Breast Cancer Risk Reduction and Counseling: Lifestyle, Chemoprevention, and Surgery

Martin C. Mahoney, MD, PhD, Buffalo, New York

Key Words
Breast cancer, prevention, clinical trials, tamoxifen, raloxifene, chemoprevention

Abstract
Qualitative and quantitative approaches to risk assessment are useful for identifying women at increased risk for developing breast cancer for whom genetics consultation, individualized surveillance recommendations, or chemoprevention may be appropriate. A comprehensive medical and family history review can be used to stratify women into categories of breast cancer risk. A quantitative estimate of the probability of developing breast cancer can be determined using risk assessment tools, such as the Gail and Claus models. Women at increased risk for breast cancer may benefit from individualized approaches to breast cancer risk reduction. Prevention strategies for reducing breast cancer risk include lifestyle modifications, chemoprevention, surgical approaches, and pharmacotherapy. (JNCCN 2007;5:800–808)

Case Vignette
Mary is a 60-year-old white woman under care for hypertension. She is up to date regarding cancer screening, including annual mammograms. During her visit, she mentions that her mother was diagnosed with breast cancer at 68 years of age and her sister was diagnosed with breast cancer last year at age 64 years. She wonders what she can do to reduce her risk for developing breast cancer.

A review of Mary's medical history reveals that her menses started at age 12 years and menopause occurred at age 51 years. She had 4 pregnancies and 3 live births (first live birth at age 21 years). She breastfed her children for variable intervals from a few weeks to 3 months. She reports using oral contraceptives for a total of approximately 4 years but never used hormone replacement therapy (HRT). Her prior mammograms have been normal, and she has no history of prior breast biopsies. She reports engaging in some walking on occasion and enjoys biking during warmer weather. She reports having a glass of wine with dinner 2 to 4 times weekly. Her body mass index is 28.4 and she has gained about 35 pounds since the birth of her first child. She is not aware of Jewish heritage.

Mary's medical history reveals no medical issues during childhood or adolescence. She reports no history of prior ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS), in addition to the 2 first-degree relatives who had breast cancer.

Based on the maternal history of breast cancer, Mary appears to be at moderate risk for developing breast cancer. Using the Gail model, Mary's 5-year breast cancer risk is calculated as 5.8% compared with 1.8% for an average-risk woman of similar age and race, and her lifetime breast cancer risk is 26.6% compared with 9.1% for a similar woman at average risk.

Mary thinks that she might be interested in a chemopreventive agent to reduce her risk for breast cancer. She understands the need for medical follow-up while taking this medication and is interested in determining whether she is eligible to enroll in a breast cancer prevention study.

Mary's physician highlights the components of a healthy diet, including a mix of vegetables, fruits, whole grains, fat-free dairy products, foods with unsaturated rather than saturated fats, and moderate intakes of processed sugar and added salt. She is also counseled to...
avoid alcohol or, if that is not possible, to limit her intake to one drink weekly. A regular exercise program of walking and bicycling is recommended as a means to achieve weight loss. The importance of risk level and age-appropriate breast self-examination, clinical breast examination, and annual mammograms are emphasized.

**Discussion**

Qualitative and quantitative approaches to risk assessment are useful for identifying women at increased risk for developing breast cancer and for whom genetics consultation, individualized surveillance recommendations, or chemoprevention may be appropriate. A comprehensive medical and family history review can be used to stratify women into categories of breast cancer risk. A quantitative estimate of the probability of developing breast cancer can be determined using risk assessment tools, such as the Gail and Claus models. Prevention strategies for reducing breast cancer risk are focused primarily on lifestyle modifications, including a diet high in fruits and vegetables, minimizing use of alcohol, avoiding use of hormone replacement therapy, maintaining a healthy body weight, and participating in regular exercise.

Tamoxifen is approved by the U.S. Food and Drug Administration (FDA) as a risk-reduction agent for women aged 35 years and older who are at increased risk for breast cancer. Clinical trial data indicate that raloxifene achieves similar reductions in invasive breast cancer incidence among women at high risk. Use of other agents for breast cancer chemoprevention, such as aromatase inhibitors, remains under investigation.

