Breast Cancer Screening Controversies

Beverly B. Green, MD, MPH, and Stephen H. Taplin, MD, MPH

Background: The Cochrane Collaborative, a respected independent review body, recently published a meta-analysis of the effectiveness of screening mammography in decreasing breast cancer mortality. Based on the results of two controlled trials they judged to be of medium validity, they concluded that screening mammography was unjustified. In contrast, the US Preventive Services Task Force recently updated their screening recommendations, and based on a meta-analysis of the same randomized controlled trials, they recommended screening mammography for all women starting at age 40 years. Additionally, the Canadian Task Force on Preventive Health Care no longer recommends breast self-examination (BSE). This article reviews the controversies regarding breast cancer screening.

Methods: We performed a systematic review of the literature using keywords and cross-referencing articles. We also used automated data from the Breast Cancer Screening Program at Group Health Cooperative to determine the sensitivity of the clinical breast examination (CBE) at our institution. For the latter we included all cancers diagnosed within 1 year of a screening examination and then determined which of those had been found by CBE.

Results: Although most screening studies have shown that mammography decreases breast cancer death, there are controversies about the validity of some of the randomized controlled screening mammography trials. These controversies have led to different conclusions about the efficacy of screening mammography. Evidence is limited about the optimal interval for screening mammography. No studies have directly tested the efficacy of the CBE in decreasing breast cancer mortality. At Group Health Cooperative, 8% of all diagnosed breast cancers were found by the CBE alone (negative mammogram). Whether this 8% incremental increase in case finding leads to decreased breast cancer deaths is unknown. There is good evidence that training women to perform BSE does not increase breast cancer diagnoses or decrease breast cancer deaths.

Conclusion: There are limitations to randomized controlled trials and meta-analyses. The balance of the evidence still favors screening mammography in women aged 40 years and older at least every 2 years. The independent incremental benefit of the CBE, when added to mammography, in decreasing breast cancer mortality is unknown. Population-based education and training to do BSE are unlikely to lead to decreased breast cancer deaths. Many women find their own breast cancers, so women need to pay attention to symptoms or changes in their breasts. (J Am Board Fam Pract 2003;16:233–41.)

In 2001 Gotzsche and Olsen 1,2 published the results of their meta-analysis on the effectiveness of mammography screening for the Cochrane Collaborative, a respected independent review body. Their conclusion was, “screening for breast cancer with mammography is unjustified.” In February 2002, the US Preventive Services Task Force published the results of their analysis of the evidence and updated recommendations for mammography screening.3 In contrast, they recommend that all women aged 40 years and older have screening mammography every 1 to 2 years based on fair evidence (a B recommendation). For clinical breast examination (CBE) and breast self-examination (BSE), they stated that the evidence was insufficient to make a recommendation. Last year, however, the Canadian Task Force on Preventive Health Care gave BSE a D recommendation, meaning that there is good evidence that it causes harm.4

In contrast, the American Cancer Society recommends that women aged 40 years and older should have an annual mammogram and an annual CBE by their health care professional, and should do a monthly BSE. The patient should have a CBE a short time before the mammogram. Women aged
20 to 39 years should have a CBE every 3 years and should perform a monthly BSE. Why is there so much disagreement about the value of mammography, CBE, and BSE and how should we be advising our patients?

**Methods**

A systematic search of the evidence was undertaken using keywords and checking cross-references. We also used internal data from Group Health Cooperative of Puget Sound, a not-for-profit health care system in the state of Washington, serving more than 600,000 members with six screening centers. Since 1985, Group Health Cooperative has had a Breast Cancer Screening Program that provides comprehensive screening and coordinated follow-up care. The patient receives a CBE by a specially trained nurse, has a 2-view mammogram, and is instructed on BSE. Abnormal results are systematically observed until breast cancer is diagnosed or ruled out. Data points exist for mammography, CBE results, and breast cancer case detection as measured by center-detected and non–center-detected cancers. From the Breast Cancer Screening Program file, a computerized study file was created in which each patient was assigned a number stripped of all identifiers. These data were used to determine which cancers were detected by the use of mammography, CBE, or both. We used Group Health Cooperative data from 1992 to 1994 to determine the performance of the CBE. Oestreich et al used the same Group Health Cooperative database for the years 1988 to 1993 in her article describing the predictors of sensitivity of the CBE and can be referred to for more details as to the methodology.

