Attribution of all-cause mortality associated with long-term average concentrations of NO₂

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ERS, WHO, HEI, ISEE meeting, Brussels 21 and 22 January 2020
Request from Defra:

- How to quantify the benefits of reducing long-term average concentrations of NO₂.
- To support the development of Air Quality Plans to reduce NO₂ concentrations

COMEAP 2018
www.comeap.org.uk
Mortality estimates for NO$_2$ - HRAPIE

<table>
<thead>
<tr>
<th>Pollutant metric</th>
<th>Health outcome</th>
<th>Group</th>
<th>RR (95% CI) per 10 µg/m$^3$</th>
<th>Range of concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO$_2$, annual mean</td>
<td>Mortality, all (natural) causes, age 30+ years</td>
<td>B*</td>
<td>1.055 (1.031–1.080)</td>
<td>&gt;20 µg/m$^3$</td>
</tr>
</tbody>
</table>

### Source of background health data

- MDB (WHO, 2013c), rates for deaths from all natural causes (ICD-10 chapters I–XVIII, codes A–R) in each of the 53 WHO Regional Office for Europe countries, latest available data

### Source of CRF

- Meta-analysis of all (11) cohort studies published before January 2013 by Hoek et al. (2013); RR based on single-pollutant models

### Comments

- Some of the long-term NO$_2$ effects may overlap with effects from long-term PM$_{2.5}$ (up to 33%); this is therefore recommended for quantification under Group B to avoid double counting in Group A analysis

Attribution of all-cause mortality associated with long-term average concentrations of NO$_2$
New meta-analysis

Attribution of all-cause mortality associated with long-term average concentrations of NO$_2$

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Cohort</th>
<th>ES (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crouse et al</td>
<td>2015b</td>
<td>CanCHEC</td>
<td>1.035 (1.029, 1.042)</td>
</tr>
<tr>
<td>Kreviski et al</td>
<td>2009</td>
<td>ACS CPS-II</td>
<td>0.995 (0.993, 0.997)</td>
</tr>
<tr>
<td>Abbey et al</td>
<td>1993</td>
<td>AHSMOG</td>
<td>1.002 (0.980, 1.024)</td>
</tr>
<tr>
<td>Lipsett et al</td>
<td>2011</td>
<td>CTS</td>
<td>0.994 (0.961, 1.019)</td>
</tr>
<tr>
<td>Hel</td>
<td>2000</td>
<td>Six Cities</td>
<td>1.078 (1.023, 1.136)</td>
</tr>
<tr>
<td>Hart et al</td>
<td>2011</td>
<td>US trucking industry cohort</td>
<td>1.054 (1.030, 1.079)</td>
</tr>
<tr>
<td>Carey et al</td>
<td>2013</td>
<td>CIRD</td>
<td>1.023 (0.998, 1.049)</td>
</tr>
<tr>
<td>Beelen et al</td>
<td>2014b</td>
<td>ESCAPE</td>
<td>1.012 (0.993, 1.031)</td>
</tr>
<tr>
<td>Bentayeb et al</td>
<td>2015</td>
<td>Gazel</td>
<td>1.070 (0.995, 1.150)</td>
</tr>
<tr>
<td>Cesaroni et al</td>
<td>2013</td>
<td>Rome longitudinal study</td>
<td>1.027 (1.020, 1.034)</td>
</tr>
<tr>
<td>Fischer et al</td>
<td>2015</td>
<td>DUELS</td>
<td>1.027 (1.024, 1.031)</td>
</tr>
</tbody>
</table>

HRs (95% CI) per 10 μg/m$^3$ for cohort studies reporting associations between NO$_2$ and all-cause mortality

Random effects summary HR: 1.023 (95% CI 1.008, 1.037) per 10 μg/m$^3$ NO$_2$

To note:

**All-cause** mortality only considered (not cause-specific mortality)

Cut-off date for literature review – **October 2015** (new studies now available)
Health Matters
Air pollution: sources, impacts and actions
Sources of air pollution

Energy industries
- PM<sub>2.5</sub>: 3.3%
- NO<sub>x</sub>: 22.4%
- SO<sub>2</sub>: 37.3%
- NH<sub>3</sub>: 0.1%
- NMVOC: 0.5%

Manufacturing industries and construction
- PM<sub>2.5</sub>: 16.1%
- NO<sub>x</sub>: 15.6%
- SO<sub>2</sub>: 21.6%
- NH<sub>3</sub>: 0.7%
- NMVOC: 2.4%

Fugitive emissions
- PM<sub>2.5</sub>: 1.1%
- NO<sub>x</sub>: 0.2%
- SO<sub>2</sub>: 1.4%
- NH<sub>3</sub>: 0.1%
- NMVOC: 15.8%

