Hot Topics in Medicine: New Guidelines and Updates in Lipid Management

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DATE

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Learning Objectives

- Describe the differences between the AHA PREVENT equations and the Pooled Cohort Equations.
- Identify when triglyceride lowering is recommended versus treatment of overall ASCVD risk.
- Explain why elevated Lp(a) is actionable today and universal screening is recommended.

New Dyslipidemia Guidelines

2018

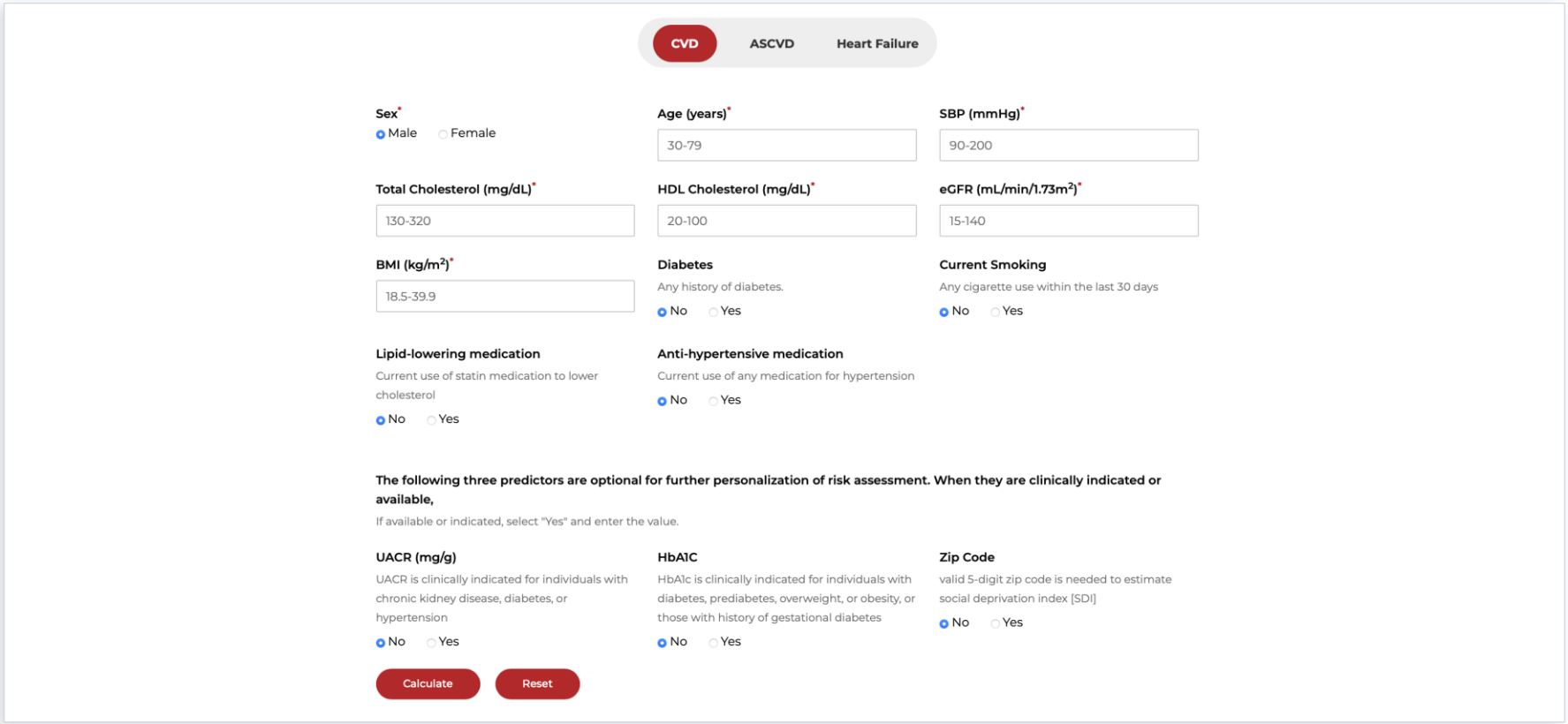
- **Pooled Cohort Equations**
- Start at age 40
- Focus on 10-year risk prediction
- Focus on ASCVD risk
- Risk categories
  - <5%
  - 5-7.5%
  - 7.5-20%%
  - >20%
- Relative LDL-C lowering

2026

- **PREVENT equations**
- Start at age 30
- 10-year and 30-year risk prediction
- ASCVD + HF risk
- Risk categories
  - <3%
  - 3-5%
  - 5-10%
  - >10%
- Thresholds + relative LDL-C lowering
- Greater incorporation of non-statin therapies, triglyceride lowering therapies
- Greater incorporation of CAC
- Universal Lp(a) testing

Blumenthal, et al, JACC 2026

AHA PREVENT Equations



PREVENT in the Guidelines

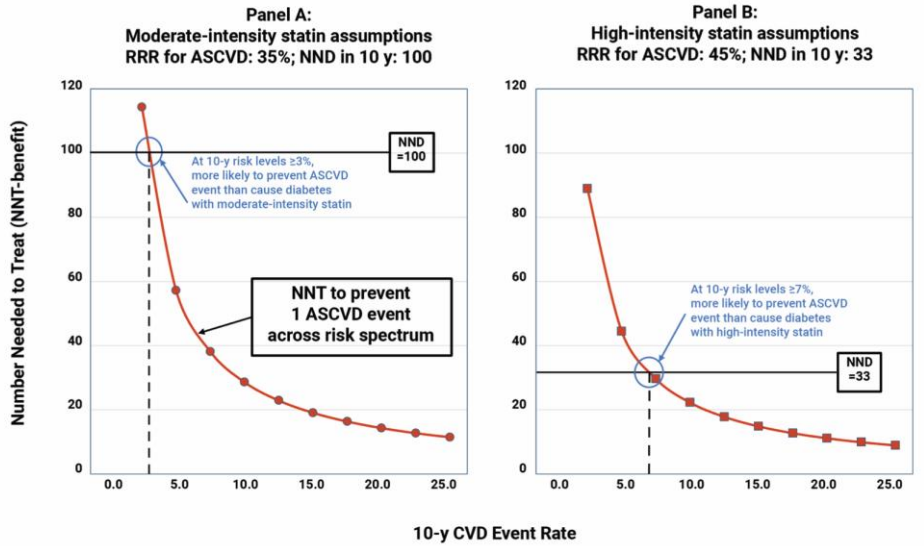
TABLE 12 Crosswalk Between 10-Year Risk ASCVD Estimates From PCE and PREVENT-ASCVD Equations

	Approximate Equivalent Ranges of 10-Year ASCVD Risk Estimates*	
Risk Group	**PCE**	**PREVENT-ASCVD**
Low	<5%	<3%
Borderline	5% to <7.5%	3% to <5%
Intermediate	7.5% to <20%	5% to <10%
High	≥20%	≥10%

*The PREVENT-ASCVD equations generally provide 10-year risk estimates that are 40% to 50% lower than the PCE estimates because the PCE calculator often over-estimated the risk for adults.

ASCVD denotes atherosclerotic cardiovascular disease; and PCE, pooled cohort equations. Adapted from Khan et al.[1,3]

Logic for Defining the Absolute Estimated 10-year ASCVD Risk for Consideration of LLT at ≥3% in Primary Prevention



Blumenthal, et al, JACC 2026

CPR

1 | B-R

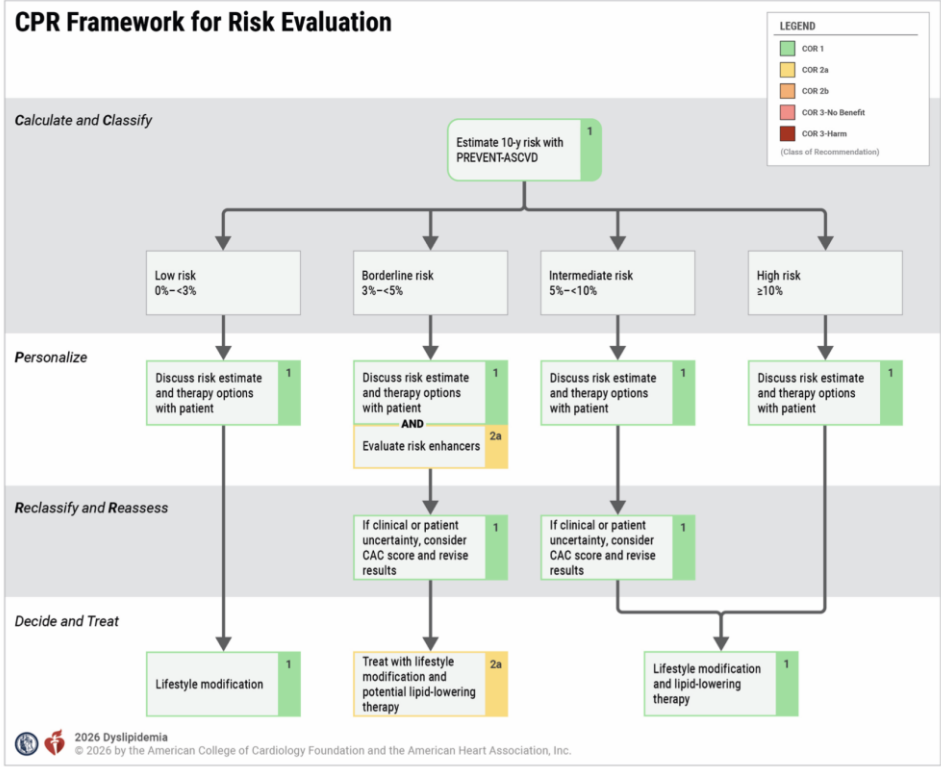
1. In adults at intermediate risk and select adults at borderline risk with no prior ASCVD, if the decision regarding LLT remains uncertain, a CAC score should be used for further risk stratification and to guide the decision to withhold, postpone, or initiate therapy.[1-4]

1 | B-NR

5. In adults with no prior ASCVD, if incidental CAC is identified on noncardiac computed tomography (CT) scans (eg, by visual estimation or a validated artificial-intelligence–based algorithm), the presence of coronary atherosclerosis should be considered during decision-making about initiation or intensification of LLT to reduce ASCVD risk.[11,12]

2b | B-NR

6. In adults with no prior ASCVD who are likely to have a high burden of noncalcified plaque (eg, inflammatory disorders, persons living with HIV, and diabetes), selective use of coronary computed tomography angiography (CCTA) may be useful to inform risk assessment and guide decisions regarding treatment intensity of LLT.[13-17]



Blumenthal, et al, JACC 2026

Return to LDL-C Goals

Lipoprotein Goals for ASCVD Risk Reduction

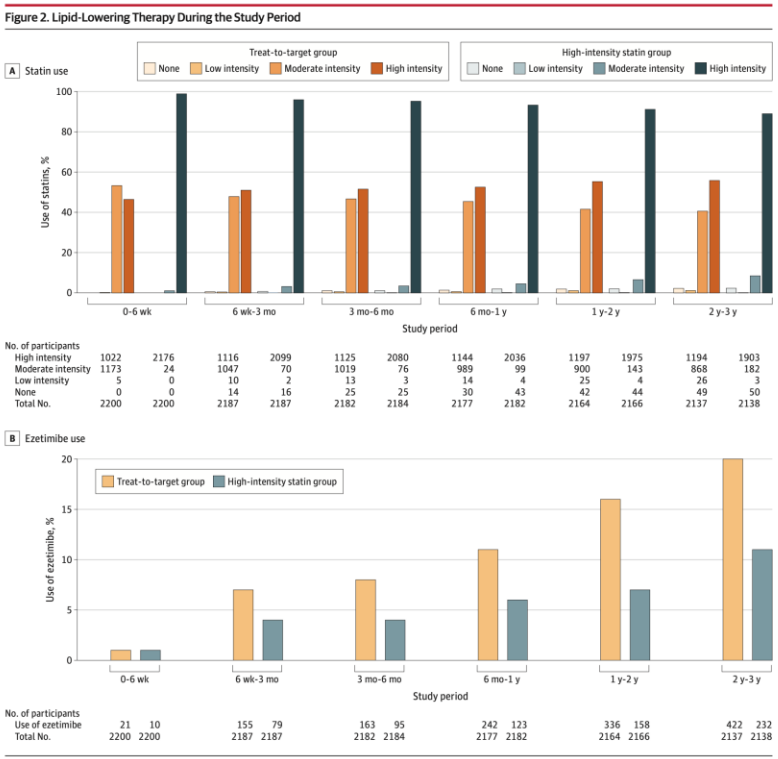
Patient population	LDL-C <100 mg/dL (2.6 mmol/L) Non–HDL-C <130 mg/dL (3.4 mmol/L)	LDL-C <70 mg/dL (1.8 mmol/L) Non–HDL-C <100 mg/dL (2.6 mmol/L)	LDL-C <55 mg/dL (1.4 mmol/L) Non–HDL-C <85 mg/dL (2.2 mmol/L)
Primary prevention	PREVENT-ASCVD <10% • If TG ≥150 mg/dL to 499 mg/dL, apoB goal: <90 mg/dL	PREVENT-ASCVD ≥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, or subclinical atherosclerosis	Severe hypercholesterolemia or HeFH with clinical ASCVD
Diabetes	**Without** ASCVD risk factors or diabetes-specific risk modifiers • apoB goal: <90 mg/dL	**With** ASCVD risk factors or diabetes-specific risk factors • 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, 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

