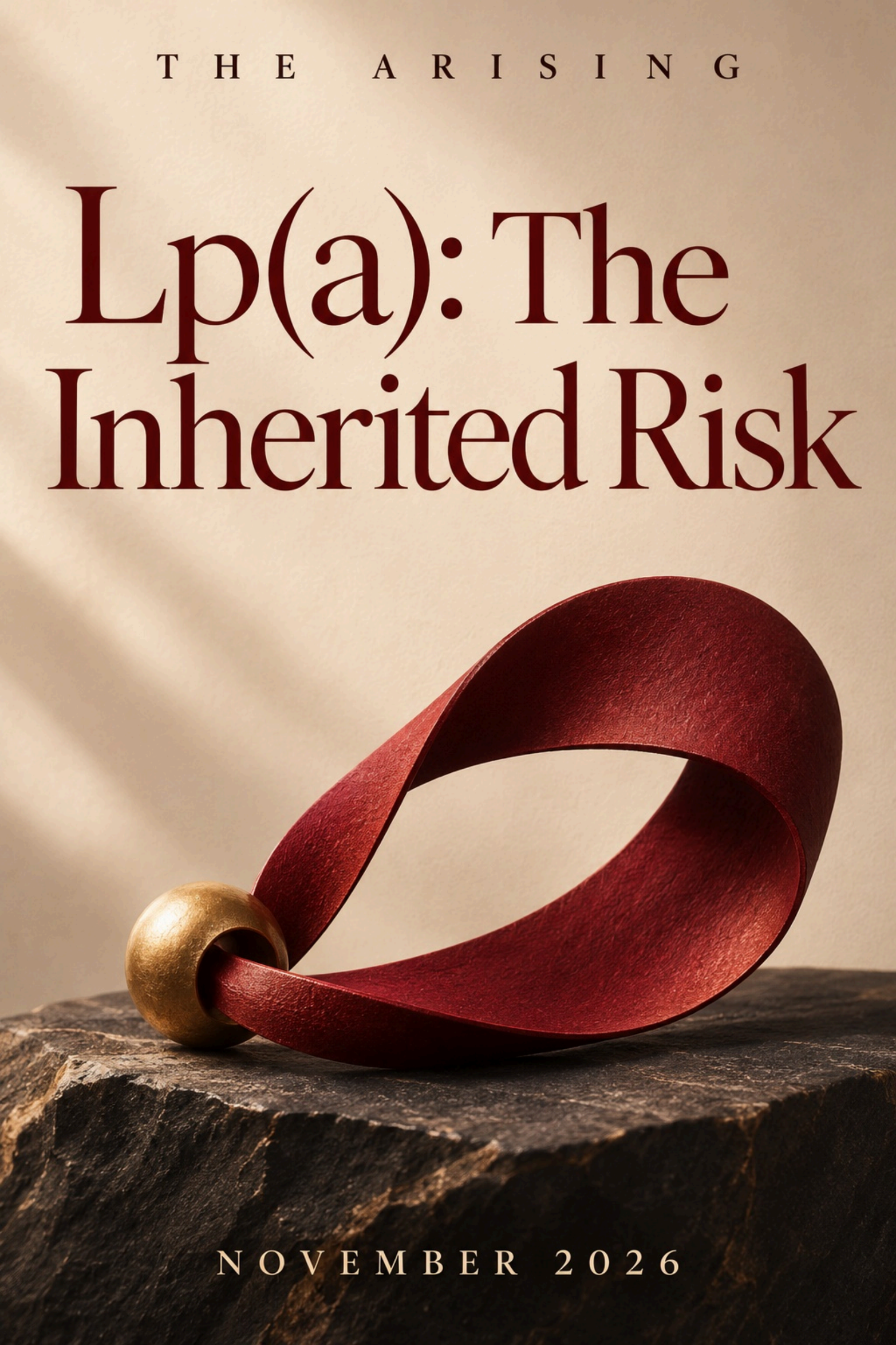
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Lp(a): The Inherited Risk



NOVEMBER 2026

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Lp(a), your family, and what comes next.

A useful question you may not have been asked

You can exercise regularly, eat thoughtfully and have a cholesterol result that looks reassuring, yet still carry an inherited cardiovascular risk that a routine cholesterol panel does not separately report. One possible reason is lipoprotein(a), usually written Lp(a) and spoken as “L-P-little-a.”