Women at increased risk for breast cancer may benefit from individualized approaches to breast cancer risk reduction. For women determined to have a substantially increased risk, surgical approaches to risk reductions can be considered. Pharmacotherapy for breast cancer risk reduction should be individualized based on medical history, family history, calculated risk estimate of developing breast cancer, and patient preferences. Clinicians are strongly encouraged to engage patients in a thorough discussion of risk and benefits as part of the shared decision-making process. Women interested in breast cancer chemoprevention are urged to consider participation in clinical trials.

Breast cancer represents the most commonly diagnosed malignancy among women in the United States, with 178,000 new cases estimated in 2007.\(^1\) Age-adjusted incidence rates seem to have trended downward in the past few years; rates are highest among white women.\(^2\) Age-specific incidence rates increase dramatically beginning at age 40 years, with peak incidence generally occurring among women between 75 and 79 years of age. The median age at diagnosis among all breast cancers cases in the United States is 61 years.\(^2\) The lifetime probability of being diagnosed with breast cancer tends to diminish as age increases. For example, at age 30 years a woman’s lifetime risk for developing breast cancer is 12.8%, at age 50 years it is 11.5%, and at age 70 years it is 6.8%.\(^2\)

A review of age-specific incidence rates suggests that the annual risk for being diagnosed with breast cancer is modest. For example, the average annual age-specific rate of breast cancer for white women between 60 and 64 years of age is 388.0 cases per 100,000 population, or less than 4 cases per 1000 women in the age interval. In other words, 996 of these 1000 women will not develop breast cancer.

**General Population Versus Increased Risk**

General population risk refers to the risk for women with no known medical conditions, family history of cancer, or specific exposures that would increase risk for developing breast cancer compared with the general population. In contrast, increased risk refers to persons who are known, or are suspected to be, at increased risk for developing certain cancers because of personal or family history of medical conditions, exposures, or prior cancers. For example, women with a close relative (e.g., mother or sister) diagnosed with breast cancer are at increased risk for developing breast cancer compared with women without this family history. Levels of increased risk are variable, and plans to reduce this risk are often individualized.

In general, personal or family histories of cancer that may suggest increased susceptibility for certain types of cancer include 2 or more affected individuals on the same side of the family (i.e., maternal or paternal lineage) with the same or "related" cancers (i.e., such as breast and ovarian cancers, or colon and uterine cancers); age of cancer diagnosis earlier than the average age of onset in the general population in at least 1 individual; presence of more than 1 primary cancer in an individual (not including metastases); or
a history of specific medical conditions associated with an increased risk for developing certain types of cancer. Patients or families with a history suggesting increased susceptibility should consider being evaluated by a cancer genetics professional to determine the significance of this family history and receive specific recommendations for surveillance or cancer risk management.

Breast Cancer Risk Assessment
Qualitative
Breast cancer incidence rates vary by age group, race/ethnicity, and multiple other risk factors. A comprehensive medical history review can be used to stratify women according to level of breast cancer risk. Women from families with 2 or more persons diagnosed with breast cancer and other related malignancies (e.g., ovarian) may be at increased risk for developing breast cancer. Women with known breast cancer gene mutations or a history of chest irradiation would be classified at high risk and those with multiple risk factors or a less strong family history of breast cancer would be at moderate risk, whereas those not in either of these groups would be classified as being at general population risk.

Risk for breast cancer is also impacted by reproductive factors (e.g., age at first live birth), breastfeeding history, menstrual history (e.g., early age at menarche, late menopause), and medical history (e.g., prior chest irradiation). Other risk factors for breast cancer can be modified, including obesity, level of exercise, alcohol consumption, and use of exogenous hormones. In addition, breast density was recently reported to impact risk for breast cancer.

Mutations involving the tumor suppressor genes breast cancer 1 (BRCA1) or 2 (BRCA2) are present in 1% to 2% of Ashkenazi Jews and, among carriers, confer a lifetime risk for breast cancer ranging between 40% and 80% and an increased risk for ovarian cancer. The prevalence of BRCA1 mutations among non-Hispanic white populations without Ashkenazi heritage is estimated to be 0.24%, suggesting that more than 500,000 non-Ashkenazi white women are at substantially increased risk for breast cancer. Other investigators have reported an overall prevalence of 0.06% for BRCA1 mutations and 0.4% for BRCA2 mutations among white and black women aged 35 to 64 years in the United States.6

Increased rates of breast cancer have been observed among female survivors of Hodgkin disease (HD) treated with chest irradiation.7,8 Risk seems to be proportional to the radiation dose to the breast.9 Surveillance guidelines for women with a history of therapeutic chest irradiation offer recommendations with regard to use of mammography and magnetic resonance imaging for this risk group.10,11

Quantitative
Breast cancer risk assessment tools can be useful for quantifying the magnitude of risk for individual patients. The Gail and Claus models are among the most widely known risk assessment tools. These models were developed based on 2 studies, the Cancer and Steroid Hormone Project–Claus Model and the Breast Cancer Detection and Demonstration Project–Gail Model, and their included variables.

