Mesothelioma Trends as Predictors of the Asbestos-Related Lung Cancer Burden

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Outline

• Background
• Estimating the lung cancer mortality burden
• Caveats
• Conclusions
  – Implications for today’s burden
  – Implications for the future burden and public health priorities
Mesothelioma Mortality Burden

- 43,000 mesothelioma deaths/year, 2005 (Driscoll et al.)
- 78% in men, 88% high income countries: 54% Europe, 26% Americas
- Latency
Asbestos Consumption 1920-2003, by region

Metric tonnes (x 000)

- Africa
- Asia, Middle East
- Central, North America
- Europe, incl Russia
- South America
- **Asbestos**: Asbestiform silicate minerals, aspect ratio 20:1
- **Serpentine**: Chrysotile
- **Amphiboles**: Amosite, Crocidolite, Tremolite, Anthophyllite, Actinolite

<table>
<thead>
<tr>
<th>Sufficient evidence of cancer in humans (all fibres)*</th>
<th>Ratios of cancer risks** Chrysotile : Amosite : Crocidolite</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesothelioma</td>
<td>1 : 100 : 500</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>1 : 10 : 10 <del>to</del> 1 : 50 : 50</td>
</tr>
<tr>
<td>Larynx</td>
<td>NK</td>
</tr>
<tr>
<td>Ovary</td>
<td>NK</td>
</tr>
</tbody>
</table>

** Hodgson and Darnton, Am J Ind Med (2000);
World asbestos production by type
1900-2003

Metric tonnes (x 000)

What is the asbestos-related lung cancer burden?

- Hidden amongst a large tobacco-related burden
- Method: Use mesothelioma deaths as an indicator of past asbestos exposure

\[
Ratio \; R_1 = \frac{Excess \; lung \; cancer \; due \; to \; asbestos}{Mesothelioma \; deaths} = \frac{(Observed - Expected) \; lung \; cancer \; deaths}{Observed \; mesothelioma \; deaths}
\]

- Extract ratio estimates from all 65 occupational cohorts
- Investigate heterogeneity in ratios by fibre type
- Combine using random effect meta-analysis

\[
Ratio \; R_2 = \frac{Excess \; lung \; cancer \; %}{Mesothelioma \; deaths \; per \; 1000 \; non-asbestos \; deaths}
\]
<table>
<thead>
<tr>
<th>Cohort</th>
<th>N</th>
<th>All deaths</th>
<th>Lung Cancer Deaths</th>
<th>Mesothelioma Deaths</th>
<th>R1</th>
<th>R2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canadian gas mask canisters</td>
<td>199</td>
<td>55</td>
<td>7</td>
<td>2.92</td>
<td>9</td>
<td>0.5</td>
</tr>
<tr>
<td>Nottingham gas masks, UK</td>
<td>951</td>
<td>166</td>
<td>12</td>
<td>1.90</td>
<td>17</td>
<td>0.3</td>
</tr>
<tr>
<td>Leyland gas masks UK.</td>
<td>757</td>
<td>219</td>
<td>13</td>
<td>2.10</td>
<td>5</td>
<td>1.4</td>
</tr>
<tr>
<td>South African crocidolite mines</td>
<td>3430</td>
<td>423</td>
<td>27</td>
<td>2.03</td>
<td>0.7</td>
<td>2.0</td>
</tr>
<tr>
<td>Tuscany rail construction Italy</td>
<td>734</td>
<td>199</td>
<td>26</td>
<td>1.24</td>
<td>5</td>
<td>1.0</td>
</tr>
<tr>
<td>Wittenoom mine/mill, Australia</td>
<td>6943</td>
<td>2408</td>
<td>281</td>
<td>2.60</td>
<td>222</td>
<td>0.8</td>
</tr>
<tr>
<td><strong>COMBINED</strong></td>
<td><strong>2.04</strong></td>
<td></td>
<td><strong>0.71</strong></td>
<td><strong>1.2</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

71 crocidolite-related lung cancers for every 100 mesotheliomas

1.2% excess lung cancers for every mesothelioma death in 1000 deaths
Ratio of Asbestos-related Lung Cancers to Mesothelioma Deaths

Ratio 1 (95% CI)

Crocidolite
0.71 (0.53, 0.94)

Crocidolite + chrysotile
1.44 (0.59, 3.49)
No excess lung cancers

Chrysotile
No mesotheliomas
6.12 (3.58, 10.45)

Amosite
4.04 (2.79, 5.87)
No excess lung cancers

Mixed
1.89 (1.38, 2.58)

