

Medical Policy:

Lipoprotein Subclassification Testing for Screening, Evaluation and Monitoring of Cardiovascular Disease

POLICY NUMBER	LAST REVIEW
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(Skip Definitions and go directly to clinical criteria)

Definitions

Lipoproteins	Blood-borne complexes of lipids and proteins that allow the transport of cholesterol throughout the body. Note: There is an association between disorders of lipoprotein metabolism and coronary heart disease, especially high serum levels of low-density lipoprotein (LDL) cholesterol and low serum levels of high-density lipoprotein (HDL) cholesterol. Tests routinely done to ascertain cardiovascular disease (CVD) include measurement of plasma levels of total cholesterol, total HDL cholesterol, total LDL cholesterol, and triglycerides. It is theorized that the evaluation of lipoprotein subclass particles (aka advanced lipoprotein testing) may contribute to improved CVD prediction and management, including coronary heart disease and ischemic stroke.
Basic lipid panel	Measures total cholesterol, triglyceride levels, HDL, and LDL cholesterol levels.
Alpha-lipoprotein (α-lipoprotein)	One with electrophoretic mobility equivalent to that of the α 1-globulins, e.g., high-density lipoprotein.
Beta-lipoprotein (β-lipoprotein)	One with electrophoretic mobility equivalent to that of the β -globulins, e.g., low-density lipoprotein.

High-density lipoprotein (HDL)	Class of plasma lipoproteins that promote transport of cholesterol from extra-hepatic tissue to the liver for excretion in the bile; serum levels have been negatively correlated with premature CAD.
Intermediate-density lipoprotein (IDL)	Class of lipoproteins formed in the degradation of very-low-density lipoproteins; some are cleared rapidly into the liver and some are degraded to low-density lipoproteins.
Low-density lipoprotein (LDL)	Class of plasma lipoproteins that transport cholesterol to extra-hepatic tissues; high serum levels have been correlated with premature CHD.
Lp(a) lipoprotein	A lipoprotein particle containing apolipoprotein B-100 as well as an antigenically unique apolipoprotein; its occurrence at high levels in plasma has been correlated with increased risk of heart disease.
Very-high-density lipoprotein (VHDL)	A class of lipoproteins composed predominantly of proteins and also containing a high concentration of free fatty acids.
Very-low-density lipoprotein (VLDL)	Class of lipoproteins that transport triglycerides from the intestine and liver to adipose and muscle tissues; they contain primarily triglycerides with some cholesteryl esters.

Guideline

- A. The basic lipid panel (CPT code 80061) (measuring total cholesterol, total HDL cholesterol, total LDL cholesterol and triglycerides) is considered **medically necessary** for the screening, evaluation and monitoring of CVD.
- B. Lipoprotein subclassification testing (aka advanced lipoprotein testing such) is **not considered medically necessary** for the screening, evaluation and monitoring of CVD (including analysis for familial dyslipidemias). Testing includes, but is not limited to:
 - 1. Apolipoprotein A1 (Apo A1)
 - 2. Apolipoprotein A2 (Apo A2)
 - 3. Apolipoprotein B (Apo B)
 - 4. Apolipoprotein E isoforms (ApoE isoforms [E2, E3, E4])
 - 5. HDL subparticles (e.g., LpAI, LPAI/AII, and or HDL3 and HDL2)
 - 6. LDL subparticles (e.g., small and large LDL particles)
 - 7. Lipoprotein remnants (e.g., intermediate density lipoproteins [IDL] and small low-density lipoproteins [sdLDL])
 - 8. Lipoprotein A (Lp([a])

(CPT codes not considered medically necessary for the screening, evaluation and monitoring of CVD: 82172, 83695, 83698, 83700, 83701, 83704, 0423T)

Limitations and Exclusions

- 1. Lipoprotein subclassification testing (e.g., Boston Heart Cholesterol Balance[®] Test) is considered investigational for all indications due to insufficient evidence of therapeutic value.
- 2. Measurement of homocysteine levels in advanced lipid testing is unproven for assessing cardiovascular risk.

