Complete Summary

GUIDELINE TITLE

Genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility: recommendation statement.

BIBLIOGRAPHIC SOURCE(S)

Genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility: recommendation statement. Ann Intern Med 2005 Sep 6;143(5):355-61. PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
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INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
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SCOPE

DISEASE/CONDITION(S)

Breast and ovarian cancer susceptibility

GUIDELINE CATEGORY

Prevention
Risk Assessment
Screening

CLINICAL SPECIALTY

Family Practice
Internal Medicine

Medical Genetics
Obstetrics and Gynecology
Oncology
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Health Care Providers
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To summarize the U.S. Preventive Services Task Force (USPSTF) recommendations on genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility and the supporting scientific evidence

TARGET POPULATION

Women seen in primary care settings who have not been diagnosed with either breast or ovarian cancer

The recommendations do not apply to:

- Women with a family history of breast or ovarian cancer that includes a relative with a known deleterious mutation in BRCA1 or BRCA2 genes; these women should be referred for genetic counseling.
- Men

INTERVENTIONS AND PRACTICES CONSIDERED

1. Routine screening for BRCA1 or 2 mutations (not recommended)
2. Risk assessment based on family and personal history
3. Referral for genetic counseling
4. Testing for BRCA1 or 2 mutations
5. Prophylactic treatment options (discussed but not specifically recommended):
    - Prophylactic mastectomy or oophorectomy
    - Chemoprevention with selective estrogen receptor modulators (SERMs)
    - Intensive screening with mammography
    - Magnetic resonance imaging (MRI)

MAJOR OUTCOMES CONSIDERED

- Key Question 1: Does risk assessment and BRCA mutation testing lead to a reduction in the incidence of breast and ovarian cancer and cause-specific or all-cause mortality?

- Key Question 2A: How well does risk assessment for cancer susceptibility by a clinician in a primary care setting select candidates for BRCA mutation testing?
- Key Question 2B: What are the benefits of genetic counseling before testing?
- Key Question 2C: Among women with family histories predicting an average, moderate, or high risk for a deleterious mutation, how well does BRCA mutation testing predict risk for breast and ovarian cancer?
- Key Question 3: What are the adverse effects of risk assessment, genetic counseling, and testing?
- Key Question 4: How well do interventions reduce the incidence and mortality of breast and ovarian cancer in women identified as high risk by history, positive genetic test results, or both?
- Key Question 5: What are the adverse effects of interventions?

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): A systematic review of the literature was prepared by the Oregon Evidence-based Practice Center (EPC) and Oregon Health & Science University for the Agency for Healthcare Research and Quality (AHRQ) for use by the U.S. Preventive Services Task Force (USPSTF) (see the "Companion Documents" field).

Literature Search Strategy

Relevant papers were identified from multiple searches of MEDLINE (1966 to 1 October 2004) and the Cochrane Library databases. Additional papers were obtained by reviewing reference lists of pertinent studies, reviews, editorials, and Web sites and by consulting experts (see Appendix Figure, available at www.annals.org).

Inclusion and Exclusion Criteria

Investigators reviewed all abstracts and determined eligibility by applying inclusion and exclusion criteria specific to key questions (See Appendix Table, available at www.annals.org). They then reviewed full-text papers of included abstracts for relevance. Studies about patients with current or past breast or ovarian cancer were excluded unless they addressed genetic testing issues in women without cancer.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The U.S. Preventive Services Task Force grades the quality of the overall evidence for a service on a 3-point scale (good, fair, poor):

Good

Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes.

Fair

Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies, generalizability to routine practice, or indirect nature of the evidence on health outcomes.

Poor

Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis
Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): A systematic review of the literature was prepared by the Oregon Evidence-based Practice Center (EPC) and Oregon Health & Science University for the Agency for Healthcare Research and Quality (AHRQ) for use by the U.S. Preventive Services Task Force (USPSTF) (see the "Companion Documents" field).

Data were extracted from each included study, entered into evidence tables, and summarized by using descriptive or statistical methods, or both. Two reviewers independently rated the quality of studies using criteria specific to different study designs developed by the U.S. Preventive Services Task Force (USPSTF) (see Appendix 1, available at www.annals.org). When reviewers disagreed, a final rating was determined by reevaluations by the two initial reviewers and a third reviewer if needed. Only studies rated good or fair in quality were included,

although studies with designs that do not have quality rating criteria, such as descriptive studies, were also included if relevant to the key questions.

