Screening for Lung Cancer in our Veterans: The risk of lung cancer from military service

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Disclosure

• “The views expressed in this lecture are those of the author and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, nor the U.S. Government”
Lung Cancer

- Estimated 224,210 in U.S. 2014\(^1\)
  - 130,270 male
  - 113,910 female

Most common cancer overall
- 2nd most common cancer in men and women
- Leading cause of cancer related death
  - More than (Breast, Prostate, Colon, and Pancreas combined)
  - 29% of cancer related deaths
- 159,260 deaths
  - Median age diagnosis 71 yrs

Seigel et al: Clinical Cancer Advances 2014
Lung Cancer Statistics

2013 Cancer Statistics

- Prostate
- Breast
- Lung
- Colon
- Melanoma
- Bladder
- Non-Hodgkin Lymphoma
- Kidney
- Thyroid
- Endometrial

Adapted from SEER (Surveillance, Epidemiology, and End Results Program located at http://seer.cancer.gov/statfacts/html/all.html)
Lung Cancer Statistics

2013 Cancer Statistics

Adapted from SEER (Surveillance, Epidemiology, and End Results Program located at http://seer.cancer.gov/statfacts/html/all.html
Lung Cancer Statistics

VA Cancer Statistics

The years lost to cancer

By Patterson Clark, Published: Feb. 17, 2014

While some cancers may claim fewer lives than others, they might cause a greater loss of potential years of life. Less common but more potent cancers that tend to be diagnosed earlier in life may have a greater impact on the population than would a more common but less virulent cancer occurring later in life. Related: New therapies targeting cancer could change everything

2010, UNITED STATES

<table>
<thead>
<tr>
<th>CANCER TYPE</th>
<th>IN THOUSANDS</th>
<th>DEATHS</th>
<th>NEW CASES</th>
<th>MEDIAN AGE* AT DIAGNOSIS AND DEATH</th>
<th>IN MILLIONS OF YEARS OF LIFE LOST</th>
<th>NCI FUNDING, IN MILLIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>LUNG</td>
<td>157</td>
<td></td>
<td>223</td>
<td>70 72</td>
<td>2.37</td>
<td>$282</td>
</tr>
<tr>
<td>COLON/RECTUM</td>
<td>51</td>
<td>143</td>
<td></td>
<td>69 74</td>
<td>0.76</td>
<td>270</td>
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<tr>
<td>BREAST</td>
<td>40</td>
<td></td>
<td>209</td>
<td>61 68</td>
<td>0.76</td>
<td>631</td>
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<tr>
<td>PANCREAS</td>
<td>37</td>
<td>43</td>
<td></td>
<td>71 73</td>
<td>0.50</td>
<td>97</td>
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<tr>
<td>LEUKEMIA</td>
<td>22</td>
<td>43</td>
<td></td>
<td>66 75</td>
<td>0.36</td>
<td>296</td>
</tr>
<tr>
<td>NON-HDG. LYMPHOMA</td>
<td>20</td>
<td>66</td>
<td></td>
<td>66 76</td>
<td>0.29</td>
<td>122</td>
</tr>
<tr>
<td>LIVER</td>
<td>19</td>
<td>24</td>
<td></td>
<td>63 68</td>
<td>0.29</td>
<td>73</td>
</tr>
<tr>
<td>BRAIN, NERVE</td>
<td>13</td>
<td>22</td>
<td></td>
<td>57 64</td>
<td>0.29</td>
<td>193</td>
</tr>
<tr>
<td>PROSTATE</td>
<td>32</td>
<td></td>
<td>218</td>
<td>66 80</td>
<td>0.27</td>
<td>301</td>
</tr>
</tbody>
</table>

Money for research

Research funding at the National Cancer Institute doesn’t necessarily correlate with a cancer’s impact. Lung cancer, which yearly robs Americans of more than 2 million years of life, receives less research funding than does prostate cancer, which...
Lung cancer and smoking

• 87% of time lung cancer occurs in either former or current smokers

• 13% occurs in never smokers
  • (~36,500 cases of lung cancer)
Risks for Lung Cancer

- Smoking and second-hand smoke cause lung cancer
- There is a 20% to 30% increase in risk of lung cancer from second-hand smoke.
- Former smokers risk of lung cancer remains elevated, 10 years after quitting 8x greater.
- Other potential carcinogens include chromium, nickel, polycyclic aromatic hydrocarbons (PAH), radon, and asbestos, which cause 3% to 4% of lung cancers.
- Family history and chronic inflammation (e.g., TB) also increase risk.

