Air pollution in association with medication of mental disorders in children and adolescents

EcoFòrum16, Terrassa

Anna Oudin

Occupational and Environmental medicine

Umeå University and Lund University

Anna.Oudin@umu.se
European perspectives on environmental burden of disease

Hänninen & Knol (eds), 2011

Overall, the environmental fraction ranges from 3% (Finland) to 6.5% (Italy) of all DALYs (years of life lost due to death or disability)

FIGURE 4-2. Relative contribution of the nine targeted stressors to the burden of disease (undiscounted, un-age-weighted DALYs) attributed to these stressors, average over the six participating countries.
Air pollution in Sweden

- 5000 people each year die prematurely in Sweden from air pollution
- 9 months shorter life in average per European
- Cost: 42 billion SEK/ 4.5 billion € annually
- PM2.5 long-distance sources, e.g. energy production in Europe
- The largest source of local particles is wear particles from studded tires
In the year 2012, ambient air pollution was responsible for 3.7 million deaths, representing 6.7% of the total deaths. Particulate matter pollution is an environmental health problem that affects people worldwide, but low- and middle-income countries disproportionately experience this burden.
Ten largest contributors to global DALYs

1. High systolic blood pressure (211.8 million)
2. Smoking (148.6 million)
3. High fasting plasma glucose (143.1 million)
4. High BMI (120.1 million)
5. Childhood undernutrition (113.3 million)
6. Ambient particulate matter (103.1 million)
7. High total cholesterol (88.7 million)
8. Household air pollution (85.6 million)
9. Alcohol use (85.0 million)
10. Diets high in sodium (83.0 million).

Based on the following outcomes:

- Lower respiratory infections
- Tracheal, bronchial, and lung cancer
- Ischaemic heart disease
- Ischaemic stroke
- Haemorrhagic stroke
- Chronic obstructive pulmonary disease
Global Burden of Disease Mental Health and Substance Use Disorders

- In 2010, mental and substance use disorders accounted for 175.3 million YLDs; 22.9% of all YLDs.
- Mental and substance use disorders were the leading cause of YLDs worldwide.
- Depressive disorders accounted for 40.5% of DALYs caused by mental and substance use disorders, anxiety disorders accounting for 14.6%, illicit drug use disorders for 10.9%, alcohol use disorders for 9.6%, schizophrenia for 7.4%, bipolar disorder for 7.0%, pervasive developmental disorders for 4.2%, childhood behavioural disorders for 3.4%, and eating disorders for 1.2%.
• In European populations the projected lifetime risk of developing any mental disorder varied from 26% in Italy to 48.9% in Ukraine (Kessler et al., 2007).

• Psychiatric disorders in young and adolescents may last the whole life. About half of all lifetime mental disorders start by the mid-teens.

• Many psychiatric disorders are not only a problem for the victim and his or her family, but is also a social and public health problem.

• Psychiatric illness may impair education, occupation, social relationships, sexual activities, dating and marriage, parenting and offspring psychological morbidity, crime and drug abuse, health and related lifestyles, financial management and driving.

• The societal cost for mental health illness in Sweden was in 2013 estimated at approximately 70 billion SEK (8 billion €) annually.

• The severe impact of child and adolescent mental health problems on society, together with the plausible and preventable association of exposure to air pollution deserves special attention.
Air pollution epidemiology
Air pollution and the brain

- Stroke
- Neuropathology (experiments)
- Long-term effects on cognition (cross-sectional studies, a few longitudinal studies on children and the elderly)
- Long-term effects on anxiety and stress
- Short-term effects on decreased cerebrovascular flow velocity and resting cerebrovascular resistance, suicide, anxiety
- Air pollution may effect olfaction. Olfactory degeneration predicts neurodegenerative disease
- Air pollution and incident dementia in Northern Sweden
There are an increasing number of studies where associations between air pollution and cognitive or mental health related outcomes have been observed.

There are experimental studies supporting a link between exposure to air pollution and mental health and cognition.

There are studies in both adults and children on air pollution in association with cognition.

There are studies in adults on long-term exposure to air pollution and anxiety and depression, but no studies on children (except ADHD and autism).

Hypothesis: Could air pollution influence mental health in children and adolescents?
Swedish National Registers

Statistics Sweden
Data on age, sex, residential address, links between parents and their offspring, socio-economy (education, income, unemployment)

Board of Health and Welfare
1. Data on dispensed medications from 2005
2. Data from the Medical Birth Registry from 1973 (smoking and BMI during pregnancy)

Residential address gives link to air pollution and group-level socio-economy
- Outcome: The medication group ‘N05’
- N05 consists of neuroleptics (antipsychotic medications), ataractics and sleeping pills.
- The majority of dispensed N05 medications are sedative medications and sleeping pills.
- It should be noted that antidepressants or attention deficit hyperactivity disorder (ADHD) medications are not included.
The empirical model was based on the ratio of the urban content contribution, the meteorological parameters and the population distribution. It includes the geographical distribution of the urban contribution. This model was used together with a model for the regional background levels to calculate the exposure of NO$_2$ and particulates for the entire Swedish population. The spatial resolution was 1 km$^2$. 
## Descriptive data

