Health Effects of Nitrogen Dioxide

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Department of Epidemiology & Public Health
Yale School of Medicine, New Haven, Connecticut
Focus

• Epidemiologic studies of human health
• Studies from North America, Europe, Australia
• Where possible, details from Canadian studies
Mechanisms of Health Effects of NO\textsubscript{2}

Allergens
Air pollutants: O\textsubscript{3}, NO\textsubscript{2}
Virus infections

Inflammation
‘Chronic eosinophilic bronchitis’

Symptoms
Cough
Chest tightness
Wheeze
Shortness of breath

Airway
Hyper-responsiveness

Triggers:
Allergens
Exercise
Cold air
Air pollutants (e.g., NO\textsubscript{2}, SO\textsubscript{2}, O\textsubscript{3}, particulates)

Major Outdoor Sources of Air Pollution

- Industrial Sources
- Domestic Sources
- Power Generation

Stationary Sources:
- Pb
- VOCs
- NOx
- PM
- SO2
- CO

Vehicle Sources:
- Diesel
- Gasoline

Major Outdoor Sources of Air Pollution

- Industrial Sources
- Domestic Sources
- Power Generation

Stationary Sources:
- Pb
- VOCs
- NOx
- PM
- SO2
- CO

Vehicle Sources:
- Diesel
- Gasoline
NO$_x$ Sources

- **Motor Vehicles**: 56%
- **Utilities**: 22%
- **Industrial / Commercial / Residential Fuel Combustion**: 17%
- **Other**: 5%

Source: US EPA
Major *Indoor* Sources

- Gas Appliances
- Gas Space Heaters
- Kerosene Space Heaters
- Tobacco Combustion
- From Outdoor Air – traffic
Exposure to NO$_2$: What health effects would cause concern?

- Death
- Serious acute illness
- Chronic illness
Exposure to NO$_2$: Epidemiology of health effects

- Death – Mortality studies
- Serious acute illness – Patterns of hospital admissions
- Chronic illness – Incidence and prevalence of asthma
Interpretation of epidemiologic studies of NO$_2$ and health effects: Cautions

- **Contaminants** - NO$_2$ found in complex mixtures and often highly correlated with other pollutants

- **Exposure assessment** – measurements averaged from central sites may misclassify personal exposure

- **Sources** - Indoor and outdoor sources of NO$_2$ rarely considered together

- **Other risk factors** - NO$_2$ exposure often confounded by other risk factors associated with low SES
Health effects of NO$_2$:
Mortality studies
Time trends in air-pollution levels and health outcomes

Epidemiologic studies reporting associations of Nitrogen dioxide or Particulates with mortality (all causes, cardiopulmonary or respiratory).

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Study Location</th>
<th>PM$_{10}$</th>
<th>NO$_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ponka et al.</td>
<td>1998</td>
<td>Helsinki</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Michelozzi et al.</td>
<td>1998</td>
<td>Rome</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Samet et al.</td>
<td>2000</td>
<td>20 US cities</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Roemer &amp; van Wijnen</td>
<td>2001</td>
<td>Amsterdam</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Vedal et al.</td>
<td>2003</td>
<td>Vancouver</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Samoli et al.</td>
<td>2003</td>
<td>9 European cities</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Burnett et al.</td>
<td>2004</td>
<td>12 Canadian cities</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Scoggins et al.</td>
<td>2004</td>
<td>Aukland</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Penttinen et al.</td>
<td>2004</td>
<td>Helsinki</td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>
# NO₂ Standards

<table>
<thead>
<tr>
<th>Standard</th>
<th>US EPA</th>
<th>Canada</th>
<th>WHO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outdoor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Annual average</td>
<td>53 ppb (100 μg/m³)</td>
<td>53 ppb (100 μg/m³)</td>
<td>21 ppb (40 μg/m³)</td>
</tr>
<tr>
<td>24-Hour average</td>
<td>106 ppb (200 μg/m³)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-Hour average</td>
<td>213 ppb (400 μg/m³)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indoor</td>
<td>53 ppb (100 μg/m³)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Annual NO$_2$ concentrations significantly associated with mortality in epidemiologic studies

