BREAST CANCER RISK ASSESSMENT & SCREENING IN AVERAGE-RISK WOMEN

TAYLOR BERTSCHY, DO  JANUARY 31, 2018 DIDACTIC LECTURE
BREAST CANCER

• MOST COMMONLY DIAGNOSED CANCER IN WOMEN IN THE US
• SECOND LEADING CAUSE OF CANCER DEATH IN AMERICAN WOMEN
• LIFETIME RISK IS 12% (1 IN 8)
• 5-YEAR SURVIVAL RATE 90%

• RISK FACTORS
  • FEMALE
  • FAMILY HISTORY
  • KNOWN GENE MUTATION
  • PRIOR BREAST BX WITH ATYPICAL HYPERPLASIA/LOBULAR CARCINOMA IN SITU
  • EARLY MENARCHE, LATE MENOPAUSE, NULLIPARITY
  • ESTROGEN & PROGESTIN HRT (WHI)
BREAST DISORDERS

- ATYPICAL DUCTAL HYPERPLASIA, ATYPICAL LOBULAR HYPERPLASIA, AND LOBULAR CARCINOMA IN SITU
  - 4-FOLD RISK OF SUBSEQUENT INVASIVE CANCER

- DENSE BREASTS DX BY MAMMOGRAPHY HAVE MODESTLY INCREASED RISK OF BREAST CANCER

- WOMEN S/P THERAPEUTIC CHEST RADIATION B/T 10 AND 30YO ARE AT INCREASED RISK OF BREAST CANCER

How breast cancer develops

Ductal breast cancer is thought to begin with abnormal tissue growth in a breast duct. A. Normal breast duct is shown. B. An overgrowth of normal cells may develop in the breast duct (hyperplasia). C. Over time, the cells develop abnormalities and continue accumulating (atypical hyperplasia). D. The abnormal cells may continue to change in appearance and multiply, evolving into ductal carcinoma in situ. E. Eventually, the cancer cells grow beyond the breast duct (invasive ductal carcinoma) and can spread to other areas of the body.
INDIVIDUAL RISK ASSESSMENT

- PATIENT HISTORY
  - REPRODUCTIVE RISK FACTORS, PRIOR BIOPSIES, IONIZING RADIATION, FAMILY HISTORY
- POTENTIAL INCREASED RISK SHOULD HAVE FURTHER ASSESSMENT
  - GAIL (WWW.CANCER.GOV/BRCAPRO), BREAST & OVARIAN ANALYSIS OF DISEASE INCIDENCE & CARRIER ESTIMATION ALGORITHM, IBIS, CLAUS MODEL

- USED TO IDENTIFY WOMEN WHO MAY BENEFIT FROM GENETIC COUNSELING, ENHANCED SCREENING, OR RISK REDUCTION STRATEGIES
Box 1. Breast Cancer Risk Factors

- Family history of breast cancer, ovarian cancer, or other hereditary breast and ovarian syndrome-associated cancer (e.g., prostate cancer, pancreatic cancer)
- Known deleterious gene mutation
- Prior breast biopsy with specific pathology
  - Atypical hyperplasia (lobular or ductal)
  - Lobular carcinoma in situ
- Early menarche
- Late menopause
- Nulliparity
- Prolonged interval between menarche and first pregnancy
- Menopausal hormone therapy with estrogen and progestin (decreased risk with estrogen alone)
- Not breastfeeding
- Increasing age
- Certain ethnicities (e.g., increased risk of BRCA mutation in Ashkenazi Jewish women)
- Higher body mass index
- Alcohol consumption
- Smoking
- Dense breasts on mammography
- Prior exposure to high-dose therapeutic chest irradiation in young women (10–30 years old)

Risk Tool

(Click a question number for a brief explanation, or read all explanations.)

1. Does the woman have a medical history of any breast cancer or ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS) or has she received previous radiation therapy to the chest for treatment of Hodgkin lymphoma?  
   - Yes
   - No

2. Does the woman have a mutation in either the BRCA1 or BRCA2 gene, or a diagnosis of a genetic syndrome that may be associated with elevated risk of breast cancer?  
   - Yes
   - No
   - Unknown

3. What is the woman's age?
   - Under 35
   - 35 to 44
   - 45 to 49
   - 50 to 59
   - 60 to 69
   - 70 to 79
   - 80 or older

   *This tool only calculates risk for women 35 years of age or older.*

4. What was the woman's age at the time of her first menstrual period?
   - 7 to 11
   - 12 to 13
   - 14 to 15
   - 16 to 17
   - 18 to 19
   - 20 or older

5. What was the woman's age at the time of her first live birth of a child?
   - No births
   - 1
   - 2
   - 3
   - 4
   - 5 or more