<table>
<thead>
<tr>
<th>County</th>
<th>Events</th>
<th>Cohort size</th>
<th>Person-time (years)</th>
<th>Events per 1000 persons</th>
<th>Annual mean NO\textsubscript{2} 50th, 5th–95th percentile (µg/m\textsuperscript{3})</th>
<th>Annual mean PM\textsubscript{10} 50th, 5th–95th percentile (µg/m\textsuperscript{3})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stockholm</td>
<td>7346</td>
<td>360 683</td>
<td>1 235 018</td>
<td>20.4</td>
<td>8.3 (3.7–21.5)</td>
<td>8.7 (3.8–21.5)</td>
</tr>
<tr>
<td>Västra Götaland</td>
<td>6004</td>
<td>270 398</td>
<td>948 035</td>
<td>22.2</td>
<td>7.7 (3.1–24.8)</td>
<td>14.2 (9.4–24.8)</td>
</tr>
<tr>
<td>Skåne</td>
<td>4248</td>
<td>218 064</td>
<td>758 504</td>
<td>19.5</td>
<td>7.4 (4.0–23.1)</td>
<td>15.8 (11.2–33.5)</td>
</tr>
<tr>
<td>Västerbotten</td>
<td>1077</td>
<td>46 972</td>
<td>165 599</td>
<td>22.9</td>
<td>2.3 (0.8–15.5)</td>
<td>5.7 (3.6–9.0)</td>
</tr>
</tbody>
</table>
HRs for a 10 µg/m³ increase in NO₂ (A) and PM₁₀ (B)  
Adjusted for age, sex, parental education, mother’s BMI, smoking, SES (group-level)  

The all-cohort estimate was 1.09 (1.06-1.12) for NO₂ and 1.04 (1.00-1.08) for PM₁₀
<table>
<thead>
<tr>
<th>County</th>
<th>Number of observations in total/in analysis/event</th>
<th>NO2 HR 95% CI</th>
<th>PM10 HR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exclude SAMS areas with a population density of &lt;1000/km²</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stockholm</td>
<td>294 728/167 711/2769</td>
<td>1.11 (1.04 to 1.18)</td>
<td>1.18 (1.07 to 1.30)</td>
</tr>
<tr>
<td>Västra Götaland</td>
<td>122 083/72 773/1288</td>
<td>1.07 (1.01 to 1.14)</td>
<td>1.11 (1.01 to 1.23)</td>
</tr>
<tr>
<td>Skåne</td>
<td>111 000/66 235/1108</td>
<td>0.89 (0.81 to 0.98)</td>
<td>0.89 (0.81 to 0.98)</td>
</tr>
<tr>
<td>Västerbotten</td>
<td>13 824/8803/142</td>
<td>0.85 (0.61 to 1.19)</td>
<td>1.13 (0.38 to 3.3)</td>
</tr>
<tr>
<td><strong>Concentrations &lt;15 µg/m³</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stockholm</td>
<td>303 380/177 831/2919</td>
<td>1.18 (1.05 to 1.32)</td>
<td>1.40 (1.19 to 1.65)</td>
</tr>
<tr>
<td>Västra Götaland</td>
<td>215 300/142 031/2494</td>
<td>1.11 (0.99 to 1.24)</td>
<td>1.19 (0.87 to 1.63)</td>
</tr>
<tr>
<td>Skåne</td>
<td>179 700/119 365/1974</td>
<td>1.15 (1.00 to 1.32)</td>
<td>0.78 (0.48 to 1.27)</td>
</tr>
<tr>
<td>Västerbotten</td>
<td>43 694/27 154/423</td>
<td>1.12 (0.89 to 1.42)</td>
<td>1.78 (0.89 to 3.36)</td>
</tr>
</tbody>
</table>
Possible confounders. Noise?

*Sensitivity analys*


Formula for how strong a confounder has to be associated with the outcome and exposure in order to completely explain the observed association with exposure and outcome (RRed):

\[ \geq \text{RRed} + \sqrt{\text{RRed}(\text{RRed}-1)} \]

Här:

\[ \geq 1.09 + \sqrt{1.09 \times 0.09} = 1.40 \]
Next?

- Outcome data - in more detail
- Air pollution data - in more detail

- Individual-level potential confounders
- Noise

Two-phase methods
Also next: Applying for funding…
Paper:

Association between neighbourhood air pollution concentrations and dispensed medication for psychiatric disorders in a large longitudinal cohort of Swedish children and adolescents

Anna Oudin, Lennart Bråbäck, Daniel Oudin Åström, Magnus Strömgren, Bertil Forsberg.

Selected references

- Guxens M, Sunyer J. A review of epidemiological studies on neuropsychological effects of air pollution. Swiss Med Wkly 2012;141:w13322
- Oudin et al. Association between neighbourhood air pollution concentrations and dispensed medication for psychiatric disorders in a large longitudinal cohort of Swedish children and adolescents. BMJ Open