Update in Breast Cancer Screening
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Disclosure information: Update in Breast Cancer Screening
Karla Kerlikowske, MD

- Grant/Research support from: National Cancer Institute
- Primary care physician at San Francisco VA; VA follows USPSTF guidelines

Outline

- Screening mammography based on age
  - When to start
  - How often to screen
  - When to stop
- Risk-based screening
- What to know about breast density

When to start screening mammography

- ACR, SBI, ACOG -- starting at age 40
- ACS -- start at age 45
- USPSTF, CDC, AAFP – start at age 50
- Most European countries and Canada start age 50
Measures of benefits and harms

**Benefits**
- Relative reduction in breast cancer mortality
- Deaths averted from cancer or NNS to avert a cancer death
- Gain in life expectancy

**Harms**
- Discomfort, cost, anxiety, inconvenience of screening test
- False-positive imaging and invasive follow-up testing
- Detection/treatment of biologically insignificant lesions

Data sources, guideline grading system, member composition, value placed on benefits vs. harms

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**Meta-analyses of screening mammography trials -- film**

<table>
<thead>
<tr>
<th>Age</th>
<th>RR (95% CI)</th>
<th>NNS*</th>
</tr>
</thead>
<tbody>
<tr>
<td>39-49</td>
<td>0.92 (0.75-1.02)</td>
<td>3333</td>
</tr>
<tr>
<td>50-59</td>
<td>0.86 (0.68-0.97)</td>
<td>1300</td>
</tr>
<tr>
<td>60-69</td>
<td>0.64 (0.45-0.92)</td>
<td>470</td>
</tr>
<tr>
<td>70-74</td>
<td>0.80 (0.51-1.28)</td>
<td>800</td>
</tr>
<tr>
<td>All cause mortality</td>
<td>0.99 (0.97-1.002)</td>
<td></td>
</tr>
</tbody>
</table>

*Number women screened for 10 years to avert a breast cancer death

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**Advanced disease reduced in screened women ages >50**

<table>
<thead>
<tr>
<th>Stage III or greater</th>
<th>RR (95% CI)</th>
<th>NNS*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ages 39-49</td>
<td>0.92 (0.75-1.02)</td>
<td>3333</td>
</tr>
<tr>
<td>Ages &gt;50</td>
<td>0.86 (0.68-0.97)</td>
<td>1300</td>
</tr>
</tbody>
</table>

---

**BCSC outcomes per 10,000 digital screens**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>40–49</th>
<th>50–59</th>
<th>60–69</th>
<th>70–74</th>
</tr>
</thead>
<tbody>
<tr>
<td>False-positives</td>
<td>1212</td>
<td>393</td>
<td>301</td>
<td>301</td>
</tr>
<tr>
<td>False-negatives</td>
<td>10</td>
<td>11</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>Invasive cancer</td>
<td>22</td>
<td>35</td>
<td>58</td>
<td>72</td>
</tr>
<tr>
<td>DCIS</td>
<td>16</td>
<td>18</td>
<td>21</td>
<td>23</td>
</tr>
</tbody>
</table>
CISNET models

Models simulate events in individual life histories

No screening

Birth | Onset | Detectable by screening | Screen diagnosed | Clinically diagnosed | Death from breast cancer

Screening

Birth | Onset | Detectable by screening | Screen diagnosed | Clinically diagnosed | Death from breast cancer

Sojourn time | Lead time | Effect of screening

Model estimates of *biennial* digital screening mammogram effectiveness

<table>
<thead>
<tr>
<th>Age</th>
<th>FP/death averted</th>
<th>Biopsy/death averted</th>
<th>FP/LYG</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-74</td>
<td>136</td>
<td>21</td>
<td>7.8</td>
</tr>
<tr>
<td>40-49</td>
<td>576</td>
<td>58</td>
<td>19.2</td>
</tr>
</tbody>
</table>

*False positive = FP; Life year gains = LYG

ACS rationale for starting screening at age 45

- Observational studies – 20-40% reduction in breast cancer mortality
- Breast cancer mortality similar 45 vs. 50
  - 40-44 -- 13.2 per 100,000
  - 45-49 -- 20.6 per 100,000
  - 50-54 -- 30.8 per 100,000
  - 55-59 -- 41.3 per 100,000
- Harms higher in women 40-44 vs. 45-49