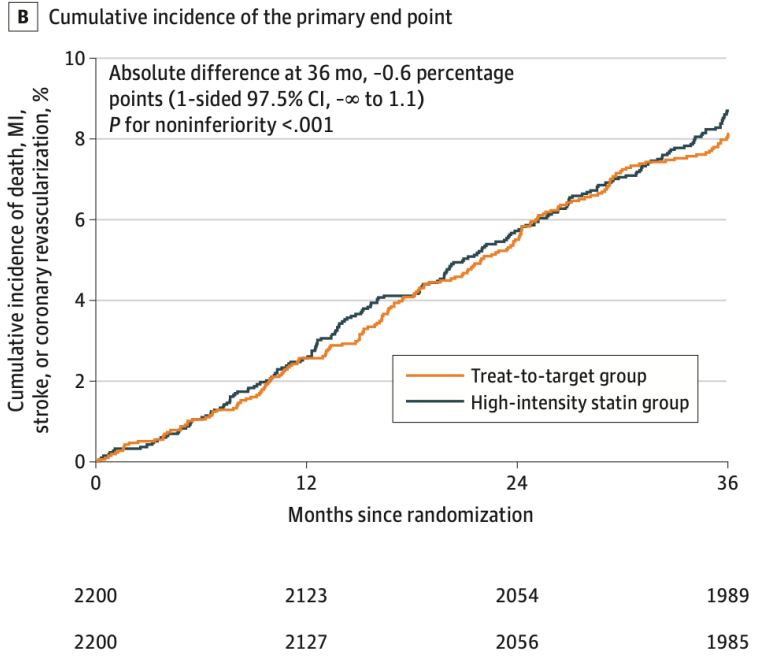
2026 Dyslipidemia

Figure 1. Lipoprotein Goals for ASCVD Risk Reduction.
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.

Blumenthal, et al, JACC 2026

Statins – treat to target?





Hong, et al, JAMA 2023

Measurement Recommendations

1 | B-NR

1. In adults and children, a standard nonfasting or fasting lipid profile is recommended to document baseline lipid levels, estimate ASCVD risk, and guide initiation of LLT.[1-4,5]

1 | B-NR

2. In adults and children 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.[4,6-10]

3: No Benefit | B-NR

6. In adults and children, routine advanced lipoprotein testing (eg, gradient gel electrophoresis, density gradient ultracentrifugation, nuclear magnetic resonance spectroscopy, ion mobility analysis) to assess lipoprotein subclasses and parameters such as LDL particle size is not recommended to estimate ASCVD risk and guide initiation of LLT.[9,10,20]

2a | B-NR

1. In adults on LLT, particularly those with ASCVD, CKM syndrome, 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.[1-8]

2b | B-NR

2. In adults not on LLT, measurement of apoB may be reasonable to enhance ASCVD risk assessment, guide decisions about initiation of LLT, and characterize inherited lipid disorders.[2,9-12]

Blumenthal, et al, JACC 2026

Measurement Recommendations

1	B-NR

1. In all adults, measurement of Lp(a) concentration is recommended at least once for ASCVD risk assessment.[1-4]

TABLE 4 ASCVD Risk Related to Lp(a) Concentrations*

Lp(a) concentration nmol/L (mg/dL)	ASCVD Relative Risk: Increase Compared With Population Median (20 nmol/L, 7 mg/dL)
430 nmol/L (180 mg/dL)	4-fold
350 nmol/L (150 mg/dL)	3-fold
250 nmol/L (100 mg/dL)	2 -fold
125 nmol/L (50 mg/dL)	1.4-fold
75-124 nmol/L (30-49 mg/dL)	1.2-fold
<75 nmol/L (<30 mg/dL)	Reference

Blumenthal, et al, JACC 2026

Primary Prevention

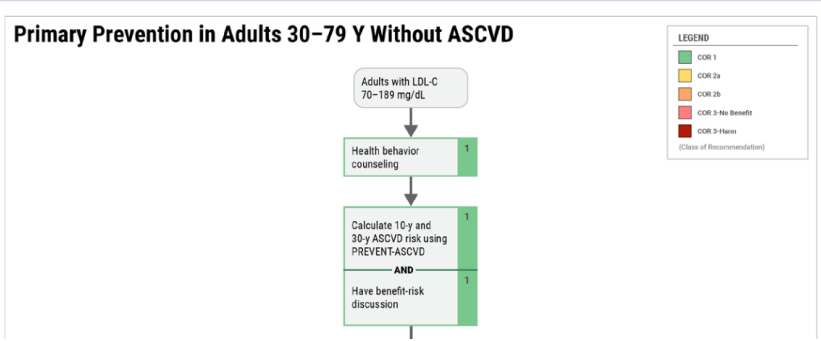
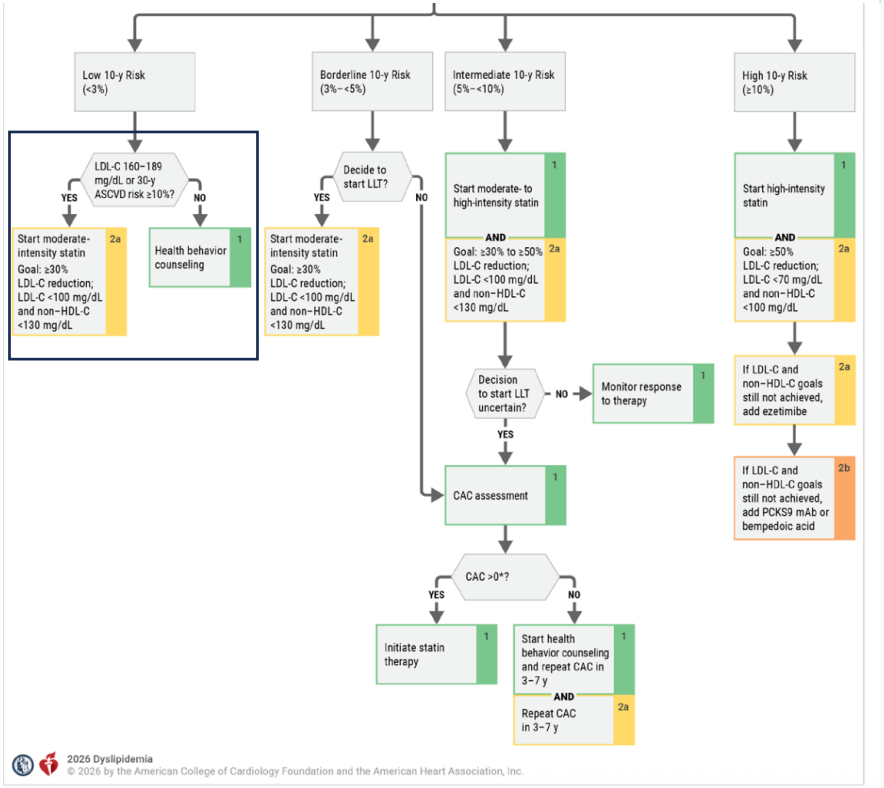


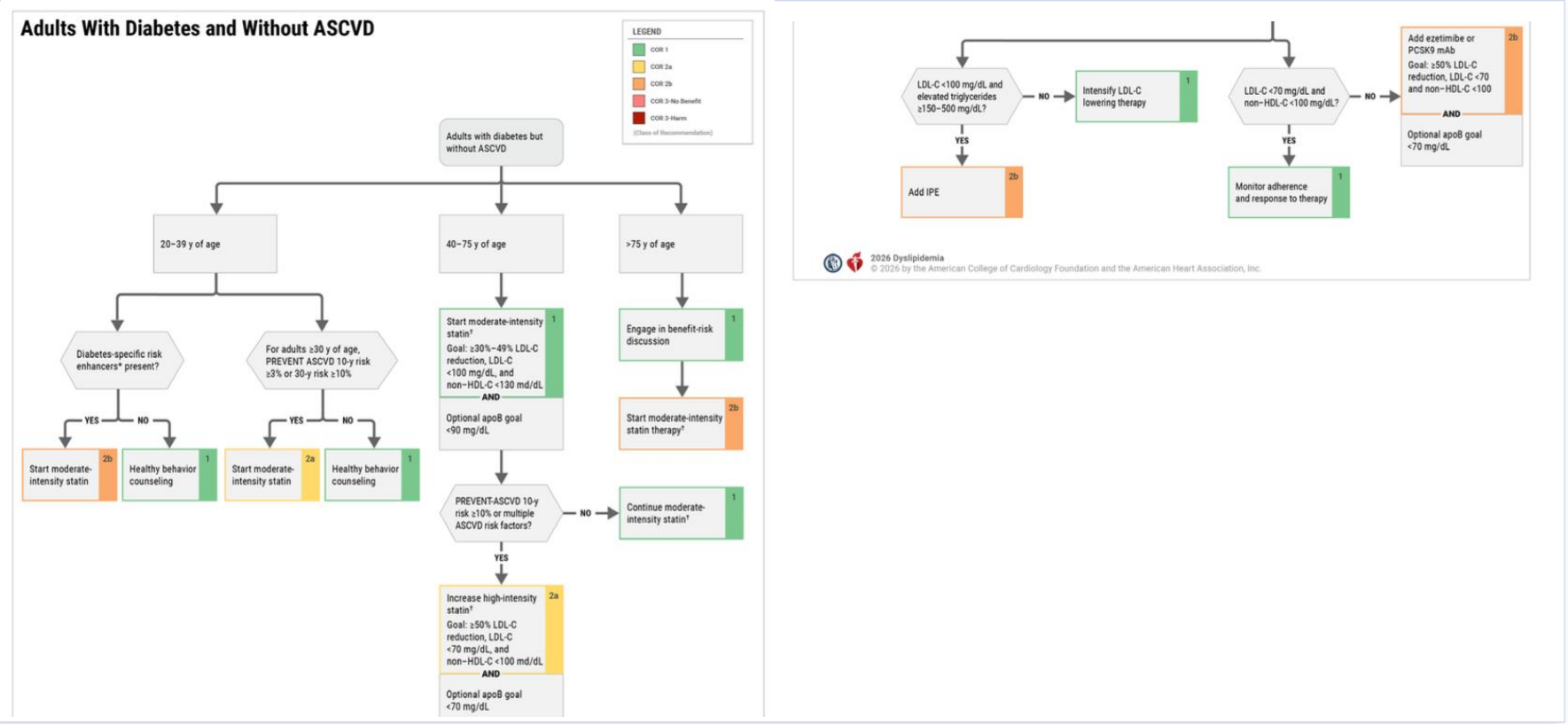
Table 13. Risk Enhancers

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) (Section 4.2.3.5, "Polygenic Risk Scores")
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; Section 4.2.3.4, "Reproductive Risk Marker")



Blumenthal, et al, JACC 2026

Diabetes



Blumenthal, et al, JACC 2026

Secondary Prevention

Secondary Prevention

- **Not very high-risk:**
  - LDL-C <70 mg/dL (50% reduction)
  - Optional <55 mg/dL
- **Very high-risk:**
  - LDL-C <55 mg/dL (50% reduction)
- Step up therapy of choice

