Effects of Fine Particulate Matter on Daily Mortality for Specific Heart Diseases in Japan

Kayo Ueda, MD; Hiroshi Nitta, DHSc; Masaji Ono, DHSc*

Background: It is thought that biological responses to air pollutants affect various heart diseases, with the magnitude of the effect dependent on the specific disease. The short-term effects of fine particulate matter (PM$_{2.5}$) on mortality for heart diseases were examined in 9 Japanese cities from 2002 to 2004.

Methods and Results: Mortality data obtained from the Ministry of Health, Labour and Welfare of Japan and PM$_{2.5}$ data from the National Institute for Environmental Studies were used in a generalized linear model to evaluate the association between PM$_{2.5}$ concentration and the mortality, adjusted for ambient temperature, relative humidity, seasonality, and day of the week. The area-specific results were combined using meta-analysis with a random-effects model. Of 67,897 deaths from heart disease, a significantly positive association was observed between heart disease mortality and PM$_{2.5}$ at lag 0. In the age-stratified analyses, the effect of PM$_{2.5}$ on acute myocardial infarction, and cardiac arrhythmia and conduction disorders was stronger at lag 0 for the younger population (0-64 years). The associations were not clear in mortality of the elderly.

Conclusions: Positive associations between PM$_{2.5}$ and heart disease mortality in Japan were observed. The effects of PM$_{2.5}$ may vary by disease and age. (*Circ J 2009; 73: 1248–1254)

Key Words: Air pollution; Heart disease; Mortality; Particulate matter

Numerous epidemiological studies, mainly from North America and Europe, have compiled evidence indicating the detrimental effects of air pollutants. Of those pollutants, acute exposure to an elevated concentration of particulate matter (PM), a complex mixture of particles with various sizes and composition, has been associated with cardiovascular mortality and cardiologists are paying increasing attention to its cardiotoxic effects. Although those studies focused on the effects of PM on overall cardiac mortality, the effects on mortality from specific heart diseases remain unclear. Inhaled PM causes various biological responses, such as alterations in sympathetic nervous system activity, systemic inflammation, an increase in fibrinogen, and arterial vasoconstriction, which subsequently lead to acute coronary syndrome, cardiac arrhythmia, and other cardiac diseases. It is possible that the magnitude of the effects and the time course differ according to the specific heart disease.

Suspended PM [SPM: particles $<$10 $\mu$m in aerodynamic diameter with a 100% cut-off level] is regularly monitored in Japan. Murakami and Ono examined the short term effects of SPM on myocardial infarction (MI) deaths in Tokyo from 1990–1996. In their analysis, they observed increased mortality from MI within only a few hours after elevated concentrations of SPM. The level of PM in Tokyo during the early 1990s was higher than at present. In addition, it has been suggested that smaller particles can reach alveoli without being trapped in the upper respiratory tract and may have a greater health impact than larger particles. Therefore, assessing the health effects of different particle sizes is another subject of interest.

Some recent studies on air pollution epidemiology have focused on the factors that could strengthen or weaken the effects of air pollutants. Of these factors, it has been shown that age can modify the effects of PM$_{10-12}$ so it is possible that disease onset and time to death can also be influenced by age.

In this study, we assessed the effects of fine PM [particles $<$2.5 $\mu$m in aerodynamic diameter (PM$_{2.5}$)], on mortality from acute MI, heart failure (HF), and cardiac arrhythmias in Japan. We analyzed the data by 3 age categories and evaluated the differences in the PM$_{2.5}$ effect on each heart disease between the age groups.

Methods

Study Areas

The Steering Committee of the Japanese Ministry of the Environment conducted a comprehensive investigation of the health effects of PM$_{2.5}$ exposure, which was released in a 2007 report. The present study involved 3 components: (1) exposure assessment for distribution of PM$_{2.5}$ concentration in both urban and rural areas in Japan, (2) epidemiologic study to compile the evidence on the health effects of PM$_{2.5}$, and (3) toxicological assessment of PM$_{2.5}$ using animal models. The short-term effects of PM$_{2.5}$ on daily mortality in Japan from 2002 to 2004 were investigated in the epidemiological study. We selected 9 areas with a population greater than 500,000 residents for the study. In those areas, the concentration of PM$_{2.5}$ has been regularly monitored by the Ministry of the Environment since 2001.
Table 1. Demographic Statistics of Mortality From Heart Disease in 9 Areas of Japan, 2002–2004

