American Cancer Society
National Lung Cancer Roundtable

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Disclosures

Olympus Respiratory America
GRAIL
Chair NCCN Lung Cancer Screening Panel
Vice-Chair NCCN NSCLC Panel
President, Thoracic Surgery Foundation
2012 → 2030

Worldwide cancer cases are projected to increase by

↑ 50%

from 14 million to 21 million

Worldwide cancer deaths are projected to increase by

↑ 60%

from 8 million to 13 million

Source: American Cancer Society: Global Cancer Facts & Figures, Second Edition
cancer.gov
### 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>Leukemia</td>
<td>28,000</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>21,780</td>
</tr>
<tr>
<td>Liver</td>
<td>21,626</td>
</tr>
<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>Lip/oral cancers</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</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>
</tr>
<tr>
<td>Parkinson's disease</td>
<td>20,552</td>
</tr>
<tr>
<td>Liver cancer</td>
<td>19,311</td>
</tr>
<tr>
<td>Homicide</td>
<td>16,591</td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>14,513</td>
</tr>
<tr>
<td>Bladder cancer</td>
<td>14,315</td>
</tr>
<tr>
<td>Brain cancer</td>
<td>14,192</td>
</tr>
<tr>
<td>Esophageal cancer</td>
<td>13,916</td>
</tr>
<tr>
<td>Kidney cancer</td>
<td>13,027</td>
</tr>
<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

Cancer screening coverage
- Breast
- Prostate
- Colon

Lung cancer disparities
- Elderly
- Low socioeconomic group
- Racial
  - “Self-inflicted” disease
Lung Cancer (C33-C34), European Age-Standardised Incidence Rates by Deprivation Quintile, England, 2006-2010
Federal Research Funding Fiscal Year 2011
(Dollars per Death)

Lung Cancer Survival

National Lung Cancer Roundtable

Mission
Create lung cancer survivors

Vision
Lower the impact of lung cancer through prevention, early detection, and optimal therapy

Values
Patient-centered  Evidence-based
Inclusive       Diverse
Proactive       Visionary
Lung Cancer Advances

- Prevention
- Diagnosis
- Staging
- Surgery
- Radiation
- Systemic therapy
- Palliative care
Lung Cancer Advances

- Prevention
- Diagnosis
- Staging
  - PET
  - EBUS
  - VATS
- Surgery
- Radiation
- Systemic therapy
- Palliative care
Lung Cancer Advances

• Prevention
• Diagnosis
• Staging
• Surgery
  – VATS
  – Sublobar resection
  – Extended resections
• Radiation
• Systemic therapy
• Palliative care
Sublobar Resection for Lung Cancer
What has changed in the past 20 years?

Wider use of CT scans → More small lung nodules
Higher resolution scans → More non-solid nodules
Lung cancer screening → Higher expectation of “doing no harm”
PET/EBUS/Med → Better clinical staging
More advanced age/comorbidity → Ablative therapies
Higher proportion of thoracic surgeons → Better decisions about extent of resection → Better outcomes
Temporal trends in outcomes following sublobar and lobar resections for small (≤2 cm) non–small cell lung cancers—a Surveillance Epidemiology End Results database analysis

Sai Yendamuri, MD, FACS, a,b,* Rohit Sharma, MD, a Michael Demmy, BS, a Adrienne Groman, MS, c Mark Hennon, MD, a Elisabeth Dexter, MD, a,b Chukwumere Nwogu, MD, a,b Austin Miller, PhD, c and Todd Demmy, MD a,b

JOURNAL OF SURGICAL RESEARCH 183 (2013) 27–32

N = 8797    lobectomy = 6636    sublobar = 2161

Minimally Invasive Lung Resection

• Thoracoscopy, Video-assisted thoracic surgery (VATS)
Maximally Invasive Lung Resection

Surgery for T3/T4 lung cancer
Lung Cancer Advances

- Prevention
- Diagnosis
- Staging
- Surgery
- Radiation
  - SBRT
  - Proton therapy
- Systemic therapy
- Palliative care
We may have reached a therapeutic plateau for treatment intensification in locally advanced disease. (More RT-0617; Induction chemo-CALGB 39801; Consolidation chemo-HOG; Surgery-INT-0139)

Introduction: Therapeutic Index

Tumor Control

Toxicity

Treatment Intensification (more RT; more chemo; more surgery has not improved outcomes)
The Physics of Protons

Depth dose curves for protons and photons.

