Association of Short-term Exposure to Air Pollution With Mortality in Older Adults

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Background

- US National Ambient Air Quality Standards (NAAQS) for fine particulate matter ($PM_{2.5}$) and ozone every are reviewed every 5 years.
- 2012 annual and 24-hour NAQQS for $PM_{2.5}$ is 35 μg/m^3 and 12 μg/m^3.
- 2012 8-hour NAQQS for ozone is 70 ppb, no annual standard
- Studies in large metropolitan areas have provided evidence for short-term exposure to $PM_{2.5}$ and ozone were associated with mortality.

Aim and Objectives

- Aim to study the effect of short-term exposure below daily NAQQS, and in rural and unmonitored areas.
- Aim to study the effect on sensitive subgoups such as those with low socio-economic status.

Data source and participants

- Participants: all deaths among all Medicare benficiaries from 2000 to 2012.
- Outcome: all-cause mortality. Individuals with validated date of death between January 1, 2020 and December 31, 2012 were included.
- Exposure: daily 24-hour $PM_{2.5}$, 8-hour maximum ozone, and daily air and dew point temperatures. Monitored data from the EPA, satellite-based measurements, and other data sets. Neural networks were used to predict 24-hour PM2.5 and 8-hour maximum ozone concentrations.
- Warm season: April 1 to September 30, which is the specific time window to examine the association between ozone and mortality

Case-cross over design

- Usage: the design has been widely used to study the association between short-term air pollution exposure and the risk of an acute adverse health event.
- Main idea: for each individual case, exposure just before the event is compared with exposure at other control ("referent") times.
- Statistical method: Conditional logistic regression.

In this study

- Case day: date of the death.
- Control days: on the same day of the week as the case day to control for potential confounding effect by day of week; before and after the case day to control for time trend; only in the same month as the case day to control for seasonal and subseasonal.
- Time window: the death day and the day before death.

Statistical analysis

- Regression model included both pollutants as main effects and natural splines of air and dew point temperatures with 3 df to control for residual confounding by weather.
- Relative risk increase (RRI) was defined as RR $-$ 1.
- The absolute risk difference (ARD) of all-cause mortality associated with air pollution was defined as $\alpha \times (RR - 1)/RR$, where α denotes the baseline daily mortality rate.

Baseline characteristics

Table 1. Baseline Characteristics of Study Population (2000-2012)

Baseline Characteristic	Value
Case days, No.	22 433 862
Control days, No.	76 143 209
Among All Cases (n = 22 433 862), %	
Age at death, y	
≤69	10.38
70-74	13.37
75-84	38.48
≥85	37.78
Sex	
Male	44.73
Female	55.27
Race/ethnicity	
White	87.34
Black	8.87
Asian	1.03
Hispanic	1.51
Native American	0.31
Medicaid Eligibility (n = 22 433 862), %	

