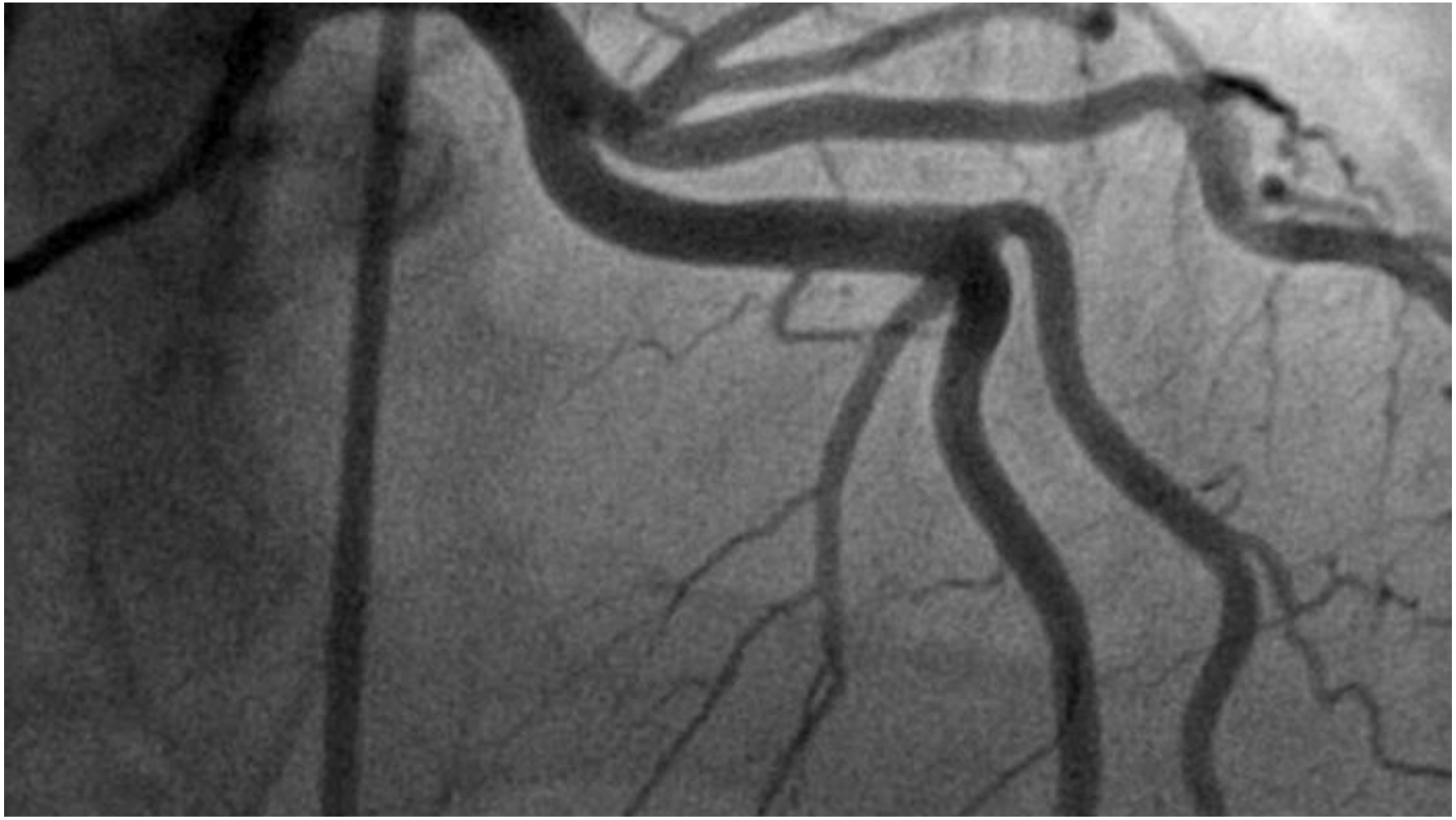
Does Your Cholesterol Matter in 2026?

Joel Kahn, MD, FACC
Clinical Professor Of Medicine
Wayne State University
School of Medicine
Kahn Center for Cardiac Longevity

American Heart Association.

Normal Coronary Angiogram: The Goal



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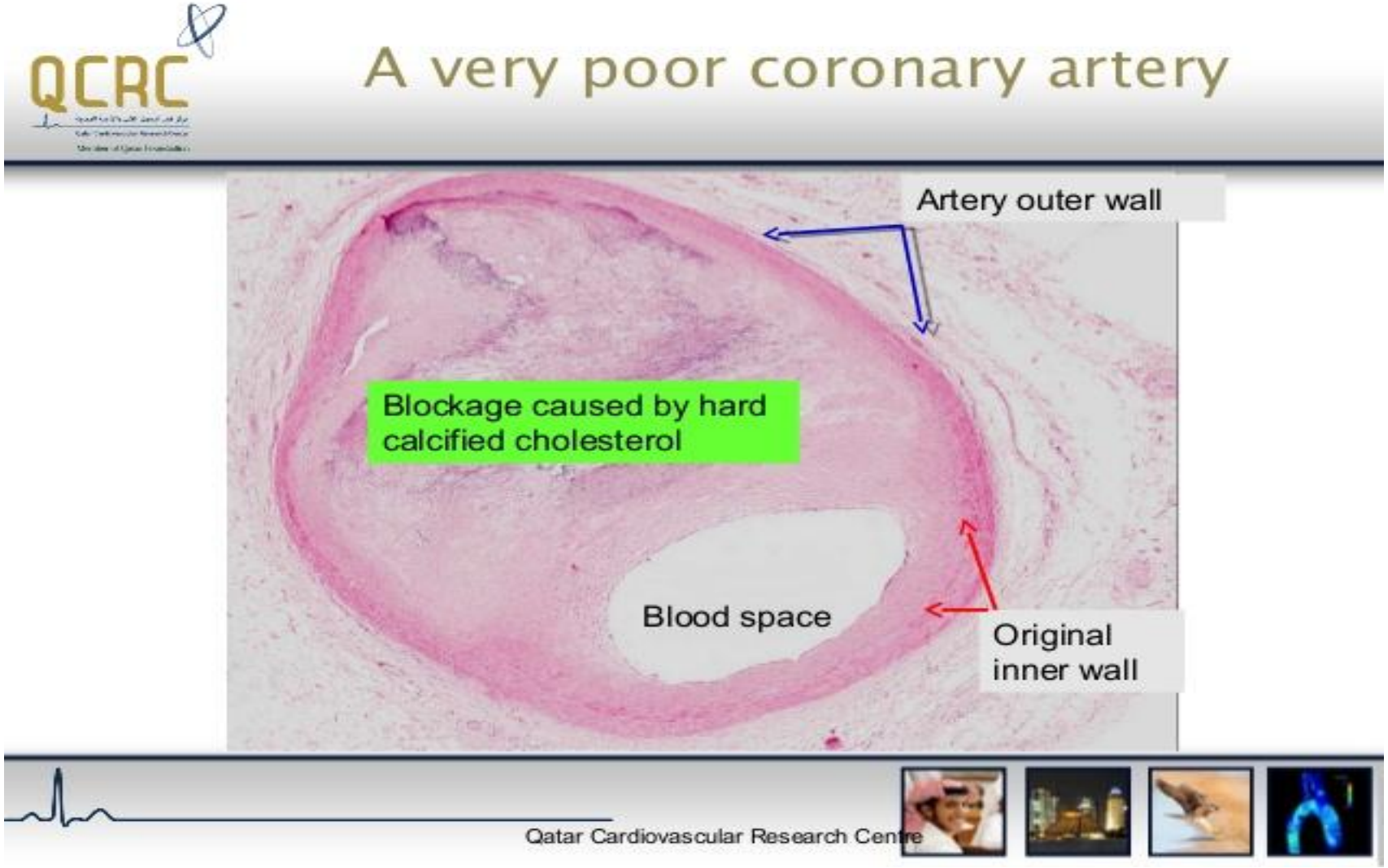
Coronary Artery Disease: The Reality



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Why Do We Clog Arteries?

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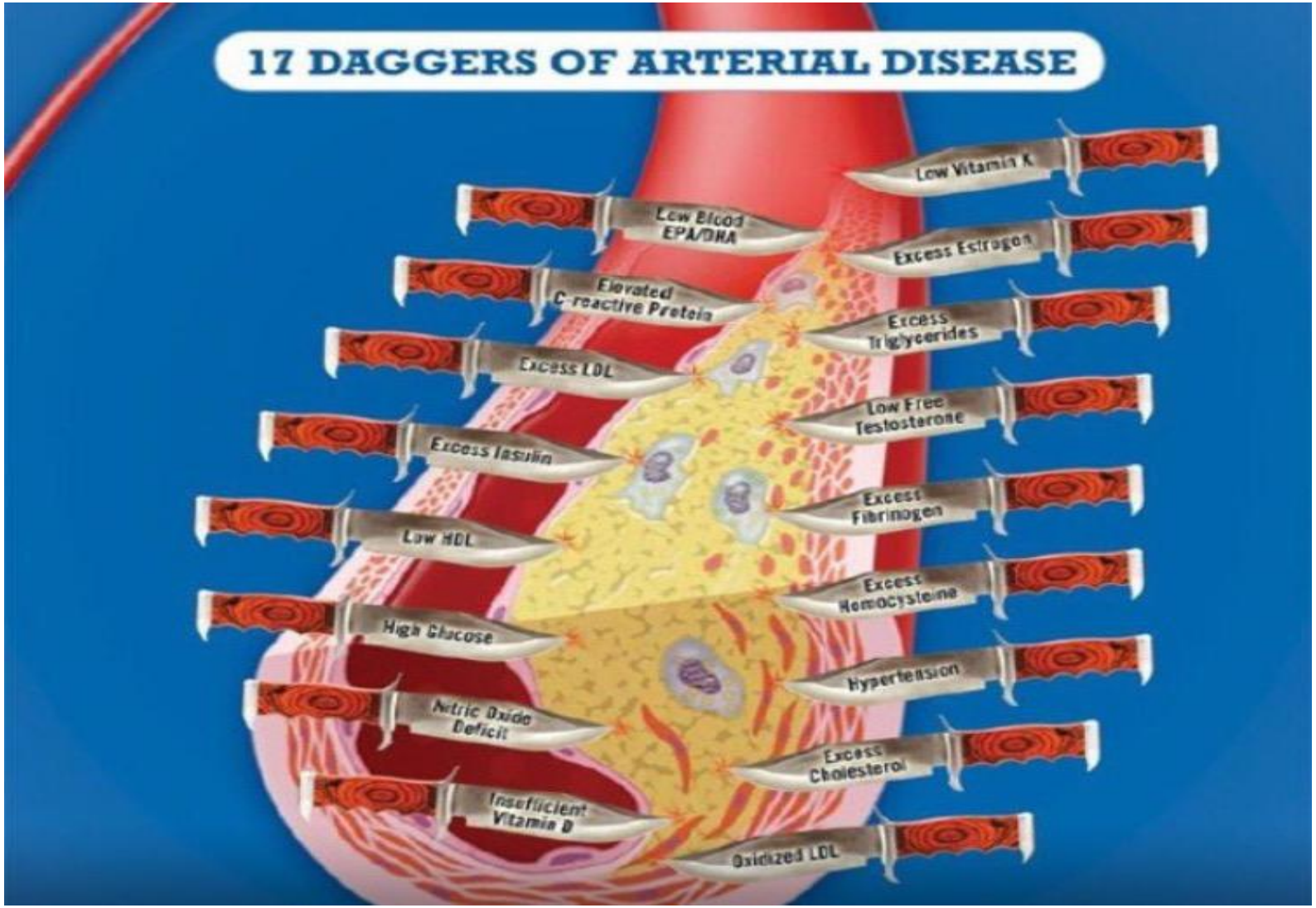
Cholesterol: A Risk Factor Not The Only Risk Factor

And More
Lipoprotein(a)
ApoE4
9p21
TMAO
Polyols
Air Pollution
Sleep
MPO
LP-PLA2
Vaping



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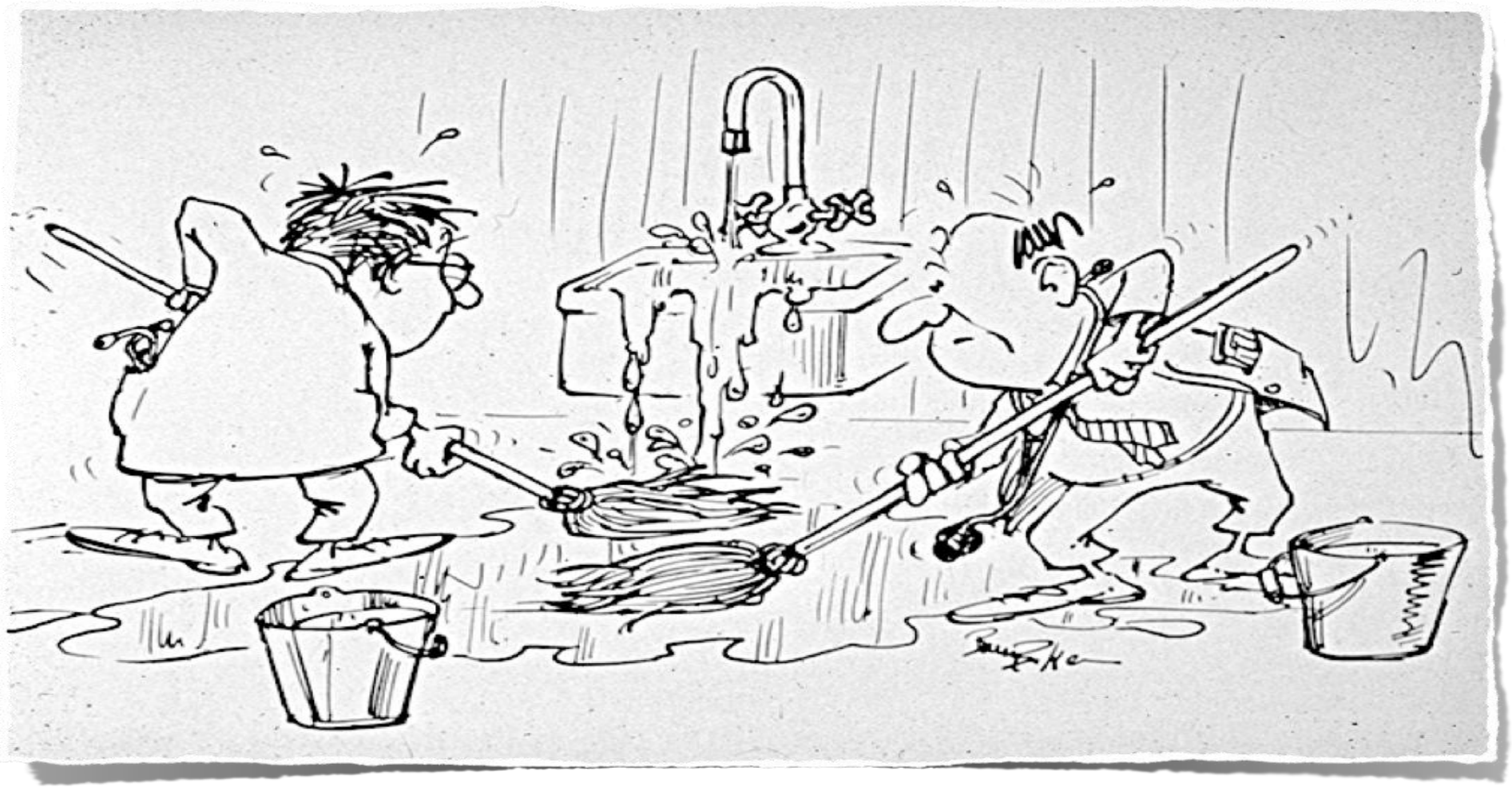
Can We Turn Off The Faucet?



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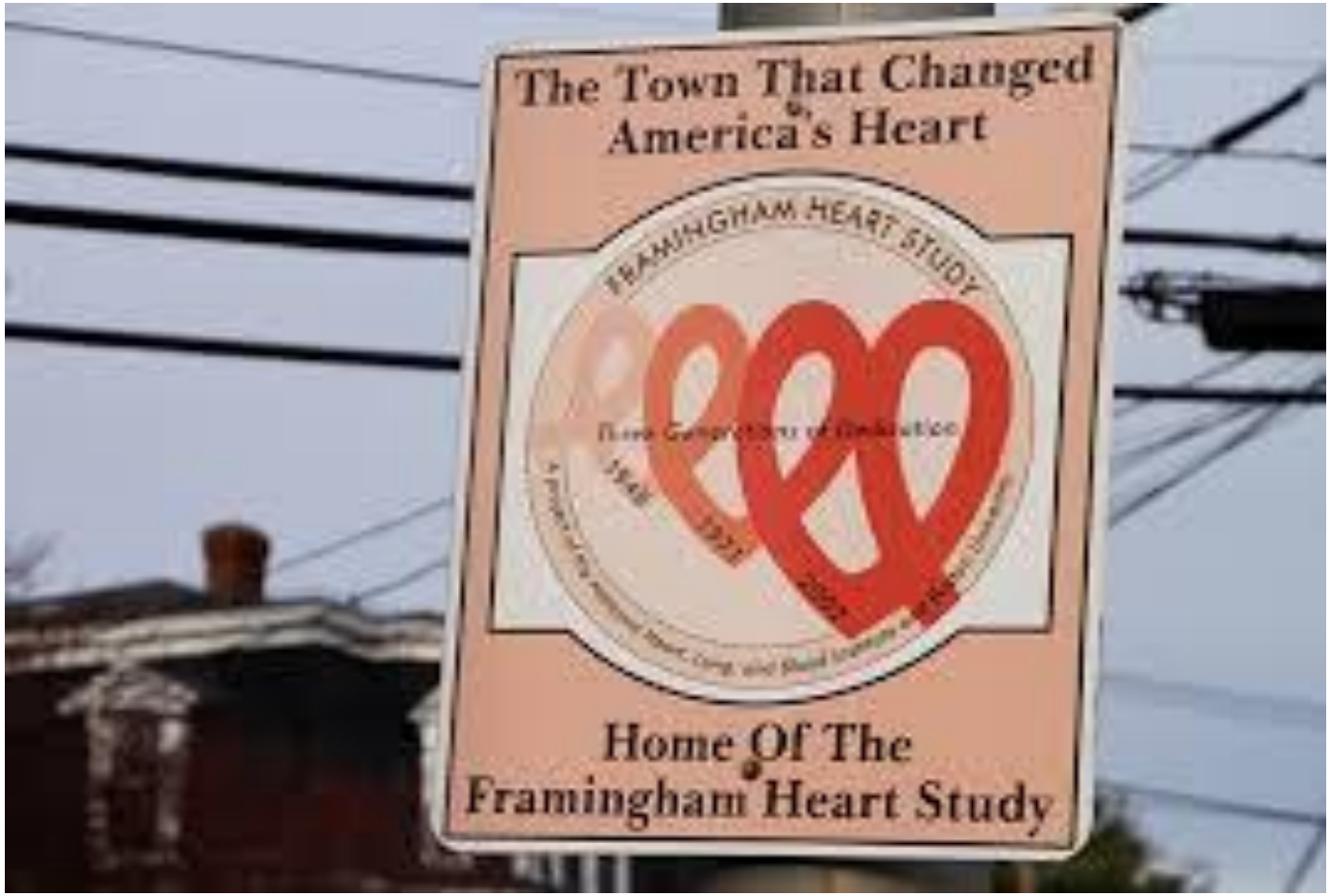
Framingham, MA



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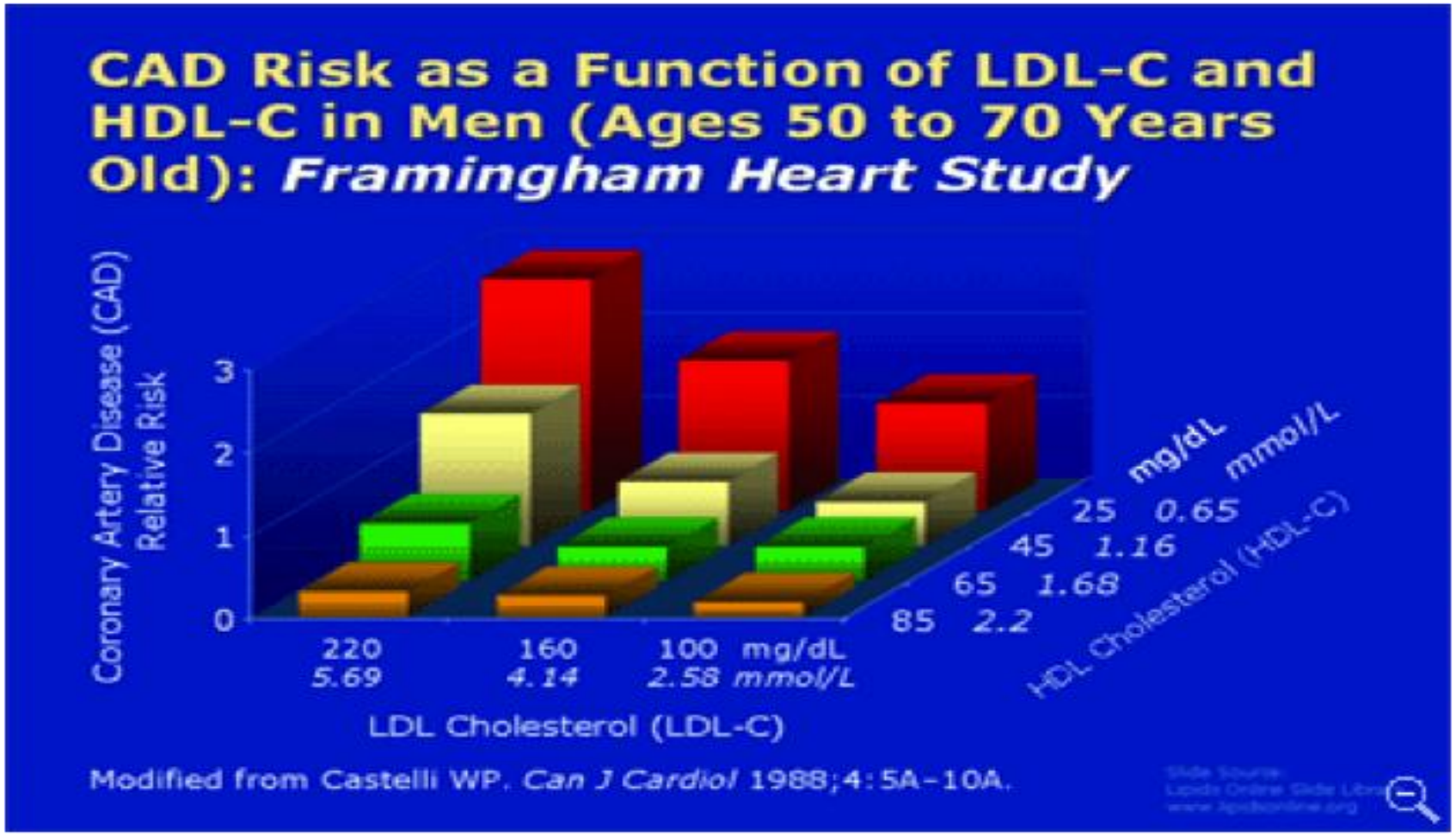
CHOLESTEROL MATTERS



