Temporal variability and health effects of air pollutants in epidemiological short-term studies

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The city of Munich, Germany

On a smog day...
The city of Munich, Germany

On a clear day...
Short-term vs. long-term effect studies

**Short-term**

- Effects of short-term exposure to ambient air pollutants
- Exposure period: hours, days, weeks
- Assessment of temporal variation
Short-term vs. long-term effect studies

**Long-term**

- Effects of long-term exposure to ambient air pollutants
- Exposure period: several years, at least one year
- Assessment of geographical variation (between study areas or participants)
Why studies on short- and long-term effects?

There are **chronic** and **acute** health effects (of air pollutants) which are independent.

Adapted from von Klot-Heydenfeldt, 2005
Why studies on short- and long-term effects?

Short-term studies assess:
- Effects of acute (transient) changes
- Potential physiological pathways

Long-term studies assess:
- Effects of moderate or high long-term (chronic) exposure and cumulative effects of repeated episodes of increased exposure
- Health benefits of clean air acts

Important for public-health!
How/why do short-term studies work?

- PM measured at a central site reflects well temporal variation near homes across urban areas.
- Correlations with the central site are usually similar for background and traffic locations.
- Using a central site in epidemiological time-series studies is therefore justifiable.
Schematic horizontal profile of ambient air pollution levels

1. near traffic station (Frankfurter Allee)
2. urban background stations
   (Nansenstrasse; Fasanenstraße)
3. regional background stations
   (Waldhof; Neuglobsow)
Temporal variation of PNC at different monitoring sites (Augsburg)

Cyrys et al., 2008
Study design of a panel study: Repeated measurements

- $Q_3 = 24.9 \mu g/m^3$
- $Q_1 = 8.7 \mu g/m^3$
- $Q_3 - Q_1 = 16.2 \mu g/m^3$
Calculation of individual exposure windows (example: individual 24-hour lags)

Important: Exposure data need to be on an hourly basis (minimum)

Principle of individual lag-times:

Time

2pm 2pm 2pm 2pm 2pm 2pm

Lag 0 Lag 1 Lag 2 Lag 3 Lag 4

5-day average exposure
Health effects of particulate air pollution based on epidemiological studies

- Mortality
- Hospital admissions
- Emergency room visits

Changes in cardiac function (heart rate variability, repolarization), cardiac symptoms, respiratory symptoms, pro-thrombotic status and increase in inflammatory markers

Sub-clinical effects in healthy subjects

Proportion of the population affected
Parts of the body that can be affected by air pollution

- Respiratory mortality
- Respiratory symptoms
- Rhinitis/Pneumonia
- Airway inflammation
- Decreased lung function
- Decreased lung growth
- Lung cancer

- Stroke
- Diseases of the central nervous system

- Cardiovascular mortality
- Cardiovascular hospital admission
- Changes in heart rate variability
- ST-segment depression
- Changes in repolarisation

- Premature birth
- Decreased birth weight
- Decreased foetal growth
- Intrauterine growth retardation
- Decreased sperm quality

Peters et al. 2011
Studies on health effects of soot (BS/BC/EC/OC) are still comparatively rare...

Table 1. Air pollutants and health outcomes.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Short-term studies</th>
<th>Long-term studies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$PM_{10}$</td>
<td>$PM_{2.5}$</td>
</tr>
<tr>
<td>Mortality</td>
<td>XXX</td>
<td>XXX</td>
</tr>
<tr>
<td>All cause</td>
<td>XXX</td>
<td>XXX</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>XXX</td>
<td>XXX</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>XXX</td>
<td>XXX</td>
</tr>
<tr>
<td>Pulmonary effects</td>
<td>XXX</td>
<td>XXX</td>
</tr>
<tr>
<td>Lung function, e.g., PEF</td>
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<td>XXX</td>
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<tr>
<td>Lung function growth</td>
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<td>XXX</td>
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<tr>
<td>Asthma and COPD exacerbation</td>
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<tr>
<td>Acute respiratory symptoms</td>
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<tr>
<td>Medication use</td>
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<tr>
<td>Lung cancer</td>
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<tr>
<td>Hospital admission</td>
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<tr>
<td>Cardiovascular effects</td>
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<tr>
<td>Hospital admission</td>
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<td>XXX</td>
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<td>ECG-related endpoints</td>
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<tr>
<td>Autonomic nervous system</td>
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<td>XXX</td>
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<tr>
<td>Myocardial substrate and vulnerability</td>
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<tr>
<td>Vascular function</td>
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<td></td>
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<tr>
<td>Blood pressure</td>
<td>XX</td>
<td>XXX</td>
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<tr>
<td>Endothelial function</td>
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<tr>
<td>Variables</td>
<td>$PM_{10}$</td>
<td>$PM_{2.5}$</td>
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<tr>
<td>Blood markers</td>
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<tr>
<td>Pro inflammatory mediators</td>
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<tr>
<td>Coagulation blood markers</td>
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<tr>
<td>Endothelial function</td>
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<tr>
<td>Reproduction</td>
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<tr>
<td>Premature birth</td>
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<tr>
<td>Birth weight</td>
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<tr>
<td>IUGR/SGA</td>
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<tr>
<td>Fetal growth</td>
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<td>Birth defects</td>
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<td>Infant mortality</td>
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<td>Sperm quality</td>
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<td>Neurotoxic effects</td>
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<tr>
<td>Diseases of the central nervous system</td>
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<td>X</td>
</tr>
</tbody>
</table>

