Benefits and Harms of Lung Cancer Screening in HIV Infected Individuals: A Simulation Study

Chung Yin Kong, Keith Sigel, R. Scott Braithwaite, Juan Wisnivesky, Kristina Crothers
Background

• Improved HIV+ patient survival with ART
• Lung cancer is the most common non-AIDS defining cancer (NADC) in HIV+
• NLST demonstrated the benefits of lung cancer screening with low-dose computed tomography (CT) in the HIV- population

What should LC screening criteria be for HIV+?
Goals

• Extend and calibrate an existing simulation model of lung cancer screening for HIV+

• Estimate the potential benefits (lung cancer mortality reduction) and harms (# of screening CT exams) of lung cancer screening among HIV+ persons and determine the optimal screening regimen(s)
Introduction to Lung Cancer Policy Model (LCPM)

- Simulate individual life-histories (microsimulation)
  - Risk of lung cancer depends on age, sex, and smoking history
  - Competing mortality depends on smoking

- Variability across cancers and individuals
  - Multiple lung cancer histologies (adenocarcinoma, squamous, large-cell, small-cell, and others)

- Part of National Cancer Institute (NCI)’s Cancer Intervention and Surveillance Modeling Network (CISNET)

Model Documentation [88 pages]
Some Prior Publications of the LCPM

• Model calibration and validation using SEER, NLST, and PLCO data\textsuperscript{1,2}

• Benefits and harms of computed tomography lung cancer screening strategies (for general population)\textsuperscript{3-5}

Smoking and Disease in HIV+ vs. HIV-

- HIV+ adults nearly **twice as likely to smoke** 37.6% [CI 34.7 – 40.6] vs. 20.6% [CI 19.9-21.3] but **less likely to quit** smoking\(^1\)

- **Higher rates of other cause mortality**, even when controlling for smoking status\(^2,3\)

- HIV+ associated with **higher rates of lung cancer** \(^4\)

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3. VACS 8 data.
Lung Cancer Screening Criteria

Centers for Medicare & Medicaid Services (CMS)
Age 55-77, history of 30 “pack-years”* of smoking, less than 15 years since quitting for former smokers

*1 pack-year = 1 pack of cigarettes/day for 1 year or 0.5 pack of cigarettes/day for 2 year, etc.

What should screening criteria be for HIV+ patients?
Simulation Results
Calibration: Smoking Behaviors in HIV+

Model Outputs vs. Observed Data

Adjusted % of Current Smokers
Quit Ratio

Model Outputs vs. Observed Data (Mdodo, 2015)
Calibration: Lung Cancer Incidence

LC Incidence Rate Ratio between HIV+ and HIV-

Model Output

Observed Ratio (Sigel, et al. 2012)
LC Mortality Reduction Comparison

CMS Criteria (Age 55-77, 30PY, Years Since Quit <15)

Screened – screened population includes only people who went through screening.
Total - total population includes never, former, and current smokers.
Examined 6 Screening Eligibility Strategies (all years-since-quit < 15)

<table>
<thead>
<tr>
<th>Notation</th>
<th>Age to begin screening</th>
<th>Age to end screening</th>
<th>Minimum PY for screening</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age_55-77-PY30 (CMS)</td>
<td>55</td>
<td>77</td>
<td>30</td>
</tr>
<tr>
<td>Age_55-77-PY20</td>
<td>55</td>
<td>77</td>
<td>20</td>
</tr>
<tr>
<td>Age_50-72-PY30</td>
<td>50</td>
<td>72</td>
<td>30</td>
</tr>
<tr>
<td>Age_50-72-PY20</td>
<td>50</td>
<td>72</td>
<td>20</td>
</tr>
<tr>
<td>Age_50-77-PY30</td>
<td>50</td>
<td>77</td>
<td>30</td>
</tr>
<tr>
<td>Age_50-77-PY20</td>
<td>50</td>
<td>77</td>
<td>20</td>
</tr>
</tbody>
</table>

Compared these strategies with no screening for HIV+ patients with CD4>500
## Results of Different Strategies

