MyCardioAdvocate™

Lipoprotein(a) & Cardiovascular Risk

When inherited risk is invisible, lifelong, and rarely measured

Updated March 2026 — Reflects the 2026 ACC/AHA/NLA Dyslipidemia Guidelines (Blumenthal et al., JACC 2026)

Why This Matters

Lipoprotein(a) — or Lp(a), pronounced "L-P-little-a" — is a genetically determined lipoprotein particle that increases cardiovascular risk independently of LDL cholesterol. Think of it as LDL's dangerous cousin: an LDL-like particle with an extra protein (apolipoprotein(a)) wrapped around it, making it stickier, more inflammatory, and more prone to causing blood clots.

Elevated Lp(a) affects approximately **1 in 5 people worldwide** — yet most have never been tested. Unlike LDL-C, which responds to diet and statins, Lp(a) is roughly **90% genetically determined**. You can't exercise it away or diet it down. It's present from birth, doesn't change much over your lifetime, and is associated with significantly increased risk of heart attack, stroke, and **calcific aortic stenosis**.

Until March 2026, no major U.S. guideline formally recommended testing Lp(a) in everyone. That changed with the 2026 ACC/AHA/NLA Dyslipidemia Guidelines — Lp(a) measurement is now a **Class I recommendation** (the strongest possible endorsement) for all adults. This is a sea change.

Why Lp(a) Flies Under the Radar

Despite its importance, Lp(a) is one of the most under-recognized and under-tested cardiovascular risk factors in clinical medicine. Here's why:

- **Not on a standard lipid panel** — Your doctor has to specifically order it. A "complete" lipid panel (total cholesterol, LDL-C, HDL-C, triglycerides) does not include Lp(a).
- **No U.S. guideline recommended universal screening until 2026** — Prior to March 2026, Lp(a) was listed only as a "risk enhancer" — something to consider, not mandate.
- **Can't be lowered by lifestyle** — Because it's genetically determined, diet and exercise don't meaningfully reduce it. This leads some clinicians to ask "why test if we can't change it?" — but knowing your Lp(a) changes *everything else* about your treatment strategy.
- **Most clinicians weren't trained on it** — Lp(a) wasn't emphasized in medical education until recently. Many practicing physicians have limited experience interpreting or acting on results.
- **Lab reporting is confusing** — Lp(a) can be reported in nmol/L or mg/dL, and the two units are **not interchangeable**. This causes confusion for both patients and clinicians.
- **Lp(a) causes aortic stenosis — not just coronary disease** — The oxidized phospholipids (OxPL) on Lp(a) particles promote inflammation and calcification of the aortic valve. Mendelian randomization studies confirm this is *causal*, not just associated. Patients with elevated Lp(a) may develop aortic stenosis earlier and more aggressively.
- **No FDA-approved Lp(a)-specific therapy — yet** — Several drugs are in Phase 3 trials (pelacarsen, olpasiran, lepodisiran, muvalaplin), but none are commercially available yet. This doesn't mean testing is pointless — it means *everything else* needs to be optimized.

What Changed in the 2026 Guidelines

Universal Lp(a) Screening: Class I (B-NR)
Measure Lp(a) at least once in ALL adults to identify those with elevated levels. This is the strongest possible recommendation — a sea change from 2018.

- **Elevated Lp(a):** ≥125 nmol/L (or ≥50 mg/dL) is a formal risk enhancer
- **Very high Lp(a):** ≥200 nmol/L (or ≥75 mg/dL) confers additional risk thresholds
- **PCSK9 monoclonal antibodies** (evolocumab, alirocumab) specifically recommended for ASCVD patients with elevated Lp(a) not at LDL-C goal (Class I, B-R) — these lower Lp(a) by ~20–25%
- **Pipeline therapies:** Pelacarsen (ASO), olpasiran and lepodisiran (siRNA), muvalaplin (oral small molecule) are in Phase 3 trials. OCEAN(a)-Outcomes results expected late 2026.