Learning about it can feel unsettling. It can also make the next conversation more useful. An elevated result is not a prediction that something terrible will happen. It is another piece of information about risk, one that can help put family history and prevention decisions into context.

The practical starting point is modest: have you had Lp(a) measured, and would knowing the result change your care?

Current professional guidance supports measuring it at least once in adulthood. The next step is to interpret it with the rest of your health, rather than treating the number as an emergency or a verdict. [1,2]

What makes this particle different?

Cholesterol travels through blood in particles called lipoproteins. Lp(a) is related to an LDL particle, with an additional protein called apolipoprotein(a) attached. That added protein helps distinguish it from the LDL cholesterol discussed in most routine visits. [1]

Your Lp(a) level is largely inherited. This is why a high result can appear in someone whose daily habits are sensible. It is not evidence that the person has failed to eat properly or exercise enough.

Evidence from genetics and population studies supports Lp(a) as a contributor to atherosclerotic cardiovascular disease, the artery disease behind many heart attacks and strokes. Elevated Lp(a) is also linked causally to calcific aortic valve stenosis, in which the valve that lets blood leave the heart becomes narrowed and stiff. [1]

Those are population-level findings about risk. A blood result does not diagnose blocked arteries or a narrowed valve. Nor does a lower result erase other risks, such as smoking, high blood pressure or an elevated LDL cholesterol level.

A useful way to understand the test is as an added layer of information, not a replacement for the rest of the picture.

Read the number with its units

Lp(a) reports may use milligrams per deciliter, written mg/dL, or nanomoles per liter, written nmol/L. The first describes mass; the second describes particle concentration. Because the size of the attached protein varies, there is no single conversion factor that works reliably for everyone. [1]

Keep the result in the units used by the laboratory. A number copied into a message without its units can create confusion that did not exist in the original report.

Common professional risk thresholds include 50 mg/dL or 125 nmol/L. These are separate thresholds used in guidance, not a promise that multiplying one by a fixed number produces the other. Risk also increases across a range; it does not suddenly appear at one dividing line. [1,2]

Imagine two people whose results both exceed a guideline threshold. One has already had a heart attack. The other is younger, has no known cardiovascular disease and has several relatives with early heart disease. Both deserve a thoughtful discussion, but their immediate decisions need not be identical. These are illustrative situations, not individual treatment recommendations.

Age, existing disease, LDL cholesterol, blood pressure, diabetes, smoking and family history all affect what an additional risk factor means. The same laboratory number can sit within quite different overall risks.

Why one measurement can be useful

Because Lp(a) is largely genetically determined, repeated frequent testing is often less useful than it is for a measure being actively changed by treatment. “At least once” does not mean “never again”: certain secondary conditions and clinical circumstances can justify reassessment. A clinician can decide whether repeating the measurement would answer a real question. [1]

An elevated result can also open a family conversation. Close relatives may share the inherited tendency, so asking whether they should be tested can be worthwhile. Family testing is an invitation to understand risk, not a way to assign blame or assume that everyone has the same result.

If you have a copy of an old laboratory report, bring it. The exact value, units and date are more useful than remembering that something was “high.”

What can change now, even if Lp(a) does not?

A common frustration is that healthy habits may have little effect on Lp(a) itself. That does not make those habits pointless. They can improve other parts of cardiovascular risk and daily health while the inherited number remains similar. [1]

Clinicians can act on LDL cholesterol, blood pressure, smoking and diabetes, and discuss physical activity and a workable eating pattern. Someone with established cardiovascular disease may need a different intensity of prevention from someone without it. A high Lp(a) result can strengthen the reason to take the whole picture seriously.

This also explains a seemingly confusing point about statins. They may modestly raise Lp(a) in some people, yet that is not a reason to stop a treatment prescribed to reduce cardiovascular risk. A change in one laboratory measure must be interpreted alongside the treatment's demonstrated benefits and the individual's situation. Medication changes belong in a clinical discussion. [1]

PCSK9-directed medicines are another part of lipid care, but they should not all be treated as interchangeable. The evidence for a particular medicine, its intended use and its effects on LDL and Lp(a) need to be kept separate. A lower Lp(a) measurement during treatment does not by itself prove that this change caused a reduction in heart attacks.

In selected patients, specialists may consider lipoprotein apheresis, a procedure that removes certain lipoproteins from blood. It is not a routine first step for everyone with an elevated test. Eligibility and access depend on the clinical situation and local rules. [1]

There is useful work to do now without promising that every part of inherited risk can be removed.