<table>
<thead>
<tr>
<th>Area</th>
<th>Tokyo</th>
<th>Osaka</th>
<th>Nagoya</th>
<th>Kobe</th>
<th>Sapporo</th>
<th>Fukuoka</th>
<th>Kawasaki</th>
<th>Sakai</th>
<th>Sendai</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of cardiac deaths</td>
<td>28,765</td>
<td>9,395</td>
<td>8,256</td>
<td>5,178</td>
<td>4,767</td>
<td>3,146</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Rates per 100,000*</td>
<td>115.4</td>
<td>119.8</td>
<td>125.5</td>
<td>114.4</td>
<td>85.8</td>
<td>76.5</td>
<td>80.4</td>
<td>107.6</td>
<td>85.4</td>
</tr>
<tr>
<td>Daily mean no. of cardiac deaths (min–max)</td>
<td>8.7 (0–40)</td>
<td>2.9 (0–16)</td>
<td>2.5 (0–18)</td>
<td>1.6 (0–11)</td>
<td>1.4 (0–12)</td>
<td>0.9 (0–9)</td>
<td>1.0 (0–10)</td>
<td>0.8 (0–8)</td>
<td>0.8 (0–7)</td>
</tr>
<tr>
<td>Age (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>0–64</td>
<td>14.7</td>
<td>16.2</td>
<td>17.4</td>
<td>19.3</td>
<td>13.2</td>
<td>19.8</td>
<td>14.4</td>
<td>16.5</td>
<td>16.0</td>
</tr>
<tr>
<td>65–74</td>
<td>18.3</td>
<td>20.8</td>
<td>19.6</td>
<td>17.2</td>
<td>18.4</td>
<td>20.2</td>
<td>18.4</td>
<td>20.5</td>
<td>17.2</td>
</tr>
<tr>
<td>75+</td>
<td>67.1</td>
<td>63.0</td>
<td>63.0</td>
<td>63.5</td>
<td>68.4</td>
<td>67.1</td>
<td>60.7</td>
<td>65.0</td>
<td>63.9</td>
</tr>
<tr>
<td>Sex (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>50.9</td>
<td>50.9</td>
<td>51.9</td>
<td>50.0</td>
<td>47.7</td>
<td>53.8</td>
<td>47.4</td>
<td>50.1</td>
<td>50.8</td>
</tr>
<tr>
<td>Women</td>
<td>49.1</td>
<td>49.1</td>
<td>48.1</td>
<td>50.0</td>
<td>52.3</td>
<td>46.2</td>
<td>52.6</td>
<td>49.9</td>
<td>49.2</td>
</tr>
<tr>
<td>Specific cardiac deaths (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMI</td>
<td>20.8</td>
<td>22.4</td>
<td>21.7</td>
<td>27.7</td>
<td>28.7</td>
<td>36.0</td>
<td>30.3</td>
<td>22.5</td>
<td>29.6</td>
</tr>
<tr>
<td>HF</td>
<td>22.2</td>
<td>25.9</td>
<td>27.5</td>
<td>33.5</td>
<td>29.8</td>
<td>32.1</td>
<td>29.7</td>
<td>27.7</td>
<td>24.1</td>
</tr>
<tr>
<td>CACD</td>
<td>8.2</td>
<td>7.8</td>
<td>18.1</td>
<td>11.6</td>
<td>10.4</td>
<td>8.5</td>
<td>14.9</td>
<td>5.2</td>
<td>20.4</td>
</tr>
</tbody>
</table>

*Average annual mortality rates during 2002–2004 calculated by dividing the average annual number of cardiac deaths by the mean of the 2000 and 2005 populations based on the census data.

AMI, acute myocardial infarction; HF, heart failure; CACD, cardiac arrhythmia and conduction disorders.