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Mendelian Randomization

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Lower LDL-Cholesterol Beginning Early in Life on the Risk of Coronary Heart Disease: A Mendelian Randomization Analysis

B. A. Ference, MD, Wonsuk Yoo, PhD, Karolina Mirowska MD, Abhishek Mewada, MD, **Joel Kahn, MD,** Luis Afonso, MD, Kim Williams Sr, MD, John Flack, MD

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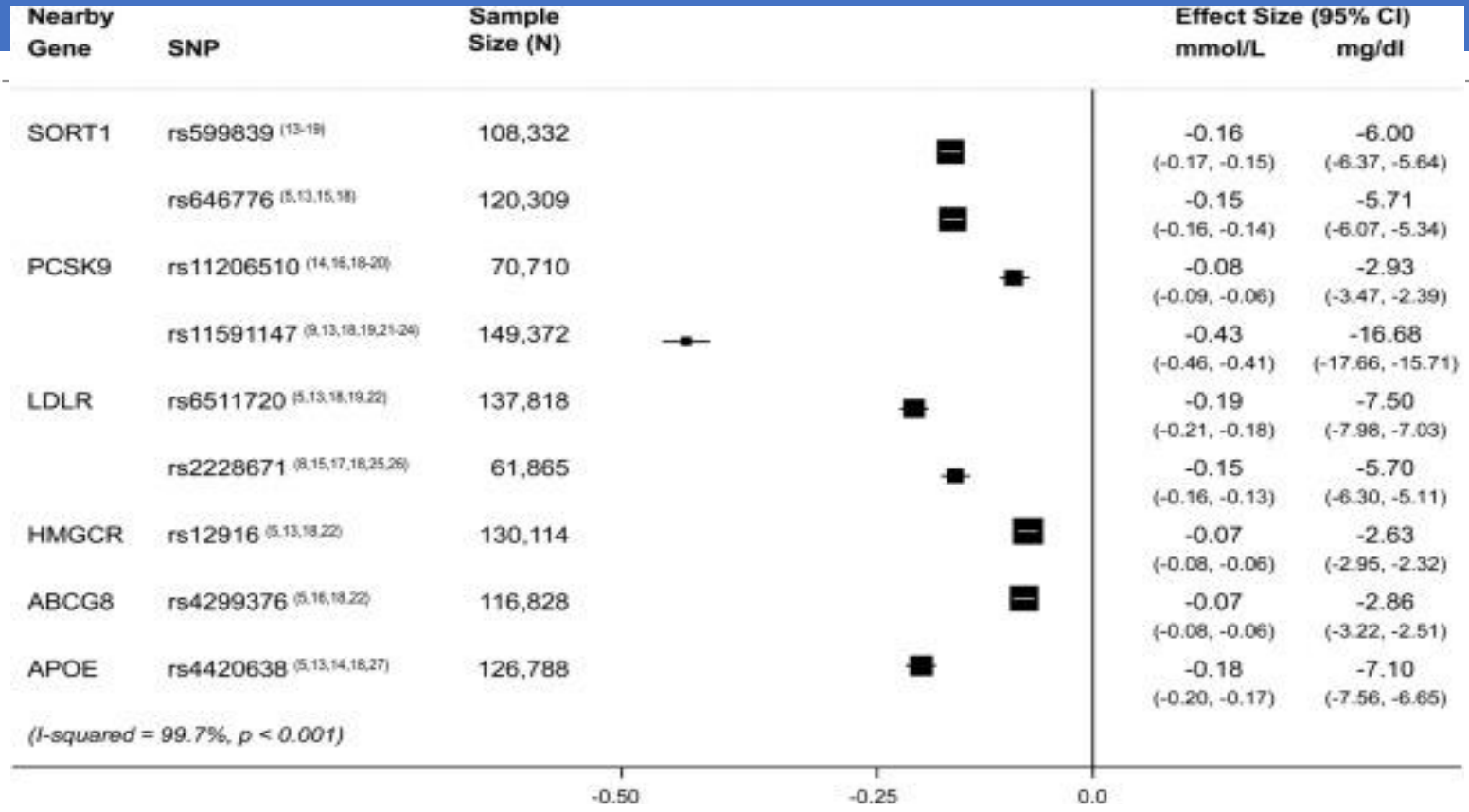
Alleles that Lower LDL Cholesterol Lifelong



Nearby Gene	SNP	Sample Size (N)	Effect Size (95% CI) mmol/L	Effect Size (95% CI) mg/dl
SORT1	rs599839 [13-19]	108,332	-0.16 (-0.17, -0.15)	-6.00 (-6.37, -5.64)
	rs646776 [5,13,15,18]	120,309	-0.15 (-0.16, -0.14)	-5.71 (-6.07, -5.34)
PCSK9	rs11206510 [14,16,18-20]	70,710	-0.08 (-0.09, -0.06)	-2.93 (-3.47, -2.39)
	rs11591147 [9,13,18,19,21-24]	149,372	-0.43 (-0.46, -0.41)	-16.68 (-17.66, -15.71)
LDLR	rs6511720 [5,13,18,19,22]	137,818	-0.19 (-0.21, -0.18)	-7.50 (-7.96, -7.03)
	rs2228671 [8,15,17,18,25,26]	61,865	-0.15 (-0.16, -0.13)	-5.70 (-6.30, -5.11)
HMGCR	rs12916 [5,13,18,22]	130,114	-0.07 (-0.08, -0.06)	-2.63 (-2.95, -2.32)
ABCG8	rs4299376 [5,16,18,22]	116,828	-0.07 (-0.08, -0.06)	-2.86 (-3.22, -2.51)
APOE	rs4420638 [5,13,14,18,27]	126,788	-0.18 (-0.20, -0.17)	-7.10 (-7.56, -6.65)

(I-squared = 99.7%, p < 0.001)

-0.50 -0.25 0.0

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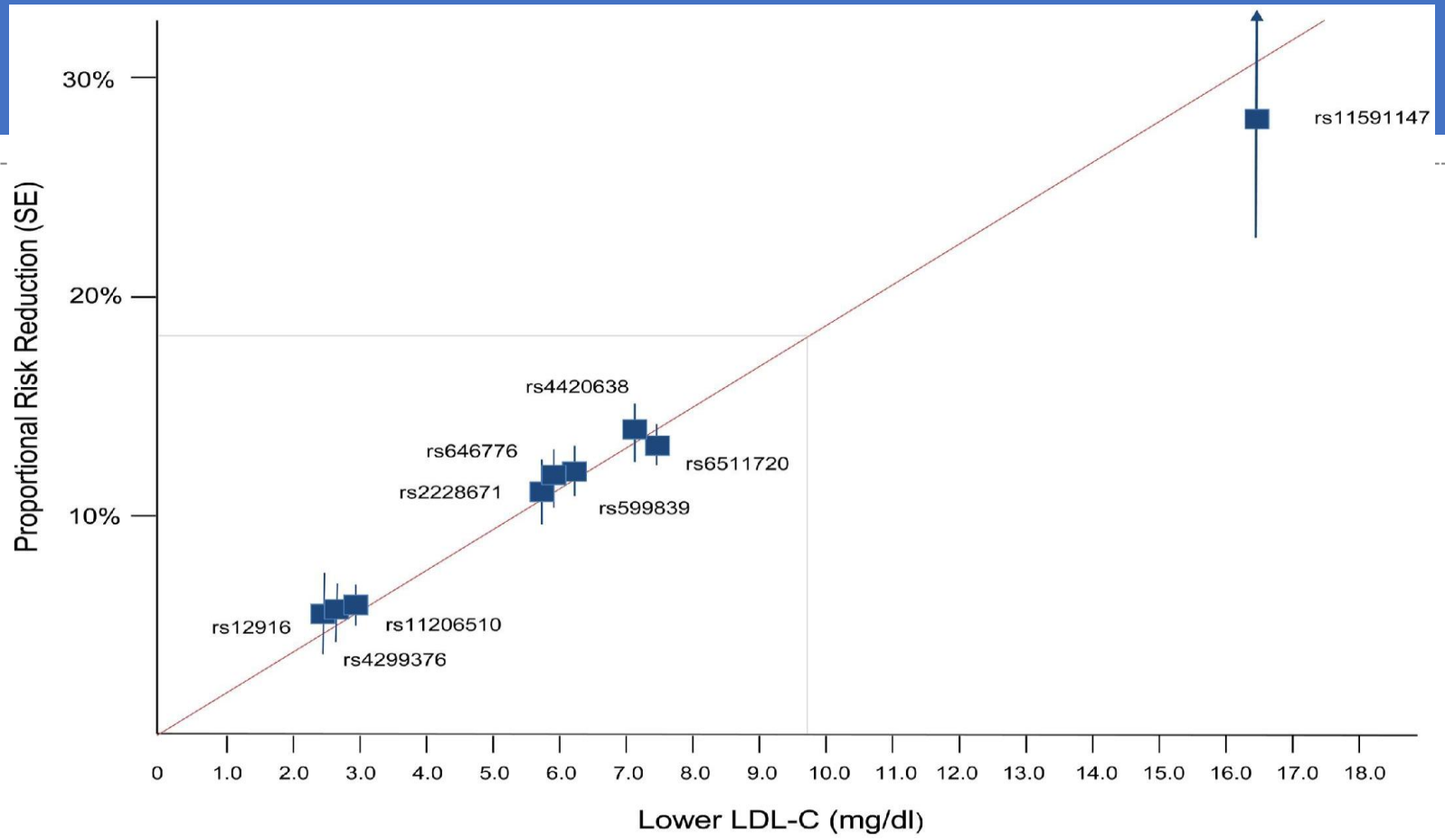
Lower LDL vs CHD Risk



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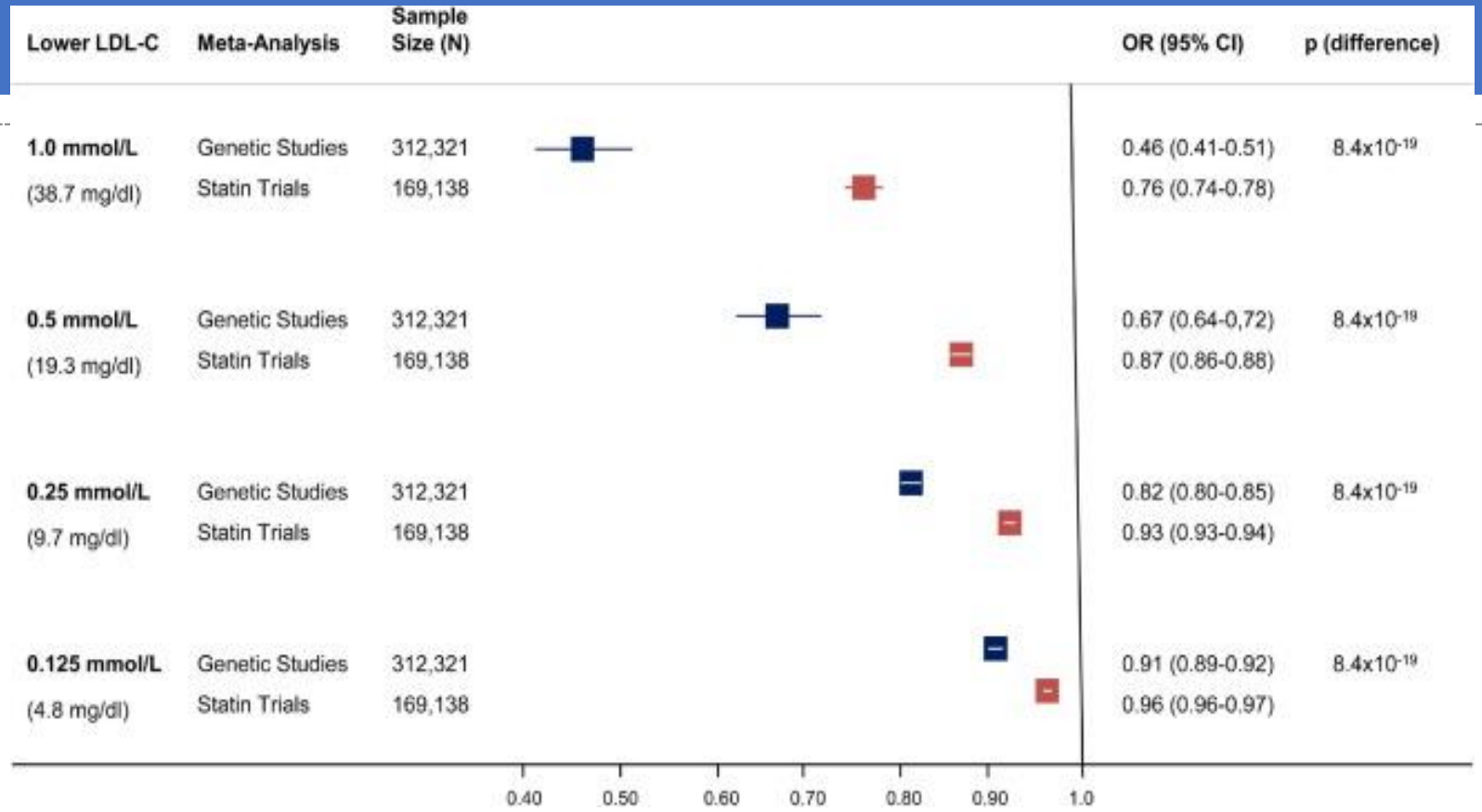
LDL Lowering: Genetics vs Statins



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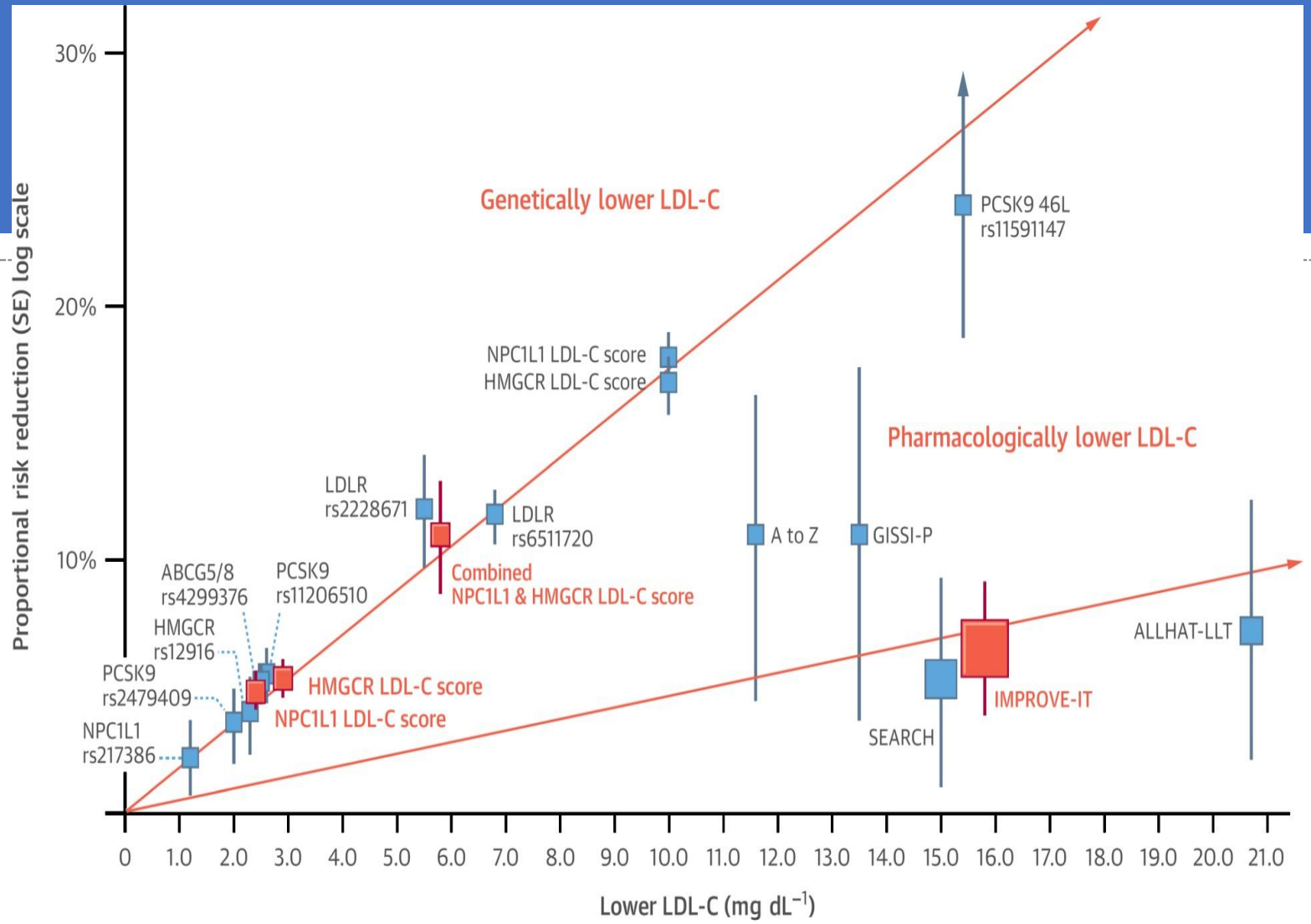
LDL Lowering: Genetics vs Statin Trials



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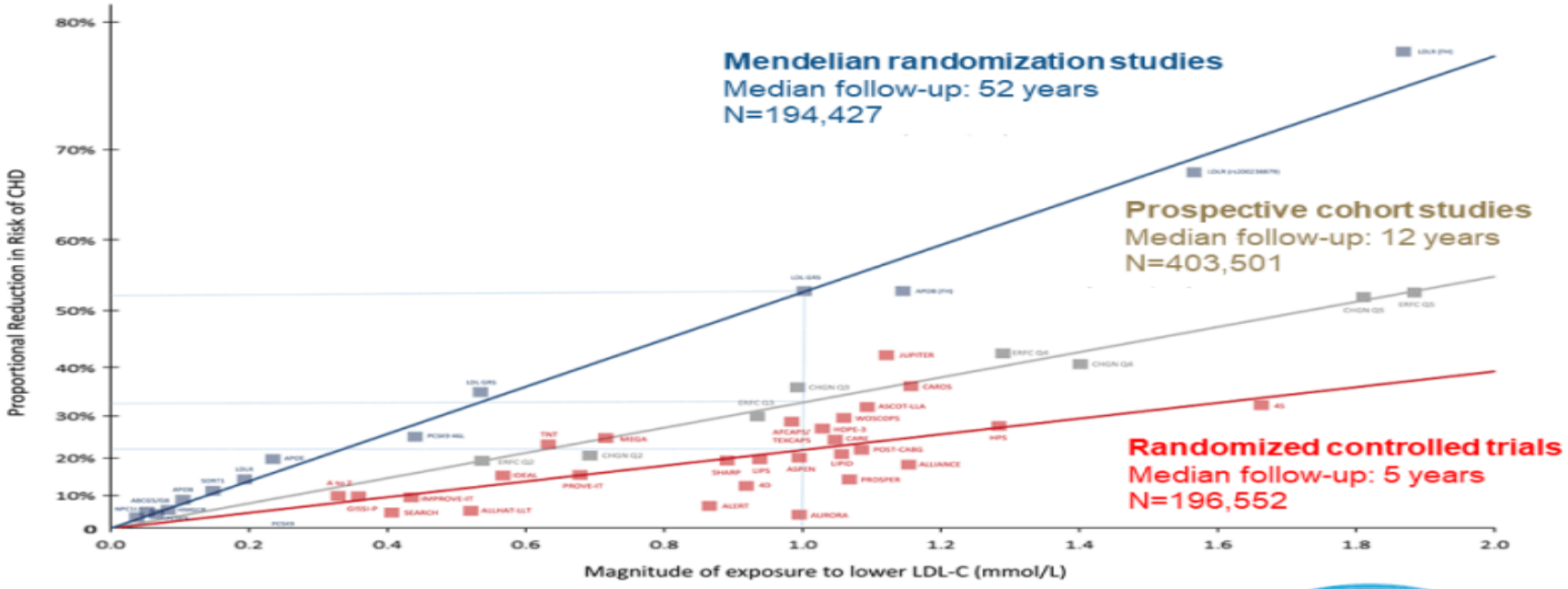
LDL-C: The Lower, The Longer, The Better

LDL is causal of atherosclerosis

Evidence from meta-analyses of **Mendelian randomization studies**, **prospective cohort studies**, and **randomized controlled trials** unequivocally establishes that LDL causes ASCVD.