Components of the Gail model (http://www.cancer.gov/bcrisktool; accessed July 19, 2007), which provides a risk estimate for the next 5 years and an estimate of lifetime risk, include age at menarche, number of prior breast biopsies and results (atypical hyperplasia: yes, no, unknown), age at first live birth, number of first-degree relatives with invasive breast cancer, patient age, and race. The Gail model was initially developed based on a cohort of white women, but also incorporates ethnicity.12 The Gail model is not applicable to women with a history of invasive breast cancer, strong family history of breast cancer, any paternal family history of breast cancer, or family history of ovarian cancer in either lineage.

The Claus model includes information on up to 2 first- or second-degree relatives with invasive breast cancer, with specification as to maternal or paternal lineage, age of patient, and age of relatives at breast cancer diagnosis. An advantage of the Claus model is the inclusion of expanded family history information; however, it can only be used among women with a family history of breast cancer or first-degree relatives with ovarian cancer.13-16

DCIS and LCIS of the breast are defined as noninvasive breast cancers, and both are excluded from risk calculations in the Gail and Claus models. This exclusion likely results in an underestimation of total (invasive and noninvasive) breast cancer risk. Neither the Gail nor Claus models are able to include a family history of ovarian or other related cancers when predicting the risk for developing breast cancer. This is significant because studies have linked a family history
Breast Cancer Risk Reduction

Lifestyle Modifications
Prevention strategies for women at general population risk of developing breast cancer are focused primarily on lifestyle modifications, such as diet, body weight, exercise, and alcohol consumption. Healthy lifestyle recommendations are discussed in detail in the article by Linos and Willett (page 809) in this issue.

HRT
Results from the Women’s Health Initiative, which examined the effects of estrogen plus progesterin (HRT) versus placebo in a randomized trial among postmenopausal women, reported an increased risk for breast cancer among women using HRT (hazard ratio, 1.26; 95% confidence interval, 1.00–1.59). This translated into an absolute excess risk of 8 more invasive breast cancers per 10,000 person years.18 Although prescribing patterns for HRT have changed dramatically as a result of these recent reports, using HRT to manage menopausal symptoms was a common practice. A large retrospective study determined that HRT was associated with an increase of about 10% in the risk for developing breast cancers for each 5 years of use.21 For women deemed to have a low or moderate risk for breast cancer, the increased risk associated with alcohol consumption or more than 5 years of HRT use translates into a small increase in actual risk.

Pharmacotherapy: Selective Estrogen Receptor Modulators
Several recent studies have reported on the use of selective estrogen receptor modulators (SERMs) to reduce breast cancer risk. This class of drugs, including tamoxifen (Nolvadex) and raloxifene (Evista), act as both estrogen agonists and antagonists. Clinicians who counsel patients about the use of SERMs must be familiar with data from the clinical trials22–26 (Table 1). Breast Cancer Prevention: The Breast Cancer Prevention Trial from the National Surgical Adjuvant Breast and Bowel Project (NSABP), also known as the P-1 study, compared the use of the first-generation SERM tamoxifen (20 mg/d for 5 years) with placebo in preventing breast cancer among women deemed to be at increased risk based on a Gail model 5-year-risk estimate of more than 1.66%. As shown in Table 2, results showed a 50% reduction in risk for invasive breast cancers with tamoxifen use (number needed to treat to prevent 1 case of breast cancer = 300).22 Use of tamoxifen resulted in an increased risk for endometrial cancers (age ≥ 50 years), pulmonary emboli (age ≥ 50 years), cataracts, and cataracts requiring surgery. Updated results from the P-1 study based on 7 years of follow-up noted similar reductions in breast cancer incidence.27

Clinicians should be aware of potential drug–drug interactions with tamoxifen. Although serotonin reuptake inhibitors are known to decrease the formation of the active metabolite of tamoxifen (endoxifen), the clinical impact of this is unclear. Citalopram and venlafaxine do not disrupt tamoxifen metabolism.