Major ASCVD Events

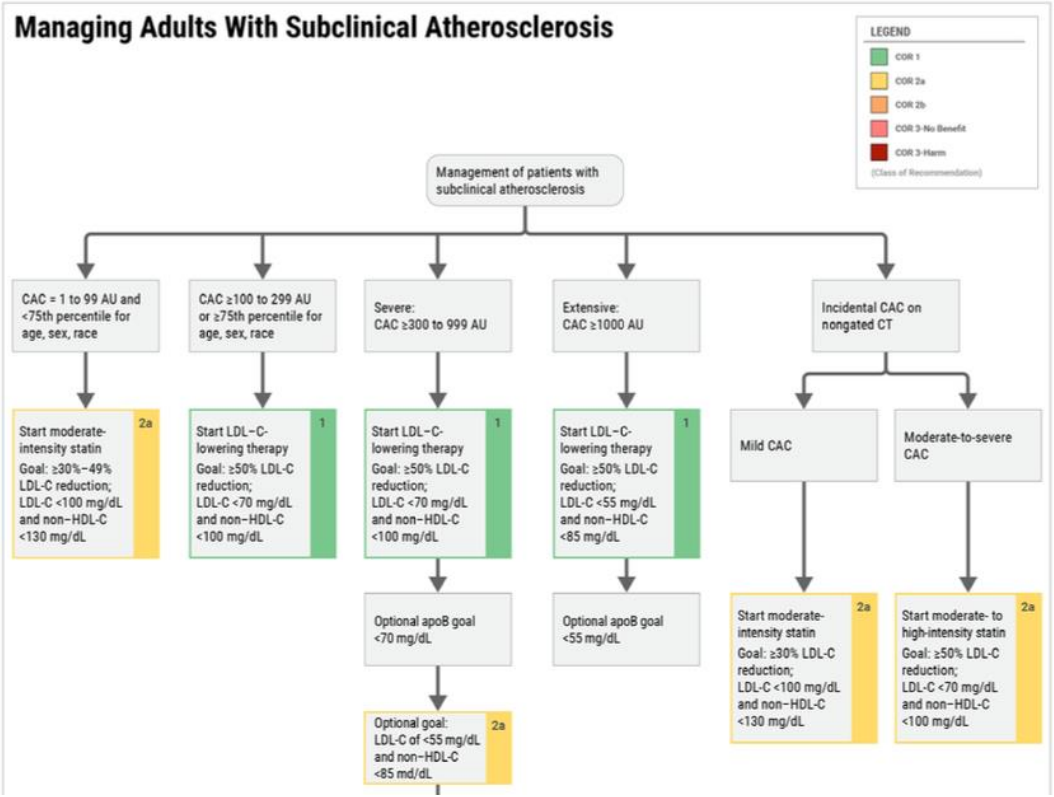
- ACS within past 12 mo
- History of MI (other than ACS above)
- History of ischemic stroke
- Symptomatic PAD

High-Risk Conditions

- Age ≥65 y
- Coronary bypass or percutaneous intervention
- Current smoker
- Diabetes
- Hx of congestive heart failure
- Hypertension
- LDL-C ≥100 mg/dL (2.6 mmol/L) despite maximally tolerated statin + ezetimibe

Blumenthal, et al, JACC 2026

Subclinical Atherosclerosis



Blumenthal, et al, JACC 2026

New Dyslipidemia Guidelines

>100 mg/dL

- <3% risk with LDL-C 160-189 mg/dL or 30-year ≥10%
- 3-10% risk
- LDL-C >190 mg/dL w/out other RFs
- Diabetes w/out other RFs
- CAC 1-99, <75th percentile

>70 mg/dL

- ≥10% risk
- LDL-C >190 mg/dL + RFs
- Diabetes + RFs
- CAC ≥100 or ≥75th percentile
- Clinical ASCVD, not very high risk

>55 mg/dL

- LDL-C >190 mg/dL + ASCVD
- CAC ≥1000, optional ≥300
- Clinical ASCVD, very high risk, optional not very high risk

Blumenthal, et al, JACC 2026

Key Dietary Recommendations

Health Behavior Interventions in Patients With Hypertriglyceridemia

Implemented shared decision-making intervention	TG ≥150 to 499 mg/dL* (1.7 to <5.7 mmol/L)	TG ≥500 to 999 mg/dL* (5.7 to <11.3 mmol/L)	TG ≥1000 mg/dL† (≥11.3 mmol/L)
Added sugars (percent calories)	<6%	<5%	Eliminate
Total fat (percent calories)	30%–35%	20%–25%‡	10%–15%§¶
Alcohol	Avoid	Abstain completely	Abstain completely
Physical activity	At least 150 minutes/week of accumulated moderate-intensity or 75 minutes/week of vigorous intensity aerobic activity (or equivalent combination of both) and 2 days/week of upper and lower body resistance exercise‖		
Weight loss (percent body weight)	Recommended weight loss goal of 5%–10% for patients who are overweight or obese with elevated TG		

2026 Dyslipidemia

3: No Benefit | B-R

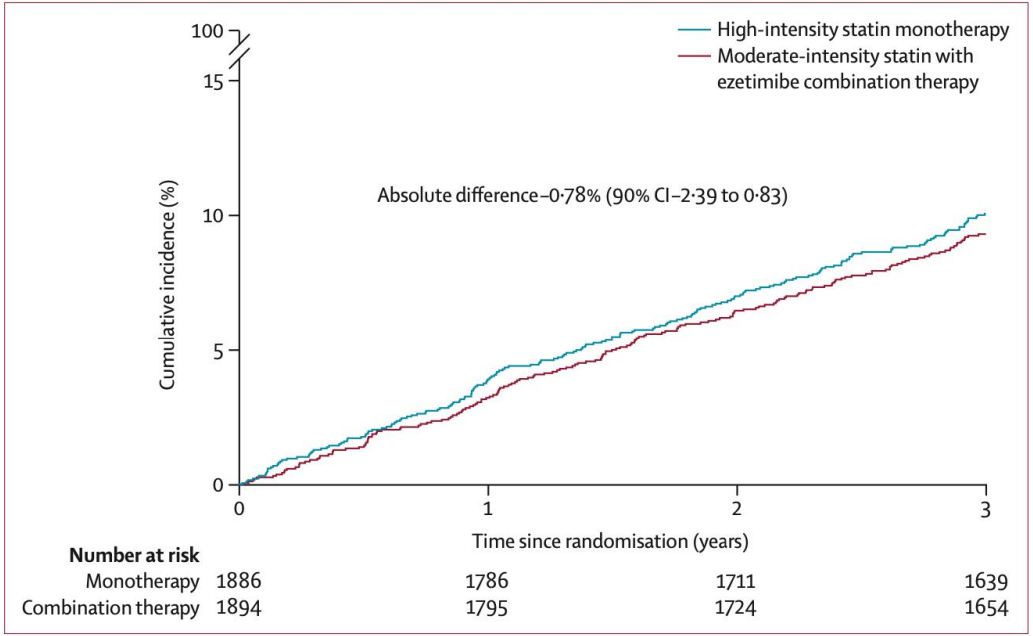
1. In individuals with dyslipidemia, the use of dietary supplements is not recommended to lower LDL-C or TG based on limited and inconsistent data and/or limited benefits in lipid-lowering and reduction in ASCVD risk.[1-4]

Blumenthal, et al, JACC 2026

SECTION 2

Updates on Statin and Non-Statin Therapies

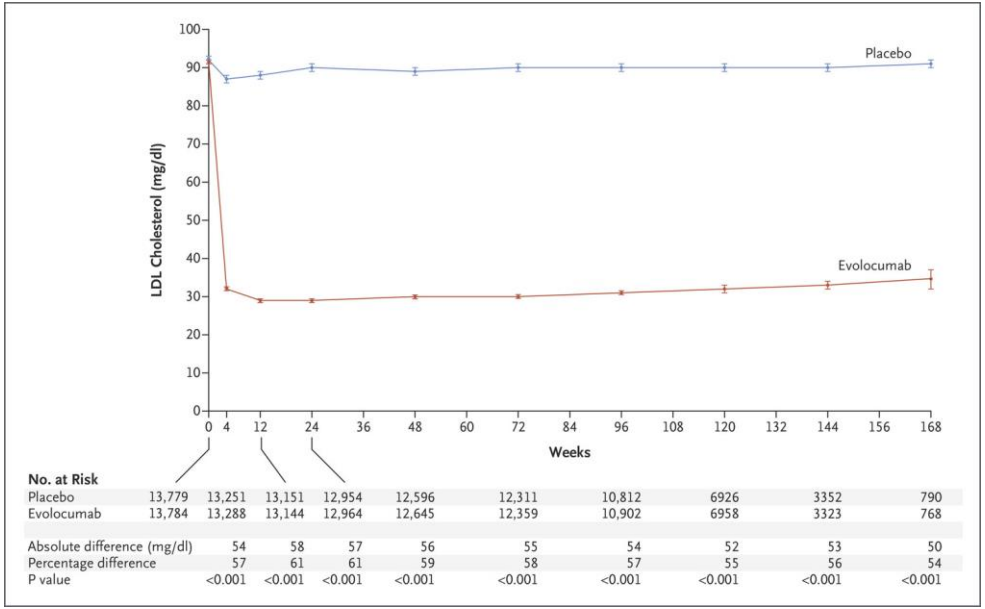
Combination therapy up front

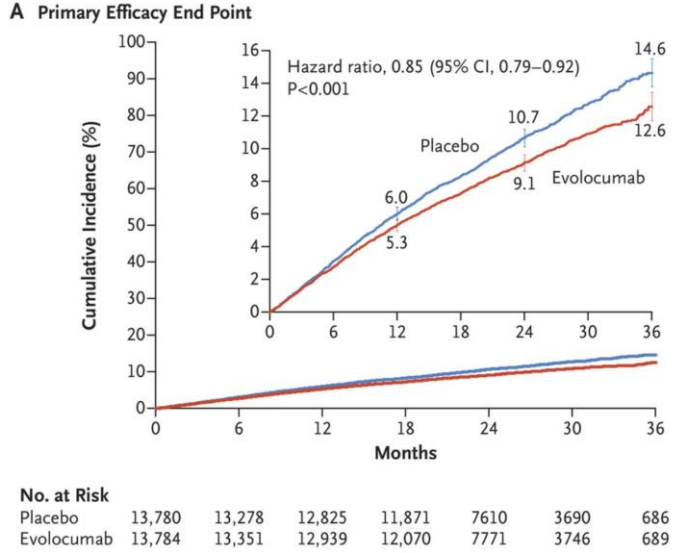


Event rate: 9.1% vs. 9.9%
LDL-C <70 mg/dL at 3 years: 72% vs. 58%
Median LDL-C at 3 years: 58 vs. 66 mg/dL
Drug discontinuation / reduction: 4.8% vs. 8.2%

