Cancer Screening 2016

Andrew Scott Pierson, MD  
Medical Oncology/Hematology  
Andrew.Pierson001@saintalphonsus.org  
Cell 208-870-2888

Goals of Lecture

1. Discuss the recommended cancer screening strategies known to increase overall survival
   ◦ Cervical
   ◦ Breast
   ◦ Colon
   ◦ Lung

2. Discuss the different recommendations for screening (e.g. breast cancer)
Cancer Screening Definition

“What cancer screening is the use of a test to detect cancer in an asymptomatic individual at an early stage with the intent to prolong life”

Why Screen?

- Cancers treated at an earlier stage have a better prognosis
- Screening in otherwise healthy individuals can improve the probability of a longer life
In Idaho, Cancer is the Leading Cause of Death. We Have Work to Do.

Figure 6. Screening Rates in Idaho (2014)

<table>
<thead>
<tr>
<th>Test Description</th>
<th>National Median</th>
<th>Idaho Percentage</th>
<th>Non-Hispanic Whites Percentage</th>
<th>Non-Hispanic Whites Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical Cancer Screening: Women Ages 21-65 Who Had a Pap Test Within the Past Three Years</td>
<td>83%</td>
<td>77%</td>
<td>83%</td>
<td>77%</td>
</tr>
<tr>
<td>Breast Cancer Screening: Women Aged 50-74 Who Had a Mammogram Within the Past Two Years</td>
<td>78%</td>
<td>69%</td>
<td>78%</td>
<td>69%</td>
</tr>
<tr>
<td>Colorectal Cancer Screening: Adults Aged 50-75 Who Were Screened for Colorectal Cancer Based on Most Recent Guidelines</td>
<td>67%</td>
<td>61%</td>
<td>68%</td>
<td>62%</td>
</tr>
</tbody>
</table>

Source: www.ccaidaho.org
CERVICAL CANCER SCREENING
Cervical Cancer Statistics-2016

- 12,990 new cases
- 4,120 deaths


Cervical Cancer Risk Factors

- HPV infection
- Smoking
- Immunosuppression
- Chlamydia
- Diet low in fruits and vegetables
- Obesity (for adenocarcinoma)
- OCPs (>5 years)

- IUD (protective)
- Poverty
- DES (diethylstibestrol)
Success of Cancer Screening Program

Cervical Cancer Incidence and Mortality in the USA

Considerable reduction of mortality from cervical cancer with the implementation of Pap smear testing.
**HPV-The Cause of Most Cervical Cancer**

**Human Papillomavirus (HPV)**

- **12 strains** of human papillomavirus (HPV) caused -50% of new cancer cases attributed to infection globally in 2008.

**In the United States, HPV Causes:**
- 96% of cervical cancer cases.
- 53% of vulvar cancers.
- 64% of vaginal cancers.
- 36% of penile cancers.
- 93% of anal cancers.
- 63% of oropharyngeal head and neck cancers.

**Preventing Infection**

Two FDA-approved vaccines can protect against infection with HPV16 and HPV18.

Both vaccines are highly effective at preventing precancerous cervical lesions.

One of the vaccines, Gardasil, was also found to prevent precancerous anal, vulvar, and vaginal lesions.

According to the CDC, safe sex practices may lower the risk of, but may not fully protect against, HPV infection.

Source: www.aacrfoundation.org

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**Incorporation of HPV into Cervical Cancer Screening**

- Women aged 30 to 65 years should be screened with cytology and HPV testing (“co-testing”) every 5 years (preferred) or cytology alone every 3 years (acceptable).

- HPV testing should not be routinely done for women between the ages of 21 and 30.
Cervical Cancer Recommendations

<table>
<thead>
<tr>
<th>Age to start</th>
<th>ACS 2012</th>
<th>USPSTF 2012</th>
<th>ACOG 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women ages 21-29</td>
<td>Cytology every 3 years</td>
<td>Cytology every 3 years</td>
<td>Cytology every 3 years</td>
</tr>
<tr>
<td>Women ages 30-65</td>
<td>Cytology every 5 years (preferred) or Every 3 years with Pap alone</td>
<td>Cytology every 5 years or Every 3 years with Pap alone</td>
<td>Cytology every 5 years (preferred) or Every 3 years with Pap alone</td>
</tr>
<tr>
<td>Women ages &gt; 65</td>
<td>Discontinue after age 65 years (adequate screen)</td>
<td>Discontinue after age 65 years -</td>
<td>Discontinue at age 65 years (adequate screen)</td>
</tr>
<tr>
<td>Total Hysterectomy</td>
<td>Discontinue (if no history of CIN2+)</td>
<td>Discontinue (if no history of CIN2+)</td>
<td>Discontinue (if no history of CIN2+)</td>
</tr>
<tr>
<td>Screening among fully vaccinated</td>
<td>Same as for non-vaccinated</td>
<td>Not reviewed</td>
<td>Same as for non-vaccinated</td>
</tr>
</tbody>
</table>

