IARC Evaluation of the Carcinogenicity of Outdoor Air Pollution

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Evaluation

• Outdoor air pollution is *carcinogenic to humans* (Group 1)

• Particulate matter in outdoor air pollution is *carcinogenic to humans* (Group 1)

Summary: [http://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(13)70487-X/fulltext](http://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(13)70487-X/fulltext)
The IARC Monographs
(http://monographs.iarc.fr/indexfr.php)

- Evaluate factors capable of causing cancer in humans
  - Environmental & occupational exposures
  - Physical, chemical & biologic agents
  - Lifestyle factors
- “The Encyclopedia of Carcinogens”
- More than 900 agents evaluated since 1971
  - >100 carcinogenic to humans
  - >300 probably or possibly carcinogenic
- National & international health agencies use the Monographs
  - To identify carcinogens
  - To support prevention or regulation
Evaluation in the IARC Monographs

- Review of all relevant studies
  - Cancer in humans
  - Cancer in animals

- Weight of the Evidence
  - Working Group: discussion & debate

- Review of Exposure Data

- Final Evaluation
  - Consensus

Review of Mechanisms of Cancer
Weight of the Evidence Evaluation

Cancer in humans
- Sufficient evidence
- Limited evidence
- Inadequate evidence
- Evidence suggesting lack of carcinogenicity

Cancer in animals
- Sufficient evidence
- Limited evidence
- Inadequate evidence
- Evidence suggesting lack of carcinogenicity

Overall Evaluation
1. Carcinogenic to humans
2A. Probably carcinogenic
2B. Possibly carcinogenic
3. Not classifiable as to carcinogenicity
4. Probably not carcinogenic

Centre international de Recherche sur le Cancer
Organisation mondiale de la Santé
Vol. 109: 24 invited experts from 11 countries
Outdoor Air Pollution is Global and Highly Variable

Sources of Principal Air Pollutants, Europe
Epidemiologic Studies

• All available studies of air pollution and cancer were reviewed (100s of studies)
• 14 studies of lung cancer were most informative
  • Cohorts from the general population in Europe, North America & Asia: millions of people and 1000s of cancer cases observed
  • Quantitative exposure information
  • Control of important confounders (smoking)
Lung Cancer and PM-2.5 (RR per 10µg/m³)
### Lung Cancer and PM-10 (RR per 10µg/m³)

<table>
<thead>
<tr>
<th>Study</th>
<th>Country/Region</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>North America</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beeson et al. 1998 USA</td>
<td></td>
<td>1.16 (1.02, 1.32)</td>
</tr>
<tr>
<td>Hart et al. 2011 USA</td>
<td></td>
<td>1.08 (0.91, 1.30)</td>
</tr>
<tr>
<td>Lipsett et al. 2011 USA</td>
<td></td>
<td>0.93 (0.81, 1.07)</td>
</tr>
<tr>
<td>McDonell et al. 2000 USA</td>
<td></td>
<td>1.23 (0.84, 1.80)</td>
</tr>
<tr>
<td>Pope et al. 2002 USA</td>
<td></td>
<td>0.98 (0.95, 1.01)</td>
</tr>
<tr>
<td>Europe</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carey et al. 2013 UK</td>
<td></td>
<td>1.03 (0.88, 1.21)</td>
</tr>
<tr>
<td>Heinrich et al. 2013 Germany</td>
<td></td>
<td>2.39 (1.35, 4.22)</td>
</tr>
<tr>
<td>Raaschou-Nielsen et al. 2013 EU</td>
<td></td>
<td>1.22 (1.03, 1.45)</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hales et al. 2012 New Zealand</td>
<td></td>
<td>1.16 (1.04, 1.29)</td>
</tr>
</tbody>
</table>

NOTE: Weights are from random effects analysis
Lung Cancer and NO$_2$ or Indicators of Exposure to Traffic
RRs for Lung Cancer and Air Pollution: Non Smokers
Meta-Analysis of Lung Cancer and Particulate Matter

