New Advances in Lung Cancer

Douglas E. Wood, MD, FACS, FRCSEd (ad hom)
Professor and Chief
Division of Cardiothoracic Surgery
Vice-Chair, Department of Surgery
Endowed Chair in Lung Cancer Research
University of Washington

Disclosure: Dr. Wood is a Research Advisor - Investigation Consultant for Spiration.
LUNG CANCER SCREENING
The Development of Guidelines and Policy
Lung Cancer is the Leading Cause of Cancer Death in Every Ethnic Group

Estimated Cancer Deaths in 2011

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Deaths 2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung and Bronchus</td>
<td>156,940</td>
</tr>
<tr>
<td>Colorectum</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>Leukemia</td>
<td>28,000</td>
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<tr>
<td>Lymphoma</td>
<td>21,780</td>
</tr>
<tr>
<td>Liver</td>
<td>21,626</td>
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<tr>
<td>Ovary</td>
<td>19,590</td>
</tr>
<tr>
<td>Bladder</td>
<td>15,460</td>
</tr>
<tr>
<td>Esophagus</td>
<td>14,990</td>
</tr>
<tr>
<td>Brain</td>
<td>14,710</td>
</tr>
<tr>
<td>Uterus/Cervix</td>
<td>13,110</td>
</tr>
<tr>
<td>Brain</td>
<td>12,410</td>
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</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 2009</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>Alzheimers</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>
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<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>
</tr>
<tr>
<td>Prostate cancer</td>
<td>28,154</td>
</tr>
<tr>
<td>Leukemia</td>
<td>22,697</td>
</tr>
<tr>
<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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<td>Bladder cancer</td>
<td>14,315</td>
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<td>Brain cancer</td>
<td>14,192</td>
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<td>Esophageal cancer</td>
<td>13,916</td>
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<td>Kidney cancer</td>
<td>13,027</td>
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<td>Stomach cancer</td>
<td>11,139</td>
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<td>HIV/AIDS</td>
<td>9,424</td>
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<tr>
<td>Melanoma</td>
<td>9,254</td>
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<tr>
<td>Lip/oral cancers</td>
<td>7,913</td>
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</tbody>
</table>

* Includes COPD, emphysema, asthma, bronchitis
Cancer screening coverage
Breast
Prostate
Colon

Lung cancer disparities
Elderly
Low socioeconomic group
Racial
“Self-inflicted” disease
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....
Previous studies have established lower stage distribution, and improved resectability and survival BUT not lower mortality

No randomized trial has had an appropriate control
Randomized control trial very difficult to perform
Previous trials have had increased incidence in screened groups - ? Overdiagnosis, length, or lead time bias
National Lung Screening Trial

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 (NCI)

- **Study design:** Randomized controlled trial
- **Interventions:** 3 screenings performed over 2 years:
  - 1\textsuperscript{st} Outcome: Lung cancer mortality assessed after 5 years of follow-up
- **Major eligibility criteria:**
  - Age 55 to 74 years
  - A cigarette smoking history of at least 30 pack-years
  - Current cigarette smokers and former smokers who quit within 15 years of randomization
- **Enrollment:** 53,454 participants at 33 sites
  - 90\% statistical power to detect a 20\% reduction in lung cancer mortality
  - Secondary endpoint of all cause mortality

National Lung Screening Trial NEJM 2011
NLST Timeline

1st Interim Analysis
2nd Interim Analysis
3rd Interim Analysis
4th Interim Analysis
5th Interim Analysis
6th Interim Analysis

T₀
T₁
T₂
### 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>
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<tr>
<td>CXR</td>
<td>143,368</td>
<td>443</td>
<td>309</td>
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</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>
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<tr>
<td>CXR</td>
<td>166,382</td>
<td>2000</td>
<td>1202</td>
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Conclusion

Screening with low dose chest CT conclusively reduces mortality from lung cancer in high risk patients.
Lung Cancer Screening


