Original Contribution

Association of Ambient Fine Particles With Out-of-Hospital Cardiac Arrests in New York City

Robert A. Silverman*, Kazuhiko Ito, John Freese, Brad J. Kaufman, Danilynn De Claro, James Braun, and David J. Prezant

* Correspondence to Dr. Robert A. Silverman, Long Island Jewish Medical Center, 270-05 76th Avenue, Queens, NY 11040 (e-mail: aresilv@aol.com; rsilverm@lij.edu).

Cardiovascular morbidity has been associated with particulate matter (PM) air pollution, although the relation between pollutants and sudden death from cardiac arrest has not been established. This study examined associations between out-of-hospital cardiac arrests and fine PM (of aerodynamic diameter $\leq$2.5 μm, or $PM_{2.5}$), ozone, nitrogen dioxide, sulfur dioxide, and carbon monoxide in New York City. The authors analyzed 8,216 out-of-hospital cardiac arrests of primary cardiac etiology during the years 2002–2006. Time-series and case-crossover analyses were conducted, controlling for season, day-of-week, same-day, and delayed/apparent temperature. An increased risk of cardiac arrest in time-series (relative risk (RR) = 1.06, 95% confidence interval (CI): 1.02, 1.10) and case-crossover (RR = 1.04, 95% CI: 0.99, 1.08) analysis for a $PM_{2.5}$ increase of 10 μg/m^3 in the average of 0- and 1-day lags was found. The association was significant in the warm season (RR = 1.09, 95% CI: 1.03, 1.15) but not the cold season (RR = 1.01, 95% CI: 0.95, 1.07). Associations of cardiac arrest with other pollutants were weaker. These findings, consistent with studies implicating acute cardiovascular effects of PM, support a link between $PM_{2.5}$ and out-of-hospital cardiac arrests. Since few individuals survive an arrest, air pollution control may help prevent future cardiovascular mortality.

air pollution; death, sudden, cardiac; emergency medical services; particulate matter

Abbreviations: PM, particulate matter; $PM_{2.5}$, particulate matter of aerodynamic diameter $\leq$2.5 μm.

Fine particulate matter (PM; particles with an aerodynamic diameter of $\leq$2.5 μm, or $PM_{2.5}$) consists of a mixture of chemical constituents generated by various combustion sources, including traffic and coal-fired power plants. Fine PM constituents vary by region and by season, depending on the relative strength of sources (1). It is estimated that in 2007 1 in 3 people in the United States lived in areas where $PM_{2.5}$ reached levels that are considered unhealthy (2). A number of reports have demonstrated a relation between ambient PM and cardiovascular morbidity and mortality (3, 4), including an increased risk of hospitalizations for ischemic heart disease, heart failure, and ventricular dysrhythmias after short-term exposure to fine particles (5). Reviews of time-series, case-crossover, and other study designs find no evidence of a safe threshold of fine particulate air pollution, and the exposure-response relation with cardiovascular health effects is near linear across reported ranges of exposure (6).

Sudden cardiac arrest accounts for more than half of all deaths of primary cardiac etiology in the United States (7), and more than 95% of sudden cardiac arrest victims do not survive to hospital discharge (8). A time-series study in New York City found an association between PM and overall cardiovascular mortality, although the study did not specifically address out-of-hospital cardiac arrests (9). Since acute ischemic events and ventricular dysrhythmias predispose to sudden death from cardiac arrests, it is hypothesized that ambient PM is a risk factor for out-of-hospital cardiac arrest. To date, however, studies that examined associations between PM and out-of-hospital cardiac arrest have shown conflicting results (10–13).

In this study we utilized a large, multiyear data set to examine the association between air pollution and out-of-hospital cardiac arrest in New York City. Our main interest was the effect of ambient $PM_{2.5}$, but we also examined ozone because of reports linking it with overall cardiovascular mortality (14). Since nitrogen dioxide is a marker of air pollution from local combustion sources (primarily motor vehicle traffic), and because recent multicity studies from Canada and Europe have suggested short-term total mortality effects (15, 16), we also evaluated the association of nitrogen dioxide with cardiac arrest. Sulfur dioxide and carbon monoxide have been shown to be more spatially variable (i.e., with an expected large exposure misclassification error) than $PM_{2.5}$, ozone, and nitrogen dioxide in the New York City metropolitan area (17); interpreting sulfur dioxide and carbon monoxide levels requires caution, but we analyzed these pollutants for reference purposes.

