of Tennessee

Policy

Reimbursement Policy

Cardiovascular Disease Risk Assessment

I. Policy Description

Cardiovascular risk assessment comprises the means and processes to predict the probability of developing a cardiovascular disease. These are a group of tests and health factors that have been proven to indicate a person's chance of having a cardiovascular event such as a heart attack or stroke.

Tests typically used to assess cardiovascular risk include lipid profiles or panels, biomarkers, and cardiovascular risk panels.

For guidance concerning lipid screening in individuals under 18 years of age, please refer to AHS-G2042-Pediatric Preventive Screening.

For guidance concerning homocysteine testing for indications other than cardiovascular disease, please refer to AHS-M2141-Testing of Homocysteine Metabolism-Related Conditions and AHS-G2014-Vitamin B12 and Methylmalonic Acid Testing.

Terms such as male and female are used when necessary to refer to sex assigned at birth.

II. Indications and/or Limitations of Coverage

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request. Specifications pertaining to Medicare and Medicaid can be found in the "Applicable State and Federal Regulations" section of this policy document.

1) For individuals 18 years of age or older, lipid panel testing (see Note 1) **MEETS COVERAGE CRITERIA** under **any** of the following conditions:
   a) To screen for cardiovascular disease (CVD) risk:
      i) Every 4 years for individuals ages 18 to 79 years.
      ii) Annually for individuals at increased risk for cardiovascular disease (as defined by 2013 ACC/AHA Pooled Cohort Equations (PCEs) to calculate 10-year risk of CVD events [see Note 2]).

b) Annually for individuals at an increased risk of dyslipidemia due to **any** of the following conditions:
   i) Obesity or metabolic syndrome
   ii) Nephrotic syndrome
   iii) Hypothyroidism
   iv) Hyperthyroidism
   v) Pancreatitis
   vi) Diabetes
   vii) Chronic kidney disease
   viii) Cushing syndrome
   ix) Pregnancy
   x) Cholestatic liver disease
   xi) Lipid metabolism disorders, such as Gaucher disease in adults

c) For individuals who are about to begin or who are currently receiving statin therapy, at the following intervals:
   i) To establish baseline levels before initiating statin therapy.
   ii) Every four to twelve weeks after initiation or change of therapy.
   iii) Annually when no medication changes have occurred.

d) Annually for individuals on a long-term drug therapy that requires lipid monitoring (e.g., Accutane, anti-psychotics).

e) For HIV positive individuals who are about to begin or who are currently receiving antiretroviral therapy (ART), at the following intervals:
   i) To establish baseline levels before initiating ART.
   ii) Every one to three months after initiation or change of therapy.
   iii) Every six to twelve months when no medication changes have occurred.

2) Measurement of apolipoprotein B (apoB) **MEETS COVERAGE CRITERIA** for **any** of the following situations:
   a) For individuals with hypertriglyceridemia.
   b) For individuals with diabetes mellitus.
   c) For individuals with obesity or metabolic syndrome.

d) For individuals with other dyslipidemias (such as very low LDL-C).

e) For individuals who are on lipid therapy.

f) For individuals who are suspected to have familial dysbetalipoproteinemia or familial combined hyperlipidemia.

3) Measurement of lipoprotein a (Lp(a)) once per lifetime (with measurement occurring when the individual is 18 years of age or older) **MEETS COVERAGE CRITERIA**.

4) For individuals for whom a risk-based treatment decision is uncertain (after quantitative risk assessment using ACC/AHA PCEs to calculate 10-year risk of CVD events [see Note 2]), testing for C-reactive protein with the high-sensitivity method (hs-CRP) **MEETS COVERAGE CRITERIA** at the following frequency:

a) One test for initial screening.

b) If the initial screen was abnormal, confirmatory testing no sooner than two weeks after the initial test.

c) Annual screening for those with elevated hs-CRP that has been confirmed.

The following does not meet coverage criteria due to a lack of available published scientific literature confirming that the test(s) is/are required and beneficial for the diagnosis and treatment of an individual's illness.

5) The following testing for CRP **DOES NOT MEET COVERAGE CRITERIA**:

a) Hs-CRP testing for all other cardiovascular disease risk assessments not described above.

b) Conventional CRP testing for cardiovascular disease risk assessment.

6) For CVD risk assessment and stratification in the outpatient setting, measurement of high-sensitivity cardiac troponin T (hs-cTnT) **DOES NOT MEET COVERAGE CRITERIA**.

7) For CVD risk assessment screening, evaluation, and management, homocysteine testing **DOES NOT MEET COVERAGE CRITERIA**.

8) For CVD risk assessment, measurement of novel lipid and non–lipid biomarkers (e.g., apolipoprotein AI, apolipoprotein E, B-type natriuretic peptide, cystatin C, fibrinogen, leptin, LDL subclass, HDL subclass) **DOES NOT MEET COVERAGE CRITERIA**.

9) Other than simple lipid panels (see Note 1), CVD risk panels consisting of multiple individual biomarkers intended to assess CVD **DO NOT MEET COVERAGE CRITERIA**.

10) For CVD risk assessment, measurement of serum intermediate density lipoproteins **DOES NOT MEET COVERAGE CRITERIA**.

11) For CVD risk assessment, measurement of lipoprotein-associated phospholipase A2 (Lp-PLA2) **DOES NOT MEET COVERAGE CRITERIA**.

12) For all situations, measurement of long-chain omega-3 fatty acids in red blood cell membranes, **DOES NOT MEET COVERAGE CRITERIA**.

13) All other tests for assessing CVD risk **DO NOT MEET COVERAGE CRITERIA**.