Kim, et al, Lancet 2022

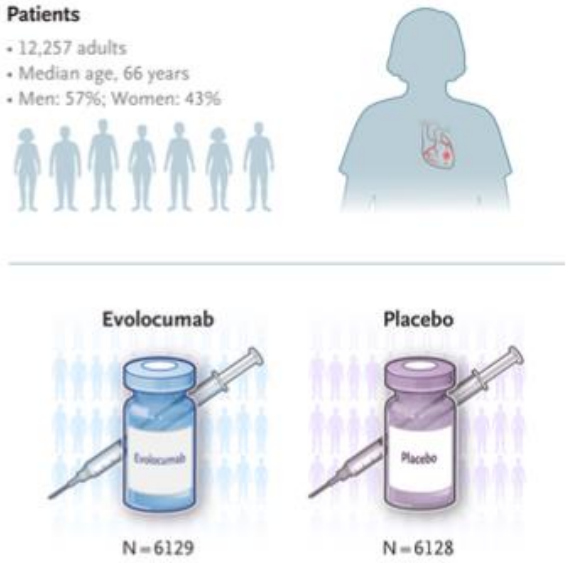
PCSK9 Inhibitors

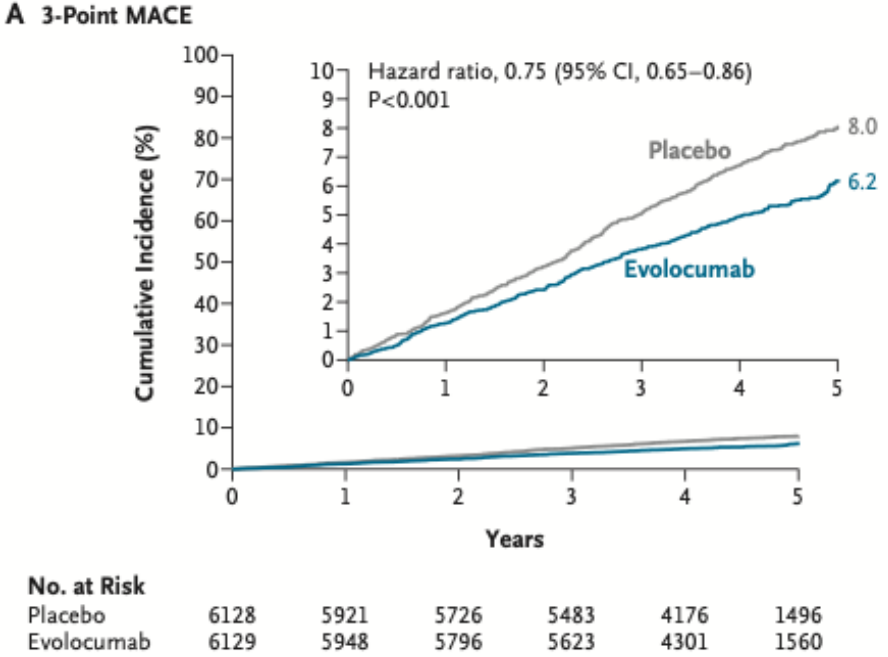




Sabatine, et al, NEJM 2017

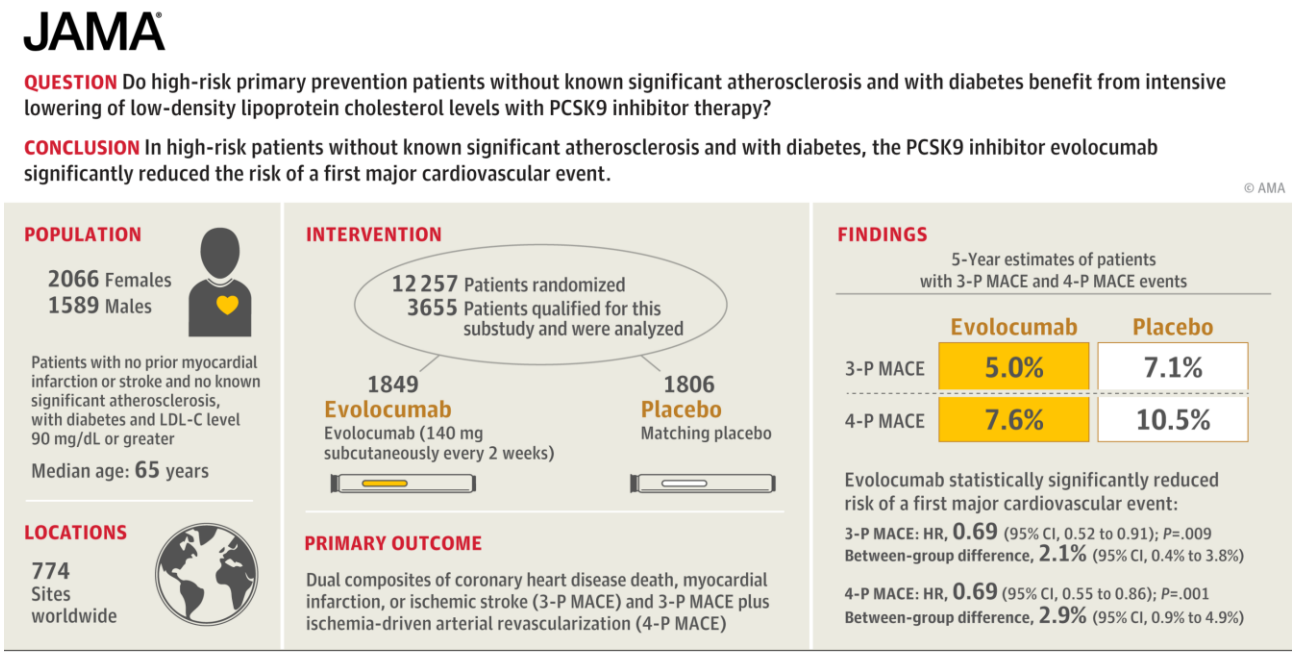
PCSK9 Inhibitors – VESALIUS-CV





Bohula, et al, NEJM 2026

PCSK9 Inhibitors – VESALIUS-CV



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

Bohula, et al, NEJM 2026

PCSK9 Inhibitors – VESALIUS-CV

The significant cardiovascular benefits with more intensive lowering of LDL-C to <55 mg/dL in patients without previous MI or stroke in VESALIUS-CV now blur the distinction between ASCVD risk categories when defining a "goal" LDL-C value. Thus, future updates to the 2026 ACC/AHA/Multisociety Dyslipidemia Guideline should include a single pathway of care for all patients with ASCVD (including prior MACE as well as coronary artery disease, peripheral artery disease, cerebrovascular disease, or at least moderate atherosclerosis on imaging without prior MI or stroke) with an optimal LDL-C goal of <55 mg/dL to be achieved via pharmacotherapy as well as lifestyle optimization.

VESALIUS-CV also redefines the benefits of more intensive LDL-C–lowering therapy to an LDL-C goal of <55 mg/dL in patients with high-risk diabetes and ≥1 additional high-risk feature. Future guideline revisions should include an evidence-based recommendation for more intensive LDL-C lowering in this high-risk population.

Blumenthal and Morris, Circulation 2026

PCSK9 Inhibitors – Inclisiran

Key Question

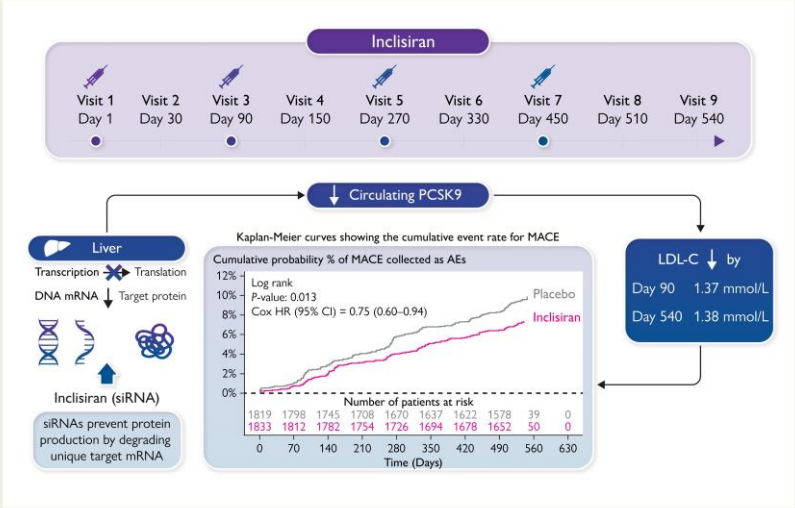
To evaluate the effect on the prespecified exploratory endpoint, cardiovascular events. This was studied in a patient-level, pooled analysis of the pivotal Phase III ORION trials (ORION-9, ORION-10 and ORION-11) over 18 months.

Key Finding

Inclisiran significantly reduced major adverse cardiovascular events (OR [95% CI] : 0.74 [0.58–0.94]), but not fatal and non-fatal myocardial infarction (OR [95% CI] : 0.80 [0.50–1.27]) and fatal and non-fatal stroke (OR [95% CI] : 0.86 [0.41–1.81]).

Take Home Message

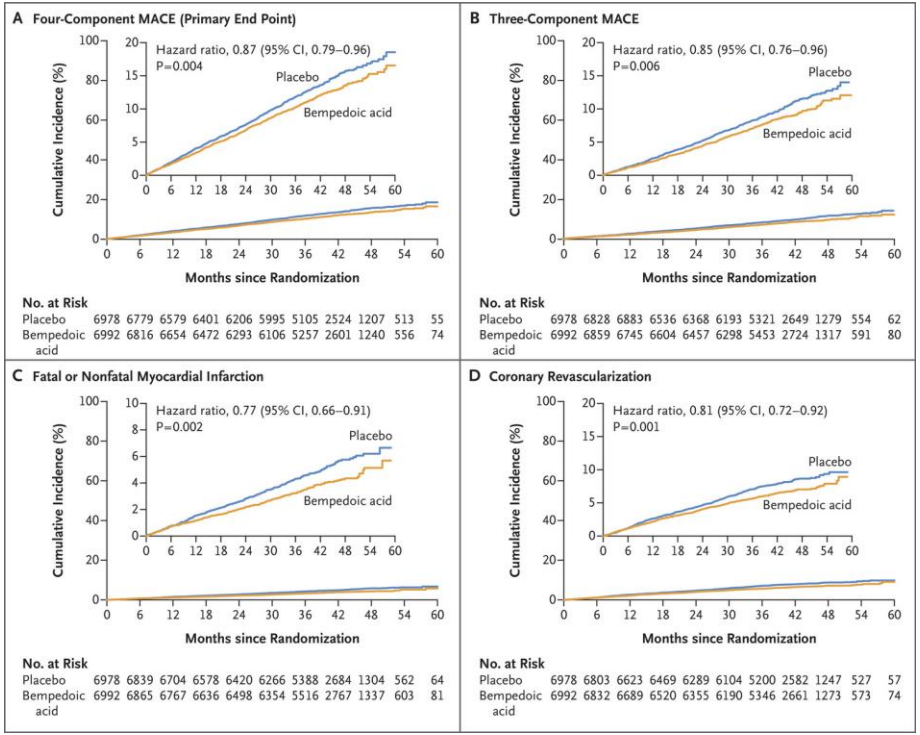
This pooled analysis offers early insights into the potential cardiovascular benefits of lowering LDL-C with inclisiran and suggests potential benefits for major adverse cardiovascular event reduction.



Inclisiran and risk of reported MACE from the patient-level pooled ORION-9, ORION-10 and ORION-11 trials.

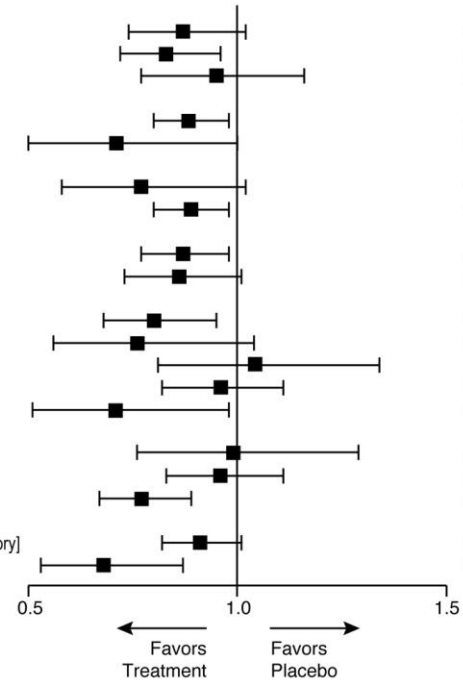
Ray, et al, EHJ 2023

Bempedoic Acid



Nissen, et al, NEJM 2023

Bempedoic Acid



Endpoints	Hazard Ratio (95% CI)	Bempedoic Acid (N=6992)	Placebo (N=6978)	Interaction P value
Age category (years)				
<65	0.87 (0.74, 1.02)	275 (9.6)	321 (11.0)	
≥65 to < 75	0.83 (0.72, 0.96)	362 (11.8)	419 (13.8)	0.60
≥75	0.95 (0.77, 1.16)	182 (17.1)	187 (17.9)	
Race				
White	0.88 (0.80, 0.98)	766 (12.0)	846 (13.4)	0.21
Non-white	0.71 (0.50, 1.00)	53 (8.9)	81 (12.6)	
Ethnicity				
Hispanic or Latino	0.77 (0.58, 1.02)	85 (7.1)	106 (9.3)	0.35
Not Hispanic or Latino	0.89 (0.80, 0.98)	734 (12.7)	821 (14.1)	
Sex				
Male	0.87 (0.77, 0.98)	537 (14.8)	598 (16.6)	0.89
Female	0.86 (0.73, 1.01)	282 (8.4)	329 (9.7)	
Region				
North America (US and Canada)	0.80 (0.68, 0.95)	247 (16.4)	301 (19.9)	
Latin America	0.76 (0.56, 1.04)	70 (7.8)	89 (10.2)	
Western Europe	1.04 (0.81, 1.34)	123 (15.6)	122 (14.7)	0.17
Eastern Europe	0.96 (0.82, 1.11)	321 (9.4)	326 (9.9)	
Other (Rest of the World)	0.71 (0.51, 0.98)	58 (14.8)	89(19.7)	
Baseline BMI category (kg/m2)				
<25	0.99 (0.76, 1.29)	117 (10.9)	108 (10.7)	
≥25 to <30	0.96 (0.83, 1.11)	345 (12.2)	360 (12.5)	0.06
≥30	0.77 (0.67, 0.89)	357 (11.6)	459 (14.8)	
Baseline CVD risk category				
Secondary prevention [Documented CVD History]	0.91 (0.82, 1.01)	708 (14.5)	766 (15.7)	0.03
Primary prevention [At high risk for CVD]	0.68 (0.53, 0.87)	111 (5.3)	161 (7.6)	

Nissen, et al, NEJM 2023

Bempedoic Acid

----------INDICATIONS AND USAGE----------

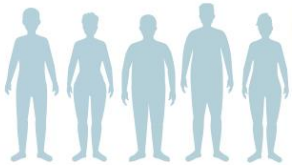
NEXLETOL, an adenosine triphosphate-citrate lyase (ACL) inhibitor, is indicated:

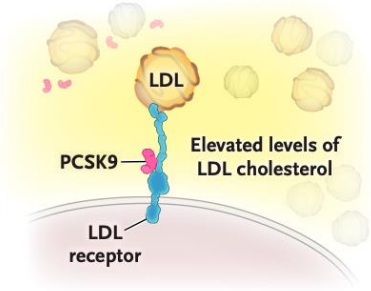
- To reduce the risk of myocardial infarction and coronary revascularization in adults who are unable to take recommended statin therapy (including those not taking a statin) with:
  - established cardiovascular disease (CVD), or
  - a high risk for a CVD event but without established CVD. (1)
- As an adjunct to diet, in combination with other low-density lipoprotein cholesterol (LDL-C) lowering therapies, or alone when concomitant LDL-C lowering therapy is not possible, to reduce LDL-C in adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH). (1)

