Women’s Interest in Chemoprevention for Breast Cancer

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Background: Chemoprevention is the use of pharmacologic or natural agents to inhibit the development of cancer. Tamoxifen citrate is the only approved chemopreventive agent for breast cancer. We sought to determine whether women are interested in taking a drug to prevent breast cancer and to assess the relationship between objective and subjective breast cancer risk and interest in chemoprevention.

Methods: We conducted telephone interviews (November 3, 1997, to May 6, 1998) among a community sample of women aged 40 to 45 and 50 to 55 years enrolled in a randomized controlled trial to evaluate the efficacy of a tailored mammography decision aid. Objective breast cancer risk was measured using the 5-year Gail score. Subjective breast cancer risk was measured using perceptions of absolute risk, perceptions of comparative risk, and worry about getting breast cancer. At 12-month follow-up (November 2, 1998, to July 20, 1999), we measured interest in taking a drug to prevent breast cancer.

Results: Among the 1273 women surveyed, 23% were interested in taking a drug to prevent breast cancer; 8% were potentially eligible for tamoxifen therapy (5-year Gail score ≥1.66%). Eligibility for chemoprevention, based on the 5-year Gail score, was not associated with interest in taking a drug to prevent breast cancer. Women who were worried about breast cancer were 3 times more likely to be interested in taking a drug to prevent breast cancer than those who were not worried.

Conclusion: Women’s interest in chemoprevention might arise more from worries about getting breast cancer than from their objective risk factors.

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CHEMOPREVENTION is the use of pharmacologic or natural agents to inhibit the development of cancer. Currently, tamoxifen citrate is the only approved chemopreventive agent for breast cancer.1 Decision making about chemoprevention for breast cancer is difficult and should require, at minimum, identification of potential risks and benefits based on a woman’s profile of breast cancer risk factors.

Given the broad range of risk factors identified for breast cancer, many women will have at least 1 risk factor. Although genetic breast cancer refers to those cancers associated with BRCA1 or BRCA2 mutations, familial breast cancer represents a much broader group of women at risk; approximately 8% of women in the general population have at least 1 first-degree relative with breast cancer.2 Additional factors that modify breast cancer risk include current age, age at menarche, nulliparity, age at first live birth, age at menopause, and benign forms of breast disease.3 The Gail model provides an overall summary score incorporating these risk factors.4,5

For women at elevated risk for breast cancer, there are several management options: close surveillance with clinical breast examination and mammography, prophylactic bilateral mastectomy or oophorectomy, and chemoprevention.6 The most recently available option is taking tamoxifen for 5 years as a chemopreventive agent. Tamoxifen, the original selective estrogen receptor modulator, has been used since the 1970s to treat localized and metastatic estrogen-receptor–positive breast cancers. Its effect as a chemopreventive agent was examined in 3 clinical trials.7-9 The US Breast Cancer Prevention Trial, sponsored by the National Surgical Adjuvant Breast and Bowel Project,7 was the largest of the 3 clinical trials and included more than 13000 women. Women were eligible for this study if they were (1) 60 years or older or (2) were 35 years or older with a 5-year calculated risk (using the Gail model) of at least 1.66% or a history of lobular car-
PARTICIPANTS AND METHODS

PARTICIPANTS

Participants were selected at random from a list provided by Blue Cross/Blue Shield of North Carolina. The sampling frame was stratified by age and mammography status based on Blue Cross/Blue Shield claims data. We included women aged 40 to 44 and 50 to 54 years enrolled with the Personal Care Plan of Blue Cross/Blue Shield. Because women aged during the study, some women in this analysis are 45 or 53 years old. About two thirds of the women were chosen because they reported having a mammogram within the previous 1 to 2 years, depending on their age. We excluded women with a previous diagnosis of breast cancer and those who had more than 1 mammogram in a 12-month period during the designated time frame.

A total of 2165 women were mailed a letter informing them of the study; 1287 (59%) consented and completed the telephone survey (Table 1); 337 (16%) refused to participate; 291 (13%) had incorrect or disconnected telephone numbers; 158 (7%) were ineligible because they were not Blue Cross/Blue Shield members at the time of the interview; 6 (0.3%) were ineligible because they had breast cancer; 6 (0.3%) were ineligible because of age; and 80 (4%) were never reached. After deleting those who were ineligible, our completion rate for the baseline survey was 76%, and our refusal rate was 20%. Women were surveyed by professional telephone interviewers from Battelle Centers for Public Health Research and Evaluation (Durham, NC) at baseline (November 3, 1997, to May 6, 1998) and at 12-month follow-up (November 2, 1998, to July 20, 1999).

MEASURES

In addition to sociodemographic measures such as age, race or ethnicity, marital status, educational level, and adequacy of income, we measured mammography use, current smoking status, and hormone replacement therapy (HRT) use (see Rimer et al12 for additional details). The main measures are described in the following paragraphs.