Figure 3
HPV Vaccination Rates of Adolescent Girls ages 13-17, by State

Completion of 3 dose HPV vaccine series among females ages 13-17, 2014

2014 U.S. average = 39.7%

NOTES: Share of females ages 13-17 who have received all 3 doses of the HPV vaccine series. *Statistically significant (p<.05) percentage point change from 2013.

Breast Cancer Statistics-2016

- 231,840 new cases
- 40,290 deaths
- #2 cause of cancer death
- Leading cause of pre-mature mortality for women
# Breast Cancer Risk Factors

- Gender
- Older Age
- Family History
- Personal History
- More Menstruation (early menarche <12 years or delayed menopause >55 years)
- Certain types of benign breast disease
- Genetics
- DES exposure
- # of Pregnancies
- OCPs
- Depot-Provera
- Post-menopausal HRT (combined estrogen/progesterone)
- Breast Feeding
- Alcohol
- Obesity
- Previous Chest Wall Radiation

## Benign Breast Disease (Non-proliferative)- Not associated with Breast Cancer

- Fibrosis and/or simple cysts
- Mild Hyperplasia
- Adenosis (non-sclerosing)
- Ductal Ectasia
- Benign Phyllodes tumor
- Papilloma
- Fat necrosis
- Periductal Fibrosis
- Squamous and apocrine metaplasia
- Epithelial related calcifications
- Other benign tumors
Proliferative Benign Breast Disease Without Atypia (1.5 to 2x Higher Risk)

- Usual Duct Hyperplasia
- Fibroadenoma
- Several Papillomas
- Radial Scar
- Sclerosing Adenosis

Proliferative Breast Lesions Associated with Atypia (3.5 to 5x Higher Risk)

- Atypical Ductal Hyperplasia (ADH)
- Atypical Lobular Hyperplasia (ALH)
Lobular Carcinoma In Situ (LCIS)

- 7- to 11-fold increased risk of developing invasive cancer in either breast
- Marker of breast cancer risk
- Does not require excision

Hereditary Breast Cancer

- 5-10% of breast cancers are associated with germline DNA mutations
- BRCA1 and BRCA2 mutations are the most common and are found more often in the Ashkenazi Jewish Population (Eastern Europe)
- Other mutations associated with Breast Cancer include: ATM, TP53, CHEK2, PTEN, CDH1, STK11 and PALB2
Breast Cancer Risk Assessment Tool (Gail Model)

http://www.cancer.gov/bcrisktool/
Breast Cancer Screening Recommendations

<table>
<thead>
<tr>
<th>Screening Modality</th>
<th>AMERICAN CANCER SOCIETY</th>
<th>AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS</th>
<th>U.S. PREVENTIVE SERVICES TASK FORCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Self Exam</td>
<td>Recommends against self breast exam, but encourages breast self awareness</td>
<td>Breast Self Awareness encouraged</td>
<td>Recommends against</td>
</tr>
<tr>
<td>Clinical Breast Exam</td>
<td>Recommends against clinical exam at any age</td>
<td>Every one to three years from 20 to 39 years of age and annually thereafter</td>
<td>Insufficient evidence to support clinical breast exams.</td>
</tr>
<tr>
<td>Magnetic Resonance Imaging</td>
<td>Offer annually to women at high risk</td>
<td>Offer annually to women at high risk</td>
<td>Insufficient evidence to support clinical breast exams.</td>
</tr>
<tr>
<td>Mammogram</td>
<td>Routine annual screening beginning at 45 years of age until age 54. And biennial screening for women 55 years or older if they have a life expectancy greater than 10 years</td>
<td>Routine annual screening beginning at 40 years of age</td>
<td>Routine biennial screening for women 50 to 74 years of age</td>
</tr>
</tbody>
</table>

USPTF Recommendations Rationale

- Screening between the ages of 40-49 is not recommended (Harms > Benefits)
  - Anxiety
  - False positives (rate of 1 false positive recall after 10 years of screening was 61.3% with annual screening). Rate of false positive leading to a biopsy was approx. 7%
  - Overdiagnosis
- The mortality benefits are small for this age group
Trends in the Annual Incidence of Late-Stage Breast Cancer and its Two Components (Regional and Distant Disease) among U.S. Women 40 Years of Age or Older, 1976–2008.
What Are the Potential Harms of Breast Cancer Screening?

