Controversies in Cancer Screening:
A Review of Current Evidence and Guidelines and the Controversies That Surround Them

Vince D. Cataldo, MD, FACP
March 11, 2016
Disclosure

I, Vince D. Cataldo, M.D., do not have any relationship(s) with commercial interests.
Early History of Cancer Screening

• 1920 – Dr. George Papanicolaou begins studying the Papanicolaou test as a method of understanding the cervical changes associated with the menstrual cycle.
• 1923 – Panpanicolaou reports his findings of cervical carcinoma by “Pap smear” and suggests its utility as a screening test.
• 1960 – The American Cancer Society endorsed the Pap Smear as a screening test.
• Late 1960s – Modern mammography techniques are developed.
• 1968 – The WHO issues its Guidelines for Screening Tests
• 1976 – The American Cancer Society recommends screening mammography.
Age-adjusted Cancer Death Rates*, Females by Site, US, 1930-2010

Per 100,000, age adjusted to the 2000 US standard population. *Uterus refers to uterine cervix and uterine corpus combined.

Note: Due to changes in ICD coding, numerator information has changed over time. Rates for cancer of the lung and bronchus, colon and rectum, and ovary are affected by these coding changes.

The Principles of Screening

  - The condition should be an important health problem.
  - There should be a treatment for the condition.
  - Facilities for diagnosis and treatment should be available.
  - There should be a latent stage of the disease.
  - There should be a test or examination for the condition.
  - The test should be acceptable to the population.
  - The natural history of the disease should be adequately understood.
  - There should be an agreed policy on whom to treat.
  - The total cost of finding a case should be economically balanced in relation to medical expenditure as a whole.
  - Case-finding should be a continuous process, not just a “once and for all” project.
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  - Case-finding should be a continuous process, not just a “once and for all” project.
“It’s not at all good when your cancer is ‘palpable’ from the outside. Carcinoma works cunningly from the inside out. Detection often works more slowly and gropingly, from the outside in.”

-Christopher Hitchens, 1949-2011
Screening for Cancer

• Colon Cancer
• Cervical Cancer
• Breast Cancer
• Prostate Cancer
• Lung Cancer
Screening for Colorectal Cancer
Risk Stratification in Colorectal Cancer Screening

• **Average Risk:**
  – Age ≥ 50 years
  – No personal history of adenoma or CRC
  – No history of IBD
  – Negative family history

• **Increased Risk:**
  – History of adenoma, CRC, or IBD
  – Positive family history

• **High-Risk Syndrome Patients:**
  – Lynch Syndrome (HNPCC)
  – Familial Adenomatous Polyposis (FAP) (and other genetic polyposis syndromes)
  – Peutz-Jeghers Syndrome, Cowden Syndrome, Li-Fraumeni Syndrome

NCCN Guidelines, 2015.
Colorectal Screening in the Average Risk Patient

• Colonoscopy preferred
  – No polyps $\Rightarrow$ Repeat colonoscopy in 10 years
  – Hyperplastic polyps (esp. left-sided and less than 1 cm) $\Rightarrow$ Repeat colonoscopy in 10 years
  – More frequent if adenoma discovered

• Where colonoscopy not available/contraindicated:
  – Evidence from randomized trials exists to support colorectal cancer mortality reduction from:
    • Guaiac-based or immunohistochemical based annual testing ± flexible sigmoidoscopy every 5 years (Reflex to colonoscopy if quaiac positive or flex sig positive for adenoma)
    • Flexible sigmoidoscopy every 5 years (Refex to colonoscopy if adenoma discovered)

NCCN Guidelines, 2015.
Random assignment between 1993-2001 of 154,900 patients aged 55-74 years to baseline screening flexible sigmoidoscopy with repeat at 3-5 years, or to “usual care”.

Death from colorectal cancer was the primary endpoint.
Is flexible sigmoidoscopy an appropriate screening modality?

- If mass or polyp found, patient referred to primary care for decisions regarding diagnostic follow-up.
- The median follow-up time was 11.9 years.

Table 2. Colorectal-Cancer Incidence and Mortality.*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Flexible-Sigmoidoscopy Group (N = 77,445)</th>
<th>Usual-Care Group (N = 77,455)</th>
<th>Relative Risk (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of participants</td>
<td>rate per 10,000 person-yr (95% CI)</td>
<td>no. of participants</td>
<td>rate per 10,000 person-yr (95% CI)</td>
</tr>
<tr>
<td>Incidence</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All colorectal cancers</td>
<td>1012</td>
<td>11.9 (11.2–12.7)</td>
<td>1287</td>
<td>15.2 (14.4–16.0)</td>
</tr>
<tr>
<td>Location of cancer†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distal</td>
<td>479</td>
<td>5.6 (5.1–6.2)</td>
<td>669</td>
<td>7.9 (7.3–8.5)</td>
</tr>
<tr>
<td>Proximal</td>
<td>512</td>
<td>6.0 (5.5–6.6)</td>
<td>595</td>
<td>7.0 (6.5–7.6)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>567</td>
<td>13.6 (12.4–14.7)</td>
<td>768</td>
<td>18.5 (17.2–19.9)</td>
</tr>
<tr>
<td>Female</td>
<td>445</td>
<td>10.3 (9.4–11.3)</td>
<td>519</td>
<td>12.0 (11.0–13.0)</td>
</tr>
<tr>
<td>Age at randomization</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>55–64 yr</td>
<td>518</td>
<td>9.4 (8.6–10.2)</td>
<td>662</td>
<td>12.1 (11.2–13.0)</td>
</tr>
<tr>
<td>65–74 yr</td>
<td>494</td>
<td>16.6 (15.1–18.1)</td>
<td>625</td>
<td>20.9 (19.3–22.5)</td>
</tr>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All colorectal-cancer deaths</td>
<td>252</td>
<td>2.9 (2.5–3.2)</td>
<td>341</td>
<td>3.9 (3.5–4.3)</td>
</tr>
<tr>
<td>Location of cancer†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distal</td>
<td>87</td>
<td>1.0 (0.8–1.2)</td>
<td>175</td>
<td>2.0 (1.7–2.3)</td>
</tr>
<tr>
<td>Proximal</td>
<td>143</td>
<td>1.6 (1.4–1.9)</td>
<td>147</td>
<td>1.7 (1.4–2.0)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>139</td>
<td>3.2 (2.7–3.8)</td>
<td>211</td>
<td>4.9 (4.3–5.6)</td>
</tr>
<tr>
<td>Female</td>
<td>113</td>
<td>2.6 (2.1–3.0)</td>
<td>130</td>
<td>2.9 (2.4–3.4)</td>
</tr>
<tr>
<td>Age at randomization</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>55–64 yr</td>
<td>133</td>
<td>2.4 (2.0–2.8)</td>
<td>157</td>
<td>2.8 (2.3–3.2)</td>
</tr>
<tr>
<td>65–74 yr</td>
<td>119</td>
<td>3.9 (3.2–4.6)</td>
<td>184</td>
<td>6.0 (5.1–6.9)</td>
</tr>
</tbody>
</table>