NOTES:

Note 1: A simple lipid panel is generally composed of the following lipid markers:

- Total cholesterol
- HDL cholesterol
- LDL cholesterol
- Triglycerides

Certain calculated ratios, such as the total/HDL cholesterol may also be reported as part of a simple lipid panel.

Other types of lipid testing (i.e., apolipoproteins, lipid particle number or particle size, lipoprotein [a]) are not considered to be components of a simple lipid profile.

Note 2: 2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk:[1]
Risk factors include gender, age, race, smoking, hypertension, diabetes, total cholesterol, high- and low-density lipoprotein cholesterol. A race- and sex-specific PCE ASCVD Risk Estimator is available at:
https://tools.acc.org/ldl/ascvd_risk_estimator/index.html#!/calulate/estimator/.

The 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol affirms that "the PCE is a powerful tool to predict population risk, but it has limitations when applied to individuals." Hence a clinician-patient risk discussion can individualize risk status based on PCE, but with the inclusion of additional risk-enhancing factors. These additional factors may include:

- A family history of premature atherosclerotic cardiovascular disease (ASCVD) (males, age <55 y; females, age <65 y)
- Primary hypercholesterolemia (LDL-C, 160–189 mg/dL [4.1–4.8 mmol/L]; non–HDL-C 190–219 mg/dL [4.9–5.6 mmol/L])

- Metabolic syndrome (increased waist circumference, elevated triglycerides [>150 mg/dL], elevated blood pressure, elevated glucose, and low HDL-C [<40 mg/dL in men; <50 in women mg/dL] are factors; tally of 3 makes the diagnosis)
- Chronic kidney disease (eGFR 15–59 mL/min/1.73 m2 with or without albuminuria; not treated with dialysis or kidney transplantation)
- Chronic inflammatory conditions such as psoriasis, RA, or HIV/AIDS
- History of premature menopause (before age 40 y) and history of pregnancy-associated conditions that increase later ASCVD risk such as preeclampsia
- High-risk race/ethnicities (eg, South Asian ancestry)
- Lipid/biomarkers: Associated with increased ASCVD risk
- Persistently elevated, primary hypertriglyceridemia (≥175 mg/dL)
- Elevated high-sensitivity C-reactive protein (≥2.0 mg/L)
- Elevated Lp(a): A relative indication for its measurement is family history of premature ASCVD. An Lp(a) ≥50 mg/dL or ≥125 nmol/L constitutes a risk-enhancing factor especially at higher levels of Lp(a)
- Elevated apoB ≥130 mg/dL: A relative indication for its measurement would be triglyceride ≥200 mg/dL. A level ≥130 mg/dL corresponds to an LDL-C ≥160 mg/dL and constitutes a risk-enhancing factor
- ABI <0.9

III. Applicable State and Federal Regulations

DISCLAIMER: If there is a conflict between this Policy and any relevant, applicable government policy for a particular member [e.g., Local Coverage Determinations (LCDs) or National Coverage Determinations (NCDs) for Medicare and/or state coverage for Medicaid], then the government policy will be used to make the determination. For the most up-to-date Medicare policies and coverage, please visit the Medicare search website: https://www.cms.gov/medicare-coverage-database/search.aspx. For the most up-to-date Medicaid policies and coverage, visit the applicable state Medicaid website.

Food and Drug Administration (FDA)

Many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88). LDTs are not approved or cleared by the U. S. Food and Drug Administration; however, FDA clearance or approval is not currently required for clinical use.

IV. Applicable CPT/HCPCS Procedure Codes

Reimbursement Policy

CPT	Code Description
80061	Lipid panel
81599	Unlisted multianalyte assay with algorithmic analysis
82172	Apolipoprotein, each
82465	Cholesterol, serum or whole blood, total
82610	Cystatin C
83090	Homocysteine
83695	Lipoprotein (a)
83698	Lipoprotein-associated phospholipase A2 (Lp-PLA2)
83700	Lipoprotein, blood; electrophoretic separation and quantitation
83701	Lipoprotein, blood; high resolution fractionation and quantitation of lipoproteins including lipoprotein subclasses when performed (eg, electrophoresis, ultracentrifugation)
83704	Lipoprotein, blood; quantitation of lipoprotein particle number(s) (eg, by nuclear magnetic resonance spectroscopy), includes lipoprotein particle subclass(es), when performed
83718	Lipoprotein, direct measurement; high density cholesterol (HDL cholesterol)
83719	Lipoprotein, direct measurement; VLDL cholesterol
83721	Lipoprotein, direct measurement; LDL cholesterol
83722	Lipoprotein, direct measurement; small dense LDL cholesterol
83880	Natriuretic peptide
84478	Triglycerides
84484	Troponin, quantitative
84512	Troponin, Qualitative
84999	Unlisted chemistry procedure
85384	Fibrinogen; activity
85415	Fibrinolytic factors and inhibitors; plasminogen activator
86140	C-reactive protein
86141	C-reactive protein; high sensitivity (hsCRP)
0019M	Cardiovascular disease, plasma, analysis of protein biomarkers by aptamer based microarray and algorithm reported as 4-year likelihood of coronary event in high-risk populations Proprietary test: SOMAmer® Lab/Manufacturer: SomaLogic
0052U	Lipoprotein, blood, high resolution fractionation and quantitation of lipoproteins, including all five major lipoprotein classes and subclasses of HDL, LDL, and VLDL by vertical auto profile ultracentrifugation Proprietary test: VAP Cholesterol Test Lab/Manufacturer: VAP Diagnostics Laboratory, Inc