<table>
<thead>
<tr>
<th>City</th>
<th>Mean ppb ($\mu g/m^3$)</th>
<th>Median ppb ($\mu g/m^3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rome</td>
<td>53 ( 99)</td>
<td>51 ( 96)</td>
</tr>
<tr>
<td>Amsterdam</td>
<td></td>
<td></td>
</tr>
<tr>
<td>background</td>
<td>24 ( 46)</td>
<td>23 ( 44)</td>
</tr>
<tr>
<td>traffic sites</td>
<td>54 (101)</td>
<td>69 (130)</td>
</tr>
<tr>
<td>Vancouver</td>
<td>16 ( 30)</td>
<td>17 ( 32)</td>
</tr>
</tbody>
</table>
Mean NO₂ concentration (ppb) and percentage change (ratio of percent change to standard error) in daily non-accidental mortality associated with a 22.4-ppb change in 3-day moving average concentration of NO₂ based on data from each of 12 study cities (1998-2000). (Significant % change indicated by striped bar.)

Data from Burnett et al. “Associations between short-term changes in nitrogen dioxide and mortality in Canadian cities” Archives of Environ Health 2004;59:228-236.
Health effects of NO₂: Hospitalization studies
## Hospital Admissions for Cardiovascular Disease

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Study Location</th>
<th>Disease</th>
<th>NO$_2$</th>
<th>Other Sig. Pollutants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morgan et al.</td>
<td>1998</td>
<td>Sydney</td>
<td>Heart disease</td>
<td>✓</td>
<td>PM, CO, O$_3$</td>
</tr>
<tr>
<td>Burnett et al.</td>
<td>1999</td>
<td>Toronto</td>
<td>Several diagnoses</td>
<td>✓</td>
<td>PM, CO, O$_3$</td>
</tr>
<tr>
<td>Linn et al.</td>
<td>2000</td>
<td>Los Angeles</td>
<td>Cardiovascular</td>
<td>✓</td>
<td>PM, CO, O$_3$</td>
</tr>
<tr>
<td>Petroeshevsky et al.</td>
<td>2001</td>
<td>Brisbane</td>
<td>Cardiovascular</td>
<td>no</td>
<td></td>
</tr>
<tr>
<td>Mann et al.</td>
<td>2002</td>
<td>Southern California</td>
<td>Ischemic heart disease</td>
<td>✓</td>
<td>CO</td>
</tr>
<tr>
<td>Grazvleviciene et al.</td>
<td>2004</td>
<td>Kaunas, Lithuania</td>
<td>Myocardial infarction (MI)</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Llorca et al.</td>
<td>2005</td>
<td>Torrelavega, Spain</td>
<td>Cardiac</td>
<td>✓</td>
<td>PM</td>
</tr>
<tr>
<td>von Klot et al.</td>
<td>2005</td>
<td>5 European cities</td>
<td>MI readmission</td>
<td>✓</td>
<td>PM</td>
</tr>
</tbody>
</table>
## Hospital Admissions for Respiratory Disease