* The median follow-up time for incidence was 11.9 years (interquartile range, 10.2 to 13.0) and for mortality was 12.1 years (interquartile range, 10.4 to 13.0).
† Distal location was defined as the rectum through the splenic flexure, and proximal as the transverse colon through the cecum. For incidence, the location was unknown for 21 cases in the flexible-sigmoidoscopy group and 23 cases in the usual-care group. For mortality, the location was unknown for 22 deaths in the flexible-sigmoidoscopy group and 19 deaths in the usual-care group.

## Costs of Colorectal Cancer Screening

<table>
<thead>
<tr>
<th>Screening Strategy</th>
<th>Cost per Life-Year Gained</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOBT</td>
<td>$5,691-$17,805</td>
</tr>
<tr>
<td>Sigmoidoscopy</td>
<td>$12,477-$39,359</td>
</tr>
<tr>
<td>FOBT plus Sigmoidoscopy</td>
<td>$13,792-$22,518</td>
</tr>
<tr>
<td>Colonoscopy</td>
<td>$9,038-$22,012</td>
</tr>
</tbody>
</table>
Screening for Cervical Cancer
Cervical Cancer Screening Guidelines
NCCN, ASCCP, and ASCP

• Age <21: No routine screening
• Age 21-29: Cytology every 3 years
  – HPV screening not recommended for this age group. Assess HPV status if ASC-US is discovered.
• Age 30-65: “Co-testing” (HPV and cytology) every 5 years
  – Cytology positive=treat accordingly
  – Cytology negative, HPV positive=repeat co-testing in 12 months or refer for colposcopy (esp if 16/18 pos)
• Age >65: No further screening following an adequate prior negative screening
  – For a history of CIN2 or more invasive disease, continue screening for at least 20 years beyond diagnosis.
• Following hysterectomy and surgical removal of cervix: No screening.
  – For those with history of cervical cancer, continue screening for at least 20 years beyond diagnosis.
• HPV Vaccinated women: Screen according to same guidelines for unvaccinated women.

NCCN Guidelines, 2015.
Human Papillomavirus and Papanicolaou Tests to Screen for Cervical Cancer

Pontus Naucler, M.D., Ph.D., Walter Ryd, M.D., Sven Törnberg, M.D., Ph.D., Anders Strand, M.D., Ph.D., Göran Wadell, M.D., Ph.D., Kristina Elfgren, M.D., Ph.D., Thomas Rådberg, M.D., Björn Strander, M.D., Bo Johansson, Ph.D., Ola Forslund, Ph.D., Bengt-Göran Hansson, Ph.D., Eva Rylander, M.D., Ph.D., and Joakim Dillner, M.D., Ph.D.

HPV Screening as Adjunct to Pap

• 12,527 Swedish women, aged 32-38, randomized to HPV screening (for 14 high-risk subgroups) plus Pap vs. Pap alone.

• Positive HPV/Negative Pap → Repeat HPV at least 1 year later

• Persistent HPV infection → Colposcopy and cervical biopsy

• Mean follow-up time was 4.1 years. Endpoints were rates of CIN grade 2-3 or invasive cervical carcinoma.

HPV Screening as Adjunct to Pap

• At initial screening, HPV+Pap group had 51% more diagnoses than the Pap alone group (114 vs. 76 (HR 1.51, 95% CI 1.13-2.02)

• Throughout entire study, HPV+Pap group had 16.8% more diagnoses than the Pap alone group, 139 vs. 119.

Can HPV Screening Replace Pap Tests?

• The prevalence of HPV among cervical cancers is suggested to exceed 99% in some large assessments.
• This represents the largest recognizable attribute ever identified for a specific malignancy.

Can HPV Screening Replace Pap Tests?

• HPV DNA testing is reproducible, is easy to perform, provides objective outcome, is more sensitive than cytologic testing in detecting high-grade CIN.

• However, the specificity of HPV testing is less specific than cytologic testing since the majority of HPV infections resolve spontaneously and will not become a clinically significant infection.

Figure 1. Natural History of HPV Infection and Cervical Cancer.

The peak prevalence of transient infections with carcinogenic types of HPV (green line) occurs among women during their teens and 20s, after the initiation of sexual activity. The peak prevalence of cervical precancerous conditions occurs approximately 10 years later (purple line) and the peak prevalence of invasive cancers at approximately 40 to 50 years of age (blue line). The conventional model of cervical-cancer prevention is based on repeated rounds of cytologic examinations, including Pap smears, and colposcopy (brown arrows). Adapted from Schiffman and Castle.6

Can HPV Screening Replace Pap Tests?

• Given the known strength of the relationship between HPV and cervical carcinoma, questions that deserve investigation include:
  – Is cytologic evaluation of the cervix necessary if the patient is HPV negative?
  – Given the lag time from persistent infection and development of carcinoma, can cytologic examination be delayed for a specified period once HPV is detected?
  – Is cytologic examination only necessary for specific subtypes of persistent HPV infections?
A trial of 5109 women, age 18-25, who self-collected a “cervical” sample for HPV DNA analysis using a Dacron swab of the high recesses of the vagina, collected 6 months after a normal cytologic evaluation of the cervix.