Interest in Chemoprevention for Breast Cancer

We asked, “Are you interested in taking a drug to prevent breast cancer?” as our main outcome measure. Response options were “interested,” “not interested,” and “don’t know.” We dichotomized responses to “interested” vs other responses, for convenience termed “not interested.”

Perceptions of Absolute Breast Cancer Risk

Absolute risk was assessed using standard verbal and numerical measures within the span of 10 years. For the verbal measures, women were asked, “How likely are you to get breast cancer in the next 10 years?” Responses were “very unlikely,” “unlikely,” “50-50 chance,” “likely,” and “very likely.” For the numerical measures, women were asked, “On a scale from 0 to 100, with 0 indicating certain not to happen and 100 indicating certain to happen, how likely are you to get breast cancer in the next 10 years?”

cinoma in situ. Tamoxifen treatment was beneficial in all age groups and within all levels of breast cancer risk, with a 49% reduction in the risk of invasive breast cancer. However, tamoxifen treatment also increased the risk of endometrial cancer and thromboembolic events compared with placebo at 47.7-month follow-up.7

Based on findings from the National Surgical Adjuvant Breast and Bowel Project, the US Food and Drug Administration approved use of tamoxifen for reduction of breast cancer risk in women at high risk, as defined by the Breast Cancer Prevention Trial (ie, 5-year Gail score $\geq 1.66\%$). Since Food and Drug Administration approval, pharmaceutical companies have begun direct marketing to women, and the National Cancer Institute has developed a “risk disk” to help women and their provid-
Perceptions of Comparative Breast Cancer Risk

We asked, “Compared with other women your age, how likely are you to get breast cancer in the next 10 years?” Responses were “much below average,” “below average,” “same average risk as other women your age,” “above average,” and “much above average.”

Worry About Getting Breast Cancer

We asked, “How worried are you about getting breast cancer in the next 10 years?” Responses were “not at all worried,” “slightly worried,” “somewhat worried,” “worried,” and “very worried.”

Assessment of Objective Breast Cancer Risk

We used the most recent Gail algorithm to assess objective breast cancer risk. The Gail model calculates an absolute risk score based on current age; race; age at menarche; mother or sisters with breast cancer; age at first live birth; and number of breast biopsies, including any with atypical hyperplasia. Using the National Surgical Adjuvant Breast and Bowel Project clinical trial criteria, we dichotomized the 5-year Gail score, using a Gail score of 1.66% or greater (elevated breast cancer risk) vs less than 1.66% (nonelevated breast cancer risk).

Depression

Because we hypothesized that depression would affect risk perceptions, we used the abbreviated 10-item Center for Epidemiological Studies–Depression scale to measure depression and considered a score of 10 or more as identifying significant depressive symptoms.

STATISTICAL ANALYSIS

We first assessed whether the Gail score’s objective measure of breast cancer risk was related to perceived breast cancer risk and worry. Stratifying our analyses by age groups (40-45 and 50-55 years), Pearson $\chi^2$ and $t$ statistics were used to compare differences between women interested and not interested in taking a drug to prevent breast cancer on demographic characteristics, health behaviors, depression, perceived risk for breast cancer, and 5-year Gail score. The analyses for this study are based on 1273 women who completed the 12-month follow-up survey. We used logistic regression to model the probability of interest in chemoprevention for breast cancer. Because we hypothesized that perceived risk and worry for breast cancer, and not actual risk, would be related to interest in taking tamoxifen, we included these as main effects in the model. We used comparative risk in the logistic regression model because other authors determined that it is a good measure of perceived susceptibility. Age group (40-45 vs 50-55 years), education, depression, smoking, and HRT use were associated with an interest in chemoprevention in bivariate analyses ($P<.10$) and were included in the logistic regression model as covariates.

RESULTS

CORRELATION OF OBJECTIVE RISK, PERCEIVED RISK, AND WORRY FOR BREAST CANCER

Overall, greater objective risk (as measured by the 5-year Gail score) was associated with greater perceived absolute risk (measured numerically on a scale from 0-100), greater perceived comparative risk, and greater worry (Table 2). Spearman correlation coefficients were less than 0.2.

POTENTIAL ELIGIBILITY FOR TAMOXIFEN THERAPY

In the entire cohort of women in this community-based sample, 8% had a 5-year Gail score of at least 1.66%. In the younger age group (40-45 years), 3% of women met criteria for high risk, and 12% in the older age group (50-55 years) were considered to be at high risk.

