

# Review: Only women with specific family histories should be referred for counseling or evaluation for *BRCA* breast and ovarian cancer susceptibility

Nelson HD, Huffman LH, Fu R, Harris EL. Genetic risk assessment and *BRCA* mutation testing for breast and ovarian cancer susceptibility: systematic evidence review for the U.S. Preventive Services Task Force. *Ann Intern Med.* 2005;143:362-79.

U.S. Preventive Services Task Force. Genetic risk assessment and *BRCA* mutation testing for breast and ovarian cancer susceptibility: recommendation statement. *Ann Intern Med.* 2005;143:355-61.

**Clinical impact ratings:** GIM/FP/GP ★★★★★☆☆☆ Oncology ★★★★★★☆☆

## QUESTION

What are the benefits and harms of genetic risk assessment and *BRCA* mutation testing for breast and ovarian cancer susceptibility in the general population of women without cancer?

## METHODS

**Data sources:** MEDLINE (1966 to October 2004); the Cochrane Library; reference lists of relevant studies, reviews, editorials, and Web sites; and experts in the field.

**Study selection and assessment:** Diagnostic accuracy studies, randomized controlled trials (RCTs), cohort studies, and case-control studies that pertained to genetic risk assessment, genetic counseling, predicting cancer risk, preventive interventions, and adverse effects of interventions in women in primary care. Studies of patients with current or past breast or ovarian cancer were excluded unless they addressed genetic testing issues in women without cancer. Study quality was assessed using criteria developed by the U.S. Preventive Services Task Force (USPTF): The strength of evidence was graded on a 3-point scale (good, fair, or poor) and recommendations reflected the strength of evidence and magnitude of net benefit (A [strongly recommend based on good evidence], B [recommend based on at least fair evidence], C [no

recommendation for or against based on at least fair evidence], D [recommend against based on at least fair evidence], and I [insufficient evidence to recommend for or against]).

**Outcomes:** Incidence of breast or ovarian cancer, and cause-specific and all-cause mortality.

## MAIN RESULTS

A primary care approach to screening for inherited breast and ovarian cancer susceptibility has not been evaluated, and evidence is lacking to determine benefits and harms for the general population. Fair evidence exists that women with specific increased-risk family histories are more likely to have *BRCA1* or *BRCA2* mutations associated with breast and ovarian cancer. About 2% of women in the general population have such a family history. Fair to good evidence suggests that such women benefit from genetic counseling, showing decreases in breast cancer worry, anxiety, and depression. Fair evidence supports the effectiveness of prophylactic surgery in women with *BRCA* mutations (mastectomy and oophorectomy). Trials of breast cancer chemoprevention with tamoxifen include too few women with *BRCA* mutations to draw conclusions about this subgroup. Magnetic resonance imaging increases sensitivity but decreases specificity when added to conventional breast cancer screening methods in

women with *BRCA* mutations. Insufficient evidence exists to recommend intensive screening for ovarian cancer in women with *BRCA* mutations. Fair evidence exists that women without specific increased-risk family histories and without Ashkenazi Jewish heritage are unlikely to have *BRCA* mutations. Fair evidence exists of important adverse ethical, legal, and social consequences resulting from routine referral and testing in such women. Such interventions as prophylactic surgery, chemoprevention, or intensive screening have known harms estimated to be small or greater in such women.

## CONCLUSIONS

Women with specific increased-risk family histories should be routinely referred for genetic counseling and evaluations for testing for mutations in the *BRCA* breast and ovarian cancer susceptibility genes. Women without specific increased-risk family histories should not be routinely referred.

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## COMMENTARY

The recently published USPTF recommendations, although accompanied by an excellent review of the relevant *BRCA* literature, fail to offer clear and concise guidelines for the use of genetic counseling and testing for primary prevention of breast and ovarian cancer. The target group for these recommendations is “women who have not received a diagnosis of breast or ovarian cancer,” but this is not apparent in the summary statements.

Deciding whether to refer a woman without a personal history of cancer for genetic counseling and testing is complex. A negative family history may be falsely reassuring in families that are small, have few women, do not share medical information, are estranged, or are from populations with increased rates of oophorectomy (e.g., African Americans). Persons from disadvantaged populations may be reluctant to use recommended genetic services, requiring extra efforts from health care providers to lessen these disparities.

*BRCA* mutations are worth finding in affected individuals. Their management is contentious, but encouraging data exist about the effectiveness of risk-reducing surgery and intensive screening. However, *BRCA* mutations are present in only a tiny minority of women without a specific increased-risk family history.

More important, therefore, is the question of whether internists and primary care providers should be restricting referral to genetic services or trying harder to identify high-risk patients. Counseling persons about risk for cancer should be beneficial, even if risk is low. The aim of counseling is to inform decisions about testing, not to ration it. The possibility of an uninformative result must be discussed before testing.

These guidelines are appropriate if the goal is to discourage unnecessary referral for genetic testing in women without a specific increased-risk family history. However, these women might benefit from being counseled that their risk is average and that testing is unnecessary. Few primary care physicians or internists are prepared to give this counseling. If the goal of these guidelines is to help busy physicians decide which women to refer to a genetic counselor, then the minimal risks associated with counseling compared with its long-term benefits for individual and family-based cancer prevention and control make these limiting recommendations troubling.

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