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Study Location</th>
<th>Disease</th>
<th>NO₂ Sig. result (✓)</th>
<th>Other Sig. Pollutants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walters et al.</td>
<td>1995</td>
<td>West Midlands, UK</td>
<td>Respiratory &lt; age 5</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Morgan et al.</td>
<td>1998</td>
<td>Sydney</td>
<td>Asthma - Children</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>COPD - adults</td>
<td>✓</td>
<td>PM</td>
</tr>
<tr>
<td>Burnett et al.</td>
<td>1999</td>
<td>Toronto</td>
<td>Respiratory</td>
<td>✓</td>
<td>PM, CO, O₃</td>
</tr>
<tr>
<td>Linn et al.</td>
<td>2000</td>
<td>Los Angeles</td>
<td>Pulmonary</td>
<td>✓</td>
<td>PM</td>
</tr>
<tr>
<td>Fusco et al.</td>
<td>2001</td>
<td>Rome</td>
<td>Total respiratory</td>
<td>✓</td>
<td>CO</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Acute respiratory</td>
<td>✓</td>
<td>O₃</td>
</tr>
<tr>
<td>Petroeschevsky et al.</td>
<td>2001</td>
<td>Brisbane</td>
<td>Respiratory</td>
<td>no</td>
<td>PM, O₃</td>
</tr>
<tr>
<td>Migliaretti et al.</td>
<td>2004</td>
<td>Turin</td>
<td>Asthma &lt; age 15</td>
<td>✓</td>
<td>PM</td>
</tr>
<tr>
<td>Llorca et al.</td>
<td>2005</td>
<td>Torrelavega, Spain</td>
<td>Respiratory</td>
<td>✓</td>
<td></td>
</tr>
</tbody>
</table>
Percentage Increase in Hospital Admissions Attributable to an Increase in Pollution Based on Multiple-pollutant Regression Models.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Ambient air pollutants</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PM</td>
</tr>
<tr>
<td>Asthma</td>
<td>4</td>
</tr>
<tr>
<td>Obstructive lung disease</td>
<td>4</td>
</tr>
<tr>
<td>Respiratory infection</td>
<td>6</td>
</tr>
<tr>
<td>Dysrhythmias</td>
<td>3</td>
</tr>
<tr>
<td>Heart failure</td>
<td>-</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>-</td>
</tr>
</tbody>
</table>

Conclusions

$NO_2$ exposure (at levels common currently in Alberta) is associated with:

- increased mortality
- increased hospital admissions for
  - cardiovascular disease
  - respiratory disease
  - asthma
Health effects of NO$_2$: 
Asthma studies
Children’s Health Study (US)

- 12 communities in southern California selected for variability in air pollution
- Children enrolled:
  - 493 with asthma
  - 653 with wheeze, no asthma
  - 2,211 with no wheeze, no asthma
- Exposure: measured in the 12 communities and averaged for 12 months

Children’s Health Study (US)

Results

Among asthmatics:

- \( \text{NO}_2 \) (per increase of 24 ppb) associated with 2 ½ times the likelihood of respiratory symptoms
- \( \text{PM}_{2.5} \) (per increase of 15 \( \mu \text{g/m}^3 \)) associated with 2 ½ times the likelihood of respiratory symptoms and bronchitis

School Study (France)

- 108 schools in 6 French cities
- Children enrolled:
  - 6,672 ages 9 - 11
- Exposure: measured at each school and averaged for 3 years

School Study (France)

Results

- NO$_2$ (per increase of 10 $\mu$g/m$^3$) associated with 23% increase in **allergic symptoms**
- O$_3$ (per increase of 10 $\mu$g/m$^3$) associated with 27% increase in **allergic symptoms**

Toronto Hospital Admissions for Asthma (Canada)

- 7,319 children ages 6 – 12 admitted to Toronto hospitals for asthma
- Exposure: averaged for up to 7 days before admission compared to control periods before and after

Toronto Hospital Admissions for Asthma (Canada)

**Results**

- NO\(_2\) (per increase of 11 ppb) associated with 10% increase in hospital admissions
- CO (per increase of 0.5 ppm) associated with 7% increase in hospital admissions

Yale Center for Perinatal, Pediatric and Environmental Epidemiology

• Summary of studies of environmental factors in the development and severity of asthma in children

• Results related NO$_2$

• New study (Study of Traffic, Air Quality and Respiratory Health [STAR])

Funded by the US National Institute of Environmental Health Sciences (NIEHS)
Yale Childhood Asthma Study

- Prospective cohort
- Mothers recruited from women delivering at 5 area hospitals (> 33,000 deliveries)
- Enrolled: 1,002 families in Connecticut and Southwestern Massachusetts
- Eligible families had a newborn infant or a child with physician-diagnosed asthma

