Tail of Two Carcinogens

The Legacy of Asbestos and Smoking

Steven Markowitz MD, DrPH
City University of New York

Ramazzini Days 2012
October 26-28
Carpi, Italy
Irving J. Selikoff, MD, 1915-1992

Director, Environmental Science Laboratory
Mount Sinai School of Medicine, 1961-1985

Co-Founder, Collegium Ramazzini
Acknowledgements

- Alfredo Morabia MD, PhD, and Al Miller, MD, Queens College
- Shannon Widman, MPH, Jordan Werbe Fuentes, Yan Guo, Queens College
- Michael Thun, MD, MS, Susan Gapstur, PhD, MPH, Yusheng Zhai, MS, MSPH, American Cancer Society
- Stephen Levin MD and Philip Landrigan MD, MSc, Mount Sinai School of Medicine
Disclosure

I have provided medico-legal opinions and testimony in asbestos tort cases, mostly involving malignant mesothelioma.
Question #1

Is it asbestosis or asbestos (or both) that raises lung cancer risk?

Question #2

How do asbestos, asbestosis, and smoking interact?
Causal Model of Asbestos, Asbestosis, Smoking and Lung Cancer
New significance

- Low-dose CT scan screening reduces lung cancer mortality (NCI 2011).
- Asbestos exposure was common in U.S. through 1980’s. Asbestosis is uncommon.
- Many asbestos-exposed workers have stopped smoking.
1.6 cm lung cancer detected by low dose CT scan, Oak Ridge DOE worker
Question #1

Is it asbestosis or asbestos (or both) that raises lung cancer risk?
COMMENTARY

Does Asbestos or Asbestosis Cause Carcinoma of the Lung?

Victor L. Roggli, MD, Samuel P. Hammar, MD, Philip C. Pratt, MD,
John C. Maddox, MD, Jacques Legier, MD, Eugene J. Mark, MD, and
Arnold R. Brody, PhD

COMMENTARY

Asbestos Inhalation, Not Asbestosis, Causes Lung Cancer

Jerrold L. Abraham, MD

Lung Cancer and Asbestos Exposure: Asbestosis is Not Necessary

David Egilman, MD MPH, and Alexander Reinert
Lung Cancer Mortality among Sheet Metal Workers, 1986-2004


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**TABLE IV.** Sheet Metal Worker Mortality by Chest X-Ray Parenchymal Category Follow-Up From Exam Date
Through December 31, 2004

<table>
<thead>
<tr>
<th>Disease category</th>
<th>Parenchymal change category</th>
<th>Obs.</th>
<th>Exp.</th>
<th>SMR</th>
<th>95% confidence limits lower</th>
<th>upper</th>
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</thead>
<tbody>
<tr>
<td>Lung cancer</td>
<td>0/− to 0/1</td>
<td>459</td>
<td>484.58</td>
<td>0.95</td>
<td>0.86</td>
<td>1.04</td>
</tr>
<tr>
<td></td>
<td>1/0 to 1/2</td>
<td>97</td>
<td>68.34</td>
<td>1.42**</td>
<td>1.15</td>
<td>1.73</td>
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<tr>
<td></td>
<td>2/1 to 2/3</td>
<td>11</td>
<td>3.65</td>
<td>3.01**</td>
<td>1.50</td>
<td>5.39</td>
</tr>
<tr>
<td></td>
<td>3/2 to 3/+</td>
<td>2</td>
<td>0.19</td>
<td>10.42*</td>
<td>1.26</td>
<td>37.63</td>
</tr>
</tbody>
</table>
Irving J. Selikoff, MD, 1915-1992

Director, Environmental Science Laboratory
Mount Sinai School of Medicine
1961-1985
Chronology of Dr. Selikoff’s Insulator Studies

- 1964: IJS initiates NA insulator study, n=17,800
- 1966: IJS publishes NY/NJ insulator mortality
- 1979: IJS examines 2,907 NA insulators
- 1981-1983: IJS publishes 10 years of NA insulator mortality and asbestos-smoking interaction
- 1991: IJS publishes 20 years of NA insulator mortality
- 1992: Publication of asbestosis mortality, 2,907 insulators