Mortality Data

We obtained data on daily mortality from heart disease among all residents in the study areas from January 2002 to December 2004, from the Ministry of Health, Labour and Welfare of Japan (permission number 137). Mortality records include sex, age, and date of death. The International Classification of Diseases, 10th revision (ICD-10) for coding the primary cause of death was used. We performed analyses for mortality from all heart diseases (ICD-10: I01–I02, I05–I09, I20–I25, I30–I52). In order to examine the disease-specific effects of air pollutants on mortality, we used the following groups: acute MI (AMI: ICD-10: I21–I22), HF (ICD-10: I50), and cardiac arrhythmia and conduction disorders (CACD: ICD-10: I44–I49).

Environmental Data

We obtained the PM2.5 data, measured at the monitoring stations located in each study area, from the National Institute for Environmental Studies. Hourly measurement of PM2.5 concentration was performed using a tapered element oscillating microbalance. Meteorological data were obtained from the Japan Meteorological Agency. The 24-h mean concentration of PM2.5, ambient temperature, and relative humidity were calculated using hourly measurements from 0 to 23 h. We excluded from our analyses the days when more than 4 measurements were missing. During the study period (1,096 days), the number of days for which the daily mean concentration of PM2.5 was missing ranged from 3 to 50 (0.3–4.6% of the days).

Statistical Methods

For each area, we used a generalized linear model to examine the association between daily mean concentration of PM2.5 and the daily mortality for all heart disease and the specific heart disease groups as defined. We applied Poisson regression with the log link function because daily counts of mortality are assumed to follow a Poisson distribution. This time-series approach that focuses on day-to-day variation of exposure is expected to eliminate the influence of individual-level risk factors of heart disease, such as gender, age, smoking, and preexisting diseases, because these risk factors do not vary over short periods of time. On the other hand, there are possible confounders that vary with time, such as seasonality, day of the week, and meteorological factors, that need to be adjusted for. It is well known that there is seasonal variation in cardiac disease mortality and morbidity. In order to control for seasonality, we used the indicator variables for every 2 months of the calendar year. We also used the indicator variables in our model to control for the day of the week. Several studies have found that the meteorological factors that correlate with PM2.5 affect the mortality and morbidity of cardiovascular disease. Generally, those studies observed an effect of ambient temperature on cardiovascular mortality. The effect was nonlinear, and both cold and hot temperatures increased cardiovascular mortality. Therefore, we used a natural cubic spline to adjust for ambient temperature. This smoothing method does not require the assumption of linearity and allows a more flexible analysis. We also used a natural cubic spline to adjust for relative humidity. We set the degrees of freedom for ambient temperature and relative humidity to 6 and 3, respectively, based on previous literature.

In order to examine the lagged effect, we used the concentrations of PM2.5 for the same day (lag 0) and the 1–2 days (lag 1 and lag 2) prior to death. We also repeated the analyses using a 2-day moving average (average of same day and 1 day prior to death) of the concentration (lag m01) and a 3-day moving average (average of same day, 1 day and 2 days prior to death) (lag m02).

We also conducted age-stratified analyses. We divided the study population into 3 age categories (0–64, 65–74, and 75+ years) for estimation of the corresponding relative risks by age category. We conducted area-specific analyses using R 2.7.0 (R Development Core Team 2008).

After obtaining area-specific results, we combined them and conducted a meta-analysis using a random-effects model which takes into account heterogeneity between areas, because we assumed that the effects of PM2.5 would vary by area. We conducted these meta-analyses and obtained risk ratios (RRs) using PROC MIXED in SAS9.1 (SAS Institute, Cary, NC, USA). All results were expressed as percent change in mortality risk, which was calculated as (RR-1)×100, with 95% confidence interval (CI) for a 10-μg/m3 increase in PM2.5. We considered a P-value less
than 0.05 to be statistically significant.

**Results**

A total of 67,897 deaths because of heart disease occurred in the 9 areas during the study period. The daily mean number of deaths varied by area from 0.8 (Sakai and Sendai) to 8.7 (Tokyo) (Table 1). Of the total cardiac deaths, 65.3% occurred in the 75+ years age group and 50.7% were males.

Table 2 shows the summary statistics for environmental variables in 9 areas of Japan, 2002–2004.