INTEREST IN CHEMOPREVENTION FOR BREAST CANCER

Overall, 23% of women were interested in taking a drug to prevent breast cancer (21% of those aged 40 to 45 years and 24% of those aged 50 to 55 years) (Table 3). Women interested in chemoprevention in the younger age group believed themselves to be at greater risk for breast cancer (measured numerically and compared with other women) and were more worried about breast cancer ($P<.01$). Women interested in taking a drug to prevent breast cancer also exhibited more depressive symptoms and were more likely to smoke ($P<.01$). However, the 5-year Gail score was not associated with interest in chemoprevention.

As in the younger age group, those aged 50 to 55 years who were interested in chemoprevention believed themselves to be at greater breast cancer risk (measured numerically and compared with other women) and were more worried about breast cancer ($P<.05$). Objective breast cancer risk (5-year Gail score $\geq$ 1.66% or $<1.66$%) was not associated with an interest in chemoprevention for this age group either.

In logistic regression analyses of the combined age groups, worry about breast cancer, comparative risk of breast cancer, current smoking status, and HRT use were significantly associated with an interest in chemoprevention (Table 4). There was a trend for women with...
depressive symptoms to be more interested in chemoprevention for breast cancer ($P = .07$).

**COMMENT**

To our knowledge, this is the first study to examine interest in chemoprevention for breast cancer and identify determinants of this interest. Although this was a predominantly low-risk community-based sample (only 8% had 5-year Gail scores $\geq 1.66$%), more than 20% expressed interest in taking a drug to prevent breast cancer. Given the new indication for tamoxifen as a breast cancer chemoprevention agent in high-risk women, the publicity tamoxifen is receiving, and the interest expressed in our sample, health care providers should initiate discussions about this controversial and complicated medical decision with their patients. Our research suggests that patients’ interest in chemoprevention for breast cancer might arise more from worries about getting breast cancer than from their objective risk factors. Thus, putting patients’ breast cancer risks in perspective should be part of the process of facilitating informed decision making about chemoprevention. Of course, we recognize that we assessed interest only, and it is likely that many women who expressed an interest would have subsequently declined to take tamoxifen when informed fully about the risks and benefits.

Although the incidence of breast cancer increases with age, previous studies have found that younger women disproportionately overestimate their risk of breast cancer. Whereas the average woman in her early 40s has a 1-in-200 chance of developing breast cancer in 5 years, and this risk increases to only 1-in-100 for the average woman in her early 50s, many women in these age ranges think that their risk is closer to 1 in 10. In our community sample, the average perceived absolute risk was 30%, or a 1-in-3

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**Table 2. Correlations Among Objective Risk and Perceptions of Risk and Worry for Breast Cancer, Stratified by Age Group***

<table>
<thead>
<tr>
<th>Objective Risk as Determined by the 5-y Gail Score</th>
<th>Absolute Risk, Numerical (0-100): Aged 40-45 y, Mean = 30, SD = 20; Aged 50-55 y, Mean = 31, SD = 22</th>
<th>Absolute Risk, Verbal (1-5): Aged 40-45 y, Mean = 2.3, SD = 0.9; Aged 50-55 y, Mean = 2.4, SD = 1.0</th>
<th>Comparative Risk, Verbal (1-5): Aged 40-45 y, Mean = 2.5, SD = 0.9; Aged 50-55 y, Mean = 2.5, SD = 0.9</th>
<th>Worry (1-5): Aged 40-45 y, Mean = 2.0, SD = 0.9; Aged 50-55 y, Mean = 1.9, SD = 0.9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aged 40-45 y (mean = 0.83, range = 0.31-7.88)</td>
<td>0.10†</td>
<td>0.01‡</td>
<td>0.15†</td>
<td>0.12†</td>
</tr>
<tr>
<td>Aged 50-55 y (mean = 1.17, range = 0.42-6.45)</td>
<td>0.14†</td>
<td>0.03‡</td>
<td>0.08‡</td>
<td>0.17†</td>
</tr>
</tbody>
</table>

*Values represent Spearman correlation coefficients. All risk perceptions and worry are for the next 10 years.
†Significant at $P < .05$.