Publication of asbestosis mortality, 2,907 insulators
HEALTH HAZARDS OF ASPEROS EXPOSURE

ANNALS OF
THE NEW YORK ACADEMY OF SCIENCES

VOLUME 330

PUBLISHED BY THE NEW YORK ACADEMY OF SCIENCES

1979 Asbestos Conference

ASBESTOS EXPOSURE, CIGARETTE SMOKING AND DEATH RATES*

E. Cuyler Hammond,† Irving J. Selikoff,‡ and Herbert Seidman†

†Department of Epidemiology and Statistics
American Cancer Society
New York, New York 10017

‡Environmental Sciences Laboratory
Mount Sinai School of Medicine
The City University of New York
New York, New York 10029
Asbestos and Smoking

Classic example of interaction

Compared insulators to blue collar cohort of Cancer Prevention Study I (CPS)
Asbestos, Smoking and Lung Cancer

(Hammond and Selikoff, 1979)

Reference, not asbestos-exposed non-smokers

Asbestos-exposed non-smokers

Smokers (not exposed to asbestos)

Asbestos-exposed smokers

RR = 53.2

RR = 10.9

RR = 5.2

RR = 1

RR Lung Cancer

CPS I

Insulators
Asbestos, Smoking and Lung Cancer
(Hammond and Selikoff, 1979)

Based on 4 lung cancer deaths

Reference non-exposed to asbestos non-smokers

Asbestos-exposed smokers

Asbestos-exposed (Insulators) Non-smokers

Smokers (not exposed to asbestos)

Asbestos-exposed smokers (Insulators who smoked)

RR = 53.2

RR = 10.9

RR = 5.2

RR = 1
Asbestos, Smoking and Lung Cancer
(Hammond and Selikoff, 1979)

RR Lung Cancer

A-S- A+ S+ A+S+

No asbestosis

With asbestosis

RR = 1

Reference not exposed to asbestos non-smokers

Asbestos-exposed (Insulators)

Smokers (not exposed to asbestos)

Asbestos-exposed (Insulators who smoked)
Chronology of Dr. Selikoff’s Insulators’ Studies

IJS initiates NA insulator study, n=17,800
1964

IJS publishes NY/NJ insulator mortality
1966

IJS examines 2,907 NA insulators
1979

IJS publishes 10 years of NA insulator mortality and asbestos-smoking interaction
1981-1983

Publication of asbestosis mortality, 2,907 insulators
1991

IJS publishes 20 years of NA insulator mortality
1992

1997
Two Groups in Current Study of Insulators

1) **Study group: North American Insulators**
   - Long term asbestos-exposed workers with known asbestosis status and smoking status (n=2,377);
   - Examined 1981-1983; mortality follow-up through 2008

2) **Reference: Cancer Prevention Study II**
   (American Cancer Society)
   - Blue collar subset not exposed to asbestos with known smoking habits (n=54,243)
   - Enrolled 1982; mortality follow-up through 2008
Study results

Baseline status of insulators (n=2,377)

1) Age at exam = mean, 58.1 years,

2) Duration of exposure = mean, 33.2 years

3) Smoking: never (19.7%) , former smokers (47.2%)

4) Asbestosis: 38.6% without asbestosis
Study results

Mortality follow-up of insulators (1981-2008)

1) Death certificate diagnosis, National Death Index

2) 1,786 died (75.1%)

3) 339 lung cancer deaths (19% deaths)

18 lung cancer deaths among non-smokers
28 year follow-up of 2,377 Insulators

Lung cancer mortality rate ratios by asbestos and smoking status, Insulators vs. CPS II, 1981-2008

- RR = 1.0 (CPS II, nonsmokers)
- RR = 5.2 (Insulators, non-smokers)
- RR = 10.3 (CPS II, smokers)
- RR = 28.4 (Insulators, smokers)

95% CI: (3.2-8.5) for A+S-
95% CI: (8.7-12.2) for S+A-
95% CI: (23.4-34.4) for A+S+
Lung cancer mortality rate ratios by asbestos and smoking status, Insulators vs. CPS II, 1981-2008

