A **TECHNICAL** REVIEW

LabCorp

Calculating Low-density Lipoprotein Cholesterol (LDL-C) Using the National Institutes of Health (NIH) Equation

LabCorp now uses the NIH equation in LDL-C calculations

Through a collaborative effort with the National Heart, Lung and Blood Institute of the National Institutes of Health (NIH), LabCorp has implemented an improved Low-density Lipoprotein Cholesterol (LDL-C) equation that overcomes the limitations of the Friedewald equation.[1] LabCorp will use the NIH LDL-C calculation [see Note 1] in place of the Friedewald equation for all lipid panels that report calculated LDL-C concentrations, and enable patients to have their blood drawn without fasting [see Note 2].

LDL-C Calculation

The NIH LDL-C equation, validated by analysis of >250,000 samples provided by LabCorp and from multiple populations from other laboratories, uses a more sophisticated process for estimating very low-density lipoprotein cholesterol (VLDL-C) than either the Friedewald or Martin equations, the latter of which employed an adjustable factor for triglyceride.[2] As a result, the NIH LDL-C equation was found to calculate LDL-C more accurately compared to the β-quantification reference method, particularly in patients with low LDL-C under 70 mg/dL, and those with elevated triglyceride levels as high as 800 mg/dL. Patient classification into correct diagnostic/prognostic categories for atherosclerotic cardiovascular disease (ASCVD) risk management is also improved, resulting in 35% less misclassification when hypertriglyceridemic patients (400-800 mg/dL) were categorized into different LDL-C treatment groups [see Note 3].[1] Importantly for patient convenience, the NIH equation performed nearly identically in fasting and non-fasting individuals.

Clinical labs traditionally calculated LDL-C levels using the Friedewald equation, which assumes total cholesterol (TC) is the sum of LDL-C, HDL-C, and VLDL-C.[3] Since VLDL-C is difficult to measure directly, its value must be estimated to enable LDL-C to be calculated as follows:

Calculated LDL-C (mg/dL) =
TC (measured) – HDL-C (measured) – VLDL-C (estimated)

The Friedewald equation makes the simplifying assumption that VLDL-C can be adequately estimated by dividing measured triglycerides (TG) by a fixed factor of 5. This assumption is invalid and calculated LDL-C unreportable when TG levels are highly elevated (≥400 mg/dL), or when the blood specimen is obtained non-fasting (the TG/5 term overestimates VLDL-C in such samples). The Friedewald calculation of LDL-C is also less reliable for clinical decision-making at lower levels of LDL-C (<70 mg/dL).[4]

Clinical Utilization

Current cholesterol management guidelines to reduce the risk of ASCVD rely heavily on low-density lipoprotein cholesterol (LDL-C) levels for therapeutic decision-making.[2] Whereas directly-measured total cholesterol and high-density lipoprotein cholesterol (HDL-C) are the laboratory measures used to calculate ASCVD risk, achieved LDL-C reductions or thresholds that match the magnitude of ASCVD risk provide the basis for determining the need for, or adequacy of, cholesterol-lowering treatment.[4]

Note 1 (NIH equation)[1]:

$$LDL\text{-}C = TC/0.948 - HDL\text{-}C/0.971 - (TG/8.56 + TG \times Non\text{-}HDL\text{-}C/2140 - TG^2/16100) - 9.44$$

Note 2: In conditions where triglyceride values provide a priori diagnostic information, such as screening for familial hypercholesterolemia or early onset heart disease, pancreatitis, or confirming hypertriglyceridemia, the patient should be counseled to fast 12-14 hours prior to blood draw.[5]

Note 3: Even with accurate LDL-C estimation, it should be noted that apolipoprotein B and other particle measures of LDL, such as LDL-P by NMR, are more closely tied to residual ASCVD risk than LDL-C when these measures are discordant.[1]

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Relevant Assays*

Test Name	Test Number
Diabetes Comorbidity Assessment	023400
Lipid Cascade With Reflex to Apolipoprotein B	363676
Lipid Cascade With Reflex to Lipoprotein Particle Assessment by NMR (With Graph)	123836
Lipid Cascade With Reflex to Lipoprotein Particle Assessment by NMR (Without Graph)	361946
Lipid Panel	303756
Lipid Panel With LDL:HDL Ratio	235010
Lipid Panel With Total Cholesterol:HDL Ratio	221010
Lipid Profile, Fasting, Pediatric	373632
Lipid Profile With Non-HDL Cholesterol	343925
NMR LipoProfile® With Lipids (With Graph)	123810
NMR LipoProfile® With Lipids (Without Graph)	884247
NMR LipoProfile® With Lipids and Insulin Resistance Markers (With Graph)	123638
NMR LipoProfile® With Lipids and Insulin Resistance Markers (Without Graph)	884000

*For the most current information regarding test options, including specimen requirements and CPT codes, please consult the online Test Menu at www.LabCorp.com.

References:
1. Sampson M, Ling C, Sun Q, et al. A new equation for calculation of low-density lipoprotein cholesterol in patients with normolipidemia and/or hypertriglyceridemia. *JAMA Cardiol.* 2020 Feb 26. doi:10.1001/jamacardio.2020.0013.
2. Martin SS, Blaha MJ, Elshazly MB, et al. Comparison of a novel method vs the Friedewald equation for estimating low-density lipoprotein cholesterol levels from the standard lipid profile. *JAMA.* 2013 Nov 20;310(19):2061-2068.
3. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem.* 1972 Jun;18(6):499-502.
4. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/ NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiololgy/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation.* 2019 Jun 18;139:e1082-e1143.
5. Driver SL, Martin SS, Gluckman MD, Clary JM, Blumenthal RS, Stone NJ. Fasting or nonfasting lipid measurements: it depends on the question. *J Amer Coll Cardiol.* 2016 Mar 15;67(10):1227-1234.

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