MATERIALS AND METHODS

Air pollution and weather data

Data from 33 $PM_{2.5}$, 16 ozone, 15 nitrogen dioxide, 14 sulfur dioxide, and 19 carbon monoxide monitors within the 20-mile (32-km) radius of the geographic center of New York City were retrieved from the US Environmental Protection Agency's Air Quality System. We computed the average of multiple monitors' data, using the 24-hour average values for $PM_{2.5}$, nitrogen dioxide, sulfur dioxide, and carbon monoxide and the daily 8-hour maximum values for ozone. The 24-hour average weather variables for LaGuardia Airport (New York) were obtained from the National Climatic Data Center.

Cardiac arrest data

We extracted medical records from a database of out-of-hospital cardiac arrest cases collected by the Emergency Medical Service of the Fire Department of New York City for the years 2002–2006. Study physicians evaluated the records to categorize the presumptive etiology of cardiac arrest utilizing the Utstein criteria for standardization of event reporting (18). We included only cardiac arrests presumed to be of primary cardiac etiology where resuscitation was attempted by paramedics in the prehospital setting.

Statistical analysis

Both time-series and case-crossover analyses were conducted to address the sensitivity of results to model uncertainty. The main difference between the 2 methods is that in the case-crossover analysis with a time-stratified referent sampling, the day-of-week and seasonal trends are adjusted by design, whereas in the time-series design these factors "compete" with the exposure variables in the model. An a priori exposure window averaging 0- and 1-day lagged air pollution levels was used (for each pollutant separately) for the main analysis, and we examined individual lag days 0 through 3 as a sensitivity analysis. Since the exposure conditions and compositions of $PM_{2.5}$ change across seasons, analyses were also conducted by season (warm season: April–September; cold season: October–March). Risk estimates were computed for an interquartile-range increment of air pollutants, which provides the magnitude-of-risk estimates that are comparable across the pollutants. Data were analyzed using the R statistical package (19).

For the time-series analysis, a Poisson generalized linear model was used to estimate the impact of air pollutants, adjusting for weather effects, seasonal/temporal trends, and day of week and accommodating overdispersion. We used natural cubic splines of days to adjust for potentially confounding temporal trends and seasonal cycles. The choice of the degrees of freedom for this temporal adjustment term (7 degrees of freedom per year) was based on the examination of the sum of absolute values of partial autocorrelation function of residuals (20). To adjust for immediate and delayed nonlinear temperature effects, natural cubic splines of the same-day and the average of past 2- and 3-day apparent temperatures were included in the model with 3 degrees of freedom over the range for each term. Apparent temperature was computed from temperature and dewpoint using the equation given by Steadman (21) to model the body's perceived temperature incorporating both temperature and humidity.

For the case-crossover analysis, we used a conditional logistic regression model with the time-stratified referent day sampling scheme in which a case was matched with control days from the same month of the year and the same day of the week (22). We included the same apparent temperature smoothing terms as in the time-series model described above. All estimated risks are expressed as relative risk rather than odds ratio, even for the case-crossover result. This is because of the equivalence of the time-series design and case-crossover design in a large population context (23), with the assumption that exposure for a given day is similar for all persons in the city.

RESULTS

A total of 8,216 cardiac arrest cases met inclusion criteria and were used in the analysis. The average age was 65.6 years, with slightly more men than women (Table 1). Table 2 shows the distribution of air pollution variables for the entire year and by season during the study period. As expected, ozone levels were much higher in the warm season than in

Table 1. Characteristics of the Study Population with Out-of-Hospital Cardiac Arrests in New York City, 2002–2006

	No.	%
All	8,216	100
Sex		
Male	4,261	51.9
Female	3,955	48.1
Age, years		
<40	484	5.9
40–69	3,293	40.1
≥70	4,439	54.0

Table 2. Distribution of Air Pollution Variables (Warm Season: April–September; Cold Season: October–March) in New York City, 2002–2006