6. How many of the woman's first-degree relatives - mother, sisters, daughters - have had breast cancer?
   - 0
   - 1
   - 2
   - 3
   - 4

7. Has the woman ever had a breast biopsy?
   - Yes
   - No

   7a. How many breast biopsies (positive or negative) has the woman had?
   - n/a
   - 1
   - 2
   - 3 or more

7b. Has the woman had at least one breast biopsy with atypical hyperplasia?
   - Yes
   - No

   8. What is the woman's race/ethnicity?
   - White
   - Black
   - Hispanic
   - Asian
   - Other

   8a. What is the sub race/ethnicity?
   - Microsoft Remote Desktop
Limitations:

- These risk calculations have been validated for women in the U.S. who are screened regularly for breast cancer.
- Risk estimates do not allow one to say precisely which woman will develop breast cancer. In fact, some women who develop breast cancer may have lower estimated risks than some women who do not develop breast cancer.
- The BCRAT was not designed to estimate risk for:
  - Women with a prior diagnosis of breast cancer, lobular carcinoma in situ (LCIS), or ductal carcinoma in situ (DCIS).
  - Women who have received previous radiation therapy to the chest for treatment of Hodgkin lymphoma.
  - Women with gene mutations in BRCA1 or BRCA2, or those who are known to have certain genetic syndromes that increase risk for breast cancer.

For women with any of the above medical history other methods to estimate breast cancer risk are better. See 'About the Tool' section for a list of references.

- Recent immigrants from parts of rural Asia, such as rural China, probably have lower risks than projected by the tool.

Race/Ethnicity:

White

5 Year Risk of Developing Breast Cancer

- This woman (age 35): 0.4%
- Average woman (age 35): 0.3%

Explanation

Based on the information provided (see below), the woman's estimated risk for developing invasive breast cancer over her lifetime (to age 90) is 12.4% compared to a risk of 12.6% for a woman of the same age and race/ethnicity from the general U.S. population.

Lifetime Risk of Developing Breast Cancer

- This woman (to age 90): 12.4%
- Average woman (to age 90): 12.6%

Explanation

Based on the information provided (see below), the woman's estimated risk for developing invasive breast cancer over the next 5 years is 0.4% compared to a risk of 0.3% for a woman of the same age and race/ethnicity from the general U.S. population. This calculation also means that the woman's risk of NOT getting breast cancer over the next 5 years is 99.6%.
MAMMOGRAPHY

Sensitivity and specificity of mammography are higher in older women than in younger
MAMMOGRAPHY AS PREFERRED SCREENING MODALITY

- **BEST STUDIED AND ONLY IMAGING TECHNIQUE THAT HAS BEEN SHOWN TO DECREASE MORTALITY**
- **MAY MISS UP TO 20% OF UNDERLYING BREAST CANCERS**
- **SUPPLEMENT WITH ULTRASOUND OR MRI**

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**Table 1** Performance Measures for 1,960,130 Screening Mammography Examinations* Performed in the US From 2002 to 2006 by Age, Based on Breast Cancer Surveillance Consortium Data as of 2009

<table>
<thead>
<tr>
<th>Age</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Recall</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>40–44</td>
<td>73.6%</td>
<td>88.2%</td>
<td>11.8%</td>
<td>1.4%</td>
</tr>
<tr>
<td>45–49</td>
<td>80.3%</td>
<td>89.0%</td>
<td>11.2%</td>
<td>2.5%</td>
</tr>
<tr>
<td>50–54</td>
<td>82.4%</td>
<td>90.5%</td>
<td>9.7%</td>
<td>3.2%</td>
</tr>
<tr>
<td>55–59</td>
<td>84.6%</td>
<td>91.5%</td>
<td>8.8%</td>
<td>4.4%</td>
</tr>
<tr>
<td>60–64</td>
<td>84.9%</td>
<td>91.9%</td>
<td>8.5%</td>
<td>5.5%</td>
</tr>
<tr>
<td>65–69</td>
<td>84.6%</td>
<td>92.3%</td>
<td>8.0%</td>
<td>6.2%</td>
</tr>
<tr>
<td>70–74</td>
<td>84.7%</td>
<td>92.9%</td>
<td>7.5%</td>
<td>7.3%</td>
</tr>
<tr>
<td>75–89</td>
<td>86.6%</td>
<td>93.4%</td>
<td>7.1%</td>
<td>9.1%</td>
</tr>
<tr>
<td>Total</td>
<td>83.5%</td>
<td>90.9%</td>
<td>9.3%</td>
<td>4.1%</td>
</tr>
</tbody>
</table>

*R: mammography examinations indicated by the radiologist to be for screening with bilateral routine views (excludes women with other mammograms within the last 6 months, and women with breast implants, a prior mastectomy, or a prior breast cancer diagnosis).

