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Mammography for symptomless women – not so wise?

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ABSTRACT

For over 20 years, medical authorities have urged asymptomatic peri/postmenopausal women to undergo frequent mammography. In a recent paper, the authors tested whether early detection reduced the incidence of previously undetected late-stage cancer and saved lives. They compared data from 1976–1978 (pre-mammography) to 2006–2008 US data. Annualized age-adjusted cancer data per 100 000 women $\geq$ 40 years old showed that early-stage cancer detection cases increased, from 105 to 178 cases of localized disease and from seven to 56 cases of ductal carcinoma *in situ*; regional invasive late-stage cancer diminished slightly, from 85 to 78 cases; distant late-stage cancer showed no decline, with 17 cases in both 1976–1978 and 2006–2008; breast cancer mortality declined by 20 per 100 000 women, from 71 to 51 cases.

Since mammogram detection produced no decline in late-stage distant cancer presentations (with high mortality rates), and an extremely modest reduction in invasive regional disease (with low mortality rates), improved treatment, not early detection, is the likely engine for the lives saved.

Overdiagnosis – estimated at about 70 000 US women per year – inflicts terror, and triggers biopsies followed by unnecessary medical treatments that are painful, potentially harmful, may impair immune responsiveness and increase the risks for other cancers. Given the availability of annual clinical exams, routine mammography screening should now be seriously questioned.

For more than 20 years, medical societies and groups like the American Cancer Society have urged asymptomatic postmenopausal women to undergo frequent mammography screenings under the propositions that breast cancer incidence is increasing, and early detection saves lives. In sharp contrast, Drs Bleyer and Welch conclude in their recent paper[1]: 'Our study raises serious questions about the value of screening mammography. It clarifies that the benefit of mortality reduction is probably smaller, and the harm of overdiagnosis probably larger than has been previously recognized.'

The authors tested whether early detection and presumably the prompt treatment that follows, in women age 40 and beyond, reduce the incidence of (previously undetected) *late-stage cancer.* Using the Survey for Epidemiology and End Results (SEER9) as their source, they chose as a baseline the period 1976–1978, before widespread screening had begun in the US, and compared data to the more recent 2006–2008 period. That later period was after the transient increase and decline in rates affected by the WHI negativity toward hormone therapy vis-à-vis breast cancer.

Key findings, comparing the annualized age-adjusted incidence of cases per 100 000 women in 1976–1978 to that of 30 years later in 2006–2008, showed:

(1) *Early-stage cancer* increased from 112 to 234 cases – an absolute increase of 122 cancers per 100 000 women. This reflects both more localized disease detection, which rose from 105 to 178 cases, and an increase of ductal carcinoma *in situ* (DCIS) detection from 7 to 56 cases;
(2) Regional invasive *late-stage cancer* diminished only slightly, from 85 to 78 cases;
(3) Distant *late-stage cancer* showed no decline, with 17 cases both in 1976 and 2006;

Meanwhile, *mortality from breast cancer* has declined by 20 cases per 100 000 women, from 71 to 51 per 100 000 women over the age of 40 per year. The smaller decrease in

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cases of late-stage cancer (of only 8 cases per 100 000), compared to the more dramatic decline in mortality (of 20 cases per 100 000), suggests to Drs Bleyer and Welch that effective treatment accounts for most of the decline in mortality, rather than mammography pre-empting late-stage disease through early detection.

The authors conclude that, if the underlying disease burden has not changed, then only eight of the 122 additional early-stage cancers were destined to progress to advanced disease, suggesting that an excess of 122 − 8 = 114 cases per 100 000 women were diagnosed. Some portion of this excess represents *overdiagnosis* – the finding of cancer that would never have come to clinical attention or significance without mammograms. The woman's natural immune defenses would either have arrested the disease or reversed it.

While the results show little benefit that can be attributed to widespread screening, they do show substantial harm. Drs Bleyer and Welch used several assumptions to test what proportion of cases of early localized cancer was due to overdiagnosis. This number matters a great deal as a woman with early-stage disease, who undergoes screening, detection and treatment before her own defense system can eliminate it, is at risk for potentially unnecessary and even harmful medical treatments.

To challenge their own hypothesis, the authors used several increasingly more extreme assumptions *in favor* of the benefits of screening to calculate the proportion of women who experienced overdiagnosis. In their 'best-guess estimate', they assume the underlying disease burden has increased by 0.25% per year over the 30-year span, while, as shown by the SEER trends, the late-stage metastatic disease has not been reduced, and the invasive late-stage regional cancers have diminished by only 8%. Since the early-stage discovery increased by 100%, this scenario suggests that over 30% of these cases would not have become clinically manifest without mammography. This translates to 1.3 million US women in the past 30 years who were told that they had breast cancer but had no life-threatening disease: over 70 000 women in 2008.

Mammograms have produced no decline at all in the late-stage distant cancers that carry a high mortality rate, and an extremely modest reduction in cases of regional disease, which have shown low mortality rates. Therefore, recommendations for routine mammography screening can now be seriously questioned by those who ask: Are asymptomatic women better served by annual clinical exams without mammography? That seems to be the case. And that is the important contribution made by this paper.

OVERVIEW

Overdiagnosis does medical harm to women. They suffer the terror of being told that they have breast cancer and then are subjected to biopsies and subsequent medical treatments that are painful, sometimes fraught with adverse events, detrimental to their overall well-being, inhibit their sexual relationship, and impair their immune system. Recent work has demonstrated that routine cancer treatments elevate the risk for future cancers in other organs, most likely because they inhibit the immune function designed to combat the ever-increasing, age-related mutations that lead to cancer[2–4]. And perhaps worse, women thus treated may erroneously believe they have been 'saved' when actually they have been harmed.

In 2009, a comprehensive analysis from the Cancer Control Division of the US CDC, presented data including all cases of breast cancer in women in 92.1% of the US population for 6 consecutive years. Dr Eheman and colleagues cited methodology stating that, in these data, one woman could be counted more than once, i.e. if she presented with more than one primary tumor[5]. Interestingly, the average age-adjusted annualized DCIS rates in the parallel age groups of the Eheman data (1999–2004) and for the 2006–2008 time period in the Bleyer and Welch article are identical (56 per 100 000 women). This is noteworthy given the fact that postmenopausal hormone use had decreased precipitously by 2006–2008, a fact that has been held responsible for a perceived decrease in early-stage breast cancer rates post-WHI in other publications using SEER data[6].

Interest groups, like the Susan Komen Race for the Cure, have encouraged public perception influencing the current routine reimbursement of the screenings and the medical treatment that follows. As a consequence, huge financial resources have gone to the construction and staffing of mammography centers, leading to both widespread marketing and media advertising to get women to use them. This investment in staff, equipment, research centers and advertising has created a huge and powerful group of financial stakeholders in maintaining this status quo. It has also supplied an enormous pool of data suggesting that over 1 million women in the US have undergone invasive and toxic treatments that likely diminished the quality of their health rather than enhanced it.

We agree with Drs Bleyer and Welch: women and their health advisers can now be clear that routine mammography is not necessarily in women's best interest.

TAKE-HOME MESSAGES

- Credible data showing most mortality reduction in breast cancer results from improved medical treatment rather than from early mammographic detection.
- Routine mammography screening produces substantial overdiagnosis that inflicts arguably more harm than good.
- Routine mammography screening should be seriously questioned, since annual clinical examinations (without mammograms) can find disease before the development of distant disease and result in less overdiagnosis that triggers unnecessary and potentially harmful treatment.

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