	5%	25%	50%	75%	95%
PM$_{2.5}$, μg/m^3					
All year	5	8	12	18	30
Warm	5	8	12	19	31
Cold	5	7	12	17	28
O$_3$, ppb					
All year	7	18	28	40	67
Warm	20	31	40	51	75
Cold	4	12	19	26	35
NO$_2$, ppb					
All year	15	21	27	32	43
Warm	14	20	26	31	42
Cold	17	23	28	34	44
SO$_2$, ppb					
All year	2.0	3.8	6.3	9.6	18.0
Warm	1.8	3.0	4.2	6.0	8.8
Cold	3.6	6.6	9.3	13.2	21.6
CO, ppm					
All year	0.6	0.7	0.9	1.0	1.5
Warm	0.6	0.7	0.8	1.0	1.3
Cold	0.6	0.7	0.9	1.1	1.6

Abbreviations: CO, carbon monoxide; NO$_2$, nitrogen dioxide; O$_3$, ozone; PM$_{2.5}$, particulate matter of aerodynamic diameter <2.5 μm; SO$_2$, sulfur dioxide.

the cold season, whereas PM$_{2.5}$ and nitrogen dioxide levels showed little seasonal differences. Sulfur dioxide levels were consistently higher in the cold season. Table 3 shows correlations among air pollutants and apparent temperature by season. PM$_{2.5}$ was moderately correlated with nitrogen dioxide, ozone, and apparent temperature in the warm season. During the cold season, ozone was negatively correlated with PM$_{2.5}$, nitrogen dioxide, sulfur dioxide, and carbon dioxide.

Table 3. Correlation Matrix Among Air Pollutants and Apparent Temperature by Season in New York City, 2002–2006

	PM$_{2.5}$	O$_3$	NO$_2$	SO$_2$	CO	AT
PM$_{2.5}$	1.00	−0.43	0.77	0.66	0.67	0.02
O$_3$	0.61	1.00	−0.38	−0.49	−0.44	0.12
NO$_2$	0.54	0.34	1.00	0.68	0.68	−0.05
SO$_2$	0.51	0.43	0.68	1.00	0.45	−0.41
CO	0.40	0.03	0.61	0.35	1.00	0.09
AT	0.51	0.46	0.05	−0.04	0.11	1.00

Abbreviations: AT, apparent temperature; CO, carbon monoxide; NO$_2$, nitrogen dioxide; O$_3$, ozone; PM$_{2.5}$, particulate matter of aerodynamic diameter <2.5 μm; SO$_2$, sulfur dioxide.
Upper diagonal shows correlation during cold season; lower diagonal shows correlation during warm season.

Table 4 shows relative risks of cardiac arrest for PM$_{2.5}$ estimated from both time-series and case-crossover analyses. The risk of a cardiac arrest was significantly higher when PM$_{2.5}$ levels were elevated. For a PM$_{2.5}$ increase of 10 μg/m^3 in the average of 0- and 1-day lags, the increased relative risk for a cardiac arrest was 1.06 (95% confidence interval: 1.02, 1.10) using a time-series design and 1.04 (95% confidence interval: 0.99, 1.08) using a case-crossover design. These associations between cardiac arrest and PM$_{2.5}$ were found only in the warm-weather seasons, and there was no apparent PM$_{2.5}$-related increase in arrests during the cold season (Table 4). There were no differences in risk between men and women or between older (ages 70 years) and younger (ages 40–69 years) adults in the all-year or seasonal analyses. These patterns of associations were similar between the time-series and case-crossover analyses, though the risk estimates obtained using the case-crossover method were generally slightly smaller than those from the time-series method.

In the sensitivity analysis of lagged associations using single-day lags, we found that PM$_{2.5}$ was positively associated at lag 0 and 1 days. The association decreased at lag day 2 and fell to null at lag day 3 (Figure 1). The estimated lag day 1 risk for cardiac arrests was similar to the lag day 0, indicating that elevated pollution levels closely preceding the event had the stronger associations. A similar pattern of lagged associations was found in the warm season, but, in the cold season, only the same-day PM$_{2.5}$ showed a positive association (results not shown).

Among the all-year time-series analysis data for the 5 pollutants, only PM$_{2.5}$ had statistically significant associations with cardiac arrests (Figure 2). The associations of each pollutant with cardiac arrest appeared stronger in warm-weather months, although, even in the warm weather, only PM$_{2.5}$ had a statistically significant association.