Reimbursement Policy

CPT	Code Description
0308U	Cardiology (coronary artery disease [CAD]), analysis of 3 proteins (high sensitivity [hs] troponin, adiponectin, and kidney injury molecule-1 [KIM-1]) with 3 clinical parameters (age, sex, history of cardiac intervention), plasma, algorithm reported as a risk score for obstructive CAD Proprietary test: HART CADhs® Lab/Manufacturer: Complete Omics, Prevencio, Inc
0309U	Cardiology (cardiovascular disease), analysis of 4 proteins (NT-proBNP, osteopontin, tissue inhibitor of metalloproteinase-1 [TIMP-1], and kidney injury molecule-1 [KIM-1]), plasma, algorithm reported as a risk score for major adverse cardiac event Proprietary test: HART CVE® Lab/Manufacturer: Complete Omics, Inc, Prevencio, Inc
0377U	Cardiovascular disease, quantification of advanced serum or plasma lipoprotein profile, by nuclear magnetic resonance (NMR) spectrometry with report of a lipoprotein profile (including 23 variables) Proprietary test: Liposcale® Lab/Manufacturer: CIMA Sciences, LLC
0415U	Cardiovascular disease (acute coronary syndrome [ACS]), IL-16, FAS, FASLigand, HGF, CTACK, EOTAXIN, and MCP-3 by immunoassay combined with age, sex, family history, and personal history of diabetes, blood, algorithm reported as a 5-year (deleted risk) score for ACS Proprietary test: SmartHealth Vascular Dx™ Lab/Manufacturer: Morningstar Laboratories, LLC
0541U	Cardiovascular disease (HDL reverse cholesterol transport), cholesterol efflux capacity, LC-MS/MS, quantitative measurement of 5 distinct HDL-bound apolipoproteins (apolipoproteins A1, C1, C2, C3, and C4), serum, algorithm reported as prediction of coronary artery disease (pCAD) score Proprietary test: HDL Reverse Cholesterol Transport Panel with pCAD Score Lab/Manufacturer: Quest Diagnostics®

Procedure codes appearing in Medical Policy documents are included only as a general reference tool for each policy. They may not be all-inclusive.

V. Evidence-based Scientific References

1. Goff DC, Jr., Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Journal of the American College of Cardiology*. Jul 1 2014;63(25 Pt B):2935-59. doi:10.1016/j.jacc.2013.11.005

2. AHA. 2025 Heart Disease and Stroke Statistics Update Fact Sheet. https://www.heart.org/en/-/media/PHD-Files-2/Science-News/2/2025-Heart-and-Stroke-Stat-Update/2025-Statistics-At-A-Glance.pdf
3. Wilson P. Overview of the possible risk factors for cardiovascular disease. Updated November 21, 2024. https://www.uptodate.com/contents/overview-of-possible-risk-factors-for-cardiovascular-disease
4. Rosenson R. Measurement of blood lipids and lipoproteins. Updated October 1, 2024. https://www.uptodate.com/contents/measurement-of-blood-lipids-and-lipoproteins
5. MacNamara J, Eapen DJ, Quyyumi A, Sperling L. Novel biomarkers for cardiovascular risk assessment: current status and future directions. *Future cardiology*. Sep 2015;11(5):597-613. doi:10.2217/fca.15.39
6. Wilson P. Atherosclerotic cardiovascular disease risk assessment for primary prevention in adults. Updated September 20, 2024. https://www.uptodate.com/contents/atherosclerotic-cardiovascular-disease-risk-assessment-for-primary-prevention-in-adults-our-approach
7. Rosenson R, Stein J, Durrington P. Lipoprotein(a). Updated April 15, 2025. https://www.uptodate.com/contents/lipoprotein-a-and-cardiovascular-disease
8. Rosenson R. Lipoprotein classification, metabolism, and role in atherosclerosis. Updated October 23, 2023. https://www.uptodate.com/contents/lipoprotein-classification-metabolism-and-role-in-atherosclerosis
9. Antonopoulos AS, Angelopoulos A, Papanikolaou P, et al. Biomarkers of Vascular Inflammation for Cardiovascular Risk Prognostication: A Meta-Analysis. *JACC Cardiovasc Imaging*. Mar 2022;15(3):460-471. doi:10.1016/j.jcmg.2021.09.014
10. Chiesa ST, Charakida M, Georgiopoulos G, et al. Glycoprotein Acetyls: A Novel Inflammatory Biomarker of Early Cardiovascular Risk in the Young. *J Am Heart Assoc*. Feb 15 2022;11(4):e024380. doi:10.1161/jaha.121.024380
11. Morita SY. Metabolism and Modification of Apolipoprotein B-Containing Lipoproteins Involved in Dyslipidemia and Atherosclerosis. *Biol Pharm Bull*. 2016;39(1):1-24. doi:10.1248/bpb.b15-00716
12. Trompet S, Packard CJ, Jukema JW. Plasma apolipoprotein-B is an important risk factor for cardiovascular disease, and its assessment should be routine clinical practice. *Curr Opin Lipidol*. Feb 2018;29(1):51-52. doi:10.1097/mol.0000000000000476
13. Robinson JG, Williams KJ, Gidding S, et al. Eradicating the Burden of Atherosclerotic Cardiovascular Disease by Lowering Apolipoprotein B Lipoproteins Earlier in Life. *J Am Heart Assoc*. Oct 16 2018;7(20):e009778. doi:10.1161/jaha.118.009778
14. Tedeschi-Reiner E, Strozzi M, Skoric B, Reiner Z. Relation of atherosclerotic changes in retinal arteries to the extent of coronary artery disease. *Am J Cardiol*. Oct 15 2005;96(8):1107-9. doi:10.1016/j.amjcard.2005.05.070
15. Lamprea-Montealegre JA, Staplin N, Herrington WG, et al. Apolipoprotein B, Triglyceride-Rich Lipoproteins, and Risk of Cardiovascular Events in Persons with CKD. *Clin J Am Soc Nephrol*. Jan 7 2020;15(1):47-60. doi:10.2215/cjn.07320619

