LUNG CANCER SCREENING
Development of Guidelines

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University of Washington
Lung Cancer is the Leading Cause of Cancer Death in Every Ethnic Group

Estimated Cancer Deaths in 2011

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Estimated Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung and Bronchus</td>
<td>156,940</td>
</tr>
<tr>
<td>Colon/Rectum</td>
<td>49,380</td>
</tr>
<tr>
<td>Breast (Female)</td>
<td>39,520</td>
</tr>
<tr>
<td>Pancreas</td>
<td>37,660</td>
</tr>
<tr>
<td>Prostate</td>
<td>33,720</td>
</tr>
<tr>
<td>Larynx/Sorel's Lung Cancer*</td>
<td>28,000</td>
</tr>
<tr>
<td>Leukemia</td>
<td>21,780</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>21,626</td>
</tr>
<tr>
<td>Liver</td>
<td>19,590</td>
</tr>
<tr>
<td>Ovary</td>
<td>15,460</td>
</tr>
<tr>
<td>Bladder</td>
<td>14,990</td>
</tr>
<tr>
<td>Esophagus</td>
<td>14,710</td>
</tr>
<tr>
<td>Brain</td>
<td>13,110</td>
</tr>
<tr>
<td>Uterus/Cervix</td>
<td>12,410</td>
</tr>
</tbody>
</table>

Lung Cancer is the Second Leading Cause of all Deaths in the United States

Actual Deaths in 2009

<table>
<thead>
<tr>
<th>Cause</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart disease</td>
<td>598,607</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>158,105</td>
</tr>
<tr>
<td>Lower respiratory disease</td>
<td>137,082</td>
</tr>
<tr>
<td>Stroke</td>
<td>128,603</td>
</tr>
<tr>
<td>Accident</td>
<td>117,176</td>
</tr>
<tr>
<td>Alzheimer's</td>
<td>78,889</td>
</tr>
<tr>
<td>Diabetes</td>
<td>68,504</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>52,462</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>50,774</td>
</tr>
<tr>
<td>Kidney disease</td>
<td>48,714</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>41,115</td>
</tr>
<tr>
<td>Suicide</td>
<td>36,547</td>
</tr>
<tr>
<td>Pancreatic cancer</td>
<td>35,872</td>
</tr>
<tr>
<td>Septicemia</td>
<td>35,587</td>
</tr>
<tr>
<td>Liver disease</td>
<td>30,444</td>
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<tr>
<td>Prostate cancer</td>
<td>28,154</td>
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<tr>
<td>Leukemia</td>
<td>22,697</td>
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<td>Lymphoma</td>
<td>21,626</td>
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<tr>
<td>Parkinson's disease</td>
<td>20,552</td>
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<tr>
<td>Liver cancer</td>
<td>19,311</td>
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<tr>
<td>Homicide</td>
<td>16,591</td>
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<tr>
<td>Ovarian cancer</td>
<td>14,513</td>
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<tr>
<td>Bladder cancer</td>
<td>14,315</td>
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<td>Brain cancer</td>
<td>14,192</td>
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<tr>
<td>Esophageal cancer</td>
<td>13,916</td>
</tr>
<tr>
<td>Kidney cancer</td>
<td>13,027</td>
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<tr>
<td>Stomach cancer</td>
<td>11,139</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>9,424</td>
</tr>
<tr>
<td>Melanoma</td>
<td>9,254</td>
</tr>
<tr>
<td>Lip/oral cancers</td>
<td>7,913</td>
</tr>
</tbody>
</table>

* Includes COPD, emphysema, asthma, bronchitis

Cancer Screening – Early Detection

Why is the Survival Rate for Lung Cancer Still So Low?

Because so Few Cases are Diagnosed at Early Stage When Cancer is Most Curable

Cancer screening coverage
Breast
Prostate
Colon

Lung cancer disparities
Elderly
Low socioeconomic group
Racial
“Self-inflicted” disease
Primary aim: to determine whether lung cancer screening using low-dose helical CT reduces lung cancer-specific mortality relative to screening with chest radiographs in a high-risk cohort.
# National Lung Screening Trial Results

