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Air Pollution and Suicide in 10 Cities in Northeast Asia: A Time-Stratified Case-Crossover Analysis

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Background: There is growing evidence suggesting an association between air pollution and suicide. However, previous findings varied depending on the type of air pollutant and study location.

Objectives: We examined the association between air pollutants and suicide in 10 large cities in South Korea, Japan, and Taiwan.

Methods: We used a two-stage meta-analysis. First, we conducted a time-stratified case-crossover analysis to estimate the short-term association between nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and particulate matter [aerodynamic diameter ≤ 10 μm (PM_{10}), aerodynamic diameter ≤ 2.5 μm ($PM_{2.5}$), and $PM_{10-2.5}$] and suicide, adjusted for weather factors, day-of-week, long-term time trends, and season. Then, we conducted a meta-analysis to combine the city-specific effect estimates for NO_2, SO_2, and PM_{10} across 10 cities and for $PM_{2.5}$ and $PM_{10-2.5}$ across 3 cities. We first fitted single-pollutant models, followed by two-pollutant models to examine the robustness of the associations.

Results: Higher risk of suicide was associated with higher levels of NO_2, SO_2, PM_{10}, and $PM_{10-2.5}$ over multiple days. The combined relative risks (RRs) were 1.019 for NO_2 (95% confidence interval [CI]: 0.999, 1.039), 1.020 for SO_2 (95% CI: 1.005, 1.036), 1.016 for PM_{10} (95% CI: 1.004, 1.029), and 1.019 for $PM_{10-2.5}$ (95% CI: 1.005, 1.033) per interquartile range (IQR) increase in the 0–1 d average level of each pollutant. We found no evidence of an association for $PM_{2.5}$. Some of the associations, particularly for SO_2 and NO_2, were attenuated after adjusting for a second pollutant.

Conclusions: Our findings suggest that higher levels of air pollution may be associated with suicide, and further research is merited to understand the underlying mechanisms. https://doi.org/10.1289/EHP2223

Introduction

Suicide is a significant public health concern. An estimated 804,000 people worldwide died by suicide in 2012, accounting for 1.4% of all deaths; suicide constitutes the 15th most common cause of death (WHO 2014). Among a broad range of contributing factors to suicide, attention has been given to environmental factors that may be associated with suicide (Sinyor et al. 2017). Numerous studies have reported evidence of a seasonal peak in suicide in spring and early summer (Christodoulou et al. 2012; Coimbra et al. 2016). Some studies have investigated the association between weather and suicide, suggesting that increases in ambient temperature are associated with increased risk of suicide (Deisenhammer 2003; Kim et al. 2016; Likhvar et al. 2011; Page et al. 2007). In addition, the association with sunlight or sunshine hours has been studied (Vyssoki et al. 2014; White et al. 2015), although it remains controversial because the association was attenuated after adjusting for the seasonality of suicide (White et al. 2015).

Emerging evidence suggests that air pollution may be another potential environmental factor associated with suicide. Several epidemiological studies have reported that higher levels of air pollutants, such as particulate matter with aerodynamic diameter ≤ 10 μm (PM_{10}) and ≤ 2.5 μm ($PM_{2.5}$), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and carbon monoxide (CO), are associated with suicide (Kim et al. 2010, Bakian et al. 2015, Lin et al. 2016, Ng et al. 2016) and with suicide attempts (Szyszkowicz et al. 2010). These studies used time-stratified case-crossover analysis, which is widely used to examine short-term associations between air pollution and health; this method is also considered the least biased method in the case-crossover design (Janes et al. 2005).

However, previous findings varied depending on the type of air pollutant and on the study location. For example, there were consistent findings of positive associations for $PM_{2.5}$ and NO_2 in three studies (Bakian et al. 2015; Kim et al. 2010; Lin et al. 2016). Other pollutants, such as PM_{10} and SO_2, were found to be associated with suicide in two of the studies (Kim et al. 2010; Lin et al. 2016) but not in the third (Bakian et al. 2015). This discrepancy may be attributed to geographical variations (e.g., the sources and components of air pollution, climate conditions, cultural backgrounds, socioeconomic factors, and suicidal behaviors). Moreover, different modeling strategies make it difficult to compare results across studies. To gain a better understanding of air pollution and suicide, a study to investigate multiple locations with a unified modeling strategy is merited.