- Insulators, non-smokers: RR = 5.2, 95% CI: (3.2-8.5)
- CPS II, smokers: RR = 10.3, 95% CI: (8.7-12.2)
- Insulators, smokers: RR = 28.4, 95% CI: (23.4-34.4)

Based on 18 lung cancer deaths.
Question #1

Is it asbestosis or asbestos (or both) that raises lung cancer risk?
Lung cancer mortality rate ratios (95% CI) by asbestos, asbestosis and smoking status, Insulators vs. CPS II

Lung Cancer Rate Ratio

Non-Smokers

Smokers
Lung cancer mortality rate ratios (95% CI) by asbestos, asbestosis and smoking status, Insulators vs. CPS II

Lung cancer mortality rate ratios (95% CI) by asbestos, asbestosis among non-smokers, Insulators vs. CPS II

Lung Cancer Rate Ratio

Non-Smokers

Smokers

A- Asb-

All A

A+ Asb-

A+ Asb+

n=7

n=11

Lung Cancer Rate Ratio

A- Asb-

All A

A+ Asb-

A+ Asb+

28.4

36.8

(30.1-45.0)

(10.7-19.4)

(8.8-12.2)

(1.7-7.6)

(3.3-8.3)

(1.7-7.6)

(4.0-13.7)
Lung cancer mortality rate ratios (95% CI) by asbestos, asbestosis among smokers, Insulators vs. CPS II.

Lung cancer mortality rate ratios by asbestos, asbestosis among smokers, Insulators vs. CPS II.

Non-Smokers

<table>
<thead>
<tr>
<th></th>
<th>Non-Smokers</th>
<th>Smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>All A</td>
<td>1.0</td>
<td>28.4</td>
</tr>
<tr>
<td>A+ Asb-</td>
<td>5.2 (1.3-3.2)</td>
<td>14.4 (10.7-19.4)</td>
</tr>
<tr>
<td>A+ Asb+</td>
<td>5.0 (4.0-13.7)</td>
<td>36.8 (30.1-45.0)</td>
</tr>
</tbody>
</table>

Smokers

<table>
<thead>
<tr>
<th></th>
<th>Non-Smokers</th>
<th>Smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>All A</td>
<td>1.0</td>
<td>28.4</td>
</tr>
<tr>
<td>A+ Asb-</td>
<td>5.2 (1.3-3.2)</td>
<td>14.4 (10.7-19.4)</td>
</tr>
<tr>
<td>A+ Asb+</td>
<td>5.0 (4.0-13.7)</td>
<td>36.8 (30.1-45.0)</td>
</tr>
</tbody>
</table>

Series 1

Series 2

Series 3

A- All A A+

Asb-

A+

Asb+
Is increased exposure to asbestos among insulators with asbestosis responsible for their increased lung cancer rates?
Duration of Insulator Work Among Insulators

<table>
<thead>
<tr>
<th></th>
<th>Non-smokers</th>
<th>Smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asbestos -</td>
<td>32.7</td>
<td>33.5</td>
</tr>
<tr>
<td>Asbestos +</td>
<td>34.9</td>
<td>32.2</td>
</tr>
</tbody>
</table>

Mean Years of Insulator Work
Conclusions

1. Asbestos alone raises risk of lung cancer.

2. Asbestosis further doubles the risk of lung cancer in smokers and non-smokers.
Question #2

*How do asbestos, asbestosis, and smoking interact?*
Asbestos, Smoking and Lung Cancer
(Hammond and Selikoff, 1979)

Reference, not asbestos-exposed non-smokers: RR = 1

Asbestos-exposed non-smokers (Insulators): RR = 5.2

Smokers (not exposed to asbestos): RR = 10.9

Asbestos-exposed smokers (Insulators who smoked): RR = 53.2
28 year follow-up of 2,377 Insulators

**Lung cancer mortality rate ratios by asbestos and smoking status, Insulators vs. CPS II, 1981-2008**

- **A-S-**
  - Lung Cancer Rate Ratio: 1.0
  - 95% CI: (3.2-8.5)

