Multi-Pollutant Exposures and Health

Particulate Matter and Health: Evaluating Alternatives to a Mass-Based PM Standard

EPRI Air Quality Research Seminar
May 26-27, 2010
Washington, DC

Helen H. Suh
Harvard School of Public Health
Posited Scenarios

Current:
- Differential toxicity
- Regional, seasonal differences
- Little consistency in component and source findings

Individual components
Classes
Sources
Component as toxicity modifier
Non-, Low toxicity component
Mixtures

Current  Future?
Longitudinal Personal–Ambient Correlation Coefficients for PM$_{2.5}$: Summer

* Median Spearman individual correlation coefficients, except for Fresno (pooled r); ¹annual correlation; ²fall
Atlanta, GA: Panel Participant Homes by Population Density

For 31 older people, repeated measurements of:
- Personal, indoor, outdoor, ambient PM$_{2.5}$, SO$_4^{2-}$, EC, NO$_2$, O$_3$
- Cardiac function (HRV)
<table>
<thead>
<tr>
<th></th>
<th>Ambient</th>
<th></th>
<th>Personal</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PM$_{2.5}$</td>
<td>EC</td>
<td>NO$_2$</td>
<td>PM$_{2.5}$</td>
</tr>
<tr>
<td>Ambient</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>--</td>
<td>-</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>EC</td>
<td>0.59$^a$</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>NO$_2$</td>
<td>0.47$^a$</td>
<td>0.58$^a$</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>O$_3$</td>
<td>0.34$^a$</td>
<td>0.26$^a$</td>
<td>0.12$^b$</td>
<td>--</td>
</tr>
<tr>
<td>Personal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>0.63$^a$</td>
<td>0.43$^a$</td>
<td>0.25$^a$</td>
<td>--</td>
</tr>
<tr>
<td>EC</td>
<td>0.46$^a$</td>
<td>0.48$^a$</td>
<td>0.33$^a$</td>
<td>0.45$^a$</td>
</tr>
<tr>
<td>NO$_2$</td>
<td>0.20$^b$</td>
<td>0.22$^a$</td>
<td>0.12$^b$</td>
<td>0.29$^a$</td>
</tr>
<tr>
<td>O$_3$</td>
<td>0.08</td>
<td>-0.01</td>
<td>-0.09</td>
<td>0.14</td>
</tr>
</tbody>
</table>

Data from Atlanta panel study of individuals with COPD and MI; spearman correlation coefficients; 24–h (approx. 9am–9am) values; $^a$ p<0.01; $^b$ 0.05<p<0.10; from Suh and Zanobetti (2010)
Overall RMSSD and 24-h Personal Exposures:

Atlanta Panel Study of MI and COPD

Table 1. Hazard ratios (95% CI) per 10 μg/m³ change in 12-month PM$_{2.5}$ for mortality and fatal CHD using alternative exposure approaches.

<table>
<thead>
<tr>
<th>Exposure Method</th>
<th>All Cause Mortality</th>
<th>Fatal CHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Space–time model</td>
<td>1.45 (1.19, 1.78)</td>
<td>2.29 (1.26, 4.18)</td>
</tr>
<tr>
<td>Nearest monitor</td>
<td>1.35 (1.08, 1.69)</td>
<td>1.47 (0.73, 2.99)</td>
</tr>
</tbody>
</table>

All estimates are based on Cox models at the monthly level, stratifying by age in months and including a number of covariates. Results reported in Paciorek et al. (2009, Ann Applied Statistics) and Puett et al. (2009, EHP).
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Individual components
Classes

Sources
Component as toxicity modifier
Non-, Low toxicity component
Mixtures

Current
Future?

?
Source Characterization

• **Source apportionment**: groups pollutants by how they co-vary from day-to-day to represent common sources.

• **Source tracers**: individual pollutants reflect exposures for specific sources.

• **Back trajectory analysis**: days or periods clustered based on the origin and route of the air parcels, representative of different pollutant-profiles.

