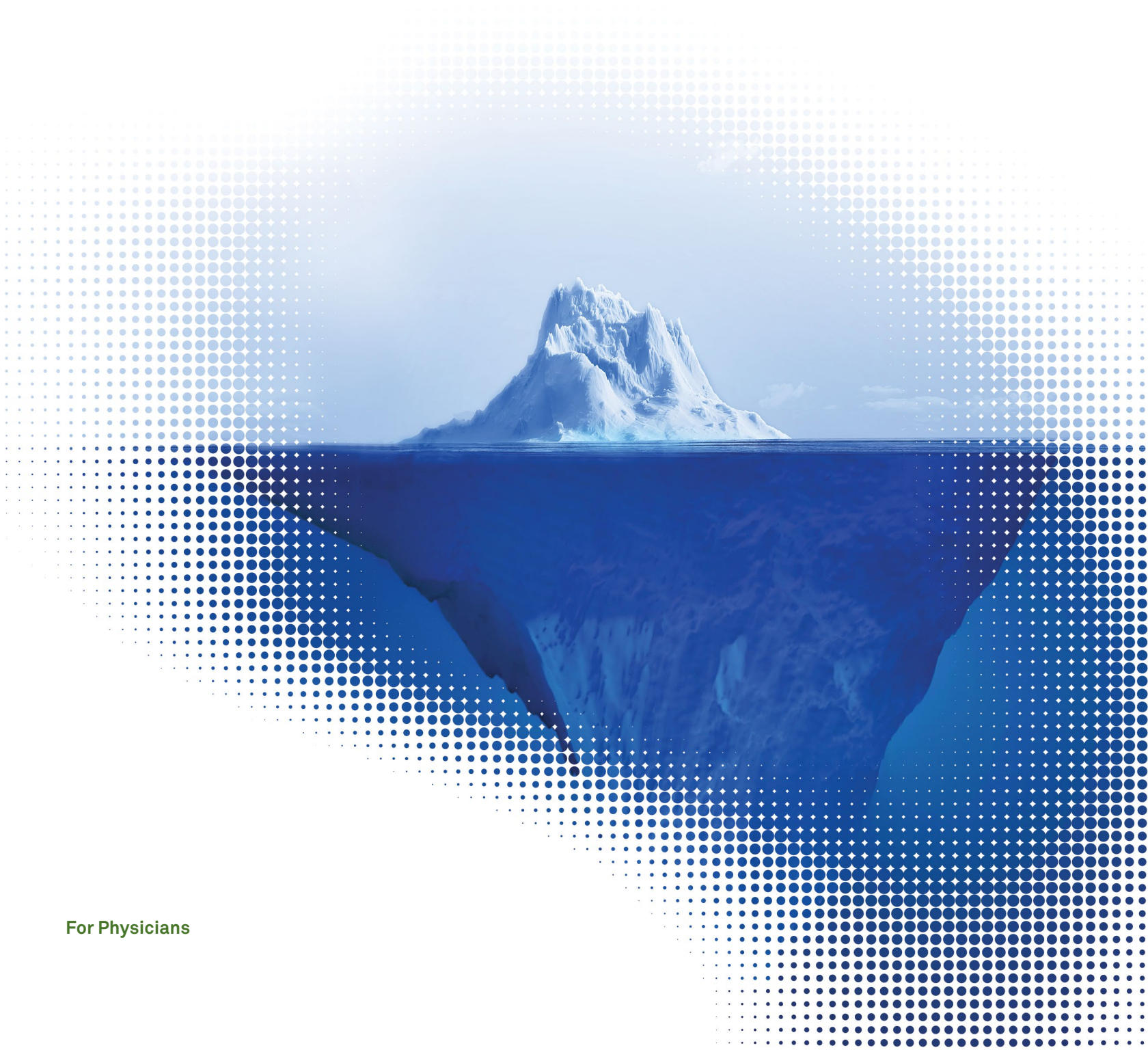
Quest Diagnostics™

Cardio IQ®

Advanced Cardiovascular Testing

Uncover Hidden Risk for Heart Attack and Stroke



For Physicians

Are traditional risk factors enough when managing cardiovascular disease?

