False-positive mammography and depressed mood in a screening population: findings from the New Hampshire Mammography Network

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ABSTRACT

Background False positives occur in approximately 11% of screening mammographies in the USA and may be associated with psychologic sequelae.

Methods We sought to examine the association of false-positive mammography with depressed mood among women in a screening population. Using data from a state-based mammography registry, women who completed a standardized questionnaire between 7 May 2001 and 2 June 2003, a follow-up questionnaire between 19 June 2003 and 8 October 2004 and who received at least one screening mammogram during this interval were identified. False positives were examined in relation to depressed mood.

Results Eligibility criteria were met by 13,491 women with a median age of 63.9 (SD = 9.6). In the study population, 2,107 (15.62%) experienced at least one false positive mammogram and 450 (3.34%) met criteria for depressed mood. Depressed mood was not significantly associated with false positives in the overall population (OR = 0.96; 95% confidence interval (CI) = 0.72–1.28), but this association was seen among Non-White women (OR = 3.23; 95% CI = 1.32–7.91).

Conclusion Depressed mood may differentially affect some populations as a harm associated with screening mammography.

Keywords depression, mammography, screening

Introduction

Women aged 40 and above are encouraged to receive screening mammograms every 1–2 years.¹ Screening mammography can help identify breast cancer at an early stage, resulting in decreased breast cancer mortality.¹ Current debates about screening mammography recommendations necessarily incorporate risk of harms into optimizing risk–benefit assessments. Screening can result in false positives, in which mammograms are ambiguous or appear to show disease indicators in the absence of breast cancer.¹ An estimated 11% of individual screening mammograms in the USA result in false positives.²–⁴ Risk increases with the number of mammograms an individual receives; estimates range from a cumulative false-positive risk of 20.8% in 10 mammograms over 20 years of screening⁵ to 49.1% over 10 years of regular screening.⁶ The chance of receiving a false positive also increases with multiple risk factors and more frequent screening.⁷ Investigations into an association between this relatively common event and depression or depressive symptoms appear to be both limited and mixed.

Although a conclusive link between a diagnosis of depression and false positives has not been found, psychologic distress and symptoms of depression may follow false positives.⁸ In a meta-analysis, Brewer et al.⁹ found that seven of nine published studies showed no effect of false positives on depression. The remaining two showed significant but conflicting results, with one finding an increase and the other a decrease in depressive symptoms following false positives.⁹ Non-significant increases in depressive symptoms were seen from 6 weeks to a year after follow-up from a
false-positive screening. Women who had received a false positive were more likely to have seen a mental health professional in the 12 months prior to interview participation.

Given the large number of women of mammography screening age, it is important to understand the potential harms of screening. In this study, we sought to examine the association of false-positive mammography and depressed mood in a screening population.

### Methods

#### Participants and data

Data for this study were collected from participants in the New Hampshire Mammography Network (NHMN) and the New Hampshire (NH) Women for Health study. The NHMN is a voluntary, state-based registry that has been collecting information on patient demographic characteristics, breast-imaging examinations and related pathology in NH since 1996. The NHMN links to the New Hampshire State Cancer Registry, recording breast cancers in a pathology database. The design and development of the registry have been described in detail elsewhere.

The NHMN was used to identify healthy women for participation in NH Women for Health, a prospective study of hormone replacement therapy and breast cancer risk. Women who consented to participate in NH Women for Health were mailed a baseline questionnaire between 7 May 2001 and 2 June 2003 and a follow-up questionnaire between 19 June 2003 and 8 October 2004. The 12-page questionnaires included validated questions capturing information about health and health behaviors. NH Women for Health questionnaire responses were linked to NHMN mammography data for all participants. For purposes of this study, only women who had completed and returned both the baseline and the follow-up questionnaires and received at least one screening mammogram in the NHMN network between 7 May 2001 and 8 October 2004 were included in the analysis. All data collection forms and procedures were approved by Dartmouth’s Committee for the Protection of Human Subjects.