Non-road transport
- PM<sub>2.5</sub>: 3.6%
- NO<sub>x</sub>: 16.8%
- SO<sub>2</sub>: 8.3%
- NH<sub>3</sub>: 0%
- NMVOC: 1.6%

Industrial processes
- PM<sub>2.5</sub>: 12.9%
- NO<sub>x</sub>: 0.1%
- SO<sub>2</sub>: 4.8%
- NH<sub>3</sub>: 1.3%
- NMVOC: 54.1%

Residential and small-scale commercial combustion
- PM<sub>2.5</sub>: 43.1%
- NO<sub>x</sub>: 10.3%
- SO<sub>2</sub>: 25.5%
- NH<sub>3</sub>: 0.8%
- NMVOC: 0.2%

Agriculture
- PM<sub>2.5</sub>: 4%
- NO<sub>x</sub>: 0.8%
- SO<sub>2</sub>: N/A
- NH<sub>3</sub>: 87.6%
- NMVOC: 14.4%

Road transport
- PM<sub>2.5</sub>: 12.4%
- NO<sub>x</sub>: 33.6%
- SO<sub>2</sub>: 0.7%
- NH<sub>3</sub>: 1.5%
- NMVOC: 3.9%

Pollution substances:
- SO<sub>2</sub> - Sulphur dioxide
- NO<sub>x</sub> - Nitrogen oxides
- NH<sub>3</sub> - Ammonia
- PM<sub>2.5</sub> - Primary particulate matter
- NMVOCs - Non-methane volatile organic compounds

Workshop convened by the Air Pollution Group, Health Protection Agency. Commissioned by the Department of Health’s Policy Research Programme

ABSTRACT
It is clear from epidemiological and laboratory studies that air pollution has adverse effects on health. However, understanding whether ambient concentrations of nitrogen dioxide (NO₂) have direct adverse effects on health has proved to be difficult, because levels in ambient air correlate closely with those of other pollutants, notably particles. This difficulty arises because NO₂ and particles have similar sources, such as traffic.
COMEAP (2015) Statement on NO₂

- Strengthening evidence for associations with NO₂
- Associations robust to adjustment for other pollutants incl PM
- May act as a marker for TRAP to some extent, but evidence suggests that it would be sensible to regard NO₂ as causing some of the health impact reported in epidemiological studies

Other assessments:
WHO REVIHAAP (2013): NO₂ might represent TRAP but
- Reasonable to infer that NO₂ has some direct effects following short-term exposure (associations robust to adjustment, some mechanistic support for causality - particularly for respiratory outcomes)
- Harder to judge independent effects of NO₂ in studies of long-term exposure. Short-term associations and mechanistic evidence, particularly on respiratory effects, suggest a causal relationship

USEPA ISA (2016)
Health Canada (2016)
Unadjusted coefficient for NO₂

Reflects:

• any causal effect of NO₂

• and also, to some extent, the effects of other pollutants correlated with NO₂

Correlated pollutants:

• PM$_{2.5}$

• other components of the air pollution mixture eg
  • Ultrafine particles
  • Black Carbon
  • Volatile Organic Compounds etc
Independence from PM mass

Using HRs (per IQR) from studies reporting results from single and two/multi-pollutant models for NO$_2$ and PM:

Compared:
- HRs from single-pollutant models
- Combined adj HRs (NO$_2$ adj for PM; PM adj for NO$_2$)

The combined effect using coefficients each adjusted for the effects of the other, is either similar to or only little higher than what would be estimated for either PM$_{2.5}$ or NO$_2$ alone.
Hazard ratios (HRs) expressed per interquartile range (IQR) from single and two pollutant models for NO$_2$ and PM$_{2.5}$