Ference BA *et al.*, Eur Heart J. 2017;38(32):2459-2472

PACE-CME

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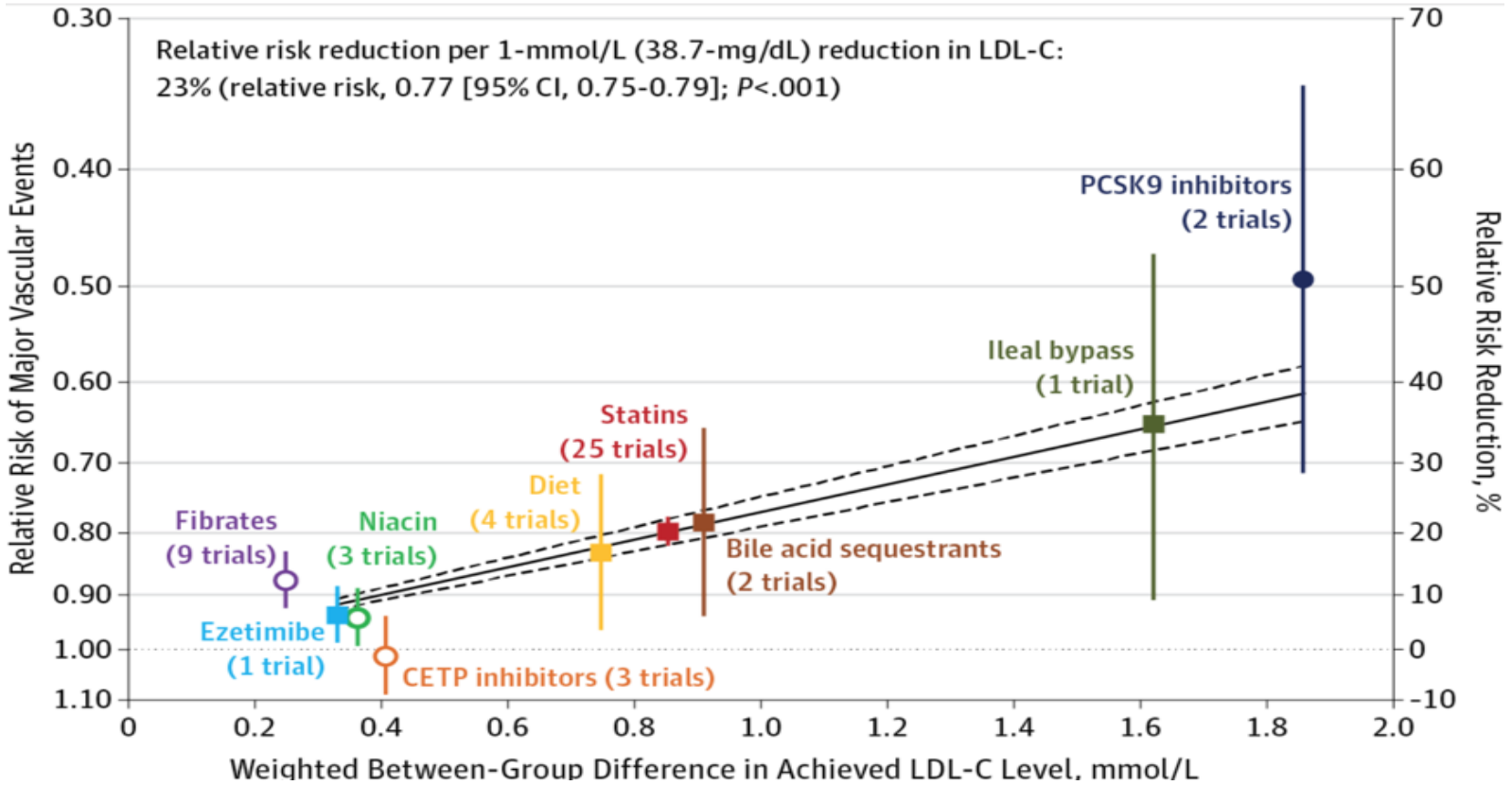
Lower LDL-C = Lower Events



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1

CHECK YOUR CHOLESTEROL EARLY AND OFTEN IN LIFE

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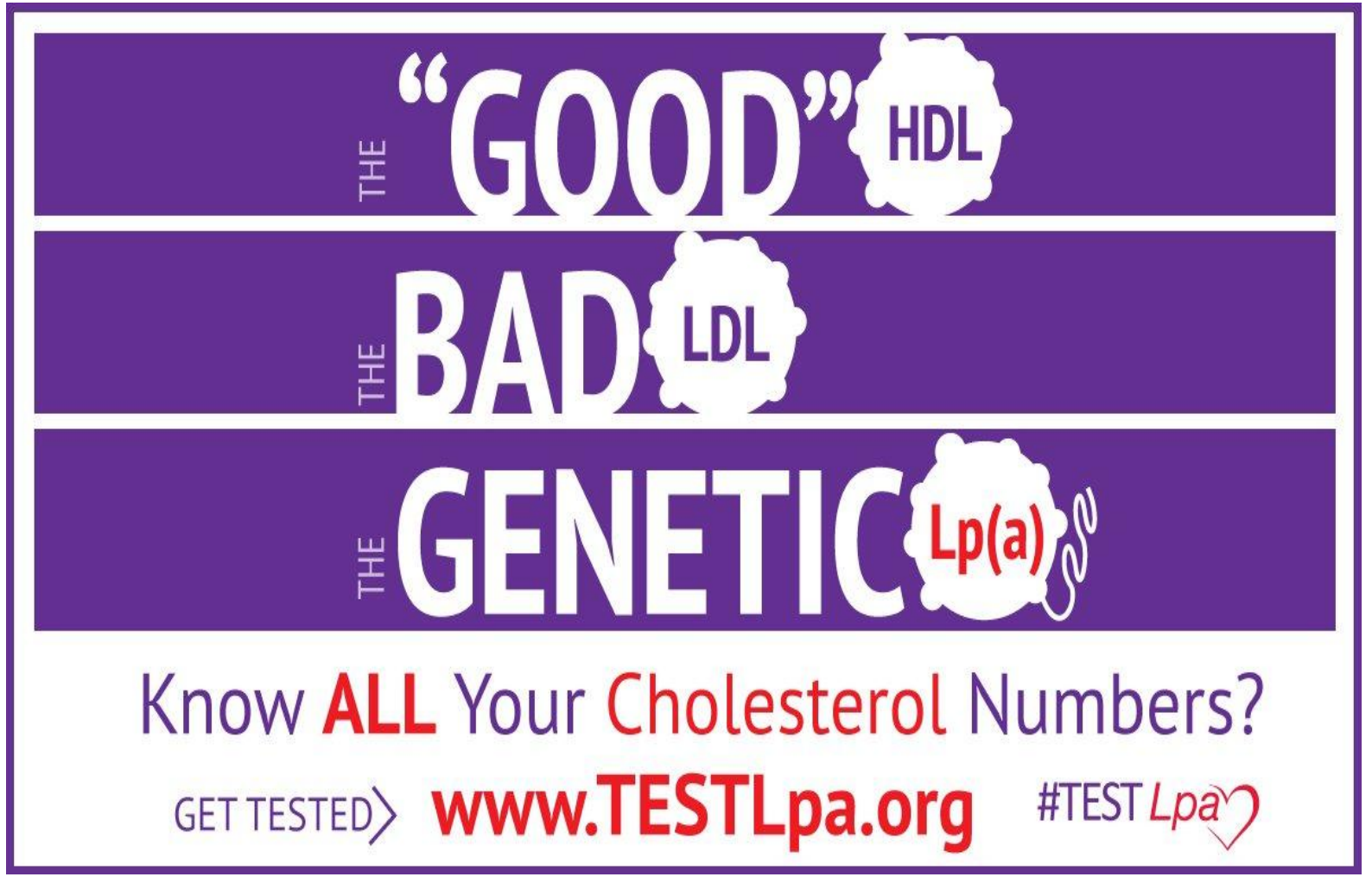
Lipoprotein(a) or Lp(a)



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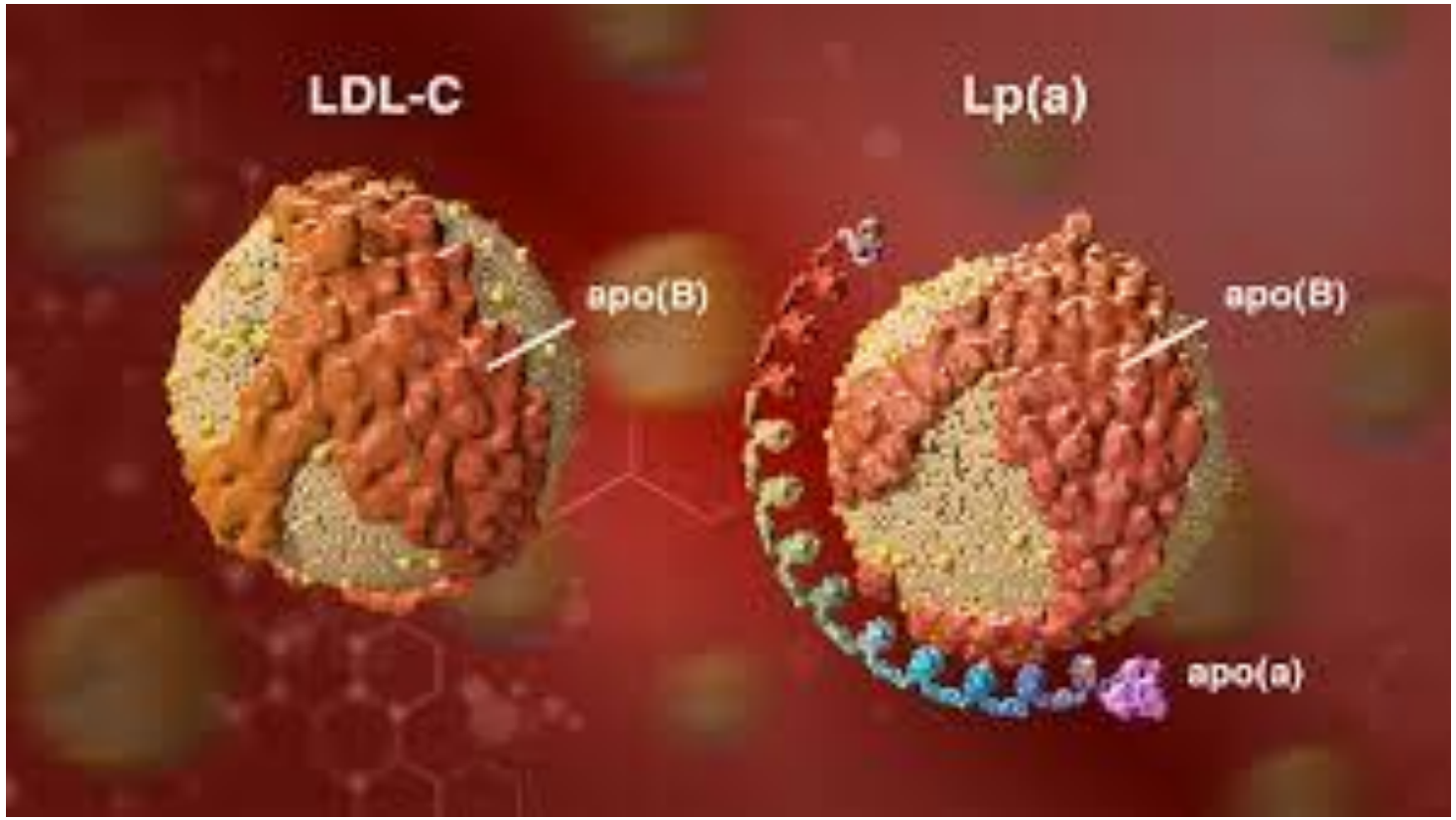
Lp(a): Like LDL-C But Worse



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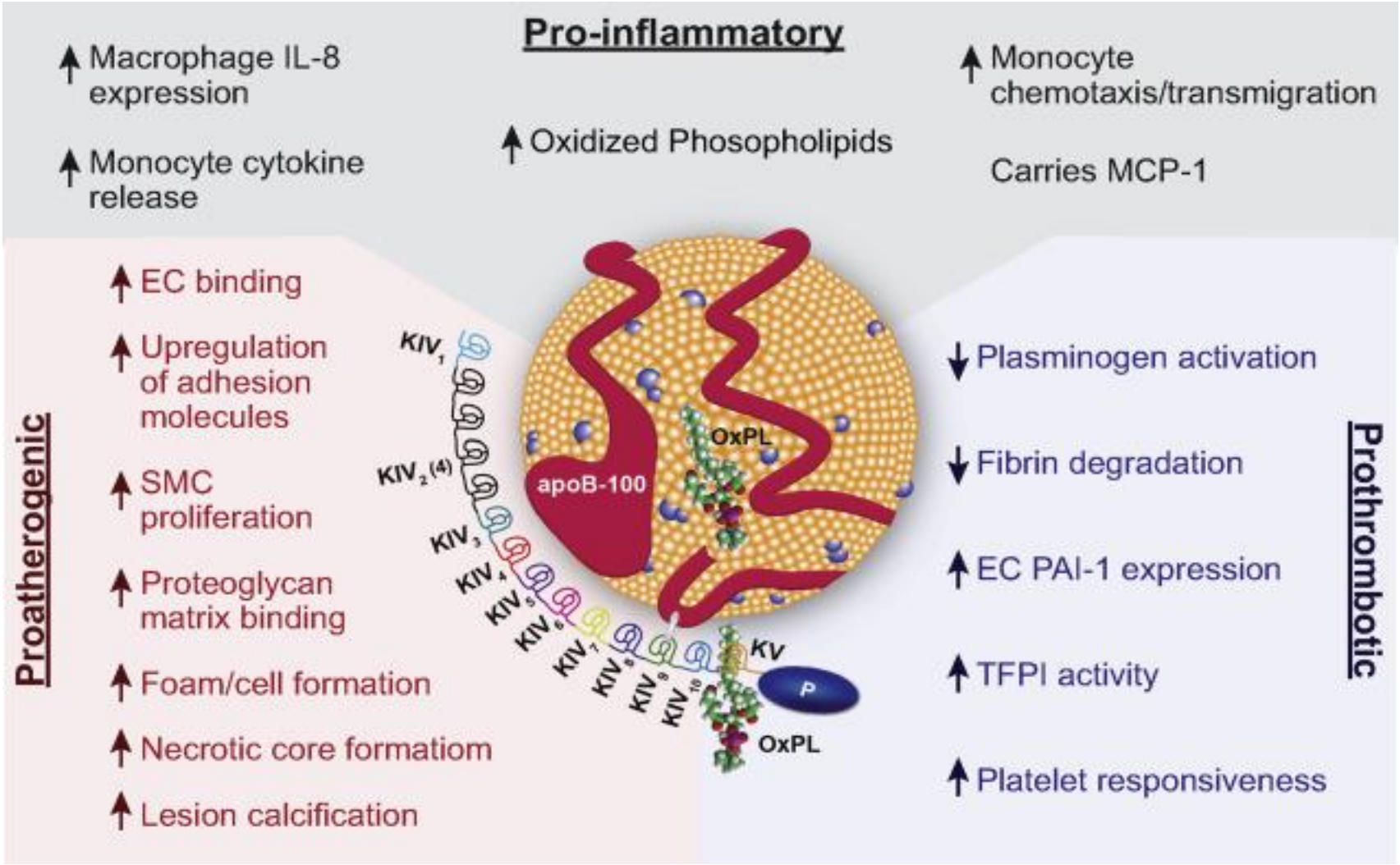
Lp(a): Triple Threat



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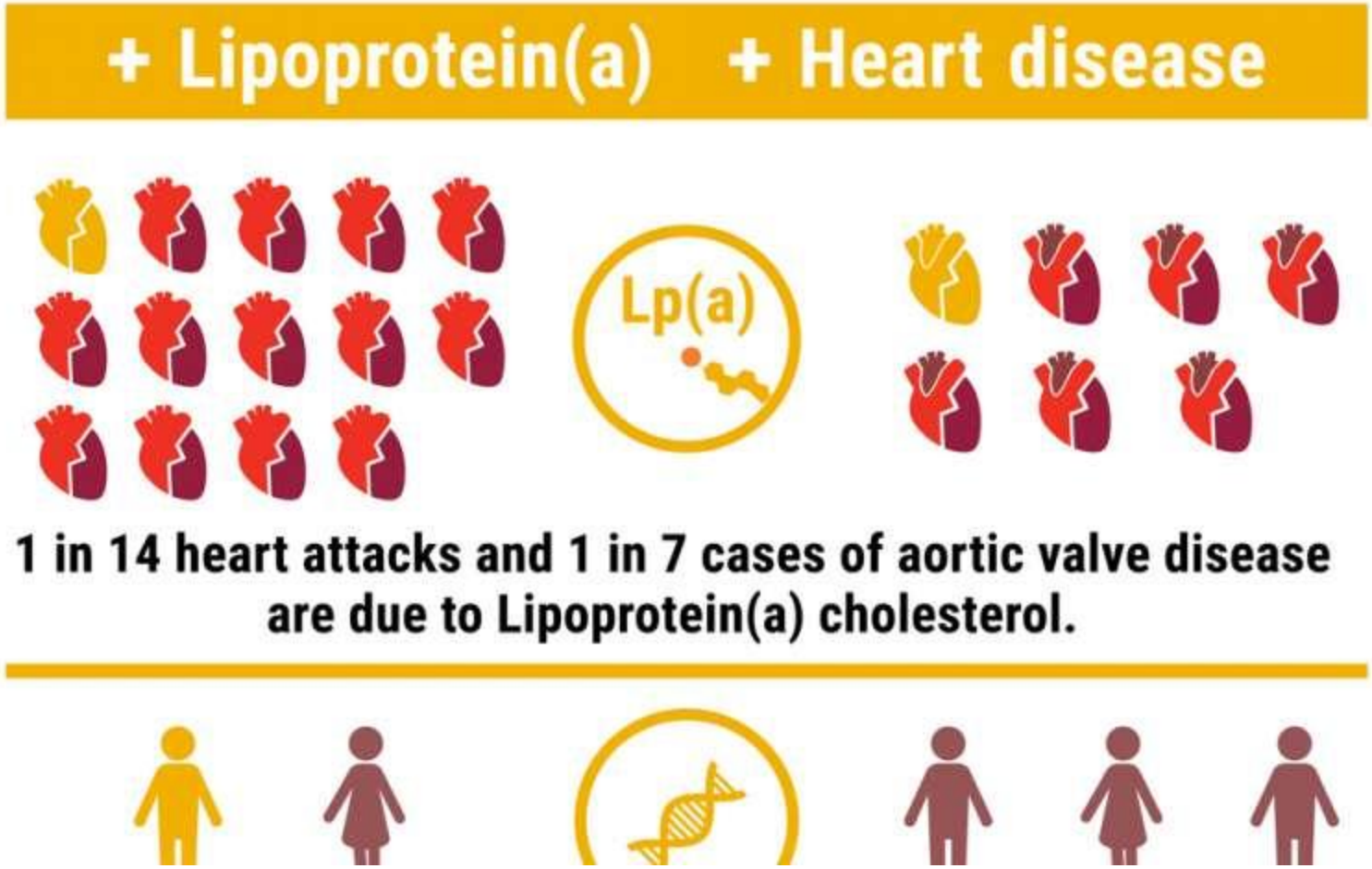
VIP: Very Important Particle



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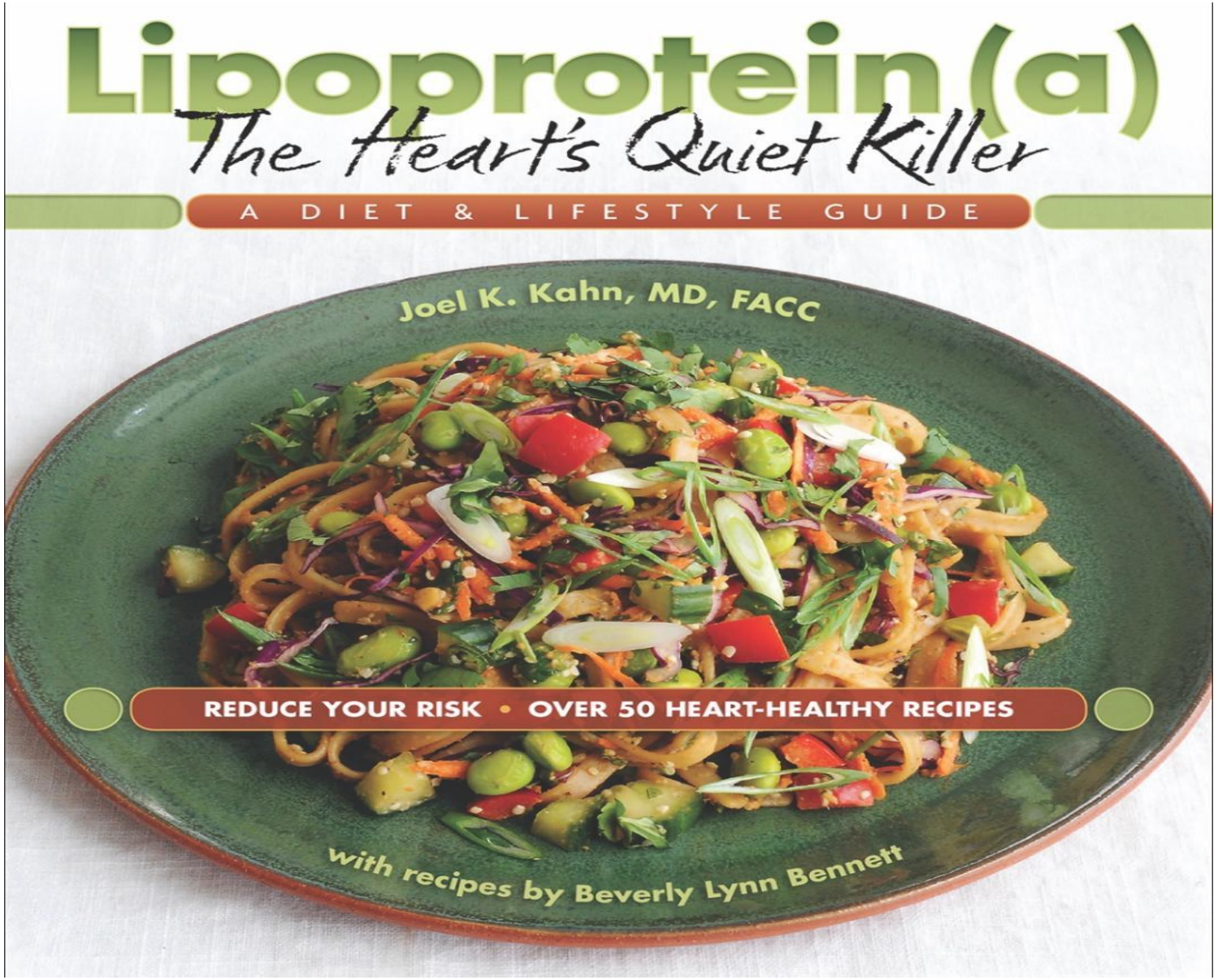

