U.S. Preventive Services Task Force

Risk Assessment, Genetic Counseling, and Genetic Testing for *BRCA*-Related Cancer: Recommendation Statement

Summary of Recommendation and Evidence

The USPSTF recommends that primary care clinicians assess women with a personal or family history of breast, ovarian, tubal, or peritoneal cancer or who have an ancestry associated with breast cancer susceptibility 1 and 2 (*BRCA1/2*) gene mutations with an appropriate brief familial risk assessment tool. Women with a positive result on the risk assessment tool should receive genetic counseling and, if indicated after counseling, genetic testing *(Table 1)*. **B recommendation.**

The USPSTF recommends against routine risk assessment, genetic counseling, or genetic testing for women whose personal or family history or ancestry is not associated with potentially harmful *BRCA1/2* gene mutations. **D recommendation.**

Rationale

IMPORTANCE

Potentially harmful mutations of the *BRCA1/2* genes are associated with increased risk for breast, ovarian, fallopian tube, and peritoneal cancer.[1-6] For women in the United States, breast cancer is the most common cancer after nonmelanoma skin cancer and the second leading cause of cancer death.[7] In the general population, *BRCA1/2* mutations occur in an estimated 1 in 300 to 500 women and account for 5% to 10% of breast cancer cases and 15% of ovarian cancer cases.[8-11] A woman's risk for breast cancer increases if she has clinically significant mutations in the *BRCA1/2* genes.[12,13] Mutations in the *BRCA1/2* genes increase breast cancer risk by 45% to 65% by age 70 years. Risk of ovarian, fallopian tube, or peritoneal cancer increases to 39% for *BRCA1* mutations and 10% to 17% for *BRCA2* mutations.[12,13]

DETECTION

Genetic risk assessment and *BRCA1/2* mutation testing is a multistep process that begins with identifying patients with family or personal histories of breast, ovarian, tubal, or peritoneal cancer; family members with known harmful *BRCA1/2* mutations; or ancestry associated with harmful *BRCA1/2* mutations. Risk for clinically significant *BRCA1/2* mutations can be further evaluated with genetic counseling by suitably trained health care clinicians, followed by genetic testing of selected high-risk individuals and posttest counseling about results. The USPSTF found adequate evidence that familial risk assessment tools are accurate in identifying women with increased likelihood of *BRCA1/2* mutations. These tools can be used by primary care clinicians to guide referrals to genetic counseling.

The USPSTF has previously established that there is adequate evidence that current genetic tests can accurately detect known *BRCA1/2* mutations.[14]

BENEFITS OF SCREENING, GENETIC COUNSELING, AND GENETIC TESTING

The USPSTF found adequate evidence that the benefits of risk assessment, genetic counseling, and genetic testing are moderate in women whose family history is associated with an increased risk for harmful mutations in the *BRCA1/2* genes.

The USPSTF found adequate evidence that the benefits of risk assessment, genetic counseling, and genetic testing are small to none in women whose family history is not associated with an increased risk for harmful mutations in the *BRCA1/2* genes.

See related Putting Prevention into Practice on page 239.

As published by the USPSTF.

This summary is one in a series excerpted from the Recommendation Statements released by the USPSTF. These statements address preventive health services for use in primary care clinical settings, including screening tests, counseling, and preventive medications.

The complete version of this statement, including supporting scientific evidence, evidence tables, grading system, members of the USPSTF at the time this recommendation was finalized, and references, is available on the USPSTF website at https://www.uspreventiveservicestaskforce.org/.

This series is coordinated by Kenny Lin, MD, MPH, deputy editor.

A collection of USPSTF recommendation statements published in *AFP* is available at https://www.aafp.org/afp/uspstf.

TABLE 1

Risk Assessment, Genetic Counseling, and Genetic Testing for *BRCA*-Related Cancer: Clinical Summary of the USPSTF Recommendation