<table>
<thead>
<tr>
<th>Strategy</th>
<th># Screening CT per 100K</th>
<th>LC Mortality Reduction among Total Population (%)</th>
<th>% Screened</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Screening</td>
<td>0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Age_55-77-PY30</td>
<td>310,299</td>
<td>10.5</td>
<td>24.9</td>
</tr>
<tr>
<td>Age_55-77-PY20</td>
<td>423,181</td>
<td>13.1</td>
<td>33.5</td>
</tr>
<tr>
<td>Age_50-72-PY30</td>
<td>393,089</td>
<td>11.5</td>
<td>28.2</td>
</tr>
<tr>
<td>Age_50-72-PY20</td>
<td>531,741</td>
<td>14.2</td>
<td>38.6</td>
</tr>
<tr>
<td>Age_50-77-PY30</td>
<td>425,187</td>
<td>12.8</td>
<td>28.6</td>
</tr>
<tr>
<td>Age_50-77-PY20</td>
<td>575,610</td>
<td>16.0</td>
<td>38.7</td>
</tr>
</tbody>
</table>
Lowering Screening Age to 50-72

- CMS recommendations
- Lower screening age to 50-72

Mortality reduction

% LC Mortality Reduction (total)

- 10.5
- 11.5

CT exams

Screening CT exams per 100,000

- 310,299
- 393,089
How to pick?

[Diagram showing a scatter plot with the x-axis labeled \# of Screening CT exams per 100K and the y-axis labeled LC Mortality Reduction. Points labeled Age_55-77-PY30 (CMS), Age_50-77-PY20, Age_55-77-PY20, Age_50-72-PY20, and Age_50-72-PY30 are plotted.]
• Minimize the resource utilization
  (screening CT exams)
• Maximize the benefit
  (lung cancer mortality reduction)
• Usually, there is no single BEST strategy
• A set of optimal strategies
Optimal Strategies Selection

- Age_55-77-PY30 (CMS)
- Age_50-77-PY20
- Age_50-72-PY30
- Age_50-72-PY20

LC Mortality Reduction vs. # of Screening CT exams per 100K

- No Screen

0% - 18%
0 - 600000

Age_55-77-PY30 (CMS)
Optimal Strategies Selection

- Age_55-77-PY30 (CMS)
- Age_50-77-PY20
- Age_50-72-PY30
- Age_50-72-PY20

# of Screening CT exams per 100K

LC Mortality Reduction
What is next?

![Graph showing LC Mortality Reduction vs. # of Screening CT exams per 100K]

- No Screen
- Age_55-77-PY30 (CMS)
- Age_50-77-PY20
- Age_50-77-PY30
- Age_50-72-PY20
- Age_50-72-PY30

The graph illustrates the relationship between the number of screening CT exams per 100K population and LC Mortality Reduction. Different cohorts are represented by specific points on the graph, indicating potential future directions for screening programs.
Optimal Strategies Selection

LC Mortality Reduction vs. # of Screening CT exams per 100K

- No Screen
- Age_55-77-PY30 (CMS)
- Age_50-77-PY20
- Age_50-72-PY20
- Age_50-77-PY30
Limitations

- Cost not included
- Not considering impact of screening on smoking behavior
- Only 6 strategies
- No data to inform increased LC risk and mortality rate prior to HIV diagnosis
Conclusions

• LC mortality reduction benefit from CT screening for HIV+ is similar to HIV-

• CMS criteria is one of the optimal strategies

• Lowering screening age-range may not be optimal
Thank You

- **Mount Sinai Hospital**
  - Keith Siegel
  - Juan Wisnivesky
- **NYU**
  - Heather Gold
  - Scott Braithwaite
- **VA Pittsburgh**
  - Kathleen McGinnis
- **Massachusetts General Hospital**
  - Deirdre Sheehan

Funding R01CA173754
LC Mortality Reduction from CT Screening for HIV+

CMS Criteria (Age 55-77, 30PY, Years Since Quit <15)

Total population includes never, former, and current smokers.
Screened population includes only people went through screening.
Predicted Life Expectancy
NO lung cancer screening (alive at age 50)