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ICD10 Approved: E78.41

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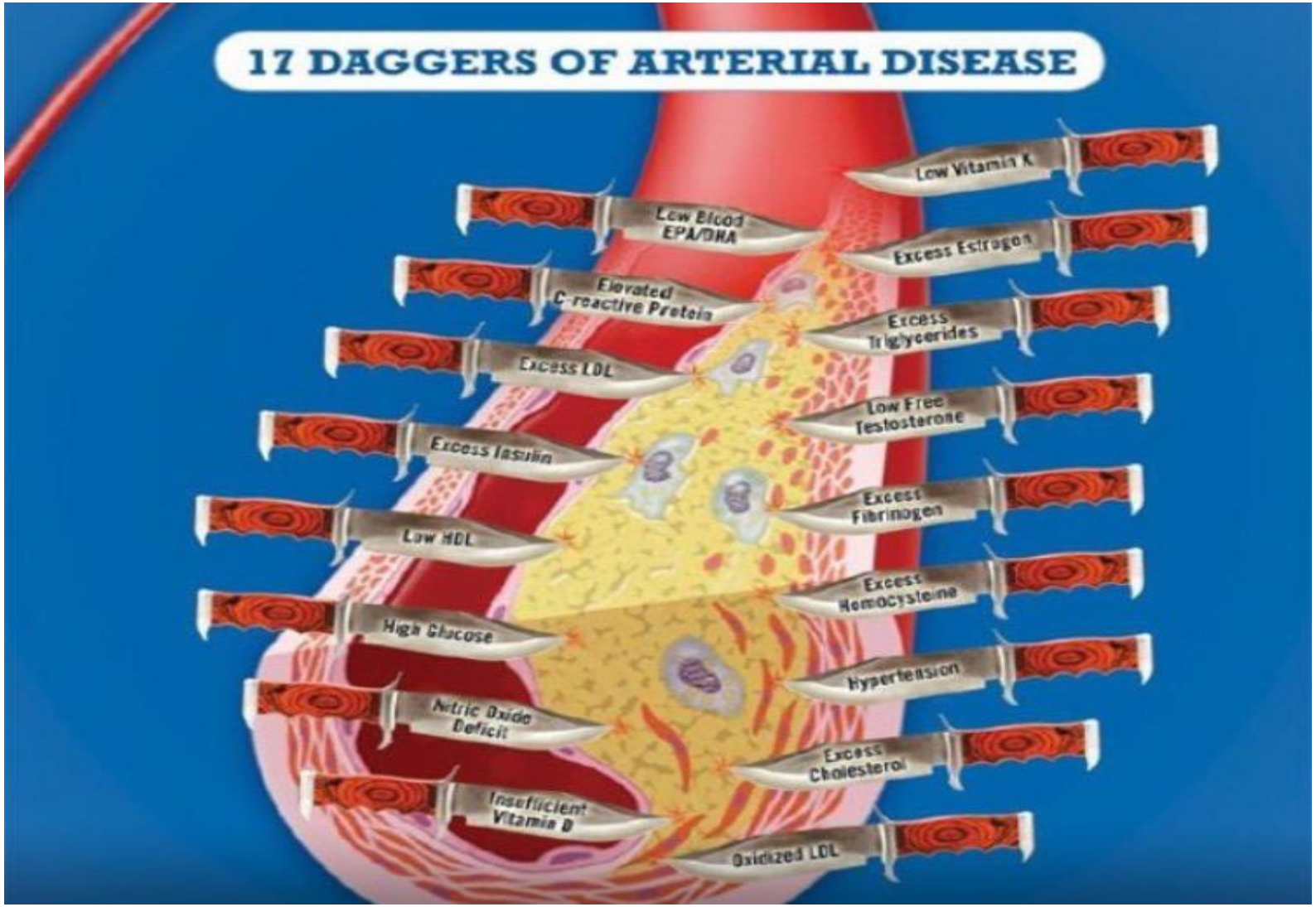
Beyond Cholesterol



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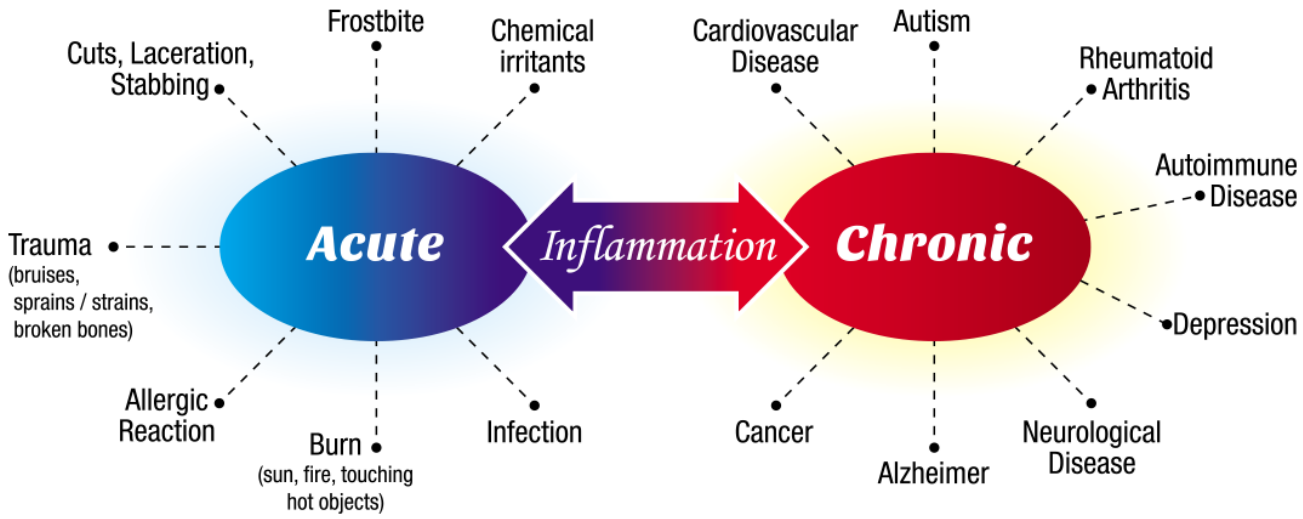
What is inflammation?



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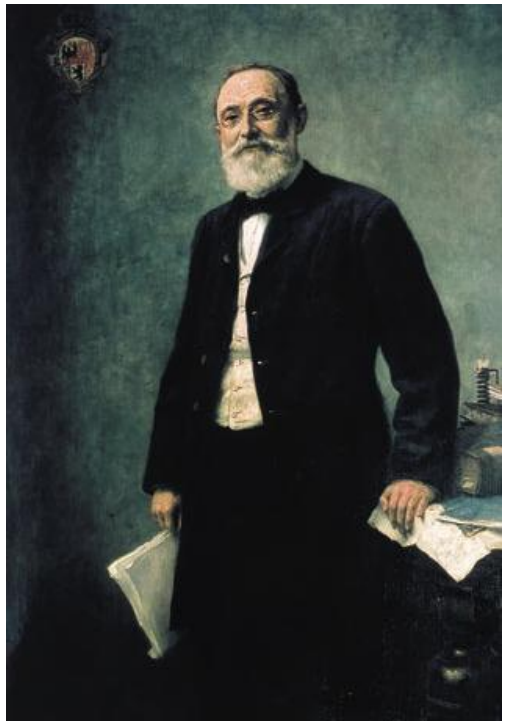
Rudolf Virchow

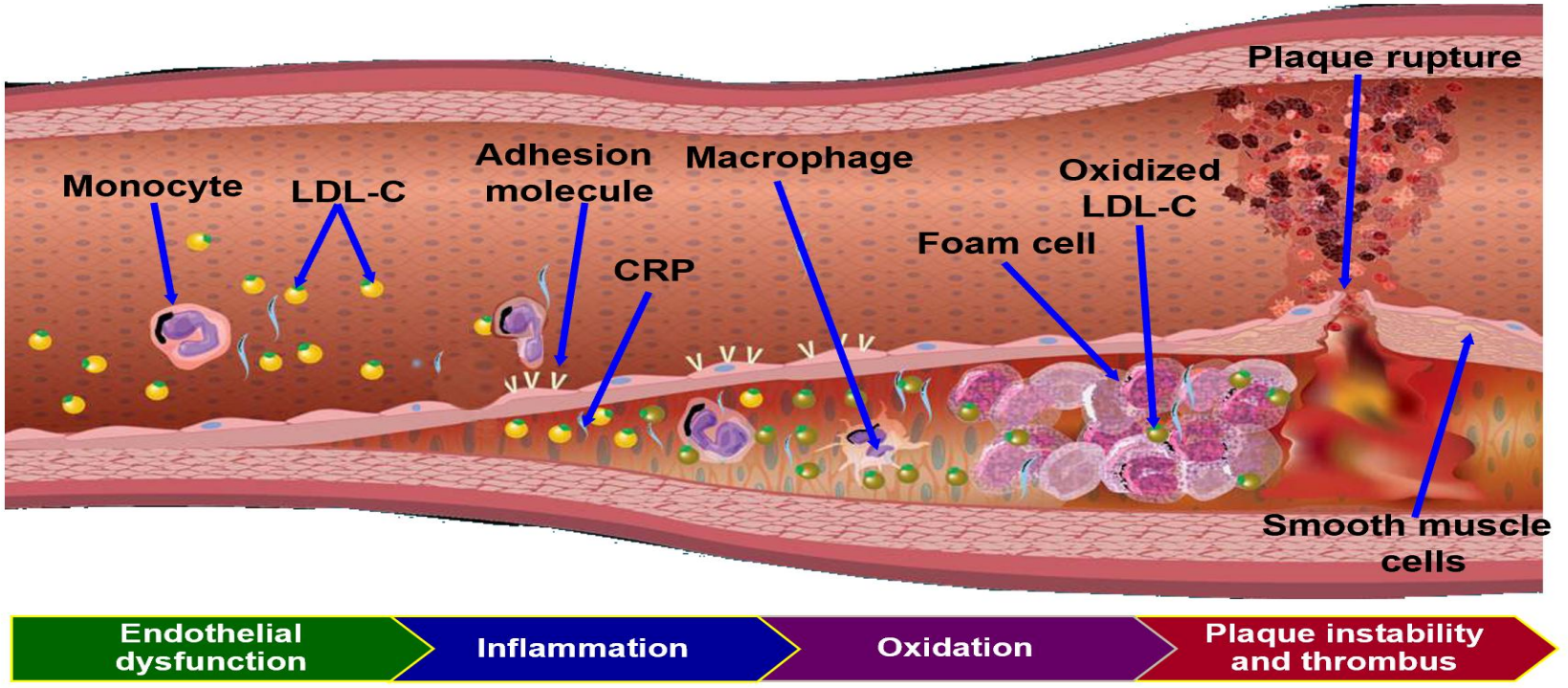
Inflammation-based arterial changes as a mechanism of primary importance in ATHEROGENESIS

mid 19th century



Lamond, B. *The American Journal of Pathology*. 2008

Atherosclerosis is an Inflammatory Disease



Libby P. *Circulation.* 2001;104:365-372; Ross R. *N Engl J Med.* 1999;340:115-126.

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EVADE CAD Trial

ePosters

American Heart Association. life is why | SCIENTIFIC SESSIONS 2017 Sessions: November 11-15 Anaheim, California

S2030 — 2017 [Board 2030] **AHA**

Anti-inflammatory Effect of Whole-Food Plant-Based Vegan Diet vs the American Heart Association - Recommended Diet in Patients With Coronary Artery Disease: The Randomized EVADE CAD Trial

The Full Poster will be available Sunday, November 12, 2017 at 3:15:00 PM US/Eastern.

Map (epsMap.cfm?id=1426)

Epidemiology, Big Data and Precision Medicine

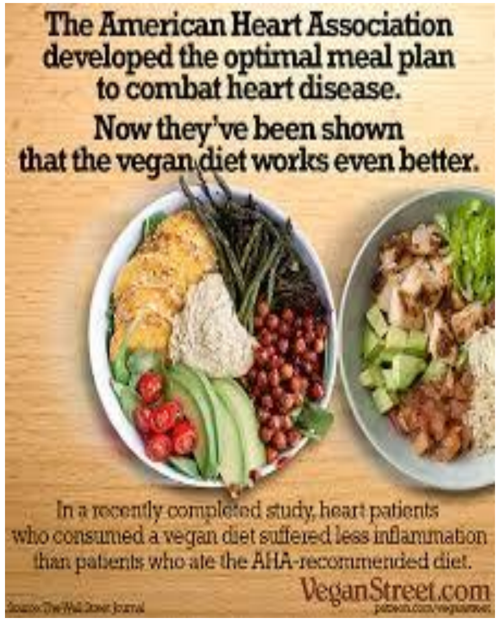
EP.APS.04 | *Physical Activity and Diet in CVD*

CAD

Presented on Sunday, November 12, 2017 3:15 PM

Author(s): Binita Shah, Jonathan Newman, Kathleen Woolf, NEW YORK UNIVERSITY, New York, NY; **Lisa Ganguzza**, NYU Langone Medical Ctr, New York, NY; Yu Guo, Edward A Fisher, Nicole Allen, NEW YORK UNIVERSITY, New York, NY; Stanley L Hazen, Cleveland Clinic, Cleveland, OH; John Larigakis, Judy Zhong, Eugenia Gianos, Francisco Ujueta, James Slater, NEW YORK UNIVERSITY, New York, NY

Background: The effect of a whole-food plant-based vegan diet vs an AHA-recommended diet on inflammatory, lipid, and glucometabolic profiles remains uncertain. **Methods**: This prospective blinded end-point trial randomized 100 patients with invasive angiographically-defined coronary artery disease (CAD) to 8 weeks of a vegan or AHA diet. Participants were provided weekly groceries for their assigned diet strategy, sample 2-week menus, tools to measure portion size, and on-going consultation with the study dietitian. Dietary adherence was measured by two weekly 24-hour dietary recalls and plasma and urine trimethylamine-*N*-oxide levels. Participants also completed a 4-day food record during the week prior to the baseline, 4-, and 8-week study visits. The primary endpoint was serum hsCRP concentration. A linear mixed effect model was used to model the log-transformed endpoints (to correct for skewness), evaluate the change in endpoint over time within treatment group, and test the interaction between time and treatment. The primary analysis was also covariate-adjusted. **Results:** Baseline characteristics are shown in Table 1. Two subjects withdrew from the vegan group after randomization, but dietary adherence remained higher in the vegan vs AHA group at the 4-week (96% vs 84%, p=0.09) and 8-week (94% vs 70%, p=0.003) visits. Endpoints are shown in Table 2. **Conclusion:** A vegan diet significantly reduced systemic inflammation, as evidenced by hsCRP, in patients with CAD on guideline-directed medical therapy, while an AHA diet did not. This is the first rigorous study to comprehensively assess multiple indices of cardiovascular risk between a vegan and AHA diet.



Binita Shah et al
Originally published Jun 2018Circulation. 2018;136:A23081

Methods

- This prospective blinded end-point trial randomized 100 patients with coronary artery disease (CAD) to 8 weeks of a vegan or AHA diet.
- Participants were provided weekly groceries for their assigned diet strategy, sample 2-week menus, tools to measure portion size, and on-going consultation with the study dietitian.
- The primary endpoint was serum hs-CRP concentration.

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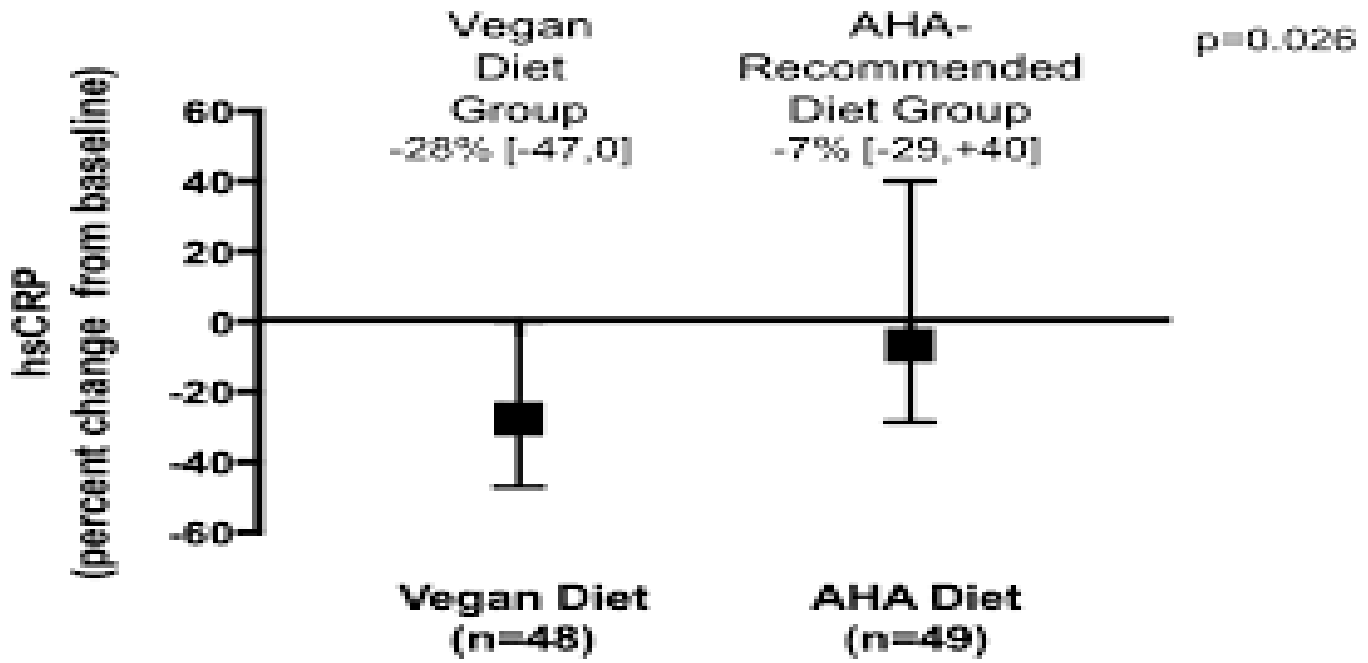
EVADE Results



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Practical Tip 2

Check your Lipoprotein(a) and hs-CRP early and often in life and eat plants

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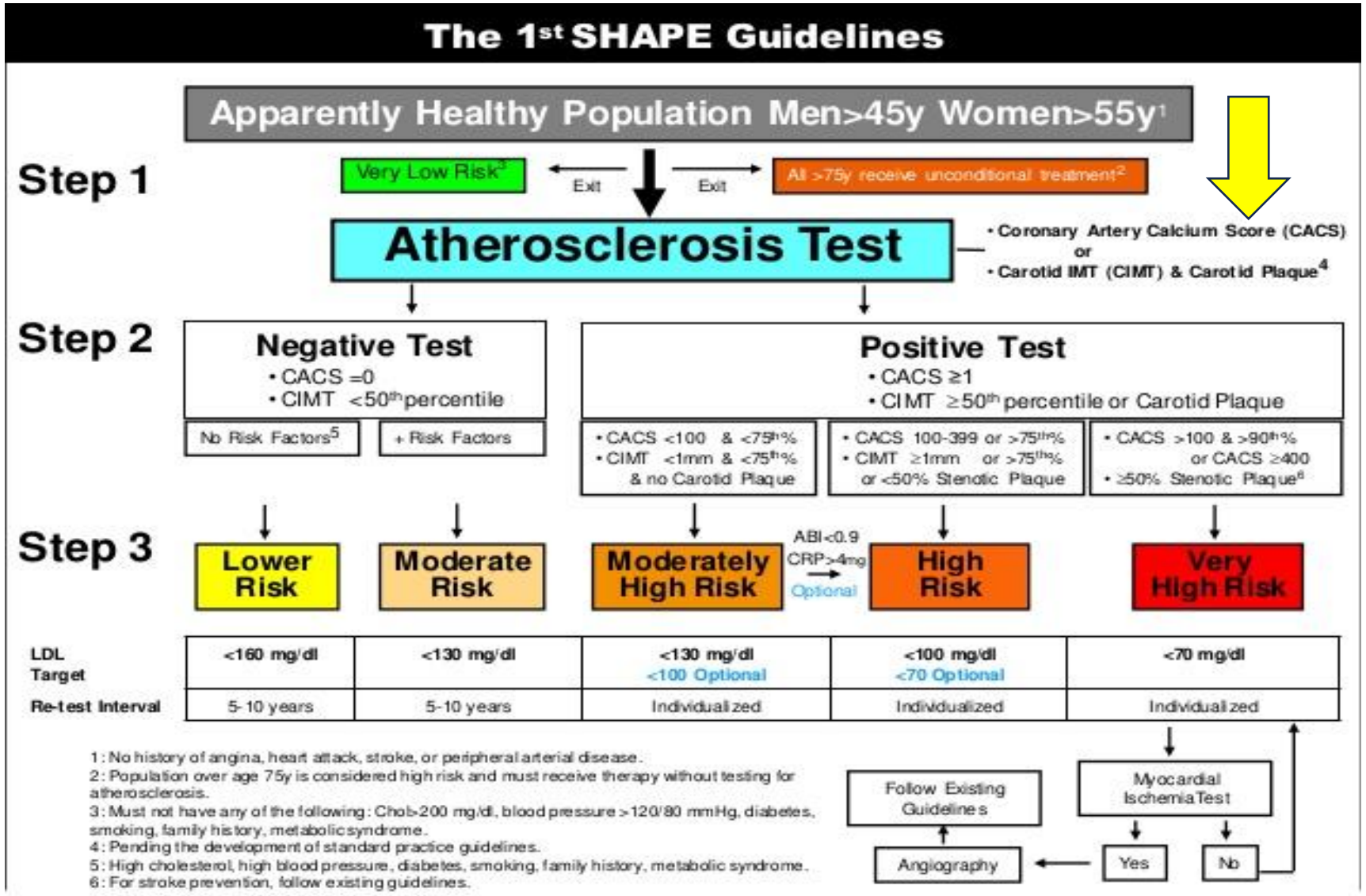
Shapesociety.org



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Coronary artery calcium score (CACS): $100

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.*

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12 Year Survival After a Coronary Calcium CT Scan. Would Rather Be 0–10 or >1000?