Prognostic factors

- Early stage
- Good performance status (0, 1)
- Female
- Race: Asian > White > Black
- Histology
  - Adenocarcinoma > Large Cell > Squamous Cell
- Presence of EGFR mutation
- Presence of ALK translocation (when treated with targeted tx)
- ABSENCE of multiple mutations
  - (i.e. K-ras and p53 mutations)
  - (increased pack years = increased number of mutations)
NSCLC Facts

• Most people are diagnosed Stage III and IV.
  - 25% stage I
  - 7% stage II
  - 32% stage III
  - 36% stage IV

• Overall 5 year survival for all stages is 15%
Military Service

- Army, Air Force, Coast Guard, Marines and Navy
- Wide range of exposures
  - Some unique to service, location, length
  - Some universal
Lung Cancer Risk of Veterans

- **Smoking** –
  - Military members have increased rates of smoking.
    - 25 to 30%
    - Second hand smoking risk
  - Deployments worsen smoking rates
    - ~50%
  - Veterans have increased rates of smoking.

- **Occupational Risks** –
  - Environmental tobacco smoke
  - Asbestos
  - Diesel fuels

Veteran Smoking

QuickStats: Current Smoking* Among Men Aged 25-64 Years, by Age Group and Veteran Status† — National Health Interview Survey (NHIS), United States, 2007-2010§

Weekly
November 16, 2012 / 61(45);929

* Defined as having smoked at least 100 cigarettes in their lifetime and now smoke everyday or some days.
Increased smoking rates associated with war

- WWII and Korean War
  - 35% excess lung cancer mortality over the general population\(^1\)

- Vietnam Veterans
  - Estimated 47% current smokers\(^2\)
  - Ever smokers 70%\(^2\)

- Gulf War Veterans
  - Estimated 47% current smokers\(^3\)

1. Bedard K et al. American Econ R, 2006:96;1-
DOD and Tobacco

• 1975 Military stopped issuing cigarettes as part of K-rations\(^1\)

1. Feigelman W. Preventive Medicine 1994;23:235-241
DOD and Tobacco

- **1975** Military stopped issuing cigarettes as part of K-rations
  
- **1996** Military stops subsidizing tobacco
  
  - DOD spent **30 million dollars** subsidizing tobacco in 1996

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1. Feigelman W. Preventive Medicine 1994;23:235-241
DOD and Tobacco

• 1975 Military stopped issuing cigarettes as part of K-rations\(^1\)
• 1996 Military stops subsidizing tobacco\(^2\)
  – DOD spent **30 million dollars** subsidizing tobacco in 1996

• **2001** DOD 1330.9
  – cigarettes must be within 5% local price\(^2\)

• **2012** DOD 1330.9
  – Cigarettes must be equal to local price

1. Feigelman W. Preventive Medicine 1994;23:235-241
NAPLES, Italy — The Navy is considering a ban on all tobacco sales on ships and bases due to health concerns over the high rate of tobacco use among sailors, officials say.

The idea is “one option on the table” as Navy Secretary Ray Mabus explores ways to further curb tobacco use among sailors, said a Navy official who who spoke on condition of anonymity because he was not authorized to speak on the subject.
Lung Cancer Risk of Veterans

- **Smoking** –
  - Military members have increased rates of smoking.
  - Deployments worsen smoking rates.
  - Veterans have increased rates of smoking.

- **Occupational Risks** –
  - Environmental tobacco smoke
  - Asbestos
  - Diesel fuels

Unique Chemicals in the military related to lung cancer and other cancers:

- polycyclic aromatic hydrocarbons (PAH)
  - Diesel Fuel
- Asbestos - (3% to 4% of lung cancers)
- Agent Orange exposure (arsenic containing) pesticides
- Depleted uranium ammunition?
Pollution has been difficult to document as a contributor to cancer.

- However, long-term exposure to high levels of air pollution may increase lung cancer risk by as much as 25%


Military “pollution”
- Oil fires in the Iraq War
- Burn pit exposures
- Diesel exhaust
Public Health

VA’s Action Plan: Burn Pits and Airborne Hazards

Registry for Veterans who may have been exposed

VA’s Airborne Hazards and Open Burn Pit Registry will allow eligible Veterans exposed to burn pit smoke and other airborne hazards to document their exposures and report health concerns. Veterans will enter information through a web-based questionnaire and have the opportunity to obtain an evaluation. Eligible Veterans include those who served in:

- Operation Enduring Freedom/Operation Iraqi Freedom/Operation New Dawn
- Djibouti, Africa after September 11, 2001
Cost of Lung Cancer in the DOD/VA

• TRICARE in 2006
  – Smoking related disabilities cost $2.1 billion in excess medical care annually\(^1\) (compared to $584 million in 1997)\(^2\)
  – Lung Cancer $564 million
  – Comparatively Prostate Cancer $42 million