#### Outcome measure

##### Depressed mood classification

The Women’s Health Questionnaire (WHQ) was included in the baseline and follow-up questionnaires, and used to determine the depressed mood and anxiety scores. The WHQ is a validated self-report instrument geared towards women at midlife. It includes 36 questions about depressed mood, somatic symptoms, anxiety and fears, vasomotor symptoms, sleep problems, sexual behavior, menstrual symptoms, memory and concentration and attractiveness. The WHQ has been previously validated against the General Health Questionnaire and the SF-36 using populations similar in age to the women in our sample (mean = 63.9, SD = 9.6). Based on previous reports, a score of 0.43 or above on the depressed mood subscale of the WHQ indicated depressed mood. Women were categorized as ‘no depressed mood’ if they had a score below 0.43 at both the baseline and the follow-up questionnaires. Women were categorized as ‘newly depressed mood’ if they had a score below 0.43 at baseline and a score of 0.43 or above at follow-up.

##### Exposure measurements

#### Mammogram status classification

False positive was derived by combining the radiologist’s assessment (BIRADS®) and recommendations from the NHMN mammography report with any existing pathology reports. If a participant had more than one screening mammogram between the baseline and the follow-up questionnaires, the mammography report proximal to the follow-up questionnaire was used; if a participant had more than one pathology report, the most severe outcome was used. Mammogram status was categorized as ‘normal’ if the NHMN mammography report indicated a recommendation of routine annual/biennial scheduling. Mammogram status was categorized as ‘false positive’ if the mammography report recommended follow-up with imaging, clinical breast examination, biopsy, fine-needle aspiration or surgical consultation, with no existing pathology report or an associated pathology report indicating a non-cancerous category. Women were excluded from analysis if a cancerous categorization was identified in their pathology report.

##### Anxiety score

Anxiety scores were calculated from the WHQ anxiety subscale, a self-report measure in the follow-up questionnaire, and categorized into tertiles (0, 0.01–0.25 and >0.25).

##### Covariates

Age was calculated using the date of the follow-up questionnaire and the participant’s date of birth. Participants
were then categorized into age groups <50, 50–59, 60–69, 70–79 and 80+. Race, family history of breast, ovarian, endometrial and colon cancer, insurance status, education and perceived risk of developing breast cancer in the next 10 years were collected by self-report in the follow-up questionnaire. Due to the low numbers of participants in all categories besides White, race was made into a dichotomous variable of ‘White’ and ‘Non-White’. Family history of several cancers was categorized into two variables: those who indicated a family history of breast cancer in at least one relative and those who indicated a family history of ovarian, endometrial, or colon cancer in at least one relative. Insurance status (private, Medicare, Medicaid, HMO, none and other) was dichotomized into ‘None’ or ‘Any’, as survey responses were not mutually exclusive. Education level was defined as ‘<high-school graduate’, ‘high-school graduate/GED’, ‘some college/technical school’ and ‘college/postgraduate’. Participants were queried about their perceived personal risk of developing breast cancer in the next 10 years compared with other women their age, using a Likert scale with possible responses ranging from ‘Much lower chance’ to ‘High chance’. These responses were collapsed into two categories, ‘Little or no chance’ and ‘Some or high chance’.

**Statistical analysis**

Descriptive analyses were performed to determine the association of the following variables with newly depressed mood: age, race, education, insurance status, family history of breast cancer, family history of other cancer, anxiety score, mammogram status and perceived risk of developing breast cancer in the next 10 years. A P-value of <0.05 was used to determine the significance. Those variables significantly associated with depressed mood were also compared with false positives to determine confounding. We hypothesized, a priori, that family history and insurance status may be effect modifiers of false positives and depressed mood; this was investigated using logistic regression and stratification of the independent variables. Based on observations, race was also checked for effect modification.