## Lung Cancer Specific Mortality

<table>
<thead>
<tr>
<th>Trial Arm</th>
<th>Person Years (py)</th>
<th>Lung Cancer Deaths</th>
<th>Lung Cancer Mortality per 100,000 py</th>
<th>Reduction in Lung Cancer Mortality (%)</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDCT</td>
<td>144,103</td>
<td>356</td>
<td>247</td>
<td><strong>20.0</strong></td>
<td>6.8 to 26.7</td>
<td>0.004</td>
</tr>
<tr>
<td>CXR</td>
<td>143,368</td>
<td>443</td>
<td>309</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## All Cause Mortality

<table>
<thead>
<tr>
<th>Trial Arm</th>
<th>Person Years (py)</th>
<th>Deaths</th>
<th>All-cause Mortality per 100,000 py</th>
<th>Reduction in All-cause Mortality (%)</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDCT</td>
<td>167,389</td>
<td>1877</td>
<td>1121</td>
<td><strong>6.7</strong></td>
<td>1.2 to 13.6</td>
<td>0.02</td>
</tr>
<tr>
<td>CXR</td>
<td>166,382</td>
<td>2000</td>
<td>1202</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

National Lung Screening Trial NEJM 2011
Conclusion

Screening with low dose chest CT conclusively reduces mortality from lung cancer in high risk patients.
At the present time, the NCCN panel does not recommend the routine use of screening CT as standard clinical practice (category 3). Available data are conflicting and thus, conclusive data from ongoing clinical trials are necessary to define the benefits and risks....
Benefits of Guidelines for Screening or Preventive Services

Especially important to identify “at risk” population
Identification of benefits and harms
Uniformity of evaluation and management protocols
Avoidance of over-testing
  Lack of knowledge by provider
  Anxiety of patient
  Financial incentives
Identification of requisite specialization
Guide correct entry points to treatment (and mitigate potential of over treatment)
Characteristics of High Quality Guideline Development Process

Explicit process
Evidence-based when possible
Level of evidence identified for each recommendation
Multidisciplinary
Expert panelists
Conflicts of interest managed
Updated frequently
Logical follow through processes of users
Supporting documentation provided
NCCN Guidelines Program

50 multidisciplinary panels with 26-30 experts per panel
62 Clinical Practice Guidelines in Oncology updated continuously
Cover continuum and all modalities of cancer care
Accepted as standard for clinical care and policy in oncology in United States
Basis for insurance coverage policy and quality evaluation
6.7 million copies downloaded in 2015 to 180 countries

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Advantages of NCCN Guidelines for Lung Cancer Screening

Wide breadth of expertise and specialties, including layperson

Not led by a medical specialty society
  - Non-partisan
  - No perceived or real conflict of interest

Evidence and consensus based
  - Evidence where evidence exists
  - Consensus of experts to help fill in gaps in evidence for practical application

Considered full spectrum of risk factors for lung cancer, not just NLST inclusion criteria

Annual updates
  - Prompt revisions responsive to new evidence
  - Corrections, improvements, and revisions based on institution feedback
NCCN Guidelines®
Minimization of Bias

Large number of panel members
Multidisciplinary
Geographic diversity
Different philosophical views represented
Institutional review
External review and input
Formal declaration of potential conflicts
EBM is “the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients”

Lack of evidence for many important practices
Only 15% of medical practice based on solid clinical trials
Prolonged period of evidence transmitted to practice
Religious fundamentalism – truth as absolute, true keepers of the faith

- Critics see the world in shades of grey and view fundamentalism as self-righteous and simplistic

Medical fundamentalism – strict and literal view of literature, undervalue non-randomized evidence, “see the literature as law, a series of sacred texts ....to be applied literally”

- “Like religious fundamentalists, medical fundamentalists tend to be self righteous and denigrate other interpretations.”
- Liberal view sees EBM in context along with non-randomized clinical trials and judgment in the application to individual patients
Evidence-based Consensus Allows Comprehensive Guideline

Continuum of disease and patient care

Evidence-based guideline

Evidence-based consensus guideline

High-level evidence exists

Gaps in evidence filled with expert consensus
NCCN Categories of Evidence and Consensus

**Category 1:** Based upon high-level evidence, there is uniform NCCN consensus (≥85%) that the intervention is appropriate.

**Category 2A:** Based upon lower-level evidence, there is uniform NCCN consensus (≥85%) that the intervention is appropriate.