The NSABP Study of Tamoxifen and Raloxifene (known as the STAR or P-2 trial) extended findings from the P-1 study by comparing 5 years of treatment with tamoxifen (20 mg/d) with 5 years of raloxifene (60 mg/d).23 After 6 years of follow-up, no difference was seen in the rates of breast cancers between tamoxifen and raloxifene, meaning that raloxifene is as effective as tamoxifen for preventing breast cancer (Table 3). The STAR trial is discussed in more detail in the article by Bevers (page 817) in this issue.

Osteoporosis Prevention: Raloxifene has been shown to be effective in treating and preventing osteoporosis among postmenopausal women.26,29 The Multiple Outcomes of Raloxifene (MORE) trial examined selected bone outcomes among postmenopausal women with osteoporosis (placebo, raloxifene 60 mg/d, or raloxifene 120 mg/d); breast cancer was a secondary end point in this study.10 After 4 years of follow-up, a 62% risk reduction was seen among the group treated with raloxifene.24 The Continuing Outcomes Relevant to Evista (CORE) trial, which extended the MORE trial to examine an additional 4 years of raloxifene (20 mg/d) on breast cancer incidence, showed a 50% reduction in the incidence of breast cancers among...
the group treated with raloxifene. The number needed to treat to prevent 1 case of breast cancer based on the MORE and CORE studies was in the range of approximately 300 to 350. When 8 years of follow-up data (both MORE and CORE) were examined, the incidence rates for venous thromboembolic events was 2.2 per 1000 person-years in the raloxifene group and 1.3 per 1000 person-years in the placebo group (number needed to harm, 1111). These trials are discussed in further detail in the article by Bevers (page 817) in this issue.

Heart Disease Prevention: The Raloxifene Use for the Heart (RUTH) trial enrolled more than 10,000 postmenopausal women with coronary heart disease (CHD) or multiple CHD risk factors into a randomized study examining raloxifene 60 mg/d (versus placebo) for CHD prevention. Although no differences were found between groups for cardiovascular disease end points, the rate of breast cancer was significantly lower among the raloxifene group (hazard ratio, 0.67; 95% confidence interval, 0.47–0.96). Rates of venous thromboembolic events did not differ between groups. The large estimate noted for the number needed to treat to prevent 1 case of breast cancer based on the RUTH trial likely reflects a study cohort that approximated the general population risk for developing breast cancer.

Currently, only tamoxifen is FDA approved for breast cancer prevention. Based on the results of the STAR trial, an application to expand the labeled use of raloxifene to include breast cancer risk reduction has been filed. The addition of raloxifene as an

Table 1 Summary of Selected Clinical Trials Examining Breast Cancer Chemoprevention