- 99.9% compliance rate
- A subset (615 patients) also received traditional cytological collection for HPV analysis at the 6-month time point to test for concordance.
- The sensitivity of HPV detection was 92% by clinician collection and 88% by self collection (HR 1.0; CI 0.9-1.2).
- There was complete concordance between both methods of collection for all 25 HPV subtypes identified (carcinogenic and non-carcinogenic included).
Costs of Cervical Cancer Screening

Cost-effectiveness Analysis for Pap Smear Screening and Human Papillomavirus DNA Testing and Vaccination

<table>
<thead>
<tr>
<th>Screening Strategy</th>
<th>Cost per Life-Year Gained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual Pap Smear</td>
<td>$31,698</td>
</tr>
<tr>
<td>HPV Testing plus Pap q 3 years</td>
<td>$36,627</td>
</tr>
<tr>
<td>HPV Vaccination plus Pap q 3 years</td>
<td>$44,688</td>
</tr>
<tr>
<td>HPV Vaccination plus q 3 year HPV Testing</td>
<td>?????????</td>
</tr>
</tbody>
</table>
Screening for Breast Cancer
General Considerations In Breast Cancer Screening

• Prior to screening, women should be counseled regarding benefits, risks, and limitations of breast screening.
• Severe comorbid conditions limiting life expectancy should influence the decision to screen.
• An upper age limit for breast cancer screening is not established.
• Ultrasound may serve as an adjunct to mammography for women with dense breasts and increased risk of breast cancer.
• Digital mammography appears to be superior to plain film mammography for young women and women with dense breasts.

NCCN Guidelines, 2015.
Breast Cancer Screening

• For asymptomatic women with a negative physical exam AND OF AVERAGE RISK, the NCCN recommends:
  – Clinical breast exam at least once every three years for women 25-39 years of age
  – Annual clinical breast exam and annual screening bilateral mammogram for women ≥ 40 years of age

NCCN Guidelines, 2015.
Breast Cancer Screening

• Women at **increased risk for breast cancer** include:
  
  – Prior history of breast cancer
  – Personal history of LCIS or **ADH/ALH**
  – Prior thoracic radiation before age 30
  – A pedigree suggestive of **OR** a known genetic predisposition for breast cancer
  – Gail Model risk suggesting a ≥ 1.7% 5-year risk of invasive breast cancer in women ≥ 35 years

NCCN Guidelines, 2015.
Risk Calculator

(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 of ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS)?

2. What is the woman's age? This tool only calculates risk for women 35 years of age or older.

3. What was the woman's age at the time of her first menstrual period?

4. What was the woman's age at the time of her first live birth of a child?

5. How many of the woman's first-degree relatives - mother, sisters, daughters - have had breast cancer?

6. Has the woman ever had a breast biopsy?

6a. How many breast biopsies (positive or negative) has the woman had?

6b. Has the woman had at least one breast biopsy with atypical hyperplasia?

7. What is the woman's race/ethnicity?

7a. What is the sub race/ethnicity?

Calculate Risk >

www.cancer.gov/bcrisktool
The Use of Breast MRI

• There are **no randomized trials** to date to suggest the most appropriate use of MRI for breast cancer screening.

• Based on **nonrandomized and screening trials**, annual screening breast MRI as an adjunct to mammography is recommended for:
  – Patients harboring a BRCA 1 or BRCA 2 mutation
  – First-degree relatives of BRCA carriers who are untested for the BRCA mutation
  – Lifetime breast cancer risk of 20% or greater as predicted by a risk assessment calculator

• The data are unclear in suggesting the age of initiation of breast MRI in these settings.

  NCCN Guidelines, 2015.
The Use of Breast MRI

• Based on expert consensus opinion, annual screening breast MRI as an adjunct to mammography is recommended for:
  – Thoracic radiation prior to the age of 30
  – Li-Fraumeni Syndrome, Cowden Syndrome, and other syndromes that confer increased breast cancer risk.

• The data are unclear in suggesting the age of initiation of breast MRI in these settings as well.

NCCN Guidelines, 2015.
The Use of Breast MRI

• There is **insufficient evidence** to recommend for or against breast MRI as an adjunct to mammography in the following settings:
  – LCIS
  – ADH
  – Dense breast tissue
  – Women with a personal history of in situ or invasive carcinoma of the breast

NCCN Guidelines, 2015.
The U.S. Preventive Services Task Force Recommendations for Breast Cancer Screening

### Screening for Breast Cancer Using Film Mammography

<table>
<thead>
<tr>
<th>Population</th>
<th>Women Aged 40–49 Years</th>
<th>Women Aged 50–74 Years</th>
<th>Women Aged ≥75 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation</td>
<td>Do not screen routinely. Individualize decision to begin biennial screening according to the patient’s context and values.</td>
<td>Screen every 2 years.</td>
<td>No recommendation.</td>
</tr>
<tr>
<td>Risk Assessment</td>
<td>This recommendation applies to women aged ≥40 years who are not at increased risk by virtue of a known genetic mutation or history of chest radiation. Increasing age is the most important risk factor for most women.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screening Tests</td>
<td>Standardization of film mammography has led to improved quality. Refer patients to facilities certified under the Mammography Quality Standards Act (MQSA), listed at <a href="http://www.fda.gov/cdrh/mammography/certified.html">www.fda.gov/cdrh/mammography/certified.html</a>.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Timing of Screening</td>
<td>Evidence indicates that biennial screening is optimal. A biennial schedule preserves most of the benefit of annual screening and cuts the harms nearly in half. A longer interval may reduce the benefit.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Balance of Harms and Benefits</td>
<td>There is convincing evidence that screening with film mammography reduces breast cancer mortality, with a greater absolute reduction for women aged 50 to 74 years than for younger women. Harm of screening include psychological harms, additional medical visits, imaging, and biopsies in women without cancer, inconvenience due to false-positive screening results, harms of unnecessary treatment, and radiation exposure. Harms seem moderate for each age group. False-positive results are a greater concern for younger women; treatment of cancer that would not become clinically apparent during a woman’s life (overdiagnosis) is an increasing problem as women age.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rationale for No Recommendation (I Statement)</td>
<td>Among women 75 years or older, evidence of benefit is lacking.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relevant USPSTF Recommendations</td>
<td>USPSTF recommendations on screening for genetic susceptibility for breast cancer and chemoprevention of breast cancer are available at <a href="http://www.preventiveservices.ahrq.gov">www.preventiveservices.ahrq.gov</a>.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
When To Initiate Screening...

