

Lipid measurements in the management of cardiovascular diseases

Lipoprotein measurements are essential for the management of patients at risk of:



Atherosclerotic coronary heart disease (CHD), leading to:

- Myocardial infarction
- Coronary death



Atherosclerotic cardiovascular disease (ASCVD) leading to:

- CHD
- Stroke



Continued improvements to lipid measuring guidelines will optimize their value as cardiovascular biomarkers.

Statement on the use of lipid measurements from the National Lipid Association.

Key principles:

Elevated cholesterol is a root cause of atherosclerosis and an underlying factor in clinical ASCVD events.



Cholesterol is carried by circulating atherogenic apolipoprotein B-containing lipoproteins:

- Non-high-density lipoprotein HDL-cholesterol (Non-HDL-C)
- Low-density lipoprotein cholesterol (LDL-C)



Non-HDL-C comprises cholesterol carried by all potentially atherogenic particles:

- Low-density lipoprotein (LDL)
- Intermediate density lipoprotein (IDL)
- Very low-density lipoprotein (VLDL) and remnants
- Chylomicron particles and remnants
- Lipoprotein(a) (Lp(a))

Non-HDL-C is a useful cardiovascular (CV) biomarker.

Pre-analytic issues



Samples should be collected from a patient in a stable metabolic state with no concurrent illness.



Non-fasting lipids can be used for initial screening.



If fasting or non-fasting triglycerides are elevated (>175 mg/dL, >2 mmol/L) an additional fasting lipid measurement is recommended.

Laboratory measurement and reporting



Laboratory tests are crucial in the determination and treatment of ASCVD risk.



Non-HDL-C can be reliably determined when fasting or non-fasting.



Advanced lipoprotein tests lack appropriate standardization and cross comparison, including:



LDL-C can be estimated from:

- Total cholesterol
- High-density lipoprotein cholesterol (HDL-C), and triglyceride (TG) determinations

- LDL particle number
- Small dense LDL-C
- Remnant cholesterol

Post-analytic issues



Lipid measurements are best reported based on an “ideal” range for cardiovascular disease prevention.



Desirable values should be noted on lipid laboratory reports to make them more informative.

Measurement	Desirable values	High Alert Values (Refer to lipid specialist)
Total cholesterol	<200 mg/dL	
HDL-C	>40 mg/dL for men >50 mg/dL for women	≤20 mg/dL
Non-HDL-C	<130 mg/dL <100 mg/dL for ASCVD or high-risk patients	≥220 mg/dL Consider inherited hyperlipidemia
LDL-C	<100 mg/dL <70 mg/dL for ASCVD or high-risk patients	<50 untreated ≥190 mg/dL Consider familial hypercholesterolemia
TG	<150 mg/dL fasting <175 mg/dL non-fasting	500-999 mg/dL - severe ≥1000 mg/dL - critical value

Points to remember:



To prevent vascular disease from advancing, clinicians should assess each patient and establish an acceptable range of values.



Clinically relevant cut points are lower for children than adults.



HDL-C concentrations are higher in women than men and in black people than white people.



Racial differences apply to Lp(a) levels, with black people having higher levels than other groups.



Recommendations: post-analytic issues

- ✓ Lipid laboratory reports recommended to include common lipid ranges. Extreme values should be highlighted for specific measures
- ✓ Reporting of measurement accuracy and precision is reasonable for specific lab measures
- ✓ Method used to calculate/measure LDL-C recommended to be described in lab reports
- ✓ LDL-C ≥190 mg/dL in adults or ≥160 mg/dL in children recommended to be reported as severe hypercholesterolemia
- ✓ Non-HDL-C in adults ≥220 mg/dL recommended to be reported as possible inherited hyperlipidemia
- ✓ Non-HDL-C recommended to be reported routinely as part of standard lipid profile
- ✓ Triglyceride concentration ≥500 mg/dL is recommended to be reported as severe hypertriglyceridemia

Clinical care laboratory considerations – Q&A:

Q

How often should lipid levels be measured in patients on lipid-altering therapy?



4-12 weeks after beginning treatment intervention (lifestyle of medication)

A



3-12 month intervals once a patient is on a stable, well-tolerated medication dose, with lipoprotein valued in the desired range

Q

How often should lipid testing be undertaken for patients undergoing lipid apheresis or injectable lipid medications?



Where patients are treated with lipid apheresis, lipids are measured before and after the procedure.

A



To assess response with lipid-lowering medication, clinicians should consider the number of days since the last injection and the interval between injections.

Q

How often should clinicians interpret lipid levels in acutely ill patients?



To avoid inaccurate lipid test results, testing should be carried out within 12 hours of the illness OR 4-8 weeks of the illness.

A



Adults with acute or chronic ASCVD or high-risk diabetes mellitus patients should be put on lipid lowering therapy with statins.