- **A+S-**
  - Lung Cancer Rate Ratio: 5.2
  - 95% CI: (3.2-8.5)

- **S+A-**
  - Lung Cancer Rate Ratio: 10.3
  - 95% CI: (8.7-12.2)

- **A+S+**
  - Lung Cancer Rate Ratio: 28.4
  - 95% CI: (23.4-34.4)
Combined Effects of Asbestos and Smoking among Insulators without Asbestosis

Study Result

- Insulators without asbestosis: A- S- = 1
- Smokers: A +, S- = 3.6
- A-, S+ = 10.3
- S+, A- = 12.9
- A+, S+ = 37.1

Additive Model

Multiplicative Model
Combined Effects of Asbestos and Smoking among Insulators with Asbestosis

**Multiplicative Model**

- Smokers: 76.2
- Insulators: 76.2

**Additive Model**

- Smokers: 36.8
- Insulators: 36.8

<table>
<thead>
<tr>
<th>Multiplicative Model</th>
<th>Additive Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Result</td>
<td>Study Result</td>
</tr>
<tr>
<td>A- S-</td>
<td>A- S-</td>
</tr>
<tr>
<td>A + S-</td>
<td>A + S-</td>
</tr>
<tr>
<td>S+ A-</td>
<td>S+ A-</td>
</tr>
<tr>
<td>A+ S+</td>
<td>A+ S+</td>
</tr>
</tbody>
</table>

- Insulators with asbestosis
- Smokers
- Combined Effects of Asbestos and Smoking
Conclusions

1. Asbestos alone and smoking raise risk of lung cancer additively.

2. Asbestosis and smoking raise lung cancer risk supra-additively.
Question #3

To what extent does smoking cessation lower lung cancer risk among asbestos workers?
Strengths of study

1. Similar, contemporaneous reference group
2. Large sample size; long-term follow-up
3. Similar follow-up method
4. Homogeneous asbestos exposure
Limitations of study

1. Homogeneous asbestos exposure; study group had heavy asbestos exposure
2. Misclassification of exposure: one-time characterization of smoking status and asbestosis status
3. Misclassification of exposure: radiographic basis for identifying asbestosis
Implications

**Public health**: Asbestos-exposed insulators, with or without smoking or asbestosis have appreciable risk (RR > 3.0) of lung cancer and are likely to benefit from lung cancer screening with low dose CT.

**Biology**: At least two pathways are likely to underlie asbestos-related lung carcinogenesis, one of which may be associated with inflammation.
Implications

**Public health**: Asbestos-exposed insulators, with or without smoking or asbestosis have appreciable risk (RR > 3.0) of lung cancer and are likely to benefit from lung cancer screening with low dose CT.

**Biology**: At least two pathways are likely to underlie asbestos-related lung carcinogenesis, one of which may be associated with inflammation.
Today’s challenge + Screen for Occupational Lung Cancer =

Early Lung Cancer Action Project: overall design and findings from baseline screening

Claudia I Henschke, Dorothy I McCauley, David F Yankelevitz, David P Naidich, Georgetaenn McGuinness, Olli S Miettinen, Daniel M Libby, Mark W Pasmanter, June Koizumi, Nasser K Altorki, James P Smith

Summary
Background The Early Lung Cancer Action Project (ELCAP) is designed to evaluate baseline and annual repeat screening by low-radiation-dose computed tomography (low-dose CT) in people at high risk of lung cancer. We report the baseline experience.

Interpretation Low-dose CT can greatly improve the likelihood of detection of small noncalcified nodules, and thus of lung cancer at an earlier and potentially more curable stage. Although false-positive CT results are common, they can be managed with little use of invasive diagnostic procedures.

Lancet 1999: 354; 99-105
I am Dr. Irving Selikoff, and I approve this message.
Questions?

