
Genetic Services Policy Project

Hereditary Breast and Ovarian Cancer: A Policy Brief

What are Hereditary Breast and Ovarian Cancers (HBOC)?

- HBOCs are cancers associated with autosomal dominant genetic mutations with reduced penetrance.
- Individuals with these mutations have a strong predisposition to breast and/or ovarian cancer, but the risk is not absolute.
- The two most widely known genes associated with HBOC are BRCA1 and BRCA2.

Who is affected by HBOC?

- Breast cancer affects nearly 180,000 women annually, and ovarian cancer is diagnosed in more than 20,000.
- Most breast and ovarian cancers are sporadic, but heredity may account for 5 to 10 percent of these cancers diagnosed each year in the United States.

What is known about the genetic contributions to HBOC?

- *BRCA* genes were first identified in the early 1990s through studies of families with multiple cases of breast and ovarian cancer.
- Myriad Genetics, a Utah-based biotechnology company, eventually sequenced and patented the genes.
- The genes have a role in DNA repair and tumor suppression, but their exact mechanism of action remains unclear even after a decade of intense study.
- More than 800 different mutations have been identified in each of the two genes.
- Prevalence of *BRCA* mutations in the general population is estimated to be 1 in 500 to 1 in 1,000. All racial and ethnic groups may be affected, but prevalence in some groups (e.g., Ashkenazi Jewish) is higher (2 percent) than others.
- In addition to high risk mutations, family history of breast and ovarian cancer may represent:
 - Other genetic causes of BOC
 - Shared environmental causes of BOC
- Other genes and environmental influences may modulate risk in individuals with a *BRCA* mutation.

What are the clinical features of HBOC?

- Women with mutations in the *BRCA1* and *BRCA2* genes have an estimated 45-65 percent lifetime risk of developing breast cancer and 11-39 percent lifetime risk of developing ovarian cancer. (Antoniou et al, 2003) Risk is higher in Ashkenazi Jewish women with *BRCA* mutations, up to 82 percent lifetime risk of breast cancer, and 23-54 percent risk of ovarian cancer. (King et al, 2003) Colon cancer risk is also increased.
- Cancer often occurs at an early age (<50 years) and may be bilateral.
- Men with altered *BRCA* genes (particularly *BRCA2*) may also develop breast cancer and are at

increased risk of prostate cancer and other cancers.

- Cancers related to *BRCA* mutations may be more aggressive than cancers not associated with *BRCA* mutations, although mortality is similar for tumors of comparable grade and stage. (Rennert, Bisland-Naggan, et al. 2007)
- Numerous factors including breast-feeding, earlier birth cohort, oral contraceptive use, and weight control are associated with decreased cancer risk in individuals with *BRCA* mutations. (Chen et al, 2006) (Jernström et al, 2004) (King et al, 2003)

What are the psychosocial impacts of HBOC?

- A cancer diagnosis is often associated with fear, uncertainty, and high levels of stress. Knowing one is at increased risk for developing cancer due to a genetic mutation or other risk factor can also be stressful. The term “pre-vivors” has been coined to acknowledge the unique issues facing these individuals.
- Genetic testing for *BRCA* mutations may bring up complex family issues and emotions. Concerns about insurance and employment discrimination may affect decisions about testing.

What is the role of genetic services in HBOC?

- Family and personal health history assessment
 - Families with HBOC are often identified by family history of cancer, on either the mother or father’s side of the family. Key elements of family history include:
 - Two first degree relatives with breast cancer, one with a diagnosis before age 50
 - Three or more first or second degree relatives, regardless of age of onset
 - Both breast and ovarian cancer among first and second degree relatives
 - First degree relative with bilateral breast cancer
 - Two or more first or second degree relatives with ovarian cancer
 - First or second degree relative with both breast and ovarian cancer
 - Male relative with breast cancer
 - In Ashkenazi Jewish families, any first degree relative (or two second degree relatives on the same side of the family) with breast or ovarian cancer (USPTF, 2005)
 - Having a limited number of female relatives may obscure a high-risk family history.
 - Personal histories of early onset cancer, bilateral breast cancer, or male breast cancer are red flags for possible HBOC.
 - A known *BRCA* mutation or other cancer syndrome in the family strongly suggests further evaluation.
- Risk assessment programs
 - Numerous risk models and computer based programs are available to assess an individual’s risk for having a *BRCA* mutation (e.g., *BRCAPRO*) or risk of breast cancer due to family or personal history (e.g., Gail model, Breast Cancer Risk Assessment Tool)
- Genetic counseling
 - Once an individual is identified as being at risk for HBOC or a high-risk mutation, genetic counseling by a qualified provider is recommended. Counseling involves assessment of personal risk for HBOC and discussion of HBOC, the risks and