To estimate risks for breast and ovarian cancer due to clinically significant BRCA mutations, the screening population was stratified into groups at average, moderate, and high risk for being a mutation carrier based on history of breast or ovarian cancer in first- and second-degree relatives. This approach allows use of published data that describe risks in similar terms. The following definitions were used: average risk--no first-degree relatives and no more than 1 second-degree relative on each side of the family with breast or ovarian cancer; moderate risk--1 first-degree relative or 2 second-degree relatives on the same side of the family with breast or ovarian cancer; high risk--at least 2 first-degree relatives with breast or ovarian cancer. On the basis of pooled data from more than 100,000 women without breast cancer from 52 epidemiologic studies, approximately 92.7% of the screening population would be expected to be average risk, 6.9% moderate risk, and 0.4% high risk according to these definitions.

Risks for developing breast and ovarian cancer in mutation carriers have been primarily calculated from families of women with existing breast and ovarian cancer. To determine benefits and adverse effects of genetic testing in average-, moderate-, and high-risk groups, EPC staff estimated mutation prevalence as well as the probability of developing cancer given the presence of the mutation (penetrance) for each risk group. Penetrance was calculated from data about the prevalence of BRCA mutations in women with and without breast and ovarian cancer, the probability of breast or ovarian cancer in the U.S. population estimated from Surveillance, Epidemiology, and End Result (SEER) data by using DevCan software, and relative risks for breast and ovarian cancer in moderate- and high-risk groups. Penetrance estimates were based on Bayes theorem and stratified by cancer type (breast or ovarian), risk group (average, moderate, and high), and age whenever data were available. Appendix 2 (available at www.annals.org) provides additional details of this method.

A meta-analysis of chemoprevention trials was performed to more precisely estimate effectiveness and adverse effects. All chemoprevention trials reported relative risk (RR) estimates, and the logarithm of the RR (logRR) and the corresponding standard errors were calculated for each trial and used in the meta-analysis. The overall estimates of RR were obtained by using a random-effects model.

EPC staff developed an outcomes table to determine the magnitude of potential benefits and adverse effects of testing for BRCA mutations in the general population based on best estimates from published studies and results of analyses when available. Variation associated with these estimates was incorporated by using Monte Carlo simulations. The sampling distributions for estimates were either the underlying distribution on which calculation of the 95% confidence interval (CI) was based when available, or one that best approximated the point estimate and CI (see Appendix 3, available at www.annals.org). The point estimates and 95% CIs of outcome variables were based on 1,000,000 simulations. Since there are no direct estimates of BRCA mutation prevalence for average- and moderate-risk groups, sensitivity analyses were conducted by assuming a range of prevalence values. Prevalence values were chosen such that when they were summed across the 3 risk groups, the total fell within the range

for the general population (1 in 300 to 500). Calculations assumed that women are cancer free at age 20 years, and outcomes were calculated to age 40 years for breast cancer, age 50 years for ovarian cancer, and age 75 years for both because results at these ages were most often reported by studies. It was assumed that half of the mutations would be in BRCA1 and half in BRCA2, and EPC staff did sensitivity analyses to determine whether this ratio (40/60, 50/50, 60/40) affects outcomes.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Balance Sheets
Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

When the overall quality of the evidence is judged to be good or fair, the U.S. Preventive Services Task Force (USPSTF) proceeds to consider the magnitude of net benefit to be expected from implementation of the preventive service. Determining net benefit requires assessing both the magnitude of benefits and the magnitude of harms and weighing the two.

The USPSTF classifies benefits, harms, and net benefits on a 4-point scale: "substantial," "moderate," "small," and "zero/negative."

"Outcomes tables" (similar to "balance sheets") are the USPSTF's standard resource for estimating the magnitude of benefit. These tables, prepared by the topic teams for use at USPSTF meetings, compare the condition specific outcomes expected for a hypothetical primary care population with and without use of the preventive service. These comparisons may be extended to consider only people of specified age or risk groups or other aspects of implementation. Thus, outcomes tables allow the USPSTF to examine directly how the preventive service affects benefits for various groups.