Steven Markowitz MD, DrPH
smarkowitz@qc.cuny.edu
Biological significance

1. There is > 1 pathway operating in asbestos-related carcinogenesis.

2. Inflammation is likely linked to carcinogenesis.

3. Carcinogenic events during period of active smoking determine lung carcinogenic events during period following smoking cessation.
Table 2.3 Causes of death, North American insulators (n=2,377), 1981-2008

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=1,786)</td>
<td>(n=482)</td>
<td>(n=769)</td>
<td>(n=535)</td>
</tr>
<tr>
<td>Cancer</td>
<td>817 45.7%</td>
<td>249 51.7%</td>
<td>378 49.2%</td>
<td>190 35.5%</td>
</tr>
<tr>
<td>Lung and trachea</td>
<td>339 19.0%</td>
<td>115 23.9%</td>
<td>151 19.6%</td>
<td>73 13.6%</td>
</tr>
<tr>
<td>Larynx</td>
<td>2 0.1%</td>
<td>1 0.2%</td>
<td>1 0.1%</td>
<td>0 0.0%</td>
</tr>
<tr>
<td>Mesothelioma*</td>
<td>103 5.8%</td>
<td>17 3.5%</td>
<td>38 4.9%</td>
<td>48 9.0%</td>
</tr>
<tr>
<td>Pleura</td>
<td>6 0.3%</td>
<td>3 0.6%</td>
<td>3 0.4%</td>
<td>0 0.0%</td>
</tr>
<tr>
<td>Peritoneum</td>
<td>40 2.2%</td>
<td>14 2.9%</td>
<td>26 3.4%</td>
<td>0 0.0%</td>
</tr>
<tr>
<td>Other, unspecified</td>
<td>57 3.2%</td>
<td>0 0.0%</td>
<td>9 1.2%</td>
<td>48 9.0%</td>
</tr>
<tr>
<td>Other Respiratory</td>
<td>2 0.1%</td>
<td>0 0.0%</td>
<td>0 0.0%</td>
<td>2 0.4%</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>104 5.8%</td>
<td>32 6.6%</td>
<td>50 6.5%</td>
<td>22 4.1%</td>
</tr>
<tr>
<td>Esophagus</td>
<td>12 0.7%</td>
<td>0 0.0%</td>
<td>11 1.4%</td>
<td>0 0.0%</td>
</tr>
<tr>
<td>Intestine and Rectum</td>
<td>35 2.0%</td>
<td>12 2.5%</td>
<td>16 2.1%</td>
<td>7 1.3%</td>
</tr>
<tr>
<td>Stomach</td>
<td>13 0.7%</td>
<td>4 0.8%</td>
<td>6 0.8%</td>
<td>3 0.6%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>27 1.5%</td>
<td>9 1.9%</td>
<td>10 1.3%</td>
<td>8 1.5%</td>
</tr>
<tr>
<td>Other</td>
<td>17 1.0%</td>
<td>6 1.2%</td>
<td>7 0.9%</td>
<td>4 0.7%</td>
</tr>
<tr>
<td>Other</td>
<td>267 14.9%</td>
<td>84 17.4%</td>
<td>138 17.9%</td>
<td>45 8.4%</td>
</tr>
<tr>
<td>Respiratory diseases</td>
<td>314 17.6%</td>
<td>72 14.9%</td>
<td>122 15.9%</td>
<td>120 22.4%</td>
</tr>
<tr>
<td>Asbestosis</td>
<td>122 6.8%</td>
<td>38 7.9%</td>
<td>57 7.4%</td>
<td>27 5.0%</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>40 2.2%</td>
<td>11 2.3%</td>
<td>16 2.1%</td>
<td>13 2.4%</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>109 6.1%</td>
<td>17 3.5%</td>
<td>31 4.0%</td>
<td>61 11.4%</td>
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<tr>
<td>Other respiratory diseases</td>
<td>43 2.4%</td>
<td>6 1.2%</td>
<td>18 2.3%</td>
<td>19 3.6%</td>
</tr>
<tr>
<td>Cardiovascular diseases</td>
<td>376 21.1%</td>
<td>96 19.9%</td>
<td>169 22.0%</td>
<td>111 20.7%</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>288 16.1%</td>
<td>78 16.2%</td>
<td>127 16.5%</td>
<td>83 15.5%</td>
</tr>
<tr>
<td>Other heart diseases</td>
<td>88 4.9%</td>
<td>18 3.7%</td>
<td>42 5.5%</td>
<td>28 5.2%</td>
</tr>
<tr>
<td>Cerebrovascular disease and other vascular diseases</td>
<td>81 4.5%</td>
<td>18 3.7%</td>
<td>31 4.0%</td>
<td>32 6.0%</td>
</tr>
<tr>
<td>Other</td>
<td>198 11.1%</td>
<td>47 9.8%</td>
<td>69 9.0%</td>
<td>82 15.3%</td>
</tr>
</tbody>
</table>

