

Cardio IQ® Advanced Cardiovascular Tests

Lipid Panel*/ASCVD (Atherosclerotic Cardiovascular Disease) Risk Panel

Lipid Panel* with Direct LDL Reflex 92061(X) and without Direct LDL Reflex 91716(X) is a panel of blood tests that serves as an initial broad medical assessment tool for abnormalities in total cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, low-density lipoprotein (LDL) cholesterol (calculated), and cholesterol/HDL ratio (calculated). A lipid panel is used to identify hyperlipidemia, which may indicate an increased risk for cardiovascular disease. If the triglycerides level is greater than 400 mg/dL, LDL will be directly measured, and not calculated, if direct LDL reflex was chosen.

Lipid Panel/ASCVD Risk Panel Assessment 92052(X) is a lipid panel with a reflex to direct LDL cholesterol (when triglycerides are greater than 400 mg/dL) and a calculation of a 10-year risk of a first ASCVD event, defined as coronary death or nonfatal myocardial infarction (MI), or fatal or nonfatal stroke—using race- and sex-specific pooled cohort evaluations, and as recommended by the *2013 ACC/AHA Guidelines on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults*. Patient information is provided by the ordering physician.

Lipoprotein Subfractionation

Ion Mobility 91604(X) is a proprietary test methodology for lipoprotein subfractionation. Individual lipoprotein subclasses are separated with high resolution, and direct quantification of lipoproteins provides precise particle counts for each lipoprotein type and subclass. Measurements

of LDL or HDL determined as part of the conventional lipid panel may be optimal, while LDL and HDL subclass analysis may indicate increased cardiovascular disease (CVD) risk.

Ion Mobility identifies small- and medium-LDL subclasses, which are highly atherogenic. There is a 1.3x increased CVD risk associated with the small LDL trait and a 1.4x increased risk for the medium LDL trait. The large HDL subclass is the most efficient cholesterol reabsorbing HDL particle and best reflects the efficacy of the reverse cholesterol transport system and cholesterol clearance by the liver. Low levels of large HDL are correlated with a 1.8x increased CVD risk.

HDL2b 36405(X) consists of the largest and most buoyant particles of the HDL subclasses. A low level of large HDL particles may reduce the efficacy of the reverse cholesterol transport process and increase CVD risk.

sdLDL 36406(X), or small dense LDL, particles are particularly atherogenic due to their increased affinity for vessel walls, increased susceptibility to oxidation, and reduced ability to be cleared by the liver, increasing the time in which these particles remain in circulation.

Apolipoproteins

ApoB 91726(X) or apolipoprotein B, is the predominant apoprotein attached to low-density lipoproteins (LDL), intermediate-density lipoproteins (IDL), and very low-density lipoproteins (VLDL). Several decades of scientific literature support the measurement of ApoB for monitoring response to statin therapy. Elevated ApoB is associated with a 2.0-2.5x increased CVD risk.

Lp(a) 91729(X), or lipoprotein (a), consists of an inherited protein attached to an LDL particle. Elevated Lp(a) is associated with increased coagulation and a 1.5-5.3x increased incidence of CVD. Lp(a) has been linked to the promotion of both early- and advanced stage atherosclerosis. When the measurement of Lp(a) is combined with other abnormal CVD risk markers, the associated risk increases further.

Inflammation

F₂-IsoPs 92771(X), or F₂-Isoprostanes, are prostaglandin-like compounds formed from free radical-mediated oxidation of arachidonic acid. F₂-IsoPs measure oxidative stress induced by lifestyle risk factors for CVD including smoking, poor diet, high red meat intake, and a sedentary lifestyle. F₂-IsoPs contribute to CVD progression through increased vasoconstriction via thromboxane production, platelet aggregation, and thrombus formation. Elevated levels of F₂-IsoPs indicate a 2.6x increased risk for CAD and a 1.8x increased risk of CVD mortality.

OxLDL 92769(X), or oxidized LDL, measures damage of the ApoB protein subunit on the surface of LDL due to oxidative modification. Oxidation of ApoB is an initiating factor in macrophage recruitment, foam cell formation, and vascular inflammation within the arterial wall. Elevated OxLDL levels indicate a 4.3x increased risk of having a coronary heart disease (CHD) event and a 3.5x increased risk of developing metabolic syndrome (MetS).

ADMA/SDMA 94153(X), or asymmetric dimethylarginine (ADMA) and symmetric dimethylarginine (SDMA), are derivatives of the amino acid L-arginine and are produced via protein degradation. ADMA is a competitive inhibitor of nitric oxide synthase and can reduce the production of nitric oxide. Nitric oxide deficiency is an early manifestation of endothelial dysfunction and atherosclerotic disease. Elevated ADMA indicates a 1.4x increased risk of CVD and CHD and a 1.6x increased risk of stroke. SDMA is primarily excreted in the urine and strongly correlates with reduced renal function.