16. Cao J, Nomura SO, Steffen BT, et al. Apolipoprotein B discordance with low-density lipoprotein cholesterol and non-high-density lipoprotein cholesterol in relation to coronary artery calcification in the Multi-Ethnic Study of Atherosclerosis (MESA). *J Clin Lipidol*. Nov 29 2019;doi:10.1016/j.jacl.2019.11.005
17. Hwang YC, Ahn HY, Han KH, Park SW, Park CY. Prediction of future cardiovascular disease with an equation to estimate apolipoprotein B in patients with high cardiovascular risk: an analysis from the TNT and IDEAL study. *Lipids Health Dis*. Aug 22 2017;16(1):158. doi:10.1186/s12944-017-0549-8
18. Mach F, Baigent C, Catapano AL, et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. *Eur Heart J*. Aug 31 2019;doi:10.1093/eurheartj/ehz455
19. Sandhu PK, Musaad SM, Remaley AT, et al. Lipoprotein Biomarkers and Risk of Cardiovascular Disease: A Laboratory Medicine Best Practices (LMBP) Systematic Review. *The journal of applied laboratory medicine*. Sep 1 2016;1(2):214-229. doi:10.1373/jalm.2016.021006
20. Kuwahara K, Nakagawa Y, Nishikimi T. Cutting Edge of Brain Natriuretic Peptide (BNP) Research - The Diversity of BNP Immunoreactivity and Its Clinical Relevance. *Circ J*. Sep 25 2018;82(10):2455-2461. doi:10.1253/circj.CJ-18-0824
21. Li N, Wang JA. Brain natriuretic peptide and optimal management of heart failure. *J Zhejiang Univ Sci B*. Sep 2005;6(9):877-84.
22. Tomcsányi J, Somlói M, Bózsik B, Frész T, Nagy E. [The value of early repeated N-terminal pro-B-type natriuretic peptide measurement in acute heart failure]. *Orv Hetil*. Jun 2018;159(25):1009-1012. Az N-terminális pro-B natriureticus peptid mérésének korai ismétlése akut szívelégtelenség miatt hospitalizált betegeken. doi:10.1556/650.2018.31095
23. Mark DB, Cowper PA, Anstrom KJ, et al. Economic and Quality-of-Life Outcomes of Natriuretic Peptide-Guided Therapy for Heart Failure. *Journal of the American College of Cardiology*. Nov 27 2018;72(21):2551-2562. doi:10.1016/j.jacc.2018.08.2184
24. Colucci W, Chen HH. Natriuretic peptide measurement in heart failure. Updated March 11, 2024. https://www.uptodate.com/contents/natriuretic-peptide-measurement-in-heart-failure
25. Januzzi JL, Jr., Ahmad T, Mulder H, et al. Natriuretic Peptide Response and Outcomes in Chronic Heart Failure With Reduced Ejection Fraction. *Journal of the American College of Cardiology*. Sep 3 2019;74(9):1205-1217. doi:10.1016/j.jacc.2019.06.055
26. Rosenson R, Durrington P. HDL cholesterol: Clinical aspects of abnormal values. Updated August 6, 2024. https://www.uptodate.com/contents/hdl-cholesterol-clinical-aspects-of-abnormal-values
27. Grundy SM, Stone Neil J, Bailey Alison L, 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 Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019/06/18 2018;139(25):e1082-e1143. doi:10.1161/CIR.0000000000000625

28. Willeit P, Ridker PM, Nestel PJ, et al. Baseline and on-statin treatment lipoprotein(a) levels for prediction of cardiovascular events: individual patient-data meta-analysis of statin outcome trials. *Lancet (London, England)*. Oct 13 2018;392(10155):1311-1320. doi:10.1016/s0140-6736(18)31652-0
29. Mehta A, Virani SS, Ayers CR, et al. Lipoprotein(a) and Family History Predict Cardiovascular Disease Risk. *Journal of the American College of Cardiology*. Aug 18 2020;76(7):781-793. doi:10.1016/j.jacc.2020.06.040
30. Rule A, Glassock, Richard. The aging kidney. Updated September 3, 2024. https://www.uptodate.com/contents/the-aging-kidney
31. Sarnak M, Gibson, Michael, Henrich, William. Chronic kidney disease and coronary heart disease. Updated May 16, 2023. https://www.uptodate.com/contents/chronic-kidney-disease-and-coronary-heart-disease
32. Maners J, Gill D, Pankratz N, Tang W. Abstract P106: Genetically Determined Fibrinogen, Gamma Prime Fibrinogen and Risk of Venous Thromboembolism and Ischemic Stroke: Evidence From Mendelian Randomization. *American Heart Association*. 2019;doi:10.1161/circ.139.suppl_1.P106
33. Pieters M, Ferreira M, de Maat MPM, Ricci C. Biomarker association with cardiovascular disease and mortality - The role of fibrinogen. A report from the NHANES study. *Thromb Res*. Dec 16 2020;198:182-189. doi:10.1016/j.thromres.2020.12.009
34. Yang H, Guo W, Li J, et al. Leptin concentration and risk of coronary heart disease and stroke: A systematic review and meta-analysis. *PloS one*. 2017;12(3):e0166360. doi:10.1371/journal.pone.0166360
35. Liu G, Dong M, Ma S, et al. Serum leptin is associated with first-ever ischemic stroke, lesion size and stroke severity in a Chinese cohort. *Neurol Res*. Feb 2019;41(2):125-131. doi:10.1080/01616412.2018.1544399
36. Pignone MP. Low-density lipoprotein cholesterol-lowering therapy in the primary prevention of cardiovascular disease. Updated June 27, 2024. https://www.uptodate.com/contents/management-of-elevated-low-density-lipoprotein-cholesterol-ldl-c-in-primary-prevention-of-cardiovascular-disease
37. Reklou A, Katsiki N, Karagiannis A, Athyros V. Effects of Lipid Lowering Drugs on Arterial Stiffness: One More Way to Reduce Cardiovascular Risk? *Curr Vasc Pharmacol*. 2020;18(1):38-42. doi:10.2174/1570161117666190121102323
38. Kongpakwattana K, Ademi Z, Chaiyasothi T, et al. Cost-Effectiveness Analysis of Non-Statin Lipid-Modifying Agents for Secondary Cardiovascular Disease Prevention Among Statin-Treated Patients in Thailand. *Pharmacoeconomics*. Oct 2019;37(10):1277-1286. doi:10.1007/s40273-019-00820-6
39. Boekholdt SM, Hovingh GK, Mora S, et al. Very low levels of atherogenic lipoproteins and the risk for cardiovascular events: a meta-analysis of statin trials. *Journal of the American College of Cardiology*. Aug 5 2014;64(5):485-94. doi:10.1016/j.jacc.2014.02.615
40. Beauchemin M, Geguchadze R, Guntur AR, et al. Exploring mechanisms of increased cardiovascular disease risk with antipsychotic medications: Risperidone alters the cardiac