• Making the case for initiation at age 50:
  – The 10-year risk of breast cancer is lower for a woman in her 40s than in her 50s
    • (1 case per 69 women vs. 1 case per 42 women)
  – 1904 women aged 40-49 would need to be invited for screening (not all are actually screened) over at least 11 years to save one life.
  – The harms of overscreening, particularly false positive findings by mammography, are considerable. (Among 1000 women screened, 4921 mammograms performed over 10 years, 470 being falsely positive requiring further investigation, and 33 false positive biopsy results.)
  – Increased exposure to radiation from additional ten years of screening mammography

Smith RA et al. NEJM, 2013.
When To Initiate Screening...

- Making the case for initiation at age 40:
  - One in 6 breast-cancer related deaths is attributable to a diagnosis of breast cancer made in a woman when she was in her 40s (Is breast cancer in younger women perhaps MORE aggressive?).
  - Breast cancer is a leading cause of premature deaths among women and **the leading cause of death in women aged 45-55**.
  - The number of women required to invite for screening in order to save a life (1904) falls to 726 needed to screen to save one life when considering those who actually undergo screening.
  - Women report that they accept the risk of false positives in favor of finding breast cancer early.

Smith RA et al. NEJM, 2013.
<table>
<thead>
<tr>
<th>Population</th>
<th>Recommendation</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women, Age 50-74 Years</td>
<td>The USPSTF recommends biennial screening mammography for women 50-74 years.</td>
<td>B</td>
</tr>
<tr>
<td>Women, Before the Age of 50 Years</td>
<td>The decision to start regular, biennial screening mammography before the age of 50 years should be an individual one and take patient context into account, including the patient’s values regarding specific benefits and harms.</td>
<td>C</td>
</tr>
<tr>
<td>Women, 75 Years and Older</td>
<td>The USPSTF concludes that the current evidence is insufficient to assess the benefits and harms of screening mammography in women 75 years and older. Go to the Clinical Considerations section for information on risk assessment and suggestions for practice regarding the I statement.</td>
<td>I</td>
</tr>
<tr>
<td>All Women</td>
<td>The USPSTF recommends against teaching breast self-examination (BSE).</td>
<td>D</td>
</tr>
<tr>
<td>Women, 40 Years and Older</td>
<td>The USPSTF concludes that the current evidence is insufficient to assess the additional benefits and harms of clinical breast examination (CBE) beyond screening mammography in women 40 years or older. Go to the Clinical Considerations section for information on risk assessment and suggestions for practice regarding the I statement.</td>
<td>I</td>
</tr>
<tr>
<td>All Women</td>
<td>The USPSTF concludes that the current evidence is insufficient to assess the additional benefits and harms of either digital mammography or magnetic resonance imaging (MRI) instead of film mammography as screening modalities for breast cancer.</td>
<td>I</td>
</tr>
</tbody>
</table>
So, have we closed the book on breast cancer screening?
Effect of Three Decades of Screening Mammography on Breast-Cancer Incidence

Archie Bleyer, M.D., and H. Gilbert Welch, M.D., M.P.H.
The Effects of Screening

• An examination of the SEER database examining trends in the diagnosis of early-stage breast cancer (DCIS and invasive carcinoma confined to breast) and late-stage breast cancer (regional carcinoma and distant disease) from 1976 to 2008

• Screening mammography has doubled the number of early-stage breast cancers diagnosed yearly.

• However,...

Table 1. Absolute Change in the Incidence of Stage-Specific Breast Cancer among Women 40 Years of Age or Older after the Introduction of Screening Mammography.*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Annual Breast-Cancer Incidence</th>
<th>Women Affected over the Three Decades†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase in cases of early-stage breast cancer</td>
<td>112</td>
<td>234</td>
</tr>
<tr>
<td>DCIS</td>
<td>7</td>
<td>56</td>
</tr>
<tr>
<td>Localized disease</td>
<td>105</td>
<td>178</td>
</tr>
<tr>
<td>Total</td>
<td>112</td>
<td>234</td>
</tr>
<tr>
<td>Decrease in cases of late-stage breast cancer</td>
<td>102</td>
<td>94</td>
</tr>
<tr>
<td>Regional disease</td>
<td>85</td>
<td>78</td>
</tr>
<tr>
<td>Distant disease</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>Total</td>
<td>102</td>
<td>94</td>
</tr>
</tbody>
</table>

* DCIS denotes ductal carcinoma in situ.
† These data exclude excess cases associated with hormone-replacement therapy.
‡ Because of rounding, the absolute change appears to be inconsistent with the subtracted values for annual breast-cancer incidence. See Table S1 in the Supplementary Appendix for precise values.
§ Without rounding, the absolute change is −0.3.

The Effects of Screening

• Mammography has resulted in a significant increase in detection of early-stage breast cancers that was not matched by a reduction in late-stage cancers.

• Estimates are an overdiagnosis of 1 million women over the past three decades and more than 70,000 women in 2008 alone (31% of all breast cancers diagnosed that year!)

• Over the same three decades, death from breast cancer has decreased from 71/100,000 women to 51/100,000 women.

• Is this due to screening or to improvement in treatment?

The Effects of Screening

- It is suggested that, since the absolute reduction in deaths (20 deaths/100,000 women) is larger than the absolute reduction of late-stage cancers diagnosed by screening mammography (8 cases/100,000 women), the contribution of early detection to decreasing deaths due to breast cancer is small and the majority of this benefit is likely due to improvements in breast cancer treatment.

- The 5 year survival rate of node positive disease is approximately 85%.

- With the advancements in treatment of clinically detectable locoregional breast cancer, does mammography offer a significant reduction in mortality?

Screening for Prostate Cancer
Screening for Prostate Cancer

Richard M. Hoffmann, M.D., M.P.H.

Screening for Prostate Cancer-
Background

• Screening by PSA and DRE resulted in an increased detected incidence of prostate cancer that peaked in the early 1990s.
• This peak has now declined and stabilized over the past decade.
• Proven risk factors for the development of prostate cancer include: older age, family history, and black race.
• Today, 90% of prostate cancers diagnosed are detected by screening.

Hoffman RM. NEJM 2011.
Age-adjusted Cancer Death Rates*, Males by Site, US, 1930-2010

*Per 100,000, age adjusted to the 2000 US standard population.

Note: Due to changes in ICD coding, numerator information has changed over time. Rates for cancer of the liver, lung and bronchus, and colon and rectum are affected by these coding changes.