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- benefits of genetic testing, and the clinical and psychosocial implications of positive, negative, or inconclusive test results.
- Genetic testing
 - In the US, *BRCA1* and *BRCA2* mutation testing is only available through Myriad and is marketed as *BRCAAnalysis*TM.
 - Testing options include full sequence analysis, single mutation analysis (for a known familial mutation), or multi-site analysis for common mutations found in the Ashkenazi Jewish population. Costs range from approximately \$300 to \$3,000 depending on type of testing done.
 - Testing an affected family member first increases the likelihood of finding a mutation; then subsequent family members can be tested for a single mutation.
 - Myriad requires that physicians or other licensed health care providers order *BRCA* tests to ensure that patients receive adequate information about the test and its implications.

What are preventive therapies for HBOC?

- For individuals identified with a *BRCA* mutation or high risk family history, there are several options including:
 - Intensive surveillance
 - Breast-clinical breast exam, mammography, and breast MRI
 - Ovarian-vaginal ultrasound, serum CA-125
 - Bilateral mastectomy (90 percent reduction in breast cancer risk)
 - Bilateral oophorectomy (96 percent reduction in ovarian cancer risk, 53 percent for breast cancer)
 - Tamoxifen: women with a *BRCA2* mutation may benefit from this treatment, but women with a *BRCA1* mutation may not (49 percent reduction in breast cancer risk)
 - Oral contraceptives: for ovarian prophylaxis (54 percent reduction in ovarian cancer risk)
- Cost-effectiveness studies comparing the above prevention strategies suggest that bilateral oophorectomy is the most cost effective strategy with the highest quality adjusted life years (QALYs) gained. (Anderson et al, 2006)
- Recent American Cancer Society guidelines recommend annual breast MRI screening as an adjunct to mammography in women with a 20 percent or higher risk of breast cancer, including women with *BRCA* mutations and/or strong family history. (Saslow et al. 2007)

Who provides care for individuals with HBOC or at risk for HBOC?

- Many different types of clinical providers may identify family history or other risk factors for HBOC, including primary care providers, genetic specialists, and cancer care specialists (oncologists, oncology nurses).
- Myriad maintains a list of “referral centers” in each state with providers who offer *BRCA* testing services. These referral centers include genetics, cancer, and breast health centers. One web-based “virtual” genetics clinic, DNA Direct, a California based company, is authorized to offer the test because they use genetic counselors and physicians in their testing process.

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- Myriad also provides patient and provider education materials, risk assessment tools, and assists patients in obtaining reimbursement from insurance companies. (Myriad, 2007)

What costs are associated with HBOC?

- There are no lifetime cost estimates specifically for HBOC.
- In a 2000 study, lifetime direct treatment costs for metastatic breast cancer were approximately \$60,000 for a cohort of women diagnosed with breast cancer in 1994. (Berkowitz, Gupta, et al, 2000) Newer treatments such as trastuzumab (Herceptin™), which cost upwards of \$60,000 per course, may add significantly to the cost of an individual's care.
- Estimates for cost of ovarian cancer treatment range from \$39,947 to \$50,562. (Bristow, 2007)
- According to one author, cost effective policies on genetic testing and preventive treatment may save up to \$800 million of the \$8 billion or more spent each year on breast cancer diagnosis, prevention, and treatment. (Anderson et al, 2006)

Who are the major stakeholders?