• **Spatial models**: estimates based on location-specific parameters, can reflect exposures to one or more source types.
Regional and Local Source Apportionment: BC

- **Black Carbon (BC) Origin:**
  - BC considered local pollutant, as mobile sources are its primary source (Schwartz et al. 2005; Suglia et al. 2008; Zanobetti and Schwartz 2006)
  - It can also travel long distances with the prevailing winds (O’Neill et al. 2005; Zanobetti and Schwartz 2006)

- **BC toxicity thought to arise from metals, PAHs, other organic compounds associated with BC** (Halonen et al. 2008; Health Effects Institute 2002; Suglia et al. 2008)

- **Aged particles may have fewer reactive components on them than fresh particles**
Two methods:

- Rural BC measurements as measure of regional BC
- Sulfate as marker of regional pollution
  - Sulfate is uniform across large areas of eastern U.S. (Maynard et al. 2007; Suh et al. 1995; Salmon et al. 1999)
  - Similar to BC in size (0.3 – 0.7 mm diameter), deposition as primary loss mechanism
  - Lack of local sources
Define the lower bound of BC/\(SO_4^{2-}\) using quantile regression (QR) (Koenker and Hallock 2001)

- QR minimizes the absolute residuals of a regression
- Residuals are asymmetrically weighted to yield a desired quantile
Local and Regional BC (ug/m³)

\[ r_{\text{total-local}} = 0.95 \]
\[ r_{\text{total-rgnl}} = 0.61 \]
\[ r_{\text{local-rgnl}} = 0.32 \]
Limitations for Health Studies

• While yielding critical information, each method is based on our knowledge of sources, concentrations, and oriented around regulatory purposes.
• As a result, these methods may group pollutants having high toxicity with some having low toxicity.
• When used in health effect analyses, may wash out the strong health effect associated with a single pollutant.
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Scenario A Approach: Classes

• **Approach:** Group pollutants based on physical and/or chemical properties
  - *Assumption:* Physical and/or chemical properties more closely linked to toxicity and thus health effects

• **Case Study:** Acute pollution–associated risks on hospital admissions differ by pollutant physical or chemical property
  - 1998–2006 air pollution databases (ARIES and AIRS)
  - Cause–specific hospital admissions from Centers for Medicare and Medicaid Services (1998–2006) for four Atlanta, GA counties
<table>
<thead>
<tr>
<th>Pollutant</th>
<th>Years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PM\textsubscript{2.5}</strong> Mass</td>
<td>1998 - 2005</td>
</tr>
<tr>
<td>Ions</td>
<td>1998 - 2005</td>
</tr>
<tr>
<td>EC (or surrogates)</td>
<td>1998 - 2002</td>
</tr>
<tr>
<td>OC</td>
<td>1998 - 2002</td>
</tr>
<tr>
<td>Metals</td>
<td>1998 - 2005</td>
</tr>
<tr>
<td>Acidity</td>
<td>1998 – 2000</td>
</tr>
<tr>
<td><strong>PM\textsubscript{coarse}</strong> Mass</td>
<td>1998 - 2005</td>
</tr>
<tr>
<td>Ions</td>
<td>1998 - 2005</td>
</tr>
<tr>
<td>Metals</td>
<td>1998 – 2005</td>
</tr>
<tr>
<td><strong>Gases</strong> Speciated VOCs</td>
<td>1998 - 2005</td>
</tr>
<tr>
<td>NH\textsubscript{3}, HNO\textsubscript{3}</td>
<td>1998 - 2005</td>
</tr>
<tr>
<td>O\textsubscript{3}, SO\textsubscript{2}, NO\textsubscript{x}, CO</td>
<td>1998 – 2005</td>
</tr>
<tr>
<td><strong>Other</strong> Meteorology</td>
<td>1998 – 2005</td>
</tr>
</tbody>
</table>

Total of 156 pollutants
- Includes multiple measurements of same pollutant
- Includes classes of pollutants

Table does not include air pollutant species that were not measured daily. Some species were not measured daily in some years.
Two Stage Approach

• **First stage:** multivariate case–crossover analysis (matched month, year, DOW; lag 0)
  - Controlled for ozone, temperature, dew pt temperature, day of week