**Category 2B:** Based upon lower-level evidence, there is NCCN consensus (50-85%) that the intervention is appropriate.

**Category 3:** Based upon any level of evidence, there is major NCCN disagreement (at least 3 institutions on each side) that the intervention is appropriate.

*All recommendations are category 2A unless otherwise noted.*
## Development of NCCN Guidelines for Lung Cancer Screening

<table>
<thead>
<tr>
<th>Date</th>
<th>Description</th>
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<tbody>
<tr>
<td>October 2009</td>
<td>Selection of chair for new guidelines panel</td>
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<tr>
<td>November 2009</td>
<td>Nominations for panel members</td>
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<tr>
<td>January 2010</td>
<td>Literature search on lung cancer screening</td>
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<tr>
<td>January 2010</td>
<td>Panel web conference to discuss guidelines development process, scope of guidelines, and panel assignments</td>
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<tr>
<td></td>
<td>- High-risk groups</td>
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<tr>
<td></td>
<td>- Risks of screening</td>
</tr>
<tr>
<td></td>
<td>- Benefits of screening</td>
</tr>
<tr>
<td></td>
<td>- Accuracy of protocols and imaging</td>
</tr>
<tr>
<td>March 2010</td>
<td>In-person panel meeting</td>
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<tr>
<td>March - Nov 2010</td>
<td>Ongoing development of evidence and guidelines through the 4 working groups</td>
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## Development of NCCN Guidelines for Lung Cancer Screening

<table>
<thead>
<tr>
<th>Month</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>November 2010</td>
<td>NLST results released</td>
</tr>
<tr>
<td>November 2010</td>
<td>Panel web conference to discuss NLST results, review workgroups, refine evidence based on NLST results</td>
</tr>
<tr>
<td>May 2011</td>
<td>Review of preliminary algorithm</td>
</tr>
<tr>
<td>June 2011</td>
<td>Preliminary draft version of NCCN Guidelines</td>
</tr>
<tr>
<td>July 2011</td>
<td>Panel web conference to review comments on the preliminary draft review</td>
</tr>
<tr>
<td>August 2011</td>
<td>Preliminary draft version distributed for Institutional Review</td>
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<tr>
<td>September 2011</td>
<td>Panel web conference to discuss the institutional review comments</td>
</tr>
<tr>
<td>October 2011</td>
<td>Updated version of guidelines sent to panel for final review</td>
</tr>
<tr>
<td>October 2011</td>
<td>NCCN Guidelines for Lung Cancer Screening Version 1.2.2012 published at NCCN website</td>
</tr>
</tbody>
</table>
Lung Cancer Screening


*J Natl Compr Canc Netw* 2012;10:240-265
NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Lung Cancer Screening

NCCN.org

NCCN Guidelines for Patients® available at www.nccn.org/patients

Continue
RISK ASSESSMENT\textsuperscript{a, b}

- Smoking history\textsuperscript{c}
- Radon exposure\textsuperscript{d}
- Occupational exposure\textsuperscript{e}
- Cancer history\textsuperscript{f}
- Family history of lung cancer in first-degree relatives
- Disease history (COPD or pulmonary fibrosis)
- Smoking exposure\textsuperscript{g} (second-hand smoke)
- Absence of symptoms or signs of lung cancer (if symptoms, see appropriate NCCN Guidelines)

RISK STATUS

**High risk:**\textsuperscript{h}
- Age 55–74 y and
- \( \geq 30 \) pack-year history of smoking and
- Smoking cessation <15 y (category 1)

or

- Age \( \geq 50 \) y and
- \( \geq 20 \) pack-year history of smoking and
- One additional risk factor (other than second-hand smoke)

**Moderate risk:**
- Age \( \geq 50 \) y and
- \( \geq 20 \) pack-year history of smoking
- or second-hand smoke exposure\textsuperscript{g}
- No additional risk factors

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

In candidates for screening, shared patient/physician decision making is recommended, including a discussion of benefits/risks\textsuperscript{i}

Lung cancer screening not recommended

Lung cancer screening not recommended

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**EVALUATION OF SCREENING FINDINGS**

- ≤ 4 mm → **Annual LDCT for 2 years (category 1) and consider annual LDCT until patient no longer eligible for definitive treatment**