Heart disease continues to be the leading cause of death in the U.S.[1]

Evolving guidelines continue to focus on traditional factors to manage cardiovascular risk

ATP I — 1988

Primary prevention of coronary heart disease (CHD), with a focus on low-density lipoprotein cholesterol (LDL-C) >160 mg/dL or those with borderline-high LDL 130–159 mg/dL

ATP II — 1993

More intensive management of LDL-C in CHD patients; focus now on LDL-C <100 mg/dL

ATP III — 2001–2004

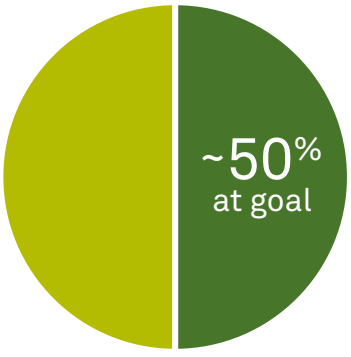
Primary prevention of CHD; focus continues on LDL-C, but new emphasis on non-HDL-C; suggest option of LDL-C <70 mg/dL in those with CHD

ACC/AHA — 2013

Goal of treatment: Primary/secondary prevention of atherosclerotic cardiovascular disease (ASCVD) in men and women with LDL-C percent reduction targets from the untreated baseline

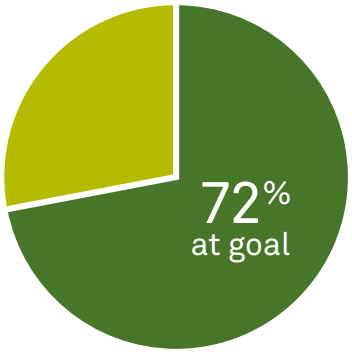
Residual cardiovascular risk is still significant despite managing traditional risk factors

LDL-C Levels <100mg/dL

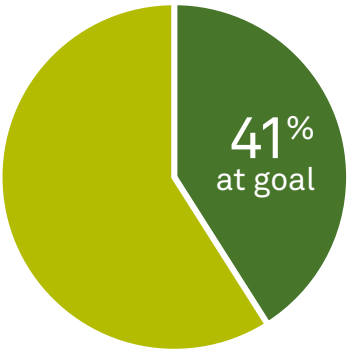


Studies show that LDL-C cholesterol levels were often not predictive of coronary artery disease (CAD). In a population of over 200,000 patients hospitalized with CAD, almost half had LDL-C levels <100 mg/dL.[2]

1st CHD Event



Recurrent CHD



The AHA Get-With-The-Guidelines® initiative analysis[2] revealed that a substantial proportion of patients with CHD events were well within guideline-recommended targets for Lipid Panel values.

Even after statin therapy, recent data suggests that residual risk still exists in many patients.[3]

Quest Diagnostics can help improve the management of cardiovascular patients

Gain deeper insights into the individual residual risks of your patients

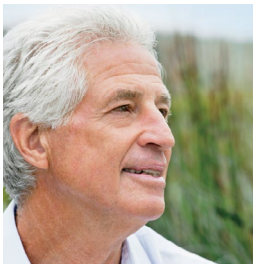
Uncovering hidden risk may benefit those patients with traditional cardiovascular disease (CVD) risk factors:

- Age (men >45 years; postmenopausal women)
- Family history of premature onset of CVD
- Unhealthy diet, excessive alcohol intake, smoking, and stress
- Obesity
- Low HDL-C

Additional risk stratification may be considered for:

- ≥5% Estimated ASCVD Risk
- Established cardiovascular disease, hypertension, or dyslipidemia
- Diabetes
- Metabolic syndrome













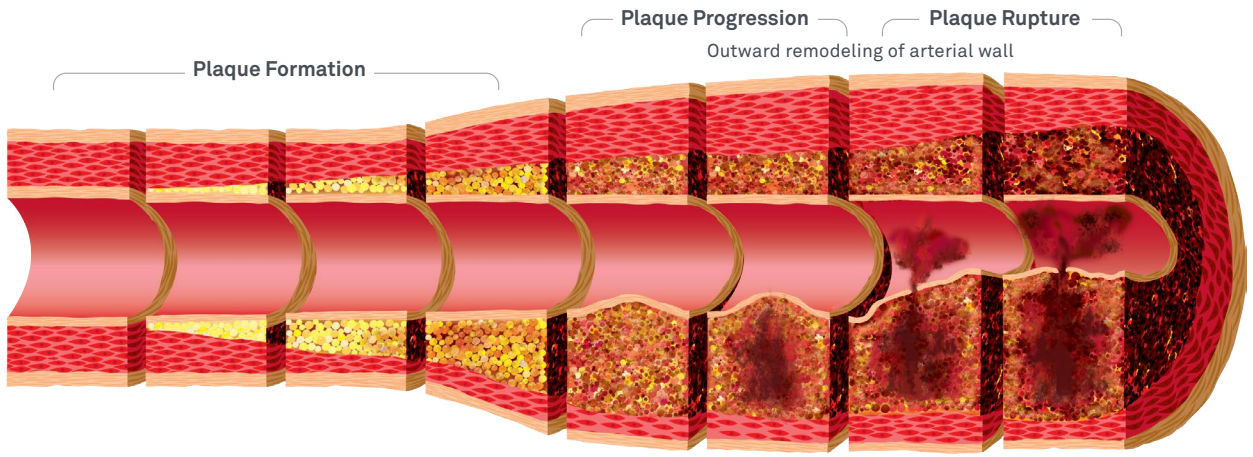
Patient types are meant to be illustrative and should not be considered a comprehensive representation.