©2014, American Cancer Society, Inc., Surveillance Research
### Probability (%) of Developing Invasive Cancers over Selected Age Intervals by Sex, US, 2005-2007*

<table>
<thead>
<tr>
<th></th>
<th>Birth to 39</th>
<th>40 to 59</th>
<th>60 to 69</th>
<th>70 and Older</th>
<th>Birth to Death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>All sites</td>
<td>1.44 (1 in 69)</td>
<td>2.12 (1 in 47)</td>
<td>8.50 (1 in 12)</td>
<td>9.01 (1 in 11)</td>
<td>15.71 (1 in 6)</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>0.02 (1 in 4,693)</td>
<td>0.38 (1 in 262)</td>
<td>0.93 (1 in 107)</td>
<td>0.98 (1 in 102)</td>
<td>3.67 (1 in 27)</td>
</tr>
<tr>
<td>Breast</td>
<td>0.48 (1 in 207)</td>
<td>3.75 (1 in 27)</td>
<td>3.45 (1 in 29)</td>
<td>6.53 (1 in 15)</td>
<td></td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>0.08 (1 in 1,270)</td>
<td>0.91 (1 in 110)</td>
<td>1.46 (1 in 69)</td>
<td>4.38 (1 in 23)</td>
<td>5.30 (1 in 19)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>0.17 (1 in 598)</td>
<td>0.22 (1 in 462)</td>
<td>0.33 (1 in 302)</td>
<td>0.78 (1 in 128)</td>
<td>1.20 (1 in 83)</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>0.03 (1 in 3,646)</td>
<td>0.93 (1 in 108)</td>
<td>2.29 (1 in 44)</td>
<td>6.70 (1 in 15)</td>
<td>7.67 (1 in 13)</td>
</tr>
<tr>
<td>Melanoma of the skin</td>
<td>0.15 (1 in 656)</td>
<td>0.64 (1 in 157)</td>
<td>0.74 (1 in 136)</td>
<td>1.85 (1 in 54)</td>
<td>2.73 (1 in 37)</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>0.08 (1 in 1,179)</td>
<td>0.31 (1 in 318)</td>
<td>0.60 (1 in 168)</td>
<td>1.73 (1 in 58)</td>
<td>3.04 (1 in 43)</td>
</tr>
<tr>
<td>Prostate</td>
<td>0.01 (1 in 8,517)</td>
<td>2.52 (1 in 40)</td>
<td>6.62 (1 in 15)</td>
<td>12.60 (1 in 8)</td>
<td>16.22 (1 in 6)</td>
</tr>
<tr>
<td>Uterine cervix</td>
<td>0.15 (1 in 656)</td>
<td>0.27 (1 in 377)</td>
<td>0.13 (1 in 762)</td>
<td>0.18 (1 in 544)</td>
<td>0.68 (1 in 147)</td>
</tr>
<tr>
<td>Uterine corpus</td>
<td>0.07 (1 in 1,423)</td>
<td>0.75 (1 in 134)</td>
<td>0.85 (1 in 117)</td>
<td>1.24 (1 in 81)</td>
<td>2.58 (1 in 39)</td>
</tr>
</tbody>
</table>

*For people free of cancer at beginning of age interval. Percentages and "1 in " numbers may not be equivalent due to rounding. † All sites excludes basal and squamous cell skin cancers and in situ cancers except urinary bladder. ‡ Includes invasive and in situ cancer cases. § Statistic is for whites only.


©2011, American Cancer Society, Inc., Surveillance Research

American Cancer Society, 2011.
Screening for Prostate Cancer - Background

- Not all prostate cancer cases will impact survival:
  - 1997 autopsy data showed 30% of men older than 50 and 70% of men older than 70 have occult prostate cancer.
  - SEER Registry data show that, in men >65, the **10-year risk of death** from prostate cancer in MEN WITH THE DIAGNOSIS was **8%** in men with well-differentiated tumors and **26%** in men with poorly differentiated tumors.
  - The 10-year risk of **death from competing causes** in this population was **60%** regardless of tumor grade.

Hoffman RM. NEJM 2011.
Screening for Prostate Cancer-

Background

• The two largest randomized controlled trials of prostate cancer screening have failed to show a reproducible reduction in prostate cancer specific mortality from screening.

• Overtreatment is not without morbidity including unnecessary urinary and bowel incontinence and erectile dysfunction.

Hoffman RM. NEJM 2011.
Schroder FH. NEJM 2009.
Andriole GL. NEJM 2009.
Screening for Prostate Cancer-Effects of Screening

• The only randomized trial that has suggested a survival advantage from routine screening was the European Randomized Study of Screening for Prostate Cancer
  – 182,000 men aged 50-74 screened with PSA every 2-4 years

Hoffman RM. NEJM 2011.
Schroder FH. NEJM 2009.
European Randomized Study of Screening for Prostate Cancer

- Results:
  - Incidence of Prostate Cancer: 8.2% in screened subjects vs. 4.8% of control subjects (71% relative increase).
  - There was a 20% relative reduction in mortality from prostate cancer in the screened cohort.
  - However, the absolute difference was only 0.7 deaths per 1000 men.
  - This means 1410 men would have to be screened over a period of 9 years and 48 men treated for prostate cancer to prevent 1 death from prostate cancer.

- Randomized studies in the U.S. have failed to reproduce these findings.

Hoffman RM. NEJM 2011.
Schroder FH. NEJM 2009.
Andriole GL. NEJM 2009.
Is It Necessary to Treat All Prostate Cancers Detected by Screening?

Radical Prostatectomy versus Watchful Waiting in Early Prostate Cancer

Anna Bill-Axelson, M.D., Ph.D., Lars Holmberg, M.D., Ph.D.,
Mirja Ruutu, M.D., Ph.D., Hans Garmo, Ph.D., Jennifer R. Stark, Sc.D.,
Christer Busch, M.D., Ph.D., Stig Nordling, M.D., Ph.D.,
Michael Häggman, M.D., Ph.D., Swen-Olof Andersson, M.D., Ph.D.,
Stefan Bratell, M.D., Ph.D., Anders Spångberg, M.D., Ph.D.,
Juni Palmgren, Ph.D., Gunnar Steineck, M.D., Ph.D.,
Hans-Olov Adami, M.D., Ph.D., and Jan-Erik Johansson, M.D., Ph.D.,
for the SPCG-4 Investigators*

NEJM; May 5, 2011
Radical Prostatectomy vs. Watchful Waiting

• 12.8 years follow-up of 695 men with early-stage prostate cancer (Up to a T2 lesion, PSA<50 and negative bone scan)
  – Prostate-cancer related deaths: 55 (prostatectomy group) vs. 81 (watchful waiting group), 14.6% vs. 20.7% risk estimated at 15 years.
  – Number needed to treat to avert 1 death: 15.

