

Corporate Medical Policy

Use of Common Genetic Variants to Predict Risk of Nonfamilial Breast Cancer

File Name: common_genetic_variants_to_predict_risk_of_nonfamilial_breast_cancer
Origination: 3/2011
Last CAP Review: 8/2011
Next CAP Review: 8/2012
Last Review: 8/2011

Description of Procedure or Service

Several single-nucleotide polymorphisms (SNPs), which are single base-pair variations in the DNA sequence of the genome, have been found to be associated with breast cancer and are common in the population, but confer only small increases in risk. Some commercially available assays test for several SNPs and combine results to predict an individual's risk of breast cancer relative to the general population in order to identify those at increased risk who might benefit from more intensive surveillance.

Background

Rare, single gene variants conferring a high risk of breast cancer have been linked to hereditary breast cancer syndromes. Examples are mutations in BRCA1 and BRCA2. These, and a few others, account for less than 25% of inherited breast cancer. Moderate risk alleles, such as variants in the CHEK2 gene, are also relatively rare and apparently supplies very little information regarding the genetic risk.

In contrast, several common SNPs associated with breast cancer have been identified primarily through genome-wide association studies of very large case-control populations. The high-risk alleles occur with high frequency in the general population, although the increased breast cancer risk associated with each is very small relative to the general population risk. Some have suggested that these common risk SNPs could be combined to achieve an individualized risk prediction either alone or in combination with traditional predictors in order to personalize screening programs in which starting age and intensity would vary by risk. In particular, the American Cancer Society has recommended that women at high risk (greater than a 20% lifetime risk) should get breast magnetic resonance imaging (MRI) and a mammogram every year, while those at moderately increased risk (15% to 20% lifetime risk) should talk with their doctors about the benefits and limitations of adding MRI screening to their yearly mammogram.

At least 9 companies (see Table) currently offer Internet-based testing for breast cancer risk profiles using SNPs. Most of these companies offer testing direct-to-consumers (DTCs), although Navigenics (Forest City, CA) appears to now offer testing only through physicians. The company does provide interested consumers with access to a network of physicians who are reported to be familiar with the company's test profile and who utilize the test.

The algorithms or risk models used for all the tests identified, except for those offered by deCODE (Reykjavik, Iceland), are proprietary and not described on company websites. In the 3 tests providing some information on the SNPs used for testing, these range from panels as small as 6 SNPs (GenePlanet, Dublin, Ireland) to as large as 16 SNPs (deCODE).

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deCODE appears to offer two separate tests for breast cancer risk: one is the deCODE BreastCancer™ test and the other is part of the deCODEme Complete Scan for risk assessment of a broad assortment of diseases. Although in the past, these two tests appeared to use different SNP combinations for testing, both are now described as 16 SNP panels. It is likely that the tests are the same, with the second of the two simply part of a larger assessment panel. The deCODE BreastCancer™ test includes a list of SNPs used and an explanation for the simple multiplicative model applied to this list.

A comprehensive list of companies offering DTC genetic testing for various diseases including breast cancer is maintained by the Genetics and Public Policy Center, available online at: http://www.dnapolicy.org/news.release.php?action=detail&pressrelease_id=137. This site was most recently updated in May 2010.

Table. Tests for Breast Cancer Susceptibility Using SNP Based Risk Panels

Company	Location	Test Offered Direct to Consumer	Number of SNPs Used in Risk Panel
23andme	Mt. View, CA	Yes	7
deCODE	Reykjavik, Iceland	Yes	deCode BreastCancer – 16; deCODE Complete Scan – 16
easyDNA	Elk Grove, CA	Yes	ND
GenePlanet	Dublin, Ireland	Yes	6
MediChecks	Nottingham, UK	Yes	ND
Navigenics	Forest City, CA	No*	ND
Pathway Genomics	San Diego, CA	Yes	ND

ND – not described

*Consumers are referred to a network of providers for testing

Regulatory Status

No test combining the results of SNPs to predict breast cancer risk has been approved or cleared by the U.S. Food and Drug Administration (FDA). These are offered as laboratory-developed tests; that is, tests developed and used at a single testing site. Laboratory developed tests, as a matter of enforcement discretion, have not been traditionally regulated by FDA in the past. They do require oversight under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) and the development, and use of laboratory developed tests is restricted to laboratories certified as high complexity under CLIA.

The FDA appears to be in the process of considering a change in its regulatory posture toward this group of DTC genetic tests (available online at: <http://www.genomicslawreport.com/index.php/2010/07/21/14-more-fda-letters/>).

The FDA has met with many of the companies listed in the Table and has sent out letters indicating the belief that premarket submissions are warranted.

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On July 19-20, 2010, the FDA held an open public meeting to allow stakeholders to comment on this issue. The FDA has not announced its final decisions about regulatory policy in the area, and so future regulatory requirements remain unclear.

Under the current regulatory program, CLIA requires that laboratories demonstrate the analytical validity of the tests they offer. However, there is no requirement for a test to demonstrate either clinical validity or clinical utility. Some states (e.g., New York) have chosen to regulate DTC laboratories. Because these reviews are not public, it is not possible to determine what scientific standard is being applied to them.

Related Policies:

Genetic Testing for Hereditary Breast and/or Ovarian Cancer
Non-BRCA Breast Cancer Risk Assessment (OncoVue)

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

Policy

Testing for one or more single nucleotide polymorphisms (SNPs) to predict an individual's risk of breast cancer is considered investigational for all applications. BCBSNC does not provide coverage for investigational services or procedures.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Use Common Genetic Variants to Predict Risk of Nonfamilial Breast Cancer is covered

Not applicable.

When Use Common Genetic Variants to Predict Risk of Nonfamilial Breast Cancer is not covered

Use of common genetic variants by testing for one or more single nucleotide polymorphisms (SNPs) to predict an individual's risk of breast cancer is considered **investigational**.

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Policy Guidelines

Common, single nucleotide polymorphisms (SNPs) have been shown to be significantly associated with breast cancer and to individually convey slightly elevated risk of breast cancer compared to the general population risk. Panels of well-documented and validated SNPs are commercially available, with results synthesized into a breast cancer risk estimate. These tests can be physician-ordered only (e.g., deCODE BreastCancer™ test) or obtained direct to consumer (e.g., part of deCODEme's deCODEme Cancer Scan, 23andme's Health Edition test, or of Navigenic's comprehensive genetic testing panel). The application of such risk panels to individual patient management or to population screening programs is premature since the majority of the genetic risk of breast cancer has yet to be explained by undiscovered gene variants and SNPs. Thus, the discrimination offered by the limited genetic factors currently known is insufficient to inform clinical practice.

Billing/Coding/Physician Documentation Information

This policy 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. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: There is no specific code for this test.

Providers may use the following CPT codes for this service: 83894, 83898, 83900, 83909, and/or 83912.

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.63, 4/8/2010

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BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.63, 5/12/11

Specialty Matched Consultant Advisory Panel - 8/2011

Policy Implementation/Update Information

3/29/11 New policy implemented. Use of common genetic variants by testing for one or more single nucleotide polymorphisms (SNPs) to predict an individual's risk of breast cancer is considered investigational. Notice given 4/12/2011. Policy effective 7/19/2011.(btw)

9/30/11 Specialty Matched Consultant Advisory Panel review 8/31/2011. "Description" section revised. No change to policy statement. References added.(btw)

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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.