Sensitivity is the percentage of biopsy-confirmed breast cancers that had a positive interpretation, i.e., American College of Radiology (ACR) Breast Imaging Reporting and Data System (BI-RADS) category 4, 5, or 6 with a recommendation for immediate follow-up.

Specificity is the percentage of non-cancers that had a negative interpretation, i.e., ACR BI-RADS category 1, 2, or 3 with no recommendation for follow-up.

Recall is the percentage of examinations with a positive interpretation.

PPV (positive predictive value) is the percentage of examinations with a positive interpretation that result in a tissue diagnosis of cancer.

Cancers = examinations with a tissue diagnosis of ductal carcinoma in situ or invasive cancer within 1 year and before the next screening mammography examination.

Noncancers = examinations without a tissue diagnosis of cancer within 1 year or before the next screening examination, whichever occurs earlier.

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BENEFITS OF MAMMOGRAM

• DECREASES BREAST CANCER MORTALITY

• REDUCED RISK OF ADVANCED BREAST CANCER IN WOMEN 50 & OLDER

• INCREASES LIFE EXPECTANCY
  • UP TO DATE: “WHILE BREAST CANCER MORTALITY HAS DROPPED DRAMATICALLY SINCE THE 1980’S, IT IS THOUGHT THAT IMPROVEMENTS IN TREATMENT ARE MORE LIKELY RESPONSIBLE THAN SCREENING.”

<table>
<thead>
<tr>
<th>Age Range (years)</th>
<th>Relative Risk (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>39–49</td>
<td>0.92 (0.75–1.02)</td>
</tr>
<tr>
<td>50–59</td>
<td>0.86 (0.68–0.97)</td>
</tr>
<tr>
<td>60–69</td>
<td>0.67 (0.54–0.83)</td>
</tr>
<tr>
<td>70–74</td>
<td>0.80 (0.51–1.28)</td>
</tr>
</tbody>
</table>

Table 2. Mammographic Screening and Breast Cancer Specific Mortality Reduction by Age Group

ADVERSE CONSEQUENCES OF MAMMOGRAPHY

- FALSE POSITIVE
- 10YR CUMULATIVE FALSE POSITIVE RATE 61% W/ ANNUAL SCREENING
- 42% WITH BIENNIAL SCREENING
- NEED FOR BIOPSY 7% FOR ANNUAL & 5% W/ BIENNUAL
- DENSE BREASTS & COMBINATION HRT ASSOCIATED W/ INCREASED LIKELIHOOD OF FALSE POSITIVE AGED 40-49
- ANXIETY
- DISCOMFORT
- OVERDIAGNOSIS & TREATMENT
- RADIATION EXPOSURE
SELF BREAST EXAM

• NOT RECOMMENDED IN AVERAGE RISK WOMEN
  • RISK OF HARM FROM FALSE POSITIVE & LACK OF EVIDENCE OF BENEFIT

• BREAST SELF-AWARENESS
  • WOMAN'S AWARENESS OF THE NORMAL APPEARANCE AND FEEL OF HER BREASTS

• 50% OF CANCER CASES IN WOMEN >50YO & 71% OF CASES IN WOMEN <50YO ARE DETECTED BY WOMEN THEMSELVES
CLINICAL BREAST EXAM

- Offered in context of shared decision-making

- 55 false positives for 1 case of cancer detected
  - 25-39yo
    - 1-3 YR
  - 40 or over
    - Annually

- ACS
  - No longer recommends due to lack of evidence for benefit, combined with increased false positive test

- USPSTF
  - Insufficient evidence to assess the benefits and harms

- NCCN
  - Continues to recommend clinical breast exam
WHEN SHOULD SCREENING MAMMOGRAPHY BEGIN?
AVERAGE-RISK WOMEN (ACOG)

- Offered screening mammogram starting at age 40yo; no later than 50yo
- Risk-benefit balance improves with age
- Should have screening mammography every 1 or 2 years
- Annual screening improves outcomes at the cost of callbacks and biopsies (particularly in younger women)
- Continue until at least age 75yo
- As long as overall health is good and have a life expectancy of 10 years or longer

**Table 5. Lifetime Benefits and Harms of Annual Versus Biennial Screening Mammography Per 1,000 Women Screened**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Annual Screening for Those Aged 50–74 Years</th>
<th>Biennial Screening for Those Aged 50–74 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fewer breast cancer deaths, n</td>
<td>9 (5–10)</td>
<td>7 (4–9)</td>
</tr>
<tr>
<td>Life-years gained</td>
<td>145 (104–180)</td>
<td>122 (75–154)</td>
</tr>
<tr>
<td>False-positive test results, n</td>
<td>1,798 (1,706–2,445)</td>
<td>953 (830–1,325)</td>
</tr>
<tr>
<td>Unnecessary breast biopsies, n</td>
<td>228 (219–317)</td>
<td>146 (121–205)</td>
</tr>
<tr>
<td>Overdiagnosed breast tumors, n</td>
<td>25 (12–68)</td>
<td>19 (11–34)</td>
</tr>
</tbody>
</table>