Model estimates of *biennial* digital screening mammogram effectiveness

<table>
<thead>
<tr>
<th>Age</th>
<th>Deaths averted*</th>
<th>No. screens</th>
<th>False positives*</th>
<th>Benign biopsy*</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-74</td>
<td>7.0</td>
<td>11,127</td>
<td>953</td>
<td>146</td>
</tr>
<tr>
<td>40-49</td>
<td>1.0</td>
<td>4,886</td>
<td>576</td>
<td>58</td>
</tr>
</tbody>
</table>

*per 1,000 women screened biennially

How often to screen with mammography

- ACR, SBI, ACOG - annual
- ACS - annual 45-54, biennial starting at 55
- USPSTF, CDC, AAFP - biennial from 50-74
- Most European countries biennial; Canada q2-3; United Kingdom q3

Potential harms of screening: false-positive mammogram and biopsy, overdiagnosis

![Image of mammography schedule]

Model estimates of digital screening mammogram effectiveness by interval

<table>
<thead>
<tr>
<th>Age &amp; Interval</th>
<th>Deaths* averted</th>
<th>LYG</th>
<th>FP*</th>
<th>Over* diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-74 y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 y</td>
<td>9</td>
<td>145</td>
<td>1,798</td>
<td>25</td>
</tr>
<tr>
<td>2 y</td>
<td>7</td>
<td>122</td>
<td>953</td>
<td>19</td>
</tr>
<tr>
<td>40-49 y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 y</td>
<td>1.3</td>
<td>47</td>
<td>1,143</td>
<td>5</td>
</tr>
<tr>
<td>2 y</td>
<td>1.0</td>
<td>30</td>
<td>576</td>
<td>2</td>
</tr>
</tbody>
</table>

*per 1,000 women screened over screening period

Overdiagnosis & overtreatment from screening mammography

- Cases not clinically detected in the absence of screening because of lack of progression or death from other causes
  - Canadian National Breast Screening Studies
    - 22% of invasive cancers
    - 37% invasive + DCIS
  - CISNET
    - 12% of detected cases

![Image of overdiagnosis and overtreatment]

Risk of late stage disease with 2 vs. 1 year screening interval

<table>
<thead>
<tr>
<th>Factor</th>
<th>Late stage</th>
<th>Tumor &gt;15mm</th>
<th>Lymph positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-49</td>
<td>+17</td>
<td>+10</td>
<td>+9</td>
</tr>
<tr>
<td>50-59</td>
<td>-2</td>
<td>+9</td>
<td>+5</td>
</tr>
<tr>
<td>60-69</td>
<td>-1</td>
<td>+13</td>
<td>-7</td>
</tr>
<tr>
<td>Premenopausal</td>
<td>+28*</td>
<td>+21*</td>
<td>+15</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>-5</td>
<td>+11*</td>
<td>-11</td>
</tr>
</tbody>
</table>

*P< 0.05

White, JNCI, 2004; Hubbard, Ann Intern Med, 2011; Miglioretti, Jama Oncol, 2015
Life expectancy for women -- 2010 US female life tables

Stopping ages based on comorbidities

When to stop screening mammography

 Lifetime risk of breast cancer death

<table>
<thead>
<tr>
<th>Risk %</th>
<th>Deaths averted†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>2.70</td>
</tr>
<tr>
<td>50-74 biennial</td>
<td>2.00 7</td>
</tr>
<tr>
<td>40-74 biennial</td>
<td>1.88 8</td>
</tr>
<tr>
<td>45-49 annual, 50-74 biennial</td>
<td>1.90 8</td>
</tr>
</tbody>
</table>

0.47 (−0.14-1.09) deaths averted per 1,000 women screened 40-49 - Age trial


When to stop screening mammography

- ACR, SBI, ACOG -- no upper age limit
- ACS -- continue if life expectancy ≥10 years
- USPSTF, CDC, AAFP -- age 74
- Most European countries and Canada stop at age 70-75