$PM_{2.5}$ times series

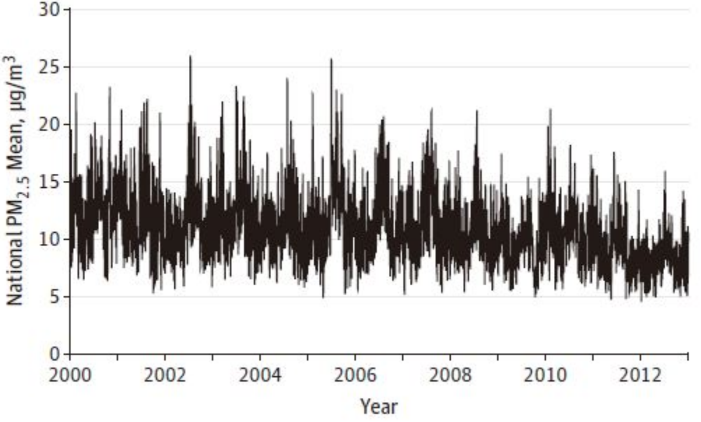


Figure 2: Daily mean fine particulate matter $PM_{2.5}$ concentrations

Ozone time series

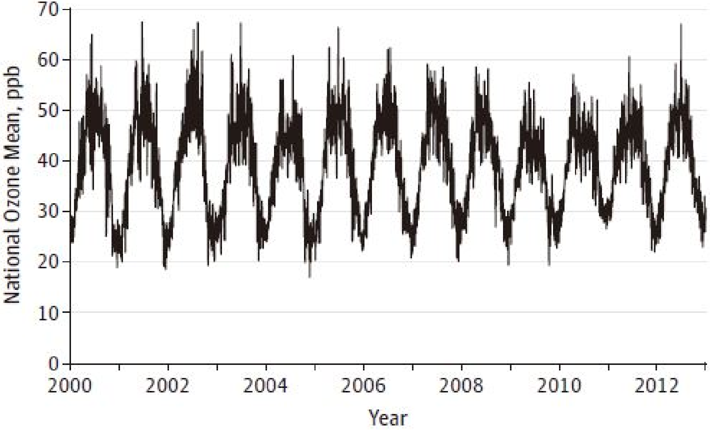


Figure 3: Daily mean 8-hour maximum ozone concentrations

Regression result

Table 2. Relative Risk Increase and Absolute Risk Difference of Daily Mortality Associated With Each 10-μg/m^3 Increase in $PM_{2.5}$ and Each 10-ppb Increase in Ozone

	Relative Risk Increase, % (95% CI)		Absolute Risk Difference in Daily Mortality Rates, No. per 1 Million Persons at Risk per Day (95% CI)[a]	
Air Pollutant Analysis	$PM_{2.5}$	Ozone[b]	$PM_{2.5}$	Ozone[b]
Main analysis[c]	1.05 (0.95-1.15)	0.51 (0.41-0.61)	1.42 (1.29-1.56)	0.66 (0.53-0.78)
Low-exposure analysis[d]	1.61 (1.48-1.74)	0.58 (0.46-0.70)	2.17 (2.00-2.34)	0.74 (0.59-0.90)
Single-pollutant analysis[e]	1.18 (1.09-1.28)	0.55 (0.48-0.62)	1.61 (1.48-1.73)	0.71 (0.62-0.79)
Nearest monitors analysis[f]	0.83 (0.73-0.93)	0.35 (0.28-0.41)	1.13 (0.99-1.26)	0.45 (0.37-0.53)

Abbreviations: $PM_{2.5}$, fine particulate matter; ppb, parts per billion.

[a] The daily baseline mortality rate was 137.33 per 1 million persons at risk per day; the warm-season daily baseline mortality rate was 129.44 per 1 million persons at risk per day.

[b] Ozone analyses included days from the warm season only (April 1 to September 30).

[c] The main analysis used the mean of daily exposure on the same day of death and 1 day prior (lag 01-day) as the exposure metric for both $PM_{2.5}$ and ozone, and controlled for natural splines of air and dew point temperatures with 3 *df*. The main analysis considered the 2 pollutants jointly included into the regression model and estimated the percentage increase in the daily mortality rate associated with a 10-μg/m^3 increase in $PM_{2.5}$ exposure adjusted for ozone and the percentage increase in daily mortality rate associated with a 10-ppb increase in warm-season ozone exposure adjusted for $PM_{2.5}$.

[d] The low-exposure analysis had the same model specifications as the 2-pollutant analysis and was constrained for days when $PM_{2.5}$ was below 25 μg/m^3 or ozone below 60 ppb.

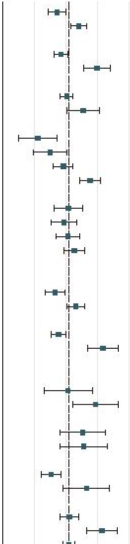
[e] The single-pollutant analysis estimated the percentage increase in the daily mortality rate associated with a 10-μg/m^3 increase in $PM_{2.5}$ exposure without adjusting for ozone and the percentage increase in the daily mortality rate associated with a 10-ppb increase in ozone exposure without adjusting for $PM_{2.5}$.