- Anxiety
- Overdiagnosis (e.g. DCIS)
- Radiation Exposure
How Much Has Mammography Decreased Breast Cancer Mortality?

- Among women 40 years of age or older, deaths from breast cancer have decreased from 71 to 51 deaths per 100,000 (28% decrease).
- Among women less than 40 years of age, deaths from breast cancer have decreased 42%.
- The estimate of the benefit of mammography ranges from 28% to 65%.
- Part of the reduction of breast cancer mortality is due to better treatment.


Mammography False Negatives

- Mammography misses about 16% of breast cancers.
- With increased breast density the false negative rate can be as high as 30%.

Current Saint Alphonsus Cancer Care Recommendations

- Breast Cancer continuum suggests screening starting at age 40 for average risk women
- The risks of screening are small compared to the potential benefit
- Even if the mortality benefit is small, there is still advantage to picking up breast cancer earlier
  - The mastectomy rate is lower
  - The patient may be spared the experience of chemotherapy
- Continue annual screening as long as the patient is healthy and life expectancy is 10 years.

Digital Tomosynthesis (3D Mammography)
Advantages of Tomosynthesis

- Better overall detection
- Better imaging for non-fatty breasts
- Less call back rates
Colorectal Cancer Statistics-2016

- 3rd most common cancer diagnosed (excluding skin cancer)
- 95,270 new cases of colon cancer
- 39,220 new cases of rectal cancer
- 49,190 deaths
- Lifetime risk is 1:21 (4.7%) men and 1:23 (4.4%) for women
Colorectal Cancer Risk Factors

- Being overweight
- Physical inactivity
- Diet high in red meat
- Eating meat cooked at high temperatures
- Smoking
- Heavy ETOH use
- Age
- Personal History of colorectal polyps or colorectal cancer
- First degree relative with h/o colorectal polyps or colorectal cancer
- Having an inherited syndrome
- Race
- Type 2 DM

Colon Cancer Screening Rates 2012

- 65.1% of adults ages 50-75 reported being screened
- The most common screening test was colonoscopy (50%)
- 27.7% were never screened
- The never screened rate was 55% without insurance and 61% for those without regular healthcare provider

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6244a4.htm
Clustering of Cancer in Families

- ~6% lifetime risk of CRC in general population
- ~20% of people with CRC have a family history:
  - ~15% of CRC is familial:
    - Environmental factors
    - Chance
    - Undiscovered gene mutation
    - Generally not eligible for genetic testing
  - ~5% of CRC cancer is hereditary:
    - Caused by an inherited gene mutation that puts them at increased risk for cancer
      - Majority is Lynch syndrome/HNPCC (Hereditary Non-Polyposis Colorectal Cancer)
      - Small fraction is Familial Adenomatous Polyposis (FAP) or other rare cancer syndromes
    - May be eligible for genetic testing
Proportion of Hereditary CRC

- Sporadic 80%
- Familial ~15%
- Hereditary ~5%
  - Lynch syndrome ~ 2-5%
  - FAP ~ <1%

Compared to sporadic cancer people with hereditary cancer have…

- A higher risk of developing cancer
- A younger age of onset of cancer
  - Generally < 50 years of age
- Multiple primary cancers
- Generally have a family history of cancer
Inherited Colorectal Cancer
Two common syndromes:

- **Lynch syndrome**
  - Also known as Hereditary Non Polyposis Colorectal Cancer or HNPCC
  - ~2 - 5% of colorectal cancer
  - Prevalence of 1 in 200 - 2,000*

- **Familial Adenomatous Polyposis (FAP)**
  - <1% of colorectal cancer
  - Prevalence of 1 in 8,000 – 14,000*

- Autosomal dominant inheritance

*Prevalence depends on population

Colorectal cancer genes… when mutated

- **Lynch syndrome (HNPCC):**
  - Mutations in DNA repair genes lead to an accumulation of mutations which may result in malignancy.