J Natl Compr Canc Netw 2012;10:240-265
Lung Cancer Screening

Version 1.2014

NCCN.org
<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Roles</th>
</tr>
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<tr>
<td>Douglas E. Wood, MD/Chair</td>
<td>University of Washington/Seattle Cancer Care</td>
<td>Chair</td>
</tr>
<tr>
<td>Ella Kazerooni, MD/Vice Chair</td>
<td>University of Michigan/Comprehensive Cancer</td>
<td>Vice Chair</td>
</tr>
<tr>
<td>Scott L. Baum, MD</td>
<td>University of Tennessee Health Science Center</td>
<td></td>
</tr>
<tr>
<td>Mark M. Dransfield, MD</td>
<td>University of Alabama at Birmingham/Comprehensive Cancer</td>
<td></td>
</tr>
<tr>
<td>George A. Eapen, MD</td>
<td>The University of Texas/MD Anderson Cancer Center</td>
<td></td>
</tr>
<tr>
<td>David S. Ettinger, MD</td>
<td>The Sidney Kimmel Comprehensive Cancer at Johns Hopkins</td>
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<tr>
<td>Lifang Hou, MD, PhD &amp; Robert H. Lurie Comprehensive Cancer Center of Northwestern University</td>
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<tr>
<td>David Jackman, MD</td>
<td>Dana-Farber/Brigham and Women’s Cancer Center</td>
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<tr>
<td>Donald Klippenstein, MD</td>
<td>Moffitt Cancer Center</td>
<td></td>
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<tr>
<td>Rudy P. Lackner, MD</td>
<td>UNMC Eppley Cancer Center at The Nebraska Medical Center</td>
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<tr>
<td>Loriliana E. Leard, MD</td>
<td>UCSF Helen Diller Family/Comprehensive Cancer</td>
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<td>Ann N. C. Leung, MD</td>
<td>Stanford Comprehensive Cancer Center</td>
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<td>Pierre P. Massion, MD</td>
<td>Vanderbilt-Ingram Cancer Center</td>
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<td>Bryan F. Meyers, MD, MPH</td>
<td>Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine</td>
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<tr>
<td>Reginald F. Munden, MD, DMD, MBA</td>
<td>The University of Texas/MD Anderson Cancer Center</td>
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<tr>
<td>Gregory A. Otterson, MD</td>
<td>The Ohio State University Comprehensive Cancer Center - James Cancer Hospital and Solove Research Institute</td>
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<tr>
<td>Kimberly Pears, MD</td>
<td>The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins</td>
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<tr>
<td>Sudhakar Pipavath, MD</td>
<td>University of Washington/Seattle Cancer Care Alliance</td>
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<td>Christie Pratt-Pozo, MA, DHSc</td>
<td>Moffitt Cancer Center</td>
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<tr>
<td>Chakravarthy Reddy, MD</td>
<td>Huntsman Cancer Institute at the University of Utah</td>
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<tr>
<td>Mary E. Reid, PhD</td>
<td>Roswell Park Cancer Institute</td>
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<tr>
<td>Arnold J. Rotter, MD</td>
<td>City of Hope Comprehensive Cancer Center</td>
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<tr>
<td>Matthew B. Schabath, PhD</td>
<td>Moffitt Cancer Center</td>
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<tr>
<td>Lucia V. Sequist, MD, MPH</td>
<td>Massachusetts General Hospital Cancer Center</td>
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<tr>
<td>Betty C. Tong, MD, MHS</td>
<td>Duke Cancer Institute</td>
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<tr>
<td>William D. Travis, MD</td>
<td>Memorial Sloan-Kettering Cancer Center</td>
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<tr>
<td>Michael Unger, MD</td>
<td>Fox Chase Cancer Center</td>
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<tr>
<td>Stephen C. Yang, MD</td>
<td>The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins</td>
<td></td>
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</tbody>
</table>
NCCN Guidelines Version 1.2013
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 Guideline)

RISK STATUS

High risk:
- 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) (category 2B)

Moderate risk:
- Age \( \geq 50\) y and
- \( \geq 20 \) 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

Routine 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.
- > 8 mm: PET/CT.
- Solid or part solid nodule:
  - Solid endobronchial nodule: LDCT in 1 mo (immediately after vigorous coughing).

