Association of Changes in Air Quality With Incident Asthma in Children in California, 1993-2014

COLLABORATIVE ON HEALTH AND THE ENVIRONMENT

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Air pollution exposure is a well-established cause of asthma exacerbation in children

Whether air pollutants play a role in the development of childhood asthma, however, remained uncertain

**Objective:** To examine whether decreasing regional air pollutants were associated with reduced incidence of childhood asthma

THE USUAL ANALYSIS

• Recruit over some geographic space
THE USUAL ANALYSIS

- Recruit over some geographic space
- Assess exposure
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- Follow for outcome
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- Compare outcome by exposure level, which is tied to geographic space
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  • Concerned about unmeasured spatial confounding
THE USUAL ANALYSIS

- Recruit over some geographic space
- Assess exposure
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- Compare outcome by exposure level, which is tied to geographic space
  - Concerned about unmeasured spatial confounding

Confounding variable: A variable (factor) that is associated with the exposure (e.g., air pollution) and is causally related to the outcome (e.g. asthma incidence), causing a spurious (artificial) association

Example: Access to green space
WHAT IF INSTEAD...

- Recruit in same geographic space, at different times
WHAT IF INSTEAD...

- Recruit in same geographic space, at different times
WHAT IF INSTEAD...

- Recruit in same geographic space, at different times

2000  2005  2010
WHAT IF INSTEAD...

- Air pollution changed over time

2000

2005

2010
WHAT IF INSTEAD...

• Follow for outcome
WHAT IF INSTEAD...

• Compare within the same geographic space
WHAT IF INSTEAD...

- Compare within the same geographic space
- Control unmeasured spatial confounders
WHAT IF INSTEAD...

• Compare within the same geographic space
  • Control unmeasured spatial confounders
    ➢ People living in the same communities will be similar to each other
BENEFIT OF THIS DESIGN

Control for unmeasured community-level [spatial] confounders

Take advantage of a natural experiment

Quantify the health benefits associated with reducing air pollution

Previously used this study design for lung function growth and bronchitis symptoms in children (Gauderman 2015; Berhane 2016)
Data from the Southern California Children’s Health Study (CHS)

Long-term study of cardiopulmonary health outcomes in children

Began in 1993 when 12 communities were selected representing air pollution levels and mixtures in Southern California.
AIR POLLUTANTS EXAMINED

Focused on 4 key air pollutants

Have legal regulatory standards

Known to have health effects

1. Nitrogen Dioxide (NO₂)
2. Ozone (O₃)
3. Particulate Matter <2.5 μm (PM₂.₅)
4. Particulate Matter <10 μm (PM₁₀)

Photo credit: Praytino via Flickr
WHAT WE DID-DETAILS

3 cohorts from the CHS (N=4,140)

Restricted to participants from the same 9 communities

Followed for 8 years (~4th grade to high school graduation)

- 1993-2001 (N=1,093)
- 1996-2004 (N=1,170)
- 2006-2014 (N=1,877)

Prospectively assessed for MD-diagnosed asthma via questionnaire (N cases=525)
WHAT WE DID-DETAILS

Multilevel Poisson model

- Random effect for cohort nested within town and fixed effect for town
- Adjusted for potential confounders identified a priori: age, sex, race, ethnicity, gas stove in home, sports participation, ambient temperature, and residential traffic

Exposure: Community-level annual average pollutant concentration in baseline year for each cohort


Outcome: Asthma incidence during follow up
TAKing ADVantage of a Natural Experiment: NO₂

Median Change
-4.3 ppb (-22%)

Year
1993 1995 1997 1999 2001 2003 2005 2007 2009 2011

Nitrogen Dioxide, ppb

Communities
Lake Gregory
San Dimas
Alpine
Mira Loma
Upland
Long Beach
Santa Maria
Lake Elsinore
Riverside

NAAQS
53 ppb
TAKING ADVANTAGE OF A NATURAL EXPERIMENT: $O_3$

Median Change: 