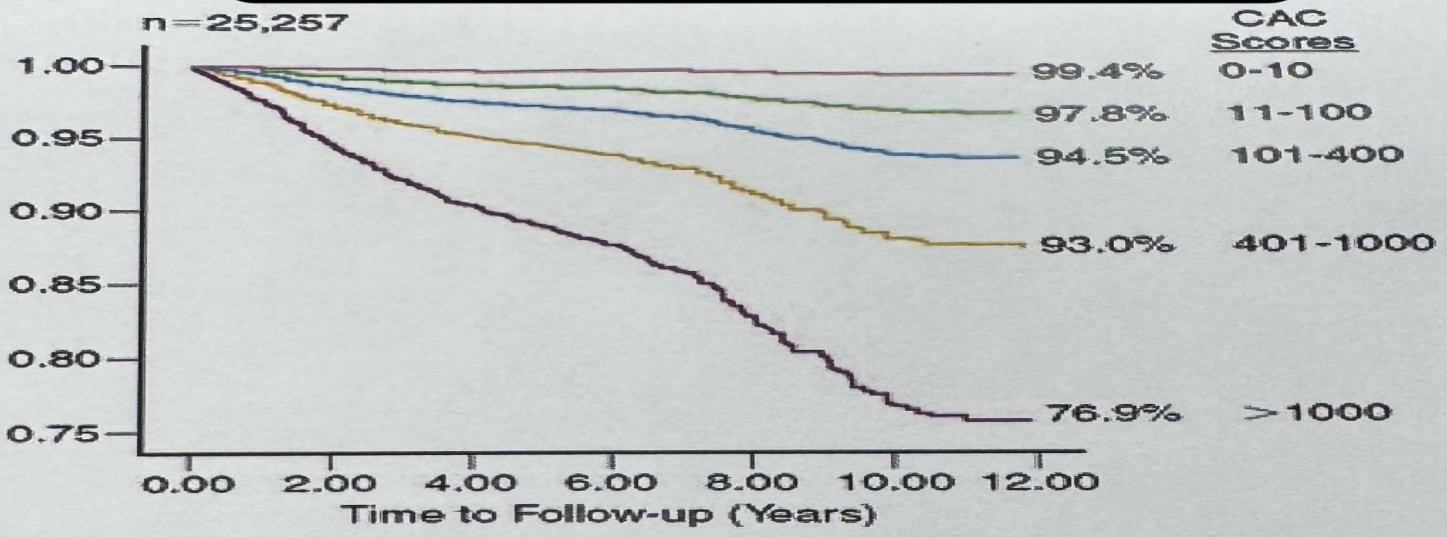

Figure 20-8 Survival rates in subjects in progressive qu
(CAC) scores. The graph shows progressively signifi
quintiles of CAC scores (<10, 11-100, 101-400, 401-100
up. The increased separation of the curves elucidates th
of CAC.

(From Budoff MJ, Shaw LJ, Liu ST, et al: Long-term
calcification: Observations from a registry of 25,253 patie
2007.)

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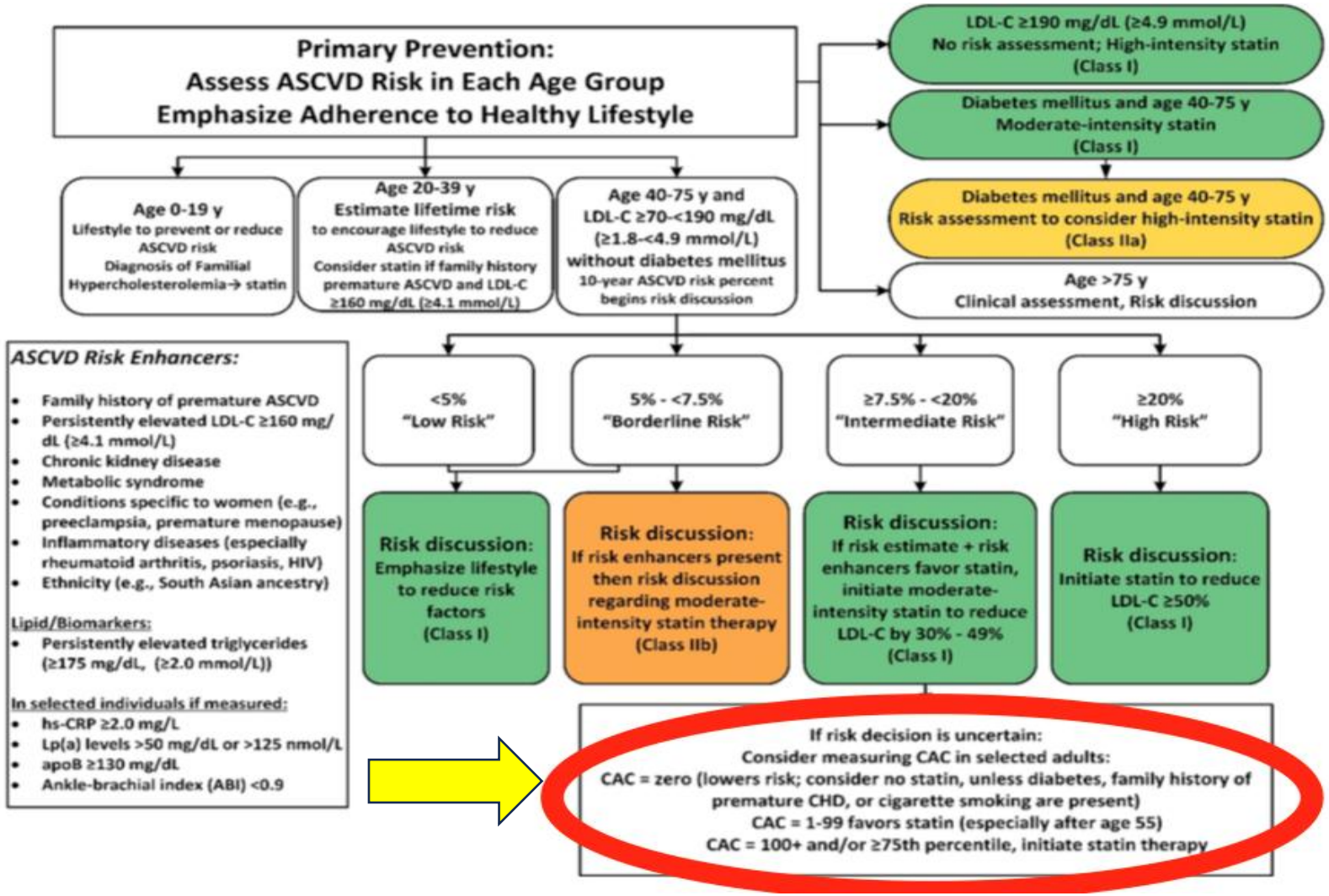
CACS: MAINSTREAM TEST AHA 2019



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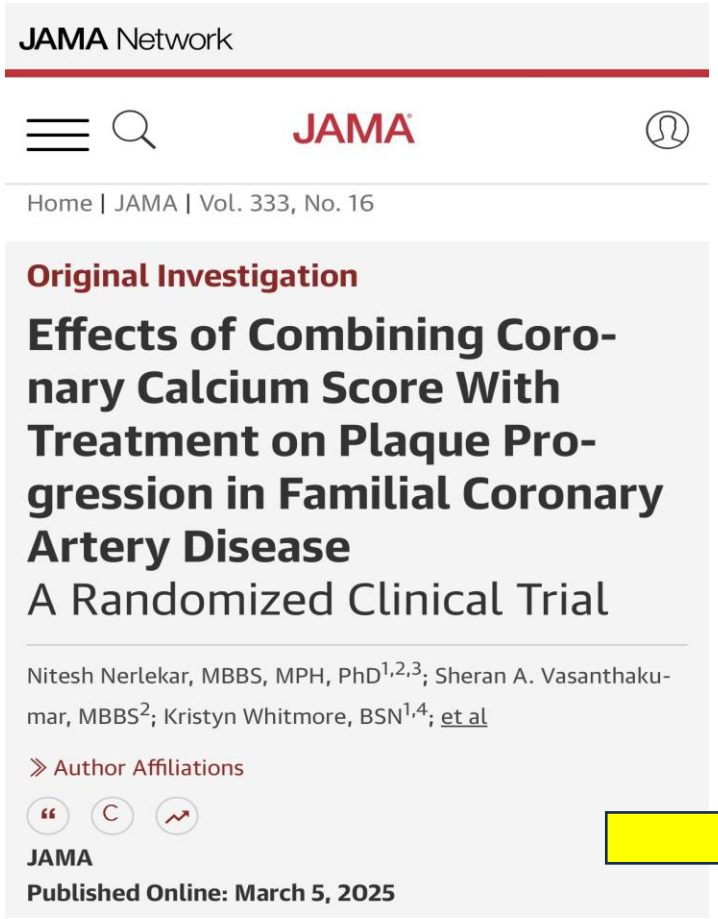
RCT: Impact of Routine calcium CT scoring



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Original Investigation

Effects of Combining Coronary Calcium Score With Treatment on Plaque Progression in Familial Coronary Artery Disease

A Randomized Clinical Trial

Nitesh Nerlekar, MBBS, MPH, PhD[1,2,3]; Sheran A. Vasanthakumar, MBBS[2]; Kristyn Whitmore, BSN[1,4]; et al

Author Affiliations

JAMA

Published Online: March 5, 2025

Key Points

Question Does the use of coronary artery calcium (CAC) scoring in intermediate-risk patients with a family history of premature coronary artery disease (CAD) lead to less progression of coronary atheroma in follow-up?

Findings Intermediate-risk participants with CAC score greater than 0 and less than 400 were randomized to usual or CAC score–informed care (which included 40 mg of atorvastatin). The CAC score–informed group showed a sustained reduction in total and low-density lipoprotein cholesterol and less progression of total, noncalcified, and fibrofatty and necrotic core plaque volumes at 3 years. The association of CAC score guidance with these plaque volume changes was independent of baseline plaque volume and risk factors.

Meaning CAC score–informed preventive strategies were associated with less plaque progression in intermediate-risk patients.

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Guideline Essentials:

American Heart Association

ADAPTED FROM:

2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia

American Heart Association.

AHA Clinical PPTX

Table 1.
Applying Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care

CLASS (STRENGTH) OF RECOMMENDATION	LEVEL (QUALITY) OF EVIDENCE‡
CLASS 1 (STRONG) **Benefit >>> Risk** **Suggested phrases for writing recommendations:** • Is recommended • Is indicated/useful/effective/beneficial • Should be performed/administered/other • Comparative-Effectiveness Phrases†: – Treatment/strategy A is recommended/indicated in preference to treatment B – Treatment A should be chosen over treatment B	**LEVEL A** • High-quality evidence‡ from more than 1 RCT • Meta-analyses of high-quality RCTs • One or more RCTs corroborated by high-quality registry studies
CLASS 2a (MODERATE) **Benefit >> Risk** **Suggested phrases for writing recommendations:** • Is reasonable • Can be useful/effective/beneficial • Comparative-Effectiveness Phrases†: – Treatment/strategy A is probably recommended/indicated in preference to treatment B – It is reasonable to choose treatment A over treatment B	**LEVEL B-R (Randomized)** • Moderate-quality evidence‡ from 1 or more RCTs • Meta-analyses of moderate-quality RCTs
CLASS 2b (Weak) **Benefit ≥ Risk** **Suggested phrases for writing recommendations:** • May/might be reasonable • May/might be considered • Usefulness/effectiveness is unknown/unclear/uncertain or not well-established	**LEVEL B-NR (Nonrandomized)** • Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies • Meta-analyses of such studies
CLASS 3: No Benefit (MODERATE) **Benefit = Risk** **Suggested phrases for writing recommendations:** • Is not recommended • Is not indicated/useful/effective/beneficial • Should not be performed/administered/other	**LEVEL C-LD (Limited Data)** • Randomized or nonrandomized observational or registry studies with limitations of design or execution • Meta-analyses of such studies • Physiological or mechanistic studies in human subjects
CLASS 3: Harm (STRONG) **Risk > Benefit** **Suggested phrases for writing recommendations:** • Potentially harmful • Causes harm • Associated with excess morbidity/mortality	**LEVEL C-EO (Expert Opinion)** • Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Concepts of expert opinion can be based on clinical experience sus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendation (COR 1 and 2a; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely-used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

American Heart Association.

Blumenthal, R. S., Morris, P. B., et al. 2026 ACC/AHA Guideline on the Management of Dyslipidemia. *Circulation*.

Screening in Adults and Children

COR	RECOMMENDATIONS
1	In adults, screening with a lipid profile is recommended beginning at age 19 years and at least every 5 years thereafter to identify treatable ASCVD risk, with frequent screening recommended for individuals with additional ASCVD risk factors.
1	In children 9 to 11 years of age not previously tested, it is recommended to screen with a lipid profile to identify familial hypercholesterolemia (FH) and other significant lipid disorders.
2a	In individuals with first- or second-degree relatives with premature ASCVD, severe hypercholesterolemia, or FH, it is reasonable to perform screening with a single lipid profile (eg, cascade screening) starting at ≥2 years of age to identify FH.

Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; and FH, familial hypercholesterolemia.

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Measurement of TC, LDL-C, HDL-C, Triglycerides, and Non-HDL-C in Adults and Children

COR	RECOMMENDATIONS
1	A standard nonfasting or fasting lipid profile is recommended to document baseline lipid levels, estimate ASCVD risk, and guide initiation of LLT.
1	With a family history of dyslipidemia or premature ASCVD, a personally known or suspected disorder in TG metabolism, or whose nonfasting lipid profile reveals a TG level ≥400 mg/dL (≥4.5 mmol/L), a fasting lipid profile should be performed to more accurately estimate the LDL-C level.
1	In those who have undergone a standard lipid profile, use of either the Martin/Hopkins equation or the Sampson/National Institutes of Health (NIH) equation is preferred over calculation by the Friedewald equation to estimate LDL-C.

Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein-cholesterol; LLT, lipid-lowering therapy; NIH, National Institutes of Health; non-HDL-C, non-high-density lipoprotein cholesterol; and TG, triglycerides.

Blumenthal, R.S., Morris, P.B., et al. 2026 ACC/AHA Guideline on the Management of Dyslipidemia. *Circulation*.

Measurement of TC, LDL-C, HDL-C, Triglycerides, and Non-HDL-C in Adults and Children (continued)

COR	RECOMMENDATIONS
1	In those who have undergone a standard lipid profile, use of either the Martin/Hopkins equation or Sampson/NIH equation is preferred over direct LDL-C measurement (other than by beta-quantification) to estimate LDL-C.
1	In those who have undergone a standard lipid profile, reporting of non–HDL-C is recommended for ASCVD risk assessment and to guide initiation and monitoring of LLT.
3: No Benefit	Routine advanced lipoprotein testing to assess lipoprotein subclasses and parameters such as LDL particle size is not recommended to estimate ASCVD risk or guide the initiation of LLT.

Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein-cholesterol; LLT, lipid-lowering therapy; NIH, National Institutes of Health; non-HDL-C, non-high-density lipoprotein cholesterol; and TG, triglycerides.

Blumenthal, R.S., Morris, P.B., et al. 2026 ACC/AHA Guideline on the Management of Dyslipidemia. *Circulation*.

Ancillary Risk Markers

Measures all atherogenic particles

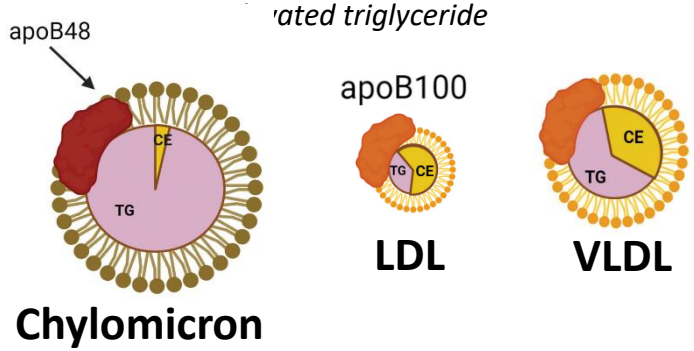
More accurate compared to LDL-C

Screening with Apolipoprotein B

In adults on LLT, particularly those with ASCVD, type 2 diabetes, and/or elevated TG, measurement of apoB is reasonable to guide decisions regarding further therapeutic intensification once LDL-C and/or Non-HDL-C goals are achieved. (2a)

In adults not on LLT, measurement of apoB may be reasonable to enhance ASCVD risk assessment, guide initiation of LLT, and characterize inherited lipid disorders. (2b)

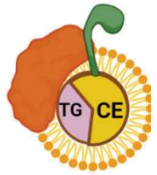
Particularly for secondary prevention, metabolic syndrome, diabetes, ...ated triglyceride



Screening with Lp(a)

Measurement of Lp(a) in all adults is recommended at least once for ASCVD risk assessment. (1)

In those with FH, premature ASCVD, or high Lp(a), cascade testing of 1st-degree relatives is recommended. (1)



Lp(a)

Lp (a) in nmol/L	ASCVD relative risk
450	4x
375	3x
250	2x
125	1.4x
75	Reference

Abbreviations: ApoB indicates apolipoprotein B; ASCVD, atherosclerotic cardiovascular disease; FH, familial hypercholesterolemia; LDL-C, low-density lipoprotein cholesterol; LLT, lipid-lowering treatment; Lp(a), lipoprotein(a); HDL-C, high-density lipoprotein cholesterol; and VLDL, very low-density lipoprotein.

Graphics from De Oliveira-Gomes, Diana et al. "Apolipoprotein B: Bridging the Gap Between Evidence and Clinical Practice." *Circulation* vol. 150,1 (2024): 62-79. doi:10.1161/CIRCULATIONAHA.124.068885

American Heart Association.

Lipoprotein Goals for ASCVD Risk Reduction

Patient population	LDL-C <100 mg/dL (2.6 mmol/L) Non-HDL-C <130 mg/dL (3.4 mmol/L)	LDL-C <70 mg/dL (1.8 mmol/L) Non-HDL-C <100 mg/dL (2.6 mmol/L)	LDL-C <55 mg/dL (1.4 mmol/L) Non-HDL-C <85 mg/dL (2.2 mmol/L)
Primary prevention	PREVENT-ASCVD < 10% • If TG ≥ 150 mg/dL to 499 mg/dL, apoB goal: <90 mg/dL	PREVENT-ASCVD ≥ 10% • If TG ≥ 150 mg/dL to 499 mg/dL, apoB goal: <70 mg/dL	N/A
Severe hypercholesterolemia	**Without** FH, ASCVD risk factors, and subclinical atherosclerosis	**With** FH, ASCVD risk factors, and subclinical atherosclerosis	Severe hypercholesterolemia or HeFH with clinical ASCVD
Diabetes	**Without** ASCVD risk factors or diabetes-specific risk modifiers • apoB goal: <90 mg/dL	**Without** ASCVD risk factors or diabetes-specific risk modifiers • apoB goal: <70 mg/dL	N/A
Subclinical atherosclerosis	CAC = 1-99 AU and <75th percentile for age, sex, and race	• CAC ≥ 100 to 299 AU or ≥75th percentile for age, sex, and race • CAC ≥ 300 to 999 AU – Optional goal: LDL-C <55 mg/dL, non-HDL-C <85 mg/dL, and consider apoB goal <55 mg/dL	CAC ≥ 1000 AU
Hypertriglyceridemia	<50 y old with no additional risk enhancers	• With clinical ASCVD not at very high risk – apoB goal: <70 mg/dL • Age 40-75 y with ≥1 ASCVD risk factor – apoB goal: <70 mg/dL	• With clinical ASCVD at very high risk – apoB goal: <55 mg/dL
Clinical ASCVD	N/A	Not at very high risk • Optional goal: LDL-C <55 mg/dL, non-HDL-C <85 mg/dL, and consider apoB goal <55 mg/dL	• At very high risk – apoB goal: <55 mg/dL • With CKD

Abbreviations: ApoB indicates apolipoprotein B; ASCVD, atherosclerotic cardiovascular disease; AU, Agatston units; CAC, coronary artery calcium; CKD, chronic kidney disease; FH, familial hypercholesterolemia; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; and TG, triglycerides.

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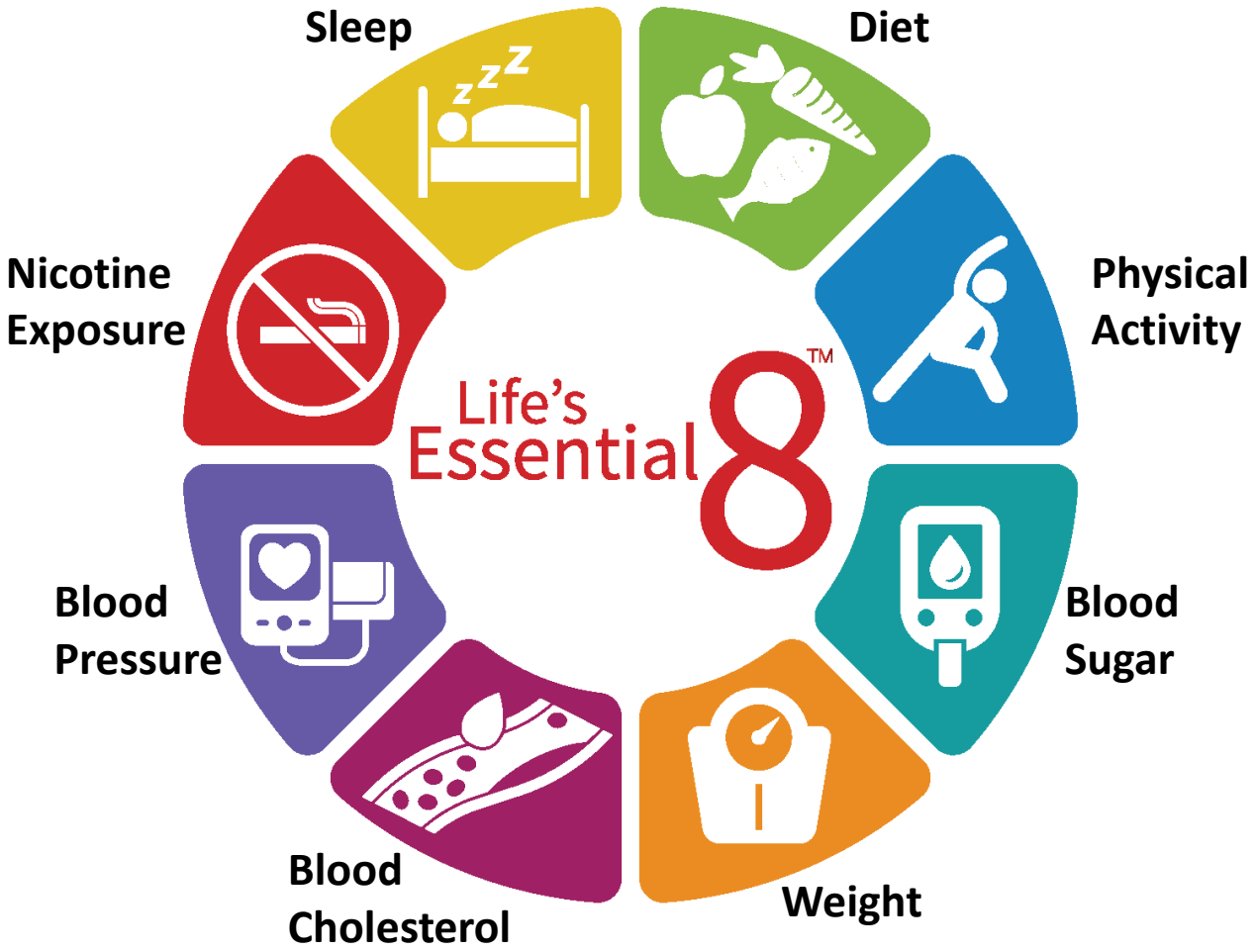
Primordial Prevention of Dyslipidemia: Childhood Through Adulthood



COR	RECOMMENDATIONS
1	In children and healthy adults, healthy dietary patterns, regular physical activity, maintenance of a healthy weight, healthy sleep, stress management, and avoidance of tobacco products should be promoted and reinforced lifelong to reduce the risk for dyslipidemia and ASCVD.

Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease.

Role of Individualized Benefit-Risk Discussion

Information

Clinician provides the best available evidence for treatment options, including the risks & benefits of each option

Patient-Centered Care

Treatment & care options take into consideration individual values & preferences

Shared Decision-Making

A collaborative decision about treatment or care is documented and shared with relevant stakeholders

COR	RECOMMENDATIONS
1	In individuals with dyslipidemia, clinicians and their patients should engage in a discussion of the patient's ASCVD risk, healthy lifestyle as the foundation of risk reduction, expected risk reduction benefits from LLT, possible harms and DDI, costs, and patient preferences to make individualized treatment decisions and/or consider additional options for evaluation to aid in decision-making.

Discussion should emphasize

- Patient's ASCVD risk
- Consideration of additional options for evaluation
- Healthy lifestyle as the foundation of risk reduction
- Expected risk reduction benefits from lipid-lowering therapies
- Possible harms and drug-drug interactions
- Costs
- Administration frequency
- Patient preferences

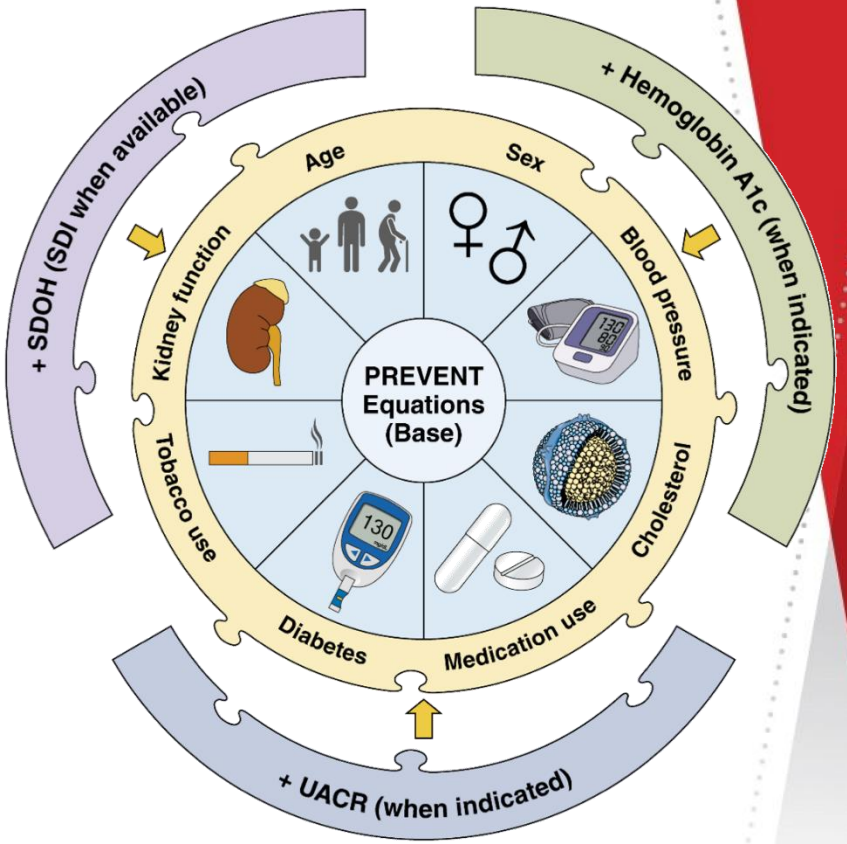
Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; DDI, drug-drug interaction; and LLT, lipid-lowering therapy.

PREVENT-ASCVD Risk Calculator

COR	RECOMMENDATIONS
1	PREVENT-ASCVD equations should be used for risk assessment in adults aged 30-79 years without ASCVD or subclinical atherosclerosis, with LDL-C 70-189 mg/dL.

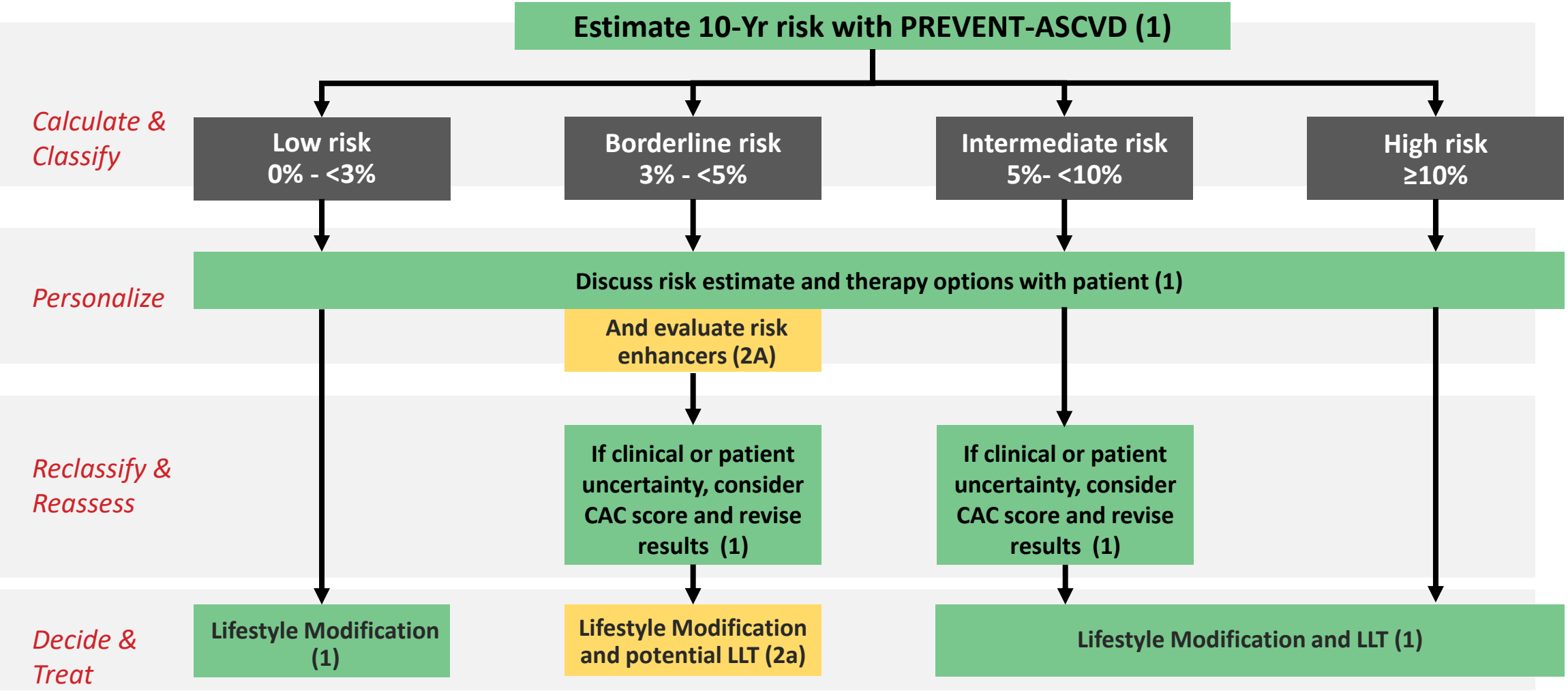
Approximate Equivalent Ranges of 10-yr ASCVD Risk Estimates

RISK	POOLED COHORT EQUATIONS	PREVENT-ASCVD
Low	<5%	<3%
Borderline	5 - <7.5%	3 to <5%
Intermediate	7.5 - <20%	5 to <10%
High	≥20%	≥10%



Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease**;** LDL-C, low-density lipoprotein cholesterol; PREVENT, Predicting Risk of cardiovascular disease EVENTS; SDI, social deprivation index; SDOH, social determinants of health; and UACR, urine albumin-to-creatinine ratio.

Calculate, Personalize, Reclassify (CPR) Framework



Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; CAC, coronary artery calcium; LLT, lipid-lowering therapy; and PREVENT, Predicting Risk of cardiovascular disease EVENTS.

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Blumenthal, R.S., Morris, P.B., et al. 2026 ACC/AHA Guideline on the Management of Dyslipidemia. *Circulation*.

Risk Enhancers

- History of premature ASCVD in a parent or sibling (onset age <55 y for men, <65 y for women)
- Higher risk ancestry (eg, South Asian, Filipino)
- High polygenic risk (if measured)
- Chronic inflammatory diseases (eg, systemic lupus, rheumatoid arthritis, advanced psoriasis, inflammatory arthritis)
- Lp(a) ≥125 nmol/L or ≥50 mg/dL
- hsCRP ≥2 mg/L on >1 occasion (if measured)
- TG persistently ≥175 mg/dL (2 mmol/L) (if nonfasting) and ≥150 mg/dL (1.7 mmol/L) (if fasting)
- CKM syndrome
- LDL-C persistently ≥160-189 mg/dL (4.1-4.9 mmol/L), non–HDL-C≥190-219 mg/dL or apoB ≥120 mg/dL
- Reproductive risk markers (premature menopause, preeclampsia, gestational diabetes, gestational hypertension, preterm delivery)

COR	RECOMMENDATIONS
2a	In adults without ASCVD with a borderline 10-year ASCVD risk estimate (3% to <5%) by the PREVENT-ASCVD equations, consideration of risk-enhancers is reasonable to personalize risk assessment and the potential benefit of initiating LLT as an adjunct to lifestyle management to reduce ASCVD risk.
2a	In adults without ASCVD with a borderline 10-year ASCVD risk estimate (3% to <5%) by the PREVENT-ASCVD equations, if high-sensitivity C-reactive protein (hsCRP) is measured and is ≥2 mg/L on 2 successive occasions with no identifiable underlying cause of hsCRP elevation, high-intensity statin therapy can be useful to reduce the risk of ASCVD events.

Abbreviations: ApoB indicates apolipoprotein B; ASCVD, atherosclerotic cardiovascular disease; HDL-C, high-density-lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein, LDL-C, low-density lipoprotein cholesterol; LLT, lipid-lowering therapy; and PREVENT, Predicting Risk of CVD Events.

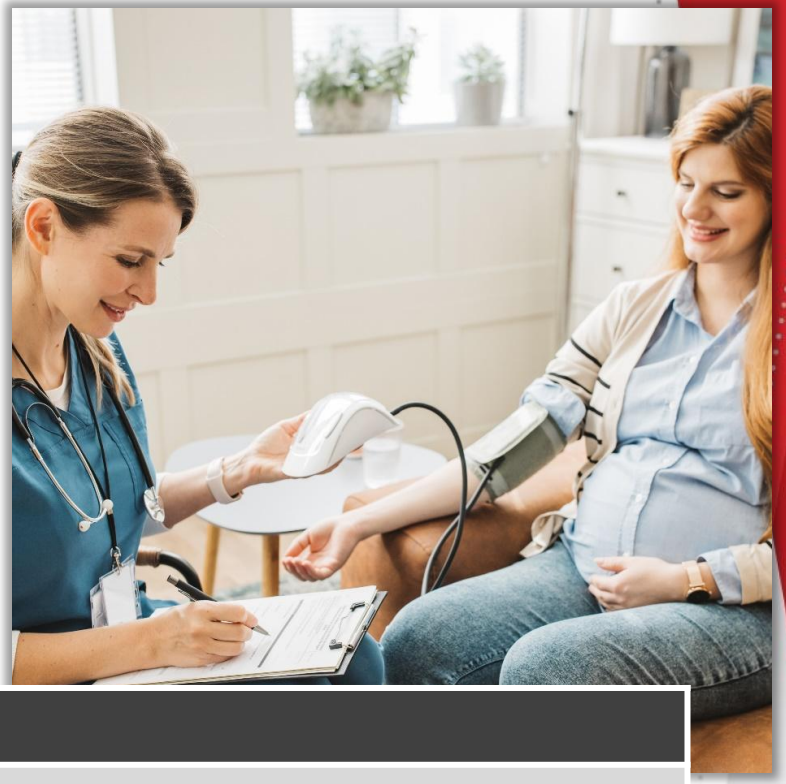
Reproductive Risk Markers

Adverse Pregnancy Outcomes with a Stronger Association with ASCVD Events

- Hypertensive disorders of pregnancy (preeclampsia, gestational hypertension)
- Gestational diabetes
- Small for gestational age (birthweight <10th percentile)
- Preterm delivery (before 37 weeks of gestation)
- Recurrent spontaneous pregnancy loss

Other Reproductive Risk Markers

- Early menarche (<10 yr old)
- Early menopause (<45 yr), especially if premature (<40 yr)
- Polycystic ovarian syndrome and irregular menses



COR	RECOMMENDATIONS
2a	In adults without ASCVD, consideration of reproductive risk markers, such as early menopause (<45 years of age) and history of adverse pregnancy outcomes is reasonable to personalize ASCVD risk assessment when considering the potential benefit of initiating LLT as an adjunct to lifestyle management for primary ASCVD prevention.

Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; and LLT, lipid-lowering therapy.

Primary Prevention 30–79 Years Without ASCVD

Adults with LDL - C 70 - 189 mg/dL

→ **Health behavior counseling (1)**

→ **Calculate 10-yr and 30-yr in ages 30-59 ASCVD risk using PREVENT-ASCVD (1)** **AND** **Have benefit-risk discussion (1)**

- Low 10-yr Risk **(<3%)**
- Borderline 10-yr Risk **(3%-<5%)**
- Intermediate 10-yr Risk **(5%-<10%)**
- High 10-yr Risk **(≥10%)**

Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol; and PREVENT-ASCVD, Predicting Risk of cardiovascular disease EVENTS–ASCVD equations.

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Primary Prevention 30-79 Years Without ASCVD

Low-Intermediate 10-y Risk (<3%-10%)	
COR	**RECOMMENDATIONS**
1	**Low risk** (<3%)+ LDL<160 mg/dL → Health behavior counseling.
2a	**Low risk** + LDL 160–189 mg/dL or high 30-yr risk → Start moderate statin. Goal: ≥30% LDL-C reduction; LDL-C<100 mg/dL and non-HDL-C <130 mg/dL
2a	**Borderline risk (3%-<5%)** → Moderate statin reasonable. Goal: ≥30% LDL-C reduction; LDL-C<100 mg/dL and non-HDL-C <130 mg/dL
1	**Intermediate risk (5%-<10%)** → Start moderate- to high-intensity statin.
AND	
2a	**Goal:** LDL-C<100 mg/dL and non-HDL-C <130 mg/dL

Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; and non-HDL-C, non–high-density lipoprotein cholesterol.

Blumenthal, R.S., Morris, P.B., et al. 2026 ACC/AHA Guideline on the Management of Dyslipidemia. *Circulation*.

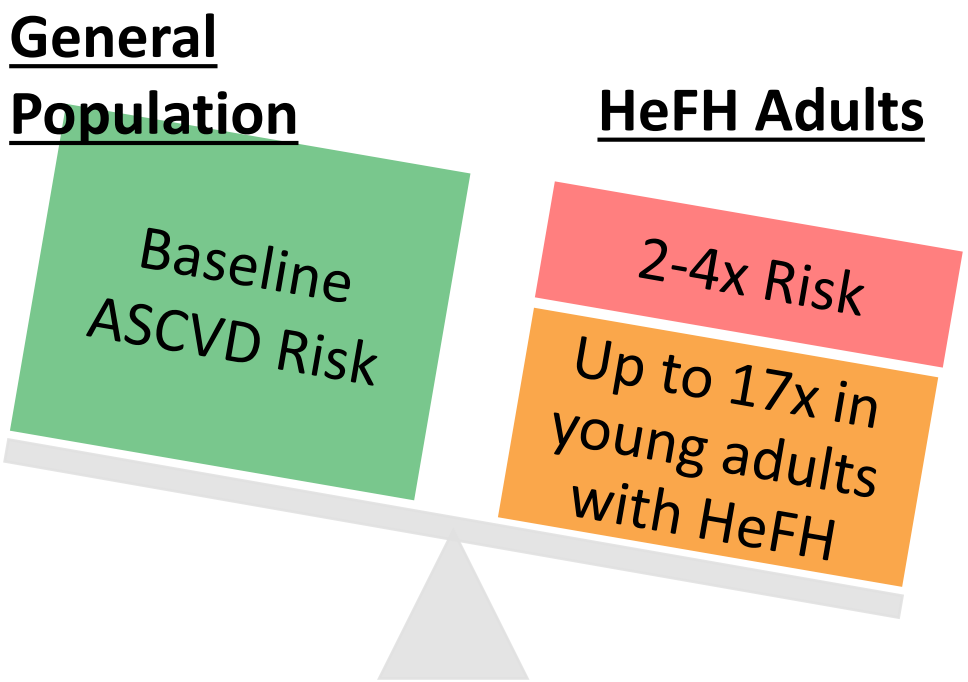
Primary Prevention 30-79 Years Without ASCVD (continued)

High 10-y Risk (≥10%)	
COR	**RECOMMENDATIONS**
1	Start high-intensity statin.
2a	**Goal:** ≥50% LDL-C reduction; LDL-C<70 mg/dL and non-HDL-C <100 mg/dL
2a	If LDL-C and non-HDL-C goals still not achieved, add ezetimibe.
2b	If LDL-C and non-HDL-C goals still not achieved, add PCSK9 mAb or bempedoic acid.

Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; non-HDL-C, non–high-density lipoprotein cholesterol; and PCSK9, proprotein convertase subtilisin/kexin type 9.

Blumenthal, R.S., Morris, P.B., et al. 2026 ACC/AHA Guideline on the Management of Dyslipidemia. *Circulation*.

Role of Risk Assessment in Heterozygous Familial Hypercholesterolemia



COR	RECOMMENDATIONS
2b	In adults with HeFH, FH-specific risk scores may be useful in predicting short-term ASCVD risk.
3: Harm	In adults with HeFH, standard risk assessment tools developed for the general population should NOT be used to calculate 10-year or 30-year ASCVD risk.

Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; CAC, coronary artery calcium; FH, familial hypercholesterolemia; and HeFH, heterozygous familial hypercholesterolemia.

Severe Hypercholesterolemia

What is severe hypercholesterolemia?

- LDL-C ≥**190 mg/dL** (or non-HDL-C >220, apoB ≥140)
- Very high *lifetime* ASCVD risk even without other risk factors
- Often due to **long-term LDL exposure**

Always exclude secondary causes first:
ketogenic/high saturated fat diet, hypothyroidism, CKD, nephrotic syndrome, steroids, etc.

COR	RECOMMENDATIONS
1	Exclude secondary causes.
1	Start maximally tolerated statin.
1	If no ASCVD/FH → add therapy to reach LDL<100.
1	If FH and CAC → intensify therapy to LDL<70.
1	If ASCVD → intensify to LDL<55.
2a	Inclisiran reasonable if LDL≥100 on therapy.

Abbreviations: ApoB indicates apolipoprotein B; ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; FH, familial hypercholesterolemia; LDL-C, low-density lipoprotein cholesterol; and non-HDL-C, non–high-density lipoprotein cholesterol.

Diabetes without ASCVD

- Most adults 40–75 years with diabetes = **intermediate or high ASCVD risk**
- First events in diabetes carry **higher morbidity and mortality**

Primary LDL Treatment Strategy

- Moderate-intensity statin indicated for ages 40–75 yrs
  - **Goal:** ≥30–49% LDL mg/dL reduction, LDL <100 mg/dL
- High-intensity statin reasonable if multiple ASCVD risk factors
  - **Goal:** ≥50% LDL reduction, LDL <70 mg/dL

COR	RECOMMENDATIONS
1	**Age 40–75 years → moderate statin (LDL<100 mg/dL).**
1	Statin-intolerant: ezetimibe/PCSK9/bempedoic.
2a	**Multiple risk factors → high-intensity statin (LDL<70 mg/dL).**
2b	TG 150–499 mg/dL→ consider icosapent ethyl.
2b	10-year risk ≥10% → consider ezetimibe/PCSK9.
2b	Age >75 years→ moderate statin reasonable.
2b	Age 20–39 years with long-duration diabetes → consider statin.

Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; LDL, and low-density lipoprotein cholesterol.

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Criteria for Defining “At Very High Risk” in ASCVD Patients

At Very High Risk

≥ 2 Major ASCVD Events

OR

1 Major ASCVD Event
+
≥2 High Risk Conditions

Major ASCVD Events

- Consider drug-drug interactions between lipid-lowering therapies and antiretroviral therapies.

High Risk Conditions

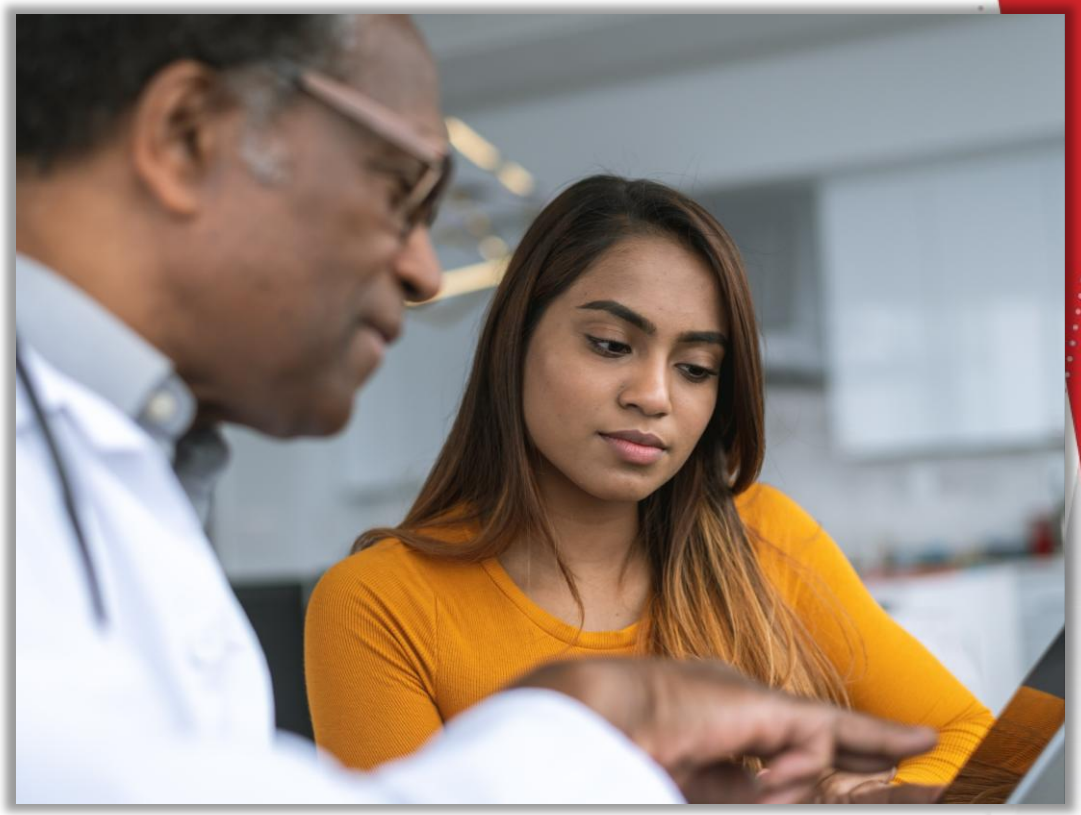
- Age ≥65
- Coronary bypass or percutaneous intervention
- Current smoker
- Diabetes
- Hx of congestive heart failure
- Hypertension
- LDL-C ≥ 100mg/dL despite maximally tolerated statin + ezetimibe

Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; and LDL-C, low-density lipoprotein cholesterol.