A Similar Study...
Radical Prostatectomy vs. Observation

- Randomized 731 men with localized prostate cancer found by PSA screening to either radical prostatectomy or observation.
- Median follow-up of 10 years.
- Death occurred in 47.0% of patients in prostatectomy group compared to 49.9% in the observation group (HR, 0.88; 95% CI, 0.71-1.08; P=0.22).
- Death from prostate cancer or from prostate cancer treatment: 5.8% in prostatectomy group vs. 8.4% in observation group (HR, 0.63; 95% CI, 0.36-1.09; P=0.09).
- Adverse events within 30 days after surgery occurred in 21.4% of prostatectomy patients (Most common: infection, sepsis, MI, need for additional surgery, bleeding, and prolonged need for catheter)

Wilt TJ. NEJM 2012.
<table>
<thead>
<tr>
<th>Dysfunction</th>
<th>Radical Prostatectomy</th>
<th>Observation</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary incontinence†</td>
<td>49/287 (17.1)</td>
<td>18/284 (6.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Erectile dysfunction‡</td>
<td>231/285 (81.1)</td>
<td>124/281 (44.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bowel dysfunction§</td>
<td>35/286 (12.2)</td>
<td>32/282 (11.3)</td>
<td>0.74</td>
</tr>
</tbody>
</table>

Table 2. Patient-Reported Urinary, Erectile, and Bowel Dysfunction at 2 Years, According to Study Group.*

Wilt TJ. NEJM 2012.
To Screen or Not to Screen

- In patients 40 years of age or older, start with a detailed history. Race and family history SHOULD affect your recommendation for screening. The closer the relative, the earlier the onset, and the more affected family members, the higher the risk.
- Discuss the risks versus benefits of screening.
- Only screen after such a discussion has taken place AND the patient understands your recommendation for biopsy if either the DRE OR the PSA are abnormal.
- Recommend against adding a PSA to routine laboratory testing without first having a detailed discussion of the implications of screening.

NCCN Guidelines, 2015.
Costs of Prostate Cancer Screening

Cost-effectiveness Analysis of Prostate Cancer Screening

<table>
<thead>
<tr>
<th>Age at Screening</th>
<th>Cost per Life-Year Gained</th>
</tr>
</thead>
<tbody>
<tr>
<td>At Age 65</td>
<td>$14,200</td>
</tr>
<tr>
<td>At Age 75</td>
<td>$51,290</td>
</tr>
</tbody>
</table>
Screening for Lung Cancer
Enrolled 53,454 people deemed to be at high risk for lung cancer between 2002-2004.

Eligible participants were aged 55-74, at least 30 pack-year tobacco use, either current smokers or smokers within 15 years of randomization.

Exclusion criteria included previous lung cancer, CT of chest within 18 months, hemoptysis, or 15 lb wt loss in the preceding one year.

Participants randomized in 1:1 fashion to low-dose CT or to chest radiography at enrollment, one year, and two years.
The NLST Screening Trial

• “Positive” tests were defined as CTs with non-calcified lung nodules 4mm or greater in size, radiographs with any non-calcified nodule, or presence of adenopathy or pleural effusion on either test modality.

• There were substantially more positive screening CTs than radiographs at each time point (T0, 27.3% vs. 9.2%; T1, 27.9% vs. 6.2%; T2, 16.8% vs. 5.0%).

• During screening, 39.1% of the participants in the CT group had at least one positive test, and 16% of participants in the radiography group had at least one positive test.

NLST Team. NEJM, 2013.
Diagnostic Follow-up of Positive Screening Results in the Three Screening Rounds.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Low-Dose CT</th>
<th>Chest Radiography</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T0</td>
<td>T1</td>
</tr>
<tr>
<td></td>
<td>7191 (100.0)</td>
<td>6901 (100.0)</td>
</tr>
<tr>
<td>Lung cancer confirmed</td>
<td>270 (3.8)</td>
<td>168 (2.4)</td>
</tr>
<tr>
<td>Lung cancer not confirmed†</td>
<td>6921 (96.2)</td>
<td>6733 (97.6)</td>
</tr>
<tr>
<td>Positive screening results with complete diag-</td>
<td>7049 (100.0)</td>
<td>6740 (100.0)</td>
</tr>
<tr>
<td>nostic follow-up information</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any diagnostic follow-up</td>
<td>6369 (90.4)</td>
<td>3866 (57.4)</td>
</tr>
<tr>
<td>Clinical procedure</td>
<td>5089 (72.2)</td>
<td>3190 (47.3)</td>
</tr>
<tr>
<td>Imaging examination</td>
<td>5717 (81.1)</td>
<td>2520 (37.4)</td>
</tr>
<tr>
<td>Chest radiography</td>
<td>1284 (18.2)</td>
<td>613 (9.1)</td>
</tr>
<tr>
<td>Chest CT</td>
<td>5153 (73.1)</td>
<td>2046 (30.4)</td>
</tr>
<tr>
<td>FDG PET or FDG PET–CT</td>
<td>728 (10.3)</td>
<td>350 (5.2)</td>
</tr>
<tr>
<td>Percutaneous cytologic examination or biopsy</td>
<td>155 (2.2)</td>
<td>74 (1.1)</td>
</tr>
<tr>
<td>Transthoracic</td>
<td>120 (1.7)</td>
<td>60 (0.9)</td>
</tr>
<tr>
<td>Extrathoracic</td>
<td>39 (0.6)</td>
<td>17 (0.3)</td>
</tr>
<tr>
<td>Bronchoscopy</td>
<td>306 (4.3)</td>
<td>178 (2.6)</td>
</tr>
<tr>
<td>With neither biopsy nor cytologic testing</td>
<td>126 (1.8)</td>
<td>95 (1.4)</td>
</tr>
<tr>
<td>With biopsy or cytologic testing</td>
<td>194 (2.8)</td>
<td>95 (1.4)</td>
</tr>
<tr>
<td>Surgical procedure</td>
<td>297 (4.2)</td>
<td>197 (2.9)</td>
</tr>
<tr>
<td>Mediastinoscopy or mediastinotomy</td>
<td>60 (9.0)</td>
<td>32 (0.5)</td>
</tr>
<tr>
<td>Thoracoscopy</td>
<td>82 (1.2)</td>
<td>56 (0.8)</td>
</tr>
<tr>
<td>Thoracotomy</td>
<td>197 (2.8)</td>
<td>148 (2.2)</td>
</tr>
<tr>
<td>Other procedures</td>
<td>168 (2.4)</td>
<td>96 (1.4)</td>
</tr>
</tbody>
</table>