proteomic signature in mice. *Pharmacol Res*. Dec 23 2019;152:104589. doi:10.1016/j.phrs.2019.104589
41. Polcwiartek C, Kragholm K, Schjerning O, Graff C, Nielsen J. Cardiovascular safety of antipsychotics: a clinical overview. *Expert Opin Drug Saf*. May 2016;15(5):679-88. doi:10.1517/14740338.2016.1161021
42. Howell S, Yarovova E, Khwanda A, Rosen SD. Cardiovascular effects of psychotic illnesses and antipsychotic therapy. *Heart*. Dec 2019;105(24):1852-1859. doi:10.1136/heartjnl-2017-312107
43. Kilicaslan EE, Karakilic M, Erol A. The Relationship between 10 Years Risk of Cardiovascular Disease and Schizophrenia Symptoms: Preliminary Results. *Psychiatry Investig*. Dec 2019;16(12):933-939. doi:10.30773/pi.2019.0063
44. Rotella F, Cassioli E, Calderani E, et al. Long-term metabolic and cardiovascular effects of antipsychotic drugs. A meta-analysis of randomized controlled trials. *Eur Neuropsychopharmacol*. Jan 6 2020;doi:10.1016/j.euroneuro.2019.12.118
45. Pile HD, Sadiq NM. Isotretinoin. *StatPearls*. StatPearls Publishing; 2019.
46. Güler E, Babur Güler G, Yavuz C, Kızılırmak F. An unknown side effect of isotretinoin: pericardial effusion with atrial tachycardia. *Anatol J Cardiol*. Feb 2015;15(2):168-9.
47. Akcay M, Yuksel S. Isotretinoin-associated possible Kounis syndrome: A case report and a review of other cardiovascular side effects reported in the literature. *Turk Kardiyol Dern Ars*. Jun 2019;47(4):324-328. Isotretinoin ile iliskili olasi Kounis sendromu: Olgu sunumu ve diger kardiyovaskuler yan etkilerin literatur derlemesi. doi:10.5543/tkda.2018.67055
48. Alan S, Unal B, Yildirim A. Premature ventricular contractions associated with isotretinoin use. *An Bras Dermatol*. Nov-Dec 2016;91(6):820-821. doi:10.1590/abd1806-4841.20165138
49. Karadag AS, Gumrukcuoglu HA, Gunes Bilgili S, et al. Does isotretinoin therapy have any effects on electrocardiography, heart rate and blood pressure? *J Dermatolog Treat*. Jun 2012;23(3):168-71. doi:10.3109/09546634.2010.546831
50. Zane LT, Leyden WA, Marqueling AL, Manos MM. A population-based analysis of laboratory abnormalities during isotretinoin therapy for acne vulgaris. *Arch Dermatol*. Aug 2006;142(8):1016-22. doi:10.1001/archderm.142.8.1016
51. Lee YH, Scharnitz TP, Muscat J, Chen A, Gupta-Elera G, Kirby JS. Laboratory Monitoring During Isotretinoin Therapy for Acne: A Systematic Review and Meta-analysis. *JAMA Dermatol*. Jan 2016;152(1):35-44. doi:10.1001/jamadermatol.2015.3091
52. Crea F, Morrow, David. C-reactive protein in cardiovascular disease. Updated November 18, 2024. https://www.uptodate.com/contents/c-reactive-protein-in-cardiovascular-disease
53. Mehta A, Blumenthal RS, Gluckman TJ, Feldman DI, Kohli P. High-sensitivity C-reactive Protein in Atherosclerotic Cardiovascular Disease: To Measure or Not to Measure? *US Cardiol*. 2025;19:e06. doi:10.15420/usc.2024.25
54. Rosenson RS, Smith CC, Bauer KA. Overview of homocysteine. Updated January 24, 2025. https://www.uptodate.com/contents/overview-of-homocysteine

