

HDL: Not so 'good' after all?

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After years of having it drilled into their heads, most people now know that LDL (low-density lipoprotein) is the "bad" cholesterol package that increases the risk of cardiovascular disease, and HDL (high-density lipoprotein) is the "good" type that helps reduce it by removing cholesterol from artery walls. So if your HDL number is high, you've probably patted yourself on the back; if it's low, you may have tried to raise it by, for instance, exercising more, losing weight, drinking a daily glass of wine, or even taking medication, such as high-dose niacin.

But before you get too hung up on HDL, you should know that while the benefits of lowering elevated LDL are proven, the evidence for raising HDL by itself remains uncertain. That's why standard cholesterol guidelines have focused almost exclusively on lowering LDL, which is

the main purpose of [statin drugs](#) (they have little effect on HDL). And recently a study in the *Lancet* raised fundamental questions about the supposed benefits of raising HDL.

[Genetic factors](#) help determine HDL levels, sometimes very strongly. In the *Lancet* paper, an international team of researchers analyzed data from 20 studies involving people with genetic variants that raise HDL but do not affect LDL, triglycerides, or related [blood lipids](#). They did a special kind of [genetic analysis](#) (called Mendelian [randomization](#)) that allowed them to determine whether high HDL, in and of itself, reduces coronary risk. Surprisingly, the evidence indicated that it does not.

An iffy link

Researchers and doctors have focused on HDL for good reason: [observational studies](#) have consistently found that people with high HDL levels are at decreased [cardiovascular risk](#). But just because there's an association between low HDL and heart disease, that doesn't mean that low HDL causes it—or that raising HDL will help prevent it. Many factors in the blood can be higher or lower with certain diseases, but relatively few actually cause the diseases. Low HDL tends to go along with other metabolic abnormalities that could directly increase risk for coronary disease, such as high levels of smaller LDL particles and increased triglycerides (fats in the blood).

So the question remains, is low HDL an independent risk factor for cardiovascular disease or merely a marker for it?

What about drugs to raise HDL?

The *Lancet* study was not the first disappointing finding about the potential benefits of raising HDL. According to the accompanying

commentary, the study confirms previous genetic analyses that "refute a causal role of HDL in coronary heart disease."

Moreover, in recent years two high-profile HDL-boosting drugs were scrapped after they failed to produce the expected benefits in pre-approval studies; one actually increased cardiovascular risk. And as we reported last year, a major study called AIM-HIGH found that prescription niacin did not further reduce the risk of heart attacks or other cardiovascular events in high-risk people who had already lowered their LDL levels via high-dose statins—even though niacin raised HDL. (Niacin also lowers LDL and triglycerides, which may explain why it was shown to be beneficial in prior studies.) Other drugs are being developed to raise HDL substantially, but in ways different from the previous drugs.

The relationship between HDL and [cardiovascular disease](#) is complicated, largely because the biochemistry of HDL is so complex. Not only does HDL interact with other lipids in the blood, but all HDL is not alike. Some HDL may do a good job at keeping arteries healthy, while other HDL may not. HDL particle size and levels of various subparticles, as well as levels of inflammation and oxidative stress in the body, may determine if, and how much, HDL is cardioprotective.

Bottom line: There are many unanswered questions about HDL. It's becoming increasingly clear that there's more to it than that single number from a basic blood test. Still, low HDL is, at the very least, a marker for increased cardiovascular risk, and should be considered in the context of your other risk factors. It may, for instance, lead your doctor to order advanced blood tests for additional cholesterol-related components such as small LDL particles. A low HDL number may also lead your doctor to more aggressively lower your LDL by medication. If you have low HDL, you should still exercise, quit smoking, and lose excess weight. Such steps help protect the heart in many ways, regardless

of their effect on HDL.

Provided by University of California - Berkeley

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