- > 4-6 mm → **LDCT in 6 mo**

- > 6-8 mm → **LDCT in 3 mo**

**FOLLOW-UP OF SCREENING FINDINGS**

- If no increase in size, LDCT in 12 mo

- If no increase in size, LDCT in 6 mo

- If increase in size → **Surgical excision**

- Annual LDCT for 2 years (category 1) and consider annual LDCT until patient no longer eligible for definitive treatment

**Solid or part solid nodule**

- > 8 mm → **Consider PET/CT**

**Suspicion of lung cancer**

- LDCT in 3 mo

- Low suspicion of lung cancer

**Suspicion of lung cancer**

- Biopsy or Surgical excision

- No cancer

- Cancer confirmed

- See appropriate NCCN Guidelines

**Solid endobronchial nodule**

- LDCT in 1 mo (immediately after vigorous coughing)

- If no resolution → **Bronchoscopy**

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Definition of a Positive Test Result in Computed Tomography Screening for Lung Cancer

A Cohort Study

Claudia I. Henschke, PhD, MD; Rowena Yip, MPH; David F. Yankelevitz, MD; and James P. Smith, MD, for the International Early Lung Cancer Action Program Investigators*

Figure. Frequency of a positive result and cases of lung cancer diagnosed within 12 mo of baseline enrollment.
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EVALUATION OF SCREENING FINDINGS

- Pure GGNs ≤5 mm
  - LDCT in 12 mo
  - Increase in size and/or becomes solid or part solid
  - Stable, resolving, or resolved
    - Annual LDCT for 2 years (category 1) and suggest annual LDCT until patient is no longer a candidate for definitive treatment
    - Consider surgical excision
  - LDCT 3–6 mo

- Multiple GGOs
  - Pure GGNs >5 mm without a dominant lesion
  - LDCT in 6 mo
  - Increase in size and/or becomes solid or part solid
  - Stable, resolving, or resolved
    - Annual LDCT for 2 years (category 1) and suggest annual LDCT until patient is no longer a candidate for definitive treatment
    - Consider surgical excision
  - LDCT 3–6 mo

- GGNs NSs
  - Dominant nodule(s) with part-solid or solid component
  - LDCT in 3–6 mo
  - Resolved
    - Annual LDCT screening
  - Persistent or increase in size
    - See LCS-3

FOLLOW-UP OF SCREENING FINDINGS

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Lung Cancer Screening

EVALUATION OF SCREENING FINDINGS

- Suspected infection/inflammation
  - Consider treatment with antimicrobials
  - Repeat LDCT in 1–2 mo

- New nodule at annual or follow-up LDCT

- No suspected infection/inflammation
  - Solid or part-solid nodule
    - See Evaluation of Screening Findings (LCS-3)
  - GGOs/GGNs/NSs
    - See Evaluation of Screening Findings (LCS-4)
  - Multiple GGOs/GGNs/NSs
    - See Evaluation of Screening Findings (LCS-5)

FOLLOW-UP OF SCREENING FINDINGS

- Resolving
  - Radiologic follow-up to resolution or stability

- Resolved
  - Annual LDCT screening (see LCS-1)
  - Low suspicion of lung cancer

- Persistent or enlarging
  - PET/CT
  - Suspicion of lung cancer
  - Biopsy or surgical excision

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RISKS/BENEFITS OF LUNG CANCER SCREENING*

**RISKS**
- Futile detection of small aggressive tumors or indolent disease
- Quality of life
  - Anxiety of test findings
- Physical complications from diagnostic workup
- False-positive results
- False-negative results
- Unnecessary testing and procedures
- Radiation exposure
- Cost
- Incidental lesions

**BENEFITS**
- Decreased lung cancer mortality
- Quality of life
  - Reduction in disease-related morbidity
  - Reduction in treatment-related morbidity
  - Improvement in healthy lifestyles
  - Reduction in anxiety/psychosocial burden
- Discovery of other significant occult health risks (e.g., severe but silent coronary artery disease, early renal mass, pole of kidney, aortic aneurysm, breast cancer)

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Concerns about Lung Cancer Screening

Benefit overestimated
Harm underestimated
Close balance of benefits and harms
Hippocrates – “Do no harm”
But in preventive services, harm presents in two forms:
- Unintended consequences of evaluation/treatment
- Denying preventive services from those who may benefit
Issues Debated in Lung Cancer Screening

• Does it work?
• Which patients should be screened?
  – What level of evidence?
• Minimizing harms
• Balancing unintended harms with benefit
• Lowering barriers to access
Which Patients Should be Screened?