Ratio 1 = Excess lung cancers to every mesothelioma death
<table>
<thead>
<tr>
<th>Asbestos Type</th>
<th>Lung cancer mortality SMR</th>
<th>Mesothelioma deaths per 1000 non-asbestos related deaths</th>
<th>Ratio $R_1$ Excess lung cancers per mesothelioma Mean (95% CI)</th>
<th>Ratio $R_2$ Excess lung cancer (%) for every mesothelioma death in 1000 non-asbestos related deaths Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crocidolite</td>
<td>2.04 (1.55, 2.69)</td>
<td>93.2 BRING THIS IN EARLIER</td>
<td>0.71 (0.53, 0.95)</td>
<td>1.2 (0.9-2.6)</td>
</tr>
<tr>
<td>Chrysotile and crocidolite</td>
<td>1.58 (1.19, 2.08)</td>
<td>7.6</td>
<td>1.44 (0.59, 3.49)</td>
<td>3.4 (0.4-9.4)</td>
</tr>
<tr>
<td>Chrysotile</td>
<td>1.68 (1.39, 2.03)</td>
<td>4.1</td>
<td>6.12 (3.58, 10.45)</td>
<td>9.1 (3.6-10.3)</td>
</tr>
<tr>
<td>Amosite</td>
<td>2.48 (1.42, 4.33)</td>
<td>18.6</td>
<td>4.04 (2.79, 5.87)</td>
<td>6.8 (5.8-10.2)</td>
</tr>
<tr>
<td>Mixed</td>
<td>1.77 (1.44, 2.20)</td>
<td>40.8</td>
<td>1.89 (1.38, 2.58)</td>
<td>2.0 (1.2-4.9)</td>
</tr>
</tbody>
</table>

McCormack et al., Brit J Cancer, 2012
Population attributable fraction (%) of Lung Cancer due to Asbestos (PAF)

<table>
<thead>
<tr>
<th>Country</th>
<th>No. Deaths</th>
<th>Meso deaths per 1000 deaths</th>
<th>% of Lung Cancer deaths</th>
<th>PAF R1=0.7 R2=1.2</th>
<th>PAF R1=1.89 R2=2.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>12768</td>
<td>1156</td>
<td>7.8</td>
<td>17.1</td>
<td>13.5</td>
</tr>
<tr>
<td>UK</td>
<td>90347</td>
<td>7362</td>
<td>6.9</td>
<td>15.4</td>
<td>12.2</td>
</tr>
<tr>
<td>New Zealand</td>
<td>3192</td>
<td>238</td>
<td>5.8</td>
<td>14.1</td>
<td>10.4</td>
</tr>
<tr>
<td>Sweden</td>
<td>8386</td>
<td>491</td>
<td>3.2</td>
<td>11.1</td>
<td>5.9</td>
</tr>
<tr>
<td>Netherlands</td>
<td>29604</td>
<td>1629</td>
<td>6.2</td>
<td>10.4</td>
<td>11.0</td>
</tr>
<tr>
<td>South Africa</td>
<td>2995</td>
<td>133</td>
<td>0.8</td>
<td>8.4</td>
<td>1.7</td>
</tr>
<tr>
<td>Iceland</td>
<td>274</td>
<td>12</td>
<td>3.7</td>
<td>8.3</td>
<td>6.8</td>
</tr>
<tr>
<td>Norway</td>
<td>5506</td>
<td>216</td>
<td>2.9</td>
<td>7.4</td>
<td>5.6</td>
</tr>
<tr>
<td>Finland</td>
<td>6557</td>
<td>252</td>
<td>2.7</td>
<td>7.3</td>
<td>5.1</td>
</tr>
<tr>
<td>Malta</td>
<td>528</td>
<td>20</td>
<td>3.3</td>
<td>7.2</td>
<td>6.2</td>
</tr>
<tr>
<td>Denmark</td>
<td>1810</td>
<td>55</td>
<td>2.6</td>
<td>5.7</td>
<td>4.9</td>
</tr>
<tr>
<td>Italy</td>
<td>24126</td>
<td>729</td>
<td>3.4</td>
<td>5.7</td>
<td>6.4</td>
</tr>
<tr>
<td>Germany</td>
<td>136953</td>
<td>4102</td>
<td>2.7</td>
<td>5.7</td>
<td>5.0</td>
</tr>
</tbody>
</table>

McCormack et al., Brit J Cancer, 2012
Caveats

- Are average ratios in occupationally exposed cohorts applicable at a country-level?

- Excess lung cancers to mesotheliomas vary by
  - Fibre type
  - Dose-response curves in cohorts vs in population
  - Time since first exposure
  - Smoking
  - Accuracy of mesothelioma coding
  - Tremolite contamination of chrysotile
Conclusions and Implications

• Today’s asbestos-related cancer burden:

  – Asbestos-related lung cancer burden is larger than the mesothelioma burden in most instances

  – 1.8 times as many lung cancers caused by asbestos as there are mesothelioma (mixed fibre types)

  – In crocidolite cohorts, the excess lung cancers are similar or less than mesothleiomas
Conclusions and Implications

Future Burden:

– Predominant burden from chrysotile will be of LUNG cancer

– A small mesothelioma burden is not an indicator of no asbestos-related lung cancer burden

– Smoking cessation especially important in previously exposed
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