MyCardioAdvocate™ Checklist

Bring this to your visit. These questions are designed to help you have a more informed conversation with your physician about Lp(a) and what it means for your cardiovascular risk.

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1. Get Tested — It Only Needs to Be Checked Once

Lp(a) is genetically determined and doesn't change much over your lifetime. A single test is usually enough to know your level.

- ■ *Has my Lp(a) ever been measured?*
- ■ *Can you add Lp(a) to my next lipid panel?*
- ■ *Which unit is the result reported in — nmol/L or mg/dL?*
- ■ **The 2026 ACC/AHA/NLA guidelines recommend Lp(a) measurement at least once in ALL adults (Class I). nmol/L is the preferred unit. The two units are not interchangeable.**

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2. Understand Your Results

Knowing your number is the first step. Understanding what it means is the next.

- ■ *Is my Lp(a) above 125 nmol/L (or 50 mg/dL)?*
- ■ *Is my Lp(a) above 200 nmol/L (or 75 mg/dL)?*
- ■ *Does my Lp(a) level change my overall cardiovascular risk category?*

Elevated (≥125 nmol/L): A formal risk enhancer — may warrant more aggressive LDL-C lowering and earlier statin consideration.
Very high (≥200 nmol/L): Equivalent to heterozygous familial hypercholesterolemia in terms of lifetime cardiovascular risk.

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3. Put It in Context — Lp(a) Amplifies Everything

Lp(a) doesn't exist in isolation. Combined with other risk factors, it amplifies risk exponentially.

- ■ *Do I have other ASCVD risk factors — smoking, hypertension, diabetes, family history?*
- ■ *Has a coronary artery calcium (CAC) score been considered to assess subclinical disease?*
- ■ *If I've had a CAC CT, was there any calcification of my aortic valve?*
- ■ *Have I been evaluated for familial hypercholesterolemia (FH) as well?*
- ■ *Given the Lp(a)–aortic stenosis connection, should I have baseline echocardiography?*

> **Pro Tip:** If you have had a coronary artery calcium (CAC) CT scan, ask your doctor: *"Was there any evidence of calcification of my aortic valve on that scan?"* Elevated Lp(a) is a **causal driver of calcific aortic stenosis** through OxPL-mediated inflammation. Incidental aortic valve calcification on a CAC CT — combined with elevated Lp(a) — may warrant closer echocardiographic surveillance and more aggressive risk management.

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4. Optimize Everything You CAN Control

Since you can't change your Lp(a), every other modifiable risk factor becomes more important.

- ■ *Is my LDL-C aggressively treated? What is my LDL-C and ApoB target?*
- ■ *Is my blood pressure at goal?*
- ■ *Am I on appropriate anti-inflammatory therapy if hsCRP is elevated?*
- ■ *Am I exercising, maintaining healthy weight, and managing metabolic risk?*
- ■ **You can't change Lp(a) — but you can relentlessly control everything else. An aggressive approach to LDL-C, blood pressure, inflammation, and metabolic health is essential.**

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5. Discuss Lp(a)-Targeting Therapies

While no FDA-approved Lp(a)-specific drug exists yet, there are options — and the pipeline is promising.

- ■ *If I have ASCVD and elevated Lp(a), am I on a PCSK9 inhibitor?*
- ■ *Does my doctor know that PCSK9 monoclonal antibodies lower Lp(a) by ~20–25%?*
- ■ *Am I aware of clinical trials for dedicated Lp(a)-lowering drugs?*
- ■ *Is Lp(a) apheresis an option for me? (FDA-approved for Lp(a) ≥60 mg/dL with FH + CAD/PAD)*

The 2026 guidelines specifically recommend PCSK9 mAbs (evolocumab, alirocumab) for ASCVD patients with elevated Lp(a) not at LDL-C goal (Class I, B-R). Dedicated Lp(a)-lowering drugs — pelacarsen, olpasiran, lepodisiran, and muvalaplin — are in Phase 3 trials with results expected 2026–2027.