Lung Cancer Screening

RISK ASSESSMENT\(^a, b\)

- Smoking history\(^c\)
- Radon exposure\(^d\)
- Occupational exposure\(^e\)
- Cancer history\(^f\)
- Family history of lung cancer in first-degree relatives
- Disease history (COPD or pulmonary fibrosis)
- Smoking exposure\(^g\) (second-hand smoke)
- Absence of symptoms or signs of lung cancer (if symptoms, see appropriate NCCN Guidelines)

RISK STATUS

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

In candidates for screening, shared patient/physician decision making is recommended, including a discussion of benefits/risks\(^i\)

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

Lung cancer screening not recommended

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Which Patients Should be Screened?

What the NLST did do:
Demonstrate a mortality reduction in patients with substantial risk factors for lung cancer

What the NLST did not do:
Define risk factors for lung cancer

- NLST was a clinical trial, eligibility criteria were never meant to define the extent of “high risk” or be the basis of public policy
- Only considered age and smoking history
- No consideration of occupational/environmental exposure, cancer history, family history, other diseases
Which Patients Should be Screened?

Key principle of NCCN Group 2 is the consideration of additional risk factors

USPSTF and CMS only considered age and smoking history (presumably on the assumption that only the NLST provides data about lung cancer risk)

Mortality benefit of patients with a certain level of lung cancer risk

What if we identified patients with a similar level of risk? Could they be extrapolated to have a similar level of mortality benefit? Do we know any risk factors for lung cancer other than age and smoking history?
Which Patients Should be Screened?

NCCN position

Group 1 high risk patients - NLST inclusion (Category 1 recommendation)

Group 2 high risk patients approximate the risk of patients included in the NLST – Category 2A “uniform consensus” from panel
Issues Debated in Lung Cancer Screening

• Does it work?
• Which patients should be screened?
  – What level of evidence?
• Minimizing harms
• Balancing unintended harms with benefit
• Lowering barriers to access
Which Patients Should be Screened?
NCCN Group 2

Evidence from randomized trial is a critical foundation

Reality that additional randomized trial data limited
  Occupational exposure
  Past cancer or family history

Is it possible to extrapolate non-randomized data regarding additional risk factors to known outcomes?

Is this more pragmatic and equitable in providing access to preventive health services?
Risk Factors for Lung Cancer

NCCN Group 2

NCCN Group 1
NLST/USPSTF/CMS
Age
Smoking

NCCN Group 2
Age
Smoking
Occupational/environmental
   Asbestos, radon, silica, etc.
Cancer history
Family history
Disease history
   COPD and pulmonary fibrosis
Previous Lung Diseases and Lung Cancer Risk: A Pooled Analysis From the International Lung Cancer Consortium

Emphysema odds ratio 2.3

# Lung Cancer Risk Assessment

<table>
<thead>
<tr>
<th></th>
<th>NLST</th>
<th>USPSTF</th>
<th>CMS</th>
<th>Brock</th>
<th>AATS</th>
<th>Bach</th>
<th>CLEAR</th>
<th>MyLungRisk</th>
<th>WashU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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</tr>
<tr>
<td>Smoking</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Cessation</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<td>+</td>
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# Risk Calculator Assessment

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<th>Bach</th>
<th>Hoggart</th>
<th>LLP</th>
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<tbody>
<tr>
<td><strong>NCCN 1 low</strong></td>
<td>0.6%</td>
<td>0.6%</td>
<td>1.8%</td>
<td>0.9%</td>
</tr>
<tr>
<td><strong>NCCN 1 med</strong></td>
<td>4.2%</td>
<td>2.3%</td>
<td>4.4%</td>
<td>2.0%</td>
</tr>
<tr>
<td><strong>NCCN 1 high</strong></td>
<td>18.9%</td>
<td>4.6%</td>
<td>5.7%</td>
<td>6.0%</td>
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<tr>
<td><strong>NCCN 2 low</strong></td>
<td>1.1%</td>
<td>0.2%</td>
<td>1.5%</td>
<td>1.3%</td>
</tr>
<tr>
<td><strong>NCCN 2 med</strong></td>
<td>4.9%</td>
<td>0.7%</td>
<td>0.1%</td>
<td>3.1%</td>
</tr>
<tr>
<td><strong>NCCN 2 high</strong></td>
<td>12.8%</td>
<td>1.7%</td>
<td>1.0%</td>
<td>6.9%</td>
</tr>
</tbody>
</table>