- **FAP:**
  - Mutations in a tumour suppressor gene cause an increase in cell proliferation and a decrease in cell death.
Lynch syndrome (HNPCC)

- Lynch syndrome is genetically heterogeneous
  - Clinical testing available for 4 genes: MLH1 & MSH2 (most common), MSH6 & PMS2
  - Research testing may be available for other genes
- High penetrance
- Characterized by:
  - Earlier onset than sporadic cancer
  - More aggressive, proximal, right sided tumours
  - Risk for extra-colonic tumours
  - Distinct tumour pathology

Cancer Risk in Individuals with Lynch syndrome (HNPCC) to Age 70 Compared to General Population

<table>
<thead>
<tr>
<th>Cancer</th>
<th>General Population Risk</th>
<th>Lynch syn. Risk</th>
<th>Mean Age of Onset in Lynch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon</td>
<td>7%</td>
<td>80%</td>
<td>45 years</td>
</tr>
<tr>
<td>Endometrium</td>
<td>2.7%</td>
<td>20-60%</td>
<td>46 years</td>
</tr>
<tr>
<td>Stomach</td>
<td>&lt;1%</td>
<td>11-19%</td>
<td>56 years</td>
</tr>
<tr>
<td>Ovary</td>
<td>1.5%</td>
<td>9-12%</td>
<td>42.5 years</td>
</tr>
<tr>
<td>Hepatobiliary tract</td>
<td>&lt;1%</td>
<td>2-7%</td>
<td>54 years</td>
</tr>
<tr>
<td>Urinary tract</td>
<td>&lt;1%</td>
<td>4-5%</td>
<td>~55 years</td>
</tr>
<tr>
<td>Small Bowel</td>
<td>&lt;1%</td>
<td>1-4%</td>
<td>49 years</td>
</tr>
<tr>
<td>Brain / CNS</td>
<td>&lt;1%</td>
<td>1-3%</td>
<td>50 years</td>
</tr>
</tbody>
</table>

from: [http://www.genetests.org](http://www.genetests.org)
Amsterdam II Criteria

- Describe the minimum requirements for a clinical diagnosis of Lynch Syndrome/Hereditary Non-Polyposis Colorectal Cancer (HNPCC)

There should be at least three relatives with a Lynch/HNPCC-associated cancer (cancer of the colorectum, endometrium, small bowel, ureter or renal pelvis) and...

- One should be a first-degree relative to the other two
- At least two successive generations should be affected
- At least one should be diagnosed before age 50
- Familial adenomatous polyposis should be excluded
- Tumors should be verified by pathological examination

Familial Adenomatous Polyposis

- Chromosome 5, APC gene
- High penetrance
- Characterized by:
  - Early onset
  - >100 adenomatous polyps
  - Variant form:
    - Attenuated FAP may occur with >10 but <100 polyps.

Consequences of FAP

- Colorectal adenomatous polyps begin to appear at an average age of 16 years (range 7-36 years)
- Average age at diagnosis: 34-43 years, when >95% have polyps

<table>
<thead>
<tr>
<th>Age</th>
<th>Individuals with colon cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>7%</td>
</tr>
<tr>
<td>45</td>
<td>87%</td>
</tr>
<tr>
<td>50</td>
<td>93%</td>
</tr>
</tbody>
</table>

From: [http://www.genetests.org](http://www.genetests.org)
COLON CANCER SCREENING FOR AVERAGE RISK PATIENTS
### Screening for Colorectal Cancer

**Clinical Summary of U.S. Preventive Services Task Force Recommendation**

<table>
<thead>
<tr>
<th>Population</th>
<th>Adults Age 50 to 75 Years*</th>
<th>Adults Age 76 to 85 Years*</th>
<th>Adults Older Than 85 Years*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommendation</strong></td>
<td>Screen with high-sensitivity FOBT, sigmoidoscopy, or colonoscopy</td>
<td>Do not screen routinely</td>
<td>Do not screen</td>
</tr>
<tr>
<td>Grade: A</td>
<td>Grade: C</td>
<td>Grade: D</td>
<td></td>
</tr>
</tbody>
</table>

For all populations, evidence is insufficient to assess the benefits and harms of screening with computed tomographic colonography and fecal DNA testing.

Grade: I (Insufficient evidence)

**Screening Tests**
High-sensitivity FOBT, sigmoidoscopy with FOBT, and colonoscopy are effective in decreasing colorectal cancer mortality. The risks and benefits of these screening methods vary.

