Management of an Inherited Predisposition to Breast Cancer

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A healthy 33-year-old woman comes to establish care. She reports no breast symptoms, her age at menarche was 14, and she has no children. She notes a family history of early-onset breast cancer in her sister (whose condition was diagnosed at the age of 35 years and who is alive at 39 years), mother (diagnosed at 37 years and alive at 60 years), and maternal aunt (diagnosed at 42 years and alive at 62 years). Her maternal grandfather died of prostate cancer. What would you advise regarding screening for breast cancer and strategies to reduce her risk?

The Clinical Problem

A family history of breast cancer, especially of early onset, is a clearly established risk factor. Although up to 15% of healthy women will have at least one first-degree relative (mother, sister, or daughter) with breast cancer, we address the treatment of women from families with multiple generations with breast cancer, often early in onset. Risk can be transmitted by either men or women, and the probability that a child will inherit a parent's susceptibility is 50%. A germ-line mutation in the \( \text{BRCA1} \) or \( \text{BRCA2} \) gene is the most commonly detectable cause of a heritable risk of breast cancer. However, only about 40 to 50% of families with multiple cases of female breast cancer but no cases of ovarian or male breast cancer are linked to these genes. Mutations in other genes may also increase breast-cancer risk (Table 1), but extensive investigation fails to detect a cause in many families.

Strategies and Evidence

Risk Assessment and Genetic Testing

A number of empirical models are available to estimate a woman's risk of having breast cancer (Table 2).\(^2\) Family history is the main determinant of risk, but some of these models incorporate personal risk factors, such as reproductive history. Risk estimates calculated by different models may vary, a factor that complicates the use of quantitative risk thresholds for making screening recommendations.\(^8\) Most of the models have been incompletely validated, and their usefulness in non-white women is particularly uncertain.

Certain models incorporate into the estimate of breast-cancer risk a Bayesian prediction of the likelihood that a woman carries a \( \text{BRCA1} \) or \( \text{BRCA2} \) mutation. Additional models are available to directly assess the likelihood that a woman carries a \( \text{BRCA} \) mutation (Table 2).\(^4\) Recent estimates of breast-cancer risk by the age of 80 years are 90% for carriers of the \( \text{BRCA1} \) mutation and 40% for carriers.
of the BRCA2 mutation, with corresponding risks of ovarian cancer of 24% and 8%, respectively9; annual risks vary according to age (Fig. 1).10 A study by Rennert et al.11 in this issue of the Journal shows that rates of survival for women with breast cancers associated with either the BRCA1 or the BRCA2 mutation are similar to those in women without these mutations. Other data have supported similar outcomes for carriers and noncarriers of the mutations, at least when adjuvant chemotherapy is used.12

If possible, a woman with either breast or ovarian cancer should be the first person in the family to undergo genetic testing. If no mutation is found, further BRCA testing in the family probably will not be helpful unless there is reason to suspect that the tested woman may have had a nonhereditary cancer (phenocopy) and that another relative is more likely to be a mutation carrier.

**SPECIALIZED BREAST-CANCER SURVEILLANCE**

**Breast Examination**

The effectiveness of breast self-examination has not been formally evaluated in women with a hereditary risk for breast cancer. A meta-analysis of studies performed in women at average risk showed no significant reduction in breast-cancer mortality with breast self-examination but did show an increase in the number of biopsies performed.13 The value of clinician-performed breast examination as an adjunct to radiographic screening is also unclear. In three large studies of women at average risk, 3 to 8% of cancers were detected solely by clinical examination.14-16 In smaller studies of women with a hereditary risk, the propor-