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6. Protect Your Family — Cascade Screening

Lp(a) is inherited. If yours is elevated, your children and siblings likely carry the same risk.

- ■ *Should my children be tested for Lp(a)?*
- ■ *Should my siblings or parents be tested?*
- ■ *Is there a family pattern of premature heart disease that Lp(a) might explain?*
- ■ **Cascade screening — testing first-degree relatives when a family member has elevated Lp(a) — can identify at-risk individuals before events occur. This is especially important for children, who can benefit from early aggressive prevention if elevated Lp(a) is confirmed.**

CPR Opportunities — Shared Decision-Making

The 2026 guidelines introduce the **CPR Framework**: **C**alculate risk, **P**ersonalize the discussion, **R**eclassify with imaging. The following topics represent gray areas in Lp(a) management where a patient-centered discussion with your clinician is especially important.

Aspirin Use in Elevated Lp(a)

The role of aspirin in primary prevention has narrowed considerably. However, emerging evidence suggests Lp(a) may be one area where aspirin retains a meaningful role — likely because Lp(a)'s pro-thrombotic properties tip the risk–benefit balance in favor of antiplatelet therapy.

- **ASPREE Trial (JACC 2022):** Among 12,815 genotyped adults ≥70 years, aspirin showed no overall benefit. But in participants with Lp(a)-elevating genotypes (rs3798220-C carriers and highest quintile of Lp(a) genetic risk score),

aspirin reduced MACE by 11.4 and 3.3 events per 1,000 person-years, respectively, without significantly increasing bleeding.

• **Women's Health Study:** Women carrying the rs3798220-C variant (Lp(a) 80–154 mg/dL) experienced approximately a 2-fold reduction in CVD risk with aspirin vs. placebo, with no increased bleeding.

• **MESA (JAHA 2024):** In 2,183 propensity-matched participants without baseline CVD, aspirin was associated with a **46% reduction in coronary heart disease events** (HR 0.54, 95% CI 0.32–0.94) among those with Lp(a) >50 mg/dL. Aspirin users with elevated Lp(a) had similar CHD risk to those with normal Lp(a).

• **CKD Cohort (JACC Advances 2025):** In patients with chronic kidney disease, aspirin was associated with substantial risk reductions for MI and ESRD specifically in those with elevated Lp(a), without increased bleeding risk.

Important limitations: Most data come from post-hoc subgroup analyses or observational studies. The ASPREE analysis used genetic markers rather than directly measured Lp(a). The optimal Lp(a) threshold for aspirin benefit remains unclear (studies use cutoffs of 44–50 mg/dL). Prospective randomized trials specifically testing aspirin in elevated Lp(a) are needed.

Applying "CPR" to the Aspirin Question:

Calculate — Use PREVENT-ASCVD for baseline 10-year and 30-year risk
Personalize — Factor in elevated Lp(a), pro-thrombotic risk, aortic valve calcification, and individual bleeding risk
Reclassify — A CAC CT showing coronary calcium and/or aortic valve calcification, combined with elevated Lp(a), may help determine whether low-dose aspirin has a net benefit

Given the lack of FDA-approved Lp(a)-lowering therapy, aspirin may represent a viable, low-cost option for selected patients with elevated Lp(a) — but benefits must be balanced against individual bleeding risk through shared decision-making.

Statin Intensity & Add-On Therapy in Elevated Lp(a)

Patients with elevated Lp(a) often have "normal" LDL-C — yet carry significantly elevated lifetime cardiovascular risk. The question of how aggressively to lower LDL-C (and whether to add PCSK9 inhibitors in primary prevention) is an evolving area of individualized decision-making.