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.
- Low suspicion of lung cancer: LDCT in 3 mo.
- Suspicion of lung cancer:
  - Biopsy or Surgical excision.
  - No cancer: See appropriate NCCN Guidelines.
  - Cancer confirmed: bronchoscopy.
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.
NCCN Guidelines Version 1.2014
Lung Cancer Screening

EVALUATION OF SCREENING FINDINGS

<6 mm
- Annually for 2 years (category 1) and consider annual LDCT until patient no longer eligible for definitive treatment

6-8 mm
- LDCT in 3 mo

Solid or part solid nodule

>8 mm
- Consider PET/CT

Solid endobronchial nodule
- LDCT in 1 mo (immediately after vigorous coughing)

FOLLOW-UP OF SCREENING FINDINGS

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

If no increase in size, LDCT in 6 mo

Low suspicion of lung cancer
- LDCT in 3 mo

Suspicion of lung cancer
- Biopsy or Surgical excision

No cancer
- See appropriate NCCN Guidelines

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

If increase in size
- Surgical excision

If no resolution
- Bronchoscopy
EVALUATION OF SCREENING FINDINGS

- Ground glass opacity (GGO)/Ground glass nodule (GGN)/Nonsolid nodule (NS)

FOLLOW-UP OF SCREENING FINDINGS

- <5 mm
  - LDCT in 12 mo
  - Stable
  - Increase in size and/or become solid or part solid

- 5-10 mm
  - LDCT in 6 mo
  - Stable
  - Increase in size and/or become solid or part solid

- >10 mm
  - LDCT in 3-6 mo
  - Stable
  - Increase in size and/or become solid or part solid

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

LDCT 3-6 mo
- or
- Consider surgical excision

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

Surgical excision
- LDCT 6-12 mo
  - or
  - Biopsy
  - Consider surgical excision

Cancer confirmed
- See appropriate NCCN Guidelines

No cancer
NCCN Guidelines Version 1.2014
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
    - Ground glass opacity (GGO)
    - Ground glass nodule (GGN)
    - Nonsolid nodule (NS)
    - Multiple GGO/GGNs

FOLLOW-UP OF SCREENING FINDINGS

- Resolving
  - Radiologic follow-up to resolution or stability

- Resolved
  - Annual LDCT screening (see LCS-3)

- Persistent or enlarging
  - PET/CT

- Low suspicion of lung cancer
  - See Evaluation of Screening Findings (LCS-4)

- Suspicion of lung cancer
  - See Evaluation of Screening Findings (LCS-5)
RISKS
- Futile detection of small aggressive tumors or indolent disease
- Quality of life
  - Anxiety of test findings
- Physical complications from diagnostic work-up
- False-positive results
- False-negative results
- Unnecessary testing
- 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
NCCN Guidelines for Patients™

Presented with the generous support of the Lung Cancer Alliance.

Dedicated to the At-Risk Public.
Medicare's Puzzling Refusal to Cover Lung-Cancer Screening

We know screening can save thousands of lives every year. But it's not provided to the group most likely to benefit.

By DOUGLAS E. WOOD And ELLA A. KAZEROONI

June 17, 2014 7:11 p.m. ET

If you could save thousands of lives, would you do it?

That's the question Medicare officials are now considering—whether to approve lung-cancer screening for Medicare beneficiaries, which we estimate could save 14,000 lives each year in that group alone. Most patients are discovered with lung cancer at a stage already too late for a cure, and cancer screening for early detection has been recommended for other common cancers for decades. The procedure has turned thousands of people into survivors rather than victims.
Congress Urges Medicare to Cover Lung Cancer Screening

Roxanne Nelson

June 05, 2014

Politicians have gotten involved and are campaigning to have lung cancer screening covered by Medicare, which insures people 65 years of age and older. Members of the US House and Senate are asking the Centers for Medicare & Medicaid Services (CMS) to approve coverage of lung cancer screening with low-dose CT.

The Senate letter has 45 signatories, and points out that the US Preventive Services Task Force has evaluated low-dose CT and given it a positive recommendation. "This means that patients with private insurance are gaining access but Medicare beneficiaries are still waiting," they write.

