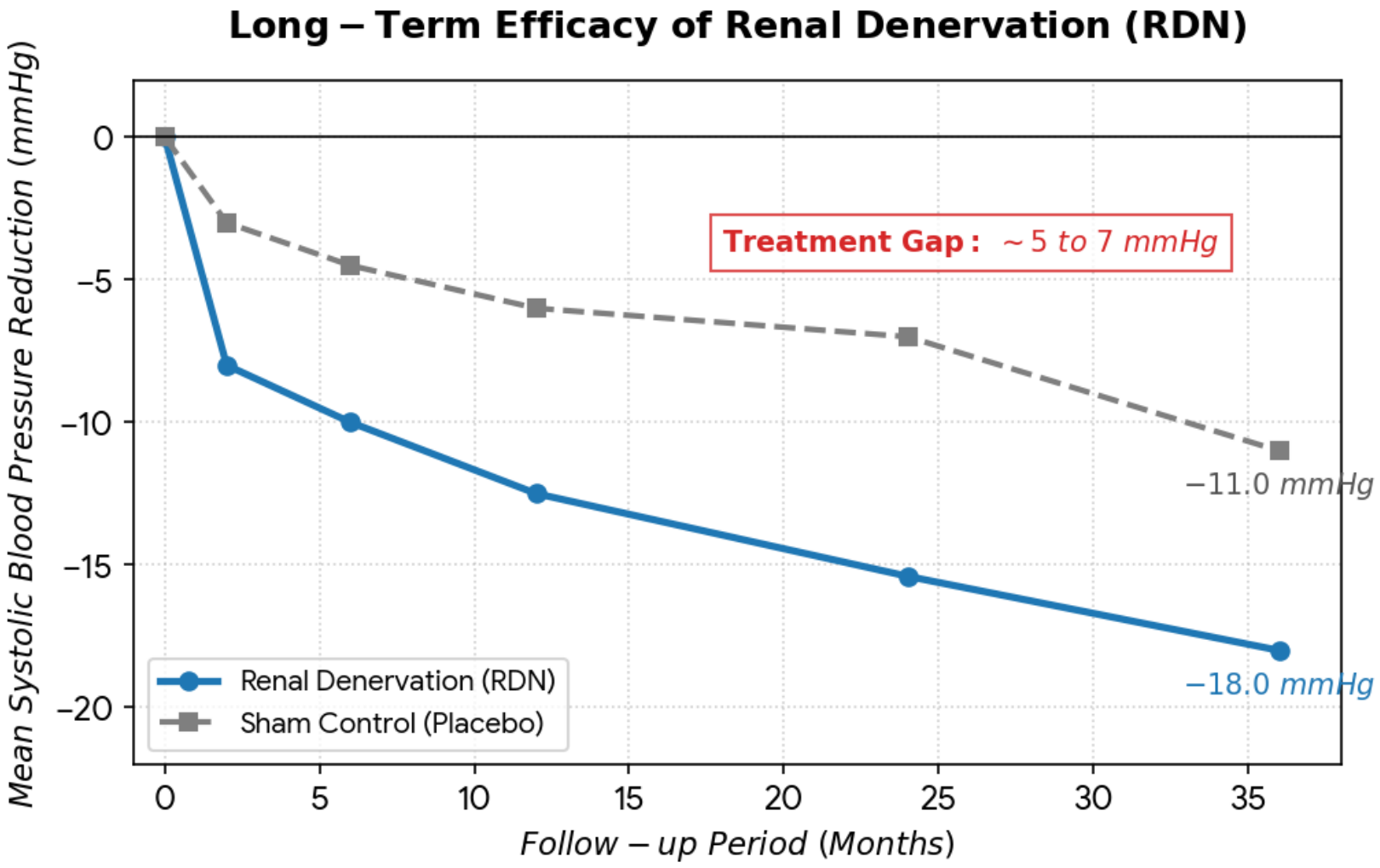
- In 536 patients, AI-QCT plaque staging based on PAV predicted MACE over 10.3 years of follow-up. Stage 3 (PAV >15%) carried a 3.6-fold increased risk of MACE compared to stages 0–1. **Adding AI-QCT to clinical risk factors + CAC improved the AUC from 0.73 to 0.82** ($P < 0.001$) [JACC. Cardiovascular Imaging. 2024. Nurmohamed NS, Bom MJ, Jukema RA, et al.]
- **CONFIRM2 Registry** (2026): In 1,916 symptomatic patients, AI-QCT significantly improved risk stratification for MACE compared with CAD-RADS alone. **Among patients without severe stenosis (<70%), only AI-QCT — not CAD-RADS — was independently associated with MACE**. [JACC. Cardiovascular Imaging. 2026. van Rosendael A, Nakanishi R, Bax JJ, et al.]
- **Plaque burden vs. CAC:** In 2,404 patients followed for a median of 7 years, AI-derived PAV demonstrated superior discriminatory power for MI prediction (AUC 0.791) compared with CAC scoring (AUC 0.699; $P < 0.001$), with noncalcified plaque volume percentage showing the highest accuracy (AUC 0.814). [European Heart Journal. Cardiovascular Imaging. 2025. Dahdal J, Jukema RA, Maaniitty T, et al.]