Procedure Codes

80061Lipid panel This panel must include the following: Cholesterol, serum, total (82465) Lipoprotein, direct measurement,
high density cholesterol (HDL cholesterol) (83718) Triglycerides (84478)

ICD-10 Diagnoses

110	Essential (primary) hypertension
111.0	Hypertensive heart disease with heart failure
111.9	Hypertensive heart disease without heart failure
113.0	Hypertensive heart and chronic kidney disease with heart failure and stage 1 through stage 4 chronic kidney disease, or unspecified chronic kidney disease
113.10	Hypertensive heart and chronic kidney disease without heart failure, with stage 1 through stage 4 chronic kidney disease, or unspecified chronic kidney disease
13.11	Hypertensive heart and chronic kidney disease without heart failure, with stage 5 chronic kidney disease, or end stage renal disease
113.2	Hypertensive heart and chronic kidney disease with heart failure and with stage 5 chronic kidney disease, or end stage renal disease
I15.0	Renovascular hypertension
115.1	Hypertension secondary to other renal disorders
115.2	Hypertension secondary to endocrine disorders
115.8	Other secondary hypertension
115.9	Secondary hypertension, unspecified
116.0	Hypertensive urgency
116.1	Hypertensive emergency
116.9	Hypertensive crisis, unspecified
120.0	Unstable angina
120.1	Angina pectoris with documented spasm
120.8	Other forms of angina pectoris
120.9	Angina pectoris, unspecified
121.01	ST elevation (STEMI) myocardial infarction involving left main coronary artery
121.02	ST elevation (STEMI) myocardial infarction involving left anterior descending coronary artery
121.09	ST elevation (STEMI) myocardial infarction involving other coronary artery of anterior wall
121.11	ST elevation (STEMI) myocardial infarction involving right coronary artery
121.19	ST elevation (STEMI) myocardial infarction involving other coronary artery of inferior wall
121.21	ST elevation (STEMI) myocardial infarction involving left circumflex coronary artery
121.29	ST elevation (STEMI) myocardial infarction involving other sites
121.3	ST elevation (STEMI) myocardial infarction of unspecified site
121.4	Non-ST elevation (NSTEMI) myocardial infarction
122.0	Subsequent ST elevation (STEMI) myocardial infarction of anterior wall
122.1	Subsequent ST elevation (STEMI) myocardial infarction of inferior wall
122.2	Subsequent non-ST elevation (NSTEMI) myocardial infarction
122.8	Subsequent ST elevation (STEMI) myocardial infarction of other sites
122.9	Subsequent ST elevation (STEMI) myocardial infarction of unspecified site
123.0	Hemopericardium as current complication following acute myocardial infarction
123.1	Atrial septal defect as current complication following acute myocardial infarction
123.2	Ventricular septal defect as current complication following acute myocardial infarction

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123.3	Rupture of cardiac wall without hemopericardium as current complication following acute myocardial infarction
123.4	Rupture of chordae tendineae as current complication following acute myocardial infarction
123.5	Rupture of papillary muscle as current complication following acute myocardial infarction
123.6	Thrombosis of atrium, auricular appendage, and ventricle as current complications following acute myocardial infarction
123.7	Postinfarction angina
123.8	Other current complications following acute myocardial infarction
124.0	Acute coronary thrombosis not resulting in myocardial infarction
124.1	Dressler's syndrome
124.8	Other forms of acute ischemic heart disease
124.9	Acute ischemic heart disease, unspecified
125.10	Atherosclerotic heart disease of native coronary artery without angina pectoris
125.110	Atherosclerotic heart disease of native coronary artery with unstable angina pectoris
125.111	Atherosclerotic heart disease of native coronary artery with angina pectoris with documented spasm
125.118	Atherosclerotic heart disease of native coronary artery with other forms of angina pectoris
125.119	Atherosclerotic heart disease of native coronary artery with unspecified angina pectoris
125.2	Old myocardial infarction
125.3	Aneurysm of heart
125.41	Coronary artery aneurysm
125.42	Coronary artery dissection
125.5	Ischemic cardiomyopathy
125.6	Silent myocardial ischemia
125.700	Atherosclerosis of coronary artery bypass graft(s), unspecified, with unstable angina pectoris
125.701	Atherosclerosis of coronary artery bypass graft(s), unspecified, with angina pectoris with documented spasm
125.708	Atherosclerosis of coronary artery bypass graft(s), unspecified, with other forms of angina pectoris
125.709	Atherosclerosis of coronary artery bypass graft(s), unspecified, with unspecified angina pectoris
125.710	Atherosclerosis of autologous vein coronary artery bypass graft(s) with unstable angina pectoris
125.711	Atherosclerosis of autologous vein coronary artery bypass graft(s) with angina pectoris with documented spasm
125.718	Atherosclerosis of autologous vein coronary artery bypass graft(s) with other forms of angina pectoris
125.719	Atherosclerosis of autologous vein coronary artery bypass graft(s) with unspecified angina pectoris
125.720	Atherosclerosis of autologous artery coronary artery bypass graft(s) with unstable angina pectoris
125.721	Atherosclerosis of autologous artery coronary artery bypass graft(s) with angina pectoris with documented spasm
125.728	Atherosclerosis of autologous artery coronary artery bypass graft(s) with other forms of angina pectoris
125.729	Atherosclerosis of autologous artery coronary artery bypass graft(s) with unspecified angina pectoris
125.730	Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with unstable angina pectoris
125.731	Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with angina pectoris with documented spasm
125.738	Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with other forms of angina pectoris
125.739	Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with unspecified angina pectoris
125.750	Atherosclerosis of native coronary artery of transplanted heart with unstable angina
125.751	Atherosclerosis of native coronary artery of transplanted heart with angina pectoris with documented spasm