• Department of Veterans Affairs
  – Smoking related disabilities cost 5 billion in 1997\(^3\)
  – Expected to grow to 9.6 billion over next decade

3. Harris J. 1997 Commissioned report Department of Veterans Affairs
Veteran’s incidence of lung cancer

Lung Cancer Rates

• At least 25%-43% higher\(^1,^3\)
• One study (Harris) reported a 76% higher rate than the national average compared to age matched SEER data\(^2\)

2. Harris et al. Cancer 1989:64;1160-1168
Screening

- **PLCO (CXR)**
  - 77,464 age 55-74 former smokers;
  - Detection of early lung cancer; no reduction in mortality

- **I-ELCAP (CT scan) (not a randomized trial)**
  - 31,567 age 40-86 former or high risk; 85% detection of early lung cancer

- **NELSON Trial (CT scan vs. no screening)**
  - 7,557 age 55-75 current or former < 10 years; 64% detection of early stage lung cancer
  - Results: 2016

- **NLST (CT scan vs. CXR)**
  - 56,456 (CT vs. CXR) (current or former) (30 pack-years)
  - Stopped Early 11/4/10 (20% reduction in lung cancer mortality)
  - Favor of CT scan: reduction in lung cancer and all cause mortality
Walter Reed Bethesda

- World’s largest military medical center
- Provides care to over a million beneficiaries a year
- Inclusive healthcare of eligible beneficiaries
- Excellent system to integrate cancer screening
- Robust disease management department

http://www.wrnmmc.capmed.mil
Developing a Lung Cancer Screening Program

• Planning 2011 – 2012

• Screening began in November 2012

• 2013 WRB and VA joint pilot for screening in 8 VA hospitals as well as 4 major military medical centers
Expected Outcomes

Outcomes of Screening

- Normal: 72%
- Abnormal: 27%
- Lung Cancer: 1%
Expected Outcomes

Outcomes of Screening

- Normal: 72%
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- Lung Cancer: 1%
Expected Outcomes

Outcomes of Screening

- Normal: 72%
- Abnormal: 27%
- Lung Cancer: 1%

Total: 100%
Organized Approach
Team Members

Roles

- Inclusion criteria for screening –
  - Radiology/Pulmonology/Oncology/Primary Care
- Radiologic Studies –
  - Radiology (LDCT)
- Guidelines for addressing abnormal screening –
  - Pulmonology/Radiology/Oncology/Primary Care
- Smoking Cessation
  - Primary Care/Smoking Cessation
- Enrollment into database for continued screening –
  - Pulmonology/Disease Management
- Database management during screening –
  - Pulmonology/Disease Management
- Clinical and radiologic assessment during screening –
  - Pulmonology/Radiology
New Patient Request for Lung Cancer Screening

If all items below are checked for either Criteria 1 or Criteria 2 and patient wishes to be screened, please order Low Dose Chest CT, complete information below and click submit.

Does the patient wish to be screened? □

**Criteria 1**
- Age 50 - 80? □
- Used Tobacco at least 30 pack years? More Info □
- Has not quit or quit less than 15 years ago? □

**OR**

**Criteria 2**
- Age 50 or greater? □
- Used Tobacco at least 20 pack years? More Info □
- One other risk factor (not second hand smoke exposure) □

**Risk Factors:**
- Occupational Exposure: Radon, Asbestos, Agent Orange, Silicon
- Patient Cancer History: Lung, HEENT, Lymphoma, CA related to smoking
- Patient Chronic Lung Disease: COPD, Pulmonary Fibrosis
- Family History: 1st Degree Relative with Lung Cancer

List other risk factor: COED
Developing Lung Cancer Screening Program

<table>
<thead>
<tr>
<th>Allergies</th>
<th>Tobacco Use</th>
<th>Military Service</th>
<th>Duty Stations</th>
<th>Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start Year</td>
<td>End Year</td>
<td>OR Number of years</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Lung Cancer Screening
# Early Outcomes of Lung Cancer Screening at WR-B