Life expectancy among those who live to at least age 50

- Current smokers:
  - HIV negative: 76.37 years
  - CD4 > 500: 67.47 years
  - CD4 200-500: 65.74 years

- Former smokers:
  - HIV negative: 79.37 years
  - CD4 > 500: 72.59 years
  - CD4 200-500: 71.76 years
## Cigarette Smoking Prevalence Among Adults With HIV Compared With the General Adult Population in the United States

### Table 3. Adjusted Prevalence and Adjusted Prevalence Difference of Current Cigarette Smoking Among Adults With HIV Who Received Medical Care (MMP) and the General Adult Population (NHIS) in the United States in 2009

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>MMP Adjusted Current Smoking Prevalence (95% CI), %*</th>
<th>NHIS Adjusted Prevalence Difference Between MMP and NHIS (95% CI), percentage points†</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>37.6 (34.7-40.6)</td>
<td>20.6 (19.9-21.3)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

### Table 4. Quit Ratios Among Former Smokers and the Weighted Number of Former Smokers and Ever-Smokers Among Adults With HIV (MMP) and the General Adult Population (NHIS) in the United States in 2009*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>MMP</th>
<th>NHIS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Former Smokers, n†</td>
<td>Ever-Smokers, n</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-29 y</td>
<td>2262</td>
<td>13861</td>
</tr>
<tr>
<td>30-39 y</td>
<td>10 053</td>
<td>40 666</td>
</tr>
<tr>
<td>40-49 y</td>
<td>29 263</td>
<td>105 889</td>
</tr>
<tr>
<td>≥50 y</td>
<td>43 865</td>
<td>103 007</td>
</tr>
</tbody>
</table>

Myocardial Infarction Among HIV+ Individuals

Higher rates of lung cancer associated with HIV+

Table 4. Adjusted lung cancer incidence rate ratios associated with HIV stratified by smoking exposure.

<table>
<thead>
<tr>
<th>Smoking strata</th>
<th>HIV-infected lung cancer cases</th>
<th>Uninfected lung cancer cases</th>
<th>IRR$^a$</th>
<th>P-value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never smoker</td>
<td>19</td>
<td>30</td>
<td>1.6</td>
<td>0.08</td>
<td>0.9–3.0</td>
</tr>
<tr>
<td>Former smoker</td>
<td>55</td>
<td>91</td>
<td>1.7</td>
<td>&lt;0.001</td>
<td>1.2–2.4</td>
</tr>
<tr>
<td>Current smoker</td>
<td>262</td>
<td>370</td>
<td>1.5</td>
<td>&lt;0.001</td>
<td>1.3–1.7</td>
</tr>
<tr>
<td>Missing smoking data</td>
<td>121</td>
<td>114</td>
<td>2.1</td>
<td>&lt;0.001</td>
<td>1.6–2.7</td>
</tr>
</tbody>
</table>

CI, confidence interval; IRR, incidence rate ratio.
$^a$Adjusted for age, sex, race/ethnicity, chronic obstructive pulmonary disease, and previous pneumonia.

Tumor Stage and Histology

HIV infected vs. No evidence of infection

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HIV infected N (%)</th>
<th>No evidence of HIV infection N (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Histology</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>131 (49)</td>
<td>687 (48)</td>
<td>0.4</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>85 (32)</td>
<td>512 (36)</td>
<td></td>
</tr>
<tr>
<td>Large cell carcinoma</td>
<td>20 (8)</td>
<td>81 (6)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>31 (12)</td>
<td>148 (10)</td>
<td></td>
</tr>
<tr>
<td><strong>Tumour stage</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>56 (21)</td>
<td>332 (23)</td>
<td>0.5</td>
</tr>
<tr>
<td>II</td>
<td>12 (5)</td>
<td>95 (7)</td>
<td></td>
</tr>
<tr>
<td>IIIA</td>
<td>34 (13)</td>
<td>193 (14)</td>
<td></td>
</tr>
<tr>
<td>IIIB</td>
<td>57 (21)</td>
<td>267 (19)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>108 (41)</td>
<td>541 (38)</td>
<td></td>
</tr>
</tbody>
</table>