• **Second stage:** meta–regression that groups pollutants by property
  - Approach used to assess associations between phenotype and single nucleotide polymorphisms (SNPs) in genetic association studies (Conti and Gauderman 2004; Thomas 2007)
  - Flexible way to summarize regression coefficients to show health effects from multiple pollutants
Key Aspect: Pollutant Groupings

• Analysis hinges on ability to group pollutants into groups with similar properties or toxicities

• Approaches
  – Literature search
  – Expert judgment

• Considerations
  – What characteristics make an appropriate physical or chemical attribute?
  – How are pollutants within a specific group correlated?
  – What pollutants should be included? Sufficient time-series, variability, >LOD, 92 pollutants
  – What is the minimum number of pollutants needed to form a group? 3 or more
  – What lag time is appropriate? 0 day
# Chemical List

<table>
<thead>
<tr>
<th>Category</th>
<th>Chemicals</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ALKENES (Olefins)</strong></td>
<td>Ethylbenzene, n-Pentane, 2,3-Dimethylhexane</td>
</tr>
<tr>
<td><strong>ALKANES (Paraffins)</strong></td>
<td>Ethane, cis-2-Pentene, 2,4-Dimethylhexane</td>
</tr>
<tr>
<td><strong>AROMATICs</strong></td>
<td>Ethylene, 1-Pentene, 2,5-Dimethylhexane</td>
</tr>
<tr>
<td>Acetic Acid</td>
<td>m-Ethyltoluene, alpha-Pinene, 2,4-Dimethylpentane</td>
</tr>
<tr>
<td>Benzaldehyde</td>
<td>o-Ethyltoluene, n-Propylbenzene, 3-Methylpentane</td>
</tr>
<tr>
<td>Benzene</td>
<td>p-Ethyltoluene, Propane, 2-Methyl-2-pentene</td>
</tr>
<tr>
<td>1,3-Butadiene</td>
<td>Total Nonmethane HCs, Propane, Heptanal</td>
</tr>
<tr>
<td>i-Butane</td>
<td>Total Identified Oxygenated HC's, Propene</td>
</tr>
<tr>
<td>n-Butane</td>
<td>Total Oxygenated HC's, Styrene, 1,3,5-Trimethylbenzene</td>
</tr>
<tr>
<td>cis-2-Butene</td>
<td>Total Unidentified Oxygenated HC's, Toluene</td>
</tr>
<tr>
<td>1-Butene</td>
<td>1,2,4-Trimethylbenzene, sec-Butylbenzene, o-Xylene</td>
</tr>
<tr>
<td>i-Butene</td>
<td>n-Heptane, 2-Methyl-1-butene, 2-Octanol</td>
</tr>
<tr>
<td>trans-2-Butene</td>
<td>Hexanal, 2-Nonanone</td>
</tr>
<tr>
<td>Cyclohexane</td>
<td>n-Hexane, 2-Methyl-2-butene, n-Octane</td>
</tr>
<tr>
<td>Cyclopentane</td>
<td>trans-2-Hexene, 3-Methyl-1-butene, i-Pentane</td>
</tr>
<tr>
<td>Cyclopentene</td>
<td>Isoprene, 3-Ethylhexane, 2,2,4-Trimethylpentane</td>
</tr>
<tr>
<td>Decanal</td>
<td>Methylcyclohexane, Total Identified HC, 2,2,4-Trimethylpentane</td>
</tr>
<tr>
<td>n-Decane</td>
<td>Methylcyclopentane, Total Unidentified HCs, 2,3,4-Trimethylpentane</td>
</tr>
<tr>
<td>2,2-Dimethylbutane</td>
<td>2-Methylhexane, m-Xylene &amp; p-Xylene, Acetone</td>
</tr>
<tr>
<td>2,3-Dimethylbutane</td>
<td>2-Methylheptane, 2-Methylpentane, 2-Butanone</td>
</tr>
<tr>
<td>2,4-Dimethylpentane</td>
<td>2-Methylpentane, 2-Butanone</td>
</tr>
</tbody>
</table>
# Chemical List (cont’d)