Multiple logistic regression analysis was used to assess the association of false positives and anxiety with depressed mood while adjusting for age, race, insurance status, education, family history of breast and other cancer and perceived breast cancer risk. We also created race-stratified models of depressed mood as a function of mammogram status to examine effect modification by race. Joint effects of mammogram status, anxiety and race on depressed mood was examined by creating a six-level interaction term between race (White and Non-White) and anxiety score (0, 0.01–0.25 and >0.25) and stratifying by mammogram status. The reference group for the interaction term was White, no anxiety (score = 0). Models were adjusted for age, education, insurance status, family history of breast and other cancer and perceived breast cancer risk. Odds ratios and 95% confidence intervals (CI) are presented. All analyses were performed using SAS software version 9.1.20

**Results**

**Participants**

Of the 25,226 women who completed both questionnaires, 1817 women were excluded due to a personal history of breast cancer, breast augmentation and/or breast reduction, indicated on a mammograms before completion of the follow-up questionnaire. We found 14,285 women who had at least one screening mammogram with complete mammographic status assessment between the baseline and the follow-up questionnaires. One hundred sixty-seven of these women were missing depressed mood information from either questionnaire, and were removed from the analysis. We excluded 627 women who reported depressed mood on the baseline questionnaire. Our final analytic population was 13,491 women.

**Depressed mood at follow-up**

Newly depressed mood was identified in 450 women (3.34%) on the follow-up questionnaire. Women with depressed mood were younger, less educated, less likely to be insured, had a higher anxiety score and had a higher perceived breast cancer risk compared with women without depressed mood. Women with and without depressed mood had similar characteristics of race, family history of breast and other cancer and did not differ by mammogram status (Table 1). Women with depressed mood were more likely to have an anxiety score in the mid-tertile range of 0.01–0.25 (OR = 4.96; 95% CI = 3.62–6.81), and had a 20-fold increased risk of developing depressed mood with anxiety scores greater than 0.25 (OR = 19.88; 95% CI = 4.91, 26.51). Women with depressed mood also had a significantly increased perceived risk of developing breast cancer (OR = 1.32; 95% CI = 1.01, 1.74) compared with women without depressed mood (Table 2).

**False positives, race, anxiety and depressed mood**

Compared with women who had normal mammograms, women with a false positive were younger (41% under 60 versus 38% under 60; P < 0.0001), less likely to be insured
Participants were categorized as either White ($n = 12,525, 93.67\%) or Non-White, comprised self-identified Black ($n = 27, 0.20\%) , Asian ($n = 30, 0.22\%$), Pacific Islander ($n = 7, 0.05\%$), American/Alaskan Indian ($n = 185, 1.37\%$), Hispanic ($n = 447, 3.31\%$) and Other ($n = 210, 1.56\%$). Categories were tallied by individual response to avoid inflation, as some women self-identified with more than one group. Results of a race-stratified multiple logistic analysis found that Non-White women were three times more likely to have depressed mood following a false-positive mammogram ($OR = 3.23; 95\% CI = 1.32, 7.91$), with a 10-fold increase in risk of depressed mood with anxiety scores.