**Results**

**Disease Burden**

Breast cancer still continues to be the most common nonskin malignancy for women, and although it ranks second after lung cancer for the most common cancer death, it causes more lost years of potential life than any other cancer, primarily because it occurs at a younger age than most cancers. At the age of 50 years women have about a 2.0% chance of developing breast cancer during the next 10 years, and this risk goes up to about 2.5% by the age of 65 years. For a woman of average risk, lifetime breast cancer incidence is 7.8% and mortality is 2.3%. Breast cancer mortality is declining in industrial nations where screening mammography is the standard of care. Some think this decline is primarily from advances in treatment, whereas others believe that earlier detection improves treatment options.

**Effectiveness of Screening Mammography**

The randomized controlled trials evaluated by the Gotzsche and Olsen for the Cochrane Collaborative and the US Preventive Services Task Force are listed in Table 1. Table 1 illustrates that almost all the trials reported decreased risk of breast cancer death in women who were randomized to receive screening. For several of the trials, however, the confidence interval included 1, meaning the benefit was not always at a 95% significance level. Even though these studies were large, the numbers of breast cancers were relatively small compared with the number screened. Meta-analysis combines the results, increasing statistical power to find important smaller benefits. The results of meta-analyses have generated most of the controversy.

There have been several meta-analyses of mammography screening before the Gotzsche and Olsen analysis. Kerlikowske et al in 1995 combined the results of the randomized trials and case-control studies and used a statistical model to combine data. They found a protective benefit for mammography of 0.74 (95% CI, 0.45–0.77) for women aged 50 to 74 years, or a 26% reduction in breast cancer mortality. They did not find a benefit for women aged 40 to 49 years. The model controlled for length of follow-up, screening interval, number of mammography views, duration of screening, whether CBE was done, and the date the study began, so that the estimate is based on comparable studies. In contrast to subsequent reviews, they did not exclude any of the major randomized trials based on the study validity.

In their meta-analysis Gotzsche and Olsen obtained additional data and records from most of the trials and performed a detailed assessment of randomization, baseline comparability of the cases and controls, exclusions after randomization, and consistency in the reported numbers of women after randomization. The authors of each trial were informed about the outcome of the initial assessment, and additional information was requested. If all the above criteria were fulfilled, the study was consid-
Table 1. Summary of Key Characteristics of Randomized Controlled Trials of Mammography Screening.

<table>
<thead>
<tr>
<th>Study (year began)</th>
<th>Age (yr)</th>
<th>Screening Provided</th>
<th>Screening Rounds (of Mammography) (No)</th>
<th>Screening Interval (mo)</th>
<th>Views</th>
<th>Compliance Rounds (%)</th>
<th>Crossovers (Controls Who Had Mammography) (%)</th>
<th>Follow-up (yr)</th>
<th>Breast Cancer Mortality* RR</th>
<th>Absolute Risk Reduction in Breast Cancer Mortality (per 1,000)</th>
<th>Number Needed to Screen 10 yr†</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIP11,12 (1963) N = 61,000</td>
<td>40–64 M + CBE vs UC</td>
<td>4</td>
<td>12</td>
<td>2</td>
<td>1 = 67</td>
<td>Data not available</td>
<td>13</td>
<td>0.83 (0.7–1.0)</td>
<td>1.4193</td>
<td>916</td>
<td></td>
</tr>
<tr>
<td>Malmo13 (1976) N = 68,000</td>
<td>45–70 M vs UC</td>
<td>9</td>
<td>18–24</td>
<td>1–2</td>
<td>1 = 74</td>
<td>25</td>
<td>11–13</td>
<td>0.81 (0.62–1.07)</td>
<td>1.0127</td>
<td>1,185</td>
<td></td>
</tr>
<tr>
<td>Two-Country14 (1977) N = 126,000</td>
<td>40–74 M vs UC</td>
<td>3</td>
<td>24–33</td>
<td>1</td>
<td>1 = 89</td>
<td>13</td>
<td>10</td>
<td>0.68</td>
<td>1.8095</td>
<td>553</td>
<td></td>
</tr>
<tr>
<td>Stockholm15,16 (1981) N = 60,000</td>
<td>40–64 M vs UC</td>
<td>2</td>
<td>24–28</td>
<td>1</td>
<td>1 = 81</td>
<td>Controls offered screening yr 5</td>
<td>7.4</td>
<td>0.71 (0.4–1.2)</td>
<td>0.3369</td>
<td>1,378</td>
<td></td>
</tr>
<tr>
<td>Gothenburg17 (1982) N = 40,000</td>
<td>39–59 M vs UC</td>
<td>5</td>
<td>18</td>
<td>1–2</td>
<td>1 = 85</td>
<td>20</td>
<td>8</td>
<td>0.86</td>
<td>0.3286</td>
<td>2,435</td>
<td></td>
</tr>
<tr>
<td>Edinburgh18,19 (1979) N = 45,000</td>
<td>45–64 M + CBE vs UC</td>
<td>4</td>
<td>24</td>
<td>1–2</td>
<td>1 = 66</td>
<td>Data not available</td>
<td>14</td>
<td>0.71 (0.54–1.37)</td>
<td>0.945</td>
<td>1,482</td>
<td></td>
</tr>
<tr>
<td>Canada120,21 (1980) N = 50,000</td>
<td>40–49 M + CBE vs single CBE</td>
<td>4–5</td>
<td>12</td>
<td>2</td>
<td>1 = 100</td>
<td>25</td>
<td>13</td>
<td>0.98 No reduction</td>
<td>Not applicable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canada22,22 (1980) N = 40,000</td>
<td>50–59 M + CBE vs CBE</td>
<td>4–5</td>
<td>12</td>
<td>2</td>
<td>1 = 100</td>
<td>16</td>
<td>10.5</td>
<td>1.14 No reduction</td>
<td>Not applicable</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