* The screenings were performed at 1-year intervals, with the first screening (T0) performed soon after the time of randomization. FDG PET denotes 18F-fluorodeoxyglucose positron-emission tomography.
† Positive tests with incomplete information on diagnostic follow-up are included in this category (142 at T0, 161 at T1, and 141 at T2 in the low-dose CT group and 39 at T0, 26 at T1, and 25 at T2 in the radiography group).

The NLST Screening Trial

• For those with positive screening tests, the most likely common next step in evaluation was additional imaging tests.

• Of those participants with positive screening tests, only 8.4% of participants in the CT screening group and 15.3% of participants in the radiography group underwent an invasive procedure. (Complication rate <2% in both groups).

NLST Team. NEJM, 2013.
The NLST Screening Trial

• There were 356 lung cancer specific deaths in the CT screening group and 443 in the radiography group (247 deaths/100,000 person-years vs. 309 deaths/100,000 person-years).

• This represents a 20.0% relative reduction in the rate of lung cancer specific death from CT screening (95% CI, 6.8 to 26.7; P=0.004).

• The number needed to screen with low-dose CT to prevent one death from lung cancer is 320.

NLST Team. NEJM, 2013.
NCCN Guidelines Version 1.2014
Lung Cancer Screening

Risk Assessment

- Smoking history
  - Present or past
- Radon exposure
- Occupational exposure
- Cancer history
- Family history of lung cancer
- Disease history (COPD or pulmonary fibrosis)
- Smoking exposure (second-hand smoke)
- Absence of symptoms or signs of lung cancer (if symptoms, see appropriate NCCN Guidelines)

Risk Status

- **High risk:**
  - Age 55-74 y and
  - ≥30 pack year history of smoking and
  - Smoking cessation <15 y (category 1)
  
  or
  - Age ≥50 y and
  - ≥20 pack year history of smoking and
  - One additional risk factor (other than second-hand smoke) (category 2B)

- **Moderate risk:**
  - Age ≥50 y and
  - ≥20 pack year history of smoking or second-hand smoke exposure
  - No additional risk factors

- **Low risk:**
  - Age <50 y and/or
  - <20 pack year history of smoking

See Screening and Findings (LCS-2)

Routine lung cancer screening not recommended

NCCN Guidelines, 2014.
NCCN Guidelines Version 1.2014
Lung Cancer Screening

**SCREENING MODALITY**

Baseline low-dose CT (LDCT)\(^h\)

- No lung nodule(s) on LDCT
  - Findings requiring follow-up for diseases other than lung cancer (e.g., suspicious for other cancers, COPD, coronary artery calcifications)

**SCREENING FINDINGS**

- Lung nodule(s) on LDCT
  - Solid or part solid nodule\(^l\)
  - Ground glass opacity (GGO)\(^y\)
  - Ground glass nodule (GGN)\(^y\)
  - Nonsolid nodule (NS)\(^l\)
  - Multiple GGO/GGNs\(^l\)

- Annual LDCT for 2 years (category 1) and consider annual LDCT until patient no longer eligible for definitive treatment\(^{h,j,k}\)
Screening for Lung Cancer: U.S. Preventive Services Task Force Recommendation Statement

Virginia A. Moyer, MD, MPH, on behalf of the U.S. Preventive Services Task Force*

Description: Update of the 2004 U.S. Preventive Services Task Force (USPSTF) recommendation on screening for lung cancer.

Methods: The USPSTF reviewed the evidence on the efficacy of low-dose computed tomography, chest radiography, and sputum cytologic evaluation for lung cancer screening in asymptomatic persons who are at average or high risk for lung cancer (current or former smokers) and the benefits and harms of these screening tests and of surgical resection of early-stage non–small cell lung cancer. The USPSTF also commissioned modeling studies to provide information about the optimum age at which to begin and end screening, the optimum screening interval, and the relative benefits and harms of different screening strategies.

Population: This recommendation applies to asymptomatic adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years.

Recommendation: The USPSTF recommends annual screening for lung cancer with low-dose computed tomography in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery. (B recommendation)

Ann Intern Med.
For author affiliation, see end of text.
* For a list of the members of the USPSTF, see the Appendix (available at www.annals.org).
This article was published online first at www.annals.org on 31 December 2013.
<table>
<thead>
<tr>
<th>Population</th>
<th>Recommendation</th>
<th>Grade (What's This?)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults Aged 55-80, with a History of Smoking</td>
<td>The USPSTF recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.</td>
<td>B</td>
</tr>
</tbody>
</table>
Lung Cancer Screening Registries

The Centers for Medicare & Medicaid Services (CMS) issued a national coverage determination (NCD) for Medicare coverage of screening for lung cancer with low dose computed tomography (LDCT) if certain eligibility requirements are met, effective February 5, 2015. Detailed information regarding the eligibility requirements are available in the NCD. Eligible radiology imaging facilities furnishing lung cancer screening with LDCT are required to submit data to a CMS-approved registry for each lung cancer LDCT screening performed. Below is the list of CMS-approved lung cancer screening registries.