10 MeV photons

Additional Dose outside the target delivered with Photons

Proton “Spread Out Bragg Peak”

Relative doses (%)
Therapeutic Index: Protons

PROBABILITY

DOSE OF RADIATION

Tumor control

Toxicity

Widening of the Therapeutic Ratio
Proton Beam

Therapeutic Index: Protons
SPECT/CT for Functional Lung Definition

Patient 1

\[^{99m}Tc\]MAA Perfusion SPECT/CT

\[^{99m}Tc\]DTPA Ventilation SPECT/CT

Functional Avoidance Regions

Patient 2

Patient 3

Courtesy of Stephen Bowen, PhD
Medically Inoperable Early Stage: SBRT

Nyman et al Lung Cancer 2006
Abscopal Effect/Immunotheapy in NSCLC

- Appears to be associated with SBRT-like regimens

- RT appears to enhance the efficacy of immunotherapy
  - Shaverdian et al (Lancet Oncol 2017) reported improved PFS and OS with RT/pembro vs pembro alone in a subset analysis of Keynote-001
  - Pacific randomized trial in stage III NSCLC reported improved PFS with consolidative durvalumab after concurrent chemoRT vs chemoRT alone

- Prospective studies are ongoing to determine optimal dose/fractionation/location for RT in combination with immunotherapy in stage III/IV NSCLC
Lung Cancer Advances

- Prevention
- Diagnosis
- Staging
- Surgery
- Radiation
- Systemic therapy
  - Targeted therapy
  - Immunotherapy
- Palliative care
New Therapies Since 2004

• Oral Tyrosine Kinase Inhibitors
• Immunotherapy
• Immunotherapy in the curative setting
Tumor Responses to Crizotinib in ROS1-Rearranged Non–Small-Cell Lung Cancer.

ROS-1 Targeting

Median Progression-Free Survival: 19.2 months
Immunotherapy in Second Line
Checkmate 017

Median survival improvement: 3.2 months (9.2 months vs 6 months)
Immunotherapy in First Line

KEYNOTE-024

Overall Survival (%)

Hazard ratio for death, 0.60 (95% CI, 0.41–0.89) P=0.005

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>Pembrolizumab</th>
<th>Chemotherapy</th>
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<tbody>
<tr>
<td>0</td>
<td>154</td>
<td>151</td>
</tr>
<tr>
<td>3</td>
<td>136</td>
<td>123</td>
</tr>
<tr>
<td>6</td>
<td>121</td>
<td>106</td>
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<td>9</td>
<td>82</td>
<td>64</td>
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<td>12</td>
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<td>15</td>
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<td>18</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>21</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Immunotherapy in the Curative Setting

Stratified hazard ratio for disease progression or death, 0.52 (95% CI, 0.42–0.65)
Two-sided P<0.001

RR
28.5% (D)
16% (P)

Lung Cancer Survival
1970s 12% → 2010s 18%
Lung Cancer Advances

- Prevention
- Diagnosis
  - LDCT for lung cancer screening
  - Navigational bronchoscopy
  - EBUS
  - cfDNA
  - SPECT perfusion
- Staging
- Surgery
- Radiation
- Systemic therapy
- Palliative care
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.
### Lung Cancer Specific Mortality

**National Lung Screening Trial Results**

<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><strong>0.004</strong></td>
</tr>
<tr>
<td>CXR</td>
<td>143,368</td>
<td>443</td>
<td>309</td>
<td></td>
<td></td>
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</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><strong>0.02</strong></td>
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<tr>
<td>CXR</td>
<td>166,382</td>
<td>2000</td>
<td>1202</td>
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</table>