| PM2.5 Al2O3 | PM2.5 Mn | PMCoarse Ti | OC |
| PM Coarse Al2O3 | PMCoarse Mn | PM2.5 WS V | DAILY 1HR MAX SO2 |
| PM2.5 Arsenic | PMCoarse WS MN | PMCoarse WS V | 24h SO2 |
| PM2.5 Bromine | PMCoarse WS MN | PM2.5 Zinc | 24h CO |
| PM Coarse Bromine | PMCoarse WS Ni | PMCoarse Zinc | DAILY 1HR MAX CO |
| PM2.5 CaO | PM2.5 Lead | PMCoarse Barium | 24h HNO3 |
| PM Coarse CaO | PMCoarse Lead | Sulfate | 24h NO3 |
| PM2.5 WS Chromium | PM2.5 Sulfur | PM2.5 Major Metal Oxides | DAILY 1HR MAX O3 |
| PM Coarse WS Chromium | PM2.5 Antimony | PMCoarse Major Metal Oxides | DAILY 8HR MAX O3 |
| PM2.5 Copper | PMCoarse Antimony | PM2.5 WS Metals | 100-1000 NM PN |
| PM Coarse Copper | PM2.5 Selenium | PMCoarse WS Metals | 100-1000 NM PAREA |
| PM2.5 WS Copper | PMCoarse Selenium | PM2.5 Nitrate | 10-100 NM PN |
| PM Coarse WS Copper | PM2.5 SiO2 | PMCoarse Nitrate | 10-100 NM PAREA |
| PM2.5 Fe2O3 | PMCoarse SiO2 | PM10 | 3-10 NM PN |
| PM Coarse Fe2O3 | PM2.5 Tin | PM2.5 | PMCoarse K2O |
| PM2.5 WS Iron | PMCoarse Sulfate | PM2.5 ACIDITY | PMCoarse TiO2 |
| PM Coarse WS Iron | PM2.5 Titanium | DAILY 8 HR MAX PM2.5 | EC |
| PM2.5 K2O | PM2.5 TiO2 | PMCOARSE MASS | … |
Pollutant Groupings: 11

- **alkene** (20 pollutants, including acetylene, butene, etc.)
- **combustible** (64 pollutants, including acetone, propane, toluene, etc.)
- **non-polar** (63 pollutants, including propane, OC, acetylene, benzene, etc.)
- **aromatic** (12 pollutants, including benzene, toluene, xylene, etc.)
- **acidic** (4 pollutants, including H\(^+\), sulfur, SO\(_2\), NO\(_2\))
- **inert** (44 pollutants, including CO, EC, 3-ethylhexane, i-butane, benzene, nitrate, S, ammonium, etc.)
- **microcrystalline oxide** (8 pollutants, including As, Ba, Br, Sb, Se, Ti, aluminum oxide, silicon oxide)
- **transition metal oxide** (8 pollutants, including Cu, Mn, Zn, Cr, Fe, Ni, V, Pb, Sn, Fe oxide)
- **polar** (10 pollutants, including acetic acid, acetone, benzaldehyde, 2-butanone, decanal, heptanal, hexanal, nonanal, octanal)
- **aldehyde** (6 pollutants, including benzaldehyde, decanal, heptanal, hexanal, nonanal, octanal)
- **alkanes** (27 pollutants, including butane, ethane, pentane, etc.)
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Approach: Second Stage

- A weighted least squares regression on a continuous response:

\[ b_j = \gamma u_j + \delta_j + \varepsilon_j \]

- \( u_j \): vector of pollutant category indicators (0/1 dummy variables)
- \( \gamma \): vector of coefficients representing the average increase in log odds ratios per mean IQR change in category’s pollutants
- \( \delta_j \): component-specific error with normal distribution of mean 0 and known variance equal to the variance-covariance matrix between pollutants obtained at the first stage of the model
- \( \varepsilon_j \): unknown, between-coefficient random errors

- Pollutant-specific betas from 1\textsuperscript{st} stage standardized by IQR in 2\textsuperscript{nd} stage

- Bootstrap method used to estimate 95% CI for \( \gamma \)
Air Pollution and CVD Hospital Admissions: All Year