Fibrinogen 91743(X) is a plasma glycoprotein that can be transformed into a fibrin clot in response

to vascular or tissue injury. The combination of elevated fibrinogen with other CVD risk factors produces an additive risk and can substantially increase disease potential.

hs-CRP 91737(X) is a highly sensitive measurement of C-reactive protein, an acute-phase reactant protein that increases in response to inflammation. In large epidemiologic studies, elevated levels of CRP have been shown to be a strong indicator of CVD. Patients with high CRP have a 1.5-2.0x increased risk of developing subsequent atherosclerotic disease compared with patients with low CRP levels. It's also been demonstrated that lowering hs-CRP, independent of lipid levels, results in a 15% risk reduction of recurrent cardiovascular events.

Lp-PLA₂ Activity 94218(X), or lipoprotein-associated phospholipase A₂, is an enzyme produced by macrophages and foam cells within the necrotic core of arterial plaque. Lp-PLA₂ Activity measures the disease activity within the arterial wall under the calcified cap of the plaque. Elevated Lp-PLA₂ Activity has been associated with a 2.0x increased risk for developing CHD independent of non-HDL cholesterol levels. Also, elevated Lp-PLA₂ Activity levels indicate a 2.0x risk of having a CHD event (MI, coronary revascularization or CHD-related death).

MPO 92814(X), or myeloperoxidase, is an inflammatory enzyme released within the vascular lumen during white blood cell activation in response to fissures, erosions, or degradation of the fibrous cap. MPO is a specific marker of vascular inflammation and is a measure of vulnerable plaque. Elevated levels of MPO independently predict 2.0-2.4x increased risk of future cardiovascular events (MI, coronary revascularization, or CVD-related death).

Metabolic Markers

Diabetes Risk Panel 92026(X) measures glucose, hemoglobin A1c (HbA1c), and lipids. It also estimates the 8-year risk of developing diabetes using laboratory test results, anthropomorphic data, and family history. The risk algorithm is based on the analysis of 3,453 individuals (ages 30-79) within the Framingham cohort. It is intended to aid in the identification of patients at risk for developing diabetes mellitus, permitting lifestyle or pharmacologic interventions.

Glucose 91947(X) measures serum glucose levels under fasting conditions. Elevated serum glucose (hyperglycemia) is associated with diabetes and insulin resistance. Low levels indicate hypoglycemia.

Hemoglobin A1c 91732(X) reflects average blood sugar levels over the preceding 90-day period. Elevated levels are associated with prediabetes and diabetes. HbA1c measurement requires no fasting or glucose loading requirement, is less sensitive than glucose to stress and illness, and is more specific for identifying individuals at increased risk for diabetes. Lowering HbA1c levels by 1% reduces the risk of microvascular complications by approximately 40%.

Insulin 91731(X) is associated with the characterization of an atherogenic lipid profile and metabolic syndrome. Abnormal fasting insulin, especially when combined with other risk factors, identifies patients at significantly higher risk for the development of CVD.

Homocysteine 91733(X) is a metabolic by-product of methionine metabolism. Progressively elevated blood levels of homocysteine are a documented risk marker for CVD events.

Omega-3 and -6 Fatty Acids (FAs) 91734(X) – A diet rich in omega-3 fatty acids is associated with a decreased risk of cardiovascular events, including sudden cardiac death (SCD). The three major omega-3 fatty acids are eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and alpha-linolenic acid. Omega-6 fatty acids are proinflammatory and prothrombotic. The major omega-6 fatty acid is arachidonic acid (AA). The omega-3 index, EPA and DHA expressed as a percentage of phospholipid FAs, is an indicator of risk for SCD and nonfatal cardiovascular events and as a therapeutic target. The EPA/AA ratio is a marker of cardiovascular risk, with higher ratios being associated with lower cardiac risk. This test measures omega-3 and -6 fatty acid levels free in serum.

OmegaCheck™ 92701(X) measures the long-chain omega-3 fatty acids: EPA, docosapentaenoic acid (DPA), DHA, and the most abundant forms of omega-6 fatty acids: AA and linoleic acid (LA). Omega-3 fatty acids have anti-oxidant, anti-inflammatory, and anti-thrombotic effects, and can help reduce triglycerides. Increased levels of omega-3 fatty acids are associated with a lower risk of sudden cardiac

death. High ratios of AA/EPA or omega-6/omega-3 are associated with increased CVD and mortality risk. The OmegaCheck test measures omega-3 and -6 fatty acid levels in whole blood.