### Table 1 Overall study participants ($n = 13,491$) characteristics by depression

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total ($n = 13,491$), $n (\text{Col%})^a$</th>
<th>No depression ($n = 13,041$, (96.66%)), $n (\text{Col%})^a$</th>
<th>New depression ($n = 450$, (3.34%)), $n (\text{Col%})^a$</th>
<th>$P$-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;50</td>
<td>798 (5.92)</td>
<td>751 (5.76)</td>
<td>47 (10.44)</td>
<td>&lt;0.0001</td>
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<tr>
<td>50–59</td>
<td>4377 (32.44)</td>
<td>4203 (32.23)</td>
<td>174 (38.67)</td>
<td></td>
</tr>
<tr>
<td>60–69</td>
<td>4617 (34.22)</td>
<td>4491 (34.44)</td>
<td>126 (28.00)</td>
<td></td>
</tr>
<tr>
<td>70–79</td>
<td>2898 (21.48)</td>
<td>2831 (21.71)</td>
<td>67 (14.89)</td>
<td></td>
</tr>
<tr>
<td>80+</td>
<td>801 (5.94)</td>
<td>765 (5.87)</td>
<td>36 (8.00)</td>
<td></td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>12,525 (93.67)</td>
<td>12,111 (93.69)</td>
<td>414 (93.03)</td>
<td>0.31</td>
</tr>
<tr>
<td>Non-white</td>
<td>847 (6.33)</td>
<td>816 (6.31)</td>
<td>31 (6.97)</td>
<td></td>
</tr>
<tr>
<td><strong>Insurance status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>214 (1.60)</td>
<td>198 (1.53)</td>
<td>16 (3.64)</td>
<td>0.001</td>
</tr>
<tr>
<td>Any</td>
<td>13,134 (98.40)</td>
<td>12,710 (98.47)</td>
<td>424 (96.36)</td>
<td></td>
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<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;High school</td>
<td>505 (3.78)</td>
<td>473 (3.66)</td>
<td>32 (7.16)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>High school or GED</td>
<td>3704 (27.69)</td>
<td>3564 (27.57)</td>
<td>140 (31.32)</td>
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</tr>
<tr>
<td>Some college</td>
<td>4106 (30.70)</td>
<td>3953 (30.58)</td>
<td>153 (34.23)</td>
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</tr>
<tr>
<td>College or post-college</td>
<td>5060 (37.83)</td>
<td>4938 (38.20)</td>
<td>122 (27.29)</td>
<td></td>
</tr>
<tr>
<td><strong>Family history of breast cancer</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>10,499 (77.82)</td>
<td>10,160 (77.91)</td>
<td>339 (75.33)</td>
<td>0.20</td>
</tr>
<tr>
<td>Any</td>
<td>2992 (22.18)</td>
<td>2881 (22.09)</td>
<td>111 (24.67)</td>
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</tr>
<tr>
<td><strong>Family history of cancer</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>11,220 (83.17)</td>
<td>10,858 (83.26)</td>
<td>362 (80.44)</td>
<td>0.12</td>
</tr>
<tr>
<td>Any</td>
<td>2271 (16.83)</td>
<td>2183 (16.74)</td>
<td>88 (19.56)</td>
<td></td>
</tr>
<tr>
<td><strong>Anxiety score</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No anxiety</td>
<td>8858 (66.58)</td>
<td>8785 (68.23)</td>
<td>73 (17.02)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>0.01–0.25</td>
<td>2809 (21.11)</td>
<td>2695 (20.93)</td>
<td>114 (26.57)</td>
<td></td>
</tr>
<tr>
<td>&gt;0.25</td>
<td>2167 (16.30)</td>
<td>1395 (10.83)</td>
<td>242 (56.41)</td>
<td></td>
</tr>
<tr>
<td><strong>Chance of breast cancer in next 10 years</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Little or None</td>
<td>10,936 (86.31)</td>
<td>10,607 (86.54)</td>
<td>329 (79.66)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Some or high</td>
<td>1734 (13.69)</td>
<td>1650 (12.46)</td>
<td>84 (20.34)</td>
<td></td>
</tr>
<tr>
<td><strong>Mammogram status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>11,384 (84.38)</td>
<td>11,004 (84.38)</td>
<td>380 (84.44)</td>
<td>0.97</td>
</tr>
<tr>
<td>False positive</td>
<td>2107 (15.62)</td>
<td>2037 (15.62)</td>
<td>70 (15.56)</td>
<td></td>
</tr>
</tbody>
</table>

*Chi-square $P$-values given for the association of participants’ characteristics with depression.

*aColumn percents presented for non-missing values. Missing $n (%)$: race, 119 (1%); insurance, 143 (1%); education, 116 (1%); anxiety score, 187 (1%) and chance of breast cancer, 821 (6%).

$^b$Family history of cancer includes endometrial, ovarian and/or colorectal cancer.

(1\% versus 2\%; $P = 0.03$), more likely to have a family history of breast cancer (25\% versus 22\%; $P < 0.001$) and had an increased perceived breast cancer risk (20\% versus 13\%; $P < 0.0001$) (data not shown).
greater than 0.25 (OR = 9.58; 95% CI = 3.54, 25.96) (Table 2). Among White women, the odds ratios for depressed mood by mammogram status, anxiety score and perceived risk of developing breast cancer were similar to the overall results.