When evidence on harms is available, the topic teams assess its quality in a manner like that for benefits and include adverse events in the outcomes tables. When few harms data are available, the USPSTF does not assume that harms are small or nonexistent. It recognizes a responsibility to consider which harms are likely and judge their potential frequency and the severity that might ensue from implementing the service. It uses whatever evidence exists to construct a general confidence interval on the 4-point scale (e.g., substantial, moderate, small, and zero/negative).

Value judgments are involved in using the information in an outcomes table to rate either benefits or harms on the USPSTF's 4-point scale. Value judgments are also needed to weigh benefits against harms to arrive at a rating of net benefit.

In making its determinations of net benefit, the USPSTF strives to consider what it believes are the general values of most people. It does this with greater confidence for certain outcomes (e.g., death) about which there is little disagreement about undesirability, but it recognizes that the degree of risk people

are willing to accept to avert other outcomes (e.g., cataracts) can vary considerably. When the USPSTF perceives that preferences among individuals vary greatly, and that these variations are sufficient to make the trade-off of benefits and harms a "close-call," then it will often assign a C recommendation (see the "Recommendation Rating Scheme" field). This recommendation indicates the decision is likely to be sensitive to individual patient preferences.

The USPSTF uses its assessment of the evidence and magnitude of net benefit to make recommendations. The general principles the USPSTF follows in making recommendations are outlined in Table 5 of the companion document cited below. The USPSTF liaisons on the topic team compose the first drafts of the recommendations and rationale statements, which the full panel then reviews and edits. Recommendations are based on formal voting procedures that include explicit rules for determining the views of the majority.

From: Harris RP, Helfand M, Woolf SH, Lohr KN, Mulrow, CD, Teutsch SM, Atkins D. Current methods of the U.S. Preventive Services Task Force: a review of the process. Methods Work Group, Third U.S. Preventive Services Task Force. Am J Prev Med 2001 Apr;20(3S):21-35.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

The U.S. Preventive Services Task Force (USPSTF) grades its recommendations according to one of five classifications (A, B, C, D, I) reflecting the strength of evidence and magnitude of net benefit (benefits minus harms):

A

The USPSTF strongly recommends that clinicians provide [the service] to eligible patients. The USPSTF found good evidence that [the service] improves important health outcomes and concludes that benefits substantially outweigh harms.

B

The USPSTF recommends that clinicians provide [this service] to eligible patients. The USPSTF found at least fair evidence that [the service] improves important health outcomes and concludes that benefits outweigh harms.

C

The USPSTF makes no recommendation for or against routine provision of [the service]. The USPSTF found at least fair evidence that [the service] can improve health outcomes but concludes that the balance of benefits and harms is too close to justify a general recommendation.

D

The USPSTF recommends against routinely providing [the service] to asymptomatic patients. The USPSTF found at least fair evidence that [the service] is ineffective or that harms outweigh benefits.

I

The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing [the service]. Evidence that the [service] is effective is lacking, of poor quality, or conflicting and the balance of benefits and harms cannot be determined.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Comparison with Guidelines from Other Groups
External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Peer Review. Before the U.S. Preventive Services Task Force makes its final determinations about recommendations on a given preventive service, the Evidence-based Practice Center and the Agency for Healthcare Research and Quality send a draft systematic evidence review to 4 to 6 external experts and to federal agencies and professional and disease-based health organizations with interests in the topic. They ask the experts to examine the review critically for accuracy and completeness and to respond to a series of specific questions about the document. After assembling these external review comments and documenting the proposed response to key comments, the topic team presents this information to the Task Force in memo form. In this way, the Task Force can consider these external comments and a final version of the systematic review before it votes on its recommendations about the service. Draft recommendations are then circulated for comment from reviewers representing professional societies, voluntary organizations, and Federal agencies. These comments are discussed before the whole U.S. Preventive Services Task Force before final recommendations are confirmed.

Recommendations of Others. Recommendations regarding genetic susceptibility testing from the following groups were discussed: The American College of Medical Genetics (ACMG); the National Comprehensive Cancer Network (NCCN); the American Society of Clinical Oncology (ASCO); and the American College of Obstetricians and Gynecologists (ACOG).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The U.S. Preventive Services Task Force (USPSTF) grades its recommendations (A, B, C, D, or I) and the quality of the overall evidence for a service (good, fair, poor). The definitions of these grades can be found at the end of the "Major Recommendations" field.