Identifying residual risk with emerging biomarkers

Biomarkers have been shown to help identify risk and thus have been adopted by several guidelines and societies.[4-6]

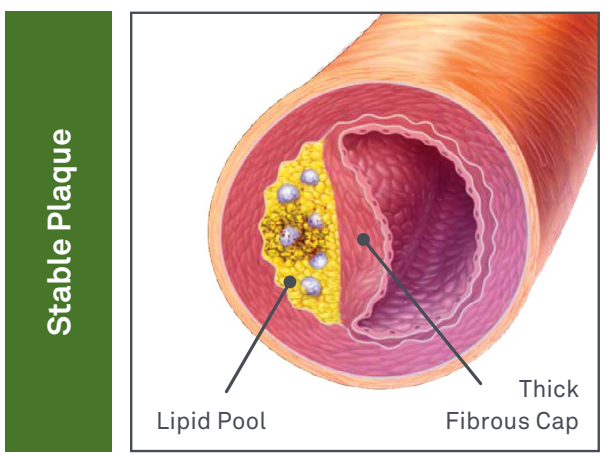
Lipoprotein Risk Factors

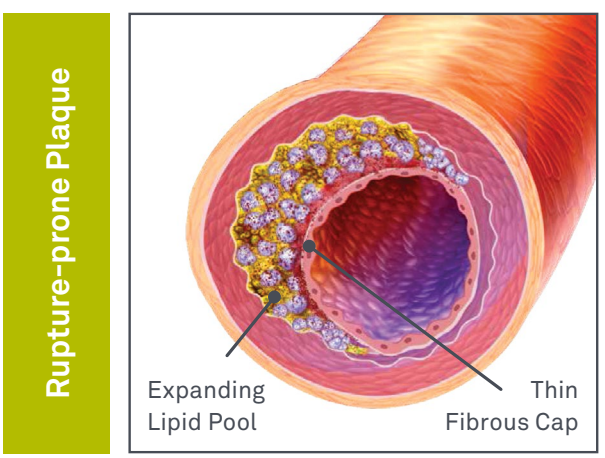
Risk Factor	Impact on Cardiovascular Disease (CVD)
LDL Particle Number	The Quebec Cardiovascular Study was the first to demonstrate that heart attack can occur when LDL particle number is high and low-density lipoprotein level is low. Greater numbers of cholesterol-containing particles in the blood means more cholesterol deposition in plaque and therefore an increased risk for heart attack.
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.
LDL Subclasses	Small LDL subclass particles cause plaque buildup to progress much faster because they 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.
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.



Inflammation Risk Factors

Risk Factor	Impact on Cardiovascular Disease (CVD)
MPO (Myeloperoxidase)	MPO is a marker of vascular-specific inflammation within the vessel lumen. Elevations occur due to white blood cell activation in response to fissures, erosions, or degradation of the fibrous cap. MPO is actively involved in atherosclerosis and is considered a near-term risk marker for cardiovascular events.
Lp-PLA_2 (Lipoprotein-Associated Phospholipase A_2)	Lp-PLA_2 measures disease activity within the artery wall below the collagen or calcified cap due to activation of macrophages. The AHA and AACE guidelines list Lp-PLA_2 as a strong and independent predictor of ASCVD events and may be valuable in identifying patients at increased CVD risk.
hs-CRP (High Sensitivity C-Reactive Protein)	The hs-CRP test is a highly sensitive quantification of CRP, an acute-phase protein released into the blood by the liver during inflammation. hs-CRP is a well-documented clinical marker of cardiac-related inflammation. 2013 ACC/AHA guidelines state hs-CRP may be useful in the evaluation of those at moderate risk for heart disease and determining whether or not more intensive treatment is warranted.
ADMA/SDMA (Asymmetric/Symmetric Dimethylarginine)	ADMA is an L-arginine derivative that inhibits nitric oxide production, an early manifestation of endothelial dysfunction and CVD progression. SDMA is a structural isomer of ADMA, but is primarily excreted in the urine and can indicate reduced renal function.
OxLDL (Oxidized LDL)	OxLDL measures oxidative protein damage of the ApoB subunit on LDL cholesterol. Elevated OxLDL promotes vascular inflammation and is associated with increased risk of metabolic syndrome, CAD, and CHD.
F_2-IsoPs (F_2-Isoprostanes)	Urinary F_2-Isoprostanes (F_2-IsoPs) measure oxidative stress in the body, primarily due to lifestyle risk factors. F_2-IsoPs contribute to CVD progression through increased risk of vasoconstriction, platelet aggregation, and thrombus formation.