<table>
<thead>
<tr>
<th>Study (additional sig figs for HRs obtained from the authors)</th>
<th>Corr NO$<em>2$/PM$</em>{2.5}$</th>
<th>NO$_2$ IQR (μg/m$^3$)</th>
<th>PM$_{2.5}$ IQR (μg/m$^3$)</th>
<th>NO$<em>2$ adj PM$</em>{2.5}$</th>
<th>PM$_{2.5}$ adj NO$_2$</th>
<th>Combined NO$_2$ adj / PM adj</th>
<th>PM$_{2.5}$ Single</th>
<th>NO$_2$ Single</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cesaroni et al 2013</td>
<td>0.79</td>
<td>10.7</td>
<td>5.7</td>
<td>1.026</td>
<td>1.004</td>
<td>1.030</td>
<td>1.023</td>
<td>1.029</td>
</tr>
<tr>
<td>Carey et al 2013 pers comm</td>
<td>0.85</td>
<td>10.7</td>
<td>1.9</td>
<td>1.001</td>
<td>1.023</td>
<td>1.024</td>
<td>1.023</td>
<td>1.022</td>
</tr>
<tr>
<td>Beelen et al 2014 14 cohorts</td>
<td>0.2-&lt;0.7</td>
<td>10.0</td>
<td>5.0</td>
<td>1.007</td>
<td>1.060</td>
<td>1.067</td>
<td>1.070</td>
<td>1.015</td>
</tr>
<tr>
<td>Fischer et al 2015 PM$_{10}$</td>
<td>0.58 (with PM$_{10}$)</td>
<td>10.0</td>
<td>2.4</td>
<td>1.019</td>
<td>1.010</td>
<td>1.029</td>
<td>1.019</td>
<td>1.027</td>
</tr>
<tr>
<td>HEI 2000 41 cities</td>
<td>-0.08</td>
<td>81.4 (min,max)</td>
<td>24.5 (min,max)</td>
<td>0.90</td>
<td>1.22</td>
<td>1.09</td>
<td>1.15</td>
<td>0.95</td>
</tr>
<tr>
<td>Jerrett et al 2013</td>
<td>0.55</td>
<td>7.7</td>
<td>5.3</td>
<td>1.025</td>
<td>1.015</td>
<td>1.040</td>
<td>1.032</td>
<td>1.031</td>
</tr>
</tbody>
</table>
Coefficient for NO$_2$ adjusted for PM$_{2.5}$

Excludes, as far as possible:

- effects associated with PM$_{2.5}$ concentrations, and other components of the air pollution mixture that are more closely correlated with PM$_{2.5}$ concentrations than with NO$_2$ concentrations

Reflects:

- any causal effect of NO$_2$ and also, to some extent, of other pollutants closely correlated with NO$_2$

➢ The extent to which the effect is likely to be causally related to NO$_2$ is unclear
Uncertainty related to causality

A key point of COMEAP’s discussions:
Uncertainty in the extent to which the effects associated with NO₂ in epidemiological studies are caused by NO₂ itself

➤ How to take the uncertainty into account quantitatively when predicting the benefits that would be expected from interventions (eg in cost-benefit assessments)

• Some Members doubtful that the evidence is sufficient to allow a robust recommendation for quantification

• The majority thought it important to attempt to estimate the possible mortality benefit from reducing NO₂ concentrations
HIA of reductions in all traffic-related pollutants:
• Use summary unadjusted NO$_2$ coefficient:
  ➢ 1.023 (95% CI 1.008, 1.037) per 10 μg/m$^3$
• (Alternatively, could assess based on PM$_{2.5}$ reductions)
HIA of interventions which target NO$_x$ emissions
• Use 25 – 55% of summary unadjusted coefficient
  ➢ 1.006 – 1.013 per 10 μg/m$^3$ – “central range”

Informal expert judgement approach equivalent to:
  o Reduction of approx 20% on adjustment for PM
  o 30 - 70% of adjusted coefficient may be causal

Advised: assessment on the basis of reductions of both NO$_2$ and PM (unadjusted) is likely to result in an overestimate
Implementation in CBA

In practice:
Modelling combines predicted changes in pollutant concentrations arising from a range of proposed interventions

- CBA guidance includes mortality benefits associated with reductions in both
  - NO₂ (reduced coefficient)
  - PM₂.₅ (unadjusted)

- Analysts should
  - Acknowledge this limitation
  - Undertake sensitivity analyses
COMEAP: Research recommendations

• Studies to reduce uncertainties in understanding the effects of long-term exposure to NO$_2$ on health
  – Toxicological, epidemiological, exposure errors

• Studies to improve quantification of effects associated with air pollution mixtures
  – Develop multi-pollutant and statistical methods

• Investigation of reasons for between-study variability in reported associations
Summary and discussion points

Science-policy interface:

• NO$_2$ has been less-studied than PM$_{2.5}$
• But evidence for independent effects of NO$_2$ grows
• Nonetheless, there is more certainty about the health benefits of interventions that reduce both PM$_{2.5}$ and NO$_2$ (and other co-pollutants)
• Communicating uncertainty is important
  – to allow informed policy decisions to be taken
• New studies and method developments will continue to inform scientific thinking and policy development
Acknowledgements

Current and former members of COMEAP and its Quantification (QUARK) subgroup, particularly:
  • Richard Atkinson, Paul Wilkinson, Fintan Hurley, Heather Walton, Frank Kelly

Current and former members of the AQPH Group and COMEAP Secretariat, particularly:
  • Karen Exley, Britta Gadeberg, Inga Mills
Thank you!