DISCUSSION

We found an association between ambient fine particle concentrations and out-of-hospital cardiac arrests in New York City. For an increase of 10 μg/m^3 in PM$_{2.5}$, there was a 4%–10% increase in the number of arrests. This study indicates that the consequences of air pollution can be acute and severe. Since an out-of-hospital arrest is usually fatal, with approximately 5% of patients surviving to hospital discharge, an increase in cardiac arrests can be considered an increase in cardiac fatalities. The likelihood of being resuscitated from an out-of-hospital cardiac arrest in large metropolitan areas is among the lowest, with survival ranging from about 1% to 3% (24, 25).

A number of previous studies have linked short-term exposure to PM with the development of acute ischemic heart disease and dysrhythmia. The possible pathobiologic mechanisms include increased platelet aggregation and clotting potential (26), inflammatory mediators, and C-reactive protein (27). PM is associated with dysregulation of the cardiac autonomic nervous system, including increased heart rate and reduced heart rate variability (28). Among individuals at high risk for sudden death with implanted defibrillators,

Table 4. Relative Risk of Cardiac Arrest per Interquartile-Range Increment Increase (10 μg/m³) of the Average of 0- and 1-Day PM₂.₅ in New York City, 2002–2006

Category and Period	Relative Risk Estimated Using Time-Series Analysis	95% CI	Relative Risk Estimated Using Case-Crossover Analysis	95% CI
All ages				
All year	1.06	1.02, 1.10	1.04	0.99, 1.08
Warm	1.09	1.03, 1.15	1.08	1.02, 1.15
Cold	1.01	0.95, 1.07	0.99	0.93, 1.06
Male, all ages				
All year	1.06	1.01, 1.13	1.04	0.98, 1.10
Warm	1.10	1.02, 1.18	1.09	1.01, 1.18
Cold	1.02	0.94, 1.11	0.99	0.90, 1.08
Female, all ages				
All year	1.05	0.99, 1.11	1.03	0.97, 1.10
Warm	1.07	0.98, 1.16	1.05	0.96, 1.14
Cold	1.00	0.92, 1.09	1.01	0.92, 1.11
Aged 40–69 years				
All year	1.04	0.97, 1.10	1.02	0.95, 1.10
Warm	1.06	0.97, 1.17	1.05	0.95, 1.15
Cold	1.00	0.91, 1.09	1.00	0.90, 1.11
Aged ≥70 years				
All year	1.06	1.00, 1.12	1.03	0.97, 1.09
Warm	1.09	1.01, 1.18	1.06	0.98, 1.15
Cold	1.00	0.92, 1.09	0.99	0.91, 1.08

Abbreviations: CI, confidence interval; PM₂.₅, particulate matter of aerodynamic diameter <2.5 μm.

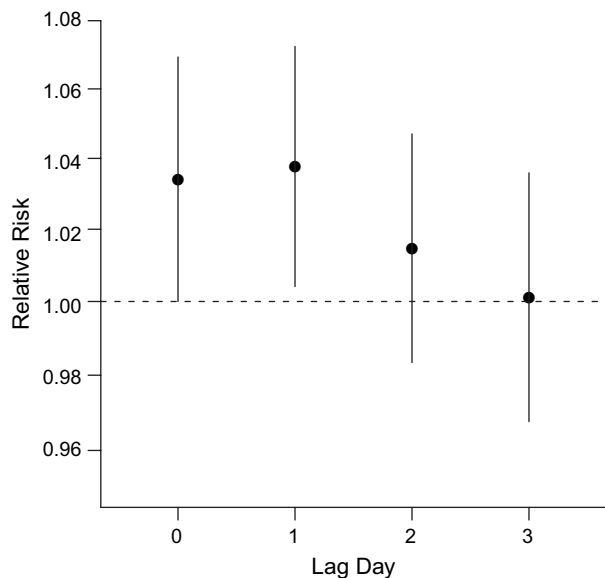an increased frequency of recorded ventricular dysrhythmias occurs with increasing ambient pollution (29, 30).

Figure 1. Lagged associations between particulate matter of aerodynamic diameter <2.5 μm (PM₂.₅) and cardiac arrests. The days 0–3 lagged associations between PM₂.₅ (per interquartile-range increase, 10 μg/m³) and cardiac arrests for all year using time-series design, New York City, 2002–2006.

Short-term exposure to PM is also associated with myocardial infarction, and the risk for an acute infarction increases with greater exposure (31, 32).