Managing residual risk with advanced insights

Advanced cardiovascular testing provides actionable information to individualize treatment options:

- Initiate/intensify statin therapy
- Identify opportunities for adjunct therapy
- Set diet, exercise, and lifestyle targets

The Cardio IQ® Enhanced Lab Report

Offering key insights for individualized patient treatment

Test results are shown in "Optimal," "Moderate," or "High" risk categories, and are **color-coded to display progressive risk** values.

Historic results of previous tests are provided with the Cardio IQ report to help monitor patient progress.

This example represents the resulting report for an order of Advanced Lipid Panel with Inflammation, which includes:

Cardio IQ Lipid Panel with Reflex to Direct LDL

Cardio IQ Ion Mobility

Cardio IQ Apo B

Cardio IQ Lp(a)

Cardio IQ hs-CRP

Cardio IQ Lp-PLA$_2$

Test Name	Units	Result and Risk Category			Result From	Risk Category Ranges		
		Optimal	Moderate	High		Optimal	Moderate	High
Lipid Panel								**Lab: EZ**
CHOLESTEROL, TOTAL	mg/dL	166				<200	200-239	>=240
HDL CHOLESTEROL	mg/dL	61				>=40	N/A	<40
TRIGLYCERIDES	mg/dL	81				<150	150-199	>=200
LDL-CHOLESTEROL	mg/dL	89				<100	100-129	>129
CHOL/HDLC RATIO	calc	2.7				<=3.5	3.6-5.0	>5.0
NON-HDL CHOLESTEROL	mg/dL	105				<130	130-159	>159
Lipoprotein Subfractions								**Lab: EZ**
LDL PARTICLE NUMBER	nmol/L		1203			<1138	1138-1409	>1409
LDL SMALL	nmol/L			236		<142	142-219	>219
LDL MEDIUM	nmol/L			373		<215	215-301	>301
HDL LARGE	nmol/L	9454				>6729	6729-5353	<5353
Apolipoproteins								**Lab: EZ**
APOLIPOPROTEIN B	mg/dL		80			<80	80-119	>=120
LIPOPROTEIN (a)	nmol/L		77			<75	75-125	>125
Inflammation								**Lab: EZ**
HS CRP	mg/L			4.5		<1.0	1.0-3.0	>3.0
LP PLA$_2$	nmol/min/mL	120				<=123	N/A	>123