Population	Women with a personal or family history of breast, ovarian, tubal, or peritoneal cancer or who have an ancestry associated with *BRCA1/2* gene mutations	Women whose personal or family history or ancestry is not associated with potentially harmful *BRCA1/2* gene mutations
Recommendation	Assess with an appropriate brief familial risk assessment tool. Grade: B	Do not perform routine risk assessment, genetic counseling, or genetic testing. Grade: D
Risk assessment	Patients with family or personal histories of breast, ovarian, tubal, or peritoneal cancer or ancestry associated with harmful *BRCA1/2* mutations should be assessed using a familial risk assessment tool. The USPSTF found adequate evidence that these tools are accurate in identifying women with increased likelihood of *BRCA1/2* mutations. Tools evaluated by the USPSTF include the Ontario Family History Assessment Tool, Manchester Scoring System, Referral Screening Tool, Pedigree Assessment Tool, 7-Question Family History Screening Tool, International Breast Cancer Intervention Study instrument (Tyrer-Cuzick), and brief versions of BRCAPRO. These tools should be used to guide referrals to genetic counseling.	
Genetic counseling	Genetic counseling about *BRCA1/2* mutation testing should be done by trained health professionals, including suitably trained primary care providers. The process of genetic counseling includes detailed kindred analysis and risk assessment for potentially harmful *BRCA1/2* mutations. It also includes identification of candidates for testing, patient education, discussion of the benefits and harms of genetic testing, interpretation of results after testing, and discussion of management options.	
Genetic testing	Tests for *BRCA1/2* mutations are highly sensitive and specific for known mutations. Testing for *BRCA1/2* mutations should be done when an individual has personal or family history that suggests an inherited cancer susceptibility, when an individual is willing to see a health professional who is suitably trained to provide genetic counseling and interpret test results, and when test results will aid in decision making.	
Treatment and interventions	In general, women with harmful *BRCA1/2* mutations are managed with a variety of interventions to lower future cancer risk. This includes intensive screening, risk-reducing medications, and risk-reducing mastectomy and salpingo-oophorectomy.	
Other relevant USPSTF recommendations	The USPSTF recommends that clinicians offer to prescribe risk-reducing medications such as tamoxifen, raloxifene, or aromatase inhibitors to women at increased risk for breast cancer and at low risk for adverse medication effects. It recommends against the routine use of medications for risk reduction of primary breast cancer in women not at increased risk for breast cancer. The USPSTF recommends against screening for ovarian cancer in women. This recommendation does not apply to women with known genetic mutations that increase their risk for ovarian cancer (e.g., *BRCA1/2* mutations). The USPSTF found insufficient evidence to assess the balance of benefits and harms of performing screening pelvic examinations in asymptomatic women for the early detection and treatment of a range of gynecologic conditions.	

Note: For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, go to https://www.uspreventiveservicestaskforce.org/.

USPSTF = U.S. Preventive Services Task Force.

HARMS OF SCREENING, GENETIC COUNSELING, AND GENETIC TESTING

The USPSTF found adequate evidence that the harms associated with risk assessment, genetic counseling, genetic testing, and interventions are small to moderate.

USPSTF ASSESSMENT

The USPSTF concludes with moderate certainty that the net benefit of risk assessment for increased risk of *BRCA1/2* mutations, testing for *BRCA1/2* mutations, and use of risk-reducing interventions outweighs the harms in women whose family or personal history is associated with an increased risk for potentially harmful mutations in the *BRCA1/2* genes.

The USPSTF concludes with moderate certainty that the harms of risk assessment for increased risk of *BRCA1/2* mutations, testing for *BRCA1/2* mutations, and use of risk-reducing interventions outweigh the benefits in women whose family

or personal history is not associated with an increased risk for potentially harmful mutations in the *BRCA1/2* genes.

Clinical Considerations

PATIENT POPULATION UNDER CONSIDERATION

This recommendation applies to women who are asymptomatic for *BRCA*-related cancer and have unknown *BRCA* mutation status. It includes women who have never been diagnosed with *BRCA*-related cancer, as well as those with a previous breast, ovarian, tubal, or peritoneal cancer diagnosis who have completed treatment and are considered cancer free but have not been previously tested. While this recommendation applies to women, the net benefit estimates are driven by biological sex (i.e., male/female) rather than gender identity. Persons should consider their sex at birth to determine which recommendation best applies to them.

ASSESSMENT OF RISK

Mutations in the *BRCA1/2* genes cluster in families, showing an autosomal dominant pattern of inheritance in either the mother's or father's family. When taking medical and family history information from patients, primary care clinicians should ask about specific types of cancer, primary cancer sites, which family members were affected, and whether relatives had multiple types of primary cancer. Clinicians should also inquire about the age at diagnosis, age at death, and sex of affected family members, both immediate (i.e., parents and siblings) as well as more distant (i.e., aunts, uncles, grandparents, and cousins).