Applying "CPR" to Statin Intensity:

Calculate — Standard risk calculators do not account for Lp(a); your true risk may be higher than the number suggests
Personalize — Elevated Lp(a) is a risk enhancer that may justify earlier and more aggressive LDL-C lowering — even in patients who appear "moderate risk" by traditional criteria
Reclassify — CAC scoring can help: a high CAC in a patient with elevated Lp(a) strongly supports aggressive statin therapy and possible add-on agents (ezetimibe, PCSK9 inhibitor)

On the Horizon

The Lp(a) landscape is changing rapidly. While no dedicated Lp(a)-lowering therapy is yet FDA-approved, multiple agents are in late-stage clinical trials — and early results are encouraging.

Dedicated Lp(a)-Lowering Therapies

• **Pelacarsen (ASO):** An antisense oligonucleotide targeting apolipoprotein(a) mRNA. The HORIZON trial — a Phase 3 cardiovascular outcomes trial — is the largest trial specifically testing whether lowering Lp(a) reduces cardiovascular events. Results expected 2026–2027.

• **Olpasiran (siRNA):** A small interfering RNA that reduces Lp(a) by >95% in Phase 2. OCEAN(a)-Outcomes — a Phase 3 cardiovascular outcomes trial enrolling ~7,200 patients — has results expected late 2026.

- **Lepodisiran (siRNA):** An Eli Lilly siRNA with ~94–95% Lp(a) reduction sustained through day 360 after a single dose in Phase 2.
- **Muvalaplin (oral small molecule):** The first oral Lp(a)-lowering agent, disrupting the apo(a)–apoB assembly. Phase 2 data shows ~60–65% Lp(a) reduction.

Lp(a) Lowering and Aortic Stenosis

Perhaps the most exciting frontier: if Lp(a)-lowering therapies prove effective at reducing cardiovascular events, they could also potentially **slow or prevent calcific aortic stenosis** — a disease for which no medical therapy currently exists (only valve replacement). The causal link between Lp(a), OxPL, and aortic valve calcification suggests that reducing Lp(a) could interrupt the disease process at its source. Additionally, emerging data on aspirin's potential to reduce OxPL-mediated inflammation raises the possibility that even current therapies could play a role in aortic stenosis prevention — an area that warrants further investigation.

Key References:

Lacaze P et al. Aspirin for Primary Prevention of CV Events in Relation to Lp(a) Genotypes. JACC. 2022.
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Razavi AC et al. Primary Prevention Aspirin, Lp(a), and Cardiorenal Outcomes in CKD. JACC Advances. 2025.
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Bhatia HS. Aspirin and Lipoprotein(a) in Primary Prevention. Curr Opin Lipidol. 2023.

Key Takeaways

- **Lp(a) measurement is now Class I** — every adult should be tested at least once (2026 ACC/AHA/NLA)
- **Elevated Lp(a) (≥125 nmol/L or ≥50 mg/dL)** is a formal cardiovascular risk enhancer
- **Lp(a) is a causal driver of calcific aortic stenosis** — not just coronary artery disease
- **~90% of Lp(a) is genetically determined** — lifestyle changes don't meaningfully reduce it
- **PCSK9 inhibitors are specifically recommended** for ASCVD patients with elevated Lp(a) (Class I)
- **Aspirin may have a role** in selected patients with elevated Lp(a) — a CPR opportunity for shared decision-making
- **The HORIZON and OCEAN(a)-Outcomes trials** will determine if dedicated Lp(a)-lowering reduces CV events
- **If Lp(a) is elevated, optimize everything else aggressively** — LDL-C, blood pressure, inflammation
- **Lp(a) is inherited** — cascade testing of family members can save lives

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Next Steps

- Ask your doctor: **"Has my Lp(a) ever been tested?"** — it only needs to be checked once
- If elevated, ask how it changes your overall risk assessment and treatment plan
- Ask whether aspirin makes sense for your individual risk profile
- If you have ASCVD + elevated Lp(a), ask about PCSK9 inhibitor therapy
- If you've had a CAC CT, ask about aortic valve calcification on that scan
- Consider cascade screening for your children and siblings

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