*Mesothelioma of the pleura, peritoneum, and other/unspecified include ICD 9 codes: 163.9, 195.2, 199.1, 235.2, 158.8, 158.9 and ICD 10 codes: C45.0, C45.1, C45.7, C45.9.
<table>
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<tr>
<th>Job Title</th>
<th>Number</th>
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<tr>
<td>Farmer, Fishing, Ranger</td>
<td>15,797</td>
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<tr>
<td>Truck, Bus Driver</td>
<td>5,346</td>
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<tr>
<td>Machinist</td>
<td>3,619</td>
</tr>
<tr>
<td>Military Personnel</td>
<td>3,095</td>
</tr>
<tr>
<td>Foreman</td>
<td>3,036</td>
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<tr>
<td>Postal Worker</td>
<td>2,733</td>
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<td>Police</td>
<td>2,383</td>
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<tr>
<td>Lab, X-ray Technician</td>
<td>2,369</td>
</tr>
<tr>
<td>Janitor</td>
<td>2,190</td>
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<tr>
<td>Warehouse Worker</td>
<td>2,078</td>
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<tr>
<td>Cook</td>
<td>1,528</td>
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<tr>
<td>Railroad Worker</td>
<td>1,165</td>
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<tr>
<td>Firefighter</td>
<td>1,164</td>
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<tr>
<td>Welder</td>
<td>1,101</td>
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<tr>
<td>Manager</td>
<td>1,020</td>
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# Overall mortality, North American Insulators, 1981-2008*

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<tr>
<th>Cause</th>
<th>Observed</th>
<th>Expected</th>
<th>SMR</th>
<th>Lower</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All Causes</strong></td>
<td>1786</td>
<td>1738.9</td>
<td>103</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>All Cancers</strong></td>
<td>817</td>
<td>462.3</td>
<td>177**</td>
<td>165</td>
<td>189</td>
</tr>
<tr>
<td>MN buccal &amp; pharynx</td>
<td>6</td>
<td>9.9</td>
<td>61</td>
<td>22</td>
<td>132</td>
</tr>
<tr>
<td>MN digestive &amp; peritoneum</td>
<td>144</td>
<td>110.3</td>
<td>131**</td>
<td>110</td>
<td>154</td>
</tr>
<tr>
<td>MN esophagus</td>
<td>12</td>
<td>12.7</td>
<td>94</td>
<td>49</td>
<td>164</td>
</tr>
<tr>
<td>MN stomach</td>
<td>13</td>
<td>13.2</td>
<td>99</td>
<td>52</td>
<td>169</td>
</tr>
<tr>
<td>MN intestine</td>
<td>34</td>
<td>39.8</td>
<td>85</td>
<td>59</td>
<td>119</td>
</tr>
<tr>
<td>MN rectum</td>
<td>1</td>
<td>8.3</td>
<td>12**</td>
<td>0</td>
<td>67</td>
</tr>
<tr>
<td>MN biliary, liver, gall bladder</td>
<td>17</td>
<td>11.6</td>
<td>147</td>
<td>85</td>
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<tr>
<td>MN pancreas</td>
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<td>23.0</td>
<td>117</td>
<td>77</td>
<td>171</td>
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<tr>
<td>MN peritoneum, other &amp; unspec. site</td>
<td>40</td>
<td>1.6</td>
<td>2,512**</td>
<td>1,794</td>
<td>3,421</td>
</tr>
<tr>
<td>MN respiratory</td>
<td>349</td>
<td>173.0</td>
<td>202**</td>
<td>181</td>
<td>224</td>
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<tr>
<td>MN larynx</td>
<td>2</td>
<td>5.4</td>
<td>37</td>
<td>4</td>
<td>133</td>
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<td>MN trachea, bronchus, lung</td>
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<td>166.2</td>
<td>204**</td>
<td>183</td>
<td>227</td>
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<td>MN pleura</td>
<td>6</td>
<td>0.5</td>
<td>1,202**</td>
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<td>2,616</td>
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<td>MN other respiratory</td>
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<td>MN male genital organs</td>
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<td>75</td>
<td>51</td>
<td>106</td>
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<td>MN prostate</td>
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<td>40.9</td>
<td>76</td>
<td>52</td>
<td>108</td>
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<tr>
<td>MN urinary</td>
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<td>24.7</td>
<td>61</td>
<td>34</td>
<td>100</td>
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<tr>
<td>MN kidney</td>
<td>10</td>
<td>11.7</td>
<td>86</td>
<td>41</td>
<td>158</td>
</tr>
<tr>
<td>MN bladder &amp; other urinary site</td>
<td>5</td>
<td>13.1</td>
<td>38*</td>
<td>12</td>
<td>89</td>
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<tr>
<td>MN other &amp; unspec. site (maj.)</td>
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<td>57.8</td>
<td>427**</td>
<td>376</td>
<td>484</td>
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<td>MN connective</td>
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<td>156</td>
<td>710</td>
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<td>31.8</td>
<td>528**</td>
<td>451</td>
<td>614</td>
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<tr>
<td>MN lymphatic &amp; hematopoietic</td>
<td>23</td>
<td>44.4</td>
<td>52**</td>
<td>33</td>
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</table>