*subject in cohort
*subject pool for 12-month follow-up Study of Asthma Severity
Map of study region for Yale Childhood Asthma Study (CHAS) showing subject residence (black dots), location of ambient air monitors (red diamonds), interstate and state highways (green lines).
Initial Home Visit

- Interview with mother to obtain demographic data, information about pregnancy, home and family characteristics

- Dust collection to measure allergens:
  - Dustmite (Der p, Der f)
  - Cat (Fel d)
  - Dog (Can f)

- Airborne mold sample to measure:
  - Total mold count
  - Cladosporium
  - Penicillium

- Air Quality sample to measure:
  - NO2
  - Nicotine (in smoking homes)
Follow-up Interviews

- Mothers were interviewed by phone every 3 months for the first three years to collect data on monthly symptoms, asthma diagnosis and medication use.

- After age 3, mothers were interviewed annually to obtain data.

- Asthma diagnosis reported by the mother was confirmed by contacting the child’s pediatrician.
Results for Index Infant
Rate of respiratory symptoms per year for infants who experienced any wheeze (41% of 880) or persistent cough (46%) in the first year of life.

Approximately one-third of the infants who experienced symptoms had the equivalent of 30 or more days of wheeze (27.5%) or persistent cough (34.9%).
Infant respiratory symptoms in the first year of life associated with:

- Infant’s gender
- Mother’s asthma
- Mother’s allergy
Infant Gender *

**Persistent Cough (days per year)**

<table>
<thead>
<tr>
<th>Frequency (%)</th>
<th>Male (n=437)</th>
<th>Female (n=443)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>&lt; 30</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>≥ 30</td>
<td>25</td>
<td>25</td>
</tr>
</tbody>
</table>

* p = 0.04

**Wheeze (days per year)**

<table>
<thead>
<tr>
<th>Frequency (%)</th>
<th>Male (n=437)</th>
<th>Female (n=443)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
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<td>50</td>
</tr>
<tr>
<td>&lt; 30</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>≥ 30</td>
<td>25</td>
<td>25</td>
</tr>
</tbody>
</table>

* p = 0.02

Mother has Asthma *

* p = 0.001

Mother has Allergies

Measured levels of NO₂: Distribution by cooking appliance. Dotted line at 20 ppb indicates the 80th percentile of the overall distribution of NO₂.
Adjusted rate ratios (aRR and 95% confidence intervals), showing the increase in the frequency of days with wheeze, persistent cough and shortness of breath, with increasing NO₂ concentrations for children from homes sampled in autumn/winter and in spring/summer separately, southern New England, USA, 1996-1998.

<table>
<thead>
<tr>
<th>Season</th>
<th>NO₂</th>
<th>1st quartile</th>
<th>2nd quartile</th>
<th>3rd quartile</th>
<th>4th quartile</th>
</tr>
</thead>
<tbody>
<tr>
<td>autumn/winter</td>
<td>Wheeze aRR (95% CI)</td>
<td>1.00</td>
<td>0.76 (0.42-1.36)</td>
<td>0.58 (0.29-1.19)</td>
<td>1.48 (0.68-3.22)</td>
</tr>
<tr>
<td></td>
<td>Persistent cough aRR (95% CI)</td>
<td>1.00</td>
<td>1.18 (0.68-2.06)</td>
<td><strong>1.86 (1.01-3.42)</strong></td>
<td><strong>2.42 (1.19-4.92)</strong></td>
</tr>
<tr>
<td></td>
<td>Shortness of breath aRR (95% CI)</td>
<td>1.00</td>
<td><strong>2.27 (1.04-4.95)</strong></td>
<td><strong>3.74 (1.60-8.73)</strong></td>
<td><strong>4.79 (1.81-12.67)</strong></td>
</tr>
<tr>
<td>spring/summer</td>
<td>NO₂</td>
<td>1st quartile</td>
<td>1.00</td>
<td><strong>1.73 (1.04-2.88)</strong></td>
<td><strong>1.71 (1.02-2.89)</strong></td>
</tr>
<tr>
<td></td>
<td>2nd quartile</td>
<td>1.00</td>
<td>0.92 (0.59-1.42)</td>
<td><strong>1.41 (0.92-2.16)</strong></td>
<td>1.50 (0.88-2.57)</td>
</tr>
<tr>
<td></td>
<td>3rd quartile</td>
<td>1.00</td>
<td><strong>1.33 (0.72-2.46)</strong></td>
<td><strong>1.49 (0.80-2.78)</strong></td>
<td><strong>2.20 (1.01-4.80)</strong></td>
</tr>
<tr>
<td></td>
<td>4th quartile</td>
<td>1.00</td>
<td><strong>1.49 (0.80-2.78)</strong></td>
<td><strong>2.20 (1.01-4.80)</strong></td>
<td><strong>4.79 (1.81-12.67)</strong></td>
</tr>
</tbody>
</table>