-8.9 ppb (-15%)
TAKING ADVANTAGE OF A NATURAL EXPERIMENT: PM$_{2.5}$

Median Change:
-8.1 µg/m$^3$ (-36%)

NAAQS:
12 µm/m$^3$
TAKING ADVANTAGE OF A NATURAL EXPERIMENT: PM$_{10}$

Particle Matter $\leq 10\ \mu m$, $\mu m/m^3$

- Median Change: $-4.0\ \mu g/m^3$ (-9%)

NAAQS 50 $\mu m/m^3$
OUR FINDINGS

Model details

1: Adjusted for age at baseline, sex, ethnicity, race, gas stove in home, sports participation, and community-level average temperature for baseline year (N=4,140)

2: Additionally adjusted for residential traffic (N=3,942)
REDUCTION IN NO\textsubscript{2} ASSOCIATED WITH LOWER ASTHMA INCIDENCE RATE

Model details

1: Adjusted for age at baseline, sex, ethnicity, race, gas stove in home, sports participation, and community-level average temperature for baseline year (N=4,140)

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REDUCTION IN NO₂ ASSOCIATED WITH LOWER ASTHMA INCIDENCE RATE

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1: Adjusted for age at baseline, sex, ethnicity, race, gas stove in home, sports participation, and community-level average temperature for baseline year (N=4,140)

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20% (10%, 29%) Lower Asthma Rate
REDUCTION IN NO$_2$ AND PM$_{2.5}$ ASSOCIATED WITH LOWER ASTHMA INCIDENCE RATE

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REDUCTION IN NO$_2$ AND PM$_{2.5}$ ASSOCIATED WITH LOWER ASTHMA INCIDENCE RATE

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20% (10%, 29%) Lower Asthma Rate

19% (2%, 33%) Lower Asthma Rate
CHANGE IN NO$_2$ AND ASTHMA INCIDENCE

Dot size indicates cohort
- ● = 1993
- ● = 1996
- ● = 2006

Communities
- Lake Gregory
- Long Beach
- San Dimas
- Santa Maria
- Alpine
- Lake Elsinore
- Mira Loma
- Riverside
- Upland
CHANGE IN PM$_{2.5}$ AND ASTHMA INCIDENCE

Dot size indicates cohort
- ● = 1993
- ○ = 1996
- ● = 2006

Communities
- Lake Gregory
- San Dimas
- Alpine
- Santa Maria
- Lake Elsinore
- Mira Loma
- Riverside
- Long Beach
- Upland

Asthma Incidence Rate (cases/100 person-years)

Particulate Matter $\leq$ 2.5 $\mu$m Concentration ($\mu$m/m$^3$)
FINDINGS FROM ADDITIONAL ANALYSES

No evidence of effects estimates differing by air pollution level (high v. low), sex, race, ethnicity, parental educational attainment, or use of Spanish (versus English) language baseline questionnaire

NO\textsubscript{2} findings held up in a variety of sensitivity analyses
SUMMARY OF RESULTS

There have been great reductions in air pollutant concentrations between 1993 and 2006 in this region, including 22% for NO$_2$ and 36% for PM$_{2.5}$

Cleaner air was related with lower rates of new-onset asthma in children

- A reduction of 4.3 ppb NO$_2$ was associated with 20% (10%, 29%) lower rate of asthma
- A reduction of 8.1 µg/m$^3$ PM$_{2.5}$ was associated with 19% (2%, 33%) lower rate of asthma

Findings for NO$_2$ were robust to a variety of sensitivities analyses

There was no evidence that the findings were driven by a subgroup of children
CONCLUDING REMARKS

Provides further evidence for the causal link between ambient NO$_2$ exposure and incident childhood asthma

Effects observed in communities with a mean baseline NO$_2$ concentration of 24 ppb—well below the current US EPA annual standard of 53 ppb

Policy implications for NO$_2$ air quality regulations
ACKNOWLEDGEMENTS

Co-authors
- Kiros T. Berhane
- Talat Islam
- Rob McConnell
- Robert Urman
- Zhanghua Chen
- Frank D. Gilliland