Blood pressure management in diabetes



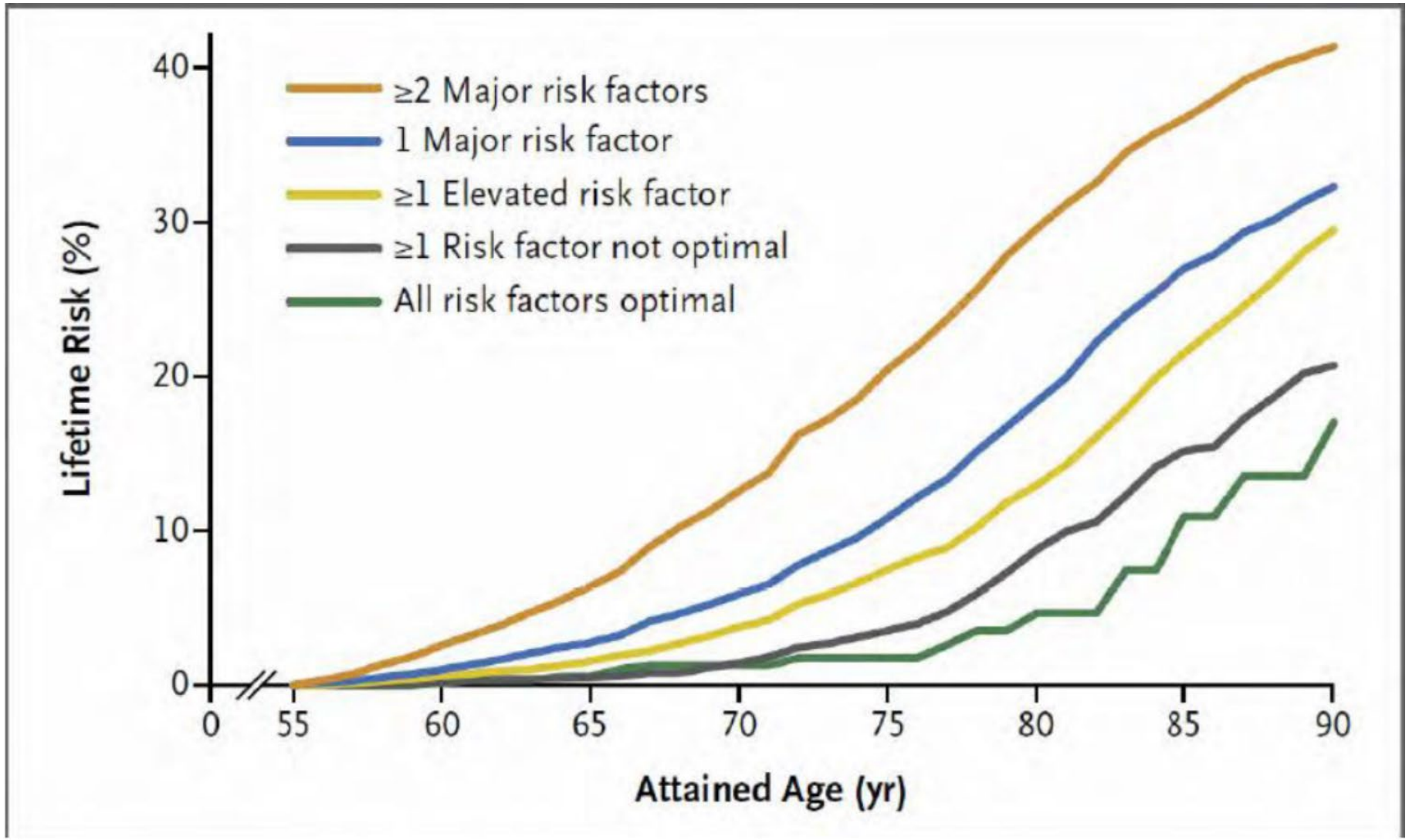
Recommendations for the treatment of confirmed hypertension in nonpregnant people with diabetes