1 Rate ratio, adjusted for parental asthma diagnosis, ethnic background, maternal education level, smoking in the home, day care, living in an apartment, the presence of siblings, and the other contaminant

* p<0.05
** p<0.01

Results for Asthmatic Sibling
Frequency (%) of wheezing by gender, ethnicity, age.
Frequency (%) of wheezing by housing type, mother’s level of education, season of nitrogen dioxide sampling
• \( \text{NO}_2 \) exposure from household sources:

  • Gas stoves
  • Gas dryers
  • Tobacco smoker in the home
Distribution of household sources of NO$_2$ among study families (n = 728)
Socioeconomic factors associated with cooking appliance use

**Ethnicity**
- White, Asian, other (490)
- Black (74)
- Hispanic (164)

**Mother's education (years)**
- < 12 (n=90)
- 12 - 15 (n=372)
- >15 (n=265)

**Housing**
- Single family (486)
- Multi-family (241)
Measured levels of NO$_2$: Distribution by housing type. Dotted line at 20 ppb indicates the 80th percentile of the overall distribution of NO$_2$. 
Estimates of odds ratios and 95% confidence intervals from logistic regression models for household sources of NO$_2$, related to respiratory symptoms in the month before sampling (Southern New England, 1998-2000)

<table>
<thead>
<tr>
<th>Factors</th>
<th>Wheeze OR (95% CI)</th>
<th>Persistent cough OR (95% CI)</th>
<th>Shortness of breath OR (95% CI)</th>
<th>Chest tightness OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Multifamily Housing</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gas stove</td>
<td>2.27 (1.15, 4.47)</td>
<td>1.19 (0.66, 2.16)</td>
<td>2.38 (1.12, 5.06)</td>
<td>4.34 (1.76, 10.69)</td>
</tr>
<tr>
<td>Gas dryer</td>
<td>0.78 (0.23, 2.57)</td>
<td>1.19 (0.40, 3.53)</td>
<td>2.39 (0.77, 7.43)</td>
<td>1.09 (0.31, 3.90)</td>
</tr>
<tr>
<td>Smoker in the home</td>
<td>1.08 (0.48, 2.39)</td>
<td>1.30 (0.64, 2.62)</td>
<td>0.98 (0.41, 2.33)</td>
<td>1.60 (0.62, 4.12)</td>
</tr>
<tr>
<td><strong>Single Family Housing</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gas stove</td>
<td>0.61 (0.35, 1.05)</td>
<td>0.92 (0.55, 1.51)</td>
<td>0.91 (0.50, 1.64)</td>
<td>0.68 (0.34, 1.32)</td>
</tr>
<tr>
<td>Gas dryer</td>
<td>1.02 (0.50, 2.12)</td>
<td>0.98 (0.49, 1.94)</td>
<td>0.93 (0.42, 2.07)</td>
<td>1.41 (0.61, 3.26)</td>
</tr>
<tr>
<td>Smoker in the home</td>
<td>1.92 (0.92, 4.04)</td>
<td>0.90 (0.41, 1.96)</td>
<td>1.26 (0.53, 2.97)</td>
<td>0.62 (0.20, 1.90)</td>
</tr>
</tbody>
</table>