RR = relative risk, N = number of participants, M = screening mammography, CBE = clinical breast examination, UC = usual care.

*Length of follow-up reported for various times up to 20 years. Data estimates were closest to 10-year point.

†Number needed to screen corrected for 10 years of screening.
erred to be high-quality data. Medium-quality data had only minor violations, and bias was not suspected or could be corrected for. If the authors detected inaccuracies of randomization, exclusions, comparability of study arms, or consistency in study numbers and bias was suspected that could not be corrected with available data, the study was considered to be of poor quality. Flawed studies that had major violations and documented important bias were excluded from all analyses.

The trials were rated based on these characteristics. The Health Insurance Plan of Greater New York (HIP) study was judged to be flawed, because people with previous breast cancer were allegedly not excluded from the control group in some cases. They also concluded that there was probable bias in the assignment of the cause of death, because the screened group was more closely observed. Their assessment contended that the Edinburgh study was also flawed. Before patients were allotted to this study, physicians in the intervention group decided whether the woman was appropriate for screening. There were some inconsistencies in randomization of the physicians and the patients, with some physicians being reallocated to the other intervention group, poor comparability of the cases and controls, and the lack of autopsy data. They also noted problems with randomization (both allocation and exclusions) in the Two-Country, Gothenburg, and Stockholm studies and determined these to be of poor validity. The only studies that were judged to be of medium validity were the Canadian study and Malmo studies. In their meta-analysis they did not include the most recent follow-up report from the Malmo study, because of inconsistencies in the numbers of women randomized compared with previous reports.

When the outcomes of the Canadian and Malmo studies were combined, screening mammography did not decrease breast cancer deaths for women younger than or older than 50 years at either 7 or 13 years of follow-up. In contrast, when the studies of poor validity were included in the meta-analysis (Two-Country, Gothenburg, and Stockholm) the results were positive. There was a significant decrease in breast cancer mortality, 15% at 7 years (RR [relative risk] = 0.85, 95% CI [confidence interval] 0.73–0.99) and 20% (RR = 0.80, 95% CI, 0.71–0.89) at 13 years. The protective effect of screening was slightly higher for women older than 50 years (25% reduction at 7 years of follow-up and 24% at 13 years).