*Model results compared with no screening
"BIENNIAL SCREENING MAMMOGRAPHY, PARTICULARLY AFTER AGE 55 YEARS, IS A REASONABLE OPTION TO REDUCE THE FREQUENCY OF HARMs, AS LONG AS PATIENT COUNSELING INCLUDES A DISCUSSION THAT WITH DECREASED SCREENING COMES SOME REDUCTION IN BENEFITS.

HEAVY EMPHASIS ON FLEXIBILITY AND SHARED DECISION MAKING

ACOG PRACTICE BULLETIN ISSUED ON JUNE 22"
Table 1. Recommendations for Breast Cancer Screening in Average-Risk Women

<table>
<thead>
<tr>
<th>Test Type</th>
<th>American College of Obstetricians and Gynecologists</th>
<th>U.S. Preventive Services Task Force</th>
<th>American Cancer Society</th>
<th>National Comprehensive Cancer Network</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Clinical Examination</td>
<td>May be offered* every 1–3 years for women aged 25–39 years and annually for women 40 years and older.</td>
<td>Insufficient evidence to recommend for or against.†</td>
<td>Does not recommend‡</td>
<td>Recommend every 1–3 years for women aged 25–39 years. Recommend annually for women 40 years and older.</td>
</tr>
<tr>
<td>Mammography Initiation Age</td>
<td>Offer starting at age 40 years.§ Initiate at ages 40–49 years after counseling, if patient desires. Recommend by no later than age 50 years if patient has not already initiated.</td>
<td>Recommend at age 50 years.¶ Age 40–49 years: The decision to start screening mammography in women before age 50 years should be an individual one.¶</td>
<td>Offer at ages 40–45 years.§ Recommend at age 45 years.*</td>
<td>Recommend at age 40 years.</td>
</tr>
<tr>
<td><strong>ACOG</strong></td>
<td><strong>USPsTF</strong></td>
<td><strong>ACS</strong></td>
<td><strong>NCCN</strong></td>
<td></td>
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<tr>
<td>------------------------</td>
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<td></td>
</tr>
<tr>
<td><strong>Mammography screening interval</strong></td>
<td>Annual or biennial§</td>
<td>Biennial‖</td>
<td>Annual for women aged 40–54 years†</td>
<td>Annual</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Biennial with the option to continue annual screening for women 55 years or older‡</td>
<td></td>
</tr>
<tr>
<td><strong>Mammography stop age</strong></td>
<td>Continue until age 75 years. Beyond age 75 years, the decision to discontinue should be based on a shared decision-making process that includes a discussion of the woman’s health status and longevity.</td>
<td>The current evidence is insufficient to assess the balance of benefits and harms of screening mammography in women 75 years and older.†</td>
<td>When life expectancy is less than 10 years‡</td>
<td>When severe comorbidities limit life expectancy to 10 years or less</td>
</tr>
</tbody>
</table>

*Offer in the context of a shared, informed decision-making approach that recognizes the uncertainty of additional benefits and harms of clinical breast examination beyond screening mammography.

†Category I recommendation

‡Qualified recommendation

§Decision between options to be made through shared decision making after appropriate counseling

‖Category B recommendation

§Category C recommendation. The Task Force notes that “Women who place a higher value on the potential benefit than the potential harms may choose to begin screening between the ages of 40 and 49 years.”

*Strong recommendation
### SUMMARY OF RECOMMENDATIONS

**LEVEL A**
- Women at average risk of breast cancer should be offered screening mammography starting @ age 40
- No earlier than 40yo
- No later than 50yo
- Should have mammogram every 1 or 2 years
- Biennial screening, particularly after 55yo, is reasonable
- Continue screening until at least age 75

**LEVEL B**
- Periodically assess breast cancer risk by reviewing patient’s history
- Women with increased risk should have further risk assessment
- Self-examination is not recommended

**LEVEL C**
- Screening clinical breast exam may be offered
- 25-39yo: 1-3 years
- >30: annually
- Counsel average-risk women about breast self-awareness
- Age alone should not be the basis to continue or discontinue screening
REFERENCES

• ACOG PRACTICE BULLETIN #179: BREAST CANCER RISK ASSESSMENT AND SCREENING IN AVERAGE-RISK WOMEN. JULY 2017

• UP TO DATE. SCREENING FOR BREAST CANCER: STRATEGIES AND RECOMMENDATIONS. 2018.