In the present study, we examined the association between air pollution and suicide in 10 large cities in three countries in Northeast Asia: South Korea, Japan, and Taiwan. The three countries share, in part, traditional cultural backgrounds, and have recorded relatively high suicide rates (31.0, 24.0, and 17.6 per 100,000 population in 2009 in South Korea, Japan, and Taiwan, respectively, compared with the global rate of 11.2 per 100,000

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population in 2010) (Chen et al. 2012; WHO 2017). We conducted a two-stage analysis to examine the city-specific association and the combined association. To our knowledge, this is the first study of the association between air pollution and suicide comparing multiple cities in multiple countries using a unified analytical framework.

Methods

Data

We collected the data on suicide, air pollutants (NO_2, SO_2, and PM_{10}) and weather in four cities in South Korea from 1 January 2001 to 31 December 2010 (10 y), in three cities in Japan from 1 April 1979 to 31 March 2009 (30 y), and in three cities in Taiwan from 1 January 1994 to 31 December 2007 (14 y) (Figure 1). All cities are considered large because the populations were >2,000,000 in 2010 (see Table S1). The study area in Tokyo covers the 23 special wards that comprise the most populous part of the metropolis. The data on $PM_{2.5}$ levels covered a shorter period and were limited to three cities: Seoul, between 1 January 2002 and 31 December 2010 (8 y); Tokyo, between 1 December 2001 and 31 January 2008 (6 y, 2 mo); and Taipei, between 1 January 2006 and 31 December 2007 (2 y).

We extracted suicide cases, defined as intentional self-poisoning and self-harm based on the *International Statistical Classification of Diseases and Related Health Problems* (ICD) [E950.0–E958.9 for ICD-9 (WHO 1978) and X60–X84 for ICD-10 (WHO 2016)] from national death registries (Statistics Korea, Ministry of Strategy and Finance in South Korea, written communication, December 2011; Ministry of Health, Labour and Welfare in Japan, written communication, December 2011; Department of Statistics, Ministry of Health and Welfare in Taiwan, written communication, June 2008). The city-specific suicide data included information on sex, age, and method of suicide. We categorized age into three groups: 10–24 y (adolescents and young adults), 25–64 y, and ≥65 years (older adults). We also dichotomized the method of suicide into violent (E950.0–E952.9 for ICD-9 and X60–X69 for ICD-10) and nonviolent (E953.0–E958.9 for ICD-9 and X70–X84 for ICD-10). The suicide reporting systems have been described in detail elsewhere (Hendin et al. 2008).

The data on the daily mean levels of NO_2, SO_2, PM_{10}, and $PM_{2.5}$ were obtained from the Research Institute of Public Health and Environment in South Korea (written communication, January 2012), the National Institute for Environmental Studies