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THANK YOU

Questions?
garc991@usc.edu
DISTRIBUTION OF SELECTED PARTICIPANT CHARACTERISTICS FROM THE CHILDREN'S HEALTH STUDY, 1993-2014

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Subjects</td>
<td>4140</td>
<td>1093</td>
<td>1170</td>
<td>1877</td>
</tr>
<tr>
<td>Person-years of follow-up</td>
<td>24254</td>
<td>6201</td>
<td>6842</td>
<td>11211</td>
</tr>
<tr>
<td>Incident asthma cases</td>
<td>525</td>
<td>139</td>
<td>184</td>
<td>202</td>
</tr>
<tr>
<td>Age at baseline</td>
<td>9.5 (0.6)</td>
<td>9.9 (0.5)</td>
<td>9.5 (0.4)</td>
<td>9.3 (0.7)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>2179 (52.6)</td>
<td>569 (52.1)</td>
<td>606 (51.8)</td>
<td>1004 (53.5)</td>
</tr>
<tr>
<td>Male</td>
<td>1961 (47.4)</td>
<td>524 (47.9)</td>
<td>564 (48.2)</td>
<td>873 (46.5)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Hispanic</td>
<td>1686 (42.2)</td>
<td>307 (28.4)</td>
<td>413 (35.5)</td>
<td>966 (55.2)</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>2310 (57.8)</td>
<td>776 (71.7)</td>
<td>750 (64.5)</td>
<td>784 (44.8)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>178 (4.6)</td>
<td>60 (5.6)</td>
<td>56 (4.8)</td>
<td>62 (3.8)</td>
</tr>
<tr>
<td>Black</td>
<td>145 (3.7)</td>
<td>50 (4.7)</td>
<td>54 (4.7)</td>
<td>41 (2.5)</td>
</tr>
<tr>
<td>Native American Indian/Other</td>
<td>890 (23)</td>
<td>182 (17)</td>
<td>249 (21.5)</td>
<td>459 (27.8)</td>
</tr>
<tr>
<td>White</td>
<td>2273 (58.6)</td>
<td>704 (65.7)</td>
<td>692 (59.8)</td>
<td>877 (53.2)</td>
</tr>
<tr>
<td>Mixed</td>
<td>392 (10.1)</td>
<td>76 (7.1)</td>
<td>106 (9.2)</td>
<td>210 (12.7)</td>
</tr>
<tr>
<td>Residential traffic-related pollution, mean (SD), ppb</td>
<td>19.6 (22.1)</td>
<td>27.5 (27.8)</td>
<td>20.5 (23.3)</td>
<td>14.9 (15.8)</td>
</tr>
</tbody>
</table>
## RESULTS TABLE

<table>
<thead>
<tr>
<th></th>
<th>Model 1</th>
<th>Model 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO₂ [-4.3 ppb]</td>
<td>0.80 (0.71, 0.90)</td>
<td>0.81 (0.72, 0.91)</td>
</tr>
<tr>
<td>O₃ [-8.9 ppb]</td>
<td>0.85 (0.71, 1.02)</td>
<td>0.86 (0.71, 1.04)</td>
</tr>
<tr>
<td>PM₂.₅ [-8.1 µg/m³]</td>
<td>0.81 (0.67, 0.98)</td>
<td>0.82 (0.67, 0.99)</td>
</tr>
<tr>
<td>PM₁₀ [-4.0 µg/m³]</td>
<td>0.93 (0.82, 1.07)</td>
<td>0.92 (0.81, 1.04)</td>
</tr>
</tbody>
</table>

Rate Ratio (RR) per median change in air pollutant concentration from 1993 to 2006

Model details

- 1: Adjusted for age at baseline, sex, ethnicity, race, gas stove in home, sports participation, and community-level average temperature for baseline year
- 2: Additionally adjusted for residential traffic (N=3,942)
## Sensitivity Analyses Results