The data that implicate PM as a risk factor for acute coronary ischemia support our findings of PM₂.₅ as a risk for cardiac arrest, since sudden cardiac arrest most typically occurs in individuals with underlying ischemic heart disease (33). Those with known coronary artery disease, as well as elderly individuals, are more likely to have ST depression when stressed on higher pollution days (PM₂.₅ or black carbon), suggesting that those most vulnerable to developing ischemia are impacted more by pollution (34). Additional evidence comes from a controlled study in which men with established coronary heart disease developed acute cardiac ischemia after a brief exposure to dilute diesel exhaust (35).

There are conflicting findings in the literature on whether pollution increases the risk of sudden death. Similar to our findings, an analysis in Rome, Italy, of 5,144 cases found associations between PM indices (estimated particle number concentration and particles with an aerodynamic diameter of ≤10 μm, or PM₁₀) and out-of-hospital cardiac deaths (12). The link between pollution and particle number concentration was stronger in the elderly. While the particle number concentration was indirectly estimated in that study, it is considered a good surrogate of ultrafine particles (which are produced mostly by local traffic) (36). Additional support comes from 2 other studies where deaths that occurred
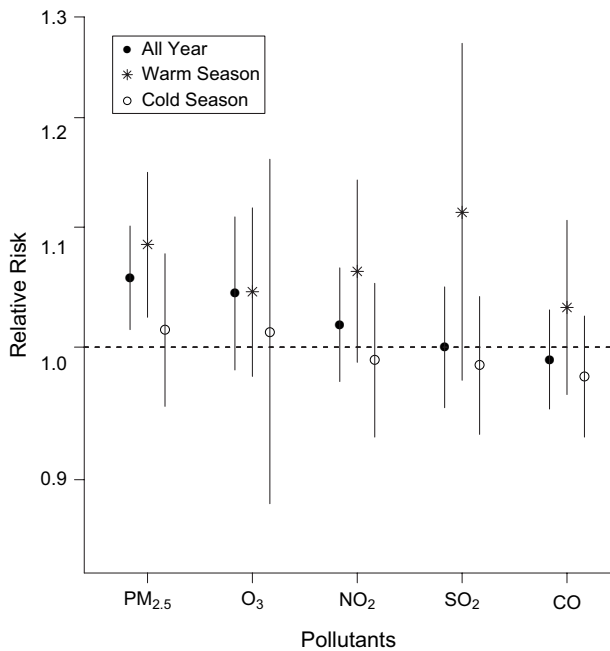
Figure 2. Seasonal cardiac arrest relative risk for air pollutants. Relative risk of cardiac arrest per interquartile-range (IQR) increase in the average of 0- and 1-day lagged air pollutants using Poisson time-series design, New York City, 2002–2006. The IQR increments are 10 μg/m^3 for particulate matter of aerodynamic diameter $\leq$2.5 μm (PM$_{2.5}$), 22 parts per billion (ppb) for ozone (O$_3$), 11 ppb for nitrogen dioxide (NO$_2$), 6 ppb for sulfur dioxide (SO$_2$), and 0.3 parts per million for carbon monoxide (CO). Warm season is April through September. Cold season is October through March.

outside of hospitals (all-cause mortality) were more strongly associated with air pollution than deaths in hospitals (37, 38). A study of sudden death from Indianapolis, Indiana, did not find associations between daily PM$_{2.5}$ and cases (n = 1,374) but did report associations between the hourly data of PM$_{2.5}$ exposure and the cardiac arrests witnessed by bystanders (n = 511) (13). Since both cardiac arrest and PM$_{2.5}$ likely have diurnal patterns, such analysis may have more accurate exposure characterization but at the same time may also reflect temporal confounding not present in the daily data.

In contrast, 2 studies of 362 and 1,206 cases from the Seattle, Washington, area that examined out-of-hospital sudden death showed no associations between fine particles (as measured by nephelometer) and cardiac arrests (10, 11). Associations between fine particles and the onset of acute myocardial infarction (5,793 cases) were evaluated in King County, Washington (39), and, in contrast to other reports evaluating acute myocardial infarction, no association was found (31, 32). Since health effects are known to vary by PM composition (and therefore by region), a possible explanation for the lack of association between fine particles and cardiac arrest in the Seattle area may be the local PM composition, which is lower in sulfate and transition metal content than northeast US cities (11). Further support for region-specific health effects is found in a study of

PM$_{2.5}$-mortality associations in 27 US cities (40), where PM$_{2.5}$ was associated with all-cause mortality in Manhattan (i.e., New York County, the only New York City county analyzed in that study) but not in Seattle.