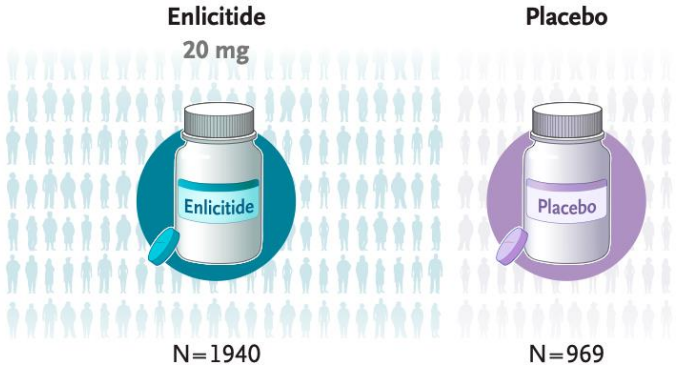
Oral PCSK9i Therapy

Participants

- 2909 adults
- Mean age, 63 years
- Men: 61%; Women: 39%

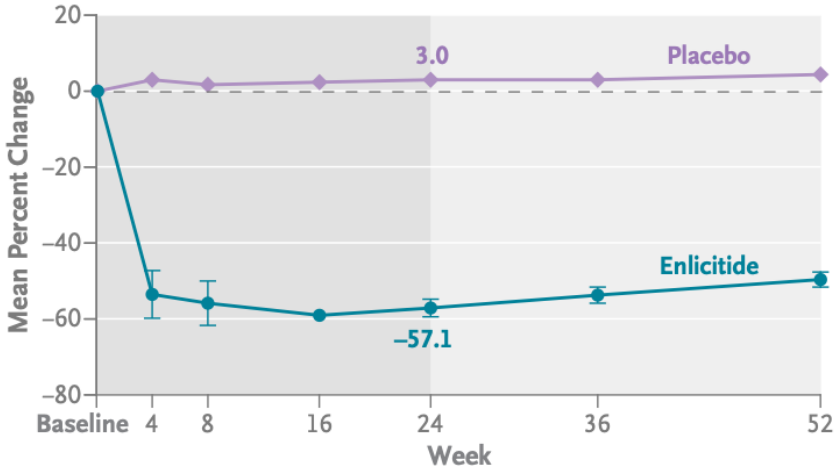






Change in LDL Cholesterol Levels

Adjusted between-group difference, −55.8 percentage points (95% CI, −60.9 to −50.7); P<0.001

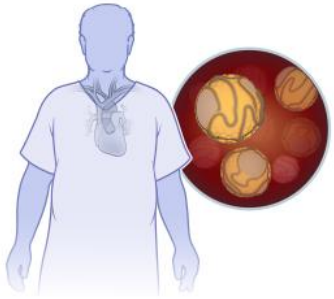


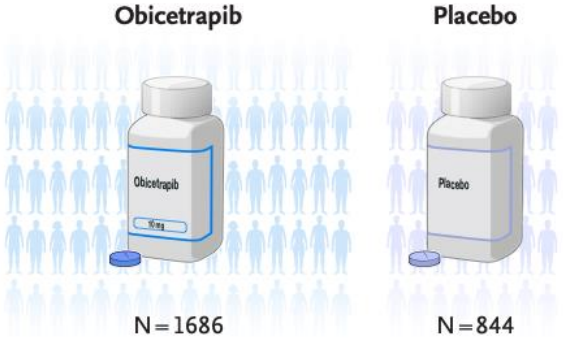
Navar, et al, NEJM 2026

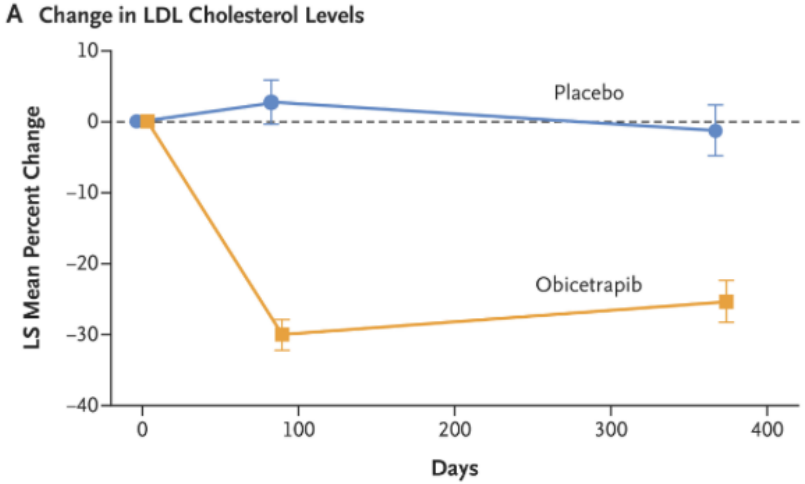
CETP Inhibition

Patients

- 2530 adults
- Mean age, 65 years
- Men: 66%; Women: 34%
- Mean baseline LDL cholesterol level: 98 mg/dl







Nichols, et al, NEJM 2025

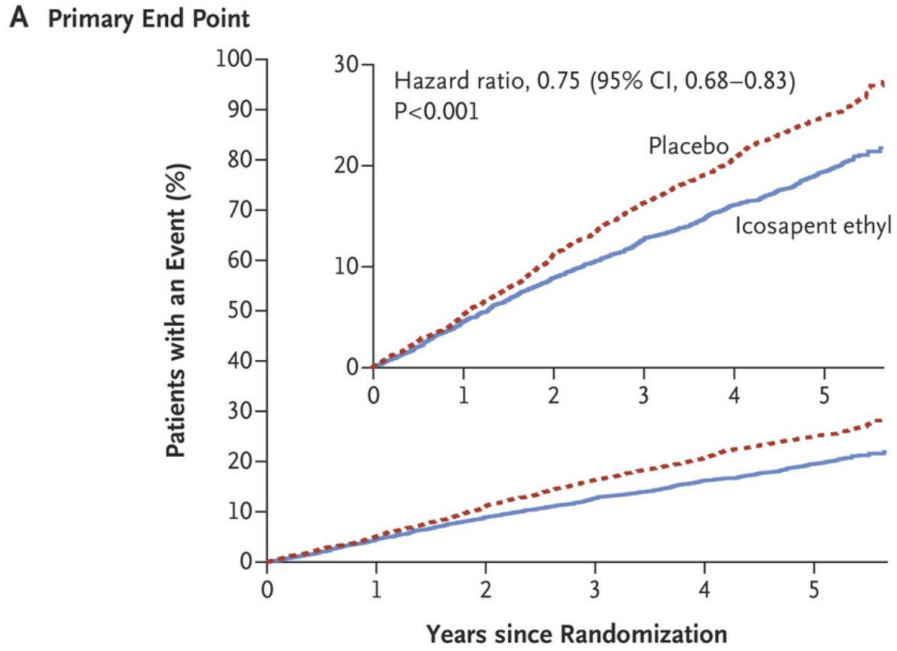
Hypertriglyceridemia

When to treat?

- **Lifestyle modification for all**
- **Increased ASCVD risk**
  - Lower LDL-C (statins), IPE
- **Pancreatitis risk**
  - Typically with very high levels, at least >500 mg/dL
  - Lower triglycerides (fibrates, omega 3 FAs, targeted therapy)
  - Think about FCS

Nichols, et al, NEJM 2025

Icosapent ethyl



Bhatt, et al, NEJM 2019

ApoC-III inhibition (Olezarsen)

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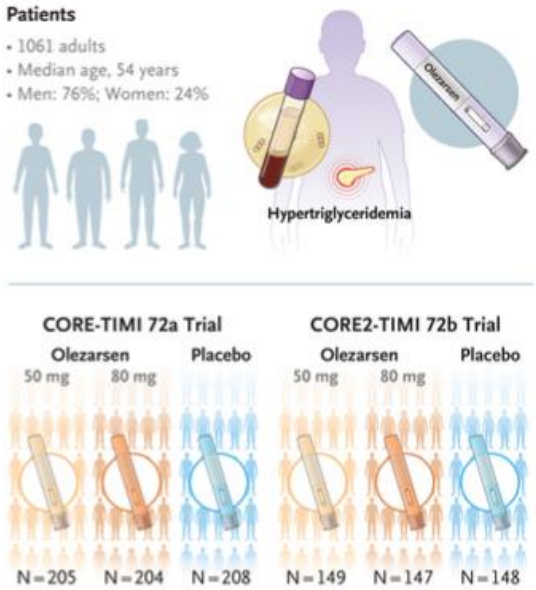
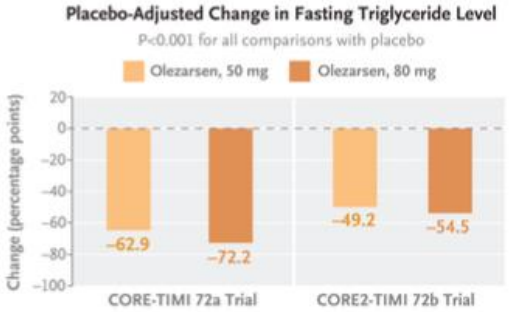
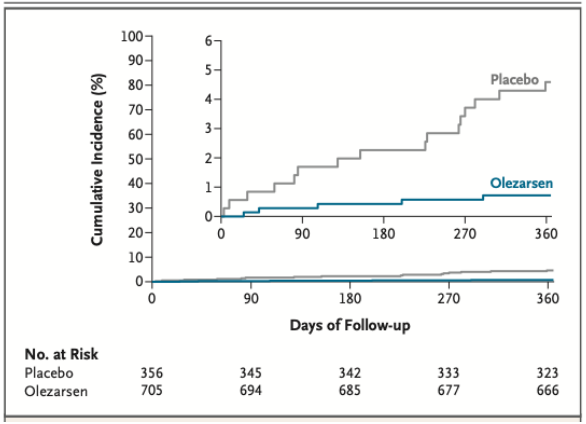
AND PHARMACEUTICAL SCIENCES
Department of Pharmacy Practice and Sciences





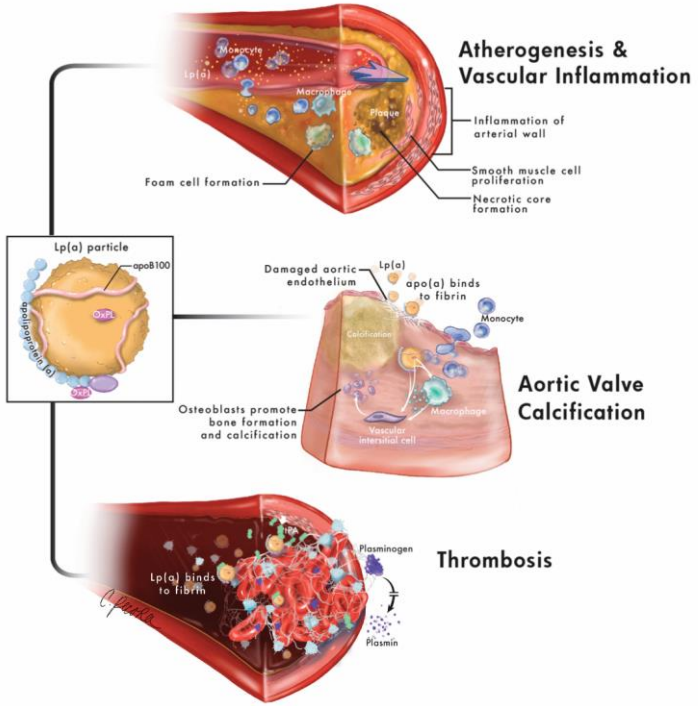


Marston et al, NEJM 2026

SECTION 3

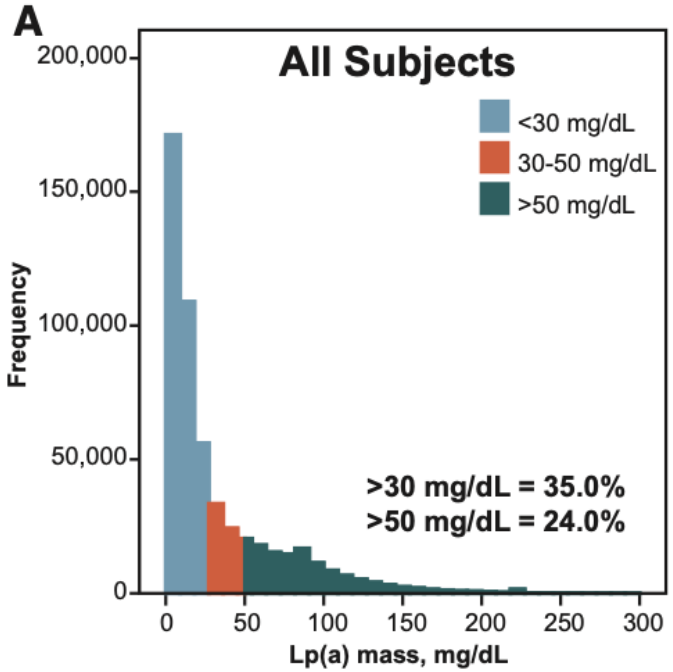
Overview of Lp(a) and Emerging Therapies