### Table 1. Genes Known to Be Associated with a Hereditary Predisposition to Breast Cancer.

<table>
<thead>
<tr>
<th>Gene</th>
<th>Syndrome</th>
<th>Relative Risk of Breast Cancer</th>
<th>Breast-Cancer Risk by Age of 70 Years</th>
<th>Major Associated Cancers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>relative risk (age range)</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td><strong>High penetrance</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BRCA1</td>
<td>HBOC</td>
<td>17 (20–29 yr); 32 (40–49 yr); 14 (60–69 yr)</td>
<td>39–87</td>
<td>Ovarian and pancreatic cancers</td>
</tr>
<tr>
<td>BRCA2</td>
<td>HBOC</td>
<td>19 (20–29 yr); 10 (40–49 yr); 11 (60–69 yr)</td>
<td>26–91</td>
<td>Ovarian, prostate, and pancreatic cancers†</td>
</tr>
<tr>
<td>p53</td>
<td>Li–Fraumeni syndrome</td>
<td>1.46 overall; 5.96 (15–29 yr)</td>
<td>56 at age 45 yr; &gt;90 at age 70 yr</td>
<td>Soft-tissue sarcoma, osteosarcoma, brain tumors, adrenocortical carcinoma, leukemia, colon cancer</td>
</tr>
<tr>
<td>PTEN</td>
<td>Cowden’s disease; Bannayan–Riley–Ruvalcaba syndrome; Proteus syndrome; Proteus-like syndrome</td>
<td>2–4</td>
<td>25–50</td>
<td>Thyroid, endometrial, and genitourinary cancers</td>
</tr>
<tr>
<td>STK11/LKB1</td>
<td>Peutz–Jeghers syndrome</td>
<td>15</td>
<td>45–54</td>
<td>Small-intestine, colorectal, uterine, testicular, and ovarian sex cord cancers; other tumors</td>
</tr>
<tr>
<td>CDH1</td>
<td>Hereditary diffuse gastric carcinoma</td>
<td>3.25</td>
<td>39</td>
<td>Lobular breast and diffuse gastric cancer; other tumors</td>
</tr>
</tbody>
</table>

**Low-to-moderate penetrance**

<table>
<thead>
<tr>
<th>Gene</th>
<th>Syndrome</th>
<th>Relative Risk of Breast Cancer</th>
<th>Breast-Cancer Risk by Age of 70 Years</th>
<th>Major Associated Cancers</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATM (heterozygote)</td>
<td>Ataxia–telangiectasia</td>
<td>3–4</td>
<td>NA</td>
<td>Undefined in heterozygotes</td>
</tr>
<tr>
<td>CHEK2</td>
<td>Li–Fraumeni variant</td>
<td>2 for women; 10 for men</td>
<td>NA</td>
<td>Undefined</td>
</tr>
<tr>
<td>BRIP1</td>
<td>Fanconi’s anemia</td>
<td>2</td>
<td>NA</td>
<td>Undefined in heterozygotes</td>
</tr>
<tr>
<td>PALB2</td>
<td>None known</td>
<td>2.3</td>
<td>NA</td>
<td>Undefined in heterozygotes</td>
</tr>
</tbody>
</table>

* High-penetrance mutations are associated with a prominent family history of breast cancer and a high risk of breast cancer. Mutations with a low-to-moderate penetrance are associated with a smaller increase in the risk of breast cancer and a less prominent family history of breast cancer. References for genes in the table are listed in the Supplementary Appendix, which is available with the full text of this article at www.nejm.org. HBOC denotes hereditary breast and ovarian cancer syndrome, and NA not available.
† Prostate cancer does not occur at an earlier age than in the general population.
tion of cancers that were identified solely by clinical screening was 0 to 4%.17-20

Mammography
A meta-analysis of the efficacy of screening mammography in the general population calculated a reduction in breast-cancer mortality of 16% in women of all age groups combined, 22% in women over the age of 50 years, and 15% in women between the ages of 40 and 49 years.21 No randomized, controlled trials of mammography-based screening have specifically analyzed data on women with a familial risk of cancer, although the performance of mammography in such women in population-screening programs is generally similar to that in women without such a family history.22 Several observational studies have described outcomes in women with a familial risk who were enrolled in specialized mammography-based screening programs. The studies varied in the baseline risk of the screened cohort, the frequency of mammography (annual or biennial), and mammographic technique (one view or two views). Among the more than 18,000 women screened in 10 series,22-31 29% of incident tumors were interval cancers (i.e., those presenting as a palpable mass after a normal screening examination), 84% of invasive cancers were smaller than 2 cm, and 66% were lymph-node–negative at the time of diagnosis (Table 1 of the Supplementary Appendix). The substantial rate of interval cancers may result from various factors. Many women who were seen at clinics specializing in the treatment