- Consumers/advocacy groups
- Professional organizations/health care providers
 - Primary care providers
 - Oncologists/oncology nurses
 - Genetic counselors/cancer genetic specialists
- Academic/research institutions
- Biotechnology industry
 - E.g., Myriad Genetics
- Public and private payers
- Retail genetics
 - E.g., DNA Direct
- Government

What genetic service delivery or policy issues does this case highlight?

- Clinical service delivery issues
 - Cancer genetic services are increasingly being integrated into clinical care, particularly in the oncology setting. More oncologists and oncology nurses are taking on genetic counseling functions. In addition, retail genetic services for HBOC are now available through the Internet. Extent, content, and overall quality of cancer genetic services in different settings (oncology vs. genetics clinic vs. retail genetics) has not been evaluated.
 - Recommendations, standards, and guidelines for genetic and other health services related to HBOC have been developed by numerous professional organizations. However, there is no organized system to measure or monitor performance related to these guidelines.
 - Despite increased availability of services, many people with genetic risk for cancer are not being identified and are not receiving services. This may be related to:
 - Limited public awareness of genetic risk factors and recommendations
 - Limited health care provider competency and confidence in providing

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- genetic risk assessment, counseling, and referral
 - Health care system barriers (e.g., traditional problem-focused office visits, inadequate time, lack of electronic health tools, lack of incentives to do risk assessment, and lack of consequences for not doing risk assessment)
 - Limited availability of counseling/testing services in certain geographic areas, or public and providers who are unaware of referral resources in their area
- Of note, physicians are much more likely to pursue genetic services for cancer susceptibility if a patient requests them, highlighting the potential benefit of increasing consumer awareness about genetic risk factors. (Freedman et al., 2003)
- Some groups (e.g., African Americans) have significantly lower rates of genetic service use, despite similar risks of having *BRCA* mutations. Additional efforts are needed to identify reasons for this disparity and to develop culturally appropriate genetic services and outreach.
- Financial factors limit access to genetic services for HBOC. This reflects the high cost of genetic testing, lack of universal health insurance access, and variations in individual health plan coverage and reimbursement policies.
- Innovative delivery models (e.g., computer-based counseling, group counseling) and educational programs (e.g., City of Hope intensive cancer genetics training for health professionals) may improve access and availability of services.
- Public and private payer issues
 - Many health plans are now covering genetic testing in select high-risk individuals but may not cover non-enrolled family members, may require co-pays, or may have other limitations. Medicare limits coverage to individuals with breast/ovarian cancer or a known *BRCA* mutation in their family. Medicaid may or may not cover testing.
 - Comprehensive information on current health plan coverage and reimbursement policies for prophylactic interventions is not available, but limitations on coverage may restrict patient options.
- Industry issues
 - Policymakers often point to Myriad and *BRCA* testing as an example of the adverse impact of gene patents on consumer access to health services. Industry representatives argue that the high price of tests is justified by research and development costs and the provision of educational and informational resources for consumers and providers.
 - Myriad's direct-to-consumer marketing of *BRCA* tests has raised concerns about increasing demand for services in inappropriate low-risk candidates and inadequate preparation of the medical community.
- Consumer/advocacy issues
 - Breast cancer is a high profile disease and advocacy is particularly strong. Facing Our Risk of Cancer Empowered (FORCE) is a support group created to address the unique issues of "pre-vivors."
 - Another group, the National Breast Cancer Coalition, has raised the concern that too much attention is paid to genetics and not enough to understanding environmental factors in the etiology of breast cancer. The group also states that genetic tests should only be used in well-designed clinical trials and research studies. (NBCC, 2006)

- Legal/regulatory issues
 - Individuals at risk for HBOC and providers counseling these individuals often cite concerns about potential genetic discrimination associated with positive genetic test results, despite limited evidence of actual discrimination. Federal protections against discrimination, as proposed in several recent bills, may decrease concerns in this area.
 - Other areas for potentially enhanced regulation include genetic testing, gene patenting, retail genetics, and direct-to-consumer marketing.
- Research issues
 - Ongoing research is needed to evaluate clinical and economic outcomes in order to enhance the evidence base for genetic services in HBOC.
 - The role of other genes and/or the environment in breast and ovarian cancer risk is also a high priority area for research.

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