**Abbreviations:** CI confidence interval; OR odds ratio.

Significant (p < 0.05) results are in shown in boldface type. Separate models were run for each symptom, and all models were adjusted for age, ethnicity, mold/mildew, water leaks, maintenance medication use, and season of sampling. Analyses were stratified by housing type.

*Am J Respir Crit Care Med* 2006;173:297-303. (Table 4)
Results of models relating symptoms in the month before sampling to levels of NO$_2$ measured *indoors* (Southern New England, 1998-2000)

<table>
<thead>
<tr>
<th>Model</th>
<th>Wheeze [OR (95% CI)]</th>
<th>Persistent cough [RR (95% CI)]</th>
<th>Shortness of breath [RR (95% CI)]</th>
<th>Chest tightness [RR (95% CI)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multifamily Housing</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Logistic regression predicting any symptom</td>
<td>1.52 (1.04, 2.21)</td>
<td>1.06 (0.75, 1.49)</td>
<td>1.28 (0.85, 1.91)</td>
<td>1.61 (1.04, 2.49)</td>
</tr>
<tr>
<td>Poisson regression predicting days of symptom</td>
<td>1.33 (1.05, 1.68)</td>
<td>1.07 (0.84, 1.35)</td>
<td>1.23 (0.95, 1.59)</td>
<td>1.51 (1.18, 1.91)</td>
</tr>
<tr>
<td>Single Family Housing</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Logistic regression predicting any symptom</td>
<td>0.99 (0.71, 1.38)</td>
<td>1.07 (0.78, 1.47)</td>
<td>0.83 (0.52, 1.31)</td>
<td>1.10 (0.78, 1.57)</td>
</tr>
<tr>
<td>Poisson regression predicting days of symptom</td>
<td>0.98 (0.78, 1.22)</td>
<td>0.91 (0.69, 1.20)</td>
<td>0.86 (0.63, 1.18)</td>
<td>0.92 (0.68, 1.25)</td>
</tr>
</tbody>
</table>

*Abbreviations:* CI confidence interval; OR odds ratio; RR rate ratio.

Significant (p < 0.05) results are in shown in boldface type. Separate models were run for each symptom, and all models were adjusted for age, ethnicity, mold/mildew, water leaks, maintenance medication use, and season of sampling. Analyses were stratified by housing type. Estimates of OR and 95% CI are from logistic regression models predicting any symptom and rate ratios (RRs) from Poisson models predicting number of days of symptoms. ORs and RRs are given for each 20-ppb increase in NO$_2$.

*Am J Respir Crit Care Med* 2006;173:297-303. (Table 5.)
### Outdoor NO₂

#### Asthma severity in children on maintenance medication

Estimates of odds ratios (OR) and 95% confidence intervals (CI) for co-pollutant logistic regression models for same- and previous-day levels of NO₂, ozone, and PM₂.₅ related to each respiratory symptom or rescue medication (bronchodilator) use of children who are users of maintenance medication (n = 130). (Southern New England, April 1 – September 30, 2001.)