### Table 2. Models Commonly Used to Predict the Risk of Breast Cancer and the Probability of Detecting a BRCA Mutation.

<table>
<thead>
<tr>
<th>Model, Description, and Access</th>
<th>Measures</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk of breast cancer for unaffected women</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gail et al.2 provide risk of breast cancer by a given age‡‡</td>
<td>Age, family history of breast cancer (FDR), reproductive factors, number of breast biopsies, personal history of atypia§</td>
<td>Does not include breast cancer in non-FDR or family history of ovarian cancer; derived from a population undergoing screening</td>
</tr>
<tr>
<td>Claus et al.3 provide 5-year and lifetime probability of breast cancer¶</td>
<td>Age, family history of breast cancer (FDR, SDR)</td>
<td>Does not include risk factors other than family history or family history of ovarian cancer; incomplete validation in nonwhite populations</td>
</tr>
<tr>
<td>Tyrer–Cuzick (Tyrer et al.4) provides 10-year and lifetime probability of breast cancer¶</td>
<td>Age, family history of breast and ovarian cancer, Ashkenazi ethnic background, reproductive factors, morphometric factors (height, weight), personal history of atypia, lobular carcinoma in situ</td>
<td>Incomplete validation, especially in nonwhite populations</td>
</tr>
<tr>
<td>BRCAPRO (Berry et al.5) provides age-specific probability of breast cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Probability of detecting BRCA mutation (affected and unaffected women)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tyrer–Cuzick4 (see listing above)</td>
<td>Personal or family history of breast and ovarian cancer, Ashkenazi ethnic background</td>
<td>Incomplete validation, especially in nonwhite populations</td>
</tr>
<tr>
<td>BRCAPRO7 (see listing above)</td>
<td>Personal or family history of breast and ovarian cancer, Ashkenazi ethnic background</td>
<td>Incomplete validation in nonwhite populations; requires information on all unaffected FDRs and SDRs</td>
</tr>
<tr>
<td>Frank et al.6 provide empirical experience of one laboratory based on 65,000 observations**</td>
<td>Personal or family history of breast and ovarian cancer, Ashkenazi ethnic background</td>
<td>Empirical model with incomplete validation; does not include unaffected family members</td>
</tr>
<tr>
<td>Manchester (Evans et al.7) provides a scoring system not available as a computer program but presented in the article</td>
<td>Personal or family history of breast and ovarian cancer</td>
<td>Uncertain applicability to nonwhite populations; does not account for ethnic background (especially Ashkenazi)</td>
</tr>
</tbody>
</table>

* FDR denotes first-degree relative, and SDR second-degree relative. 
† The model is available as an interactive tool at www.cancer.gov/bcrisktool. 
‡ The model is available for download at www4.utsouthwestern.edu/breasthealth/cagene/default.asp and at www.tucows.com/preview/221909. 
§ Reproductive risk factors include the age at menarche, menopause, and first childbirth and the number of live births. 
¶ The model is available on request; send e-mail to ibis@cancer.org.uk. 
‖ The model is available for download at astor.som.jhmi.edu/BayesMendel/brcapro.html. 
** The model is available for download at www.myriadtests.com/provider/brc-a-mutation-prevalence.htm.
of patients with a familial risk of cancer were younger than 40 years of age, and interval cancers appear to be more common in this age group.\textsuperscript{32} The reduced sensitivity of mammography in younger women probably results from both increased breast density and a propensity for the development of rapidly growing cancers.\textsuperscript{33} Specialized mammography-based screening programs have not been shown to result in downstaging or improved survival for women with a familial risk. The sensitivity of mammography is also suboptimal in women with BRCA mutations. In 361 women with BRCA mutations who underwent mammography-based surveillance, only 11 of 21 incident cancers were detected radiographically, and 10 cancers developed between annual screenings.\textsuperscript{17,19} Risk factors for interval cancer, such as increased breast density and shorter doubling times, may be associated with a hereditary predisposition.\textsuperscript{34,35} In addition, BRCA1-associated cancers frequently demonstrate a “basal-like” phenotype, which has been associated with interval presentation in other studies.\textsuperscript{36}