- 58 yo male 30 pk-yr, stopped 13 years ago, no other risk factors
- 65 yo male 40 pk-yr, stopped 5 years ago, family history
- 74 yo female 55 pk-yr, current smoker, previous cancer
- 50 yo female 25 pk-yr, stopped 15 years ago, previous cancer
- 65 yo male 25 pk-yr, current smoker, asbestos, pulmonary fibrosis
- 78 yo male 35 pk-yr, stopped smoking 1 year ago, previous cancer, COPD
Experience With a CT Screening Program for Individuals at High Risk for Developing Lung Cancer

Brady J. McKee, MD\textsuperscript{a}, Jeffrey A. Hashim, MD\textsuperscript{a}, Robert J. French, MD\textsuperscript{a}, Andrea B. McKee, MD\textsuperscript{b}, Paul J. Hesketh, MD\textsuperscript{c}, Carla R. Lamb, MD\textsuperscript{d}, Christina Williamson, MD\textsuperscript{c}, Sebastian Flacke, MD, PhD\textsuperscript{c}, Christoph Wald, MD, PhD\textsuperscript{a}

Experience With a CT Screening Program for Individuals at High Risk for Developing Lung Cancer


Table 2. Prevalence Exam Results

<table>
<thead>
<tr>
<th>Result</th>
<th>Total Screened (n = 1,760)</th>
<th>NCCN Group 2 (n = 464)</th>
<th>NCCN Group 1 (n = 1,296)</th>
<th>P (Group 2 vs Group 1)</th>
<th>NLST (TO)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total positive</td>
<td>481</td>
<td>116</td>
<td>365</td>
<td>0.1</td>
<td>27.3%</td>
</tr>
<tr>
<td>Probably benign</td>
<td>412</td>
<td>103</td>
<td>309</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Suspicious</td>
<td>69</td>
<td>13</td>
<td>56</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Probable infection</td>
<td>114</td>
<td>28</td>
<td>86</td>
<td>0.8</td>
<td>NR</td>
</tr>
<tr>
<td>Significant incidental findings</td>
<td>108</td>
<td>28</td>
<td>80</td>
<td>0.1</td>
<td>10.2%</td>
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</tbody>
</table>

Table 4. Malignancy rate and average follow-up

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall</th>
<th>Group 2</th>
<th>Group 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall malignancy rate</td>
<td>23/1,328 (1.7%)</td>
<td>6/331 (1.8%)</td>
<td>17/997 (1.7%)</td>
</tr>
<tr>
<td>Average follow-up (mo)</td>
<td>12.5</td>
<td>12.1</td>
<td>12.7</td>
</tr>
<tr>
<td>Annualized malignancy rate</td>
<td>1.6%</td>
<td>1.8%</td>
<td>1.6%</td>
</tr>
<tr>
<td>Time to diagnosis (mo)</td>
<td>4.1</td>
<td>5.6</td>
<td>3.7</td>
</tr>
<tr>
<td>Average follow-up from diagnosis (mo)</td>
<td>7.8</td>
<td>5.3</td>
<td>8.6</td>
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</tbody>
</table>
Issues Debated in Lung Cancer Screening

• Does it work?
• Which patients should be screened?
  – What level of evidence?
• Minimizing harms
• Balancing unintended harms with benefit
• Lowering barriers to access
Minimizing Harms of Lung Cancer Screening

Limit Access
Further narrow, or prevent widening of, eligibility criteria
Expose fewer people to risks
Use policy to override shared decision-making
Disenfranchise and potentially harm others at high risk