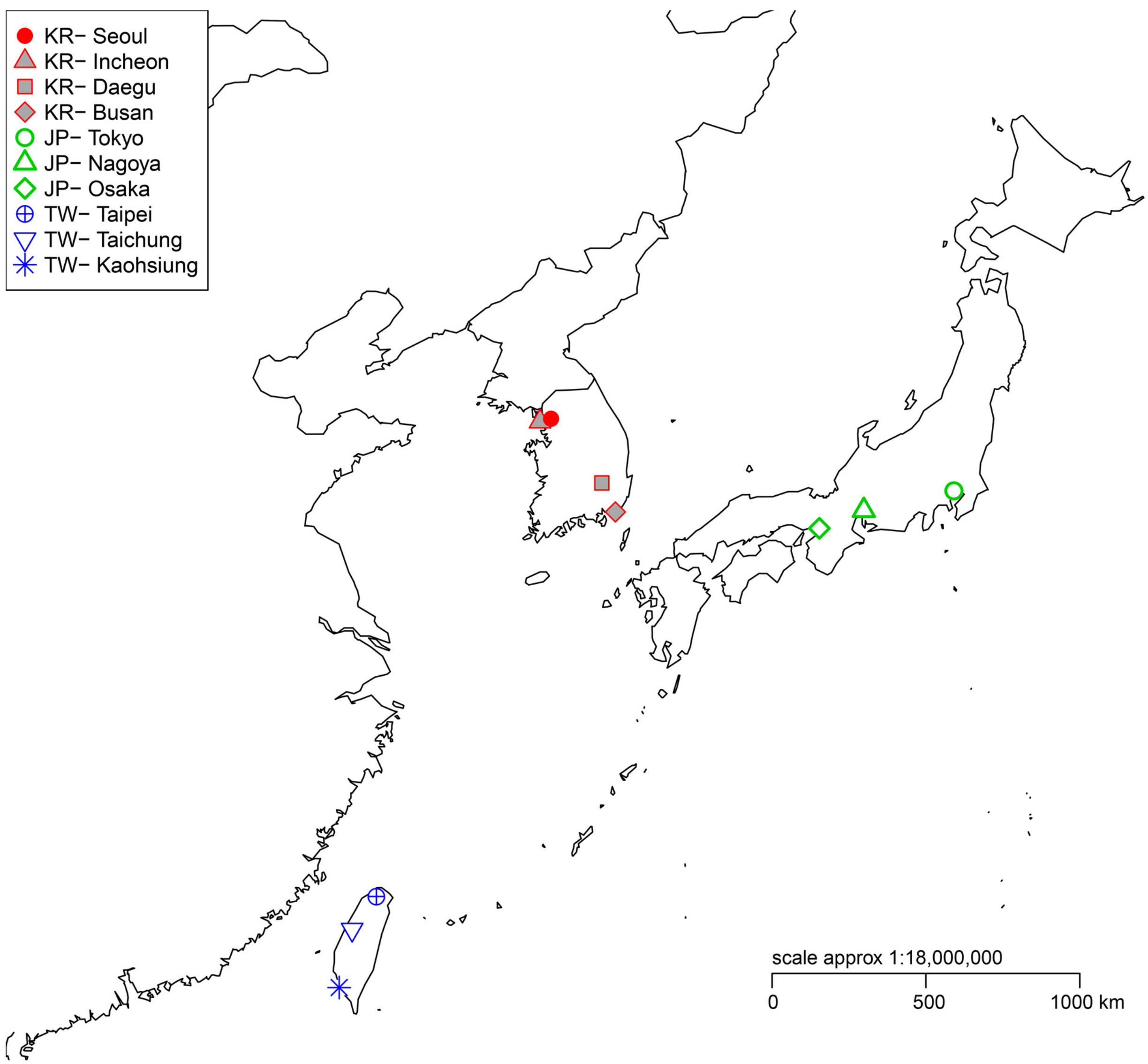

Figure 1. Study location of 10 cities in South Korea (KR), Japan (JP), and Taiwan (TW).

in Japan (written communication, April 2011), and the Taiwan Environmental Protection Administration in Taiwan (https://taqm.epa.gov.tw/taqm/en/default.aspx). The data originally included hourly concentrations of each pollutant measured by multiple monitoring stations in each city. We first calculated hourly means across the stations and from these values, we calculated the daily 24-h average concentrations in each city. Daily levels of coarse particles ($PM_{10-2.5}$) were obtained by subtracting daily concentrations of $PM_{2.5}$ from those of PM_{10}. For four cities in Korea, we identified extremely high concentrations of PM_{10} and $PM_{2.5}$, that is to say, daily mean PM_{10} levels $>400\ \mu g/m^3$ (6 d in Seoul, 5 d in Incheon, and 4 d in Busan and Daegu) and the daily mean $PM_{2.5}$ for the same 6 d in Seoul (on average, $226.2\ \mu g/m^3$). These values are considered outliers according to the Asian dust warning system (advisory) of the Korea Meteorological Administration (KMA 2016). Air pollution data were unavailable for some days; the missing rates were $\leq 0.33\%$ for NO_2 and SO_2, $\leq 0.44\%$ for PM_{10}, and $\leq 0.40\%$ for $PM_{2.5}$ over the study periods.

