Medical Policy
Cardiovascular Risk Panels

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Policy Number: 664
BCBSA Reference Number: 2.04.100
NCD/LCD: N/A

Related Policies
- Novel Lipid Risk Factors in Risk Assessment and Management of Cardiovascular Disease, #283
- Measurement of Lipoprotein-Associated Phospholipase A2 - Lp-PLA2- in the Assessment of Cardiovascular Risk, #558
- Ultrasonographic Measurement of Carotid Intima-Medial Thickness as an Assessment of Subclinical Atherosclerosis, #547
- Homocysteine Testing in the Screening, Diagnosis, and Management of Cardiovascular Disease, #016
- Genotyping for 9p21 Single Nucleotide Polymorphisms to Predict Risk of Cardiovascular Disease or Aneurysm, #340
- Gene Expression Testing to Predict Coronary Artery Disease, #349

Policy
Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO BlueSM and Medicare PPO BlueSM Members

Cardiovascular risk panels, consisting of multiple individual biomarkers intended to assess cardiac risk, are INVESTIGATIONAL.

Prior Authorization Information
Pre-service approval is required for all inpatient services for all products.
See below for situations where prior authorization may be required or may not be required for outpatient services.
Yes indicates that prior authorization is required.
No indicates that prior authorization is not required.
N/A indicates that this service is primarily performed in an inpatient setting.

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Cardiovascular (CV) disease remains the single largest cause of morbidity and mortality in the developed world. As a result, accurate prediction of CV risk is a component of medical care that has the potential to focus and direct preventive and diagnostic activities. Current methods of risk prediction in use in general clinical care are not highly accurate, and as a result there is a potential unmet need for improved risk prediction instruments.

Components of cardiovascular risk include family history, cigarette smoking, hypertension, and lifestyle factors such as diet and exercise. In addition, numerous laboratory tests have been associated with cardiovascular (CV) risk, most prominently lipids such as low-density lipoprotein (LDL) and high-density lipoprotein (HDL). These clinical and lipid factors are often combined into simple risk prediction instruments, such as the Framingham risk score (FRS). (1) The Framingham risk score provides an estimate of the 10-year risk for developing cardiac disease and is currently used in clinical care to determine the aggressiveness of risk factor intervention, such as the decision to treat hyperlipidemia with statins.

Many additional biomarkers, genetic factors and radiologic measures have been associated with increased risk of CV disease. Over 100 emerging risk factors have been proposed as useful for refining estimates of cardiovascular risk. (2-4) Some general categories of these potential risk factors are as follows:

- **Lipid markers.** In addition to LDL and HDL, other lipid markers may have predictive ability, including the apolipoproteins, lipoprotein (a), lipid subfractions, and/or other measures.
- **Inflammatory markers.** Many measures of inflammation have been linked to the likelihood of CV disease. High-sensitivity C-reactive protein (CRP) is one example of an inflammatory marker; others include fibrinogen, interleukins, and tumor necrosis factor.
- **Metabolic syndrome biomarkers.** Measures associated with metabolic syndrome, such as specific dyslipidemic profiles or serum insulin levels, have been associated with increased risk of CV disease.
- **Genetic markers.** A number of mutations associated with increased thrombosis risk, such as the MTHFR mutation or the prothrombin gene mutations, have been associated with increased CV risk. In addition, numerous single nucleotide polymorphisms (SNPs) have been associated with CV disease in large genome-wide studies.

CV risk panels may contain measures from one or all of the above categories, and may include additional measures not listed above such as radiologic markers (carotid CMT, calcium score). Some cardiovascular risk panels are relatively limited, including a few markers in addition to standard lipids. Others include a wide variety of potential risk factors from a number of different categories, often including both genetic and nongenetic risk factors. Other panels are composed entirely of genetic markers.

Some examples of commercially available CV risk panels are as follows:
Health Diagnostics Cardiac Risk Panel: MTHFR gene analysis, common variants; vitamin D, 1,25 dihydroxy; B-type natriuretic peptide (BNP); Lp-PLA2; myeloperoxidase; apolipoprotein; immune complex assay; lipoprotein, blood; electrophoretic separation and quantitation; very long chain fatty acids; total cholesterol; HDL; LDL; triglycerides; (high-sensitivity CRP, hsCRP); lipoprotein (a); insulin, total; fibrinogen; apolipoprotein analysis; multiple single-nucleotide polymorphisms (SNPs) associated with coronary artery disease (CAD).