Comorbidities

<table>
<thead>
<tr>
<th>Ref</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age stop</td>
<td>74</td>
<td>76</td>
<td>72</td>
<td>70</td>
</tr>
<tr>
<td>Deaths averted*</td>
<td>0.9</td>
<td>1.0</td>
<td>0.8</td>
<td>0.9</td>
</tr>
<tr>
<td>Overdiagnosed*</td>
<td>0.8</td>
<td>0.7</td>
<td>0.6</td>
<td>0.9</td>
</tr>
</tbody>
</table>

*per 1,000 women screened

Mild: history of MI, acute MI, ulcer, or rheumatologic disease
Moderate: vascular disease, cardiovascular disease, paralysis or diabetes, or combinations of diabetes with MI, ulcer, or rheumatologic disease
Severe: AIDS, COPD, mild liver disease, severe liver disease, chronic renal failure, dementia, or congestive heart failure

Stopping ages based on comorbidities


Oeffinger et al, Jama, 2015
When should screening clinical breast examination be performed?

a) Starting at age 40, annually
b) Starting at age 50, annually
c) Starting at age 40, biennially
d) Starting at age 50 biennially
e) None of the above

Risk-based screening to optimize clinical outcomes

- Implement prevention strategies based on individual disease risk
- Assess breast cancer risk
- Determine if woman above or below average risk for her age
- Starting age and screening frequency based on risk

BCSC model ONLINE includes strong & prevalent risk factors

https://tools.bcsc-scc.org/BC5yearRisk/calculator.htm

Breast Imaging Reporting and Data System (BI-RADS)

- Almost entirely fat
- Scattered fibroglandular densities
- Heterogeneously dense
- Extremely dense

Engemann et al., Jama Oncol, In press
### 5-year risk (%) for 45-49y women

<table>
<thead>
<tr>
<th>Density</th>
<th>BCSC</th>
<th>5-yr risk</th>
<th>No Family Hx</th>
<th>Bx</th>
<th>Family Hx</th>
<th>No bx</th>
<th>Bx</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>.4</td>
<td>.3</td>
<td>.5</td>
<td>.5</td>
<td>.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b</td>
<td>0.8</td>
<td>0.7</td>
<td>1.0</td>
<td>1.0</td>
<td>1.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>c</td>
<td>1.2</td>
<td>1.0</td>
<td>1.7</td>
<td>1.6</td>
<td>2.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>d</td>
<td>1.6</td>
<td>1.3</td>
<td>2.1</td>
<td>2.1</td>
<td>3.3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Average risk 1.4% in next 5 years for woman 50-54 years

Tice et al., Ann Intern Med, 2008; Tice et al., JCO, 2015

### 5-year risk (%) for 50-54y women

<table>
<thead>
<tr>
<th>Density</th>
<th>BCSC</th>
<th>5-yr risk</th>
<th>No Family Hx</th>
<th>Bx</th>
<th>Family Hx</th>
<th>No bx</th>
<th>Bx</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>.5</td>
<td>.4</td>
<td>.7</td>
<td>0.7</td>
<td>1.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b</td>
<td>1.0</td>
<td>0.9</td>
<td>1.4</td>
<td>1.4</td>
<td>2.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>c</td>
<td>1.6</td>
<td>1.3</td>
<td>2.2</td>
<td>2.1</td>
<td>3.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>d</td>
<td>2.1</td>
<td>1.7</td>
<td>2.8</td>
<td>2.7</td>
<td>4.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Tice, Ann Intern Med, 2008; Tice, JCO, 2015

### Mammography Strategies Age 40-49

- 20% offer biennial screening with BCSC risk ≥1.4%
- Dense breasts & 1-2 risk factors
- Scattered density & 2 risk factors

<table>
<thead>
<tr>
<th>BI-RADS-c or d + 1 or 2 risk factors</th>
<th>BI-RADS-b + 2 risk factors</th>
<th>BI-RADS-c or d + 0 risk factors</th>
<th>BI-RADS-b + 0 or 1 risk factor</th>
<th>BI-RADS-a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mammo Every 2 Years</td>
<td>None Until Age 50</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Schousboe, Ann Intern Med, 2011