de Boer et al. American Diabetes Association. Diabetes Care 2017;40:1273–1284



Google AI-generated graphical summary of the typical long-term efficacy of Renal Denervation (RDN) compared to a placebo (Sham control) group, based on pooled data from modern randomized trials (such as the SPYRAL HTN and RADIANCE programs).

Lipid Management in Diabetes



Berry, J.D., et al. N Engl J Med, 2012. **366**(4): p. 321-329.

TABLE 1 Criteria for Defining Patients at Very High Risk* of Future ASCVD Events

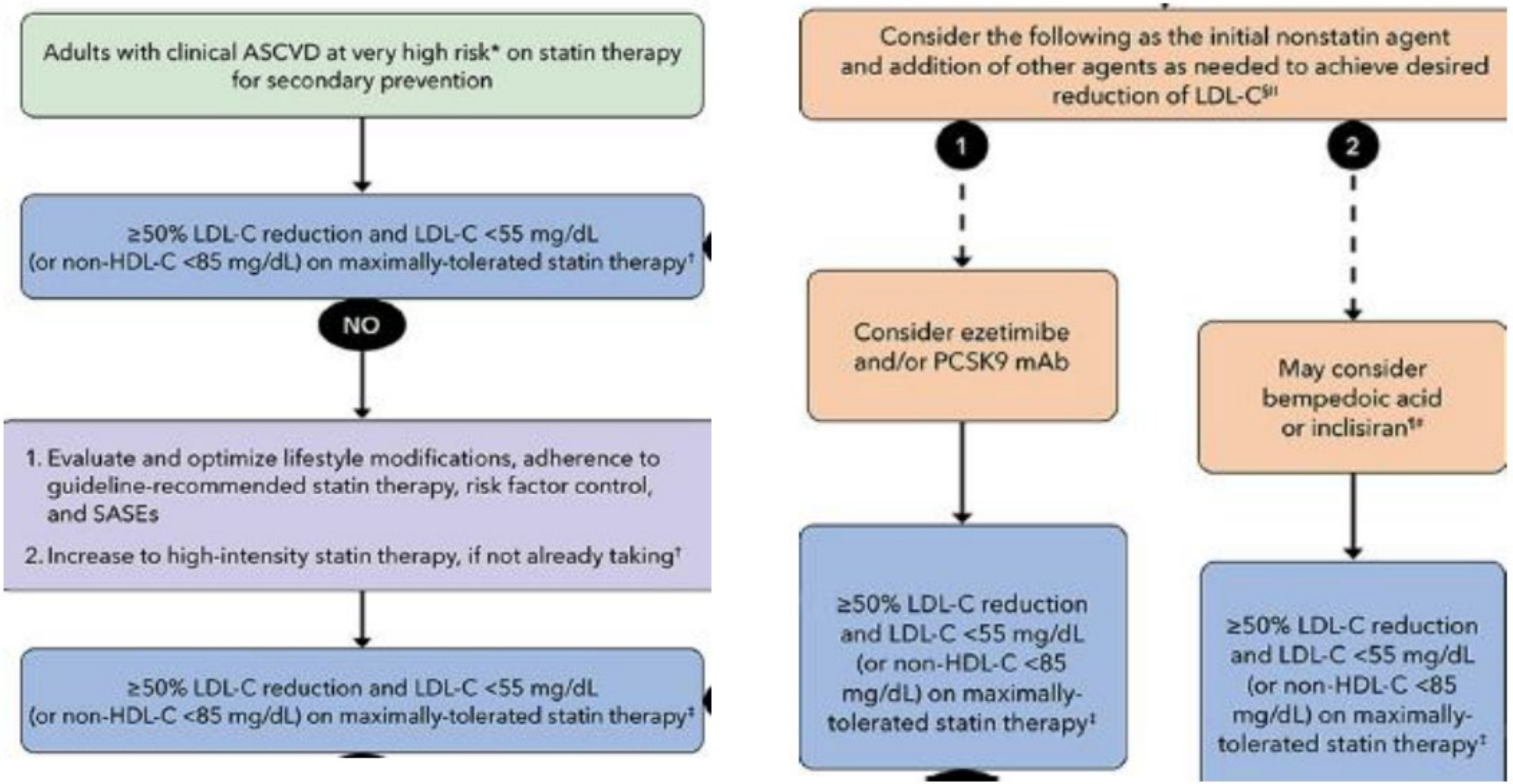
Major ASCVD Events
Recent ACS (within the past 12 months)
History of MI (other than recent ACS event listed above)
History of ischemic stroke
Symptomatic PAD (history of claudication with ABI <0.85 or previous revascularization or amputation)
High-Risk Conditions
Age ≥65 years
Heterozygous familial hypercholesterolemia
History of prior coronary artery bypass surgery or percutaneous coronary intervention outside of the major ASCVD event(s)
Diabetes
Hypertension
CKD (eGFR 15-59 mL/min/1.73 m^2)
Current smoking
Persistently elevated LDL-C (LDL-C ≥100 mg/dL [≥2.6 mmol/L]) despite maximally tolerated statin therapy and ezetimibe
History of congestive HF