125.758	Atherosclerosis of native coronary artery of transplanted heart with other forms of angina pectoris
125.759	Atherosclerosis of native coronary artery of transplanted heart with unspecified angina pectoris
125.760	Atherosclerosis of bypass graft of coronary artery of transplanted heart with unstable angina
125.761	Atherosclerosis of bypass graft of coronary artery of transplanted heart with angina pectoris with documented spasm
125.768	Atherosclerosis of bypass graft of coronary artery of transplanted heart with other forms of angina pectoris
125.769	Atherosclerosis of bypass graft of coronary artery of transplanted heart with unspecified angina pectoris
125.790	Atherosclerosis of other coronary artery bypass graft(s) with unstable angina pectoris
125.791	Atherosclerosis of other coronary artery bypass graft(s) with angina pectoris with documented spasm
125.798	Atherosclerosis of other coronary artery bypass graft(s) with other forms of angina pectoris
125.799	Atherosclerosis of other coronary artery bypass graft(s) with unspecified angina pectoris
125.810	Atherosclerosis of coronary artery bypass graft(s) without angina pectoris
125.811	Atherosclerosis of native coronary artery of transplanted heart without angina pectoris
125.812	Atherosclerosis of bypass graft of coronary artery of transplanted heart without angina pectoris
125.82	Chronic total occlusion of coronary artery
125.83	Coronary atherosclerosis due to lipid rich plaque
125.84	Coronary atherosclerosis due to calcified coronary lesion
125.89	Other forms of chronic ischemic heart disease
125.9	Chronic ischemic heart disease, unspecified
150.1	Left ventricular failure, unspecified
150.20	Unspecified systolic (congestive) heart failure
150.21	Acute systolic (congestive) heart failure
150.22	Chronic systolic (congestive) heart failure
150.23	Acute on chronic systolic (congestive) heart failure
150.30	Unspecified diastolic (congestive) heart failure
150.31	Acute diastolic (congestive) heart failure
150.32	Chronic diastolic (congestive) heart failure
150.33	Acute on chronic diastolic (congestive) heart failure
150.40	Unspecified combined systolic (congestive) and diastolic (congestive) heart failure
150.41	Acute combined systolic (congestive) and diastolic (congestive) heart failure
150.42	Chronic combined systolic (congestive) and diastolic (congestive) heart failure
150.43	Acute on chronic combined systolic (congestive) and diastolic (congestive) heart failure
150.810	Right heart failure, unspecified
150.811	Acute right heart failure
150.812	Chronic right heart failure
150.813	Acute on chronic right heart failure
150.814	Right heart failure due to left heart failure
150.82	Biventricular heart failure
150.83	High output heart failure
150.84	End stage heart failure
150.04	

150.9	Heart failure, unspecified
151.0	Cardiac septal defect, acquired
151.1	Rupture of chordae tendineae, not elsewhere classified
151.2	Rupture of papillary muscle, not elsewhere classified
151.3	Intracardiac thrombosis, not elsewhere classified
151.4	Myocarditis, unspecified
151.5	Myocardial degeneration
151.7	Cardiomegaly
151.81	Takotsubo syndrome
151.89	Other ill-defined heart diseases
151.9	Heart disease, unspecified
Z13.6	Encounter for screening for cardiovascular disorders

References

National Institutes of Health. National Heart Lung Blood Institute website. June 2016. <u>http://www.nhlbi.nih.gov/health/health-topics/topics/hd/</u>. Accessed July 13, 2022.

