



Size and density matter: how advanced lipid testing can uncover residual risk

Despite advancements in treatment, including statin therapies, cardiovascular disease (CVD) continues to be the leading cause of death in the U.S.¹ While there are many reasons for this, one contributing factor may be the continued focus on traditional markers to manage cardiovascular risk, as supported by guidelines.



CVD continues to be the leading cause of death in the U.S.¹

Cardiovascular risk assessment has evolved beyond standard lipid panel values. More specifically, the response-to-injury hypothesis brought to light the role of inflammation in atherosclerosis and CVD.² This theory was further advanced with the response to retention hypothesis that suggested that the retained and modified lipoproteins in the arterial wall were the stimulus for the inflammatory response.³ The Québec Cardiovascular Study (1997) was the first to suggest that the presence of small, dense low-density lipoprotein (LDL) particles may be associated with an increased risk of developing CVD.⁴

Assessing LDL particle number, size, and density—using biomarkers—can help identify residual risk among patients already being monitored or treated with statin therapy.⁵⁻⁷

This paper reviews:

- **Why assessing traditional risk factors isn't enough**—size and density matter
- **Which additional markers can help** accurately assess risk
- **What can be done** to address risk once it's known

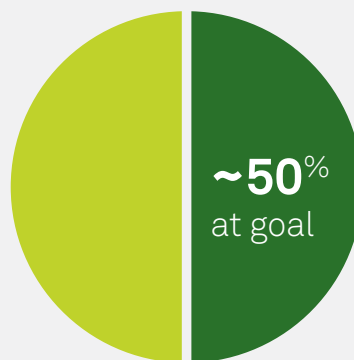


Residual risk: why size and density matter

Standard lipid screening—assessing LDL levels—plays an important role in cardiovascular risk assessment, but it may not always be predictive of adverse events. Residual cardiovascular risk can still be significant despite managing traditional risk factors.⁴

Even with intensive statin therapy, some patients remain at significant residual cardiovascular risk⁸

Studies show that LDL-C levels are often not predictive of coronary artery disease (CAD). In a population of more than 200,000 patients hospitalized with CAD, almost half had LDL-C levels <100 mg/dL.⁹

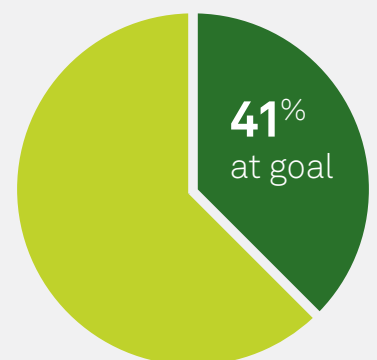


LDL-C Levels <100mg/dL

The AHA Get-With-The-Guidelines® initiative analysis⁹ revealed that a substantial proportion of patients with coronary heart disease (CHD) were well within guideline-recommended targets for lipid panel values.



1st CHD Event



Recurrent CHD

Additional studies support the need to identify residual risk in those with traditional CVD risk factors or those already being treated with statin therapies.

- An assessment of 1,919 participants from the prospective, population-based Malmö Diet and Cancer Study Cardiovascular Cohort revealed that the risk of CVD was 2.3x greater among those with higher LDL-P (LDL particle number) compared to those with lower numbers.¹⁰
- Small dense LDL-C (sdLDL-C) was measured in 11,419 men and women in the prospective Atherosclerosis Risk in Communities (ARIC) study and was found to be associated with incident CHD.¹¹
- An expert panel convened by the National Lipid Association to evaluate the use of selected biomarkers concluded that for patients with intermediate risk, a family

history of premature CVD, and those with recurrent events, measurement of apolipoprotein B (ApoB) would enable the best possible management of modifiable factors for cardiovascular risk. Among other conclusions, the panel also indicated that because elevated levels of lipoprotein(a) are additive to risk, anyone presenting with vascular disease should have this measurement.⁶

~30%–40%

of those with low LDL-C
may have elevated LDL-P¹²

Lipoprotein biomarkers and what they reveal

Emerging biomarkers have been shown to help identify residual risk in patients with traditional CVD risk factors and thus have been adopted by several guidelines and societies.⁵⁻⁷

Lipoprotein risk factors include the following:

- **LDL particle number:** the Quebec Cardiovascular Study⁴ was the first to demonstrate that heart attack can occur when LDL particle number is high and low-density lipoprotein level is low. Greater numbers of cholesterol-containing particles in the blood may suggest more cholesterol deposition in plaque and therefore an increased risk for heart attack.
- **LDL subclasses:** small LDL subclass particles may cause plaque buildup to progress much faster because they may enter the artery wall more easily than large LDL particles. A predominance of smaller LDL particles, referred to as Pattern B lipid phenotype, represents an atherogenic lipid profile that is associated with CVD.
- **HDL subclasses:** a low level of large HDL particles may reduce the efficacy of the reverse cholesterol transport process. The large HDL subclass was identified in the Malmö Diet and Cancer Study to be inversely correlated with CHD risk.¹⁰
- **ApoB:** ApoB is the primary apolipoprotein attached to all atherogenic particles. It is involved in the metabolism and transport of lipids. A high ApoB number indicates increased risk for heart disease.
- **Lp(a):** Lipoprotein(a) is an inherited protein that is attached to LDL. High levels of lipoprotein(a) increase risk of coagulation and contribute to atherosclerosis.

Taking action against residual risk

Advanced cardiovascular testing can provide actionable information to individualize treatment options, including:

- Initiating or intensifying statin therapy
- Identifying opportunities for adjunct therapy
- Setting more specific diet, exercise, and lifestyle goals

A patient with an elevated LDL particle number, for example, may benefit from diet and exercise, statins, ezetimibe, a balloon aortic valvuloplasty (BAV), or PCSK9 inhibitors; while a patient with elevated Lp(a) may benefit from a more aggressive plan to lower LDL (both LDL-C and LDL-P) or ApoB.

Ultimately, assessing lipoprotein risk factors—beyond traditional risk factors—can help physicians improve their management of cardiovascular patients, for better health and practice outcomes.

A lab that's committed to helping physicians identify residual risk

Quest Diagnostics is committed to helping physicians prevent, diagnose, and manage CVD. Our advanced cardiovascular solutions, including testing for both inflammatory and lipoprotein biomarkers, can help physicians uncover residual risk and make treatment decisions more targeted to the individual patient.



Interested in learning more? Visit [QuestDiagnostics.com/AdvancedLipidTesting](https://www.questdiagnostics.com/AdvancedLipidTesting).

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