Colorectal cancer and flexible sigmoidoscopy (to a lesser degree) entail possible serious complications.

**Screening Test Intervals**

<table>
<thead>
<tr>
<th>Intervals for recommended screening strategies:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual screening with high-sensitivity FOBT</td>
</tr>
<tr>
<td>Sigmoidoscopy every 5 years, with high-sensitivity FOBT every 3 years</td>
</tr>
<tr>
<td>Screening colonoscopy every 10 years</td>
</tr>
</tbody>
</table>

**Balance of Harms and Benefits**

The benefits of screening outweigh the potential harms for 50- to 75-year-olds.

The likelihood that detection and early intervention will yield a mortality benefit declines after age 75 because of the long average time between adenoma development and cancer diagnosis.

**Implementation**
Focus on strategies that maximize the number of individuals who get screened.

Practice shared decision making; discussions with patients should incorporate information on test quality and availability.

Individuals with a personal history of cancer or adenomatous polyps are followed by a surveillance regimen, and screening guidelines are not applicable.

**Relevant USPSTF Recommendations**
The USPSTF recommends against the use of aspirin or nonsteroidal anti-inflammatory drugs for the primary prevention of colorectal cancer. This recommendation is available at www.preventiveservices.ahrq.gov.

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### CRC Screening for Average-Risk

<table>
<thead>
<tr>
<th>Screening Test</th>
<th>ACS-USMSTF-ACR</th>
<th>USPSTF</th>
<th>Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitive gastric fecal occult blood test</td>
<td>Recommended if &gt;50% sensitivity for CRC</td>
<td>Recommended</td>
<td>1 year</td>
</tr>
<tr>
<td>Fecal immunochemical test</td>
<td>Recommended if &gt;50% sensitivity for CRC</td>
<td>Recommended, only if high sensitivity test used</td>
<td>1 year</td>
</tr>
<tr>
<td>Stool DNA test</td>
<td>Recommended if &gt;50% sensitivity for CRC</td>
<td>Not recommended due to insufficient evidence to assess sensitivity and specificity of fecal DNA</td>
<td>Uncertain</td>
</tr>
<tr>
<td>Flexible Sigmoidoscopy</td>
<td>Recommended if sigmoidoscope is inserted to 40 cm or to the splenic flexure</td>
<td>Recommended with gastric fecal occult blood test every 3 yrs</td>
<td>5 years</td>
</tr>
<tr>
<td>Barium Enema</td>
<td>Recommended, but only if other tests are not available</td>
<td>Not recommended</td>
<td>5 years</td>
</tr>
<tr>
<td>CT Colonography</td>
<td>Recommended, with referral for colonoscopy if polyps &gt;6 mm are detected</td>
<td>Not recommended</td>
<td>5 years</td>
</tr>
</tbody>
</table>

Colonoscopy Recommended Recommended 10 year

Stool Test: Immunochemical (FIT)

- Specific for human blood and for lower GI bleeding
- Results not influenced by foods or medications
- Some types require only 1 or 2 stool specimens
- Higher sensitivity than older forms of guaiac-based FOBT
- Slightly more costly than guaiac tests

*FIT use in the US will likely increase due to recent elimination of guaiac-based testing by LabCorp and Quest Labs*
Stool DNA Test (sDNA)

- Rationale
  - Fecal occult blood tests detect blood in the stool – which is intermittent and non-specific
  - Colon cells are shed continuously
  - Polyps and cancer cells contain abnormal DNA
  - Stool DNA tests look for abnormal DNA from cells that are passed in the stool*

*All positive tests should be followed with colonoscopy

Colognard®: Foundation to our success

- FDA-approved & Medicare-covered
- Developed in collaboration with Mayo Clinic
- New England Journal of Medicine results:
  - 92% cancer sensitivity (all stages)
  - 69% high grade dysplasia sensitivity
  - 87% specificity
  - 94% sensitivity for stages I to II cancer
- Included in American Cancer Society guidelines

Source: American Cancer Society Cancer Facts & Figures 2013; Atlanta: American Cancer Society 2013
LUNG CANCER SCREENING

Lung Cancer Statistics 2016

- 2\textsuperscript{nd} most common cancer in both men and women
- 224,390 new cases
- 158,080 deaths
- Each year more people die of lung cancer than of colon, breast and prostate cancer combined
- Average age at diagnosis is 70
Lung Cancer Risk Factors