Weather data were obtained from the KMA (written communication, September 2012), the Japan Meteorological Agency (http://www.jma.go.jp), and the Taiwan Central Weather Bureau (written communication, May 2012). We collected daily mean ambient temperature (°C); daily sum of sunshine hours, defined as hours with direct sunlight $\geq 120\ W/m^2$ (WMO 2014); daily mean relative humidity (%); daily mean sea-level atmospheric pressure (hPa); and daily total precipitation (mm). The missing rates were $\leq 0.03\%$ for temperature, $\leq 0.05\%$ for sunshine duration, $\leq 0.11\%$ for humidity, $\leq 0.04\%$ for atmospheric pressure, and $\leq 11.5\%$ for precipitation over the study periods.

Statistical Analyses

A two-stage meta-analysis was conducted to analyze the multicity time-series data. In the first stage, we used a time-stratified case-crossover analysis to estimate the short-term association between suicide and air pollutants for each city. In the second stage, we used a meta-analysis to combine the city-specific estimates. We used R (version 3.2.3; R Development Core Team) with the packages "gnm" and "dlnm" for the time-stratified case-crossover analysis and "metafor" for the meta-analysis.

First-Stage Modeling

We used a time-stratified case-crossover design for comparing exposure levels between case and control days matched within a stratum. We defined a stratum as a combination of year, month, and day-of-week; each case was matched to controls on the same day-of-week in the same month and year (i.e., 1:3 or 1:4 matching depending on the length of a month). This design allows for the adjustment of long-term time trend, seasonality, and day-of-week, and it assumes that unmeasured time-varying confounders are constant within a stratum (Lu et al. 2008).

We fitted a conditional Poisson regression model with quasi-Poisson family to accommodate an over-dispersion (Armstrong et al. 2014). We assumed a linear association between air pollutants and suicide upon confirming by an F-test that nonlinearity is unnecessary. To examine a delayed effect of the association, we used an average exposure of air pollutant levels over multiple days from the current day up to 9 preceding days (i.e., 0–1 to 0–9 lag days) and estimated associations across different lengths of exposure. We included potential time-varying confounders (temperature and sunshine hours) and an indicator of public holidays (except on Saturday and Sunday) in the model. The weather factors were incorporated as distributed lag nonlinear functions with a maximum lag of 5 d. Specifically, we used a natural cubic spline with three internal knots placed at the 25th, 50th, and 75th percentiles of exposure distribution and the same spline for lags with an intercept and two equally spaced internal knots in the log scale.

We started with a single-pollutant model to estimate marginal association, followed by a two-pollutant model adjusting for a second pollutant to assess the robustness of the association. To obtain comparable results between the two models, we fitted the single-pollutant model using a subset of data without any missing second pollutant. In the two-pollutant model, we examined possible multicollinearity based on the variance inflation factor (VIF) (O'brien 2007).

We analyzed the total population and conducted subgroup analyses by sex, age, and method of suicide using single-pollutant models. All city-specific analyses were performed without the missing values described above. We excluded the days with extreme PM_{10} and $PM_{2.5}$ levels in the Korean cities from the analysis.

Second-Stage Modeling

To combine the city-specific results estimated from the first-stage modeling, we performed a meta-analysis based on a random-effect model (Borenstein et al. 2009; Viechtbauer 2010). To investigate the heterogeneity, we calculated I^2 and tested the uncertainty of the heterogeneity using a chi-squared test for Cochran's Q statistic (Borenstein et al. 2009; Higgins et al. 2003).