Low-dose CT is already covered by the Department of Veterans Affairs, the Department of Energy, and a number of large private insurers, such as WellPoint, Blue Cross Blue Shield affiliates, and Anthem affiliates.

In the letter from the House, the 134 signatories point out that "Americans pay into Medicare throughout their working lives and deserve to have access to potentially life-saving evidence-based screening."

Many major medical societies have come out in favor of lung cancer screening, including the American Association for Thoracic Surgery, the American Cancer Society, the American College of Radiology, the American Society of Clinical Oncology, the Lung Cancer Alliance, and the Society for Thoracic Surgeons.

September X, 2014

Tamara S. Syrek Jensen, J.D.
Acting Director, Coverage and Analysis Group
Centers for Medicare & Medicaid Services
Mail Stop C1-09-06
7500 Security Boulevard
Baltimore, MD 21244

Re: National Coverage Analysis for Lung Cancer Screening with Low Dose Computed Tomography (CAG-00439N)

Dear Ms. Syrek Jensen:

In follow up to the stakeholder letter dated March 12th, 2014 and the June 19th, 2014 meeting with the Centers for Medicare and Medicaid Services Coverage and Analysis Group (CMS CAG), the undersigned organizations and groups continue to strongly support broad national coverage for annual screening for lung cancer with low-dose computed tomography.
The American Association of Physicists in Medicine (AAPM)
The Academy of Radiology Research
American Association for Thoracic Surgery (AATS)
The American Board of Radiology (ABR)
The American Board of Radiology Foundation
American College of Surgeons’ Commission on Cancer
American Roentgen Ray Society (ARRS)
American Society for Radiation Oncology (ASTRO)
Association of University Radiologists (AUR)
Blanchard Valley Hospital, Findlay, Ohio
The Fleischner Society
Global Institute of Public Health, New York University
Henry Ford Medical Group
Hollings Cancer Center
Houston Methodist Hospital
International Association for the Study of Lung Cancer (IASLC)
International Early Lung Cancer Action Program (I-ELCAP)
Lahey Hospital and Medical Center
Mary Horrigan Connors Center for Women’s Health
Massachusetts General Hospital
Montefiore Einstein Center for Cancer Care
National Council of Asian Pacific Islander Physicians (NCAPIP)
National Comprehensive Cancer Network (NCCN)
National Jewish Health Lung Cancer Screening CT Program
Oakland University
William Beaumont School of Medicine
Penn Lung Center of the University of Pennsylvania
Prevent Cancer Foundation
Quantitative Imaging Biomarkers Alliance (QIBA)
Radiological Society of North America (RSNA)
Society of Chairs of Academic Radiology Departments
Society of Computed Body Tomography and Magnetic Resonance (SCBT-MR)
Society of Thoracic Radiology (STR)
Tobacco Exposure Program at City of Hope Medical Center
The University of Chicago
University of Michigan Comprehensive Cancer Center
Upstate Medical University
WellStar Medical Group.
Medicare Plans to Pay for Lung Cancer Screening
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.

26.7%

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 approximately 2 million eligible for screening
Additional estimate of averted lung cancer deaths ≈ 3000

Cancer 2013;119:1381-5
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
Lung Cancer Screening Status

LDCT now established with a significant mortality benefit for lung cancer screening in high risk groups

- Appears cost-effective: approx $1/month per covered life in under 65 and $2-3/month in Medicare population

USPSTF recommendation requires coverage as a benefit under the ACA

Medicare now providing coverage for beneficiaries

Probably biggest impact on lung cancer management and outcomes in our generation
Minimally Invasive and Maximally Invasive Surgery for Lung Cancer
Minimally Invasive Lung Resection

AKA: thoracoscopy, Video-assisted thoracic surgery (VATS)
Thoracotomy

Division of chest wall muscle and rib spreading

- Impairment of respiratory function
- Immune suppression
- Air leak / chest tube drainage
- Pain/recovery/hospital LOS
Thoracoscopic lobectomy