We found that significant associations between fine particles and out-of-hospital cardiac arrests appear to be found mainly in the warm season. This is consistent with several analyses of PM and all-cause mortality in which the strongest associations were found in summer (40–43). The reasons are not known, but there are several possible explanations. The stronger association in the warm season may be related to the higher penetration rate of outdoor PM into indoors (44). In addition, among studies of specific PM components and mortality in Phoenix, Arizona (45), and Washington, DC (46), sulfate-related PM showed the strongest associations among the source-apportioned PM components. One possible explanation is that sulfate particles are more harmful; another potential explanation is that a higher warm-weather rate of photochemical conversion from sulfur dioxide to sulfuric acid may make transition metals more water soluble and therefore more bioavailable to cells (47).

We also analyzed cardiac arrests relative to changes in ozone, nitrogen dioxide, sulfur dioxide, and carbon monoxide but found that these gaseous pollutants' associations with cardiac arrest were weaker than that for PM$_{2.5}$. In our study, ozone was not significantly associated with out-of-hospital cardiac arrest. This contrasts with the positive and significant association other studies found with ozone for all-cause or circulatory mortality in New York City (9, 48). One possible explanation is that our study is far smaller in terms of daily counts (~4.4 cardiac arrest/day) compared with daily mortality for all-cause (~180/day) or circulatory mortality (~87/day), limiting its statistical power. Nitrogen dioxide was also not significantly associated with cardiac arrest in our analysis, but the magnitude of risk estimate for the warm season was similar to the trend of increased risk found in Rome (12). In the Rome study, carbon monoxide was significantly associated with cardiac deaths but in our study was not. The lack of associations for carbon monoxide and sulfur dioxide in our study may be due in part to the expected larger exposure misclassification for these pollutants compared with PM$_{2.5}$, ozone, or nitrogen dioxide (17), as representativeness of exposures relevant to the residents for these local combustion sources may vary from city to city.

In using both time-series and case-crossover designs, the risk estimates in our study results from case-crossover analysis were slightly less significant, which was expected. The time-stratified referent day sampling scheme (the same day of week in the same month/year) in the case-crossover method we applied effectively uses 12 degrees of freedom/year, as compared with 7 degrees of freedom/year for time-series design, to adjust for season/temporal trends and may explain the slightly smaller risk estimates in the case-crossover result. A recent study compared time-series, case-crossover, and extended Cox regression designs in an analysis of a cohort of myocardial infarction survivors in 5 European cities to assess the probability of recurrent hospitalizations (49). These methods gave similar results, and findings suggested that time-series analysis might also be most practical. Since

time-series analysis involves selection of degrees of freedom for temporal adjustment, case-crossover analysis provides an alternative to ensure that the result is not dependent on model specifications. However, a recent study that discussed the equivalency of these 2 methods pointed out that the case-crossover analysis does not account for overdispersion of the Poisson variance (23). Thus, while the 2 methods may produce generally similar results, they may be used as model-checking methods for each other.

Among study limitations, the derivation of this data set comes from only cases treated by paramedics of the Fire Department of New York City and not by voluntary ambulance crews. Though the data set represents the majority of calls within the 5 boroughs, the New York City 911 system comprises not only the Fire Department of New York City but also a number of voluntary hospital ambulance systems, representing 65% and 35% of the available paramedic units, respectively. We do not suspect the data would be biased based on whether a municipal or a voluntary ambulance crew responded to the call, especially since our endpoint was cardiac arrest and not death. In addition, we did not follow patients to either admission to or discharge from the hospital. For large cities, however, because an out-of-hospital cardiac arrest almost always results in death, the arrest endpoint is nearly equivalent and, regardless, represents a substantial cardiac event.

In conclusion, fine particles are associated with an increased risk of sudden out-of-hospital cardiac arrests. These observations are supported by previous data linking ischemic heart disease and dysrthymias with PM. Since few individuals survive an out-of-hospital cardiac arrest, controlling air pollution may be a preventable means to decrease cardiovascular mortality.

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