$x$, few studies; $xx$, many studies; $xxx$, large number of studies.

Rückerl et al., 2011
Health effects of particulate air pollution based on epidemiological studies

- Mortality
- Hospital admissions
- Emergency room visits
- Changes in cardiac function (heart rate variability, repolarization), cardiac symptoms, respiratory symptoms, pro-thrombotic status and increase in inflammatory markers
- Sub-clinical effects in healthy subjects

Proportion of the population affected
Comparison between effects of black carbon particles and PM$_{10}$ on health – a review

34 included publications, mostly studies conducted in Europe

Health outcomes:

Daily mortality due to all causes, cardiovascular diseases, respiratory diseases

Hospital admissions due to respiratory diseases, asthma, cardiac diseases and ischemic heart diseases

Results:

- Most studies show an increase in health outcome with increased air pollution
- Effects per an 10µg/m³ increase are higher for BCP than for PM$_{10}$
- Results are similar when IQR is used

Janssen et al., 2011
PM$_{10}$ vs. BS/BC/EC/OC in studies on daily all-cause mortality

Janssen et al., 2011
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Sub-clinical effects in healthy subjects

Proportion of the population affected
### Examples for short-term studies on BS/BC/EC/OC and inflammatory/prothrombotic blood biomarkers

<table>
<thead>
<tr>
<th>Reference</th>
<th>Air pollutants</th>
<th>CRP</th>
<th>MPO</th>
<th>Fibrinogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rückerl, 2006</td>
<td>EC/OC</td>
<td>o</td>
<td>n.m.</td>
<td>o</td>
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<tr>
<td>Delfino, 2008</td>
<td>EC/OC/BC/Ocpri/SOC</td>
<td>+</td>
<td>o</td>
<td>o</td>
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<tr>
<td>Hildebrandt, 2009</td>
<td>EC/OC</td>
<td>o</td>
<td>n.m.</td>
<td>+</td>
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<tr>
<td>Delfino, 2009</td>
<td>EC/OC/BC/Ocpri/SOC</td>
<td>+</td>
<td>n.m.</td>
<td>n.m.</td>
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<tr>
<td>Bind, 2012</td>
<td>BC</td>
<td>o</td>
<td>n.m.</td>
<td>+</td>
</tr>
<tr>
<td>Rückerl, 2014</td>
<td>BC</td>
<td>++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Li, 2016</td>
<td>BC</td>
<td>n.m.</td>
<td>+</td>
<td>n.m.</td>
</tr>
</tbody>
</table>

O: no association; +: positive association; –: negative association; n.m.: not measured

**CRP**: C-reactive protein – biomarker of systemic inflammation  
**MPO**: Myeloperoxidase - pro-oxidant enzyme/indicator of neutrophil activation  
**Fibrinogen**: important role in blood coagulation  
**OC_{pri}/SOC**: estimated primary and secondary organic carbon
Study objective:
Description of health endpoint in susceptible groups

Study location: Area of Augsburg, Germany.

Study period: Mar 2007 - Dec 2008

Study design:
Panel study with up to seven repeated measurements every four to six weeks
Associations between 5-day average exposure of air pollutants and CRP

CRP: C-reactive protein – biomarker of systemic inflammation

- Non-diabetic subjects with a potential genetic predisposition on the detoxifying pathway (GSTM-1 null), n=87
- Patients with Type II diabetes or impaired glucose tolerance, n=187

Rückerl, 2014
Rückerl, 2016
Associations between 5-day average exposure of air pollutants and MPO

Non-diabetic subjects with a potential genetic predisposition on the detoxifying pathway (GSTM-1 null), n=87

Patients with Type II diabetes or impaired glucose tolerance, n=187

MPO: Myeloperoxidase - pro-oxidant enzyme/indicator of neutrophil activation

Rückerl, 2014
Rückerl, 2016
Associations between 5-day average exposure of air pollutants and fibrinogen

Non-diabetic subjects with a potential genetic predisposition on the detoxifying pathway (GSTM-1 null), n=87

Patients with Type II diabetes or impaired glucose tolerance, n=187

Fibrinogen: important role in blood coagulation

Rückerl, 2014
Rückerl, 2016
Thank you for your attention!