### Model estimates of biennial vs. triennial for low density & risk - 50-74

<table>
<thead>
<tr>
<th>Density</th>
<th>RR†</th>
<th>Deaths averted*</th>
<th>False positives*</th>
<th>FP/death averted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biennial 50-74</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a (bi)</td>
<td>1.3</td>
<td>5.3</td>
<td>612</td>
<td>151</td>
</tr>
<tr>
<td>a (tri)</td>
<td>1.3</td>
<td>4.4</td>
<td>484</td>
<td>110</td>
</tr>
</tbody>
</table>

*per 1,000 women screened; †Relative risk

Model estimates of biennial vs. triennial for low density & risk - 50-74

<table>
<thead>
<tr>
<th>Density</th>
<th>RR†</th>
<th>Deaths averted*</th>
<th>False positives*</th>
<th>FP/death averted</th>
</tr>
</thead>
<tbody>
<tr>
<td>b (bi)</td>
<td>1.0</td>
<td>5.2</td>
<td>1009</td>
<td>194</td>
</tr>
<tr>
<td>b (tri)</td>
<td>1.0</td>
<td>4.0</td>
<td>781</td>
<td>195</td>
</tr>
<tr>
<td>Biennial 50-74</td>
<td>7.0</td>
<td>953</td>
<td>136</td>
<td></td>
</tr>
<tr>
<td>b (bi)</td>
<td>1.3</td>
<td>6.5</td>
<td>994</td>
<td>153</td>
</tr>
<tr>
<td>b (tri)</td>
<td>1.3</td>
<td>5.1</td>
<td>767</td>
<td>150</td>
</tr>
</tbody>
</table>

*per 1,000 women screened; †Relative risk


---

Model estimates of biennial vs. triennial for low density & risk - 65-74

<table>
<thead>
<tr>
<th>Density</th>
<th>RR†</th>
<th>Deaths averted*</th>
<th>False positives*</th>
<th>FP/death averted</th>
</tr>
</thead>
<tbody>
<tr>
<td>a (bi)</td>
<td>1.0</td>
<td>2.1</td>
<td>343</td>
<td>163</td>
</tr>
<tr>
<td>a (tri)</td>
<td>1.0</td>
<td>1.7</td>
<td>230</td>
<td>135</td>
</tr>
<tr>
<td>Biennial 65-74</td>
<td>2.9</td>
<td>307</td>
<td>106</td>
<td></td>
</tr>
<tr>
<td>a (bi)</td>
<td>1.3</td>
<td>2.6</td>
<td>335</td>
<td>129</td>
</tr>
<tr>
<td>a (tri)</td>
<td>1.3</td>
<td>2.1</td>
<td>223</td>
<td>106</td>
</tr>
</tbody>
</table>

*per 1,000 women screened; †Relative risk


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Breast Cancer Risk Factors

- **RR= 1.3**
  - >25g alcohol/day
  - Postmenopausal HT
  - Nulliparity or age first birth >30
  - Body mass index ≥30 kg/m²
  - First-degree relative with breast cancer
  - Hx of breast biopsy
- **RR= 2.0**
  - Two first-degree relatives with breast cancer
  - History of proliferative disease without atypia
- **RR= 4.0**
  - LCIS or ADH

Model estimates of *biennial* vs. *annual* by high density & risk - 50-74

<table>
<thead>
<tr>
<th>Density</th>
<th>RR†</th>
<th>Deaths averted*</th>
<th>False positives*</th>
<th>FP/death averted</th>
</tr>
</thead>
<tbody>
<tr>
<td>c (bi)</td>
<td>2.0</td>
<td>10.6</td>
<td>1125</td>
<td>106</td>
</tr>
<tr>
<td>c (an)</td>
<td>2.0</td>
<td>14.3</td>
<td>1984</td>
<td>139</td>
</tr>
<tr>
<td>Biennial 50-74</td>
<td>7.0</td>
<td>953</td>
<td>136</td>
<td></td>
</tr>
<tr>
<td>c (bi)</td>
<td>4.0</td>
<td>15.8</td>
<td>1016</td>
<td>64</td>
</tr>
<tr>
<td>c (an)</td>
<td>4.0</td>
<td>21.0</td>
<td>1778</td>
<td>85</td>
</tr>
</tbody>
</table>