The USPSTF recommends against routine referral for genetic counseling or routine breast cancer susceptibility genes (BRCA) testing for women whose family history is not associated with an increased risk for deleterious mutations in breast cancer susceptibility gene 1 (BRCA1) or breast cancer susceptibility gene 2 (BRCA2). D recommendation

The USPSTF found fair evidence that women without certain specific family history patterns, termed here "increased risk family history" (see Clinical Considerations for a definition of this term) have a low risk for developing breast or ovarian cancer associated with BRCA1 or 2 mutations. Thus, any benefit to routine screening of these women for BRCA1 or 2 mutations, or routine referral for genetic counseling, would be small or zero.

The USPSTF found fair evidence regarding important adverse ethical, legal, and social consequences that could result from routine referral and testing of these women. Interventions such as prophylactic surgery, chemoprevention, or intensive screening have known harms. The USPSTF estimated that the magnitude of these potential harms is small or greater.

The USPSTF concluded that the potential harms of routine referral for genetic counseling or BRCA testing in these women outweigh the benefits.

The USPSTF recommends that women whose family history is associated with an increased risk for deleterious mutations in BRCA1 or BRCA2 genes be referred for genetic counseling and evaluation for BRCA testing. B recommendation

The USPSTF found fair evidence that women with certain specific family history patterns ("increased risk family history") have an increased risk for developing breast or ovarian cancer associated with BRCA1 or 2 mutations. The USPSTF determined that these women would benefit from genetic counseling that allows informed decision-making about testing and further prophylactic treatment. This counseling should be done by suitably trained health care providers. There is insufficient evidence to determine the benefits of chemoprevention or intensive screening in improving health outcomes in these women if they test positive for deleterious BRCA1 or 2 mutations. However, there is fair evidence that prophylactic surgery for these women significantly decreases breast and ovarian cancer incidence. Thus, the potential benefits of referral and discussion of testing and prophylactic treatment for these women may be substantial.

The USPSTF also found insufficient evidence regarding important adverse ethical, legal, and social consequences that could result from referral and testing high risk women. Prophylactic surgery is associated with known harms. The USPSTF estimated that the magnitude of these potential harms is small.

The USPSTF concluded that the benefits of referring women with an increased risk family history to suitably trained healthcare providers outweigh the harms.

Clinical Considerations

- This recommendation applies to women who have not been diagnosed with either breast or ovarian cancer. It does not apply to women with a family

history of breast or ovarian cancer that includes a relative with a known deleterious mutation in BRCA1 or BRCA2 genes; these women should be referred for genetic counseling. This recommendation does not apply to men.

- While there currently are no standardized referral criteria, women with an increased risk family history (see below) should be considered for genetic counseling to further evaluate their potential risks.
- Certain specific family history patterns are associated with an increased risk for deleterious mutations in BRCA1 or 2 genes. Both maternal and paternal family histories are important. For non-Ashkenazi Jewish women, these patterns include:
    - Two first-degree relatives with breast cancer, one of whom was diagnosed at age 50 or younger
    - A combination of 3 or more first- or second-degree relatives with breast cancer, regardless of age of diagnosis
    - A combination of both breast and ovarian cancer among first- and second- degree relatives
    - A first-degree relative with bilateral breast cancer
    - A combination of 2 or more first- or second-degree relatives with ovarian cancer, regardless of age of diagnosis
    - A first- or second-degree relative with both breast and ovarian cancer, at any age
    - A history of breast cancer in a male relative
- For women of Ashkenazi Jewish heritage, an increased risk family history includes any first-degree relative (or 2 second-degree relatives on the same side of the family) with breast or ovarian cancer.
- About 2% of adult women in the general population have an increased risk family history as defined above. Women without one of these family history patterns have a low probability of having a deleterious mutation in BRCA1 or BRCA2 genes.
- Computational tools are available to predict the risk for clinically important BRCA mutations (i.e., BRCA mutations associated with the presence of breast and/or ovarian cancer), but these tools have not been verified in the general population. There is no empirical evidence concerning what level of risk for a BRCA mutation merits referral for genetic counseling.
- Not all women with a potentially deleterious BRCA mutation will develop breast or ovarian cancer. The probability of developing breast or ovarian cancer by the age of 70 in a woman who has a clinically important BRCA mutation is estimated to be 35% to 84% for breast cancer and 10% to 50% for ovarian cancer.
- Appropriate genetic counseling helps women make informed decisions and can improve their knowledge and perception of absolute risk for breast and ovarian cancer and often reduce anxiety. Genetic counseling includes elements of counseling, risk assessment, pedigree analysis, and, in some cases, recommendations for testing for BRCA mutations in affected family members and/or the presenting patient. It is best delivered by a suitably trained healthcare provider.
- Ordering a BRCA test typically is done by a physician. When done in concert with genetic counseling, the test assures the linkage of testing with appropriate management decisions. Genetic testing may lead to potential adverse ethical, legal, and social consequences, such as insurance and employment discrimination; these issues should be discussed in the context of genetic counseling and evaluation for testing.