Proposed Advantages

Less pain
Decreased morbidity
Shorter chest tube duration
Reduced cost
Faster return to full function
Better tolerance for adjuvant therapy
Minimally Invasive Lobectomy
Directed Towards Frail and High Risk Patients


Post-Operative Pain (3 weeks)

- OPEN
  - 6% severe
  - 31% moderate
  - 25% mild
  - 65% none

- VATS
  - 38% severe
  - 31% moderate
  - 25% mild
  - 6% none
Discharge Disposition

*P* = 0.015
Shorter length of stay with the VATS approach……

• Average = 3 days
• Consistently less than with open thoracotomy
• N >2000 patients

McKenna R. Chest Surgery Clinic of North America, Nov 1998
Swanson S et al, Proc ASCO 2002; 21: 290a
VATS Lobectomy

Multiple case series and database reviews strongly suggesting several advantages:

- Diminished postoperative pain
- Shorter length of stay
- Less morbidity

BUT...

- Small randomized trials demonstrate no advantage (or disadvantage)
- No sizable modern randomized trial data
A meta-analysis of unmatched and matched patients comparing video-assisted thoracoscopic lobectomy and conventional open lobectomy

Christopher Cao\textsuperscript{1,2}, Con Manganas\textsuperscript{2}, Su C. Ang\textsuperscript{2}, Tristan D. Yan\textsuperscript{1}

### Table A

<table>
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<tr>
<th>Study or Subgroup</th>
<th>VATS Events</th>
<th>VATS Total</th>
<th>Thoracotomy Events</th>
<th>Thoracotomy Total</th>
<th>Weight</th>
<th>M-H. Random, 95% CI</th>
<th>Risk Ratio</th>
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<td>Ilonen 2011</td>
<td>1</td>
<td>116</td>
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<td>212</td>
<td>9.0%</td>
<td>[0.05, 4.04]</td>
<td>0.46</td>
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<tr>
<td>Paul 2010</td>
<td>6</td>
<td>1281</td>
<td>43</td>
<td>5042</td>
<td>58.9%</td>
<td>[0.23, 1.29]</td>
<td>0.55</td>
</tr>
<tr>
<td>Villamizar 2009</td>
<td>4</td>
<td>697</td>
<td>10</td>
<td>382</td>
<td>32.1%</td>
<td>[0.07, 0.69]</td>
<td>0.22</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>11</td>
<td>2084</td>
<td>5636</td>
<td>100.0%</td>
<td>0.40</td>
<td>[0.21, 0.77]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td></td>
<td>57</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 0.00; \chi^2 = 1.50, df = 2 (P = 0.45), I^2 = 0$

Test for overall effect: $Z = 2.73 (P = 0.006)$

### Table B

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>VATS Events</th>
<th>VATS Total</th>
<th>Thoracotomy Events</th>
<th>Thoracotomy Total</th>
<th>Weight</th>
<th>M-H. Random, 95% CI</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ilonen 2011</td>
<td>1</td>
<td>116</td>
<td>2</td>
<td>116</td>
<td>13.5%</td>
<td>[0.05, 5.44]</td>
<td>0.50</td>
</tr>
<tr>
<td>Paul 2010</td>
<td>6</td>
<td>1281</td>
<td>8</td>
<td>1281</td>
<td>69.2%</td>
<td>[0.26, 2.16]</td>
<td>0.75</td>
</tr>
<tr>
<td>Villamizar 2009</td>
<td>1</td>
<td>284</td>
<td>6</td>
<td>284</td>
<td>17.3%</td>
<td>[0.02, 1.38]</td>
<td>0.17</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>8</td>
<td>1681</td>
<td>1681</td>
<td>100.0%</td>
<td>0.55</td>
<td>[0.23, 1.32]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td></td>
<td>16</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 0.00; \chi^2 = 1.51, df = 2 (P = 0.45), I^2 = 0$

Test for overall effect: $Z = 1.35 (P = 0.18)$

http://www.annalscts.com/article/viewFile/473/598
A meta-analysis of unmatched and matched patients comparing video-assisted thoracoscopic lobectomy and conventional open lobectomy