*per 1,000 women screened; †Relative risk


Risk-based strategy better harm-benefit ratios

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Risk-based vs Biennial 45-74</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screen frequency</td>
<td>40% q3</td>
</tr>
<tr>
<td></td>
<td>43% q2</td>
</tr>
<tr>
<td>Life expectancy</td>
<td>+0.5%</td>
</tr>
<tr>
<td>False positives</td>
<td>-23%</td>
</tr>
<tr>
<td>Overdiagnosis</td>
<td>-12%</td>
</tr>
<tr>
<td>False-negatives</td>
<td>-22%</td>
</tr>
</tbody>
</table>


Model estimates of *biennial* vs. *annual* for high density & risk - 50-74

<table>
<thead>
<tr>
<th>Density</th>
<th>RR†</th>
<th>Deaths averted*</th>
<th>False positives*</th>
<th>FP/death averted</th>
</tr>
</thead>
<tbody>
<tr>
<td>d (bi)</td>
<td>2.0</td>
<td>10.8</td>
<td>872</td>
<td>81</td>
</tr>
<tr>
<td>d (an)</td>
<td>2.0</td>
<td>14.7</td>
<td>1540</td>
<td>105</td>
</tr>
<tr>
<td>Biennial 50-74</td>
<td>7.0</td>
<td>953</td>
<td>136</td>
<td></td>
</tr>
<tr>
<td>d (bi)</td>
<td>4.0</td>
<td>15.4</td>
<td>776</td>
<td>50</td>
</tr>
<tr>
<td>d (an)</td>
<td>4.0</td>
<td>20.5</td>
<td>1359</td>
<td>66</td>
</tr>
</tbody>
</table>

*per 1,000 women screened; †Relative risk


What should be done for women with dense breasts?

a) Order screening ultrasound  
b) Order screening MRI  
c) Discuss supplemental imaging  
d) No action
Legislation mandates women be notified of dense breasts

- Women notified regardless of age or other breast cancer risk factors, ~47% of screened women
- Notifications suggest discussing need for supplemental imaging with your primary provider

**27.6 million women 40-74 with dense breast in U.S.**


---

High breast density masks interval invasive tumors

<table>
<thead>
<tr>
<th>BIRADS Density</th>
<th>Screen-detected Interval cancer*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Film</td>
</tr>
<tr>
<td>a</td>
<td>1.2</td>
</tr>
<tr>
<td>b</td>
<td>2.3</td>
</tr>
<tr>
<td>c</td>
<td>3.2</td>
</tr>
<tr>
<td>d</td>
<td>4.2</td>
</tr>
</tbody>
</table>

64% of interval cancers in women with BI-RADS c or d

*per 1,000 women 50-59 screened


---

Half of women with dense breasts are low risk

<table>
<thead>
<tr>
<th>BI-RADS density</th>
<th>a</th>
<th>b</th>
<th>c</th>
<th>d</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BCSC risk</strong></td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Low/av (0-1.66%)</td>
<td>90</td>
<td>68</td>
<td>51</td>
<td>53</td>
</tr>
<tr>
<td>Interim (1.67-2.49%)</td>
<td>9</td>
<td>21</td>
<td>29</td>
<td>22</td>
</tr>
<tr>
<td>High (&gt;2.5%)</td>
<td>1</td>
<td>11</td>
<td>20</td>
<td>25</td>
</tr>
</tbody>
</table>


---

BCSC Risk Calculator

FREE iPhone & iPad app

Tice J, et al., *JCO*, 2015
High risk, high density - interval cancer rate >1 per 1000 exams