The US Preventive Services Task Force performed their own meta-analysis of the same trials that were analyzed by Gotzsche and Olsen for the Cochrane Collaborative. The criteria for rating the quality of the study included assembly of comparable groups, maintenance of comparable groups, and the outcome assessment. The Edinburgh trial was rated as poor because many more cases than controls were of a high socioeconomic status. Excluding the Edinburgh trial from the meta-analysis did not change the results significantly. For the other seven studies, the US Preventive Services Task Force was concerned about the flaws found by the Gotzsche and Olsen review, but they did not feel the flaws influenced the outcomes significantly. The pooled effect of the seven valid studies that included women aged 40 years and older was 0.84 (95% CI, 0.77–0.91), which is a 16% reduction in breast cancer deaths in women who were screened. The number to screen (NNS) to prevent 1 death was 1,008 (95% CI, 531–2,128). For women aged 50 years and older, the summary relative risk was 0.78 (95% CI, 0.70–0.87) after 14 years of observation. The number to screen to prevent 1 death was 838 (95% CI, 494–1,676).

The Canadian studies have been the only randomized trials to show no benefit from screening mammography. Different from the other trials of mammography screening, they assumed for women aged 50 years and older, mammography was beneficial. For this age-group a CBE was done yearly and compared with CBE and mammography yearly with no difference in breast cancer mortality found. A possible interpretation of their negative findings is that a thorough CBE (5 to 10 minutes per breast) is as effective a screening tool as mammography. For women aged 40 to 49 years, for whom the efficacy of screening mammography is less certain, controls received one baseline CBE, whereas intervention subjects had annual mammograms and CBEs. There was no benefit from screening for this age-group.

Criticisms about the Canadian studies include using a volunteer population (not a population invited for screening) after randomization at the initiation of the intervention, and many more cases than controls had breast cancers with a poorer prognosis (four or more lymph nodes involved). That CBE was done before randomization possibly
introduced bias. Also fewer than expected breast cancer deaths occurred in both groups; as a result, the study was not sufficiently powered to show an effect size of less than 40% difference in mortality.\textsuperscript{26} In contrast, all the other studies that included women younger than 50 years found some benefit, with the US Preventive Services Task Force finding a 15% reduction in breast cancer deaths of 0.85 (95% CI, 0.73–0.99; NNS = 1,792). It took at least 8 years to see these effects, so some women were already older than 50 years before they benefited from screening. The Canadian study was excluded in a second analysis, because its participants were prescreened volunteers, and they might have been different from women in the general population. This increased the risk reduction of a breast cancer death to 20% and decreased the NNS to 1,385.

There is also controversy about whether the Malmo trial can be labeled as a negative study. Positive results emerged and persisted after the eighth year for women aged 55 to 69 years, which were published by Andersson in 1997.\textsuperscript{27} Because of inconsistencies of the number of patients assigned to each group, as compared with their previous article, Gotzsche and Olsen did not include it in their meta-analysis. It has been argued that had the data been analyzed differently, important benefits of screening would have emerged.\textsuperscript{28}

Little is known about the optimal interval for mammography. In a recently published trial women aged 50 to 62 years who received baseline mammograms were randomized to either receive annual screening for 3 years or a single mammogram 3 years after the baseline study. After 3 years of follow-up, there were no differences between the groups for late-stage disease or breast cancer mortality. Although the study was quite large, (more than 70,000 women participated), power calculations were not available, and so a smaller effect might have been missed. It is also possible that it would take longer than 3 years to see a benefit.\textsuperscript{29} Of the screening trials, the Swedish Two-Country study had the longest screening interval (24–33 months) and the greatest reduction in breast cancer mortality. The HIP trial and the Canadian studies both used 12-month intervals. The HIP trial found a 17% reduction in breast cancer mortality, whereas the Canadian studies found no benefit of mammography. While these studies do not provide conclusive evidence, they suggest that the benefit of annual mammography is likely to be small, if it exists.

### Limitations of Controlled Trials and Meta-Analyses

Randomized controlled trials are not true efficacy studies in the classic sense of testing a technology under ideal conditions. In the breast cancer screening studies, compliance with screening was not complete and often decreased further after several rounds of screening. All the trials reported crossover contamination with control groups receiving screening. This crossover was as high as 25% in the Malmo and Canadian studies, in part because the benefits of screening were being advertised. Additionally, randomized controlled trials are analyzed as intent-to-treat studies. The study analyzed women by the group to which they were assigned, regardless of whether they complied with the intervention as intended. This design controls for any selection biases that might be related to characteristics of those that participate but underestimates the efficacy of the intervention. Tabar et al.\textsuperscript{30} reanalyzed the Swedish Two-Country trial and found a 63% reduction in breast cancer death among women who actually underwent screening.