Average increase in log odds ratio per average IQR increase in category pollutants; lag 0; 95% CI determined w/bootstrap methods

Average Gamma (95% CI)

-0.010
-0.005
0.000
0.005
0.010
0.015

Inert, Polar, Aromatic, Aldehyde, Alkanes, Acidic, Combustible, Transition Metal Oxides*10, Microcrystalline Oxides*10

Average increase in log odds ratio per average IQR increase in category pollutants; lag 0; 95% CI determined w/bootstrap methods
Pollutant–Specific Coefficients: 1st Stage

Distribution of pollutant-specific betas per IQR increase in pollutant levels; lag 0; Stage 1
**Air Pollution and CVD Hospital Admissions: Summer**

Average increase in log odds ratio per average IQR increase in category pollutants; lag 0; 95% CI determined w/bootstrap methods
Air Pollution and CVD Hospital Admissions: Winter

Gamma per IQR increase in pollutant concentration

Gamma (95% CI)

-0.020
-0.015
-0.010
-0.005
0.000
0.005
0.010
0.015
0.020

Winter

Group A
Group B

Inert, Polar, Aromatic, Aldehyde, Alkanes, Acidic, Combustible, Transition Metal Oxides *10, Microcrystalline Oxides *10

Gamma (95% CI)
Air Pollution and Respiratory Hospital Admissions: All Year

Average increase in log odds ratio per average IQR increase in category pollutants; lag 0; 95% CI determined w/ bootstrap methods.
Source–apportioned ambient PM$_{2.5}$ for CVD ED visits (Atlanta:Nov 1998–Dec 2002)

**Transition Metal (TM)**

**Sources:**
- Mobile sources
- Fuel Oil
- Smelters, incinerators, metal processing
- Crustal

**Biological Properties:**
- React w/oxygen to yield ROS
- ROS linked to adverse impacts (Lay et al., 1999; Ghio et al., 2000; Gonzalez–Flecha 2004; Rison et al., 2005; Dhalla et al., 2000)
- Studies found associations between TM and increased inflammation, oxidative stress (Park et al., 2006)
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The Air Quality Index (AQI): Is it a robust measure of air quality and health?

Sun Hwa Chung, Antonella Zanobetti, Helen Suh

Harvard School of Public Health
Today’s Air Quality

Air Quality Index 111
Health Category Unhealthy for Sensitive Groups

Pollutant concentration*

- O₃
- PM₂.₅
- SO₂
- NO₂
- CO

AQIs for pollutants

- O₃ 99
- PM₂.₅ 111
- SO₂ 25
- NO₂ 90
- CO 27

0 - 50 Good
51-100 Moderate
101-150 USG
151-200 Unhealthy
201-300 Very Unhealthy
301-500 Hazardous

NAAQS = 100
Objectives

- Examine the relation between AQI measures and short-term mortality
- Assess whether AQI is an appropriate exposure measure for air pollutant mixtures
- Several AQI measures:
  - Maximum AQI: Current US method
  - Aggregate AQI: Sum of individual pollutant AQI
  - Calculated based on US NAAQS and WHO guidelines
Study Areas: 6 MSAs

- Boston, MA
- Baltimore, MD
- Chicago, IL
- Philadelphia, PA
- Houston, TX
- Los Angeles, CA

US–Based AQI Values

Average AQI values of Individual Pollutants

Pollutants Determining Max AQI at Unhealthy categories

% Increase in Mortality *

Boston, MA

<table>
<thead>
<tr>
<th>Pollutants</th>
<th>O3</th>
<th>PM25</th>
<th>SO2</th>
<th>NO2</th>
<th>CO</th>
<th>Max</th>
<th>US</th>
<th>WHO</th>
<th>Agg</th>
</tr>
</thead>
</table>

Philadelphia, PA

<table>
<thead>
<tr>
<th>Pollutants</th>
<th>O3</th>
<th>PM25</th>
<th>SO2</th>
<th>NO2</th>
<th>CO</th>
<th>Max</th>
<th>US</th>
<th>WHO</th>
<th>Agg</th>
</tr>
</thead>
</table>