American College of Radiology (ACR) Lung Cancer Screening Registry (LCSR)
Email: nrdr@acr.org
Phone: 1-800-227-5463, extension 3535
http://www.acr.org/Quality-Safety/National-Radiology-Data-Registry/Lung-Cancer-Screening-Registry

Related Links

- Decision Memo for Screening for Lung Cancer with Low Dose Computed Tomography (LDCT)
- Medicare Coverage Database
- Medicare Coverage Center
The NLST Screening Trial

• Issues:
  – Is this protocol ready for “prime time”? Can communities effectively implement a screening protocol? There are over 7 million Americans who currently meet the NLST inclusion criteria and nearly 100 million current/former smokers in the U.S.
  – Is there an added advantage to ongoing screening beyond three yearly screening tests?
  – How do we effectively address the high false positive rate?
  – Can we effectively identify independent risk factors beyond the selection criteria that could potentially address the high false positive rate?
• The screening protocol as conducted in the NLST cost $1,631 per person randomized to low-dose CT screening and $469 per person randomized to chest radiograph screening.

• Screening by low-dose CT added an additional 0.0316 life-years per person screened, corresponding to a cost of $52,000 per life-year gained.
“It remains an astonishing, disturbing fact that in America – a nation where nearly every new drug is subjected to rigorous scrutiny as a potential carcinogen, and even the bare hint of a substance’s link to cancer ignites a firestorm of public hysteria and media anxiety – one of the most potent and common carcinogens known to humans can be freely bought and sold at every corner store for a few dollars.”

-Siddhartha Mukherjee, M.D.

*The Emperor of All Maladies*
Questions?

vincedcataldo@gmail.com
Frequency of Screening After Adenoma

- **Low-Risk Adenomatous Polyps**: Every 5 years
  - ≤ 2 in number
  - < 1 cm
  - Tubular

- **High-Risk Adenomatous Polyps**: 3 years, then every 5 years if normal
  - High-grade dysplasia
  - ≥ 1 cm
  - Villous (> 25% villous)
  - Between 3 and 10 in number (>10-consider a polyposis syndrome)

NCCN Guidelines, 2015.
rad.usuhs.edu
Commons.wikimedia.org
Frequency of Screening After CRC

• 1 year following resection of the CRC
  – Yearly if adenomas are discovered
• Then, 2-3 years,
• Then, 3-5 years if colonoscopies remain normal

NCCN Guidelines, 2015.
Frequency of Screening with IBD

• Begin screening with colonoscopy within ten years of onset of symptoms of colitis.

• Then, colonoscopy every 1-2 years with extensive sampling of strictures and masses, polypectomy when appropriate with sampling of surrounding mucosa, and extensive 4 quadrant biopsies when IBD is clinically quiescent.

NCCN Guidelines, 2015.
Frequency of Screening with Family History of CRC

• One 1\textsuperscript{st} degree relative with CRC aged <50 years OR two 1\textsuperscript{st} degree relatives with CRC at any age:
  – Colonoscopy at age 40 or 10 years prior to earliest age of diagnosis then every 3-5 years.

• One 1\textsuperscript{st} degree relative with CRC aged ≥50 years:
  – Colonoscopy at age 50 or 10 years prior to earliest age of diagnosis then every 5 years.

NCCN Guidelines, 2015.
Breast Cancer Screening in High Risk Populations

• Women with a previous history of breast cancer:
  – There is NO evidence to suggest that mammography more frequent than once yearly in the asymptomatic breast cancer survivor improves overall survival.
  – Clinical breast examination is warranted every 6-12 months.

NCCN Guidelines, 2015.
High Risk Populations

• History of LCIS
  – Beginning at the time of diagnosis of LCIS, annual bilateral screening mammography and clinical breast exam every 6-12 months.

NCCN Guidelines, 2015.
High Risk Populations

• History of thoracic radiation prior to the age of 30
  – There is a lag time of increased incidence of breast cancer following thoracic radiation of approximately 8-10 years after radiation.
    • For patients < 25 years, annual clinical breast exam beginning 8-10 years after radiation
    • For patients ≥ 25 years, annual bilateral screening mammography and clinical breast exam every 6-12 months beginning 8-10 years after radiation or age 40, whichever occurs first.

NCCN Guidelines, 2015.
High Risk Populations

• Gail Model risk suggesting a $\geq 1.7\%$ 5-year risk of invasive breast cancer in women $\geq 35$ years
  – Can be used for any woman aged $\geq 35$ to calculate her 5-year and lifetime risk of breast cancer
  – Interactive online calculators available
  – Factors affecting the risk score include: Age, age at menarche, age at first live birth, history of lcis/dcis/adh, history of breast biopsy for any reason, family history of breast cancer, and race.
  – Annual bilateral screening mammography and clinical breast exam every 6-12 months beginning at the time elevated risk discovered or age 40, whichever occurs first.

NCCN Guidelines, 2015.
Prostate Screening Guidelines.

- Assuming that the first PSA and DRE are performed at age 40 and are normal:
  - Continue annual screening if the PSA $\geq 1$, African American Race, or Family History
  - If PSA < 1 and DRE normal, repeat screening at 5 year intervals until 50, then annually
- PSA Velocity:
  - In men with PSA < 4 ng/mL, a PSA velocity of $\geq 0.35$ ng/mL/yr is suspicious for cancer.
  - In men with PSA 4-10 ng/mL, a PSA velocity of $\geq 0.75$ ng/mL/yr is suspicious for cancer.
- DRE:
  - If at any time the DRE is positive, proceed to TRUS-guided biopsy.

NCCN, 2014.
Is flexible sigmoidoscopy an appropriate screening modality?

• Flexible sigmoidoscopy compared with usual care was associated with a relative **reduction in overall colorectal-cancer mortality of 26%** and a **21% relative reduction in the incidence of colorectal cancer**.

• Comparing the two groups, there was a **50% reduction in mortality from distal colorectal cancer**, and the incidence of distal colorectal cancer was **reduced by 29%** in the study group.

• Comparing the two groups, there was a **14% reduction in the incidence of proximal colorectal cancer** in the study group, but there was **NO reduction in mortality related to proximal colorectal cancers**.

• Does this actually lend support to colonoscopy as the preferred screening modality for colon cancer?

182,000 men randomized to PSA-based screening vs. no screening

At 11 years median follow up, there was a 21% relative risk reduction in prostate-specific mortality in the screening group.

The absolute reduction in mortality in the screening group was 0.1 deaths per 1000 person-years (1.07 deaths per 1000 men screened). (Number needed to screen=1055, Number needed to detect and treat=37)

No difference in all-cause mortality between the two groups