Sensitivity Analysis

We performed several sensitivity analyses to evaluate the robustness of our results. First, as an alternative to the distributed lag nonlinear function, we adjusted for temperature and sunshine duration using the natural cubic splines of their average of 0–5 lag days with four degrees of freedom. Second, we added other weather variables—relative humidity, atmospheric pressure, and precipitation—one at a time to the final model. We used the distributed lag nonlinear function with the same specifications as temperature or sunshine duration to humidity and pressure, and with different knot placement (at the 80th, 90th, and 99th percentiles) to precipitation after natural log transformation because of the skewness. Third, we redefined the stratum from the original year, month, and day-of-week combination to every 2 or 3 wk matched by day-of-week to assess whether our length of stratum was sufficiently short to control for seasonality in the time-stratified case-crossover design (Guo and Barnett 2015). Finally, we performed the same analysis including the days with extremely high concentrations of particulate matter (PM_{10}, $PM_{2.5}$, and $PM_{10-2.5}$) in Korean cities.

Results

Table 1 shows summary statistics for suicide, air pollutants, and weather variables. The total number of suicides ranged from 3,352 in Taichung to 46,519 in Tokyo during the study periods. The daily mean suicide count was the highest in Seoul at 5.3 ± 2.9 [mean $\pm$ SD (standard deviation)] and the lowest in Taichung at 0.7 ± 0.8). Air pollution levels varied depending on pollutant and location. NO_2 levels were higher in larger cities, such as Seoul and Tokyo (capital cities) and Osaka (the second-largest city in Japan). SO_2 levels were higher in Kaohsiung and Osaka. The PM_{10} level was highest in Kaohsiung, which is located in Taiwan's industrial area. Among the three capital cities, the $PM_{2.5}$ level was lowest in Tokyo. The cities in Taiwan had smaller variations in temperature and humidity given its location in the subtropical zone, with a warmer and more humid climate than Korea and Japan (Table 1; see also Table S1).

Association between Suicide and Air Pollutants

We found evidence of short-term associations between suicide and air pollutants (NO_2, SO_2, PM_{10} and $PM_{10-2.5}$), estimated as the

Table 1. Summary statistics of suicide (daily mean and standard deviation), air pollutants and weather factors (median and interquartile range) for each city.

Country	City	Total number of suicide	Daily mean suicide counts	NO_2 (ppb)	SO_2 (ppb)	PM_{10} ($\mu g/m^3$)	$PM_{2.5}$ ($\mu g/m^3$)	$PM_{10-2.5}$ ($\mu g/m^3$)	Temperature (°C)	Sunshine duration (hour)
South Korea	Seoul	19,218	5.3 ± 2.9	35.0 ± 18.1	4.7 ± 2.7	53.0 ± 38.3	26.0 ± 20.0	25.0 ± 18.9	14.4 ± 17.8	5.4 ± 7.1
	Busan	8,971	2.5 ± 1.7	22.8 ± 12.5	5.6 ± 3.2	49.9 ± 28.8	—	—	15.7 ± 12.9	7.0 ± 6.9
	Incheon	6,204	1.7 ± 1.4	27.1 ± 15.1	6.6 ± 3.2	53.2 ± 34.2	—	—	13.9 ± 16.9	6.8 ± 7.0
	Daegu	5,420	1.5 ± 1.3	22.8 ± 13.4	5.2 ± 3.2	50.4 ± 30.8	—	—	15.7 ± 16.3	6.9 ± 6.7
Japan	Tokyo[a]	46,519	4.2 ± 2.3	30.3 ± 14.8	6.7 ± 7.1	40.2 ± 32.4	17.8 ± 11.9	11.1 ± 10.5	16.5 ± 13.4	5.6 ± 8.0
	Nagoya	11,685	1.1 ± 1.1	26.2 ± 13.1	6.2 ± 4.9	40.1 ± 30.9	—	—	16.3 ± 15.0	6.4 ± 7.4
	Osaka	18,911	1.7 ± 1.4	31.7 ± 15.9	7.3 ± 6.1	38.6 ± 30.6	—	—	17.2 ± 14.8	5.9 ± 6.9
Taiwan	Taipei	9,481	1.9 ± 1.6	26.9 ± 10.0	4.6 ± 3.7	47.6 ± 29.7	25.8 ± 18.8	20.5 ± 9.9	23.8 ± 8.6	3.4 ± 7.1
	Taichung	3,352	0.7 ± 0.8	22.3 ± 11.2	3.7 ± 2.6	56.2 ± 41.7	—	—	24.8 ± 7.6	6.5 ± 6.2
	Kaohsiung	5,050	1.0 ± 1.1	24.5 ± 17.1	9.3 ± 5.9	80.6 ± 66.8	—	—	26.3 ± 5.8	6.8 ± 5.5