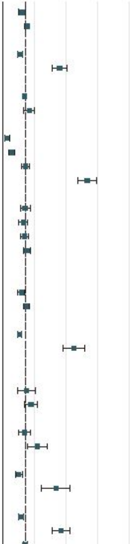
[f] $PM_{2.5}$ and ozone monitoring data were retrieved from the US Environmental Protection Agency Air Quality System, which provides the daily mean of $PM_{2.5}$ and daily 8-hour maximum ozone levels at each monitoring site. Daily ozone concentrations were averaged from April 1 to September 30. Individuals were assigned to the $PM_{2.5}$ and ozone levels from the nearest monitor site within 50 km. Those living 50 km from any monitoring site were excluded.

Subgroup analysis

Figure 3. Relative Risk Increase and Absolute Risk Difference of Daily Mortality Associated With 10-µg/m³ Increase in Fine Particulate Matter ($PM_{2.5}$)

Model	Relative Risk Increase in Mortality per 10-µg/m³ Increase in $PM_{2.5}$, % (95% CI)	P Value for Effect Modification	Absolute Risk Difference in Mortality, No. per 1 Million at Risk per Day (95% CI)	P Value for Effect Modification
Sex				
Male	0.86 (0.72-1.00)	[Reference]	1.24 (1.03-1.45)	[Reference]
Female	1.20 (1.07-1.33)	<.001[a]	1.56 (1.39-1.72)	.02[a]
Medicaid eligibility				
Noneligible	0.92 (0.81-1.03)	[Reference]	1.11 (0.98-1.24)	[Reference]
Eligible	1.49 (1.29-1.70)	<.001[a]	3.59 (3.11-4.08)	<.001[a]
Race/ethnicity				
White	1.01 (0.91-1.12)	[Reference]	1.38 (1.24-1.52)	[Reference]
Nonwhite	1.27 (1.01-1.53)	.07	1.69 (1.34-2.03)	.11
Age, y				
≤69	0.55 (0.25-0.86)	[Reference]	0.27 (0.12-0.42)	[Reference]
70-74	0.75 (0.48-1.01)	.35	0.57 (0.37-0.78)	.02[a]
75-84	0.96 (0.80-1.11)	.02[a]	1.46 (1.23-1.69)	<.001[a]
≥85	1.38 (1.23-1.54)	<.001[a]	5.35 (4.75-5.95)	<.001[a]
Population density				
Low	1.04 (0.81-1.27)	[Reference]	1.43 (1.12-1.74)	[Reference]
Medium low	0.97 (0.76-1.17)	.64	1.31 (1.04-1.58)	.56
Medium high	1.03 (0.84-1.22)	.95	1.39 (1.14-1.65)	.86
High	1.13 (0.97-1.30)	.52	1.54 (1.31-1.77)	.57
Whites				
Sex				
Male	0.83 (0.67-0.99)	[Reference]	1.19 (0.97-1.42)	[Reference]
Female	1.16 (1.02-1.30)	.002[a]	1.51 (1.33-1.70)	.03[a]
Medicaid eligibility				
Noneligible	0.88 (0.77-1.00)	[Reference]	1.07 (0.93-1.21)	[Reference]
Eligible	1.58 (1.34-1.83)	<.001[a]	4.49 (3.81-5.17)	<.001[a]
Nonwhites				
Sex				
Male	1.03 (0.65-1.42)	[Reference]	1.52 (0.96-2.08)	[Reference]
Female	1.47 (1.12-1.82)	.01	1.80 (1.37-2.22)	.44
Medicaid eligibility				
Noneligible	1.26 (0.91-1.62)	[Reference]	1.40 (1.01-1.79)	[Reference]
Eligible	1.28 (0.90-1.66)	.94	2.21 (1.56-2.85)	.04[a]
Medicaid eligibility, males				
Noneligible	0.77 (0.61-0.93)	[Reference]	1.03 (0.82-1.24)	[Reference]
Eligible	1.32 (0.96-1.69)	.006	3.37 (2.45-4.28)	<.001[a]
Medicaid eligibility, females				
Noneligible	1.06 (0.90-1.21)	[Reference]	1.17 (1.00-1.33)	[Reference]
Eligible	1.57 (1.32-1.82)	<.001[a]	3.69 (3.12-4.26)	<.001[a]
Overall	1.05 (0.95-1.15)		1.42 (1.30-1.55)	