<table>
<thead>
<tr>
<th>Study Name</th>
<th>N</th>
<th>Eligibility Criteria</th>
<th>Outcome</th>
<th>Annual Breast Cancer Incidence Rate/1000</th>
<th>Risk Ratioa (95% CI)</th>
<th>Absolute Rate Difference per 1000 (%)</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSABP, P-1</td>
<td>13,388</td>
<td>5-year Gail risk ≥1.66% or history of LCIS; 6 years of follow-up; median follow-up 54.6 months</td>
<td>Invasive breast cancers</td>
<td>6.76 3.43</td>
<td>0.51 (0.39–0.66)</td>
<td>-3.33</td>
<td>300</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ER+, invasive breast cancers</td>
<td>5.02 1.58</td>
<td>0.31 (0.22–0.45)</td>
<td>-3.44</td>
<td>291</td>
</tr>
<tr>
<td>STAR (P-2)</td>
<td>19,747</td>
<td>Postmenopausal women with 5-year Gail risk ≥1.66%; 6 years of follow-up</td>
<td>Invasive breast cancers</td>
<td>4.30 3.04</td>
<td>1.02 (0.82–1.28)</td>
<td>No difference between tamoxifen and raloxifene</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ER+, invasive breast cancers</td>
<td>4.41 2.86</td>
<td>0.93 (0.72–1.24)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MORE</td>
<td>7,705</td>
<td>Postmenopausal women with osteoporosis; mean age 66 years, 4 years follow-up</td>
<td>All breast cancers</td>
<td>5.3 1.9</td>
<td>0.38 (0.24–0.58)</td>
<td>-3.4</td>
<td>294</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ER+, invasive breast cancers</td>
<td>3.7 0.6</td>
<td>0.16 (0.09–0.30)</td>
<td>-3.1</td>
<td>323</td>
</tr>
<tr>
<td>CORE</td>
<td>5,213</td>
<td>4-year extension of MORE trial; follow-up to 8 years</td>
<td>All breast cancers</td>
<td>5.5 2.7</td>
<td>0.50 (0.30–0.82)</td>
<td>-2.80</td>
<td>357</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ER+, invasive breast cancers</td>
<td>3.9 1.3</td>
<td>0.34 (0.18–0.66)</td>
<td>-2.60</td>
<td>385</td>
</tr>
<tr>
<td>RUTH</td>
<td>10,101</td>
<td>Postmenopausal women with documented CHD or multiple risk factors for CHD; mean age 67 years, median follow-up 5.6 years</td>
<td>All breast cancers</td>
<td>0.29 0.20</td>
<td>0.67 (0.47–0.96)</td>
<td>-0.09</td>
<td>11,111</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ER+, invasive breast cancers</td>
<td>0.27 0.09</td>
<td>0.45 (0.28–0.72)</td>
<td>-0.18</td>
<td>5,556</td>
</tr>
</tbody>
</table>

* Risk ratio, ratio of rates between treatment group.
† Absolute rate difference = difference between groups for indicated comparisons.
‡ Risk estimate based on hazard ratio.

Abbreviations: CHD, coronary heart disease; CI, confidence interval; CORE, Continuing Outcomes Relevant to Evista; ER, estrogen receptor; LCIS, lobular carcinoma in situ; MORE, Multiple Outcomes of Raloxifene; NNT, number needed to treat to prevent one undesired outcome; NSABP, National Surgical Adjuvant Breast and Bowel Project; RUTH, Raloxifene Use for the Heart; STAR, Study of Tamoxifen and Raloxifene; TAM, tamoxifen; RAL, raloxifene.
### Table 2 Summary of Selected Outcomes in the NSABP Breast Cancer Prevention Trail (P-1) Comparing Placebo Versus Tamoxifen

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Annual Rate per 1000</th>
<th>Absolute Rate Difference* per 1000</th>
<th>NNH: (Favors Placebo)</th>
<th>NNT: (Favors Tamoxifen)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
<td>Tamoxifen</td>
<td>Risk Ratio* (95% CI)</td>
<td>(Favors Placebo)</td>
</tr>
<tr>
<td>Endometrial cancer</td>
<td>≤ 49 years</td>
<td>1.09</td>
<td>1.32</td>
<td>1.21 (0.41–3.60)</td>
</tr>
<tr>
<td></td>
<td>≥ 50 years</td>
<td>0.76</td>
<td>3.05</td>
<td>4.10 (1.70–10.90)</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>≤ 49 years</td>
<td>0.78</td>
<td>1.08</td>
<td>1.39 (0.51–3.99)</td>
</tr>
<tr>
<td></td>
<td>≥ 50 years</td>
<td>0.88</td>
<td>1.51</td>
<td>1.71 (0.85–3.58)</td>
</tr>
<tr>
<td>Stroke</td>
<td>≤ 49 years</td>
<td>0.39</td>
<td>0.30</td>
<td>0.76 (0.11–4.49)</td>
</tr>
<tr>
<td></td>
<td>≥ 50 years</td>
<td>1.26</td>
<td>2.20</td>
<td>1.75 (0.98–3.20)</td>
</tr>
<tr>
<td>Pulmonary embolus</td>
<td>≤ 49 years</td>
<td>0.10</td>
<td>0.20</td>
<td>2.03 (0.11–119.62)</td>
</tr>
<tr>
<td></td>
<td>≥ 50 years</td>
<td>0.31</td>
<td>1.00</td>
<td>3.19 (1.12–11.15)</td>
</tr>
<tr>
<td>Fracture</td>
<td>≤ 49 years</td>
<td>2.24</td>
<td>1.98</td>
<td>0.88 (0.46–1.68)</td>
</tr>
<tr>
<td></td>
<td>≥ 50 years</td>
<td>7.27</td>
<td>5.76</td>
<td>0.79 (0.60–1.05)</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>all</td>
<td>2.37</td>
<td>2.73</td>
<td>1.15 (0.81–1.64)</td>
</tr>
<tr>
<td>Cataracts</td>
<td>all</td>
<td>21.72</td>
<td>24.82</td>
<td>1.14 (1.01–1.29)</td>
</tr>
<tr>
<td>Cataracts with surgery</td>
<td>all</td>
<td>3.00</td>
<td>4.72</td>
<td>1.57 (1.16–2.14)</td>
</tr>
<tr>
<td>Invasive breast cancer</td>
<td>all</td>
<td>6.76</td>
<td>3.43</td>
<td>0.51 (0.39–0.66)</td>
</tr>
</tbody>
</table>