*compared to US white male population
<table>
<thead>
<tr>
<th>Cause</th>
<th>Observed</th>
<th>Expected</th>
<th>SMR</th>
<th>Lower</th>
<th>Upper</th>
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<tr>
<td>Benign &amp; unspec. nature neoplasms</td>
<td>6</td>
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<td>108</td>
<td>40</td>
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<tr>
<td>Dis. blood &amp; blood-forming organs</td>
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<td>6.7</td>
<td>75</td>
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<td>174</td>
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<td>Diabetes mellitus (major)</td>
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<td>35.9</td>
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<td>8</td>
<td>40</td>
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<td>Mental &amp; psych. disorders</td>
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<td>20</td>
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<td>31</td>
<td>4</td>
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<td>Nervous system disorders</td>
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<td>86</td>
<td>59</td>
<td>121</td>
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<td>Heart diseases</td>
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<td>623.1</td>
<td>60**</td>
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<td>Ischemic heart disease</td>
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<td>516.9</td>
<td>56**</td>
<td>49</td>
<td>63</td>
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<td>Other dis. circulatory system</td>
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<td>58**</td>
<td>46</td>
<td>72</td>
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<td>Cerebrovascular disease</td>
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<td>59**</td>
<td>44</td>
<td>77</td>
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<td>Dis. respiratory system</td>
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<tr>
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<td>126*</td>
<td>104</td>
<td>152</td>
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<td>Asbestosis</td>
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<td>20,348**</td>
<td>16,897</td>
<td>24,296</td>
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<td>Other pneumoconiosis</td>
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<td>74</td>
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<td>Other respiratory diseases</td>
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<td>22.1</td>
<td>190**</td>
<td>137</td>
<td>257</td>
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<tr>
<td>Diseases digestive system</td>
<td>51</td>
<td>70.8</td>
<td>72*</td>
<td>54</td>
<td>95</td>
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<td>Cirrhosis &amp; other liver dis.</td>
<td>22</td>
<td>34.6</td>
<td>64*</td>
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<td>Dis. skin &amp; subcutaneous</td>
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<td>Dis. musculoskeletal &amp; connective</td>
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<td>27.2</td>
<td>40**</td>
<td>20</td>
<td>72</td>
</tr>
<tr>
<td>Sympt. &amp; ill-def. cond. (maj.)</td>
<td>7</td>
<td>15.6</td>
<td>45*</td>
<td>18</td>
<td>93</td>
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<td>Transportation injuries</td>
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<td>20**</td>
<td>7</td>
<td>43</td>
</tr>
<tr>
<td>Falls</td>
<td>6</td>
<td>11.0</td>
<td>55</td>
<td>20</td>
<td>119</td>
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<td>Other injury (major)</td>
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<td>24.6</td>
<td>53*</td>
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<td>Violence</td>
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<td>32.5</td>
<td>22**</td>
<td>9</td>
<td>44</td>
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<td>Tuberculosis &amp; HIV</td>
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<td>7</td>
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<td>32</td>
<td>32.5</td>
<td>98</td>
<td>67</td>
<td>139</td>
</tr>
</tbody>
</table>