Although imperfect, annual mammography is recommended for women with BRCA mutations beginning between the ages of 25 and 30 years, when breast-cancer risk begins to increase.\textsuperscript{10,37} For women without documented BRCA mutations who have a substantial familial risk of breast cancer, screening is suggested to begin at an age that is 5 to 10 years earlier than the youngest age at diagnosis in the family. The recent Digital Mammographic Imaging Screening Trial (DMIST) reported that digital mammography may be more accurate than mammography without computer-aided detection in younger women or in those with dense breasts.\textsuperscript{38}

\textit{Magnetic Resonance Imaging}

Several single-center and multicenter studies have evaluated screening magnetic resonance imaging (MRI) in women with a hereditary risk for breast cancer (Fig. 2). Prospective studies involving 3991 high-risk patients, including 913 with BRCA mutations, showed that MRI detects more than twice as many cancers as does simultaneously performed mammography or sonography\textsuperscript{18,20,39-42} (Table 2 of the Supplementary Appendix). In the studies, MRI detected 64 to 100% of cancers, whereas mammography and ultrasonography each detected 16 to 40%. Of all cancers identified, 78% were detected by MRI, 38% by mammography, and 42% by ultrasonography (when performed). Rates of interval cancer were less than 10% when MRI was performed. Of the cancers identified by MRI, 12 to 27% were ductal carcinoma in situ (DCIS). Of the invasive tumors, 75 to 94% were 2 cm or smaller, and axillary nodal metastases were identified in 17 to 25%. Of the 155 cancers that were detected by screening in these series, 18 (12 DCIS and 8 invasive) were detected on mammography but not on MRI (12%). Therefore, MRI should be considered as a complement to mammography, rather than as a replacement.

Concern has been expressed about the specificity of breast MRI. The definition of a positive examination has varied from study to study, which has complicated comparisons of specificity and positive predictive value. In the prospective studies, specificities were generally more than 95% (range, 81 to 97).\textsuperscript{18,20,39,40} Approximately 11% of
examinations resulted in recalls for additional evaluation. In 7 to 12% of patients, either short-interval follow-up was recommended or the study was interpreted as probably benign, corresponding to the definition for category 3 of the Breast Imaging and Reporting Data System (BI-RADS). The overall rate of biopsy (percutaneous or surgical) was 5 to 11% for women undergoing combined MRI and mammographic screening. The rate of additional imaging required for indeterminate lesions appeared to decline with ongoing screening, as did rates of benign findings on biopsy, dropping from 11 to 5% by the third round of annual screening in one study. The positive predictive value of an MRI that was interpreted as “suspicious for cancer” or “highly suggestive of cancer,” corresponding to the BI-RADS category 4 or 5 definition, was more than 45%. The positive predictive value is expected to be lower in lower-risk populations, and MRI screening is likely to be most cost-effective for mutation carriers (as opposed to women at lower risk), particularly for BRCA1 carriers and for the subgroup of BRCA2 carriers with dense breasts.

**Ultrasonography**

The addition of ultrasonography to screening mammography in asymptomatic women with nonfatty breasts yielded a rate of breast-cancer detection of 0.35 percentage point. The benefit in women with a familial risk has not been established. In three studies of women with a hereditary risk who underwent screening with mammography, ultrasonography, and MRI, only 2 of 83 cancers were detected solely by annual ultrasonography. Two additional nonpalpable cancers were detected by screening ultrasonography performed at 6-month intervals in one study. Ultrasonography did identify a significant number of mammographically occult tumors. Of the 83 cancers in these series, only 32 (39%) would have been identified by mammography alone, whereas 45 (54%) would have been detected by a combination of mammography and ultrasonography. This finding suggests that ultrasonography may add benefit beyond mammography alone in women with a hereditary risk but provides little incremental benefit in women undergoing screening with MRI.

**SCREENING FOR OTHER CANCERS**

Screening for other BRCA-associated cancers (e.g., ovarian, prostate, male breast, and pancreatic cancers) is often recommended even though there
is no clear proof of benefit. In particular, serum CA-125 measurements and transvaginal ultrasonography have not been shown to downstage ovarian tumors in BRCA mutation carriers at the time of detection or to improve survival with ovarian cancer. In families with a hereditary predisposition not related to BRCA1 or BRCA2, screening for other component tumors is commonly recommended but generally has not proved to be beneficial.