- Statistical analysis combining results from 14 studies in Europe, Asia & North America
- Random effects model
- Meta-RR 1.09 (1.04-1.14) per 10 µg/m$^{-3}$ PM$_{2.5}$
- Meta-RR 1.08 (1.00-1.17) per 10 µg/m$^{-3}$ PM$_{10}$
- RR not substantially affected by gender, smoking status, or social class

(Hamra et al., in press)
Air pollution and lung cancer incidence in 17 European cohorts: prospective analyses from the European Study of Cohorts for Air Pollution Effects (ESCAPE)

Ole Raaschou-Nielsen, Zorana J Andersen, Rob Beelen, Evangelia Samoli, Massimo Stafoggia, Gudrun Weinmayr, Barbara Hoffmann, Paul Fischer,

Figure 2: Distribution of particulate matter air pollution at participant addresses in each cohort

Figure 3: Risk for lung cancer according to concentration of particulate matter in each cohort study

Lung cancer risk per 5 μg/m³
Summary – Human Studies

- Lung cancer is positively associated with indicators of air pollution in nearly all studies.
- The associations with particulate matter are the most consistent.
- Risk increases about 10% per 10 µg/m\(^3\) of PM.
- Associations are not explained by smoking or other confounders.
- Limited evidence of an association with bladder cancer.
- Inadequate data for other cancers (breast, leukemia, childhood cancer).
Evaluation: Cancer in humans

- There is *sufficient evidence* in humans for the carcinogenicity of *outdoor air pollution*. Outdoor air pollution causes *cancer of the lung*. A positive association has been observed for cancer of the urinary bladder.

- There is *sufficient evidence* in humans for the carcinogenicity of *particulate matter in outdoor air pollution*. Particulate matter in outdoor air pollution causes *cancer of the lung*.
Cancer in experimental animals

There is *sufficient evidence* in experimental animals for the carcinogenicity of:

- **Organic solvent-extracted material from particles collected from outdoor air pollution**
- **Particulate matter in outdoor air pollution**
  - Solvent-extracted materials collected from outdoor air
  - Diesel engine exhaust
- **Outdoor air pollution**
  - Promotion of tumours in animals exposed to polluted outdoor air
  - Updating and confirming previous IARC evaluations, including: diesel engine exhaust, coal combustion, wood combustion
Other relevant data

- Review of 100s of studies of mechanisms of cancer in exposed humans, animals and experimental systems.
- **Strong mechanistic support**: Exposures to outdoor air pollution, or particulate matter in polluted outdoor air, are associated with increases in genetic damage that have been shown to be predictive of cancer in humans.
Other relevant data

Key findings:

- Atmospheric mutagenic potency is quantitatively related to levels of atmospheric particulate matter.
- Cytogenetic damage, DNA damage and mutations in animals, birds and plants exposed to outdoor air pollution.
- Altered expression of genes involved in DNA damage and repair, cell cycle control, inflammation, and oxidative stress response in people occupationally or environmentally exposed to outdoor air pollution.
- Increased frequencies of chromosome aberrations and micronuclei in exposed outdoor workers.
Mutagenic potency of PM extracts and atmospheric PM concentration in 26 countries

$r^2 = 0.10, F$ ratio = 56.8
$n = 501, p < 0.0001, RMSE = 0.54$
Cytogenic effects in humans exposed to polluted outdoor air