Christopher Cao¹,², Con Manganas², Su C. Ang², Tristan D. Yan¹

Table 1 Summary of perioperative outcomes of unmatched and propensity score-matched patients who underwent video-assisted thoracic surgery (VATS) versus open thoracotomy for non-small cell lung cancer in three selected studies

<table>
<thead>
<tr>
<th>Measured outcome</th>
<th>Unmatched patients</th>
<th>Matched patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>VATS n=2,094</td>
<td>Open n=5,636</td>
</tr>
<tr>
<td>Perioperative mortality</td>
<td>VATS &lt; Open</td>
<td>NS</td>
</tr>
<tr>
<td>Perioperative morbidity</td>
<td>VATS &lt; Open</td>
<td>NS</td>
</tr>
<tr>
<td>Prolonged air leak</td>
<td>VATS &lt; Open</td>
<td>NS</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>VATS &lt; Open</td>
<td>NS</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Atrial arrhythmias</td>
<td>VATS &lt; Open</td>
<td>NS</td>
</tr>
<tr>
<td>Bleeding</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Empyema</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Sepsis</td>
<td>VATS &lt; Open</td>
<td>NS</td>
</tr>
<tr>
<td>Length of stay</td>
<td>VATS &lt; Open</td>
<td>NS</td>
</tr>
</tbody>
</table>

*"<" indicates statistically lower rate or duration according to meta-analysis; NS, not significant

http://www.annalscts.com/article/viewFile/473/598
# Thoracoscopic Lobectomy versus Open Lobectomy in Stage I Non-Small Cell Lung Cancer: A Meta-Analysis

Yi-xin Cai, Xiang-ning Fu, Qin-zi Xu, Wei Sun, Ni Zhang*

<table>
<thead>
<tr>
<th>Study</th>
<th>% for OPEN</th>
<th>% for VATS</th>
<th>OR</th>
<th>95%LB</th>
<th>95%UB</th>
<th>Z-statistics</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total complications</td>
<td>0.57</td>
<td>0.18</td>
<td>0.17</td>
<td>0.10</td>
<td>0.29</td>
<td>-6.45</td>
<td>0.000</td>
</tr>
<tr>
<td>Ilonen IK (2011)</td>
<td>0.28</td>
<td>0.17</td>
<td>0.54</td>
<td>0.29</td>
<td>0.99</td>
<td>-1.98</td>
<td>0.047</td>
</tr>
<tr>
<td>Park BJ (2007)</td>
<td>0.30</td>
<td>0.24</td>
<td>0.74</td>
<td>0.53</td>
<td>1.02</td>
<td>-1.83</td>
<td>0.067</td>
</tr>
<tr>
<td>Flores RM (2009)</td>
<td>0.09</td>
<td>0.06</td>
<td>0.64</td>
<td>0.18</td>
<td>2.26</td>
<td>-0.70</td>
<td>0.486</td>
</tr>
<tr>
<td>Shigemura N (2006)</td>
<td>0.27</td>
<td>0.27</td>
<td>1.00</td>
<td>0.27</td>
<td>3.77</td>
<td>0.00</td>
<td>1.000</td>
</tr>
<tr>
<td>Sugihara H (1999)</td>
<td>0.52</td>
<td>0.20</td>
<td>0.23</td>
<td>0.08</td>
<td>0.73</td>
<td>-2.50</td>
<td>0.013</td>
</tr>
<tr>
<td>Kirby TJ (1995)</td>
<td>0.45</td>
<td>0.24</td>
<td>0.84</td>
<td>-2.48</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Odds ratio and 95% CI

Relative weight

<table>
<thead>
<tr>
<th>Relative weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>20.32</td>
</tr>
<tr>
<td>19.55</td>
</tr>
<tr>
<td>22.46</td>
</tr>
<tr>
<td>12.33</td>
</tr>
<tr>
<td>11.77</td>
</tr>
<tr>
<td>13.58</td>
</tr>
</tbody>
</table>

PLoS ONE 8(12): e82366. doi:10.1371/journal.pone.0082366