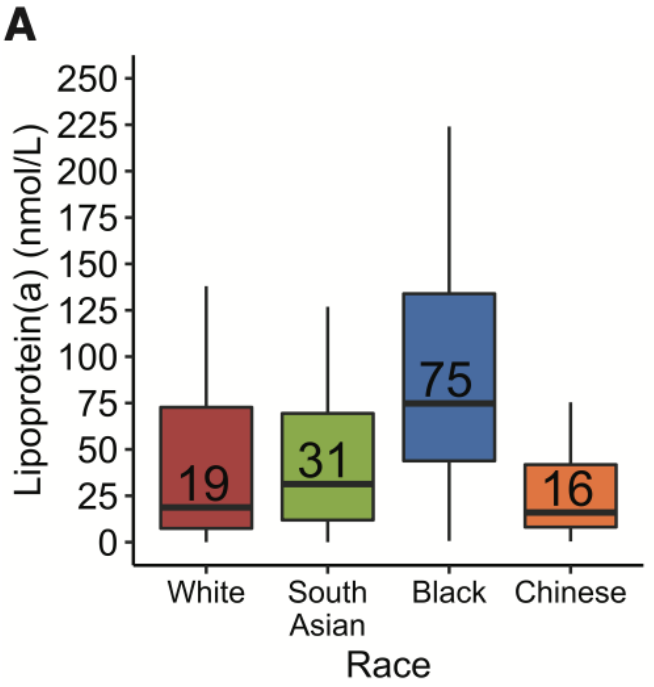
Lipoprotein(a)



Bhatia, et al, J Clin Med 2022

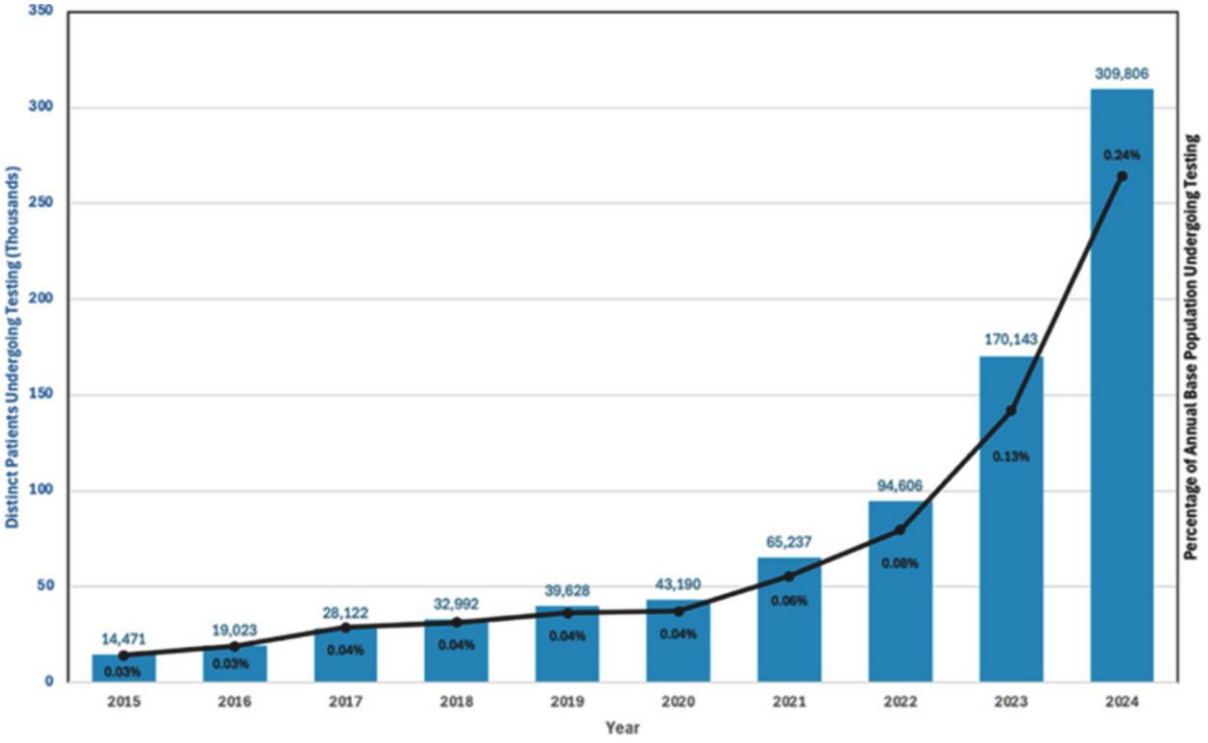
Elevated Lp(a) is Highly Prevalent





Varvel et al, ATVB 2016; Patel et al, ATVB 2021

The Problem: Lp(a) is Very Under-Tested

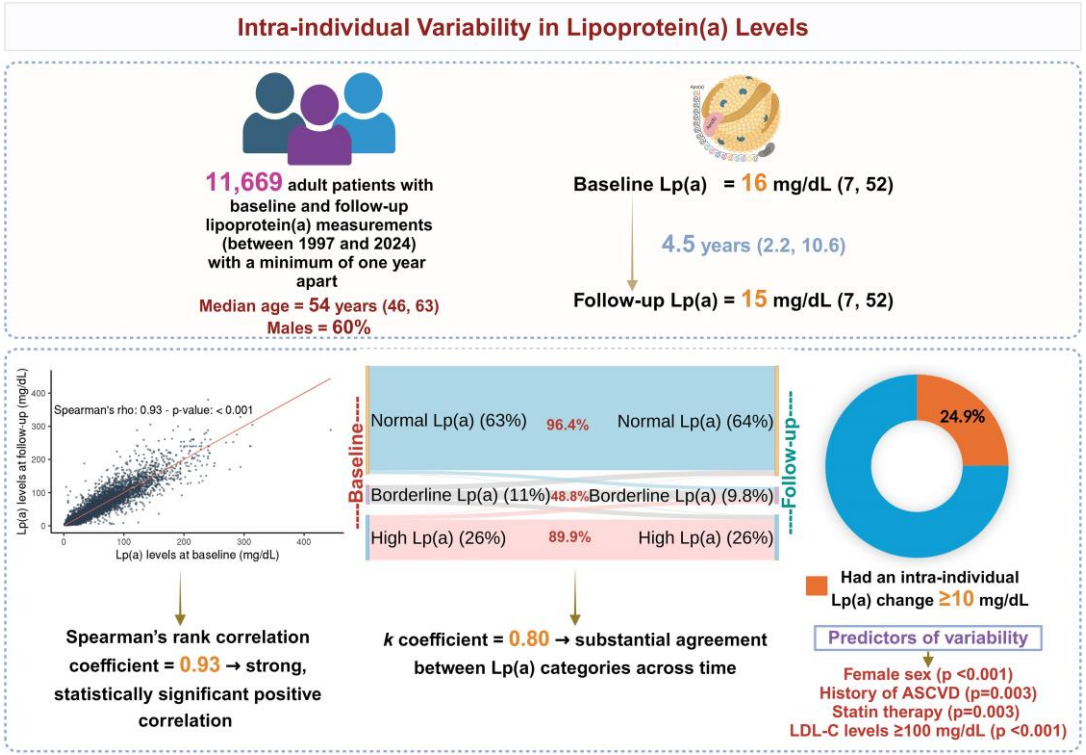


Ramsis and Bhatia, et al, JACC Advances 2025

Potential Barriers to Lp(a) Testing

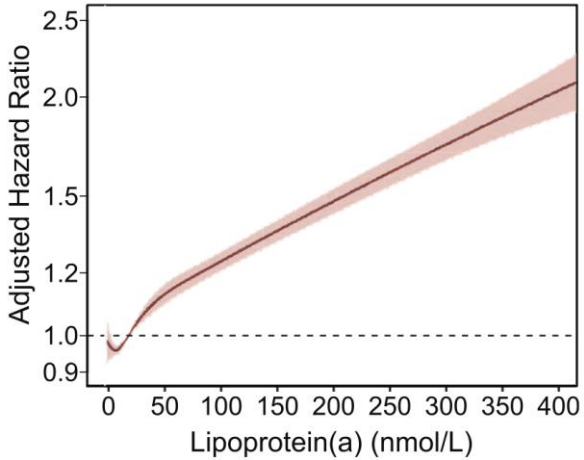
- Knowledge
- Complexity of medicine
- Guidelines
- Concerns about cost
- Complexity of measurement / units
- “There’s nothing you can do about it”

Test Most People Once



Awad et al, EJPC 2025

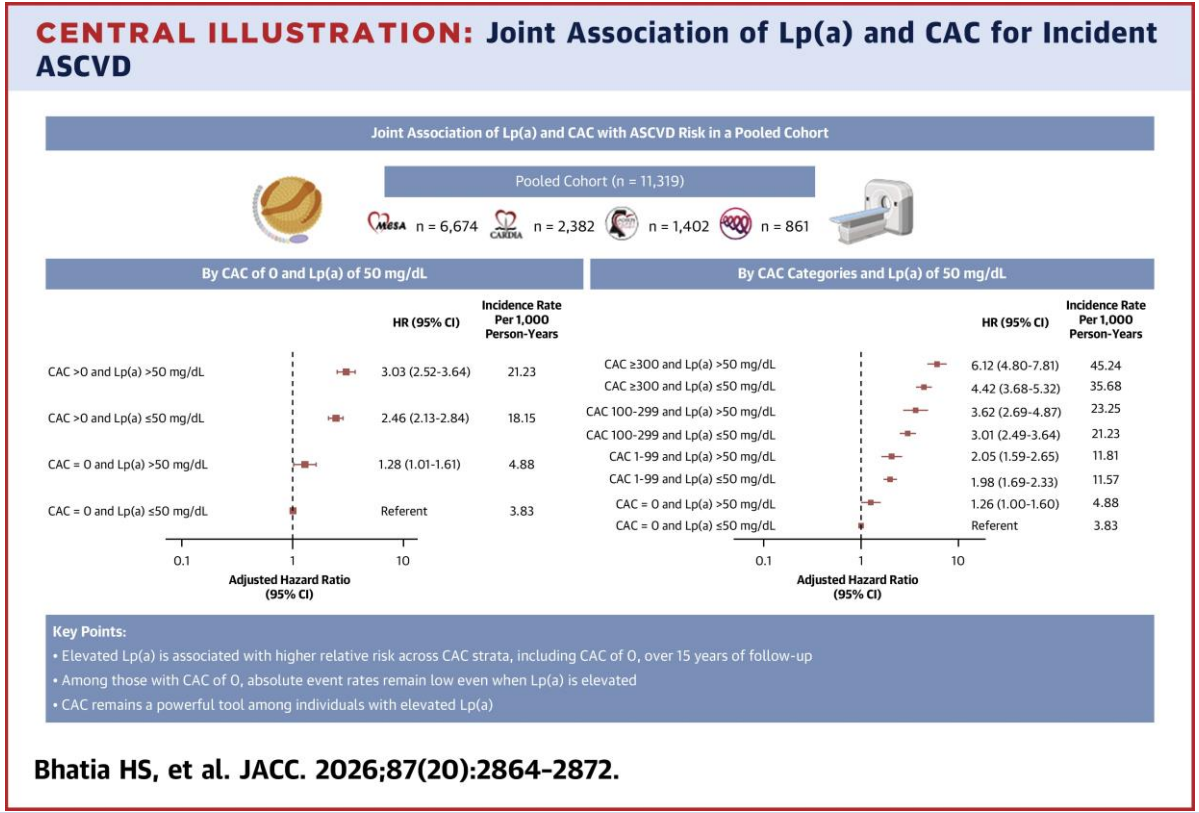
Tailoring Risk Assessment



Patient example: For a patient with 10-y risk estimate of 10.0%, who has an Lp(a) level of 250 nmol/L, the updated predicted risk estimate would be 16.9%: $10.0\ \% \times 1.11^{(250/50)} = 10.0\% \times 1.115 = 10.0\% \times 1.69 = 16.9\%$