The new result that changes the treatment story

A major question has been whether a drug designed to lower Lp(a) will also prevent cardiovascular events. The HORIZON trial tested pelacarsen in people with established cardiovascular disease and high Lp(a). Its results were published in November 2026. [3]

Its main outcome was the first occurrence of cardiovascular death, a nonfatal heart attack, a nonfatal ischemic stroke, or urgent coronary revascularization requiring hospitalization: an urgent procedure to restore blood flow in the heart’s arteries.

The report described 8,350 people randomized to pelacarsen or placebo, with 8,322 included in the efficacy analysis. Over a median follow-up of 4.7 years, the main cardiovascular outcome occurred in 511 of 4,157 participants receiving pelacarsen, or 12.3%, and 503 of 4,165 receiving placebo, or 12.1%. The trial did not demonstrate a cardiovascular benefit despite markedly lowering Lp(a). [3]

The estimated hazard ratio was 1.02. In everyday language, the observed rates over time were very similar. The 95% confidence interval, an uncertainty range from 0.90 to 1.15, allowed for some benefit or some harm; it did not establish an improvement. This was not a result showing that a dramatic laboratory change reliably delivered better health outcomes.

The trial also involved treatment burdens. An investigator-institution account reported more flu-like symptoms and injection-site reactions, with treatment discontinuations due to adverse events in 20.6% versus 7.5%. A drug's ability to lower a number is only one part of deciding whether its use helps people. [4]

This result matters, but its meaning should not be stretched. It does not show that Lp(a) is irrelevant, erase the genetic evidence, or prove that every other approach must fail. It tells us that this drug, in this studied population and follow-up, did not demonstrate the hoped-for cardiovascular benefit.

It is a reason to be precise, not a reason to abandon either curiosity or prevention.

Other approaches still have to answer the outcome question

Other investigational medicines aim to reduce production of Lp(a), including olpasiran and lepodisiran. Their large outcome trials address the question that a striking drop in a biomarker cannot settle on its own: do fewer people experience important cardiovascular events? [5,6]

The retrieved trial records list both studies as active but not recruiting, with no results posted. Their estimated primary completion dates are in 2028 and 2029, respectively. Those dates are plans, not guarantees, and a registry entry is not a result. [5,6]

Different medicines may have different effects, harms and practical burdens. An encouraging early change in Lp(a) should therefore be described as a laboratory finding until clinical outcomes support a stronger claim. An investigational treatment is not a reason to postpone appropriate care available now.

Bring the result back to a person

A useful next appointment does not have to become a debate about every drug in development. A few concrete questions can move it forward:

• Have I had Lp(a) measured? What were the exact value and units?

• How does it change the interpretation of my family history and overall risk?

• Which parts of my risk can we act on now?

• Does my LDL cholesterol plan still fit, given this additional information?

• Should close relatives discuss testing with their clinicians?

• Would repeat testing or specialist advice answer a specific question?

For someone with a high result, the goal is neither panic nor dismissal. It is a clearer prevention plan. For someone whose result is lower, the goal is not permission to ignore the rest of cardiovascular health.

Inherited risk is information about where you begin. Understanding it can help you and your clinician decide what to do next.

Sources and further reading

[1] Kronenberg F, Mora S, Stroes ESG, et al. Lipoprotein(a) in atherosclerotic cardiovascular disease and aortic stenosis: a European Atherosclerosis Society consensus statement. *European Heart Journal*. 2022. Full text.

[2] Blumenthal RS, Morris PB, Gaudino M, et al. 2026 ACC/AHA multisociety guideline on the management of dyslipidemia. *Circulation*. 2026;153:e1154–e1276. Publication. Official summary.

[3] Cho L, Nicholls SJ, Frndak S, et al. Pelacarsen and Cardiovascular Outcomes in Patients with High Lipoprotein(a). *New England Journal of Medicine*. Published November 7, 2026. Primary report.

[4] Cleveland Clinic. Lipoprotein(a) reduction with pelacarsen has no impact on cardiac events.

[5] OCEAN(a)-Outcomes. Trial record NCT05581303.

[6] ACCLAIM-Lp(a). Trial record NCT06292013.

HORIZON was funded by Novartis. The Cleveland Clinic account comes from the investigators’ institution; it is not an independent trial.