- Among women with BRCA1 or 2 mutations, prophylactic mastectomy or oophorectomy decreases the incidence of breast and ovarian cancer; there is inadequate evidence for mortality benefits. Chemoprevention with selective estrogen receptor modulators (SERMs) may decrease breast cancer incidence of estrogen receptor-positive cancers; however, it is also associated with adverse effects such pulmonary embolism, deep vein thrombosis, and endometrial cancer. Most breast cancers associated with BRCA1 mutations are estrogen-receptor negative and thus not prevented by tamoxifen. Intensive screening with mammography has poor sensitivity, and there is no evidence of benefit of intensive screening for women with BRCA1 or BRCA2 gene mutations; magnetic resonance imaging (MRI) may detect more cancers, but the effect on mortality is not clear.
- Women with an increased risk family history are at risk not only for deleterious BRCA1 or BRCA2 mutations, but potentially for other unknown mutations as well. Women with an increased risk family history who test negative for BRCA1 and BRCA2 mutations may also benefit from surgical prophylaxis.
- The USPSTF has made recommendations on mammography screening for breast cancer, screening for ovarian cancer, and chemoprevention of breast cancer, which can be accessed at: www.preventiveservices.ahrq.gov.

Definitions:

Strength of Recommendations

The USPSTF grades its recommendations according to one of five classifications (A, B, C, D, I) reflecting the strength of evidence and magnitude of net benefit (benefits minus harms):

A

The USPSTF strongly recommends that clinicians provide [the service] to eligible patients. The USPSTF found good evidence that [the service] improves important health outcomes and concludes that benefits substantially outweigh harms.

B

The USPSTF recommends that clinicians provide [this service] to eligible patients. The USPSTF found at least fair evidence that [the service] improves important health outcomes and concludes that benefits outweigh harms.

C

The USPSTF makes no recommendation for or against routine provision of [the service]. The USPSTF found at least fair evidence that [the service] can improve health outcomes but concludes that the balance of benefits and harms is too close to justify a general recommendation.

D

The USPSTF recommends against routinely providing [the service] to asymptomatic patients. The USPSTF found at least fair evidence that [the service] is ineffective or that harms outweigh benefits.

I

The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing [the service]. Evidence that the [service] is effective is lacking, of poor quality, or conflicting and the balance of benefits and harms cannot be determined.

Strength of Evidence

The USPSTF grades the quality of the overall evidence for a service on a 3-point scale (good, fair, poor):

Good

Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes.

Fair

Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies, generalizability to routine practice, or indirect nature of the evidence on health outcomes.

Poor

Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

CLINICAL ALGORITHM(S)

None available

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is identified in the "Major Recommendations" field.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate assessment, referral, and testing for breast and ovarian cancer susceptibility

Subgroups Most Likely to Benefit:

- Certain specific family history patterns are associated with an increased risk for deleterious mutations in BRCA1 or 2 genes. Both maternal and paternal family histories are important. For non-Ashkenazi Jewish women, these patterns include:
    - Two first-degree relatives with breast cancer, one of whom was diagnosed at age 50 or younger.
    - A combination of 3 or more first- or second-degree relatives with breast cancer, regardless of age of diagnosis.
    - A combination of both breast and ovarian cancer among first- and second- degree relatives.
    - A first-degree relative with bilateral breast cancer.
    - A combination of 2 or more first- or second-degree relatives with ovarian cancer, regardless of age of diagnosis.
    - A first- or second-degree relative with both breast and ovarian cancer, at any age.
    - A history of breast cancer in a male relative.
- For women of Ashkenazi Jewish heritage, an increased risk family history includes any first-degree relative (or 2 second-degree relatives on the same side of the family) with breast or ovarian cancer.