Improve management
Refine management algorithms to minimize false positives
Require expertise in evaluation/treatment to optimize outcomes
Empower shared decision-making
Provide access to similar risk patients
Add cost to payers
Risk of evaluation/treatment added to new patients with less proof of benefit
<table>
<thead>
<tr>
<th>Category</th>
<th>Category Descriptor</th>
<th>Category</th>
<th>Findings</th>
<th>Management</th>
<th>Probability of Malignancy</th>
<th>Estimated Population Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incomplete</td>
<td></td>
<td>0</td>
<td>prior chest CT examination(s) being located for comparison part or all of lungs cannot be evaluated</td>
<td>Additional lung cancer screening CT images and/or comparison to prior chest CT examinations is needed</td>
<td>n/a</td>
<td>1%</td>
</tr>
<tr>
<td>Negative</td>
<td>No nodules and definitely benign nodules</td>
<td>1</td>
<td>no lung nodules</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>nodule(s) with specific calcifications: complete, central, popcorn, concentric rings and fat containing nodules</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benign</td>
<td>Nodules with a very low likelihood of becoming a clinically active cancer due to size or lack of growth</td>
<td>2</td>
<td>solid nodule(s): &lt; 6 mm new &lt; 4 mm</td>
<td>Continue annual screening with LDCT in 12 months</td>
<td>&lt; 1%</td>
<td>90%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>part solid nodule(s): &lt; 6 mm total diameter on baseline screening</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>non solid nodule(s) (GGN): &lt; 20 mm OR ≥ 20 mm and unchanged or slowly growing</td>
<td>category 3 or 4 nodules unchanged for ≥ 3 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probably Benign</td>
<td>Probably benign finding(s) - short term follow up suggested, includes nodules with a low likelihood of becoming a clinically active cancer</td>
<td>3</td>
<td>solid nodule(s): ≥ 6 mm to &lt; 8 mm at baseline OR new 4 mm to &lt; 6 mm</td>
<td>6 month LDCT</td>
<td>1-2%</td>
<td>5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>part solid nodule(s) ≥ 6 mm total diameter with solid component &lt; 6 mm OR new &lt; 6 mm total diameter</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suspicious</td>
<td>Findings for which additional diagnostic testing and/or tissue sampling is recommended</td>
<td>4A</td>
<td>solid nodule(s): ≥ 8 mm to &lt; 15 mm at baseline OR growing &lt; 8 mm OR new 6 to &lt; 8 mm</td>
<td>3 month LDCT; PET/CT may be used when there is a ≥ 8 mm solid component</td>
<td>5-15%</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>part solid nodule(s): ≥ 6 mm with solid component ≥ 6 mm to &lt; 8 mm OR with a new or growing &lt; 4 mm solid component</td>
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<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>endobronchial nodule</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>4B</td>
<td>solid nodule(s) ≥ 15 mm OR new or growing, and ≥ 8 mm</td>
<td>chest CT with or without contrast, PET/CT and/or tissue sampling depending on the probability of malignancy and comorbidities. PET/CT may be used when there is a ≥ 8 mm solid component.</td>
<td>&gt; 15%</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>part solid nodule(s) with: a solid component ≥ 8 mm OR a new or growing ≥ 4 mm solid component</td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>4X</td>
<td>Category 3 or 4 nodules with additional features or imaging findings that increases the suspicion of malignancy</td>
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False-positive rate

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<th>LungRADS</th>
<th>Improvement w/LungRADS</th>
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<tr>
<td>Baseline</td>
<td>26.6%</td>
<td>12.8%</td>
<td>52%</td>
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<tr>
<td>After baseline</td>
<td>21.8%</td>
<td>5.3%</td>
<td>76%</td>
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Lung Cancer Screening Guidelines

Nov 2010    NLST results
Oct 2011    National Comprehensive Cancer Network (NCCN)
Apr 2012    American Lung Association
May 2012    American College of Chest Physicians and ASCO
Jun 2012    NCCN Update
Jul 2012    American Association for Thoracic Surgery
Jan 2013    American Cancer Society
Jun 2013    NCCN Update
Jul 2013    American Academy of Family Practice
Jul 2013    Society of Thoracic Surgeons
Dec 2013    US Preventive Services Task Force
July 2014    NCCN Update
Nov 2014    Centers for Medicare and Medicaid Services
July 2015    NCCN Update
July 2016    NCCN Update
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<tr>
<th>Lung Cancer Guidelines</th>
<th>NLST</th>
<th>USPSTF</th>
<th>CMS</th>
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<th>Cancer Care Ontario</th>
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<th>ALA</th>
<th>ACCP</th>
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<td>55-79</td>
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<td>≥30</td>
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<td>&gt;20 pk-yr Add risk factor</td>
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<tr>
<td>Lung Cancer Guidelines</td>
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<td>Risk calc</td>
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</table>
Issues Debated in Lung Cancer Screening