<table>
<thead>
<tr>
<th>BCSC risk</th>
<th>a</th>
<th>b</th>
<th>c</th>
<th>d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (0-1%)</td>
<td>0.14</td>
<td>0.21</td>
<td>0.63</td>
<td>0.72</td>
</tr>
<tr>
<td>Average (&gt;1-1.66%)</td>
<td>0.31</td>
<td>0.38</td>
<td>0.58</td>
<td>0.89</td>
</tr>
<tr>
<td>Interm (1.67-2.49%)</td>
<td>0.48</td>
<td>0.43</td>
<td>0.83</td>
<td>1.17</td>
</tr>
<tr>
<td>High (&gt;2.5%)</td>
<td>--</td>
<td>0.90</td>
<td></td>
<td>1.48</td>
</tr>
</tbody>
</table>

24% of women with dense breasts at high risk of missed cancer


Examples of BCSC 5-year risk

Age: 62
Race/ethnicity: White
1st-degree relative diagnosed of breast cancer: Yes
Prior breast biopsy: No
Breast density: Heterogeneously dense

Estimated risk for developing invasive breast cancer over the next 5 years is **2.79%**
The average risk for a woman the same age and race/ethnicity is **1.96%**

Assessment; discuss alternative screening strategies

Alternative imaging strategies for women with dense breasts

- Change screening frequency
- Screening ultrasound -- hand held; whole breast
- Tomosynthesis (3D)
- Breast MRI

Odds of late stage disease with 2 vs. 1 year screening interval

<table>
<thead>
<tr>
<th>Age group</th>
<th>Heterogeneously dense</th>
<th>Extremely dense</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-49</td>
<td>1.32 (0.93-1.88)</td>
<td>1.89 (1.06-3.39)</td>
</tr>
<tr>
<td>50-74</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No HT</td>
<td>1.21 (0.92-1.61)</td>
<td></td>
</tr>
<tr>
<td>E+P</td>
<td>1.56 (0.88-2.80)</td>
<td></td>
</tr>
<tr>
<td>E only</td>
<td>1.19 (0.66-2.13)</td>
<td></td>
</tr>
</tbody>
</table>

Low cancer detection for women with dense breasts by ultrasound

<table>
<thead>
<tr>
<th></th>
<th>Parris</th>
<th>Hooley</th>
<th>Weigert</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exams</td>
<td>5519</td>
<td>935</td>
<td>8647</td>
</tr>
<tr>
<td>Cancers</td>
<td>10</td>
<td>3</td>
<td>24</td>
</tr>
<tr>
<td>Biopsy rate %</td>
<td>3.3</td>
<td>5.0</td>
<td>5.0</td>
</tr>
<tr>
<td>Cancer rate %</td>
<td>.18</td>
<td>.32</td>
<td>.28</td>
</tr>
<tr>
<td>NNS</td>
<td>552</td>
<td>312</td>
<td>309</td>
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Whole breast US for women with dense breasts – 1.9 per 1000 exams


Supplemental screening ultrasound is expensive

- Digital mammography + ultrasound
- 10,000 women 50-75 dense breasts
- 12 rounds of screening
- Cost per QALY – $338,000
- Additional 3 deaths averted
- 3500 more false-positive biopsies
- NNS 3300 to avert 1 breast cancer death

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Cancer detection by extent of density for DM vs. DBT

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<th>Digital + Tomo</th>
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<td>Invasive cancer rate*</td>
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<tr>
<td>Non-dense</td>
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<td>4.0</td>
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<tr>
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<td>4.2</td>
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<tr>
<td>Recall rate*</td>
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<td>79</td>
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<tr>
<td>Dense</td>
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<td>109</td>
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*per 1,000 exams, P< 0.001

Biopsy rate: 18.1 vs. 19.3

Rafferty et al, JAMA, 2016

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Maximize chance of benefit & minimize chance of harm

- Offer screening biennially from age 50-74 or 13 mammograms in a woman’s lifetime
  - Consider triennial screening if low density & average to low risk ~32% of women
  - Consider annual screening if high density & risk
  - Stop screening before 70 for women with moderate to severe comorbidities
- Consider biennial screening age 40-49 if 5-year breast cancer risk >1.4%, i.e., average-risk of woman 50-54

Dense breasts

- Digital mammography effective for most women with dense breasts
- Women with dense breasts at high risk of interval cancer, consider tomosynthesis or supplemental screening ultrasound

Thank you