- Tobacco Smoke (80% of lung cancer is smoking related)
- Second hand smoke
- Radon exposure
- Asbestos exposure
- Other workplace exposures (uranium, diesel exhaust, etc.)
- Previous radiation to the lungs
- Air Pollution (5% of all lung cancer deaths worldwide)
- Personal or family history of lung cancer

National Lung Screening Trial (NLST)

- Asymptomatic men and women 55 to 74 years of age were randomly assigned to low dose CT scan or chest radiography to be done annually for 3 years
  - Participants had to have a 30 pack year smoking history or greater
  - Participants were either current smokers or had been smokers within the previous 15 years

Enrollment and Follow-up of the Study Participants after the Initial Screening


NLST: Stage Groupings

Table 5. Stage and Histologic Type of Lung Cancers in the Two Screening Groups, According to the Result of Screening.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Positive Screening Test (N=649)</th>
<th>Negative Screening Test (N=447)</th>
<th>No Screening Test (N=367)</th>
<th>Total (N=146)</th>
<th>Positive Screening Test (N=279)</th>
<th>Negative Screening Test (N=137)</th>
<th>No Screening Test (N=229)</th>
<th>Total (N=641)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>329/665 (51.0)</td>
<td>5/44 (11.4)</td>
<td>82/361 (22.7)</td>
<td>50/275 (18.0)</td>
<td>16/135 (11.9)</td>
<td>90/916 (10.0)</td>
<td>97/925 (10.5)</td>
<td>196/929 (21.1)</td>
</tr>
<tr>
<td>IB</td>
<td>71/665 (11.2)</td>
<td>2/44 (4.5)</td>
<td>31/361 (8.6)</td>
<td>25/275 (9.1)</td>
<td>4/135 (3.0)</td>
<td>46/916 (5.0)</td>
<td>42/925 (4.5)</td>
<td>99/929 (10.0)</td>
</tr>
<tr>
<td>II A</td>
<td>26/665 (4.1)</td>
<td>2/44 (4.5)</td>
<td>7/361 (1.9)</td>
<td>16/275 (5.8)</td>
<td>2/135 (1.5)</td>
<td>16/916 (1.7)</td>
<td>18/925 (1.9)</td>
<td>32/929 (3.4)</td>
</tr>
<tr>
<td>II B</td>
<td>20/665 (3.1)</td>
<td>3/44 (6.8)</td>
<td>15/361 (4.2)</td>
<td>10/275 (3.6)</td>
<td>3/135 (2.2)</td>
<td>25/916 (2.7)</td>
<td>28/925 (3.0)</td>
<td>53/929 (5.7)</td>
</tr>
<tr>
<td>III A</td>
<td>59/665 (9.3)</td>
<td>3/44 (6.8)</td>
<td>37/361 (10.2)</td>
<td>35/275 (12.7)</td>
<td>3/135 (2.2)</td>
<td>57/916 (6.3)</td>
<td>71/925 (7.6)</td>
<td>109/929 (12.7)</td>
</tr>
<tr>
<td>III B</td>
<td>40/665 (6.7)</td>
<td>5/44 (11.4)</td>
<td>58/361 (16.1)</td>
<td>22/275 (8.0)</td>
<td>24/135 (17.8)</td>
<td>7/916 (0.8)</td>
<td>7/925 (0.8)</td>
<td>49/929 (5.4)</td>
</tr>
<tr>
<td>IV</td>
<td>81/665 (22.8)</td>
<td>14/44 (31.8)</td>
<td>113/361 (31.3)</td>
<td>226/275 (82.7)</td>
<td>57/135 (42.4)</td>
<td>21/916 (2.3)</td>
<td>21/925 (2.3)</td>
<td>232/929 (24.9)</td>
</tr>
</tbody>
</table>

20% reduction in lung-cancer specific mortality with LDCT
6.7% reduction in overall mortality with LDCT

Lung Cancer Screening

RISK ASSESSMENT

- Smoking history
  - Present or past
  - Riton exposure
  - Occupational exposure
  - Cancer history
  - Family history of lung cancer
  - Obesity (BMI > 30)
  - History of pulmonary fibrosis
  - Smoking exposure (second-hand smoke)
  - Absence of symptoms or signs of lung cancer (if symptoms, see separate guidelines)