POTENTIAL HARMS

The U.S. Preventive Services Task Force (USPSTF) examined the evidence on harms of screening and intervention.

- Approximately 12% of high risk families without a BRCA1 or BRCA2 coding-region mutation may have other clinically important genomic rearrangements. Approximately 13% of tests report mutations of unknown significance; however, the harms associated with such test results are not known.
- Although not well quantified in the literature, it is clear that routine referral for genetic counseling and consideration of BRCA1 and BRCA2 testing carries important psychological, ethical, legal, and social implications. Among these are the potential for burdening patients with the knowledge of mutations of unknown importance and the potential for affecting family members beyond the individual patient. The potential harms of intensive screening include overdiagnosis and overtreatment.
- There is good quality evidence on the harms of prophylactic tamoxifen; these harms include thromboembolic events, endometrial cancer, and hot flashes.
- There is fair quality evidence on the potential harms of prophylactic surgery: prophylactic mastectomy potential harms include hematoma, infection, contracture, or implant rupture (with reconstruction); harms from prophylactic oophorectomy include infection, bleeding, urinary tract or bowel injury, and premature menopause.

Overall, the USPSTF estimates that the magnitude of these potential harms is at least small.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

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

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The experiences of the first and second U.S. Preventive Services Task Force (USPSTF), as well as that of other evidence-based guideline efforts, have highlighted the importance of identifying effective ways to implement clinical recommendations. Practice guidelines are relatively weak tools for changing clinical practice when used in isolation. To effect change, guidelines must be coupled with strategies to improve their acceptance and feasibility. Such strategies include enlisting the support of local opinion leaders, using reminder systems for clinicians and patients, adopting standing orders, and audit and feedback of information to clinicians about their compliance with recommended practice.

In the case of preventive services guidelines, implementation needs to go beyond traditional dissemination and promotion efforts to recognize the added patient and clinician barriers that affect preventive care. These include clinicians' ambivalence about whether preventive medicine is part of their job, the psychological and practical challenges that patients face in changing behaviors, lack of access to health care or of insurance coverage for preventive services for some patients, competing pressures within the context of shorter office visits, and the lack of organized systems in most practices to ensure the delivery of recommended preventive care.

Dissemination strategies have changed dramatically in this age of electronic information. While recognizing the continuing value of journals and other print formats for dissemination, the Agency for Healthcare Research and Quality will make all U.S. Preventive Services Task Force (USPSTF) products available through its Web site. The combination of electronic access and extensive material in the public domain should make it easier for a broad audience of users to access U.S. Preventive Services Task Force materials and adapt them for their local needs. Online access to U.S. Preventive Services Task Force products also opens up new possibilities for the appearance of the annual, pocket-size Guide to Clinical Preventive Services.

To be successful, approaches for implementing prevention have to be tailored to the local level and deal with the specific barriers at a given site, typically requiring the redesign of systems of care. Such a systems approach to prevention has had notable success in established staff-model health maintenance organizations, by addressing organization of care, emphasizing a philosophy of prevention, and altering the training and incentives for clinicians. Staff-model plans also benefit

from integrated information systems that can track the use of needed services and generate automatic reminders aimed at patients and clinicians, some of the most consistently successful interventions. Information systems remain a major challenge for individual clinicians' offices, however, as well as for looser affiliations of practices in network-model managed care and independent practice associations, where data on patient visits, referrals, and test results are not always centralized.

IMPLEMENTATION TOOLS

Foreign Language Translations
Patient Resources
Personal Digital Assistant (PDA) Downloads
Pocket Guide/Reference Cards
Tool Kits

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility: recommendation statement. Ann Intern Med 2005 Sep 6;143(5):355-61. PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1996 (revised 2005)

GUIDELINE DEVELOPER(S)

United States Preventive Services Task Force - Independent Expert Panel

GUIDELINE DEVELOPER COMMENT

The U.S. Preventive Services Task Force (USPSTF) is a federally-appointed panel of independent experts. Conclusions of the U.S. Preventive Services Task Force do not necessarily reflect policy of the U.S. Department of Health and Human Services (DHHS) or its agencies.