<table>
<thead>
<tr>
<th>Reference</th>
<th>Endpoint</th>
<th>Control subjects</th>
<th>Results</th>
<th>Exposed subjects</th>
<th>Results</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chen et al. 1999 [37]</td>
<td>CA*</td>
<td>Indoor police officers in Hebi, Henan (n = 30)</td>
<td>0.40%</td>
<td>Traffic policemen exposed to outdoor air pollution from coal combustion and automobile exhaust in Hebi, Henan (n = 45)</td>
<td>0.98%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Cui et al. 1991 [29]</td>
<td>CA</td>
<td>Chorionic villi in pregnant women in Dalian, Liaoning (n = 827)</td>
<td>0.11%</td>
<td>Chorionic villi in pregnant women in Shenyang, Liaoning (n = 811)</td>
<td>1.66%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Zhao et al. 1998 [29]</td>
<td>MNb</td>
<td>Household register police officers in Lanzhou, Gansu (n = 34)</td>
<td>3.22±1.31</td>
<td>Traffic policemen exposed to outdoor air pollution from automobile exhaust in Lanzhou, Gansu (n = 67)</td>
<td>5.72±2.57</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Zhao et al. 1998 [29]</td>
<td>SCEc</td>
<td>Household register police officers in Hebei (n = 34)</td>
<td>3.73±1.51</td>
<td>Traffic policemen exposed to outdoor air pollution from automobile exhaust in Lanzhou, Gansu (n = 67)</td>
<td>8.11±1.83</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Bai et al. 2005 [30]</td>
<td>MNd</td>
<td>Indoor police officers in Tangshan, Hebei (n = 49)</td>
<td>1.97±0.21</td>
<td>Traffic policemen exposed to outdoor air pollution from automobile exhaust at crossroads in Tangshan, Hebei (n = 65)</td>
<td>4.27±0.68</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Bai et al. 2005 [30]</td>
<td>SCEc</td>
<td>Indoor police officers in Hebei (n = 49)</td>
<td>2.69±0.35</td>
<td>Traffic policemen exposed to outdoor air pollution from automobile exhaust at crossroads in Tangshan, Hebei (n = 65)</td>
<td>4.32±0.58</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Peng et al. 1995 [31]</td>
<td>MNb</td>
<td>Botanical garden officers, Shanghai (n = 36)</td>
<td>0.69±0.06</td>
<td>Bus drivers or bus ticket officers on route through DaPu tunnel in Shanghai (n = 40)</td>
<td>1.28±1.02</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Peng et al. 1995 [31]</td>
<td>SCEc</td>
<td>Botanical garden officers, Shanghai (n = 36)</td>
<td>4.50±0.99</td>
<td>Bus drivers or bus ticket officers on route through DaPu tunnel in Shanghai (n = 40)</td>
<td>5.94±1.23</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Ishikawa et al. 2006 [32]</td>
<td>MNd</td>
<td>Female residents in rural areas in Shenyang, Liaoning (n = 63)</td>
<td>1.02</td>
<td>Female residents in urban and industrial areas in Shenyang, Liaoning (n = 66)</td>
<td>1.56</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

CA, chromosomal aberration; MN, micronucleus; SCE, sister chromatid exchange. *The results are expressed as the percentage of cells with CA, with 100 metaphases examined for each subject. †The results are expressed as the number of MNs per 1,000 cells. ‡The results are expressed as the number of SCEs per cell. §The results are expressed as the number of MN-containing cells per 1,000 binucleated cells.

Loomis et al., Chin J Cancer; 2014; Vol. 33 Issue 4
www.cjcsysu.com
Importance of the Evaluation

- The evaluation of outdoor air pollution concerns the complex mixture of pollutants from all sources.
- The evaluation of particulate matter includes all sizes and sources of particles, primary and secondary.
- The monographs do not formally quantify risk, but studies indicate risks comparable to passive smoking at levels of air pollution existing in Europe.
- Independent data indicate 223,000 lung cancer deaths worldwide (15% of all lung cancer) are related to air pollution.
Attributable Cancer Deaths in Comparison

PM Air Pollution

Secondhand Smoke

High BMI

High Red Meat Consumption

Data from Global Burden of Disease 2010
http://www.healthmetricsandevaluation.org/gbd/visualizations/country
Ranges of Lung Cancer RR and Exposure Concentration for Studies of PM-2.5
Conclusions

- Millions of people are exposed to air pollution at high levels, but the dimensions of the problem are not yet fully known.
- Nevertheless, classifying air pollution as a carcinogen is an important step forward.
- Effective measures for reducing air pollution are available; most require collective response.
- The IARC evaluation of air pollution is a call to take action.