subgroup analysis

$$Z = \frac{RR_{\text{male}} - RR_{\text{female}}}{\sqrt{se(RR_{\text{male}})^2 + se(RR_{\text{female}})^2}}$$

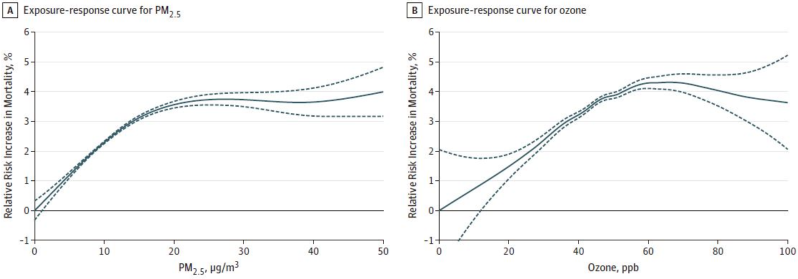
Figure 5: subgroup analysis of Ozone

p-value

two sample test $Z = \frac{RR_{male} - RR_{female}}{\sqrt{(se(RR_{male})^2 - se(RR_{female})^2)}}$

Dose-response

Figure 5. Estimated Exposure-Response Curves for Short-term Exposures to Fine Particulate Matter ($PM_{2.5}$) and Ozone



A 2-pollutant analysis with separate penalized splines on $PM_{2.5}$ (A) and ozone (B) was conducted to assess the percentage increase in daily mortality at various pollution levels. Dashed lines indicate 95% CIs. The mean of daily exposure on the same day of death and 1 day prior (lag 01-day) was used as metrics of exposure to $PM_{2.5}$ and ozone. Analysis for ozone was restricted to the warm season (April to September). Ppb indicates parts per billion.

Figure 6: Estimated Exposure-Response Curves for Short-term Exposures to Fine Particulate Matter ($PM_{2.5}$) and Ozone

Conclusions

In the US Medicare population from 2000 to 2012, short-term exposures to $PM_{2.5}$ and warm-season ozone were significantly associated with increased risk of mortality. This risk occurred at levels below current national air quality standards, suggesting that these standards may need to be reevaluated.

Thanks!
Today Slides and Articles

Bi-directional sampling

$P(D|E) = 0.001$ and $P(D|\bar{E})$

	Period 1				Period 2			
Community 1	E	1002	D	2				
			D̄	1000	Ē	1000	D	1
							D̄	999
Community 2	Ē	2002	D	2				
			D̄	2000	E	2000	D	4
							D̄	1996

Risk in each time period is 0.001 for unexposed subjects, 0.002 for exposed subjects. True risk ratio is 2.

	Control		
		Exposed	Unexposed
case	Exposed	0	4
	Unexposed	1	0

$\text{OR}_{mh} = 4$ $\text{OR}_{true} = 2$

	Control		
		Exposed	Unexposed
case	Exposed	0	6
	Unexposed	3	0

$\text{OR}_{mh} = 2$

Bi-directional sampling

	Control		
		Exposed	Unexposed
case	Exposed	0	6
	Unexposed	3	0

$\mathrm{OR}_{mh} = 2$

Bi-directional sampling

$$E \to \bar{E} \to E$$
$$\bar{E} \to E \to \bar{E}$$

$\mathsf{OR}_{mh} = 1$

$$E \to \bar{E} \to \bar{E}$$

$$\bar{E} \to E \to E$$

$\mathsf{OR}_{mh} = 4$