**STRATEGIES FOR REDUCING RISKS**

**Chemoprevention**

In the large, randomized Breast Cancer Prevention Trial, tamoxifen given for 5 years was shown to reduce the incidence of breast cancer by 43% in women at increased risk. However, tamoxifen is associated with an increased risk of uterine cancer and venous thromboembolism. Another randomized trial comparing raloxifene with tamoxifen showed that raloxifene was associated with a reduction in the risk of breast cancer that was similar to that of tamoxifen but with a lower risk of endometrial cancer and venous thromboembolism. A subgroup analysis of the Breast Cancer Prevention Trial did not show a significant benefit in women with BRCA mutations, but a benefit was not excluded. The effect of raloxifene in such women has not been studied. Adjuvant tamoxifen reduces the risk of contralateral breast cancer in affected BRCA mutation carriers.

Case–control studies examining the effect of oral contraceptives on the risk of ovarian cancer in BRCA mutation carriers have demonstrated a substantially lower risk (up to 60%) in women who have had 3 or more years of exposure. Other studies have suggested that oral contraceptives may increase the risk of breast cancer in mutation carriers. BRCA2 mutation carriers using oral contraceptives for 5 or more years had twice the risk of breast cancer in one study; in another study, the risk for BRCA1 carriers increased by 30%.

**Surgery**

Risk-reducing salpingo-oophorectomy (RRSO) is an important preventive intervention in BRCA mutation carriers. Although this surgery has not been evaluated in randomized trials, retrospective and prospective cohort studies indicate a reduction in the risk of BRCA-associated gynecologic cancer of 80 to 96% and a reduction in the risk of breast cancer of approximately 50%, most likely through the induction of premature menopause. RRSO is also associated with reduced overall and cancer-specific mortality. Surgically induced menopause may diminish the quality of life; short-term low-dose estrogen replacement may be prescribed for symptoms, but there is a theoretical concern that such therapy may reduce the protective effect of RRSO against breast cancer.

Risk-reducing mastectomy (RRM) reduces the risk of breast cancer by at least 90% in mutation carriers. The cosmetic effect of the procedure may be mitigated by newer reconstructive techniques, but women undergoing surgery may still find it has a detrimental effect on self-image and sexual function.

RRSO and RRM do not entirely prevent the risk of subsequent breast or ovarian cancer. The residual risk of primary peritoneal cancer after RRSO has been reported to be 0.2% annually. The absolute risk after RRM has not been clearly defined.

**AREAS OF UNCERTAINTY**

Randomized, controlled trials of surgical interventions to prove mortality benefits are not likely to be feasible. Even if preventive mastectomy reduces the risk of breast-cancer mortality, the degree to which it improves survival beyond that achieved with RRSO and surveillance (including MRI), with or without tamoxifen or raloxifene, is not clear. Also uncertain are the roles of mammography and MRI screening in BRCA mutation carriers who are either under 30 or over 65 years of age, the role of screening ultrasonography, and the optimal sequencing of screening examinations. Additional data are needed to address the concern that repeated mammography may induce breast cancer in mutation carriers, although recent studies have not supported such an association. Data are also needed regarding the optimal duration and time to initiate hormonal chemoprevention in young women identified as having a hereditary risk for breast cancer. Finally, the potential role of preimplantation genetic diagnosis in women who carry BRCA mutations warrants consideration; data are needed regarding the safety of hormonal treatments that are used to induce ovulation in these women.
Table 3. Published Recommendations for Breast-Cancer Screening for Women with a Hereditary Risk.*