Meta-analyses also have limitations. The interventions combined differed; some included CBEs, whereas others did not. Some used one-view mammography and others used two views. Number of screening rounds and intervals between screenings also were not the same. The degree of compliance and crossover contamination varied. A meta-analysis combines results from many studies, but as studies are excluded, the analytic power decreases. In the Gotzsche and Olsen meta-analysis, their conclusions were based on only two studies. Additionally, unlike the investigators in a clinical trial, the authors in meta-analyses know the outcomes of the individual studies before they begin their analysis, which might introduce subtle forms of bias. Because of all these potential concerns, the results of meta-analyses are generally thought to be of a weaker grade of evidence than a well-conducted controlled trial.

When this much controversy exists, it means at a minimum there are some unanswered questions and most likely insufficient evidence to determine an answer. A reasonable conclusion to the current controversy might be that there are problems with most of the mammography trials. This is not to say mammography does not work; it simply acknowl-
edges that there are weaknesses in the studies. The more important question is whether the weaknesses are so serious that they invalidate the results. The US Preventive Services Task Force and others did not think that was the case. Based on the complexities of these analyses and the weight of the evidence, we agree with the US Preventive Services Task Force findings.

Adverse Events Related to Mammography

The Gotzsche and Olsen meta-analysis also noted that women in the screening groups were 23% more likely to have radical mastectomy, 35% more likely to have simple mastectomy or lumpectomy, and 25% more likely to have radiotherapy. Screening will pick up cancers that might have remained silent and treatment would not have been needed. It is generally not possible to determine which women could be spared treatment in favor of decreasing the mortality rates for others. Also, women have a 6.5% chance of a false-positive screening result with each mammogram, leading to increased visits, follow-up mammographies, and biopsies. After 10 years, women have a 1 in 3 chance of having had a false-positive mammogram (24%) or CBE (13%). The result is increased anxiety in some women and increased patient-initiated visits. In general, women are willing to tolerate false-positive results because of beliefs about the favorable aspects of screening. Many women, however, might overestimate the benefits and might not be aware of the potential harms of screening. It is possible the current controversy has tempered women’s faith in mammography, and it will be important to find out how much. There are some concerns that controversy will discourage women from seeking mammography.

The Effectiveness of the Clinical Breast Examination

The US Preventive Services Task Force recommends routine mammography every 1 to 2 years starting at age 40 years, but CBE received an I rating, meaning there is insufficient evidence to make a recommendation. There are no studies that have directly compared CBE with no screening. Screening trials have either combined CBE with mammography or used mammography alone. Much of what we know about the benefit of the CBE is derived from indirect evidence based on its performance. The sensitivity of CBE ranges from 69% in picking up breast cancers in women who have not had much screening to about 31% in those that have had regular screening. The performance of CBE by age is shown in Table 2. The sensitivity of the CBE is higher in women younger than 50 years (in contrast to screening mammography, which is less sensitive in younger women). Because breast cancer is not as common in women younger than 50 years, however, a mass found in an older woman on CBE is four times more likely to be a cancer than is a mass in a younger woman. About 3 to 5 women of each 100 women examined will have a false-positive CBE.


<table>
<thead>
<tr>
<th>Age</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive Predictive Value (%)</th>
<th>Incremental Increase in Case Finding (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40–49 yr</td>
<td>37.5</td>
<td>96.5</td>
<td>2.1</td>
<td>8.3</td>
</tr>
<tr>
<td>50–64 yr</td>
<td>36.0</td>
<td>97.3</td>
<td>8.8</td>
<td>9.6</td>
</tr>
<tr>
<td>65–74 yr</td>
<td>23.6</td>
<td>97.3</td>
<td>9.3</td>
<td>3.7</td>
</tr>
<tr>
<td>75+ yr</td>
<td>30.6</td>
<td>97.5</td>
<td>9.9</td>
<td>8.1</td>
</tr>
<tr>
<td>All ages combined</td>
<td>30.6</td>
<td>97.1</td>
<td>7.1</td>
<td>7.0</td>
</tr>
</tbody>
</table>

Note: all clinical breast examinations (CBEs) were performed by registered nurses in screening centers. Only invasive breast cancers were analyzed. A total of 42,647 women had CBEs and 297 cases of invasive breast cancer were diagnosed, screened and nonscreened.