*Risk ratio, tamoxifen group compared to placebo group.
†Absolute rate difference = difference between groups (tamoxifen versus placebo).

Abbreviations: CI, confidence interval; NNH, number needed to harm or number needed to cause one undesired outcome; NNT, number needed to treat to prevent one undesired outcome; NSABP, National Surgical Adjuvant Breast and Bowel Project.


FDA-approved breast cancer risk reduction agent could lead to the expanded use of breast cancer chemoprevention in general medical practice. Primary care clinicians are already familiar with raloxifene in the treatment of osteoporosis. In contrast, primary care clinicians have generally been unenthusiastic about tamoxifen for chemoprevention given its original use by oncologists in breast cancer treatment, combined with concerns about serious adverse events.31-31

The major trials examining the impact of pharmacologic risk reduction strategies (the P-1, STAR, MORE, CORE, and RUTH trials) enrolled a limited proportion of non-whites, and findings from those trials are difficult to generalize to other population subgroups. These clinical trials also used somewhat different eligibility criteria regarding breast cancer risk status, such as a history of chest wall irradiation and a history of atypical hyperplasia.31

**Pharmacotherapy: Other Agents**

Aromatase inhibitors (AIs), including anastrozole, exemestane, and letrozole, block the conversion of androgens to estrogens by aromatase and lower circulating estrogen levels. AIs have proven effective in breast cancer treatment among postmenopausal women with hormone-sensitive tumors. Clinical trial data from 3 studies show that AIs decrease the incidence of contralateral breast cancers by 37% to 55%.34-36 The safety profile for AIs seems favorable compared with that for tamoxifen. Clinical trials assessing the chemopreventive potential of AIs among women at increased risk for breast cancer are currently underway. AIs are not FDA-approved for breast cancer prevention.

Regular use of aspirin and other nonsteroidal anti-inflammatory agents has been reported to decrease the risk for breast cancer.37,38 However, other retrospective studies have noted inconsistent relationships because of limited information about dosage and duration of use. An article from the Women’s Health
Table 3 Summary of Selected Adverse Outcomes in the NSABP Breast Cancer Prevention Trial (STAR, P-2) Comparing Tamoxifen Versus Raloxifene

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Tamoxifen Rate per 1000</th>
<th>Raloxifene Rate per 1000</th>
<th>Risk Ratio (Favors Tamoxifen)</th>
<th>Absolute Rate Difference† per 1000 (Favors Tamoxifen)</th>
<th>NNH: (Favors Tamoxifen)</th>
<th>NNT: (Favors Raloxifene)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometrial cancer</td>
<td>2.00</td>
<td>1.25</td>
<td>0.62 (0.35–1.08)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>2.29</td>
<td>1.69</td>
<td>0.74 (0.53–1.03)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>1.39</td>
<td>1.33</td>
<td>0.96 (0.64–1.43)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary embolus</td>
<td>1.41</td>
<td>0.90</td>
<td>0.64 (0.41–1.00)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fracture</td>
<td>2.73</td>
<td>2.51</td>
<td>0.92 (0.68–1.22)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>3.00</td>
<td>3.29</td>
<td>1.10 (0.85–1.43)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cataracts</td>
<td>12.30</td>
<td>9.72</td>
<td>0.79 (0.68–0.92)</td>
<td></td>
<td>−2.58</td>
<td>388</td>
</tr>
<tr>
<td>Cataracts with surgery</td>
<td>8.03</td>
<td>6.62</td>
<td>0.82 (0.68–0.99)</td>
<td></td>
<td>−1.41</td>
<td>709</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>4.30</td>
<td>4.41</td>
<td>1.02 (0.82–1.28)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Outcomes are not stratified by age group because only 9% of the study population was younger than 50 years.

