MyCardioAdvocate™

HDL Cholesterol

When 'good' cholesterol isn't good enough.

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Why This Matters

For decades, HDL cholesterol earned its nickname 'good cholesterol' and became the poster child of cardiovascular protection. Patients memorized the mantra: 'Get your HDL high, get your LDL low.' Yet the past 15 years of clinical trials have delivered a humbling message: raising HDL cholesterol does not reduce heart attacks or strokes. This paradigm shift—from HDL quantity to HDL function—represents one of the most consequential reframes in cardiology, one that many patients and providers have yet to fully absorb.

The result: enormous resources have been devoted to raising HDL-C through medications (CETP inhibitors) that failed to improve clinical outcomes, while the focus on what actually matters—HDL function, ApoB particle burden, and anti-inflammatory state—has been neglected. Understanding why higher HDL does not equal better outcomes is critical to making sense of modern lipid management.

Why HDL Flies Under the Radar

The intuitive simplicity trap. 'High HDL is good, low HDL is bad' is so intuitive and has been repeated for so long that it has become gospel. Questioning it feels contrarian, even though the evidence has moved on.

CETP inhibitor trials revealed the paradox. Torcetrapib (ILLUMINATE) raised HDL by 72% but showed no CV benefit and increased mortality. Dalcetrapib (dal-OUTCOMES) raised HDL by 31% and showed no benefit. Evacetrapib (ACCELERATE) raised HDL but failed to reduce CV events. Yet many patients still ask their provider for 'something to raise HDL.'

HDL is heterogeneous; number masks dysfunction. A lab report showing HDL = 60 mg/dL tells you nothing about HDL particle size, composition, or function. In inflammatory states or metabolic syndrome, HDL becomes dysfunctional ('pro-inflammatory HDL') despite normal or high HDL-C levels.

Very high HDL may paradoxically increase risk. A U-shaped curve has emerged in some populations: extremely high HDL (>80-90 mg/dL) is associated with higher mortality than moderate HDL. This flies in the face of conventional wisdom.

What Changed in 2026

HDL-C raising abandoned as a therapeutic target. ACC/AHA guidelines no longer recommend treatments whose primary goal is HDL raising. Drugs like CETP inhibitors have fallen out of favor.

Obicetrapib mechanism reconsidered. Obicetrapib (BROADWAY, TANDEM trials) lowers LDL-C as its primary mechanism—not raises HDL. This reframing emphasizes LDL and ApoB reduction over HDL manipulation.

HDL particle count and function emphasized. When HDL is discussed, the focus has shifted to particle count (apoA-I) and antioxidant function, not total HDL-C number.

MyCardioAdvocate™ Checklist

Use this checklist to reframe your understanding of HDL and cholesterol:

1. Don't rely on HDL number alone for reassurance.

A high HDL-C does not guarantee CV protection. Focus instead on overall lipid pattern: Is LDL-C low? Is ApoB low? Are triglycerides controlled?

2. Understand HDL function, not just quantity.

Ask your provider: 'Does my HDL look normal and functional, or is there evidence of inflammation that might make it dysfunctional?' Inflammatory markers (hs-CRP) can hint at HDL dysfunction.

3. If your HDL is exceptionally high (>80 mg/dL), ask whether it's protective.

Very high HDL in some patients correlates with worse outcomes. Understanding the context (genetics, presence of metabolic syndrome, inflammation) is important.

4. Focus on ApoB and LDL-C, not HDL raising.

Modern lipid therapy targets LDL-C and ApoB reduction. If a provider suggests a drug primarily to 'raise HDL,' ask whether the drug reduces ApoB or LDL-C. If not, it probably won't help.

Key Takeaways

- Higher HDL-C does not reduce heart attack and stroke risk. Major CETP inhibitor trials showed no benefit.
- HDL function (particle number, antioxidant activity) matters more than HDL number.
- Very high HDL may paradoxically increase mortality in some populations.
- Modern lipid therapy targets LDL-C and ApoB, not HDL raising.

Next Steps & Related Content

- Stop asking for 'something to raise HDL.' Ask for LDL-C and ApoB reduction instead.
- Request a full lipid panel: LDL-C, non-HDL-C, triglycerides, HDL, and ApoB.
- If your HDL is very high (>80), discuss whether it's truly protective in your clinical context.

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