*Sensitivity—percent of invasive breast cancers detected by CBE, unrelated to mammography.

†Specificity—percent of women without invasive breast cancer with normal findings on CBE.

‡Positive predictive value—percent of positive CBEs that were invasive breast cancer.

§Percent of cases of breast cancer found by CBE alone, eg, mammography negative and CBE.
cancers detected by CBE are somewhat less (59% to 84% at 10 years) than those detected by mammography alone (77% to 93%).

Barton, comparing a variety of studies, showed that providers who took longer than 2 minutes for the CBE and had more correct techniques (a systematic search pattern, thoroughness, varying palpation pressure, three fingers, finger pads, and circular motion) performed significantly better than those who did not (P < .001) in silicone models.

The Effectiveness of Breast Self-Examination
The US Preventive Services Task Force also gave breast self-examination an I recommendation in its 2002 update. The Canadian Task Force on Preventive Health Care however gave it a D recommendation, stating that there was no evidence of benefit and some evidence of harm and they no longer recommend it.

The best study of BSE is a controlled trial of Chinese women who were randomized by workplace. Women in the BSE intervention group received intensive instruction and follow-up. After 5 years of follow-up, there were no differences in breast cancer incidence or mortality rates between the two groups. There were two times as many biopsies in the BSE group. This study has recently been completed, and the final outcomes are unchanged. In another ongoing study, Russian women who were randomized by workplace to receive an education session and information campaign had similar proportions of late-stage breast cancer and breast cancer deaths as those who did not receive the intervention. The US Preventive Services Task Force was concerned about the applicability of these studies to women in the United States. Additionally, results might be different for a highly motivated woman.

The observational studies include a large cohort study in which women were asked a single question, whether they did BSE. No difference for breast cancer mortality was found between those who responded yes and those who responded no (RR = 1.04, 95% CI, 0.95–1.13). A case-control study asked women with advanced-stage breast cancer questions about their practice of BSE and compared their responses with those without breast cancer. Doing BSE and the frequency of BSE were not associated with a decreased risk of late-stage disease. Women who practiced BSE with high proficiency did have a decreased risk of breast cancer deaths, but the retrospective design could not eliminate the possibility of recall bias.

Women do find breast cancers by self-examination. In women ages 40 to 45 years (before many have routine mammography), 65% of the cancers were self-detected. Self-detection was divided equally between those who did routine BSE and those who accidentally found a breast lump. In a series of 3,197 invasive cases of cancer diagnosed in Wisconsin from 1988 to 1990, women detected their own cancers 55% of the time. Tumors found by mammography or CBE were much more likely to be localized.

Conclusion
What to Advise Women About Mammography?
There has been much media coverage about the controversies surrounding screening mammography, and many women might have questions. The simplest message to tell women is that some studies showing screening mammography to be beneficial had errors which might have affected the quality of the results. Scientists do not agree how important these errors were.

The Gotzsche and Olsen meta-analysis represents a single meta-analysis that looks at the same trials reviewed by other groups. The US Preventive Services Task Force did not find most of these same trials to have major deficiencies and therefore reached different conclusions, eg, that screening mammography is effective in decreasing breast cancer deaths. Although the evidence is not as strong as we would like, there are no convincing studies that breast cancer screening does not work compared with no screening at all.

Should Physicians Perform Clinical Breast Examinations?
There is insufficient evidence to answer this question. CBE increases case finding of breast cancer, but it is unknown whether this increased case finding improves outcomes. Using better techniques and taking a longer time to do the examination improve the accuracy of CBE.

Should Physicians Instruct Women Patients In Breast Self-Examinations?
Currently there is no convincing data that BSE increases breast cancer detection rates or decreases...
breast cancer mortality. Some women might want to do all they can to detect breast cancer earlier. For women who choose to do BSE, they should be assisted in learning to do it proficiently. If they choose not to do it, they do not need to feel guilty; however, they should not ignore such breast symptoms as bleeding, discharge, pain, or a lump found by accident.

References

26. Boyd NF, Jong RA, Yaffe MJ, Trichtler D, Lockwood G, Zylak CJ. A critical appraisal of the Cana-