*compared to US white male population
Do smoking habits differ between the CPS II blue collar cohort and insulators?
Smoking Habits, CPS II and Insulators

- Never Smoked: 19.7%
- Former Smoker: 47.2%
- Current Smoker: 34.7%

CPS II
- Never Smoked: 37.0%
- Former Smoker: 33.1%
- Current Smoker: 28.3%
Quantity Smoked (mean pack years), CPS II and Insulators

Number of Pack Years

Former Smoker

Current Smoker

Insulators

CPS II

35.4

32.6

48.8

50.2
Is increased smoking among insulators with asbestosis responsible for their increased lung cancer rates?
### Lung Cancer Mortality in Asbestos-exposed Cohorts

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Observed</th>
<th>Expected</th>
<th>SMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wittenoom—miners, millers</td>
<td>87</td>
<td>48.7</td>
<td>179</td>
</tr>
<tr>
<td>Paterson—factory</td>
<td>98</td>
<td>20.5</td>
<td>478</td>
</tr>
<tr>
<td>New Orleans-cement factory</td>
<td>31</td>
<td>17.7</td>
<td>175</td>
</tr>
<tr>
<td>US/Canada—insulators</td>
<td>934</td>
<td>256.8</td>
<td>364</td>
</tr>
<tr>
<td>Rochdale—textile factory</td>
<td>56</td>
<td>37.1</td>
<td>151</td>
</tr>
<tr>
<td>Johns Manville-insulation factory</td>
<td>73</td>
<td>28.4</td>
<td>257</td>
</tr>
<tr>
<td>South Carolina-textile factory</td>
<td>112</td>
<td>46</td>
<td>244</td>
</tr>
<tr>
<td>Quebec—miners, millers</td>
<td>587</td>
<td>431.6</td>
<td>136</td>
</tr>
</tbody>
</table>
Asbestos, Smoking and Lung Cancer
(Hammond and Selikoff, 1979)

RR Lung Cancer

A-S-  A+  S+  A+S+

Reference non-smokers

Asbestos-exposed (Insulators)

Smokers (not exposed to asbestos)

Asbestos-exposed (Insulators who smoked)

No asbestosis

With asbestosis

Current smoker

Former smoker

RR = 1

RR Lung Cancer
Decline in lung cancer with smoking cessation
CPS II versus Insulators

Adjusted for age categories and pack-years; reference group is Cancer Prevention Study II, never smokers
Decline in lung cancer with smoking cessation
CPS II versus Insulators

Adjusted for age categories and pack-years; reference group is Cancer Prevention Study II, never smokers
Does an insulator with asbestosis also benefit from smoking cessation?
Decline in lung cancer with smoking cessation
CPS II versus insulators, with and without asbestosis

*adjusted for age categories and pack-years; reference group is Cancer Prevention Study II, never smokers
Decline in lung cancer with smoking cessation
CPS II versus insulators without asbestosis

*adjusted for age categories and pack-years; reference group is Cancer Prevention Study II, never smokers
Decline in lung cancer with smoking cessation
CPS II versus insulators with asbestosis

*adjusted for age categories and pack-years; reference group is Cancer Prevention Study II, never smokers