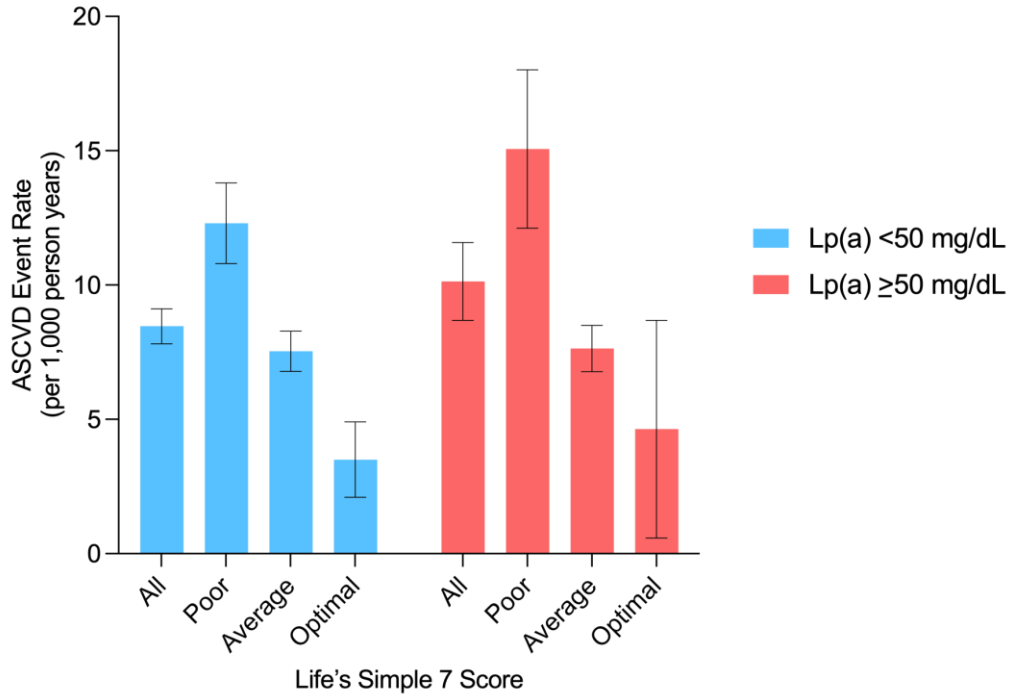
Patel et al, ATVB 2021; Reyes-Soffer et al, ATVB 2022

Coronary Artery Calcium Scoring



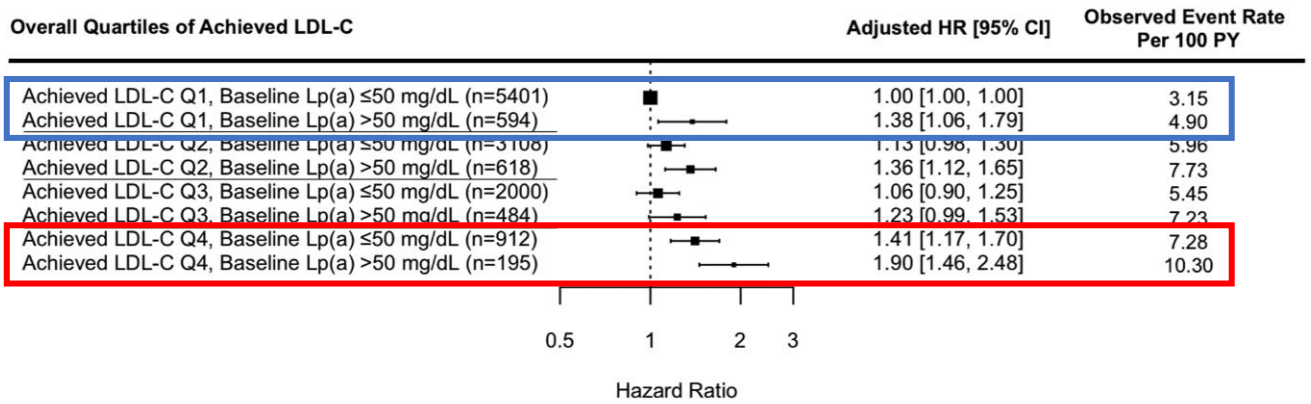
Bhatia et al, JACC 2026

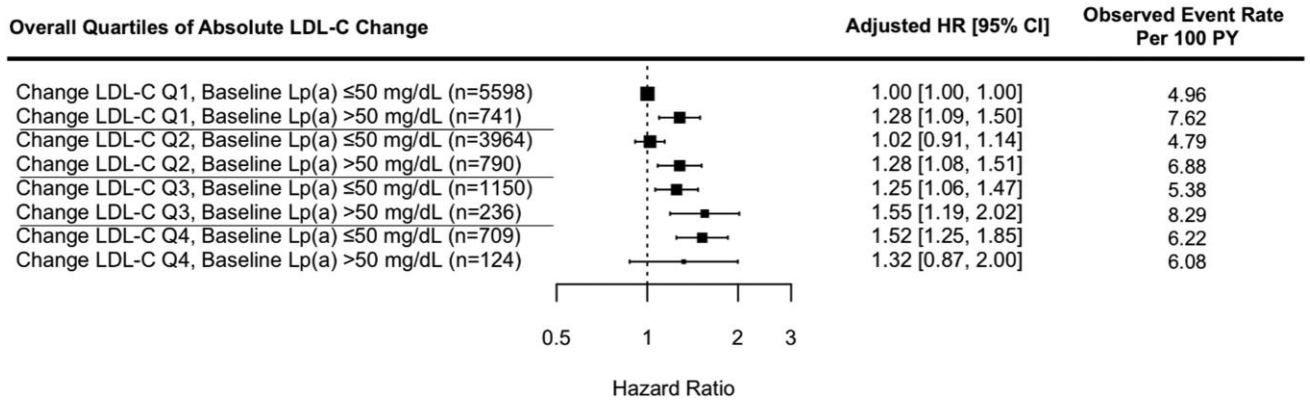
Targeting Aggressive Risk Factor Modification



Razavi and Bhatia, et al, EJPC 2025

More aggressive lipid lowering therapy





Bhatia, et al, Circulation 2024

Use of PCSK9i

PCSK9 Inhibitors and Lipoprotein(a)

Study of 6 academic medical centers

453 participants
Mean 62 years of age, 42% women
Baseline Lp(a) 91.3 mg/dL
On-treatment Lp(a) 75.0 mg/dL

Lp(a) Reduction with PCSK9i

All Individuals
Median 17.3%
Median 11.3 mg/dL

Lp(a) >50 mg/dL
Median 17.7%
Median 19.2 mg/dL

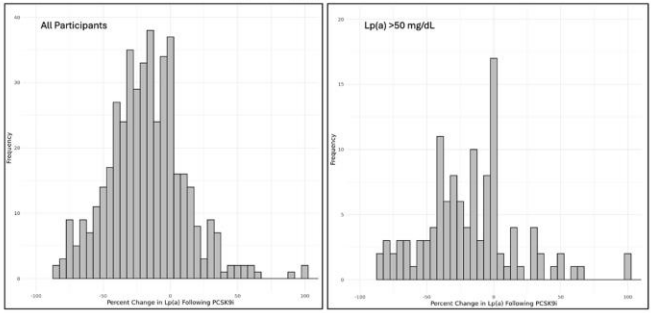
By Sex
Women: median 16.2%
Men: median 18.6%

By Assay Type
Mass (mg/dL): median 18.6%
Molar (nmol/L): median 17.4%

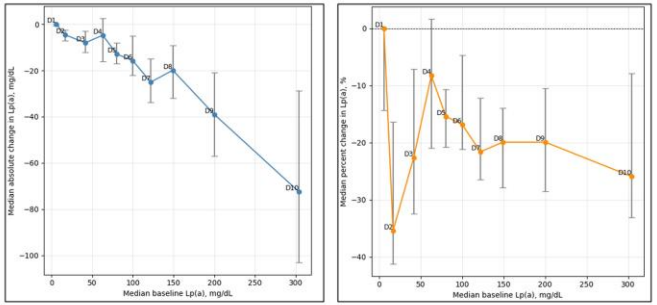
Predictors of Response

Baseline Lp(a) level ↑
Female sex ↓

Distribution of Percent Change in Lp(a) with PCSK9i

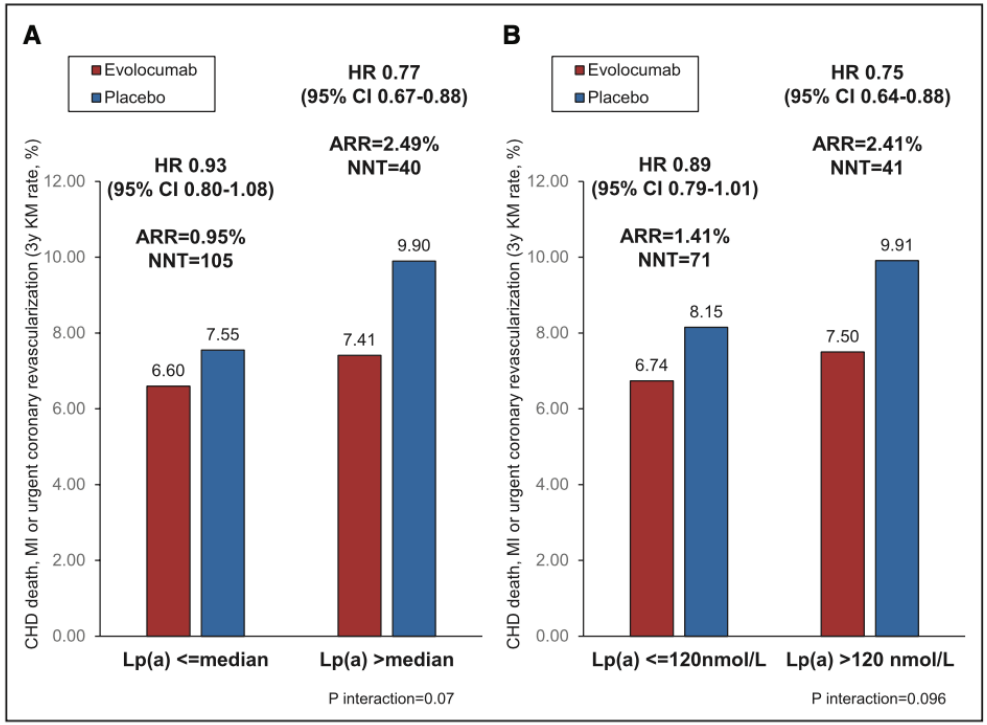


Absolute and Percent Change in Lp(a) with PCSK9i by Baseline Lp(a)