*Very high risk includes a history of multiple major ASCVD events or 1 major ASCVD event and multiple high-risk conditions. Reprinted with permission from Grundy et al.[7]

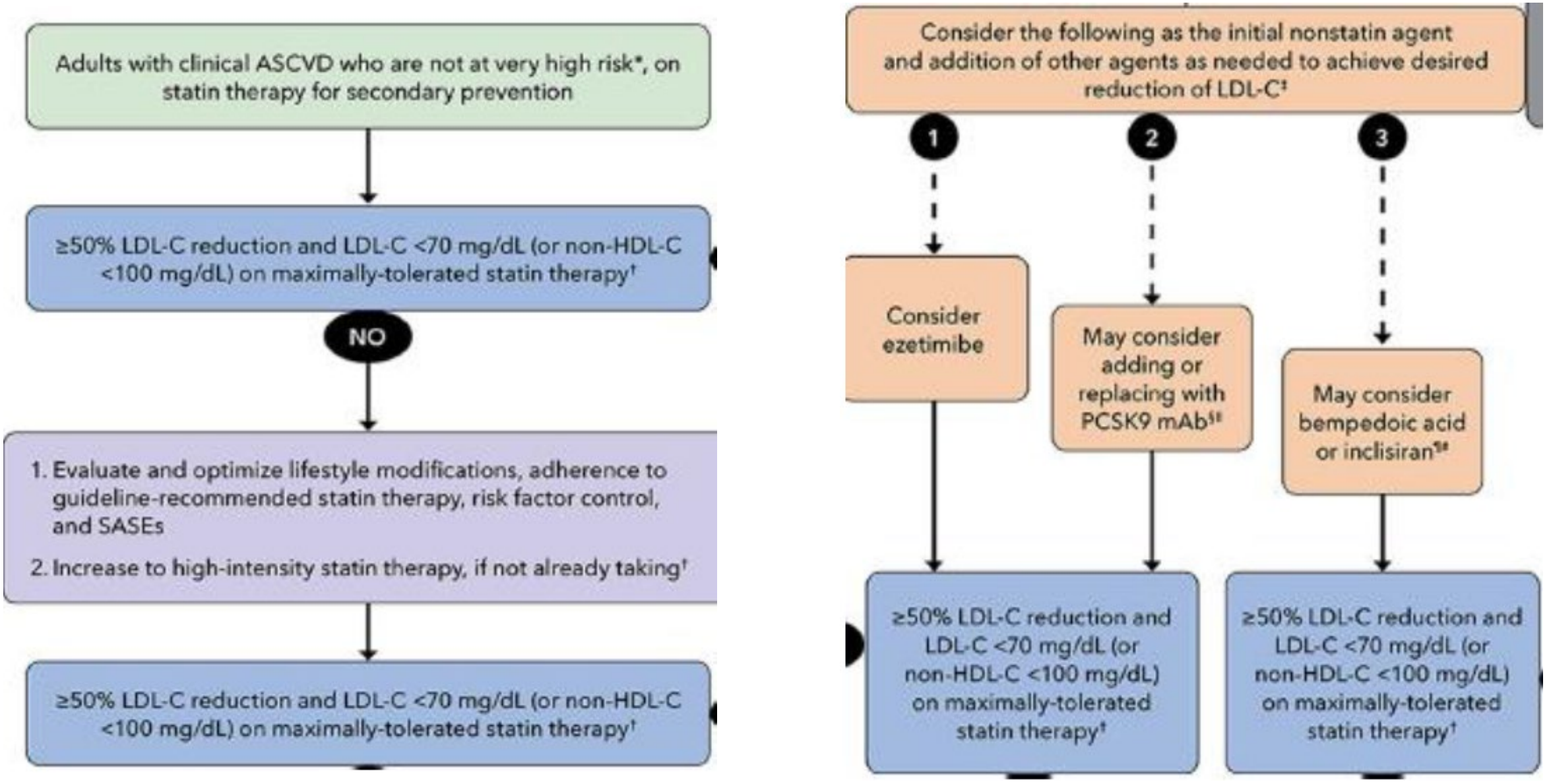
Risk-Enhancing Factors

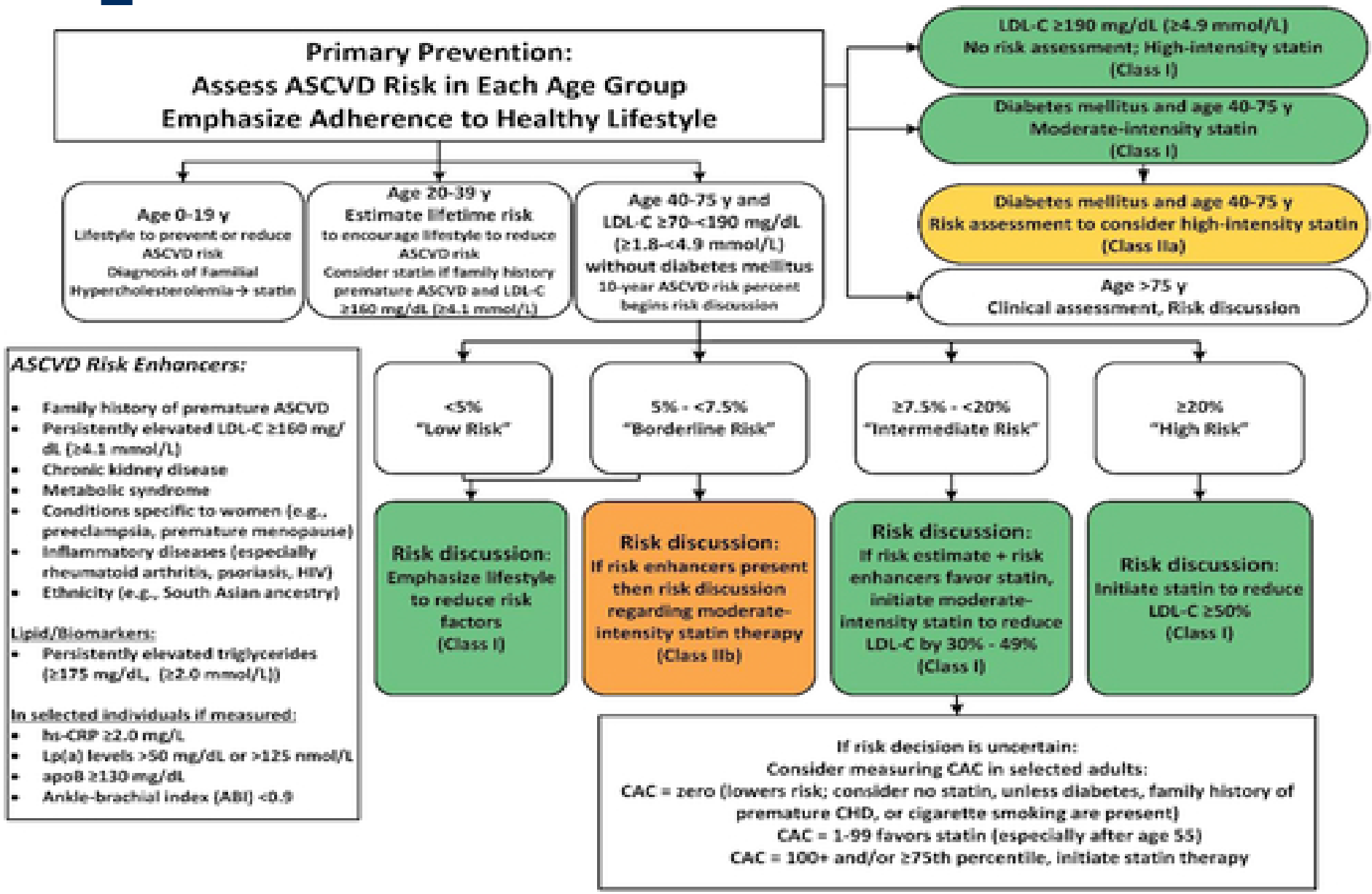
- **Family history of premature ASCVD** (men aged <55 years; women aged <65 years)
- **Primary hypercholesterolemia** (LDL-C 160-189 mg/dL [4.1-4.8 mmol/L); non-HDL-C 190-219 mg/dL [4.9-5.6 mmol/L]*
- **Metabolic syndrome** (increased waist circumference, elevated triglycerides [≥150 mg/dL], elevated blood pressure, elevated glucose, and 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/1.73 m^2 with or without albuminuria; not treated with dialysis or kidney transplantation)
- **Chronic inflammatory conditions** such as psoriasis, RA, or HIV/AIDS