* Risk ratio, raloxifen group compared to tamoxifen group.
† Absolute rate difference, difference between groups (raloxifene versus tamoxifen).

Abbreviations: CI, confidence interval; NNH, number needed to harm or number needed to cause one undesired outcome; NNT, number needed to treat to prevent one undesired outcome; NSABP, National Surgical Adjuvant Breast and Bowel Project; STAR, Study of Tamoxifen and Raloxifene.

Source: Data are based on Vogel VG, Constantino JP, Wicherham DL, et al., Effects of tamoxifen vs raloxifene on the risk of developing invasive breast cancer and other disease outcomes: the NSABP Study of Tamoxifen and Raloxifene (STAR) P-2 trial. JAMA 2006;295:2727–2741.

Study reported no difference in breast cancer incidence with use of 100 mg of aspirin on alternative days after 10 years of follow-up. It could be argued that the use of a daily coated aspirin may afford additional benefits beyond cardioprotection among women without a contraindication to use.

Use of pharmacotherapy for breast cancer risk reduction should be individualized to each patient based on medical history, family history, quantified estimate of developing breast cancer, and patient preferences. Women who opt to undergo pharmacotherapy for breast cancer risk reduction and those participating in clinical trials of breast cancer prevention should understand the importance of adhering with surveillance recommendations for the prompt detection of breast cancer and the need to seek medical evaluation for specific adverse effects, such as abnormal vaginal bleeding and vision problems.

All women considering breast cancer chemoprevention should be counseled on modifying lifestyle factors as an initial approach to risk reduction. Qualitative and quantitative approaches to risk assessment should be used to identify women at increased risk for breast cancer for whom genetics consultation, individualized surveillance, or chemoprevention may be appropriate. Women interested in breast cancer chemoprevention are urged to consider participation in clinical trials.

Surgical Approaches

Surgical options for women at substantially increased risk for breast cancer include prophylactic mastectomy and prophylactic salpingo-oophorectomy. The surgical approach is limited to women at markedly increased risk based on the presence of known or suspect genetic mutations (BRCA1, BRCA2, p53, PTEN) or a family history of breast or ovarian cancers among first- and second-degree relatives. Among women at moderate and high risk, bilateral risk reduction mastectomy can substantially reduce breast cancer risk. Clinicians have recommended that bilateral salpingo-oophorectomy as a breast cancer risk reduction strategy should be limited to women with BRCA1 and BRCA2 mutations. However, clinicians may deem it appropriate to also discuss bilateral salpingo-oophorectomy with additional premenopausal women judged to be at high risk, including those carrying a BRCA or other high-risk mutation, those with LCIS, or those who...
underwent prior thoracic radiation therapy at an early age. Women wishing to contemplate risk-reduction surgery are recommended to undergo presurgical evaluations, including consultation and genetic testing with a cancer genetics professional and a psychological evaluation, to assure that they fully understand the magnitude of risk and breadth of potential harms and benefits.25

Summary
Breast cancer risk-reduction strategies should be individualized to each patient based on medical history, family history, quantified estimate of developing breast cancer, and patient preferences. Clinicians are strongly encouraged to engage patients in a thorough discussion of risks and benefits as part of a shared decision-making process.

Women who opt to use pharmacotherapy to achieve breast cancer risk reduction and those participating in clinical trials of breast cancer prevention should understand the importance of adhering with surveillance recommendations for the prompt detection of breast cancer and the need to seek medical evaluation for specific symptoms of potential adverse events, such as abnormal vaginal bleeding and vision problems.

Patients being considered for breast cancer chemoprevention should be counseled regarding modifiable lifestyle factors as an initial approach to risk reduction. Qualitative and quantitative approaches to risk assessment should be used to identify women at increased risk for breast cancer who might benefit from chemoprevention, individualized surveillance, or chemoprevention may be appropriate. Women interested in breast cancer chemoprevention are urged to consider participating in clinical trials.

References