<table>
<thead>
<tr>
<th>Pollutant</th>
<th>Wheeze</th>
<th>Cough</th>
<th>Shortness of breath</th>
<th>Chest tightness</th>
<th>Bronchodilator use</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td><strong>Same day</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NO₂ (15 ppb, 1-h max)</td>
<td>1.14 (1.03, 1.26)</td>
<td>1.05 (0.97, 1.13)</td>
<td><strong>1.14 (1.01, 1.30)</strong></td>
<td><strong>1.12 (1.00, 1.27)</strong></td>
<td>1.02 (0.98, 1.05)</td>
</tr>
<tr>
<td>O₃ (50 ppb, 1-h max)</td>
<td>0.99 (0.81, 1.20)</td>
<td>0.97 (0.81, 1.14)</td>
<td>1.03 (0.85, 1.26)</td>
<td>1.03 (0.84, 1.26)</td>
<td>1.03 (0.97, 1.10)</td>
</tr>
<tr>
<td>PM₂.₅ (10mg/m³, 24-h ave)</td>
<td>1.00 (0.93, 1.07)</td>
<td>1.02 (0.96, 1.07)</td>
<td>1.07 (0.98, 1.17)</td>
<td>1.06 (0.97, 1.15)</td>
<td>1.01 (0.99, 1.03)</td>
</tr>
<tr>
<td><strong>Previous day</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NO₂ (15 ppb, 1-h max)</td>
<td>1.00 (0.92, 1.09)</td>
<td>1.00 (0.94, 1.06)</td>
<td>1.01 (0.91, 1.12)</td>
<td>0.99 (0.89, 1.10)</td>
<td>1.00 (0.98, 1.03)</td>
</tr>
<tr>
<td>O₃ (50 ppb, 1-h max)</td>
<td>1.06 (0.91, 1.23)</td>
<td><strong>1.09 (1.00, 1.21)</strong></td>
<td><strong>1.26 (1.07, 1.48)</strong></td>
<td><strong>1.22 (1.02, 1.45)</strong></td>
<td>1.02 (0.97, 1.06)</td>
</tr>
<tr>
<td>PM₂.₅ (10mg/m³, 24-h ave)</td>
<td>1.02 (0.96, 1.09)</td>
<td>1.01 (0.96, 1.05)</td>
<td>1.06 (0.98, 1.15)</td>
<td>1.07 (0.98, 1.17)</td>
<td>0.99 (0.97, 1.02)</td>
</tr>
</tbody>
</table>

Significant (p < 0.05) ORs are in boldface type.

Separate logistic regression analyses were performed for each outcome measure. All models include same- and previous-day levels of NO₂ (1-hr max), ozone (1-hr max), and PM₂.₅ (24-hr average) adjusted for maximum daily temperature. Logistic regressions were performed using generalized estimating equations and specifying a one-day lagged autoregressive structure (AR1) for the correlation matrix.
Conclusions

**Indoor NO$_2$** exposure associated with:
- respiratory symptoms in infants at risk for asthma
- respiratory symptoms in asthmatic children

**Outdoor NO$_2$** exposure associated with:
- increased respiratory symptoms in asthmatic children using maintenance medication
Interpretation of epidemiologic studies of NO$_2$ and health effects: Cautions

- **Contaminants** - NO$_2$ found in complex mixtures and often highly correlated with other pollutants

- **Exposure assessment** – measurements averaged from central sites may misclassify personal exposure

- **Sources** - Indoor and outdoor sources of NO$_2$ rarely considered together

- **Other risk factors** - NO$_2$ exposure often confounded by other risk factors associated with low SES
Study of Traffic, Air Quality and Respiratory Health (STAR)

- Asthma severity associated with
  1) Indoor & outdoor NO$_2$
  2) Traffic emission
  3) Interaction between allergens & NO$_2$
Yale STAR study

• Recruiting 1500 asthmatic children in Connecticut

• Measuring NO₂ for 1 month in each season
  – indoors in child’s bedroom & playroom
  – outdoors outside of child’s home

• Estimating traffic exposure within 2 km of child’s home
Yale STAR study

- Health outcomes recorded daily
  - respiratory symptoms
  - medication use
  - physician visits
Estimated average daily level of NO₂ along major roadways in Connecticut. Model based on traffic density data from the State Dept. of Transportation and outdoor NO₂ measurements taken at study subjects’ homes (1997 – 2000).
Yale Center for Perinatal, Pediatric and Environmental Epidemiology

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• Theodore Holford
• Elizabeth Triche

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