Blumenthal, R.S., Morris, P.B., et al. 2026 ACC/AHA Guideline on the Management of Dyslipidemia. *Circulation*.

Secondary Prevention of ASCVD in Adults not at Very High Risk

Clinical ASCVD in adults not at very high risk:	
COR	**RECOMMENDATIONS**
1	High-intensity statin therapy should be initiated to achieve ≥50% reduction in LDL-C and a goal of LDL-C <70 mg/dL and non-HDL-C <100 mg/dL to reduce the risk of recurrent ASCVD events.
2a	For those on on maximally tolerated statin therapy, it is reasonable to add ezetimibe, a PCSK9 mAb, or bempedoic acid* to achieve a goal of LDL-C <70 mg/dL and non-HDL-C <100 mg/dL to reduce the risk of ASCVD events.
2a	For those on on maximally tolerated statin therapy, it is reasonable to add ezetimibe, a PCSK9 mAb, or bempedoic acid to achieve a goal LDL-C <55 mg/dL and non-HDL-C <85 mg/dL and to reduce the risk of ASCVD events.



Abbreviations: ASCVD, atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol; non-HDL-C, non–high-density lipoprotein cholesterol; and PCSK9, proprotein convertase subtilisin/kexin type 9.

American Heart Association.

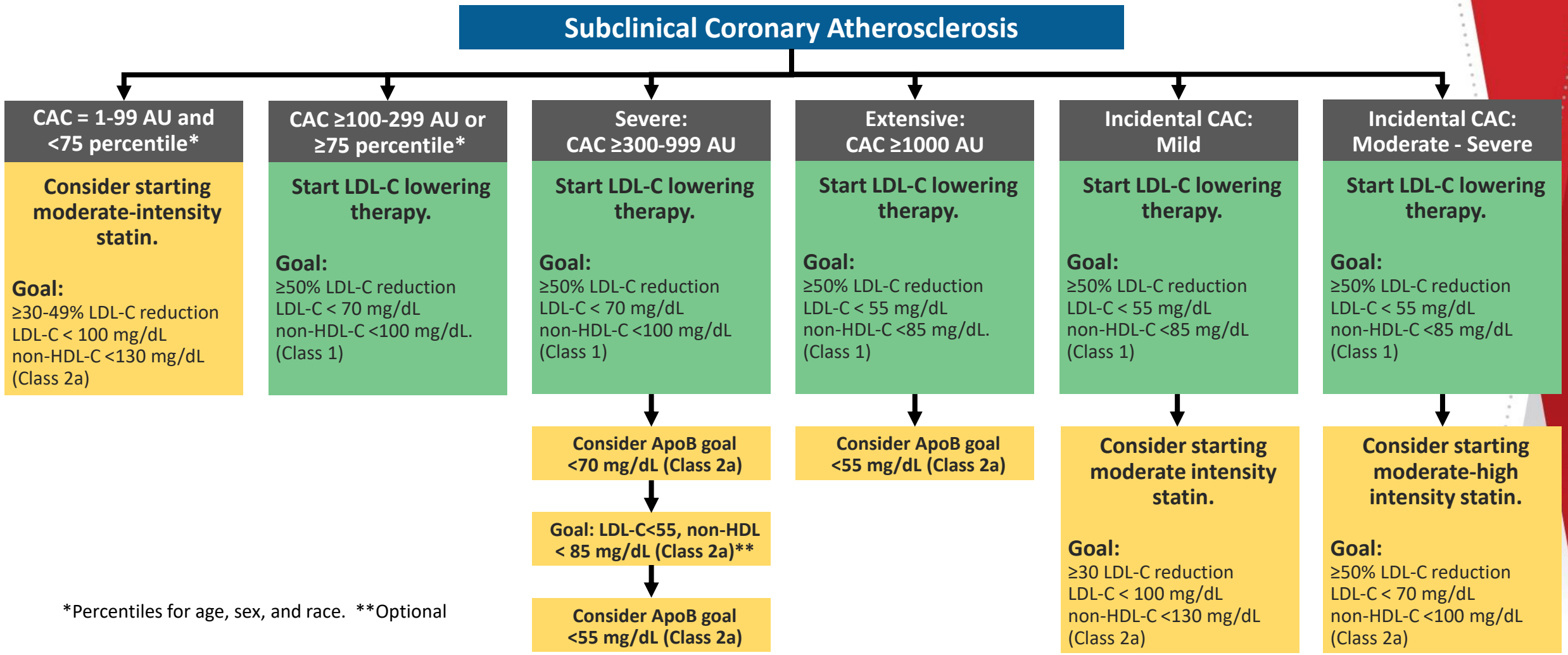
Secondary Prevention of ASCVD in Adults at Very High Risk

Clinical ASCVD in adults at very high risk:	
COR	**RECOMMENDATIONS**
1	High-intensity statin therapy should be initiated to achieve ≥50% lowering in LDL-C and a goal LDL-C <55 mg/dL and non-HDL-C <85 mg/dL and to reduce the risk of ASCVD events.
1	For those on maximally tolerated statin therapy, ezetimibe and/or a PCSK9 mAb should be added to achieve a goal of LDL-C <55 mg/dL and non-HDL-C <85 mg/dL to reduce risk of ASCVD events.
2a	For those on maximally tolerated statin, it is reasonable to add bempedoic acid to a statin, with or without ezetimibe and/or PCSK9 mAb, to reach an LDL-C goal <55 mg/dL and non-HDL-C <85 mg/dL to reduce the risk of ASCVD events.
2a	For those on maximally tolerated statin therapy with or without ezetimibe, it is reasonable to add inclisiran in those unable to tolerate or obtain evolocumab or alirocumab or have a strong preference for less frequent dosing to achieve an LDL-C goal <55 mg/dL and non-HDL-C <85 mg/dL.

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol; non-HDL-C, non–high-density lipoprotein cholesterol; and PCSK9, proprotein convertase subtilisin/kexin type 9.

American Heart Association.

Subclinical Coronary Atherosclerosis



*Percentiles for age, sex, and race. **Optional

Abbreviations: ApoB indicates apolipoprotein B; LDL-C, low-density lipoprotein cholesterol; and HDL-C, high-density lipoprotein cholesterol.

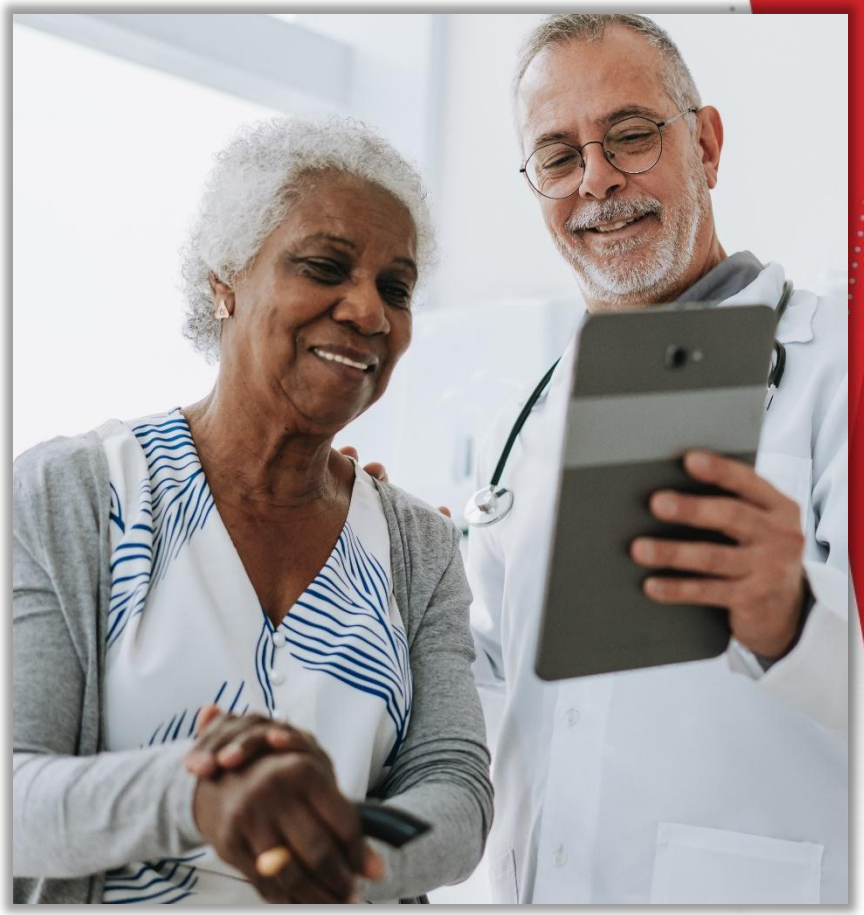
Children, Adolescents, and Young Adults

COR	RECOMMENDATIONS
1	In young adults (age 19-39), dietary, physical activity, and weight optimization recommendations should be provided to reduce cumulative atherogenic lipid exposure and lifetime ASCVD risk.
1	In children and adolescents with lipid abnormalities, lifestyle management is recommended to improve LDL-C, triglyceride, and non-HDL-C.
1	In children and adolescents ≥8 years of age with an LDL-C level persistently ≥160 mg/dL (4.1 mmol/L) and a presentation consistent with FH who do not respond sufficiently after 3 to 6 months of lifestyle management, initiation of statin and other LLT as necessary is recommended to lower LDL-C.
2a	In children and adolescents with a clinical presentation consistent with FH, genetic testing for FH-causing genetic variants can be useful to guide diagnosis, cascade testing, and treatment.

Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; FH, familial hypercholesterolemia; and LDL-C, low-density lipoprotein cholesterol.

Recommendations for Older Adults

COR	RECOMMENDATIONS
1	In older adults, the benefit-risk discussion should include patient priorities, functional status, multimorbidity, frailty, polypharmacy, and life expectancy, and should not be based solely on chronological age when considering the decision to discontinue LLT.
2a	In adults aged >75 years with an estimated life expectancy of at least 2.5 years, it may be reasonable to initiate moderate-intensity statin therapy after a clinician–patient discussion of potential benefits and risks to reduce ASCVD risk.
2a	In patients with a life expectancy of <1 year, it may be reasonable to discontinue LDL-lowering therapy to avoid unnecessary medication use or adverse medication effects.
2b	In adults aged >75 years with an estimated life expectancy of at least 2.5 years, and for whom the decision regarding LLT is uncertain, it may be reasonable to measure CAC to reclassify those with minimal (1-10) or no CAC to avoid LLT.



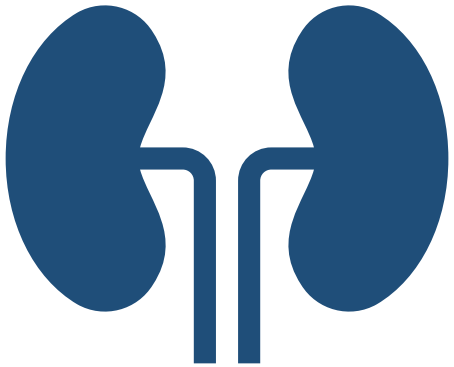
Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; CAC, coronary artery calcification; LDL, low-density lipoprotein; and LLT, lipid-lowering therapy.

Adults with Heart Failure

Adults with HFrEF	
COR	**RECOMMENDATIONS**
3: No Benefit	In adults with heart failure with reduced ejection fraction (HFrEF) who do not have clinical ASCVD or another indication for LLT, initiation of LLT is not recommended to reduce clinical events or mortality.

Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; LTT, lipid-lowering therapy; and HFrEF, heart failure with reduced ejection fraction.

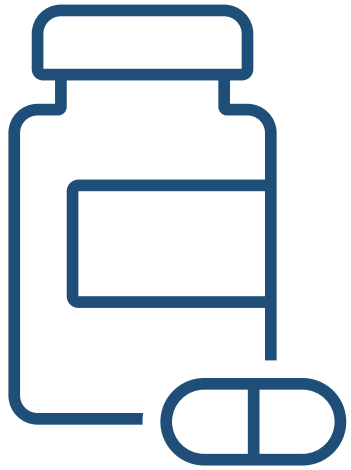
Adults with Chronic Kidney Disease



Adults with CKD	
COR	**RECOMMENDATIONS**
1	In adults 40 to 75 years of age with CKD Stage 3 or higher and an LDL-C of 70-189 mg/dL (1.8-4.9 mmol/L), moderate-intensity statin therapy (± ezetimibe) is recommended to reduce ASCVD risk.
1	In adults with CKD Stage 3 or higher and clinical ASCVD, LLT with high-intensity statin therapy (± ezetimibe) and/or a PCSK9 mAb, is recommended to achieve ≥50% reduction in LDL-C levels and a goal of LDL-C <55 mg/dL (1.4 mmol/L) and non-HDL-C <85 mg/dL (2.2 mmol/L) to reduce ASCVD risk.
2b	In adults with CKD who require maintenance hemodialysis, it may be reasonable to continue statin therapy to reduce the risk of ASCVD events. Treatment decisions should be individualized, considering expected survival, other comorbidities, and severity of ASCVD.

Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; CKD, chronic kidney disease; HDL-C, high-density lipoprotein cholesterol; HFrEF, heart failure with reduced ejection fraction; LDL-C, low-density lipoprotein cholesterol; LTT, lipid-lowering therapy; and PCSK9, proprotein convertase subtilisin/kexin type 9.

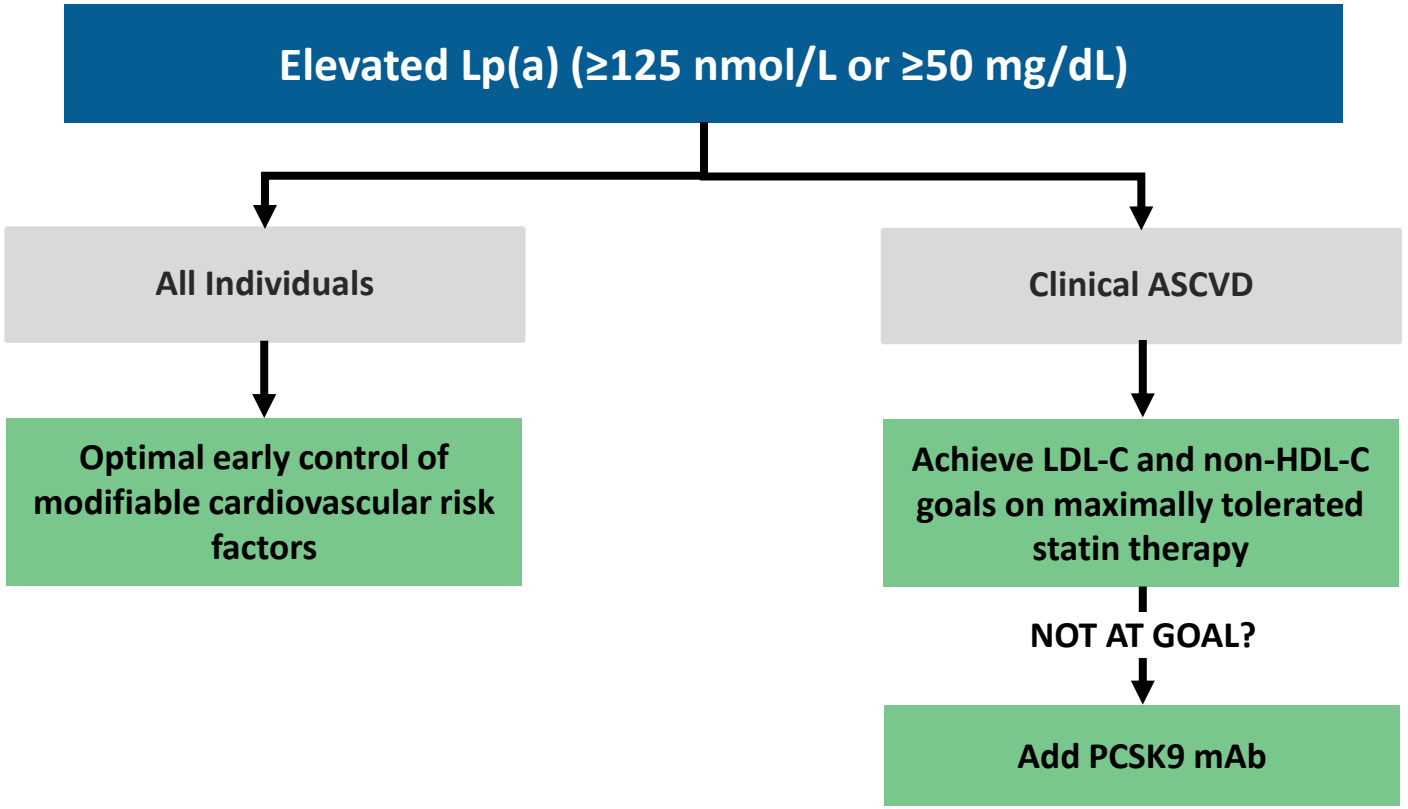
Adults with Cancer or a History of Cancer



Adults with Cancer or a History of Cancer	
COR	**RECOMMENDATIONS**
1	Adult cancer survivors with life expectancy of at least 2 years who otherwise qualify for LLT should be treated similarly to people without history of cancer to reduce the risk of ASCVD events.
1	In adults with active cancer currently on statin therapy, treatment should be continued to reduce ASCVD risk unless there is concern for a specific drug interaction or life expectancy is <1 year.
2b	In adults with active cancer, initiation of statin therapy may be considered to prevent anthracycline-induced cardiotoxicity.

Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; and LLT, lipid-lowering therapy.

Approach to Patients with Elevated Lp(a)



Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein-cholesterol; Lp(a), lipoprotein(a); mAb, monoclonal antibody; and PCSK9, Proprotein Convertase Subtilisin/Kexin type 9.

American Heart Association.

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ORIGINAL ARTICLE

Intensive LDL Cholesterol Targeting in Atherosclerotic Cardiovascular Disease

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ABSTRACT

BACKGROUND

Despite guideline recommendations, evidence from randomized trials evaluating the appropriate low-density lipoprotein (LDL) cholesterol target for secondary prevention in patients with atherosclerotic cardiovascular disease remains limited.

METHODS

In this open-label superiority trial conducted in South Korea, we randomly assigned patients with atherosclerotic cardiovascular disease in a 1:1 ratio to a target LDL cholesterol level of less than 55 mg per deciliter (1.4 mmol per liter) (intensive-targeting group) or less than 70 mg per deciliter (1.8 mmol per liter) (conventional-targeting group). The primary end point was a composite of death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, any revascularization, or hospitalization for unstable angina at 3 years. Safety was also assessed.

RESULTS

Of 3048 patients who underwent randomization, 1526 were assigned to the intensive-targeting group and 1522 to the conventional-targeting group. The median follow-up was 3.0 years. The median LDL cholesterol level during the trial was 56 mg per deciliter (1.4 mmol per liter) in the intensive-targeting group and 66 mg per deciliter (1.7 mmol per liter) in the conventional-targeting group. A primary end-point event occurred in 100 patients (Kaplan–Meier estimate of cumulative incidence, 6.6%) in the intensive-targeting group and in 147 patients (Kaplan–Meier estimate of cumulative incidence, 9.7%) in the conventional-targeting group (hazard ratio, 0.67; 95% confidence interval, 0.52 to 0.86; P=0.002). The incidence of prespecified safety end points was similar in the two trial groups, except for a lower incidence of creatinine elevation in the intensive-targeting group.

CONCLUSIONS

Among patients with atherosclerotic cardiovascular disease, targeting an LDL cholesterol level of less than 55 mg per deciliter resulted in a lower risk of cardiovascular events at 3 years than targeting a level of less than 70 mg per deciliter. (Funded by the Cardiovascular Research Center and Yuhan; Ez-PAVE ClinicalTrials.gov number, NCT04626973.)

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*A complete list of the Ez-PAVE investigators is provided in the Supplementary Appendix, available at NEJM.org.

Yong-Joon Lee and Seung-Jun Lee contributed equally to this article.

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American Heart Association.

Blumenthal, R.S., Morris, P.B., et al. 2026 ACC/AHA Guideline on the Management of Dyslipidemia. *Circulation*.