For women who have family members with breast, ovarian, tubal, or peritoneal cancer or have a personal history of these types of cancer, primary care clinicians may use appropriate brief familial risk assessment tools to determine the need for in-depth genetic counseling. Tools evaluated by the USPSTF include the Ontario Family History Assessment Tool (*Table 2*[15-18]), Manchester Scoring System (*Table 3*[16,18-21]), Referral Screening Tool (*Table 4*[22]), Pedigree Assessment Tool (*Table 5*[23,24]), 7-Question Family History Screening Tool (*Table 6*[25,26]), International Breast Cancer Intervention Study instrument (Tyrer-Cuzick) (*Table 7*[26,27]), and brief versions of BRCAPRO. Each of these tools has been validated and accurately estimates the likelihood of carrying a harmful *BRCA1/2* mutation. They can be used to guide referrals to genetic counseling for more definitive risk assessment.[28] General breast cancer risk assessment models (e.g., the National Cancer Institute Breast Cancer Risk Assessment Tool, which is based on the Gail model) are not designed to identify *BRCA*-related cancer risk and should not be used for this purpose.

In general, these brief familial risk assessment tools include factors associated with increased likelihood of potentially harmful *BRCA1/2* mutations. These include breast cancer diagnosis before age 50 years, bilateral breast cancer, presence of both breast and ovarian cancer in one individual, male family members with breast cancer, multiple cases of breast cancer in the family, 1 or more family members with 2 primary types of *BRCA*-related cancer (such as ovarian cancer), and Ashkenazi Jewish ancestry. The USPSTF recognizes that each risk assessment tool has advantages and limitations and found insufficient evidence to recommend one over another.

TABLE 2

Ontario Family History Assessment Tool*

Risk factor	Points
Breast and ovarian cancer	
Mother	10
Sibling	7
Second-/third-degree relative	5
Breast cancer relatives	
Parent	4
Sibling	3
Second-/third-degree relative	2
Male relative (add to above)	2
Breast cancer characteristics	
Onset age, y	
20-29	6
30-39	4
40-49	2
Premenopausal/perimenopausal	2
Bilateral/multifocal	3
Ovarian cancer relatives	
Mother	7
Sibling	4
Second-/third-degree relative	3
Ovarian cancer onset, y	
< 40	6
40-60	4
> 60	2
Prostate cancer onset	
Age < 50 y	1
Colon cancer onset	
Age < 50 y	1
Family total:	____
Referral†	≥10

*—See Gilpin, et al.[15]; Oros, et al.[16]; Panchal, et al.[17]; and Parmigiani, et al.[18]

†—Referral with score of 10 or greater corresponds to doubling of lifetime risk for breast cancer (22%).

TABLE 3

Manchester Scoring System*†

Risk factor (age at onset for relative in direct lineage)	*BRCA1* score	*BRCA2* score
Female breast cancer, y		
<30	6	5
30-39	4	4
40-49	3	3
50-59	2	2
≥60	1	1
Male breast cancer, y		
<60	5‡	8§
≥60	5‡	5§
Ovarian cancer, y		
<60	8	5
≥60	5	5
Pancreatic cancer		
Any age	0	1
Prostate cancer, y		
<60	0	2
≥60	0	1
Total individual genes	10	10
Total for combined = 15		

*—See Oros, et al.[16]; Parmigiani, et al.[18]; Antoniou, et al.[19]; Barcenas, et al.[20]; and Evans, et al.[21]
†—A score of 10 in either column or a combined score of 15 for both columns would be equivalent to a 10% chance of identifying a *BRCA1* or *BRCA2* mutation.
‡—If testing for *BRCA2*.
§—If testing for *BRCA1*.

TABLE 4

Referral Screening Tool*†

History of breast or ovarian cancer in the family? If yes, complete checklist.

Risk factor	Breast cancer at age ≤50 y	Ovarian cancer at any age
Yourself	☐	☐
Mother	☐	☐
Sister	☐	☐
Daughter	☐	☐
Mother's side		
Grandmother	☐	☐
Aunt	☐	☐
Father's side		
Grandmother	☐	☐
Aunt	☐	☐
≥2 cases of breast cancer after age 50 y on same side of family	☐	☐
Male breast cancer at any age in any relative	☐	☐
Jewish ancestry	☐	☐

*—See Bellcross, et al.[22]
†—Referral if 2 or more checks in table.

TABLE 5

Pedigree Assessment Tool*†

Risk factor	Score for every family member with breast or ovarian cancer diagnosis, including second-/third-degree relatives
Breast cancer at age ≥50 y	3
Breast cancer at age <50 y	4
Ovarian cancer at any age	5
Male breast cancer at any age	8
Ashkenazi Jewish heritage	4
Total:	_____

*—See Hoskins, et al.,[23] and Teller, et al.[24]
†—Score of 8 or greater is the optimal referral threshold.