The joint effects of mammogram status, race and anxiety score on depressed mood are demonstrated in Table 3. The interaction term for each of the fully adjusted models of mammogram status, normal and false positive, was significant ($P < 0.0001$). With respect to the reference group in each mammogram strata, the odds of developing newly depressed mood increased across levels of anxiety for both White and Non-White women. However, the odds for depressed mood increased similarly for White women regardless of mammogram status across all levels of anxiety, whereas odds for depressed mood among Non-White women increased significantly following a false positive compared with a normal mammogram for each increasing level of anxiety.

### Discussion

#### Main finding of this study

We hypothesized that false positives would be associated with depressed mood in this population. While this has not been seen in past research, distress and symptoms of depression seem to be common. This, along with the mixed results of past studies, our large sample size and the condensed time span between false positives and the follow-up questionnaire suggested a priori that any existing association could be found.
We did not find an association between false positives and depressed mood in our population overall. However, there was a significantly increased likelihood of newly depressed mood after a false positive among Non-White women. We also found that the risk of depressed mood following a false-positive mammogram may be modified by anxiety, with an especially pronounced effect of anxiety in interaction with race. These associations have not previously been reported, but there is a paucity of published data on the relationship between false positives and depression among racial groups.

What is already known on this topic
The few studies that have analyzed psychologic outcomes of false positives by race have found some limited differences. Jatoi et al. found that among Hispanics, non-Hispanic Whites and non-Hispanic Blacks, Black women were more likely to feel restless than White women, and had a non-significant trend towards feelings of worthlessness. Alderete et al. found that among White, Asian, Latina and Black women, Black women were more likely than Whites or Latinas to report depressive symptoms within a year following an abnormal mammogram. Asian women were less likely to report recent depressive symptoms than all groups. Overall, however, little is known about the experiential aspects of breast cancer screening among minority women, particularly among Hispanic and American Indian women, a large proportion of the Non-White women in our sample. Attitudes towards breast cancer and screening are multifactorial, and may differ among women of different race/ethnicities in part as a function of differing family and community experiences with cancer, health literacy, access to screening and cultural beliefs about risks and mortality. These differences may be related to variation in psychologic outcomes.

What this study adds
Our results, indicating that Non-White women may be at increased risk for depressed mood following a false positive, and that women with moderate to high anxiety, especially Non-White women, may be particularly vulnerable to depressed mood following a false-positive mammogram, add compelling evidence to the need for more detailed investigations into risk–benefit analyses of screening mammography, particularly as these effects were seen despite our small Non-White population.

Limitations of this study
This study had limitations that may have influenced the findings. Our data came from a screening population, with women maintaining scheduled preventive health care and willing and able to comply with time-consuming study guidelines. This sample may not, therefore, be representative of the general screening-age population. Additionally, NH is largely rural with a primarily White population, further limiting generalizability to other screening populations. The small minority population reflected in the sample led us to group all Non-White women into one category, limiting interpretability of the effects of race/ethnicity in different minority groups. Much of the information on health and health behaviors collected, including the primary outcome measure, was based on self-report, and therefore subject to potential bias. Finally, differences in practice cannot be determined in this study, and may have influenced the mammographic interpretation leading to classification of false positives as well as each woman’s experience and psychologic outcome.

Despite these limitations, the study also had considerable strengths. Foremost among these is the large population from which data were drawn. While NH’s population is relatively homogeneous, this homogeneity may increase the internal validity of the findings. The condensed timeframe of the observations, spanning from Spring 2001 to Fall 2004, strengthens the association of outcomes to the exposure, as a relatively short time could have passed between mammography and the depression assessment and overall data collection. Finally, the WHQ, used to assess depressed mood and anxiety, is well validated for women in midlife.

Conclusion
In this study, we sought to examine the association of false-positive mammography and depressed mood in a screening population. This association was not found in the sample overall. However, we did find an association between false-positive mammography and depressed mood among Non-White women. We also found significant risk modification by anxiety and the interaction of race and anxiety, which suggests that an interplay of factors may be related to harms of screening.

False positives will occur in the course of regular screening. It is therefore important to better understand the potential psychologic implications of screening mammography. Identifying women at the greatest risk of harms associated with screening will help patients and providers to use screening most appropriately for each woman.
Funding

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References