National Lung Screening Trial NEJM 2011
**Conclusion**

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

<table>
<thead>
<tr>
<th>Date</th>
<th>Organization</th>
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<tbody>
<tr>
<td>Nov 2010</td>
<td>NLST results</td>
</tr>
<tr>
<td>Oct 2011</td>
<td>National Comprehensive Cancer Network (NCCN)</td>
</tr>
<tr>
<td>Apr 2012</td>
<td>American Lung Association</td>
</tr>
<tr>
<td>May 2012</td>
<td>American College of Chest Physicians and ASCO</td>
</tr>
<tr>
<td>Jun 2012</td>
<td>NCCN Update</td>
</tr>
<tr>
<td>Jul 2012</td>
<td>American Association for Thoracic Surgery</td>
</tr>
<tr>
<td>Jan 2013</td>
<td>American Cancer Society</td>
</tr>
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<td>Jun 2013</td>
<td>NCCN Update</td>
</tr>
<tr>
<td>Jul 2013</td>
<td>American Academy of Family Practice</td>
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<tr>
<td>Jul 2013</td>
<td>Society of Thoracic Surgeons</td>
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<tr>
<td>Dec 2013</td>
<td>US Preventive Services Task Force</td>
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<tr>
<td>July 2014</td>
<td>NCCN Update</td>
</tr>
<tr>
<td>Nov 2014</td>
<td>Centers for Medicare and Medicaid Services</td>
</tr>
<tr>
<td>July 2015</td>
<td>NCCN Update</td>
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<td>July 2016</td>
<td>NCCN Update</td>
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<td>July 2017</td>
<td>NCCN Update</td>
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</table>
Draft Recommendation Statement

Note: This draft Recommendation Statement is not the final recommendation of the U.S. Preventive Services Task Force. This draft is distributed solely for the purpose of pre-release review. It has not been disseminated otherwise by the USPSTF. It does not represent and should not be interpreted to represent a USPSTF determination or policy.

This draft Recommendation Statement is based on an evidence review that was published on July 30, 2013 (available at http://www.uspreventiveservicestaskforce.org/uspsf13/lungcancer/lungcanart.htm).

The USPSTF makes recommendations about the effectiveness of specific preventive care services for patients without related signs or symptoms.

It bases its recommendations on the evidence of both the benefits and harms of the service, and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decisionmaking to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

This draft Recommendation Statement was available for comment from July 30 until August 26, 2013 at 5:00 PM ET. A fact sheet that explains the draft recommendations in plain language is available here.

Screening for Lung Cancer: U.S. Preventive Services Task Force Recommendation Statement DRAFT

Summary of Recommendation and Evidence

The U.S. Preventive Services Task Force (USPSTF) recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in persons at high risk for lung cancer based on age and smoking history.

This is a Grade B recommendation.
Medicare Plans to Pay for Lung Cancer Screening
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
Performance of Lung-RADS in the National Lung Screening Trial
A Retrospective Assessment
Paul F. Pinsky, PhD; David S. Gierada, MD; William Black, MD; Reginald Munden, MD; Hrudaya Nath, MD; Denise Aberle, MD; and Ella Kazerooni, MD

False-positive rate

<table>
<thead>
<tr>
<th></th>
<th>NLST</th>
<th>LungRADS</th>
<th>Improvement w/LungRADS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>26.6%</td>
<td>12.8%</td>
<td>52%</td>
</tr>
<tr>
<td>After baseline</td>
<td>21.8%</td>
<td>5.3%</td>
<td>76%</td>
</tr>
</tbody>
</table>

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%
Screening Efficiency
Number Needed to Screen

Screening mammography$^{1,2}$  780 - 2000
Screening colonoscopy$^2$  1250
Screening LDCT (in NLST)  320

Balancing curability and unnecessary surgery in the context of computed tomography screening for lung cancer

Lung Cancer Survival

Current Lung Cancer Survival

I-ELCAP


National Lung Cancer Roundtable

Mission
Create lung cancer survivors

Vision
Lower the impact of lung cancer through prevention, early detection, and optimal therapy

Values
Patient-centered  Evidence-based
Inclusive        Diverse
Proactive        Visionary
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
National Lung Cancer Roundtable

- Provider engagement and outreach
- Lung cancer screening implementation strategies
- Tobacco cessation in the context of lung cancer screening
- Triage for appropriate treatment
- Shared decision making
- Lung cancer in women
- Advanced imaging
- Policy action
National Lung Cancer Roundtable

Support interdisciplinary communication
Enhance opportunities for collaboration
Do not duplicate effort
Identify resources, knowledge gaps, opportunities
Create synergies
Increase awareness, priority, and urgency
Accelerate the mission – to create lung cancer survivors