National Institutes of Health, US National Library of Medicine. July 2015. <u>http://www.nlm.nih.gov/medlineplus/ency/article/007115.htm</u>. Accessed July 13, 2022.

Roger VL, Go AS, Lloyd-Jones DM, et al. Heart disease and stroke statistics--2011 update: a report from the American Heart Association. Circulation. 2011;123(4):e18-e209. http://circ.ahajournals.org/content/123/4/e18.full.pdf. Accessed July 13, 2022.

Castelli WP, Anderson K, Wilson PW, Levy D. Lipids and risk of coronary heart disease. The Framingham Study. Ann Epidemiol. 1992 Jan-Mar;2(1-2):23-8.

Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentifuge. Clin Chem. 1972; 18:499-502.

Cromwell WC, Otvos JD. Low-density lipoprotein particle number and risk for cardiovascular disease. Curr Atheroscler Rep. 2004;6:381-387.

Otvos JD, Jeyarajah EJ, Cromwell WC. Measurement issues related to lipoprotein heterogeneity. Am J Cardiol. 2002;90(suppl):22i-29i.

Cleeman JL. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA. 2001;285:2486-2497.

Cromwell WC, Otvos JD, Keyes MJ, et al. LDL particle number and risk of future cardiovascular disease in the Framingham Offspring Study -Implications for LDL management. J Clin Lipidol. 2007;1(6):583-592.

Cromwell WC, Barringer TA. Low-density lipoprotein and apolipoprotein B: clinical use in patients with coronary heart disease. Curr Cardiol Rep. Nov 2009;11(6):468-475.

Otvos JD, Mora S, Shalaurova I, Greenland P, Mackey RH, Goff DC, Jr. Clinical implications of discordance between low-density lipoprotein cholesterol and particle number. J Clin Lipidol. Mar-Apr 2011;5(2):105-113.

Brunzell JD, Davidson M, Furberg CD, et al. Lipoprotein management in patients with cardiometabolic risk: consensus conference report from the American Diabetes Association and the American College of Cardiology Foundation. J Am Coll Cardiol. Apr 15 2008;51(15):1512-1524.

Contois JH, McConnell JP, Sethi AA, et al. Apolipoprotein B and cardiovascular disease risk: position statement from the AACC Lipoproteins and Vascular Diseases Division Working Group on Best Practices. Clin Chem. Mar 2009;55(3):407-419.

Davidson MH, Ballantyne CM, Jacobson TA, et al. Clinical utility of inflammatory markers and advanced lipoprotein testing: Advice from an expert panel of lipid specialists. J Clin Lipidol. Sep 2011;5(5):338-367.

Jellinger PS, Smith DA, Mehta AE, Ganda O, Handelsman Y, Rodbard HW, Shepherd MD, Seibel JA; AACE Task Force for Management of Dyslipidemia and Prevention of Atherosclerosis, Kreisberg R, Goldberg R. American Association of Clinical Endocrinologists' Guidelines for Management of Dyslipidemia and Prevention of Atherosclerosis. Endocr Pract. 2012 Mar-Apr;18 Suppl 1:1-78

Helfand M, Carson S. Screening for Lipid Disorders in Adults: Selective Update of 2001 US Preventive Services Task Force Re view. Agency for Healthcare Research and Quality; Rockland, MD 2008.

Specialty matched clinical peer review.

Revision History

Jul. 8, 2022	Added language communicating that measurement of homocysteine levels in advanced lipid testing is unproven for assessing cardiovascular risk ConnectiCare adopts clinical criteria of its parent corporation EmblemHealth
Jun. 11, 2021	Added Boston Heart Cholesterol Balance Test, as example of an investigational subclassification test
Jun. 12, 2020	Added familial dyslipidemias as not medically necessary for lipoprotein subclassification testing