<table>
<thead>
<tr>
<th>Organization</th>
<th>Risk Group</th>
<th>Method (Age to Begin)</th>
<th>BSE</th>
<th>CBE</th>
<th>MMG</th>
<th>US</th>
<th>MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Comprehensive Cancer Network*</td>
<td>1.7% at ≥35 yr</td>
<td>Encouraged</td>
<td>Every 6–12 mo</td>
<td>Annual (35 yr)</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Strong family history</td>
<td>Encouraged</td>
<td>Every 6–12 mo</td>
<td>Annual (varies)†</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Genetic high risk</td>
<td>Monthly (18 yr)</td>
<td>Every 6 mo (25 yr)</td>
<td>Annual (25 yr)</td>
<td>NA</td>
<td>Annual (25 yr)</td>
<td></td>
</tr>
<tr>
<td>Cancer Genetics Studies Consortium*</td>
<td>BRCA mutation</td>
<td>Monthly (18 yr)</td>
<td>Every 6 mo (20–25 yr)</td>
<td>Annual (20–25 yr)</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>National Institute for Health and Clinical Excellence (United Kingdom)*</td>
<td>&gt;8% (30–39 yr) or &gt;20% (40–49 yr) or &gt;12% (40–49 yr) plus dense breast tissue or BRCA mutation or p53</td>
<td>NA</td>
<td>NA</td>
<td>Annual digital (40 yr)</td>
<td>NR</td>
<td>Annual (30 yr; 20 yr for p53)</td>
<td></td>
</tr>
<tr>
<td>French National Ad Hoc Committee*</td>
<td>&gt;20%</td>
<td>NR</td>
<td>Every 4–6 mo (20 yr)</td>
<td>Annual (30 yr)</td>
<td>NA</td>
<td>Ongoing research</td>
<td></td>
</tr>
<tr>
<td>American Cancer Society*</td>
<td>BRCA mutation; untested close relative of carrier; lifetime risk of at least 20–25%; chest radiation at age 10–30; Li–Fraumeni and close relative with breast cancer; Cowden and close relative with breast cancer</td>
<td>Annual‡</td>
<td>Annual‡</td>
<td>Annual‡</td>
<td>Annual‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>U.S. Preventive Services Task Force*§</td>
<td>Mutation carriers</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*BSE denotes breast self-examination, CBE clinician-performed breast examination, MMG mammography, US ultrasonography, MRI magnetic resonance imaging, NA not available, and NR not recommended.
†Mammography should begin 5 to 10 years before the youngest age at the time of diagnosis in the family.
‡Both mammography and screening MRI should be performed annually.
§Evidence is insufficient to determine the benefits of chemoprevention or intensive screening.

**Recommendations from Professional Societies**

Published guidelines for management of breast-cancer risk in women with a hereditary risk are presented in Table 3. No randomized, controlled trials of screening methods or prophylactic interventions have been conducted specifically in mutation carriers; guidelines are based largely on expert opinion and on observational studies and trials involving women at high risk for cancer.

**Summary and Conclusions**

The woman described in the vignette is clearly at increased risk for breast cancer. Risk-prediction models based on family history indicate that her lifetime risk is 30 to 40%. BRCAPRO, the most commonly used model for predicting the presence of a mutation, indicates a 37% probability of detecting a BRCA mutation. BRCA testing should be offered to the patient’s sister. Even if no mutation is found in the family, this young woman is still at increased risk for breast cancer, and mammography should begin by the age of 40 years or 5 to 10 years before the youngest age at which breast cancer was diagnosed in a family member, whichever is earlier.

In women with a BRCA mutation, screening should begin by the age of 25 to 30 years. Although no studies have shown a mortality benefit, the American Cancer Society recommends MRI screening in addition to mammography for women with a BRCA mutation or for women who, like this patient, have a lifetime breast-cancer risk of at least 20 to 25% on the basis of family history. Ultrasonography and breast examination may increase detection rates slightly but at a cost of more false positive results and additional evaluations. Preventive mastectomy and salpingooophorectomy for BRCA mutation carriers are options that should be discussed with women who are at increased risk. Oophorectomy is performed after childbearing, since the greatest increase in the risk of ovarian cancer occurs later.
than that of breast cancer in BRCA mutation carriers.65 Risks and benefits of chemoprevention (e.g., with tamoxifen or raloxifene) should also be discussed. In many circumstances, patients may be referred to genetic counselors and physicians with expertise in clinical cancer genetics and with access to targeted prevention trials. Finally, the patient should be made aware of the inherited nature of breast-cancer risks and should be encouraged to refer family members for consideration of genetic testing and of strategies for prevention and early detection.70

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REFERENCES


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