Genova Diagnostics CV Health Plus Genomics™ Panel: apo E; prothrombin; factor V leiden; fibrinogen; HDL; HDL size; HDL particle number; homocysteine; LDL; LDL size; LDL particle number; lipoprotein (a); LP-PLA2; MTHFR gene; triglycerides; very low-density lipoprotein (VLDL); VLDL size; vitamin D; hs-CRP.

Cleveland HeartLab CVD Inflammatory Profile: hs-CRP, urinary microalbumin, myeloperoxidase, Lp-PLA2, F2-isoprostanes.


Genetiks Genetic Diagnosis and Research Center Cardiovascular Risk Panel: factor V leiden, factor V R2, Prothrombin gene, factor XIII, fibrinogen -455, PAI-1, GPIIIs (HPA-1), MTHFR, ACE I/D, Apo B, Apo E.

Singulex® Cardiac-Related Test Panels: Several panels of markers related to cardiac dysfunction, vascular inflammation and dysfunction, dyslipidemia, and cardiometabolic status are offered by Singulex (Alameda, CA). Some of these panels are offered in conjunction with a CV disease testing and wellness management service. The test panels use an immunoassay method referred to as “Proprietary high-precision Single Molecule Counting [SMC] technology.”5
  - Cardiac Dysfunction panel: SMC™ cTnl (high-sensitivity troponin), N-terminal pro-B-type natriuretic peptide
  - Vascular Inflammation and Dysfunction panel: SMC™ IL-6, SMC™ IL-17A, SMC™ TNFα, SMC™ Endothelin, Lp-PLA2, hs-CRP, homocysteine, vitamin B12, folate.
  - Dyslipidemia panel: total cholesterol, LDL-C (direct), apo B, small dense LDL, HDL cholesterol, apo AI, HDL2b, triglycerides, Lp(a).
  - Cardiometabolic panel: parathyroid, vitamin D, calcium, magnesium, leptin, adiponectin, ferritin, cortisol, cystatin C, hemoglobin A1c, glucose, insulin, thyroid-stimulating hormone (TSH), T3 and free T4, uric acid, liver panel, renal panel, thyroid peroxidase antibody, thyroglobulin antibody.

In addition to panels that are specifically focused on CV risk, a number of commercially available panels include markers associated with CV health, along with a range of other markers that have been associated with inflammation, thyroid disorders and other hormonal deficiencies, and other disorders. Examples of these panels include:

Singulex Cardiometabolic Panel: described above.

WellnessFX (San Francisco, CA) Premium6: total cholesterol, HDL, LDL, triglycerides, Apo AI, Apo B, LP(a), Lp-PLA2, omega-3 fatty acids, free fatty acids, lipid particle numbers, lipid particle sizes, blood urea nitrogen/creatinine, aspartate aminotransferase and alanine aminotransferase, total bilirubin, albumin, total protein, dehydroepiandrosterone, free testosterone, total testosterone, estradiol, sex hormone binding globulin, cortisol, insulin-like growth factor 1, insulin, glucose, hemoglobin A1c, total T4, T3 uptake, free T4 index, TSH, total T3, free T3, reverse T3, free T4, hs-CRP, fibrinogen, homocysteine, complete blood count with differential, calcium, electrolytes, bicarbonate, ferritin, total iron binding capacity, vitamin B12, red blood cell magnesium, 25-hydroxy vitamin D, progesterone, follicle-stimulating hormone, luteinizing hormone.

Summary

Cardiovascular risk panels refer to different combinations of cardiac markers that are intended to evaluate risk of cardiovascular (CV) disease. There are numerous commercially available risk panels that include different combinations of lipids, noncardiac biomarkers, measures of inflammation, metabolic parameters, and/or genetic markers. Risk panels report the results of multiple individual tests, as distinguished from
quantitative risk scores that combine the results of multiple markers into 1 score.

The evidence for the use of CV risk panels in individuals who have risk factors for CV disease includes multiple cohort and case-control studies and systematic reviews of these studies. Relevant outcomes are test accuracy and validity, other test performance measures, change in disease status, and morbid events. The available evidence from cohort and case-control studies indicates that many of the individual risk factors included in CV risk panels are associated with increased risk of CV disease. However, it is not clear how the results of individual risk factors impact management changes, so it is also uncertain how the panels will impact management decisions. Given the lack of evidence for clinical utility of any individual risk factor beyond simple lipid measures, it is unlikely that the use of CV risk panels improves outcome. Studies that have evaluated the clinical validity of panels of multiple markers have not assessed management changes that would occur as a result of testing, or demonstrated improvements in outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

Policy History

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Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:

- Medical Policy Terms of Use
- Managed Care Guidelines
- Indemnity/PPO Guidelines
- Clinical Exception Process
- Medical Technology Assessment Guidelines

References