<table>
<thead>
<tr>
<th>Sensitivity Analysis</th>
<th>N</th>
<th>N cases</th>
<th>NO$_2$ RR (95% CI)</th>
<th>PM$_{2.5}$ RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excluded one town</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alpine</td>
<td>3665</td>
<td>471</td>
<td>0.80 (0.71, 0.90)</td>
<td>0.80 (0.65, 0.99)</td>
</tr>
<tr>
<td>Lake Elsinore</td>
<td>3724</td>
<td>468</td>
<td>0.77 (0.68, 0.87)</td>
<td>0.73 (0.59, 0.90)</td>
</tr>
<tr>
<td>Lake Gregory</td>
<td>3651</td>
<td>466</td>
<td>0.80 (0.71, 0.91)</td>
<td>0.84 (0.69, 1.02)</td>
</tr>
<tr>
<td>Long Beach</td>
<td>3731</td>
<td>466</td>
<td>0.86 (0.75, 0.98)</td>
<td>0.87 (0.71, 1.06)</td>
</tr>
<tr>
<td>Mira Loma</td>
<td>3645</td>
<td>477</td>
<td>0.80 (0.71, 0.90)</td>
<td>0.80 (0.65, 1.00)</td>
</tr>
<tr>
<td>Riverside</td>
<td>3679</td>
<td>464</td>
<td>0.80 (0.70, 0.90)</td>
<td>0.71 (0.56, 0.89)</td>
</tr>
<tr>
<td>San Dimas</td>
<td>3715</td>
<td>467</td>
<td>0.77 (0.67, 0.89)</td>
<td>0.84 (0.67, 1.04)</td>
</tr>
<tr>
<td>Santa Maria</td>
<td>3650</td>
<td>471</td>
<td>0.81 (0.72, 0.91)</td>
<td>0.82 (0.67, 0.99)</td>
</tr>
<tr>
<td>Upland</td>
<td>3660</td>
<td>450</td>
<td>0.80 (0.70, 0.91)</td>
<td>0.84 (0.67, 1.05)</td>
</tr>
<tr>
<td>Excluded subjects reporting wheeze or 3+ months of cough in prior 12 months at baseline</td>
<td>3723</td>
<td>411</td>
<td>0.81 (0.71, 0.92)</td>
<td>0.79 (0.62, 0.99)</td>
</tr>
<tr>
<td>Adjusted for:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Income, education, and insurance</td>
<td>4140</td>
<td>525</td>
<td>0.79 (0.70, 0.89)</td>
<td>0.80 (0.65, 0.98)</td>
</tr>
<tr>
<td>In utero smoking exposure</td>
<td>4140</td>
<td>525</td>
<td>0.80 (0.71, 0.90)</td>
<td>0.81 (0.66, 0.98)</td>
</tr>
<tr>
<td>Pests, pets, and carpet</td>
<td>4140</td>
<td>525</td>
<td>0.81 (0.71, 0.91)</td>
<td>0.82 (0.68, 1.00)</td>
</tr>
</tbody>
</table>

Rate ratios scaled to -4.3 ppb for NO$_2$ and -8.1 µg/m$^3$ for PM$_{2.5}$.

Models adjusted for community as a fixed effect, age at baseline, sex, ethnicity, race, gas stove in home, participation in sports, and community-level average temperature for baseline year.
RECENT META-ANALYSIS ON AIR POLLUTION & INCIDENT CHILDHOOD ASTHMA

Meta-analysis of 21 papers published before Sept 2016 (Khreis 2017)

<table>
<thead>
<tr>
<th>Pollutant</th>
<th>Random-effect risk estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO$_2$</td>
<td>1.05 (1.02, 1.07) per 4 µg/m$^3$</td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>1.03 (1.01, 1.05) per 1 µg/m$^3$</td>
</tr>
<tr>
<td>PM$_{10}$</td>
<td>1.05 (1.02, 1.08) per 2 µg/m$^3$</td>
</tr>
</tbody>
</table>