* Percent change in mortality by IQR increase of each variable
% Increase in Mortality *

Boston, MA

Philadelphia, PA

* Percent change in mortality by IQR increase of each variable
% Increase in Mortality *

Boston, MA

Philadelphia, PA

* Percent change in mortality by IQR increase of each variable
### Environmental Standards Scenarios

<table>
<thead>
<tr>
<th>Pollutants*</th>
<th>EPA NAAQS</th>
<th>WHO Final AQG</th>
</tr>
</thead>
<tbody>
<tr>
<td>O3</td>
<td>0.075</td>
<td>0.05</td>
</tr>
<tr>
<td>PM2.5</td>
<td>35</td>
<td>25</td>
</tr>
<tr>
<td>SO2</td>
<td>0.14</td>
<td>0.008</td>
</tr>
<tr>
<td>NO2</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>CO</td>
<td>9</td>
<td>9</td>
</tr>
</tbody>
</table>

* Averaging time: 24 hours for SO2 and PM2.5, 8 hours for O3 and CO, 1 hour for NO2
Units: ppm except PM2.5 (ug/m3)

- AQI of each pollutant were rescaled to the WHO guideline and calculated using the same method
Pollutants Determining Maximum US- and WHO-based AQI: Unhealthy Categories

<table>
<thead>
<tr>
<th>City</th>
<th>Boston</th>
<th>Philadelphia</th>
<th>Baltimore</th>
<th>Chicago</th>
<th>Houston</th>
<th>Los Angeles</th>
</tr>
</thead>
<tbody>
<tr>
<td>US NAAQS scenario</td>
<td>O3</td>
<td>PM25</td>
<td>SO2</td>
<td>NO2</td>
<td>CO</td>
<td></td>
</tr>
<tr>
<td>WHO AQS scenario</td>
<td>O3</td>
<td>PM25</td>
<td>SO2</td>
<td>NO2</td>
<td>CO</td>
<td></td>
</tr>
</tbody>
</table>
% Increase in Mortality *

Boston, MA

Philadelphia, PA

* Percent change in mortality by IQR increase of each variable
% Increase in Mortality *

Baltimore, MD

Chicago, IL

* Percent change in mortality by IQR increase of each variable

Pollutants | % Increase in Mortality |
--- | --- |
O3 | US | WHO |
PM25 | Max | Agg |
SO2 | Max | Agg |
NO2 | Max | Agg |
CO | Max | Agg |
% Increase in Mortality *

Houston, TX

Los Angeles, CA

* Percent change in mortality by IQR increase of each variable
AQI–Mortality Dose–Response

US

US

OHM

WHO

Baltimore, MD

Chicago, IL

% Change in Mortality

AQI Index

US

WHO

Agg

Max
AQI–Mortality Dose–Response

Houston, TX

Los Angeles, CA

US

WHO

Agg

Max

% Change in Mortality

AQI Index
Classification of Zones by Max AQI US and Agg AQI WHO

WHO-Based Aggregate AQI

US-Based Maximum AQI

Zone I

Zone 2

Zone 3

Healthy?

90th percentile

Referent

Unhealthy

0

100

200

300

0

400

800
% Increase in Mortality by Zone

Referent
Zone 1
Zone 2
Zone 3
Referent
Zone 1
Zone 2
Zone 3
Referent
Zone 1
Zone 2
Zone 3
Referent
Zone 1
Zone 2
Zone 3
Boston Philadelphia Baltimore Chicago Houston LA
Conclusions

• AQI was a robust exposure measure that captured daily variation in air pollution (vs. Individual pollutants)
  – Depends on air pollution mixture but less so on season
  – Less sensitive in the ozone-dominating cities

• Aggregate AQI was a robust and sensitive predictor of daily mortality risk as compared to maximum AQI)
  – Presented clear, linear dose–response relation with daily mortality

• Dose–response of US–based AQI tended to be flatten at higher values unlike WHO–based values
  – Perhaps due to behavior modification
  – False negatives (healthy) may be occur when maximum AQI values are depict healthfulness of air quality
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