- **History of premature menopause (before age 40 years) and history of pregnancy-associated conditions that increase later ASCVD risk, such as preeclampsia**
- **High-risk races/ethnicities** (eg, South-Asian ancestry)
- **Lipids/biomarkers:** Associated with increased ASCVD risk
  - **Persistently* elevated, primary hypertriglyceridemia** (≥175 mg/dL)
  - If measured:
    1. **Elevated high-sensitivity C-reactive protein** (≥2.0 mg/L)
    2. **Elevated Lp(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).
    3. **Elevated apoB ≥130 mg/dL:** A relative indication for its measurement would be triglycerides ≥200 mg/dL. A level ≥130 mg/dL corresponds to LDL-C ≥160 mg/dL and constitutes a risk-enhancing factor
    4. **ABI** <0.9

"VERY HIGH RISK"



"HIGH RISK"


Adults with clinical ASCVD who are not at very high risk*, on statin therapy for secondary prevention
≥50% LDL-C reduction and LDL-C <70 mg/dL (or non-HDL-C <100 mg/dL) on maximally-tolerated statin therapy†
NO
1. Evaluate and optimize lifestyle modifications, adherence to guideline-recommended statin therapy, risk factor control, and SASEs
2. Increase to high-intensity statin therapy, if not already taking†
≥50% LDL-C reduction and LDL-C <70 mg/dL (or non-HDL-C <100 mg/dL) on maximally-tolerated statin therapy†
Consider the following as the initial nonstatin agent and addition of other agents as needed to achieve desired reduction of LDL-C‡
1
2
3
Consider ezetimibe
May consider adding or replacing with PCSK9 mAb§‖
May consider bempedoic acid or inclisiran§#
≥50% LDL-C reduction and LDL-C <70 mg/dL (or non-HDL-C <100 mg/dL) on maximally-tolerated statin therapy†
≥50% LDL-C reduction and LDL-C <70 mg/dL (or non-HDL-C <100 mg/dL) on maximally-tolerated statin therapy†



Scott M. Grundy et al. *J Am Coll Cardiol* 2018; 73:e285-e350.

Questions?