• Does it work?
• Which patients should be screened?
  – What level of evidence?
• Minimizing harms
• Balancing unintended harms with benefit
• Lowering barriers to access
Screening Efficiency

Number Needed to Screen

Screening mammography\textsuperscript{1,2} \hspace{1cm} 780 - 2000
Screening colonoscopy\textsuperscript{2} \hspace{1cm} 1250
Screening LDCT (in NLST) \hspace{1cm} 320

Issues Debated in Lung Cancer Screening

• Does it work?
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  – What level of evidence?
• Minimizing harms
• Balancing unintended harms with benefit
• Lowering barriers to access
Applying the National Lung Screening Trial eligibility criteria to the US population: what percent of the population and of incident lung cancers would be covered?

Paul F Pinsky and Christine D Berg

SEER (Surveillance, Epidemiology and End Results)
United States Census
National Health Interview Survey
Two statistical models of lung cancer risk

Proportion of those diagnosed with lung cancer that would be covered by the NLST-based eligibility criteria.

27%

Annual Number of Lung Cancer Deaths Potentially Avertable by Screening in the United States

Jiemin Ma, PhD, MHS; Elizabeth M. Ward, PhD; Robert Smith, PhD; and Ahmedin Jemal, DVM, PhD

8.6 million Americans eligible for screening
Annual number of lung cancer deaths averted – 12,250

Experience With a CT Screening Program for Individuals at High Risk for Developing Lung Cancer

NCCN Group 2 adds 2 million eligible for screening
Additional estimate of averted lung cancer deaths ≈ 3000

Cancer 2013;119:1381-5
An overarching objective of the American Cancer Society’s 2015 challenge goals is to eliminate disparities in the cancer burden among different segments of the US population, defined in terms of socioeconomic status (income, education, insurance status, etc.), race/ethnicity, geographic location, sex, and sexual orientation.

Lung cancer patient disparities:
Older – 68% Medicare population
Higher mortality amongst African-Americans
Lower socioeconomic groups mortality 4-5 times greater
Rural access to screening and treatment
Balancing curability and unnecessary surgery in the context of computed tomography screening for lung cancer

Lung Cancer Survival

Current Lung Cancer Survival

I-ELCAP


Lung Cancer Screening

Summary

Lung cancer screening reduces mortality in a high risk population. Randomized trial data, and USPSTF eligibility, do not consider risk factors other than age and smoking. Non-randomized data exists to validate other risk factors. Rigid adherence to NLST inclusion criteria ignores important data regarding lung cancer risk, disenfranchises patients at legitimate risk, lost opportunity of maximizing benefit of lung cancer screening, and violates principles of equity and elimination of health care disparities. Data supports NCCN Group 2 as having similar risk to NLST. Policy should extend screening to patients similar to NCCN Group 2. Screening risk minimized by algorithmic management and multidisciplinary expertise. Shared decision making important to balance risks and benefits.
NCCN Member Institutions

Fred Hutchinson Cancer Research Center/Seattle Cancer Care Alliance

Huntsman Cancer Institute at the University of Utah

UCSF Helen Diller Family Comprehensive Cancer Center
Stanford Cancer Institute

UC San Diego Moores Cancer Center

City of Hope Comprehensive Cancer Center

Mayo Clinic Cancer Center

University of Colorado Cancer Center

University of Michigan Comprehensive Cancer Center

Ohio State University Comprehensive Cancer Center - James Cancer Hospital and Solove Research Institute

University of Alabama at Birmingham Comprehensive Cancer Center

University of Wisconsin Carbone Cancer Center

Robert H. Lurie Comprehensive Cancer Center of Northwestern University

Barnes-Jewish Hospital and Washington University School of Medicine

St. Jude Children’s Research Hospital/The University of Tennessee Health Science Center

University of Texas MD Anderson Cancer Center

The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

Vanderbilt-Ingram Cancer Center

Roswell Park Cancer Institute

Case Comprehensive Cancer Center/University Hospitals Seidman Cancer Center and Cleveland Clinic Taussig Cancer Institute

Dana-Farber/Brigham and Women’s Cancer Center
Massachusetts General Hospital Cancer Center

Dana-Farber Cancer Institute
Yale Cancer Center/Smilow Cancer Hospital
Memorial Sloan Kettering Cancer Center
Fox Chase Cancer Center

Duke Cancer Institute

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