



## Evidence Based Guideline

# High-Sensitivity C-Reactive Protein in Cardiac Disease Risk Assessment

**File Name:** high\_sensitivity\_c\_reactive\_protein\_in\_cardiac\_disease\_risk\_assessment  
**Guideline Number:** EBG.MED1496  
**Origination:** 9/2009  
**Last CAP Review:** not applicable  
**Next CAP Review:** 9/2011  
**Last Review:** 9/2009

### Description of Procedure or Service

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C-reactive protein (CRP) is an acute phase reactant produced by the liver that has long been used to monitor inflammatory processes, such as infection and autoimmune diseases. Recent studies have suggested that low-level chronic inflammation may play a role in atherogenesis, and thus measurement of CRP has been investigated in various settings of cardiovascular disease, i.e., in patients with known cardiovascular disease, in patients with risk factors for cardiovascular disease, and as a general risk assessment tool for cardiovascular disease.

Conventional methodologies for measuring CRP in acute inflammatory diseases have a detection limit of 3-5 mg/L. However, in the setting of the low levels of chronic inflammation in otherwise healthy individuals, this level of detection is not adequate. To be used as a risk assessment tool, a greater precision at lower levels of CRP is needed such that the range of values collected in epidemiologic studies can be subdivided into quartiles and quintiles; in this way, the data from large epidemiologic studies can be applied to individual patients. Such new technologies, collectively known as high-sensitivity C-reactive protein (hs-CRP) include enzyme linked immunoabsorbent assays (ELISA) and various other techniques based on monoclonal antibodies. While the ELISA test is still primarily used as a research tool, various immunoassays have been automated and are commercially available. Several of the high-sensitivity C-reactive protein tests have received 510(k) marketing clearance from the U.S. Food and Drug Administration (FDA).

**\*\*\*Note: This Evidence Based Guideline is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

### Evidence Based Guideline for high-sensitivity C-reactive protein in cardiac disease risk assessment

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Measurement of high-sensitivity C-reactive protein may not be appropriate as a method of cardiac risk stratification.

### Medical Evidence regarding high-sensitivity C-reactive protein in cardiac disease risk assessment:

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A BCBSA TEC Special Report completed in 2002 concluded that a large body of well-done observational cohort studies demonstrates an association between C-reactive protein levels and risk of future coronary heart disease (CHD) events. There are, however, uncertainties as to the exact role C-reactive protein plays in

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the pathogenesis of CHD and the reliability of C-reactive protein assessment.

The 2002 TEC Special Report offered the following conclusions:

- While the existing observational evidence suggests that using CRP as a component of a risk assessment tool will result in a more accurate cardiac risk prediction, at this point in time, there appears to be no scientific literature that directly and experimentally tests the hypothesis that measurement of C-reactive protein to assess CHD risk results in improved patients outcomes. In addition, there appears to be no generally accepted risk assessment tool available using C-reactive protein that translates into risk estimates to which established treatment guidelines can be applied (e.g., Adult Treatment Panel III sponsored by the National Cholesterol Education Program).
- There is no general agreement on how management of the patient would be changed in patients with high C-reactive protein levels.

The American Heart Association/Centers for Disease Control and Prevention (AHA/CDC) Scientific Statement was published in January 2003. None of the recommendations received a Class I recommendation, and the AHA/CDC recognize that the benefits of using hs-CRP as a cardiac risk assessment tool are uncertain. This BCBSNC guideline is based on this acknowledged lack of direct evidence linking a risk assessment incorporating hs-CRP to changes in therapy and ultimately to improvement in health outcomes. The strongest recommendation by the CHD/AHA (i.e., IIa) suggests that the results of hs-CRP may help identify patients at intermediate risk who may benefit from primary prevention of CVD. It is estimated that some 30%–40% of the population may fall into this intermediate risk group. If the results of the hs-CRP measurement are considered high, patients may then be offered various interventions, frequently including the initiation of statin therapy. Therefore, the use of hs-CRP as one component of a risk assessment tool may ultimately result in considerably more patients being placed on life-long drug therapy.

Evaluation of any risk assessment tool for primary prevention is complicated by the fact that, in general, recommendations for primary prevention are in part based on cost-effective analyses. Risk assessment typically involves setting cut-off points to determine candidacy for an intervention, since the population of patients that could benefit from primary prevention is quite broad. These cutoff points for interventions are typically based in part on cost effectiveness. For example, lowering LDL-cholesterol through lifestyle changes or drug therapy appears to be an effective prevention strategy regardless of the particular risk factors a person has for CVD or their absolute risk of CHD. Nevertheless, the guidelines of the National Cholesterol Education Program (NCEP), which have been widely adopted to identify candidates for risk reduction, do not target the general population but focus on those with a higher baseline risk of CVD who will achieve a greater absolute reduction in risk with an intervention. These NCEP guidelines are in part based on concepts of cost effectiveness. Cost-effective analysis of using hs-CRP as part of the risk assessment tool may be particularly important given that some 30%–40% of the population may fall into an intermediate risk group, and a certain proportion of those may be considered for primary intervention when hs-CRP is used as part of the assessment tool.

The available published studies confirm or extend what is known about hs-CRP as a predictor of cardiovascular risk. This information alone is not sufficient to justify the use of hs-CRP in routine care without having adequate tools and guidelines to incorporate hs-CRP into routine clinical decision-making.

### Benefits Application

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Please refer to certificate for availability of benefit. This guideline relates only to the services or supplies described herein. Benefits may vary according to benefit design; therefore certificate language should be reviewed before applying the terms of the guideline.

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### Billing/Coding/Physician Documentation Information

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This guideline may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at [www.bcbsnc.com](http://www.bcbsnc.com). They are listed in the Category Search on the Medical Policy search page.

*Applicable codes: 86141*

*Determination of high-sensitivity C-reactive protein (hs-CRP) may be included as a component of a comprehensive cardiovascular risk assessment offered by reference laboratories. Comprehensive risk assessment may include evaluation of small low-density lipoproteins, subclassification of high-density lipoproteins, evaluation of apolipoprotein E genotype or phenotype, total plasma homocysteine, apolipoprotein B, and lipoprotein a.*

### Scientific Background and Reference Sources

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BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.22, 1/08/09

BCBSA 2002 TEC Assessments; Tab 23 (Special Report)

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* 2003; 107(3):499-511

National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). 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) final report. *Circulation* 2002; 106(25):3143-421. Available online at <http://circ.ahajournals.org/cgi/reprint/106/25/3143>.

Senior Medical Director review 9/2009

### Policy Implementation/Update Information

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10/26/09 New Evidence Based Guidelines issued. Measurement of high-sensitivity C-reactive protein may not be appropriate as a method of cardiac risk stratification. (adn)

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Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.