RISK STATUS

High risk:
- Age 55-79 y
- 10 pack-year history of smoking
- Smoking cessation < 15 y

Moderate risk:
- Age 50 y
- 20 pack-year history of smoking
- No additional risk factors

Low risk:
- Age < 50 y
- < 10 pack-year history of smoking

SCREENING MODALITY

- Baseline low-dose computed tomography (LDCT)
- Annual LDCT screening for 3 years and until age 74

SCREENING FINDINGS

- No lung nodules on LDCT
- Lung nodules on LDCT
  - Solid or part solid nodule
  - Ground glass opacity (GGO)
  - Nodule growth

- Surgical excision
- No cancer
- Cancer confirmed

See Evaluation of Screening Findings (LCS-2)
See Evaluation of Screening Findings (LCS-3)
Annual LDCT screening for 3 years and until age 74

EVALUATION OF SCREENING FINDINGS

- Follow-up CT scans should be performed at low dose (100-120 kVp) and 40-60 ms or less, unless evaluating mediastinal abnormalities or lymph nodes, where standard dose CT with kV contrast might be appropriate.
- There should be a systematic process for appropriate follow-up.
- Without bronchial pattern of calcification, fat in nodules is not transmural, or features suggesting inflammatory etiology. When multiple nodules are present and current infection or inflammation is possible, an added option is a course of a broad-spectrum antibiotic with aminocaproic acid, followed by LDCT 1-2 months later.
- If confidence in annual or follow-up LDCT, see LCS-2. Nodule density is defined as 33 HU in mean diameter.
- Level of suspicion for lung cancer is based on size, shape, and number of nodules.
- PET is a better modality for tumors with less than 8 mm of solid component.
- Nodules > 3 cm in size have a lower likelihood of malignancy, especially if the history of surrounding lung parenchyma, regardless of absolute SUV.
- If nodules < 15 mm in diameter, increased in diameter 22 mm in any nodule or if on the solid portion of a partial nodule compared to baseline scan. For nodules >15 mm increase in mean diameter of 15% compared to baseline scan.
- Note: All recommendations are category A unless otherwise indicated.
- Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
NLST - False Positives

- 24.2% of CT screens were positive

- False Positive: 3.6%
- True Positive: 96.4%

NLST - Positive Studies

- 92% of positive CT screens had a diagnostic evaluation

- 16 deaths within 60 days
- 6 of 16 had benign pathology
Overdiagnosis in Low-Dose Computed Tomography Screening for Lung Cancer

Overdiagnosis: Detection of disease that does not contribute to death

Results in unnecessary treatment, morbidity, cost, worry

Lung Cancer (LDCT) 18%
Breast Cancer (Mammo) 30-54%
Prostate Cancer (PSA) 29-44%

Etzioni et al. JNCI 2002; 94: 981-990
Published online December 8, 2014.

An Actuarial Analysis Shows That Offering Lung Cancer Screening As An Insurance Benefit Would Save Lives At Relatively Low Cost

- Cost per life-year saved would be below $19,000 (ages 50-64)

Pyrenese et al. Health Affairs 31, No.4 770-779: April 2012
LDCT Radiation Exposure

- Mean dose in NLST per scan 1.4 mSv
  - 1/5 the dose of standard CT scan
  - Annual ambient radiation dose 8 mSv
- Mean dose in mammography 0.7 mSv
- Based on risk models from atomic bombings and medical imaging, LDCT screening will cause one cancer death from radiation per 2500 screened
- Risk is low but not trivial

JAMA 2012; 307:2418-2429

Radiation Exposure

<table>
<thead>
<tr>
<th>LDCT</th>
<th>&lt;1 mSv</th>
<th>Years of annual lung screening</th>
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</thead>
<tbody>
<tr>
<td>Mammogram</td>
<td>.7 mSv</td>
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<tr>
<td>Lumbar Spine Films</td>
<td>2 mSv</td>
<td>2</td>
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<tr>
<td>Diagnostic Chest CT</td>
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<td>Background Exposure Colorado</td>
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<td>4.5 mSv/year</td>
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<tr>
<td>Occupational Exposure</td>
<td>50 mSv/year</td>
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<tr>
<td>Transatlantic Flight</td>
<td>.1 mSv</td>
<td>7 flights = 1 LDCT</td>
</tr>
</tbody>
</table>

10 -30 year latency period to develop secondary malignancies from RT exposure

Average age of patients in screening trials is 62
QUESTIONS?