SOURCE(S) OF FUNDING

United States Government

GUIDELINE COMMITTEE

U.S. Preventive Services Task Force (USPSTF)

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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*Members of the Task Force at the time this recommendation was finalized. For a list of current Task Force members, go to www.ahrq.gov/clinic/uspstfab.htm.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The U.S. Preventive Services Task Force has an explicit policy concerning conflict of interest. All members and evidence-based practice center (EPC) staff disclose at each meeting if they have an important financial conflict for each topic being discussed. Task Force members and EPC staff with conflicts can participate in discussions about evidence, but members abstain from voting on recommendations about the topic in question.

From: Harris RP, Helfand M, Woolf SH, Lohr KN, Mulrow, CD, Teutsch SM, Atkins D. Current methods of the U.S. Preventive Services Task Force: a review of the process. Methods Work Group, Third U.S. Preventive Services Task Force. Am J Prev Med 2001 Apr;20(3S):21-35.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the U.S. Preventive Services Task Force (USPSTF) Web site. Also available from the Annals of Internal Medicine Online.

Print copies: Available from the Agency for Healthcare Research and Quality (AHRQ) Publications Clearinghouse. For more information, go to http://www.ahrq.gov/news/pubsix.htm or call 1-800-358-9295 (U.S. only).

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

Evidence Reviews:

- 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 Sep 6;143(5):362-79.

Electronic copies: Available from the U.S. Preventive Services Task Force (USPSTF) Web site. Also available from the Annals of Internal Medicine Online.

Background Articles:

- Woolf SH, Atkins D. The evolving role of prevention in health care: contributions of the U.S. Preventive Services Task Force. Am J Prev Med 2001 Apr;20(3S):13-20.
- Harris RP, Helfand M, Woolf SH, Lohr KN, Mulrow, CD, Teutsch SM, Atkins D. Current methods of the U.S. Preventive Services Task Force: a review of the

process. Methods Work Group, Third U.S. Preventive Services Task Force. Am J Prev Med 2001 Apr;20(3S):21-35.

- Saha S, Hoerger TJ, Pignone MP, Teutsch SM, Helfand M, Mandelblatt JS. The art and science of incorporating cost effectiveness into evidence-based recommendations for clinical preventive services. Cost Work Group of the Third U.S. Preventive Services Task Force. Am J Prev Med 2001 Apr;20(3S):36-43.

Electronic copies: Available from U.S. Preventive Services Task Force (USPSTF) Web site.

The following are also available:

- The guide to clinical preventive services, 2005. Recommendations of the U.S. Preventive Services Task Force. Rockville (MD): Agency for Healthcare Research and Quality (AHRQ), 2005. 192 p. Electronic copies available from the AHRQ Web site.

Print copies: Available from the Agency for Healthcare Research and Quality Publications Clearinghouse. For more information, go to http://www.ahrq.gov/news/pubsix.htm or call 1-800-358-9295 (U.S. only).

The Interactive Preventive Services Selector tool, which enables users to search USPSTF recommendations by patient age, sex, and pregnancy status, is available as a web-based version or PDA application. It is available from the AHRQ Web site.

PATIENT RESOURCES

The following is available:

- The Pocket Guide to Good Health for Adults. Rockville (MD): Agency for Healthcare Research and Quality (AHRQ); 2003.

  Electronic copies: Available from the U.S. Preventive Services Task Force (USPSTF) Web site. Copies also available in Spanish from the USPSTF Web site.

  Print copies: Available from the Agency for Healthcare Research and Quality (AHRQ) Publications Clearinghouse. For more information, go to http://www.ahrq.gov/news/pubsix.htm or call 1-800-358-9295 (U.S. only).

- Genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility: U.S. Preventive Services Task Force Recommendations. Ann Intern Med. 2005 Sep 6;143(5):I-47.

  Electronic copies: Available from the Annals of Internal Medicine Online.

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NGC STATUS

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