55. Varbo A, Benn M, Tybjaerg-Hansen A, Jorgensen AB, Frikke-Schmidt R, Nordestgaard BG. Remnant cholesterol as a causal risk factor for ischemic heart disease. *Journal of the American College of Cardiology*. Jan 29 2013;61(4):427-36. doi:10.1016/j.jacc.2012.08.1026
56. Jepsen A-MK, Langsted A, Varbo A, Bang LE, Kamstrup PR, Nordestgaard BG. Increased Remnant Cholesterol Explains Part of Residual Risk of All-Cause Mortality in 5414 Patients with Ischemic Heart Disease. *Clinical Chemistry*. 2016;62(4):593. doi:10.1373/clinchem.2015.253757
57. Joshi PH, Khokhar AA, Massaro JM, et al. Remnant Lipoprotein Cholesterol and Incident Coronary Heart Disease: The Jackson Heart and Framingham Offspring Cohort Studies. 2016-05-01 2016;doi:10.1161/JAHA.115.002765
58. Varbo A, Benn M, Nordestgaard BG. Remnant cholesterol as a cause of ischemic heart disease: evidence, definition, measurement, atherogenicity, high risk patients, and present and future treatment. *Pharmacology & therapeutics*. Mar 2014;141(3):358-67. doi:10.1016/j.pharmthera.2013.11.008
59. Di Angelantonio E, Sarwar N, Perry P, et al. Major lipids, apolipoproteins, and risk of vascular disease. *Jama*. Nov 11 2009;302(18):1993-2000. doi:10.1001/jama.2009.1619
60. Rosenson RS, Stafforini DM. Modulation of oxidative stress, inflammation, and atherosclerosis by lipoprotein-associated phospholipase A2. *Journal of lipid research*. Sep 2012;53(9):1767-82. doi:10.1194/jlr.R024190
61. LPSC. Lipoprotein-associated phospholipase A2 and risk of coronary disease, stroke, and mortality: collaborative analysis of 32 prospective studies. *The Lancet*. 2010/05/01 2010;375(9725):1536-1544. doi:10.1016/S0140-6736(10)60319-4
62. Garg PK, McClelland RL, Jenny NS, et al. Lipoprotein-associated phospholipase A2 and risk of incident cardiovascular disease in a multi-ethnic cohort: The multi ethnic study of atherosclerosis. *Atherosclerosis*. Jul 2015;241(1):176-82. doi:10.1016/j.atherosclerosis.2015.05.006
63. Sudhir K. Lipoprotein-associated phospholipase A2, vascular inflammation and cardiovascular risk prediction. *Vascular health and risk management*. 2006;2(2):153-6.
64. Mohler ER, 3rd, Ballantyne CM, Davidson MH, et al. The effect of darapladib on plasma lipoprotein-associated phospholipase A2 activity and cardiovascular biomarkers in patients with stable coronary heart disease or coronary heart disease risk equivalent: the results of a multicenter, randomized, double-blind, placebo-controlled study. *Journal of the American College of Cardiology*. Apr 29 2008;51(17):1632-41. doi:10.1016/j.jacc.2007.11.079
65. De Stefano A, Mannucci L, Tamburi F, et al. Lp-PLA2, a new biomarker of vascular disorders in metabolic diseases. *Int J Immunopathol Pharmacol*. Jan-Dec 2019;33:2058738419827154. doi:10.1177/2058738419827154
66. Mozaffarian D. Fish oil: Physiologic effects and administration. Updated August 14, 2024. https://www.uptodate.com/contents/fish-oil-physiologic-effects-and-administration
67. de Oliveira Otto MC, Wu JH, Baylin A, et al. Circulating and dietary omega-3 and omega-6 polyunsaturated fatty acids and incidence of CVD in the Multi-Ethnic Study of Atherosclerosis. *J Am Heart Assoc*. Dec 18 2013;2(6):e000506. doi:10.1161/jaha.113.000506

68. Superko HR, Superko AR, Lundberg GP, et al. Omega-3 Fatty Acid Blood Levels Clinical Significance Update. *Curr Cardiovasc Risk Rep*. 2014;8(11)doi:10.1007/s12170-014-0407-4
69. Itakura H, Yokoyama M, Matsuzaki M, et al. Relationships between plasma fatty acid composition and coronary artery disease. *J Atheroscler Thromb*. 2011;18(2):99-107. doi:10.5551/jat.5876
70. Bosch J, Gerstein HC, Dagenais GR, et al. n-3 fatty acids and cardiovascular outcomes in patients with dysglycemia. *The New England journal of medicine*. Jul 26 2012;367(4):309-18. doi:10.1056/NEJMoa1203859
71. Rizos EC, Ntzani EE, Bika E, Kostapanos MS, Elisaf MS. Association between omega-3 fatty acid supplementation and risk of major cardiovascular disease events: a systematic review and meta-analysis. *Jama*. Sep 12 2012;308(10):1024-33. doi:10.1001/2012.jama.11374
72. Siscovick DS, Barringer TA, Fretts AM, et al. Omega-3 Polyunsaturated Fatty Acid (Fish Oil) Supplementation and the Prevention of Clinical Cardiovascular Disease: A Science Advisory From the American Heart Association. *Circulation*. Apr 11 2017;135(15):e867-e884. doi:10.1161/cir.0000000000000482
73. Gibson M, Morrow, D. Elevated cardiac troponin concentration in the absence of an acute coronary syndrome. Updated April 17, 2024. https://www.uptodate.com/contents/elevated-cardiac-troponin-concentration-in-the-absence-of-an-acute-coronary-syndrome
74. Jaffe A. Troponin testing: Analytical considerations. Updated April 17, 2024. https://www.uptodate.com/contents/troponin-testing-analytical-considerations
75. Ford I, Shah AS, Zhang R, et al. High-Sensitivity Cardiac Troponin, Statin Therapy, and Risk of Coronary Heart Disease. *Journal of the American College of Cardiology*. Dec 27 2016;68(25):2719-2728. doi:10.1016/j.jacc.2016.10.020
76. Tang O, Matsushita K, Coresh J, et al. High-Sensitivity Cardiac Troponin I for Risk Stratification in Older Adults. *J Am Geriatr Soc*. Nov 4 2020;doi:10.1111/jgs.16912
77. Suthahar N, Meems LMG, van Veldhuisen DJ, et al. High-Sensitivity Troponin-T and Cardiovascular Outcomes in the Community: Differences Between Women and Men. *Mayo Clin Proc*. Jun 2020;95(6):1158-1168. doi:10.1016/j.mayocp.2020.01.017
78. Genova Diagnostics. Cardio Check. https://www.gdx.net/core/sample-reports/Cardio-Check-Sample-Report.pdf
79. Cleveland HeartLab. The Science. https://www.clevelandheartlab.com/providers/the-science/
80. Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. Sep 10 2019;140(11):e596-e646. doi:10.1161/cir.0000000000000678
81. Greenland P, Alpert JS, Beller GA, et al. 2010 ACCF/AHA guideline for assessment of cardiovascular risk in asymptomatic adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Journal of the American College of Cardiology*. Dec 14 2010;56(25):e50-103. doi:10.1016/j.jacc.2010.09.001