EZ-PAVE STUDY RESULTS

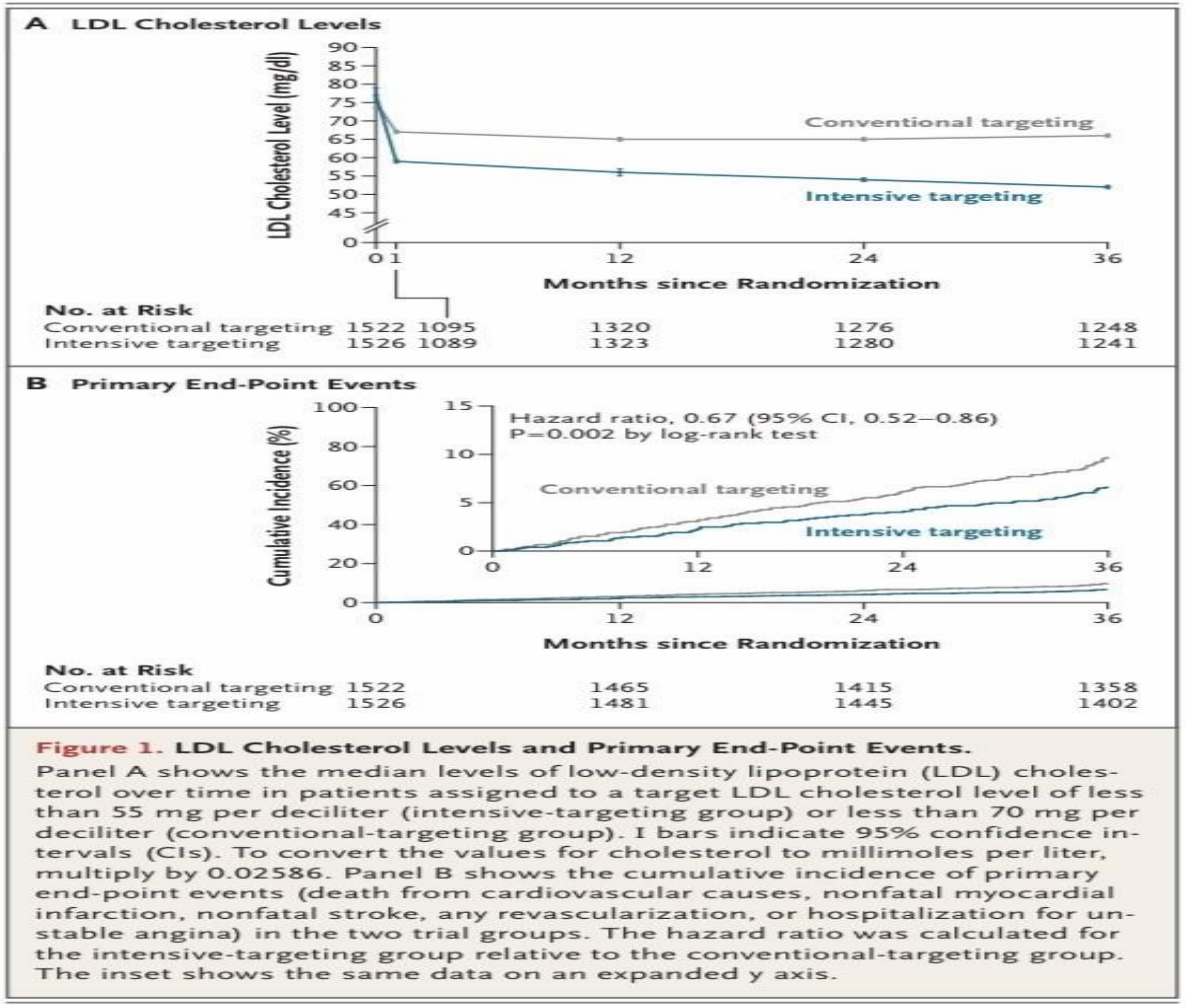

Figure 1. LDL Cholesterol Levels and Primary End-Point Events.
Panel A shows the median levels of low-density lipoprotein (LDL) cholesterol over time in patients assigned to a target LDL cholesterol level of less than 55 mg per deciliter (intensive-targeting group) or less than 70 mg per deciliter (conventional-targeting group). I bars indicate 95% confidence intervals (CIs). To convert the values for cholesterol to millimoles per liter, multiply by 0.02586. Panel B shows the cumulative incidence of primary end-point events (death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, any revascularization, or hospitalization for unstable angina) in the two trial groups. The hazard ratio was calculated for the intensive-targeting group relative to the conventional-targeting group. The inset shows the same data on an expanded y axis.

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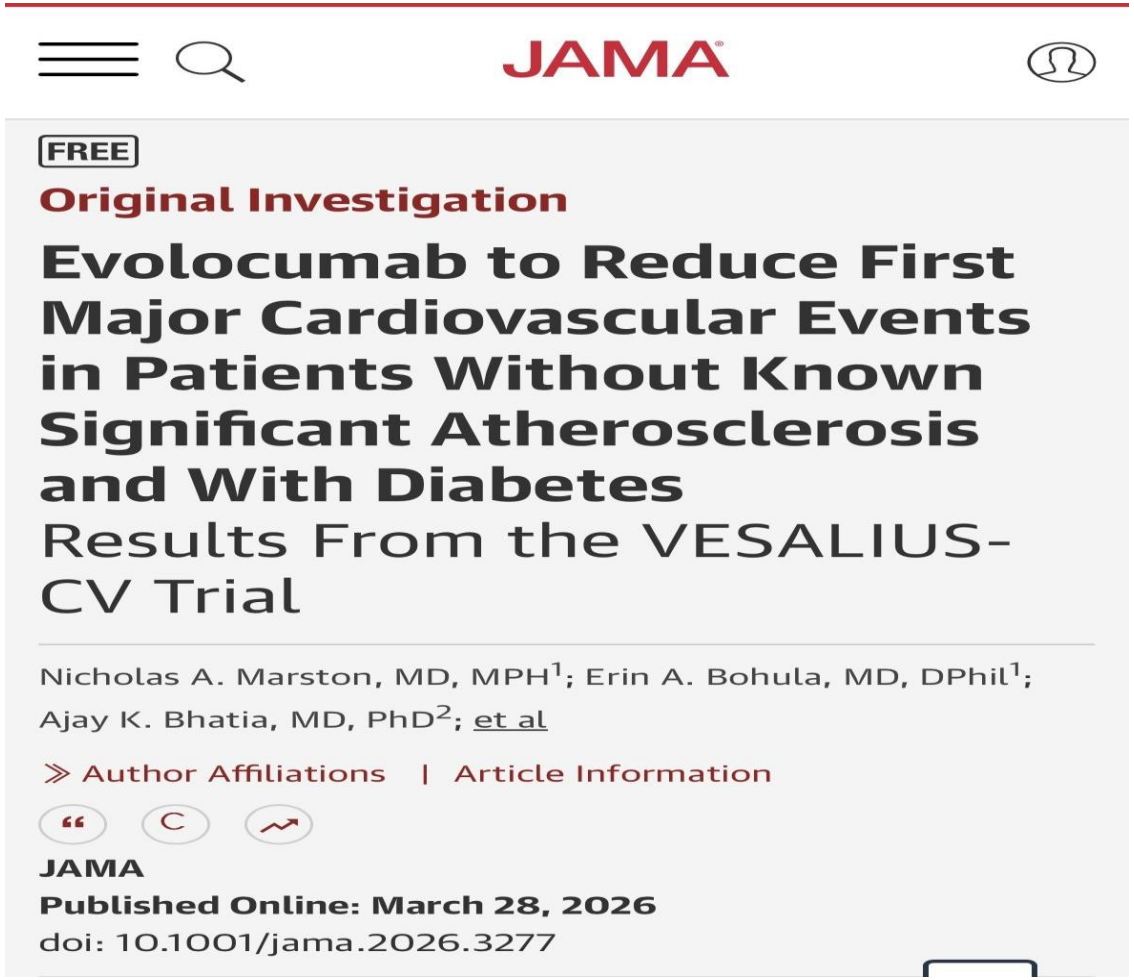
VESALIUS-CV IN DIABETICS



JAMA

FREE

Original Investigation

Evolocumab to Reduce First Major Cardiovascular Events in Patients Without Known Significant Atherosclerosis and With Diabetes

Results From the VESALIUS-CV Trial

Nicholas A. Marston, MD, MPH[1]; Erin A. Bohula, MD, DPhil[1]; Ajay K. Bhatia, MD, PhD[2]; et al

≫ Author Affiliations | Article Information

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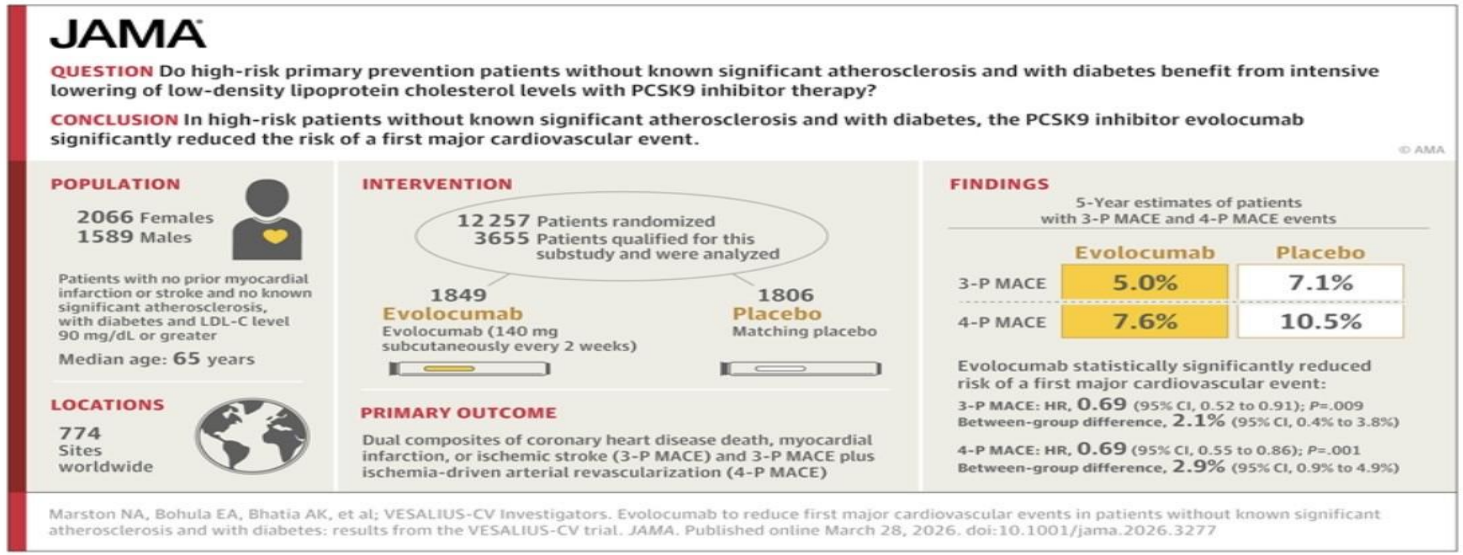
American Heart Association.

VESALIUS-CV IN DIABETICS: RESULTS

Abstract



JAMA

QUESTION Do high-risk primary prevention patients without known significant atherosclerosis and with diabetes benefit from intensive lowering of low-density lipoprotein cholesterol levels with PCSK9 inhibitor therapy?

CONCLUSION In high-risk patients without known significant atherosclerosis and with diabetes, the PCSK9 inhibitor evolocumab significantly reduced the risk of a first major cardiovascular event.

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POPULATION

2066 Females
1589 Males

Patients with no prior myocardial infarction or stroke and no known significant atherosclerosis, with diabetes and LDL-C level 90 mg/dL or greater

Median age: 65 years

LOCATIONS

774 Sites worldwide

INTERVENTION

12 257 Patients randomized
3655 Patients qualified for this substudy and were analyzed

1849 Evolocumab
Evolocumab (140 mg subcutaneously every 2 weeks)

1806 Placebo
Matching placebo

PRIMARY OUTCOME

Dual composites of coronary heart disease death, myocardial infarction, or ischemic stroke (3-P MACE) and 3-P MACE plus ischemia-driven arterial revascularization (4-P MACE)

FINDINGS

5-Year estimates of patients with 3-P MACE and 4-P MACE events

	Evolocumab	Placebo
3-P MACE	5.0%	7.1%
4-P MACE	7.6%	10.5%

Evolocumab statistically significantly reduced risk of a first major cardiovascular event:

3-P MACE: HR, 0.69 (95% CI, 0.52 to 0.91); P=.009
Between-group difference, 2.1% (95% CI, 0.4% to 3.8%)

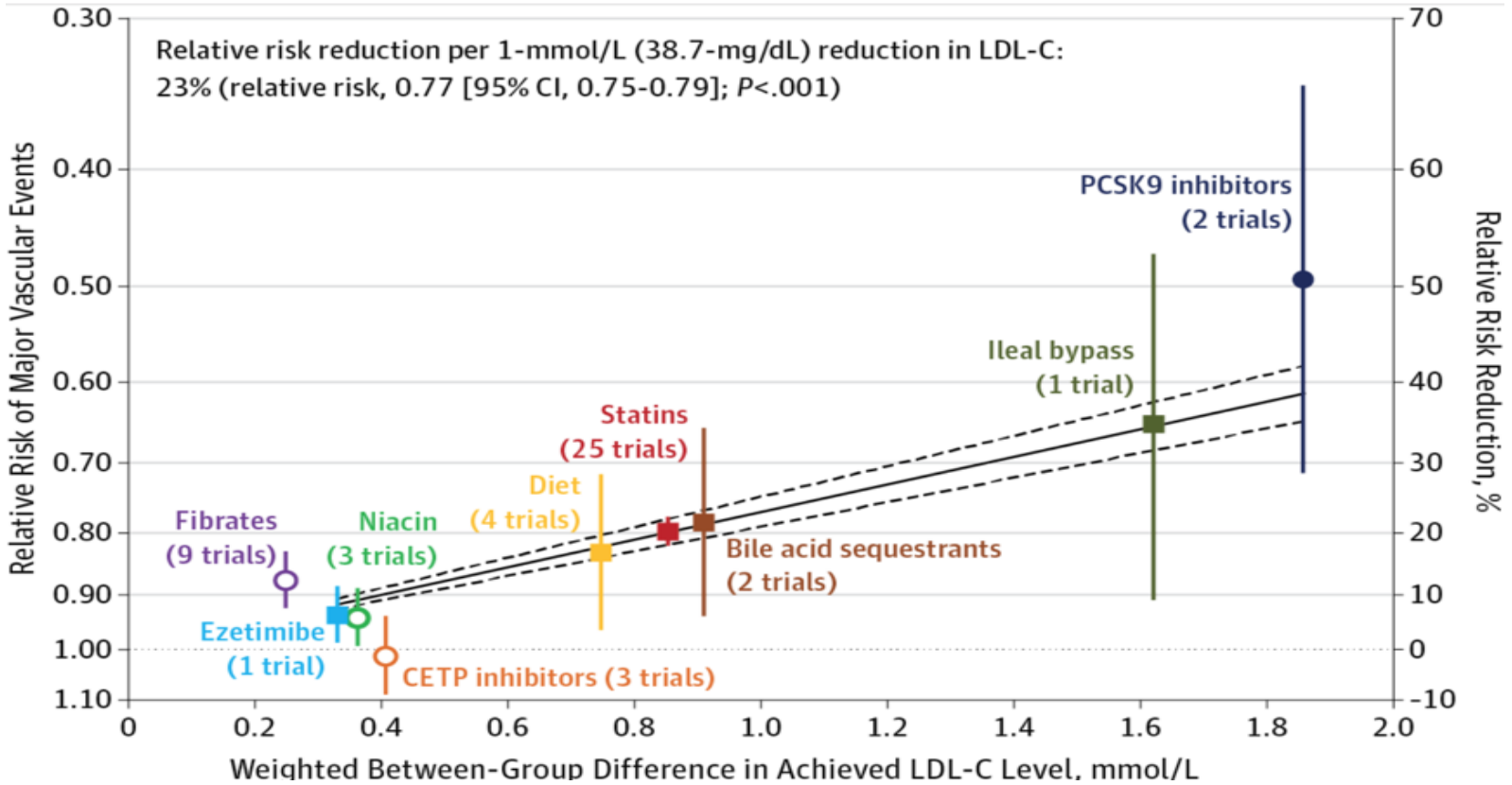
4-P MACE: HR, 0.69 (95% CI, 0.55 to 0.86); P=.001
Between-group difference, 2.9% (95% CI, 0.9% to 4.9%)

Marston NA, Bohula EA, Bhatia AK, et al; VESALIUS-CV Investigators. Evolocumab to reduce first major cardiovascular events in patients without known significant atherosclerosis and with diabetes: results from the VESALIUS-CV trial. *JAMA*. Published online March 28, 2026. doi:10.1001/jama.2026.3277

Evolocumab to Reduce First Major Cardiovascular Events in Patients Without Known Significant Atherosclerosis and With Diabetes

American Heart Association.

Lower LDL-C = Lower Events



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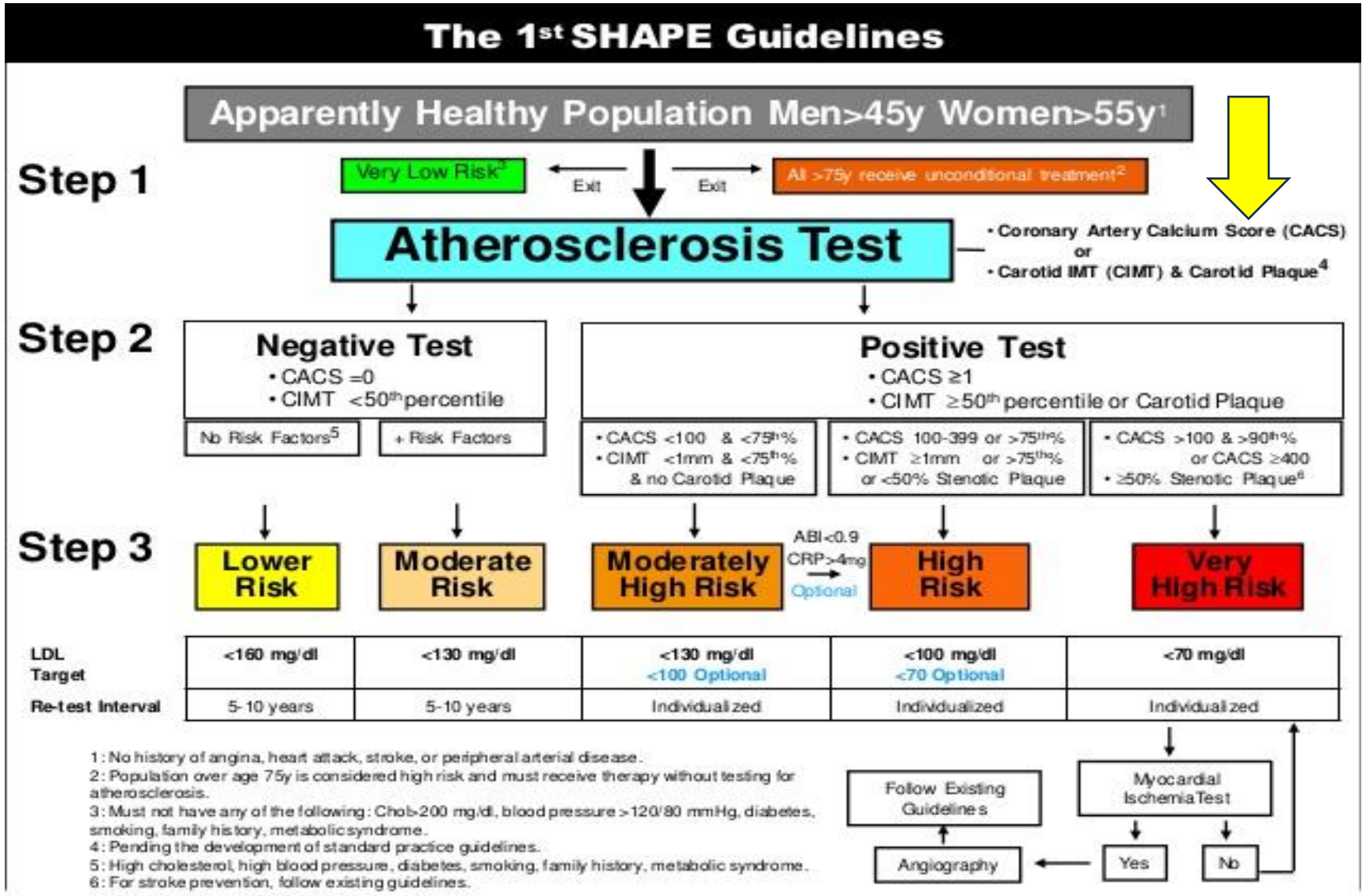
LIVE FIERCE

Shapesociety.org



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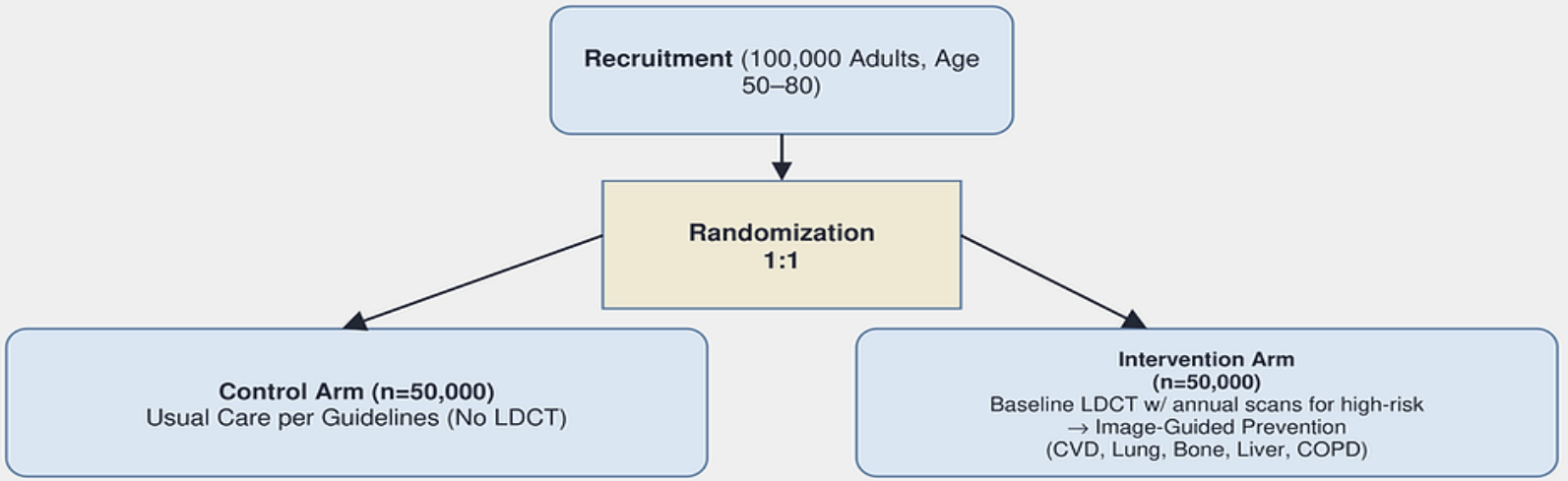
LIVE FIERCE

LDCT Mega Trial: Study Design Overview



Follow-up: 5 Years Primary Endpoint + 5 Years Extended Observation

Primary (Composite) Endpoint:

- All-cause Mortality
- Major adverse cardiovascular events (MACE) including MI, stroke, MALE (PAD), HF hospitalization
- Late-stage (III/IV) /100,000
- COPD hospitalization

Secondary Endpoints:

- Each component of the primary endpoint
- CVD mortality
- Lung cancer mortality
- ESRD / progression to dialysis
- Late-stage (III/IV) / early stage (I/II)
- Cost-effectiveness
- CKD / hospitalization
- Quality of Life / SF12
- hip/vertebral fractures
- Vaccination rates

Governance: LIFEMAP Foundation (Nonprofit)

Collaborators: WHO, NIH, IELCAP, SHAPE, Major Academic Centers