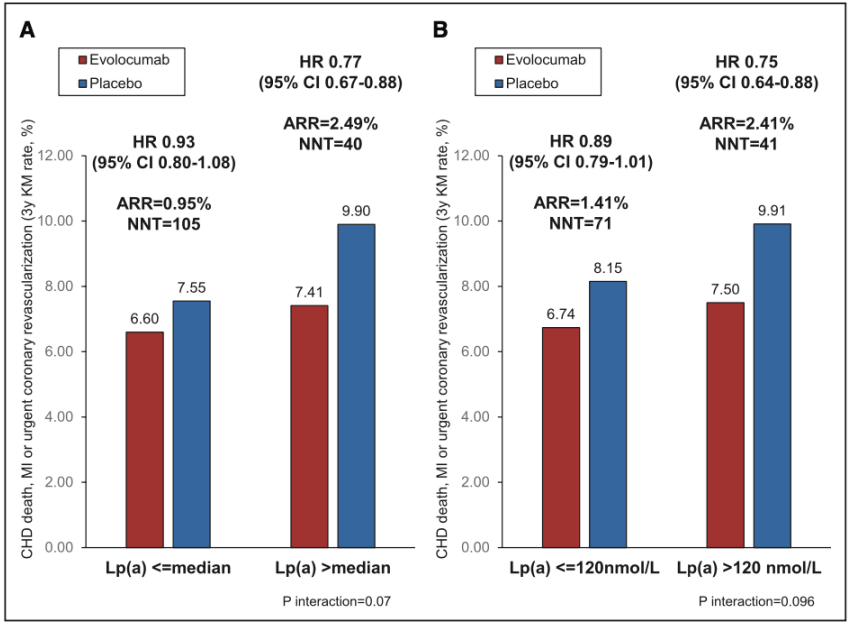
Bhatia, et al, EJPC 2025

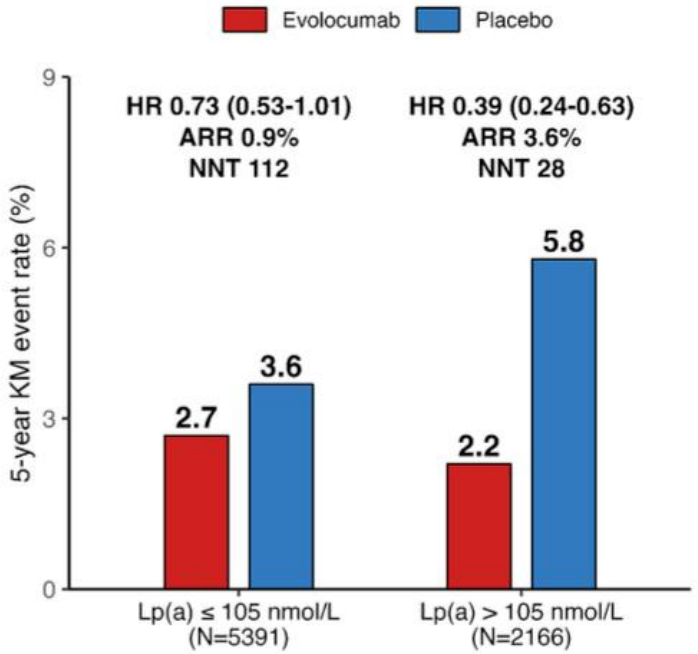
Use of PCSK9i



O'Donoghue et al, Circulation 2019

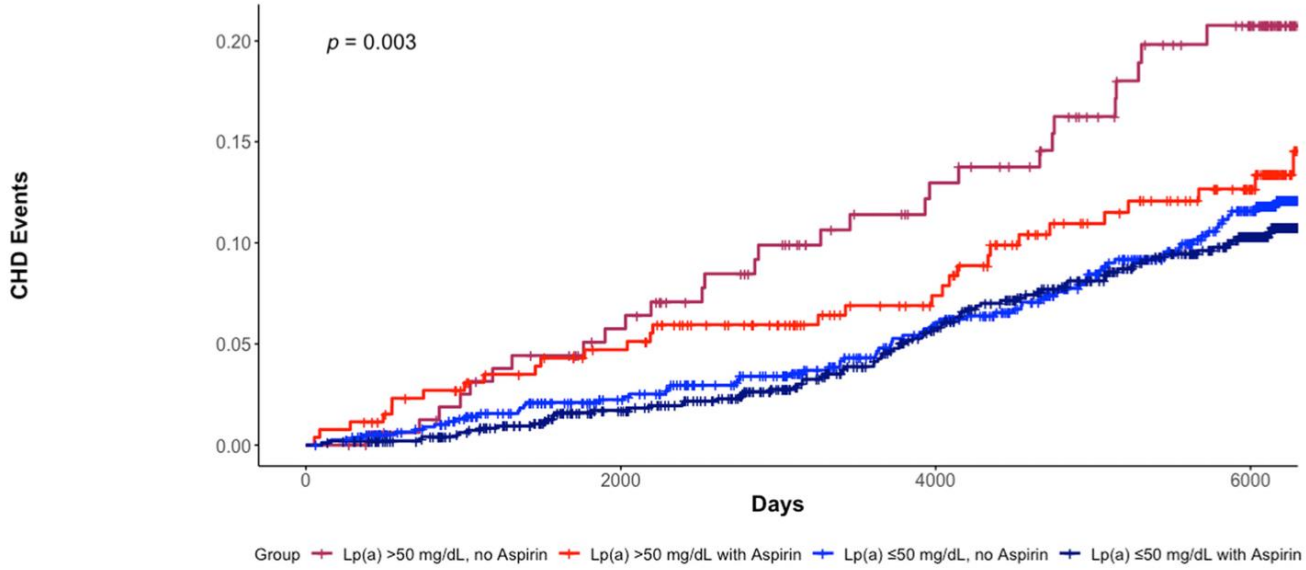
Use of PCSK9i





O'Donoghue et al, Circulation 2019; Monguillon et al, Circulation 2026

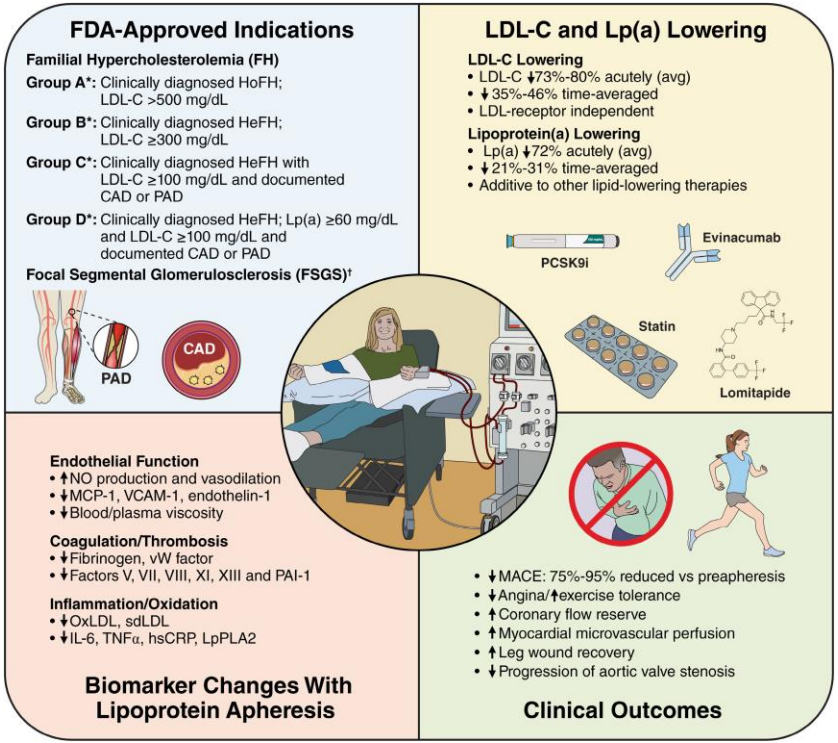
Potential Role for Aspirin Therapy in Primary Prevention



HR for aspirin: **0.54 (0.31-0.93) among Lp(a) >50 mg/dL**
0.80 (0.58-1.10) among Lp(a) ≤50 mg/dL

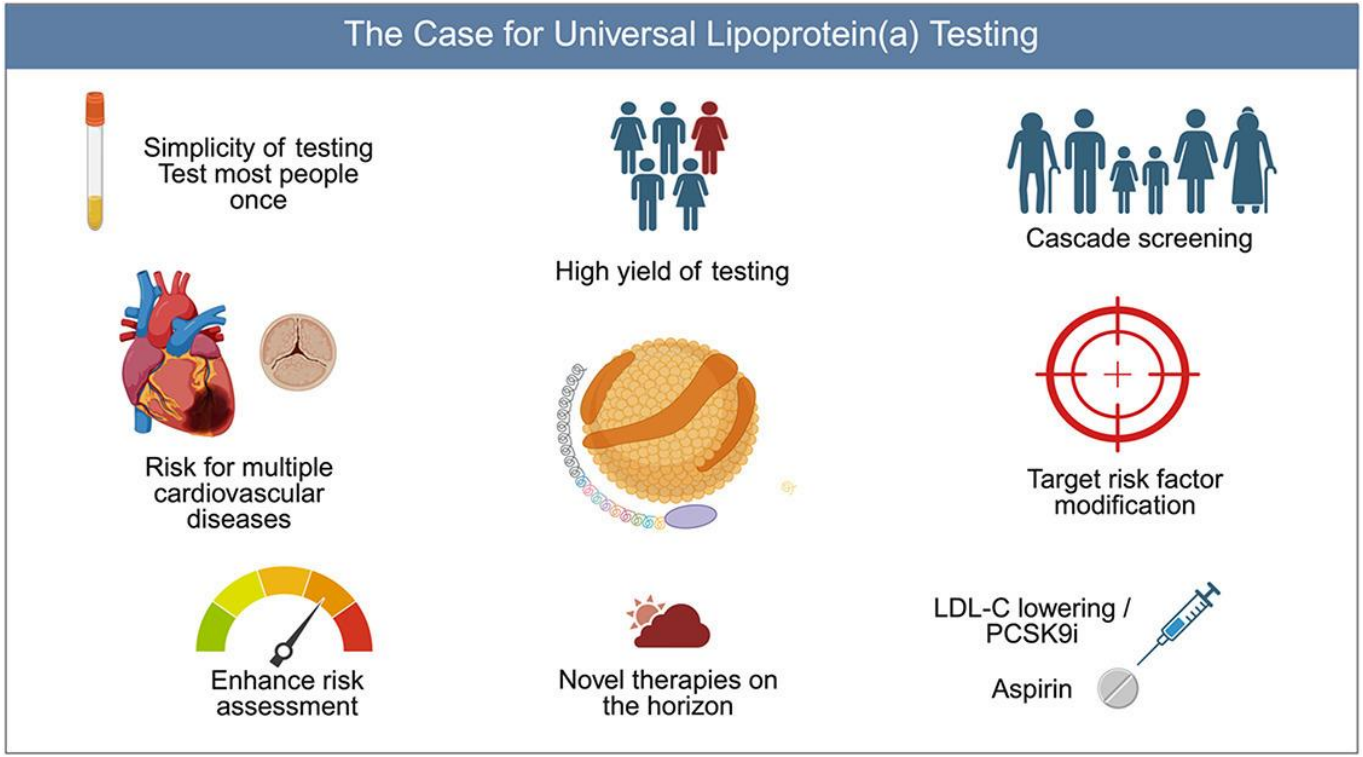
Bhatia, et al, JAHA 2024

Lipoprotein apheresis



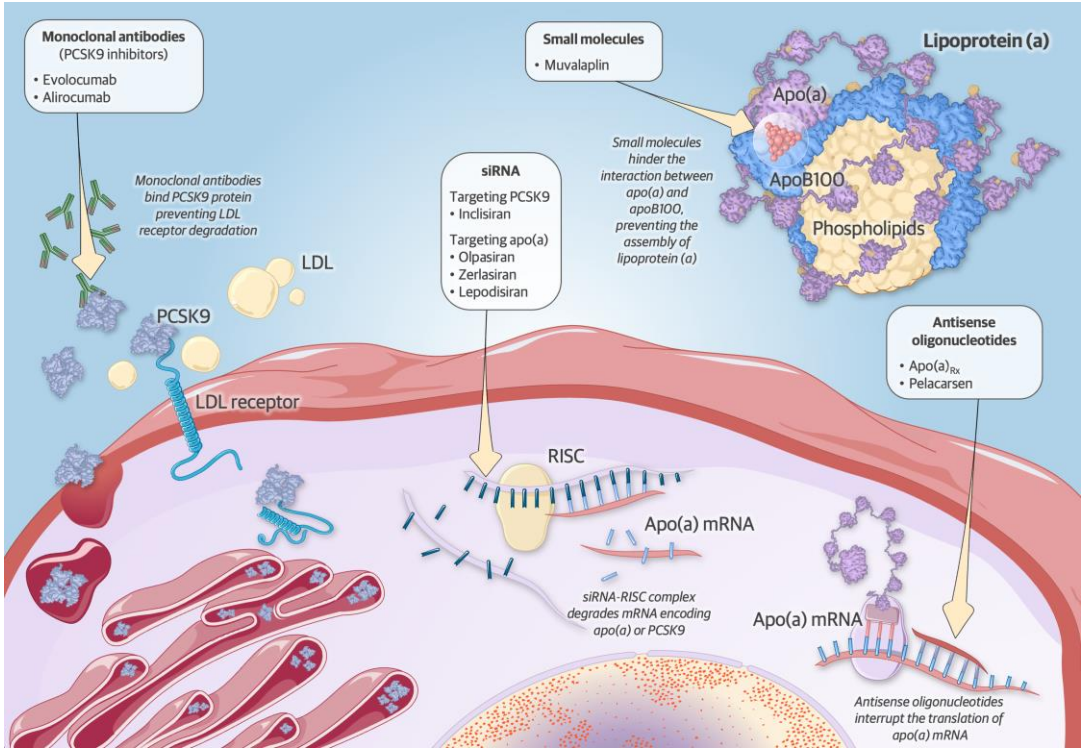
Gianos, et al. ATVB, 2024.

Universal Lp(a) Testing



Bhatia, et al, AJPC 2025

Emerging Therapies



Greco et al, Circulation 2025

Emerging Therapies

Drug	Mechanism	Lp(a) lowering	Trial	Est. Completion
Pelacarsen	ASO	80%	Lp(a)HORIZON (2˙ prevention) Lp(a)FRONTIERS CAVS (AS)	2026 2030
Olpasiran	siRNA	>95%	OCEAN(a)-Outcomes (2’) OCEAN(a)-PreEvent (1’)	2028 2031
Lepodisiran	siRNA	~95%	ACCLAIM-Lp(a) (1’ and 2’)	2029
Muvalaplin	Small molecule	70-86%	MOVE-Lp(a) (1’ and 2’)	2031
Zerlasiran	siRNA	~86%	Phase 3 TBD	TBD
HRS-5346	Small molecule		Phase 2	TBD
AZD4954	Small molecule		Phase 1	2026

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Thank you!

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