Dyslipidemic patients should be evaluated for secondary hyperlipidemia, with consideration of:

- Excessive alcohol consumption
- Pancreatitis
- Non-lipid medication side effects
- Hepatic disease
- Nephrotic syndrome
- Uncontrolled diabetes
- Hypothyroidism
- Hyperthyroidism
- Primary biliary cholangitis
- HIV infection

LDL-C estimating equations

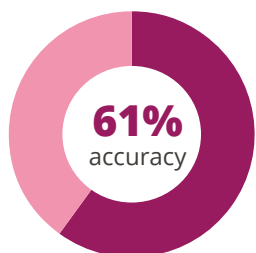
The Friedewald equation:



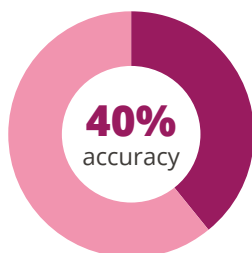
Simple and accurate for most patients with LDL-C ≥ 100 mg/dL and TG < 150 mg/dL



Can be inaccurate with patients with low LDL-C and higher TG



(LDL-C < 70 mg/dL and TG of 150-199 mg/dL)



(TG level of 200-399 mg/dL)

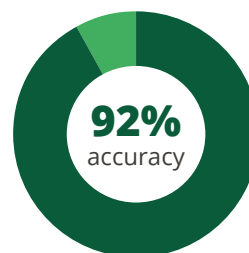
The Martins/Hopkins formula:



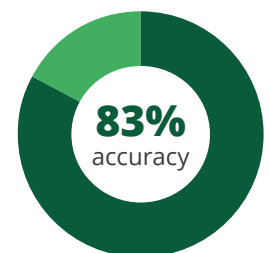
Uses TG, HDL-C and total cholesterol to estimate LDL-C



Preferred method overall, particularly for samples with LDL-C < 100 mg/dL and TG 150-400 mg/dL



(LDL-C < 70 mg/dL and TG of 150-199 mg/dL)



(TG level of 200-399 mg/dL)

LDL-C estimating equations are not recommended for TG > 400 mg/dL due to inaccuracy.

Laboratory measurement and reporting



LDL-C and non-HDL-C can be used for:

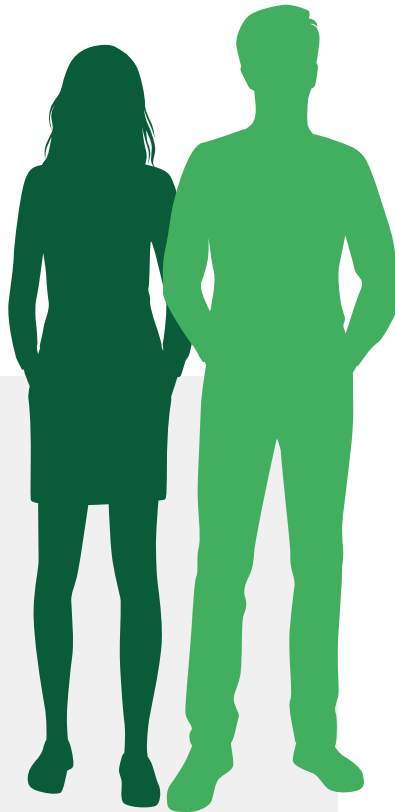
- Screening
- Initial evaluation
- Tracking patient care
- Calculating ASCVD risk



Patients with the atherogenic phenotype, characterized by increased small dense LDL over larger LDL particles, appear to have increased ASCVD risk.



More men than women have the atherogenic phenotype and it is associated with higher apolipoprotein B (apoB) levels.



Lp(a) is a class of atherogenic particles and is an independent risk factor for ASCVD.



Lp(a) elevations are generally genetically determined but can also be elevated with low estrogen levels, severe hyperthyroidism and chronic kidney disease.



The NLA recommends measuring Lp(a) using an immunochemical assay calibrated against WHO/IFCC secondary reference material, measuring in nmol/L.



Measuring Lp(a) can be valuable in patients:

- With a family history of ASCVD
- Who do not respond fully to statin therapy
- Those who have an ASCVD event while on evidence-based lipid-lowering therapy

Specific considerations for traditional and advanced lipid testing



For patients with high ASCVD risk (LDL-C <70 mg/dL), residual atherogenic burden can be assessed by measuring non-HDL-C, apoB and LDL Particle Number (LDL-P).



ApoB or LDL-P measurements can identify patients with increased ASCVD risk due to higher atherogenic lipoprotein burden, who may benefit from high dose statins plus ezetimibe or PCSK9 inhibitors.



High concentrations of non-HDL-C can indicate increased likelihood of ASCVD events.



Clinical consensus that apoB >130 mg/dL is high.

European Society of Cardiology Guideline says apoB levels that should result in intensification of lipid therapy are:

>65 mg/dL

very high

>80 mg/dL

high

>100 mg/dL

moderate



- Measurement of apoB can help guide therapy as part of initial lipid evaluation for some patients or guide lipid therapy.



- Measuring LDL-P can guide therapy after initial lipid evaluation, although LDL-P assays are not standardized.



- Measuring Lp(a) can help guide therapy for patients with primary hypercholesterolemia or high ASCVD risk.

It is difficult to compare advanced lipoprotein tests due to a lack of standardization.