82. ACC. 2018 Guideline on the Management of Blood Cholesterol. Updated June 2019. https://www.acc.org/~/media/Non-Clinical/Files-PDFs-Excel-MS-Word-etc/Guidelines/2018/Guidelines-Made-Simple-Tool-2018-Cholesterol.pdf
83. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension (Dallas, Tex : 1979)*. Jun 2018;71(6):1269-1324. doi:10.1161/hyp.0000000000000066
84. American Diabetes Association Professional Practice C. 10. Cardiovascular Disease and Risk Management: Standards of Care in Diabetes-2025. *Diabetes Care*. Jan 1 2025;48(Supplement_1):S207-S238. doi:10.2337/dc25-S010
85. ElSayed NA, Aleppo G, Aroda VR, et al. 10. Cardiovascular Disease and Risk Management: Standards of Care in Diabetes-2023. *Diabetes Care*. Jan 1 2023;46(Suppl 1):S158-S190. doi:10.2337/dc23-S010
86. American Diabetes A. 10. Cardiovascular Disease and Risk Management: Standards of Medical Care in Diabetes-2021. *Diabetes Care*. Jan 2021;44(Suppl 1):S125-S150. doi:10.2337/dc21-S010
87. American Diabetes Association Professional Practice C. 14. Children and Adolescents: Standards of Care in Diabetes-2024. *Diabetes Care*. Jan 1 2024;47(Suppl 1):S258-S281. doi:10.2337/dc24-S014
88. Wilson DP, Jacobson TA, Jones PH, et al. Use of Lipoprotein(a) in clinical practice: A biomarker whose time has come. A scientific statement from the National Lipid Association. *J Clin Lipidol*. May-Jun 2019;13(3):374-392. doi:10.1016/j.jacl.2019.04.010
89. Wilson PWF, Jacobson TA, Martin SS, et al. Lipid measurements in the management of cardiovascular diseases: Practical recommendations a scientific statement from the national lipid association writing group. *Journal of Clinical Lipidology*. 2021;15(5):629-648. doi:10.1016/j.jacl.2021.09.046
90. CDC. Cardiovascular Disease Biomarker Standardization Programs. Updated April 24, 2024. https://www.cdc.gov/clinical-standardization-programs/php/cvd/
91. CDC. Heart Disease Risk Factors. Updated December 2, 2024. https://www.cdc.gov/heart-disease/risk-factors/
92. CDC. LSP: Lipids Standardization Program. Updated December, 2023. https://wwwn.cdc.gov/dlsdata/lspds/pdf/UserManual.pdf
93. Pearson TA, Mensah GA, Alexander RW, et al. Markers of inflammation and cardiovascular disease: application to clinical and public health practice: A statement for healthcare professionals from the Centers for Disease Control and Prevention and the American Heart Association. *Circulation*. Jan 28 2003;107(3):499-511. doi:10.1161/01.cir.0000052939.59093.45
94. CMS. Lipid Testing https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?NCDId=102

95. Reyes-Soffer G, Ginsberg HN, Berglund L, et al. Lipoprotein(a): A Genetically Determined, Causal, and Prevalent Risk Factor for Atherosclerotic Cardiovascular Disease: A Scientific Statement From the American Heart Association. *Arterioscler Thromb Vasc Biol*. Jan 2022;42(1):e48-e60. doi:10.1161/ATV.0000000000000147
96. Jellinger PS, Handelsman Y, Rosenblit PD, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Guidlines for Management of Dyslipidemia and Prevention of Cardiovascular Disease. *Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists*. Apr 2017;23(Suppl 2):1-87. doi:10.4158/ep171764.appgl
97. AACE. Consensus Statement by The American Association Of Clinical Endocrinologists And American College Of Endocrinology On The Management Of Dyslipidemia And Prevention Of Cardiovascular Disease Algorithm – 2020 Executive Summary. 2021;
98. Garber AJ, Handelsman Y, Grunberger G, et al. Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm– 2020 Executive Summary. *Endocrine Practice*. 2020/01/01 2020;26(1):107-139. doi:10.4158/CS-2019-0472
99. Visseren FLJ, Mach F, Smulders YM, et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice: Developed by the Task Force for cardiovascular disease prevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies With the special contribution of the European Association of Preventive Cardiology (EAPC). *European Heart Journal*. 2021;42(34):3227-3337. doi:10.1093/eurheartj/ehab484
100. Catapano AL, Graham I, De Backer G, et al. 2016 ESC/EAS Guidelines for the Management of Dyslipidaemias. *Eur Heart J*. Oct 14 2016;37(39):2999-3058. doi:10.1093/eurheartj/ehw272
101. Cosentino F, Grant PJ, Aboyans V, et al. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: The Task Force for diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and the European Association for the Study of Diabetes (EASD). *European Heart Journal*. 2020;41(2):255-323. doi:10.1093/eurheartj/ehz486
102. Newman CB, Blaha MJ, Boord JB, et al. Lipid Management in Patients with Endocrine Disorders: An Endocrine Society Clinical Practice Guideline. *The Journal of Clinical Endocrinology & Metabolism*. 2020;105(12):3613-3682. doi:10.1210/clinem/dgaa674
103. Rosenzweig JL, Bakris GL, Berglund LF, et al. Primary Prevention of ASCVD and T2DM in Patients at Metabolic Risk: An Endocrine Society* Clinical Practice Guideline. *J Clin Endocrinol Metab*. Jul 31 2019;doi:10.1210/jc.2019-01338
104. ASCP. American Society for Clinical Pathology. https://www.ascp.org/content/docs/default-source/get-involved-pdfs/20-things-to-question.pdf