GENETIC COUNSELING

The process of genetic counseling includes detailed kindred analysis and risk assessment for potentially harmful *BRCA1/2* mutations. It also includes identification of candidates for testing, patient education, discussion of the benefits and harms of genetic testing, interpretation of results after testing, and discussion of management options. Genetic counseling about *BRCA1/2* mutation testing should be performed by trained health professionals, including suitably trained primary care clinicians. Several professional organizations describe the skills and training necessary to provide comprehensive genetic counseling.

GENETIC TESTING

Testing for *BRCA1/2* mutations should be performed only when an individual has personal or family history that suggests an inherited cancer susceptibility, when an individual is willing to talk with a health professional who is suitably trained to provide genetic counseling and interpret test results, and when test results will aid in decision-making. Clinical practice guidelines recommend that *BRCA1/2* mutation testing begin with a relative with known *BRCA*-related cancer, including male relatives, to determine if a clinically significant mutation is detected

TABLE 6

7-Question Family History Screening Tool*†

No.	Questions
1	Did any of your first-degree relatives have breast or ovarian cancer?
2	Did any of your relatives have bilateral breast cancer?
3	Did any man in your family have breast cancer?
4	Did any woman in your family have breast *and* ovarian cancer?
5	Did any woman in your family have breast cancer before age 50 y?
6	Do you have 2 or more relatives with breast *and/or* ovarian cancer?
7	Do you have 2 or more relatives with breast *and/or* bowel cancer?

*—See Ashton-Prolla, et al.,[25] and Fischer, et al.[26]
†—One positive response initiates referral.

TABLE 7

International Breast Cancer Intervention Study Instrument*†

No.	Risk factor
1	Personal history: current age, age at menopause, age at menarche, childbirth history, menopausal status, use of menopausal hormone therapy
2	Personal breast history, breast density (optional), prior breast biopsy, history of cancer (breast or ovarian), genetic testing
3	Ashkenazi Jewish inheritance
4	Family history (genetic risk)—relatives with breast or ovarian cancer, age at diagnosis, genetic testing

*—See Fischer, et al.,[26] and Cuzick.[27]
†—Referral for genetic testing if the personal risk level for a mutation in breast cancer susceptibility gene 1 or 2 is 10% or greater.

in the family before testing individuals without cancer.[29] If an affected family member with a *BRCA*-related cancer is not available, then the relative with the highest probability of mutation should be tested. The type of mutation analysis required depends on family history. Individuals from families with known mutations or from ancestry groups in which certain mutations are more common (e.g., Ashkenazi Jewish founder mutations) can be tested for these specific mutations. Because risk assessment is primarily based on family history, it is unclear how women with a limited or unknown family history should be assessed for *BRCA1/2* mutation risk and potential referral to counseling or genetic testing.

Tests for *BRCA1/2* mutations are highly sensitive and specific for known mutations. The availability of testing options has changed since the 2013 U.S. Supreme Court ruling that determined human genes are not patentable (*Association for Molecular Pathology v Myriad Genetics, Inc.*).[30] Previously, *BRCA1/2* mutation testing in the United States was mainly conducted by 1 laboratory. Since the ruling, the number of testing options has significantly increased, with more than 80 multigene panels that include *BRCA1/2*, as well as tests marketed directly to consumers.[31]

Guidelines from the American College of Medical Genetics and Genomics, which were updated in 2015, recommend new standard terminology for reporting *BRCA1/2* mutations identified by genetic tests. These include a 5-tier terminology system using the terms "pathogenic," "likely pathogenic," "uncertain significance," "likely benign," and "benign."[32]

TREATMENT AND INTERVENTIONS

Management of increased cancer risk related to *BRCA1/2* mutations is beyond the scope of this Recommendation Statement. In general, care for women with harmful *BRCA1/2* mutations consists of a variety of interventions to lower future cancer risk. This includes intensive screening, risk-reducing medications, and risk-reducing mastectomy and salpingo-oophorectomy.

ADDITIONAL TOOLS AND RESOURCES

The National Cancer Institute Cancer Genetics Services Directory provides a list of professionals who offer services related to cancer genetics, including cancer risk assessment, genetic counseling, and genetic testing.[33]

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The "Other Related USPSTF Recommendation," Other Considerations," "Discussion," "Update of Previous USPSTF Recommendation," and "Recommendations of Others" sections of this recommendation statement are available at https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/brca-related-cancer-risk-assessment-genetic-counseling-and-genetic-testing1.

The USPSTF recommendations are independent of the U.S. government. They do not represent the views of the Agency for Healthcare Research and Quality, the U.S. Department of Health and Human Services, or the U.S. Public Health Service.

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