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Screened</th>
<th>Nodules</th>
<th>Lung Cancer Detected</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Henschke</td>
<td>1999</td>
<td>1000</td>
<td>23.3 % 9.7% (&gt;5mm)</td>
<td>2.7%</td>
<td></td>
</tr>
<tr>
<td>Sone</td>
<td>2001</td>
<td>5483</td>
<td>5.1%</td>
<td>0.4%</td>
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</tr>
<tr>
<td>Diederich</td>
<td>2002</td>
<td>817</td>
<td>50.1% 18.8% (&gt;5mm)</td>
<td>1.35%</td>
<td></td>
</tr>
<tr>
<td>Nawa</td>
<td>2002</td>
<td>7956</td>
<td>26.4% 6.8% (&gt;8mm)</td>
<td>0.45%</td>
<td></td>
</tr>
<tr>
<td>Sobue</td>
<td>2002</td>
<td>1611</td>
<td>11.5%</td>
<td>0.81%</td>
<td></td>
</tr>
<tr>
<td>Swensen</td>
<td>2002</td>
<td>1520</td>
<td>51.4% 31.3%</td>
<td>1.38%</td>
<td></td>
</tr>
<tr>
<td>Titola</td>
<td>2002</td>
<td>602</td>
<td>18.4% 8.0% (&gt;5mm)</td>
<td>0.83%</td>
<td></td>
</tr>
<tr>
<td>NLST Research Team</td>
<td>2011</td>
<td>53454 (26,722 LDCT)</td>
<td>27.3% (first round) 39.1% (during 3 rounds)</td>
<td>1.0% (first round) 3.9% (during 3 rounds)</td>
<td>20% reduction in lung cancer deaths.</td>
</tr>
<tr>
<td>WR-B</td>
<td>2013-2014</td>
<td>150</td>
<td>&gt;55%</td>
<td>4 %</td>
<td>Offered now as standard of care</td>
</tr>
</tbody>
</table>
Smoking Cessation

• Increased referrals to smoking cessation
  – (added 50 new patients)

• Smoking Cessation for screening program:
  – 50% of patients

• Smoking Reduction Rates:
  – 25 % (reduced number of cigarettes)
  – Follow-up smoking cessation >50%
• Which nodules are malignant?
• How can we improve screening?
• Are the lung cancers we are seeing in the military different?
• 2011 Congressionally Directed Medical Research Programs (CDMRP) grant (13M)

• The Detection of Early Lung Cancer Among Military Personnel
DECAMP Consortium

• C0-PI Avrum Spira, MD, MSc Boston Univ,
• Co-PI Mitchell Schnall, MD, PhD ACRIN
• 4 designated Military Treatment Facilities (MTF)
• 7 Veterans Administration Hospitals (VAH),
• One academic hospital
• several molecular biomarker laboratories, along with Biostatics, Bioinformatics, Pathology and Biorepository cores
• Pathology Core: MD Anderson (Ignacio Wistuba MD)
Murtha Cancer Center Bio-Bank

• Banked Lung cancer specimens:
  – Approx. 300 samples
  – frozen tissue and paraffin blocks (FFPE)
  – blood and serum, urine
  – Linked to radiographic images
  – clinical data, and deployment exposures, etc
Research Direction

1) How Many Lives Can we Save in the National Capital Area
   – (enhanced Multi-Service Market) for the Defense Health Agency
   – Statistical Analysis focusing on COST for the military

2) Natural History Study for Lung Cancer Screening the Military
   – Includes optional BIOBANKING
     • Blood, Urine, and Nasal tissue

3) Understanding the Immunosuppressive microenvironment of tumorigenesis (focusing on KRAS mutated lung cancer)
Future Direction

- Integrative analysis of the Microbiome and their metabolites
Future Directions

- Understanding and validating unique **Urinary Metabolic Profiling**

**Figure 1.** Four metabolites are best predictors of lung cancer status and prognosis independent of race and gender. 

A. Receiver Operating Characteristic (ROC) Analysis depicting diagnostic utility of the four metabolites individually and their combination in all cases. 

B. Kaplan-Meier analysis showing that the combination of four metabolites leads to a stronger association with prognosis.

**Figure 2.** Receiver Operating Characteristic (ROC) Analysis. Thirteen metabolites are best classifiers of lung cancer diagnosis in African Americans (top). This diagnostic classifier is robust in Stage I NSCLC (bottom) (Haznadar, M, et.al, In Prep).
Future Directions

- Addition of a BIOMARKER to the Low Dose CT scan

  - **PAULA’s test:**
    - 20/20 Gene Assay: 3 tumor proteins and one autoantibody
      Sens.: (0.83) Spec.: (0.80)
    - Addition of additional autoantibody-based biomarkers identified through collaboration with the Rush Thoracic-Oncology research program
    - Increase Sensitivity to 0.90 and Specificity to 0.90
Summary

• Military service appears to increase risk for lung cancer
  – Unique exposures and deployments
  – Increased smoking

• Military medicine is invested in the early detection of lung cancer and prevention

• As screening experience grows, patient inclusion criteria will need to be modified for pertinent risk factors. Military service may be a unique factor.

• Screening, coupled with aggressive smoking cessation, likely provides the best method to reduce the mortality impact of lung cancer
  – Couple cessation with continued measures to limit access to tobacco and smoking in the military
Thank you