**Table 3. Level of Interest in Chemoprevention for Breast Cancer Among Women, Stratified by Age Group***

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Women Aged 40-45 y</th>
<th>Women Aged 50-55 y</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Characteristics</strong></td>
<td><strong>Interested</strong> (n = 118)</td>
<td><strong>Not Interested</strong> (n = 455)</td>
<td><strong>Interested</strong> (n = 137)</td>
</tr>
<tr>
<td><strong>Demographics, %</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Currently married</td>
<td>79</td>
<td>83</td>
<td>.3</td>
</tr>
<tr>
<td>African American</td>
<td>17</td>
<td>15</td>
<td>.6</td>
</tr>
<tr>
<td>College education</td>
<td>64</td>
<td>71</td>
<td>.1</td>
</tr>
<tr>
<td>Adequate income</td>
<td>90</td>
<td>93</td>
<td>.2</td>
</tr>
<tr>
<td><strong>Perceived vulnerability</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Likely or very likely to get breast cancer in the next 10 y (verbal), %</td>
<td>5</td>
<td>4</td>
<td>.7</td>
</tr>
<tr>
<td>Chances of getting breast cancer in the next 10 y, 0-100 (numerical), mean (SD)</td>
<td>35 (20)</td>
<td>29 (19)</td>
<td>.007</td>
</tr>
<tr>
<td>Likely or very likely to get breast cancer in the next 10 y compared with other women of the same age, %</td>
<td>15</td>
<td>8</td>
<td>.03</td>
</tr>
<tr>
<td>Worried about getting breast cancer in the next 10 y, %</td>
<td>10</td>
<td>3</td>
<td>.001</td>
</tr>
<tr>
<td><strong>Breast cancer risk factors, %</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First-degree relative with breast cancer</td>
<td>14</td>
<td>8</td>
<td>.06</td>
</tr>
<tr>
<td>High risk ($\geq 1.66$ 5-y Gail score)</td>
<td>3</td>
<td>3</td>
<td>.8</td>
</tr>
<tr>
<td><strong>Health behaviors, %</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ever had a mammogram</td>
<td>84</td>
<td>87</td>
<td>.4</td>
</tr>
<tr>
<td>Ever had an abnormal mammogram result</td>
<td>24</td>
<td>18</td>
<td>.2</td>
</tr>
<tr>
<td>Ever used HRT</td>
<td>23</td>
<td>17</td>
<td>.1</td>
</tr>
<tr>
<td>Currently using HRT</td>
<td>17</td>
<td>11</td>
<td>.09</td>
</tr>
<tr>
<td>Currently smoking cigarettes</td>
<td>30</td>
<td>13</td>
<td>.001</td>
</tr>
<tr>
<td>Depression, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CES-D scale score $\geq$10</td>
<td>38</td>
<td>24</td>
<td>.003</td>
</tr>
</tbody>
</table>

*HRT indicates hormone replacement therapy; CES-D, Center for Epidemiological Studies-Depression.
The prevalence of depressive symptoms in this community sample of women was higher than reported in the general population. This high prevalence of depressive symptoms was noted in a similar community sample of women (aged 45-54 years) and could be attributed to the overlap between depression and climacteric symptoms, which are both measured using the abbreviated Center for Epidemiological Studies–Depression scale.

An informed decision to use tamoxifen for chemoprevention would require a thorough risk-and-benefit analysis. Although tamoxifen has protective antiestrogenic effects on the breast, its other estrogenic effects can be harmful, although these are estimated to be very low. For example, through its estrogenic effect on the uterus, tamoxifen can increase the risk of endometrial cancer, depending on age and menopausal status. On the other hand, tamoxifen can decrease cholesterol levels and increase bone density in postmenopausal women. Tamoxifen can also increase the risk of stroke, pulmonary embolism, and deep vein thrombosis. In addition, use of tamoxifen has been associated with a decrease in bone density among premenopausal women, worsening climacteric symptoms in postmenopausal women, and an increase in the incidence of depression.

Results of this study should be considered in light of a few limitations. First, interest in taking a drug to prevent breast cancer was measured by self-report and was not assessed behaviorally. Our estimates are likely much higher than if we assessed rates of tamoxifen prescriptions for chemoprevention. Second, hysterectomy status was not examined and might be a potential factor related to interest in chemoprevention because women without a uterus do not have to consider the potential risk of endometrial cancer associated with tamoxifen use. Third, we used only single-item measures to assess perceptions of breast cancer risk and worry. Although age is the most important risk factor for breast cancer, in this study we addressed interest in chemoprevention of women in their early 40s and 50s. Further research is needed to explore interest in using chemoprevention for breast cancer among women aged 60 years and older. Finally, because the major purpose of our study was to obtain data about mammography use, we could not collect in-depth

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information about correlates of tamoxifen use that would have been ideal. Many women in their 40s and 50s say that they are interested in breast cancer chemoprevention despite the fact that for most of them, consideration of tamoxifen therapy seems completely unwarranted. This unwarranted interest in chemoprevention might stem from their overestimation of breast cancer risk. Women need help assessing their breast cancer risks and risk-reducing options and weighing the risks and benefits of taking tamoxifen. Physicians might need guidance about how to counsel patients about breast cancer risk and assessing the appropriateness of tamoxifen treatment. Decision aids for breast cancer chemoprevention are needed to maximize the scarce time of health care professionals. Such decision aids should address breast cancer risks, perceptions of risk and worry about breast cancer, HRT use, and smoking status and should take into account additional risk factors for endometrial cancer, thromboembolic events, and depression. Ultimately, there are no right or wrong answers for most patients. The goal should be to help individuals decide what is best for them.

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