105. Wong ND, Budoff MJ, Ferdinand K, et al. Atherosclerotic cardiovascular disease risk assessment: An American Society for Preventive Cardiology clinical practice statement. *Am J Prev Cardiol*. Jun 2022;10:100335. doi:10.1016/j.ajpc.2022.100335
106. NICE. Cardiovascular disease: risk assessment and reduction, including lipid modification. Updated December 14, 2023. https://www.nice.org.uk/guidance/ng238
107. Bibbins-Domingo K, University of California SF, Grossman DC, et al. Statin Use for the Primary Prevention of Cardiovascular Disease in Adults: US Preventive Services Task Force Recommendation Statement. *Jama*. 2017;316(19):1997-2007. doi:10.1001/jama.2016.15450
108. Chou R, Dana T, Blazina I, Daeges M, Bougatsos C, Jeanne TL. Screening for Dyslipidemia in Younger Adults: A Systematic Review for the U.S. Preventive Services Task Force. *Annals of internal medicine*. Oct 18 2016;165(8):560-564. doi:10.7326/m16-0946
109. USPSTF. Risk assessment for cardiovascular disease with nontraditional risk factors: Us preventive services task force recommendation statement. *Jama*. 2018;320(3):272-280. doi:10.1001/jama.2018.8359
110. USPSTF. Screening for abnormal blood glucose and type 2 diabetes mellitus: U.s. preventive services task force recommendation statement. *Annals of internal medicine*. 2015;163(11):861-868. doi:10.7326/M15-2345
111. USPSTF. Screening for Cardiovascular Disease Risk With Electrocardiography: US Preventive Services Task Force Recommendation Statement. *Jama*. 2018;319(22):2308-2314. doi:10.1001/jama.2018.6848
112. Moyer VA. Screening for primary hypertension in children and adolescents: U.S. Preventive Services Task Force recommendation statement. *Annals of internal medicine*. Nov 5 2013;159(9):613-9. doi:10.7326/0003-4819-159-9-201311050-00725
113. USPSTF. High Blood Pressure in Children and Adolescents: Screening. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/blood-pressure-in-children-and-adolescents-hypertension-screening
114. USPSTF. Hypertension in Adults: Screening. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/hypertension-in-adults-screening
115. Pearson GJ, Thanassoulis G, Anderson TJ, et al. 2021 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in Adults. *Can J Cardiol*. Aug 2021;37(8):1129-1150. doi:10.1016/j.cjca.2021.03.016
116. Thompson MA, Horberg MA, Agwu AL, et al. Primary Care Guidance for Persons With Human Immunodeficiency Virus: 2020 Update by the HIV Medicine Association of the Infectious Diseases Society of America. *Clinical Infectious Diseases*. 2020;73(11):e3572-e3605. doi:10.1093/cid/ciaa1391
117. Aberg JA, Gallant JE, Ghanem KG, Emmanuel P, Zingman BS, Horberg MA. Primary Care Guidelines for the Management of Persons Infected With HIV: 2013 Update by the HIV

Medicine Association of the Infectious Diseases Society of America. *Clinical Infectious Diseases*. 2014;58(1):e1-e34. doi:10.1093/cid/cit665

118. O'Malley PG, Arnold MJ, Kelley C, et al. Management of Dyslipidemia for Cardiovascular Disease Risk Reduction: Synopsis of the 2020 Updated U.S. Department of Veterans Affairs and U.S. Department of Defense Clinical Practice Guideline. *Annals of internal medicine*. Nov 17 2020;173(10):822-829. doi:10.7326/m20-4648

VI. Revision History

Revision Date	Summary of Changes
06/04/2025	Reviewed and Updated: Updated the background, guidelines and recommendations, and evidence-based scientific references. Literature review necessitated the following changes to coverage criteria: CC3 edited to clarify that Lp(a) screening is once per lifetime AND should happen after the individual is 18 years of age. Now reads: "3) Measurement of lipoprotein a (Lp(a)) once per lifetime (with measurement occurring when the individual is 18 years of age or older) MEETS COVERAGE CRITERIA." CC4 edited to clarify that hs-CRP screening is a total of two measurements, with at least two weeks in between each one of those measurements, and that when those two tests have confirmed elevated CRP, annual measuring thereafter. Subcriteria now read: "a) One test for initial screening. b) If the initial screen was abnormal, confirmatory testing no sooner than two weeks after the initial test. c) Annual screening for those with elevated hs-CRP that has been confirmed." CC5 edited to define the use of both hs-CRP and conventional CRP measurement for CVD risk assessment. Now reads: "5) The following testing for CRP DOES NOT MEET COVERAGE CRITERIA: a) Hs-CRP testing for all other cardiovascular disease risk assessments not described above. b) Conventional CRP testing for cardiovascular disease risk assessment." Updated code description for CPT code 0308U, 0309U
03/05/2025	Off-cycle coding modification: Added CPT code 0541U (effective date 4/1/2025) Revised laboratory name for CPT code 0308U, 0308U (effective date 4/1/2025)