<table>
<thead>
<tr>
<th>Area</th>
<th>No. of days analyzed</th>
<th>PM$_{2.5}$ (μg/m$^3$)</th>
<th>Ambient temperature (°C)</th>
<th>Relative humidity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tokyo</td>
<td>1,093</td>
<td>21.1±9.9</td>
<td>16.8±7.7</td>
<td>59.9±15.1</td>
</tr>
<tr>
<td>Osaka</td>
<td>1,046</td>
<td>21.5±10.5</td>
<td>17.4±8.2</td>
<td>64.3±11.0</td>
</tr>
<tr>
<td>Nagoya</td>
<td>1,052</td>
<td>20.5±9.8</td>
<td>16.3±8.4</td>
<td>66.7±12.7</td>
</tr>
<tr>
<td>Kobe</td>
<td>1,093</td>
<td>19.7±10.0</td>
<td>17.3±8.1</td>
<td>65.7±11.1</td>
</tr>
<tr>
<td>Sapporo</td>
<td>1,087</td>
<td>13.2±6.9</td>
<td>9.3±9.1</td>
<td>67.5±10.9</td>
</tr>
<tr>
<td>Fukuoka</td>
<td>1,054</td>
<td>21.8±11.7</td>
<td>17.5±7.6</td>
<td>65.2±11.0</td>
</tr>
<tr>
<td>Kawasaki</td>
<td>1,093</td>
<td>19.9±9.5</td>
<td>16.7±7.7</td>
<td>63.6±15.8</td>
</tr>
<tr>
<td>Sakai</td>
<td>1,070</td>
<td>20.1±10.0</td>
<td>17.4±8.2</td>
<td>64.3±11.0</td>
</tr>
<tr>
<td>Sendai</td>
<td>1,092</td>
<td>14.1±7.8</td>
<td>12.3±7.8</td>
<td>70.9±13.4</td>
</tr>
</tbody>
</table>

Values are mean±SD.

PM$_{2.5}$, particulate matter with aerodynamic diameter <2.5 μm.

The area-specific analyses showed that the estimated percent change in mortality for all heart disease at lag 0 ranged from –0.5% (95% CI, −4.0–3.1%) in Fukuoka to 4.7% (95% CI, 1.4–8.1%) in Kobe (Figure 2). In the combined analyses, we found significantly positive associations between mortality for all heart disease and PM$_{2.5}$ concentration at lag 0 (Table 3). We repeated the same analyses to examine the effects of PM$_{2.5}$ on mortality from AMI, HF, and CACD. In general, we found positive associations between deaths from these diseases and PM$_{2.5}$, but the associations were not significant.

Age-stratified analyses revealed different patterns of association between deaths from specific heart disease and PM$_{2.5}$ concentrations (Figure 3). An increase in mortality from AMI was observed on the same day of exposure to PM$_{2.5}$ for the younger population aged 0–64 years (5.4%, 95% CI 0.2–10.8%), but there was no clear effect for those aged 65 years and over. The PM$_{2.5}$ effect on HF remained positive for the age category 0–64 years and 65–74 years.
from lag 0 to lag 2, although the effects were not significant on the single lag days. The strongest effect in mortality from CACD was observed for the age category 0–64 years at lag 0 (9.1%, 95%CI –0.1–19.2%) and the estimates diminished at lag 1 and lag 2. The effect on CACD mortality was almost zero among those aged 75+. Figure 4 shows area-specific results of percent changes in mortality from AMI and CACD for those aged less than 65 years at lag 0. Although the combined results were positive, regional heterogeneity was observed. When we repeated the analyses using values of moving average (lag m01, lag m02), we found a significant increase in mortality risks for HF for the population aged 65–74 years (8.5%, 95%CI 0.6–17.0% at lag m01; 10.0%, 95%CI 1.9–18.8% at lag m02).
Discussion

In this study, we found that an increase in PM$_{2.5}$ concentration was associated with increased mortality from heart disease in Japan. Generally, the effect on heart disease mortality was stronger on the day of death (lag 0) and decreased with days prior to death (lag 1 and lag 2). The analyses for mortality from specific categories of heart disease showed similar patterns. The age-stratified analyses suggested that the PM$_{2.5}$ effect was larger among the younger population for particular diseases. The areas used for the analyses consisted of 9 large areas from all over Japan. Our findings provide robust evidence for the association between PM$_{2.5}$ and heart disease mortality in Japan.