TMAO 94154(X), or trimethylamine-N-oxide, is a metabolite produced by the gut microbiome following consumption of food products containing the precursors L-carnitine, choline, and phosphatidylcholine (lecithin), which are abundant in various animal-derived products (dairy, egg yolk, and red meat) as well as dietary supplements and energy drinks. TMAO impacts physiological processes that can increase risk of atherosclerosis, enhance platelet hyperreactivity, and increase thrombosis. Elevated TMAO is associated with a 2.5x increased risk of incident major adverse cardiovascular events (MACE). A meta-analysis also demonstrated a 7.6% increase in relative risk for CVD mortality for every 10µmol/L increase in TMAO.

Vitamin D, 25 Hydroxy, LC/MS/MS 91735(X) low levels are associated with increased risk of CVD events and death due to heart failure, sudden cardiac death, and stroke. The cardiovascular impact of low vitamin D is via activation of the renin-angiotensin-aldosterone system, as well as via increased parathyroid hormone levels (which predispose individuals to increased insulin resistance associated with diabetes, hypertension, inflammation, and increased cardiovascular risk).

Heart Failure (HF)

NT-proBNP 91739(X), or N-terminal pro b-type natriuretic peptide, is an endogenously produced neurohormone secreted from the cardiac ventricular myocytes in response to cardiac stress. Elevated levels indicate the presence of ongoing myocardial stress and potentially an underlying cardiac disorder. As a highly sensitive marker for cardiac dysfunction, elevated NT-proBNP levels are prognostic of future cardiovascular events, even in the setting of undiagnosed, subclinical CVD.

ST2, Soluble (sST2) 91823(X) can be used in risk assessment of patients with acute and chronic heart failure. The sST2 biomarker binds and removes Interleukin-33 from the circulation, thus eliminating the protective effect the IL-33 provides to the cardiac muscle. Patients with HF and elevated

sST2 levels are at increased risk for progression, heart transplantation, and possibly death. sST2 is not affected by confounding factors as is BNP/NT-proBNP. Using sST2 alongside BNP/NT-proBNP can help improve the risk stratification of patients with chronic HF. High levels of both sST2 and BNP/NT-proBNP, compared with high levels of only one, better predict HF progression.

Galectin-3 82777(X) is a carbohydrate-binding lectin that increases collagen production and cardiac fibroblast proliferation. Elevated levels of galectin-3 have been associated with macrophage infiltration, cardiac fibrosis, and cardiac hypertrophy, which contribute to progression of heart failure and poor cardiovascular outcomes. Measuring galectin-3 in conjunction with BNP/NT-proBNP and ST2 can further enhance risk stratification to monitor and treat HF and CVD.

Genetic Cardiovascular Markers

4q25 AF Risk Genotype Test 90948(X) may help predict risk of atrial fibrillation (AF) and cardioembolic (CE) stroke. 4q25 AF Risk carriers may have up to a 1.7x increased risk of AF and up to a 1.5x increased risk of CE stroke related to AF. Physicians may benefit from knowledge of their patient's increased AF risk, and therefore consider additional clinical follow-up for these patients.

Apolipoprotein E (ApoE) Genotype Test 90649(X) may help predict risk of CVD and response to different diets.

9p21 Genotype Test 90648(X) may help predict risk of early onset MI, abdominal aortic aneurysm (AAA), and MI/CHD. Identification of 9p21 carriers may allow clinicians to take steps to characterize and reduce risk factors that may contribute to the development or progression of disease.

CYP2C19 Genotype Test 90668(X) may help predict response to Plavix® (clopidogrel). Patients carrying one or two copies of nonfunctional alleles may not receive the full benefits of Plavix and therefore may benefit from alternative dosing strategies or an anti-platelet agent other than Plavix.

KIF6 Genotype Test 90645(X) may help predict risk of a CHD event and response to Lipitor® (atorvastatin) or Pravachol® (pravastatin). In certain studies, atorvastatin and pravastatin therapy was found to reduce CHD event risk more effectively in KIF6 carriers compared with noncarriers.

LPA Aspirin Genotype Test 90553(X) may help predict risk of CVD and response to aspirin therapy. In the Women's Health Study (WHS), low-dose aspirin therapy resulted in a greater reduction of CVD events in LPA Aspirin carriers than in noncarriers.

LPA Intron 25 Genotype Test 90655(X) may help predict risk of CHD, providing additional insight into a patient's risk for CHD beyond traditional risk factors.



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- on each of our Cardio IQ Advanced
- Cardiovascular Tests. Use the search
- function to locate the specific test and
- available information.

*Lipid panel components may be ordered separately: Cholesterol, Total 91717(X)/334 (CPT 82465); Triglycerides 91718(X)/896 (CPT 84478); HDL Cholesterol 91719(X)/608 (CPT 83718). If triglyceride result is >400 mg/dL, Direct LDL Cholesterol will be performed at an additional charge (CPT 83721).†

†The CPT codes provided are based on American Medical Association guidelines and are for informational purposes only. CPT coding is the sole responsibility of the billing party. Please direct any questions regarding coding to the payer being billed.

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