Test Results	Relative Risk	Treatment Options‡§	Goal‡§
Elevated LDL Cholesterol	1.6x[7]	• Diet and exercise • Statins, ezetimibe, bile acid sequestrants (BAS), PCSK9 inhibitors	LDL Cholesterol <100 mg/dL LDL Cholesterol reduction 30% to <50% Moderate-intensity statin dose group LDL Cholesterol reduction >50% High-intensity statin dose group
Elevated Triglycerides	1.7–4.0x[7]	• Diet and exercise • Fibrates, high-dose omega-3 fatty acids, nicotinic acid	Triglycerides <150 mg/dL
Elevated LDL Particle Number	1.4–2.3x[8*,9,10]	• Diet and exercise • Statins, ezetimibe, BAS, PCSK9 inhibitors	<1138 nmol/L
Elevated Small LDL Particles	1.3–2.1x[8*,9,10] 1.5x (sdLDL)[11]	• Diet and exercise • Address excess LDL-P or ApoB • Consider therapies to address insulin resistance (e.g., Metformin)	Small <142 nmol/L sdLDL ≤40.0 mg/dL
Elevated Medium LDL Particles	1.4–2.2x[8*,9,10]	• Diet and exercise • Address excess LDL-P or ApoB • Consider therapies to address insulin resistance (e.g., Metformin)	Medium <215 nmol/L
Suboptimal Large HDL	1.8x (Large HDL)[8*] 1.9x (HDL2b)[12]	• Diet and exercise • May consider nicotinic acid	Large HDL >6729 nmol/L HDL2b >26% (Males); HDL2b >28% (Females)
Elevated ApoB Particles	2.0–2.5x[13]	• Diet and exercise • Statins, ezetimibe, BAS, PCSK9 inhibitors	ApoB <80 mg/dL
Elevated Lp(a)	1.5–5.3x[14]	• More aggressive lowering of LDL‡ or ApoB • Consider nicotinic acid	Lp(a) <75 nmol/L
Elevated F_2-Isoprostanes	1.8-2.6x[15,16]	• Diet, exercise, and smoking cessation • Assure optimal LDL‡ levels	F_2-Isoprostanes <0.86 ng/mg creatinine
Elevated OxLDL	3.5-4.3x[17,18]	• Diet and exercise • Address LDL‡ and insulin sensitivity	OxLDL <60 U/L
Elevated ADMA/ SDMA	1.4x (ADMA)[19]	• Diet and exercise • Statins • Assure major CVD risk factor goals are achieved	ADMA <100 ng/mL SDMA 73-135 mg/mL
Elevated hs-CRP	2.3-2.9x[20,21]	• Diet and exercise • Address etiology • Consider subclinical CAD or insulin resistance	hs-CRP <1 mg/L
Elevated Lp-PLA_2	2.0x[22†]	• Diet and exercise • More aggressive lowering of LDL‡ or ApoB • Consider omega-3 fatty acids	Lp-PLA_2 ≤123 nmol/min/mL
Elevated MPO	2.0-2.4x[23,24†]	• Diet and exercise • Assure major CVD risk factor goals are achieved	MPO <470 pmol/L

* Expected risk of highest tertile versus lowest tertile assuming measure is normally distributed and risk increases linearly.

† The risk associated with elevated Lp-PLA_2 or MPO levels is substantially increased in patients when either Lp-PLA_2[22] or MPO[23] is elevated with CRP.

‡ Includes LDL-C and LDL-P.

§ The treatment considerations are provided for informational purposes only and are not intended as medical advice. A physician's test selection and interpretation, diagnosis, and patient management decisions should be based on his/her education, clinical expertise, and assessment of the patient.For more information on treatment options and goals per test, please see the Test Guide and/or Test Summary posted within the specific test's section at QuestDiagnostics.com/TestCenter.

Ordering Information

Test Name	Test Code*	CPT Code(s)*
Cardio IQ Advanced Lipid Panel with Inflammation**	94220(X)	80061, 83704, 82172, 83695, 86141, 83698
Includes:		
Cardio IQ Lipid Panel with Reflex to Direct LDL**	92061(X)	80061
Cardio IQ Lipoprotein Fractionation, Ion Mobility	91604(X)	83704
Cardio IQ Apolipoprotein B	91726(X)	82172
Cardio IQ Lipoprotein (a)	91729(X)	83695
Cardio IQ hs-CRP	91737(X)	86141
Cardio IQ Lp-PLA_2	94218(X)	83698
Cardio IQ MPO	92814	83876
Cardio IQ ADMA/SDMA	94153	82542
Cardio IQ OxLDL	92769	83520
Cardio IQ F_2-Isoprostane/Creatinine	92771	82542/82570

Other cardiometabolic testing

We offer additional advanced CVD tools for personalization of risk management in your patients. Options include deeper insight into functional areas important in managing CVD risk patients, such as inflammation status, myocardial stress, cardiometabolic state, and cardiovascular genetics.

*Test codes may vary by location. Please contact your laboratory for more information. The CPT codes provided are based on AMA 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.

**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).

For more information, contact your Quest Diagnostics sales representative or visit us at **QuestDiagnostics.com/Education.**

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1. Benjamin EJ, Virani SS, Callaway CW, *et al.*On behalf of the American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics 2018 update: a report from the American Heart Association. *Circulation*. DOI: 10.1161/CIR.0000000000000558. **2.** Sachdeva A, Cannon CP, Deedwania PC, *et al*. on behalf of the Get-With-The-Guidelines (GWTG) Steering Committee and Hospitals. *AHJ*. 2009;157:111-117.e2.(1) **3.** Reith C and Armitage J. Management of residual risk after statin therapy. *Atherosclerosis*. 2016;245:161-170 **4.** Third Report of the National Cholesterol Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Final Report. *Circulation*. 2002;106(25):3143-3412. **5.** Davidson MH, Ballantyne CM, Jacobson TA, *et al*. 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