Many reports have shown that PM has adverse effects on overall heart disease mortality$^{1-5}$ and recently, more attention has been drawn to the effects of air pollutants on specific heart diseases. However, some of the results have been inconsistent. For sudden cardiac death, Rosenthal et al found an association between PM$_{2.5}$ exposure and out-of-hospital cardiac arrests in Indiana.$^{21}$ On the other hand, Levy et al did not observe an association between PM$_{10}$ and out-of-hospital primary cardiac arrest in Seattle and Washington.$^{22}$ In Japan, most of the research interest involving air pollutant epidemiology has focused on impacts on the respiratory system and we are aware of only a few reports that examined the association between air pollutants and cardiovascular disease.$^{8,23}$ There have been concerns about an increasing trend in the incidence of coronary heart disease and the prevalence of its risk factors. An increase in age-adjusted coronary heart disease incidence was observed among men and women in the Takashima AMI Registry$^{24}$ and among middle-aged men in a Japanese urban community.$^{25}$ Furthermore, an increase in the prevalence of hypercholesterolemia and high blood glucose was observed among middle-aged men.$^{25}$ Therefore, research on various risk factors of cardiovascular disease would be relevant from a public health perspective to prevent disease. Although there are numerous studies on lifestyle-related risk factors, it is also important to address the environment-related factors.

Previous epidemiologic studies indicated that particulate air pollution triggers AMI$^{26}$ exacerbates congestive HF$^{27}$ and increases the risk of ventricular arrhythmias$^{28}$ which could lead to death. As the epidemiologic evidence accumulates, researchers are considering the potential mechanisms that could explain the link between the exposure to PM and acute cardiac mortality/morbidity. It has been suggested that exposure to PM leads to acute systemic inflammation and increases in platelet adhesiveness, fibrinogen concentration, sympathetic nervous system activity, and arterial vasoconstriction$^{29,30}$ which could subsequently trigger acute coronary syndrome, cardiac arrhythmias, and other cardiac diseases.$^{6}$ Another possible mechanism involves direct cardiovascular toxicity of ultrafine particles with a diameter of less than 0.1 $\mu$m$^{31}$ The analyses in the current study specific for each category of heart disease provide an insight into the mechanisms linking exposure to PM$_{2.5}$ with cardiac death.

Murakami and Ono observed an increase in MI deaths a few hours after exposure to high levels of SPM in Tokyo from 1990 to 1994.$^8$ Levels of SPM during the period of the present study (2002–2004) were lower than those in the 1990s and met environmental quality standards in most areas of Japan.$^{32}$ Our results showed that a positive association between heart disease mortality and PM$_{2.5}$ occurs at concentrations below the current environmental quality standards of SPM in Japan.$^{33}$ In addition, it has been suggested that fine PM can reach deeper into the lung and may have greater toxicity than coarse particles.$^{6,9}$ Although there are numerous findings on the cardiovascular effects of PM in North America and Europe, factors that can affect the susceptibility to cardiovascular disease, such as genetic background, lifestyle, weather, and the healthcare system, differ between Japan and those countries. Therefore, it is necessary to accumulate evidence on the health effects of PM$_{2.5}$.
PM$_{2.5}$ in Japan. The percent increases in mortality risk because of HF were high at lag 0 and lag 1, but the association was insignificant. Similarly, previous studies found no significant association between air pollution and mortality for congestive HF$^{23,35}$ On the other hand, there is a study that reported a significant association between HF admissions and PM$^{27}$ If it is possible that the effect of PM is relevant for exacerbation of HF, but not for death from HF. However, there is another possible explanation. A study that investigated the characteristics of patients with HF in Japan revealed that some of these patients died suddenly$^{36}$ and the cause of death on death certificates for those could be counted as other diseases, such as cardiac arrhythmia, ischemic heart disease, or even stroke.

Some researchers have investigated the association between air pollution and ventricular arrhythmias using the records from implantable cardioverter defibrillator devices$^{28,37}$ These arrhythmias are life-threatening and could be a cause of death. We examined the association between CACD and PM$_{2.5}$ and found a marginal association at lag 0 only for the younger population (<65 years). The pathophysiology of CACD differs. Although we wanted to focus on cardiac arrhythmias, those particular data were not available, so we used the data on CACD as a proxy for cardiac arrhythmias, which may have obscured the association between fatal arrhythmias and air pollution.

The results we obtained using age-stratified analyses were inconsistent with those from several previous studies$^{10-12}$ that showed the elderly were more sensitive to air pollutants. This discrepancy may have arisen from differences in lifestyle and housing among countries. Given that more exposure to air pollutants causes greater health impacts, differences in the size of the effect among age groups could be explained by differences in the amount of exposure to PM$_{2.5}$. There was a significant association among the younger population (<65 years) on the day of death for AMI and CACD, which are common causes of sudden cardiac death$^{23,39}$ It is assumed that elderly are more sedentary and likely to stay in a hospital or nursing home in the time preceding death. Because most of these facilities in Japan are considered to be equipped with an air-conditioning system$^{40}$ the inmates might have had less exposure to outside air. On the other hand, the younger population is less likely than the elderly to have a preexisting disease that confines them to their house or a hospital, so the chance of exposure to ambient air pollutants could be higher for the younger group. This could be an explanation for the age-related differences; another is that we could not capture the effect among the elderly because we used mortality data and the primary diagnosis might not reflect the true cause of death.

It is suggested that the impact of PM on cardiovascular mortality is more immediate than that on respiratory mortality$^{2}$ In our study, the estimated effects of PM$_{2.5}$ were largest at lag 0 for mortality from AMI and CACD in the all-population analyses. Besides, in the age-stratified analyses, this lag pattern was observed only for the younger group, which suggested that the time period in which air pollutants affect mortality differs by type of disease and age. The detailed mechanism remains unclear and further study is needed.

We observed regional heterogeneity in the estimated effects of PM$_{2.5}$ on cardiac disease mortality. In particular, a significant negative association between PM$_{2.5}$ levels and mortality from CACD was observed in Osaka, despite a positive association with the combined result. Although we do not have concrete evidence to explain this, it is possible that there are differences in the composition of PM and socioeconomic status among regions, which could modify the PM$_{2.5}$ effect on health and account for regional heterogeneity. Further investigation will be necessary to clearly define the reason for the observed negative association.

**Study Limitations**

First, in this type of air pollutant epidemiology, it is common to use the values measured at the monitoring station in the same city as a proxy for individual exposure to air pollutants. Exposure measurement errors might be substantial, especially in cities with a large area, such as Sapporo. Consequently, these errors could obscure the true relationship between exposure and outcome. Second, inaccuracy of the cause of death may have influenced the results. It is known that vital statistics based on death certificates do not necessarily reflect the underlying cause of death$^{41}$ Although the accuracy of death certificate diagnosis for HF has improved since the ICD-10 in 1995$^{42}$ it is likely that some misclassification remains and could also be a source of bias. Third, misclassification of exposure time may have underestimated the true risk of death. We used 24-h (0–23h) mean concentration as an index of exposure to PM$_{2.5}$. If the death occurred early in the day, the value of PM$_{2.5}$ at "lag 0", in which most of the hourly values were those after the time of death, would not represent the true exposure. New indices that take into account of time of exposure$^{43}$ will be necessary for further analyses. We assumed that the period between exposure to air pollutants and death was short, from a few hours to a few days$^{23,28}$ Our focus was the short-term effect of PM$_{2.5}$ on heart disease mortality, especially on the diseases that could cause sudden cardiac death. Therefore, we believe that the results obtained in this study reflect the true effect, despite the possibility of underestimation. Finally, we did not adjust for other gaseous co-pollutants. It is suggested that adjusting for co-pollutant would need cautious interpretation because these co-pollutants might work as a surrogate rather than a confounder$^{44}$ Besides, previous studies showed that adjustment for co-pollutants did not substantially change the central estimates of the association between PM and mortality, but that it resulted in wider CLs$^{45}$ Therefore, we think that interpretation based on the model without co-pollutants would represent the true effect, although uncertainty might remain.

The results obtained in this study provide robust evidence for the short-term health effects of air pollutants on heart disease mortality in Japan. The overall effect of fine PM on heart disease mortality was subtle compared with other lifestyle-related risk factors. However, accumulating evidence in Japan is necessary in order to reduce preventable deaths because of air pollution.

**Acknowledgments**

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