Note: —, data unavailable; NO_2, nitrogen dioxide; $PM_{2.5}$, particulate matter with aerodynamic diameter ≤ 2.5 μm; PM_{10}, particulate matter with aerodynamic diameter ≤ 10 μm; $PM_{10-2.5}$, coarse particulate matter; SO_2, sulfur dioxide. Study period varies by city: 10 years in Korean cities, 30 years in Japanese cities, and 14 years in Taiwanese cities. The data on $PM_{2.5}$ and $PM_{10-2.5}$ were limited to 8 years in Seoul; 6 years, 2 months in Tokyo; and 2 years in Taipei. The summary statistics of the particulate matter were calculated after excluding extremely high concentrations.

[a]23 special wards covering the most populous area of Tokyo.

relative risk (RR) per interquartile range (IQR) increase in the average of each pollutant at varying lag periods from the current day to lag 0–5 d. (Figure 2; see also Figure S1). Statistical significance was determined if the 95% CI for the RR excluded 1. The combined RR was the highest at the lags of 0–1 d for NO_2 [RR = 1.019 (95% CI: 0.999, 1.039)], 0–3 d for SO_2 [RR = 1.026 (95% CI: 1.008, 1.044)], and 0–2 d for PM_{10} [RR = 1.020 (95% CI: 1.007, 1.033)] and $PM_{10-2.5}$ [RR = 1.023 (95% CI: 1.007, 1.038)]. We found no evidence of an association for $PM_{2.5}$ on any of the lag days.

Figure 3 shows the city-specific effect estimates from the first-stage modeling at a lag of 0–1 d. Although the variability across cities was small in general, some cities had stronger signals than others (e.g., Tokyo for NO_2, SO_2, and PM_{10}; Osaka for SO_2). Among the capital cities, there was evidence of elevated RRs for $PM_{2.5}$ and $PM_{10-2.5}$ in Taipei and Seoul, respectively.

In two-pollutant models, some associations observed in the single-pollutant models were attenuated after adjusting for a second pollutant (Table 2). In particular, the association between SO_2 and suicide weakened substantially after adding NO_2 into the model. The combined RR for SO_2 also decreased after adjusting for PM_{10}. Similarly, the estimates for NO_2 decreased after adjusting for either SO_2 or PM_{10}, and the 95% CIs became wider. The association for PM_{10} weakened after adjusting for NO_2 but remained significant after adjusting for SO_2. The estimated association for $PM_{10-2.5}$ varied slightly after adjusting for NO_2 or SO_2. The VIFs were <10 in all the two-pollutant models.

The chi-squared test for Cochran's Q statistic showed no evidence of strong heterogeneity across cities based on the estimates from the single- or the two-pollutant models ($p > 0.10$) with I^2 values ranging from 0 to 61.0%, except for $PM_{2.5}$ (p for Cochran's Q test = 0.03 and $I^2 = 77.9\%$ at lag 0).

In subgroup analyses, there was no clear pattern of effect modification by sex, age, or method of suicide (Figure 4; see also Figures S2–S4). The confidence intervals among the subgroups largely overlapped covering the point estimates, suggesting that large uncertainty exists when comparing estimates across the groups. Nevertheless, we found some differences by age group in some cities (see Figure S3). Based on the city-specific results estimated from the first-stage modeling at a lag of 0–1 d, the associations for NO_2, SO_2, and PM_{10} were higher in the young age group (10–24 y) in Tokyo and Taipei.

Sensitivity Analysis

The effect estimates for NO_2, SO_2, and PM_{10} were generally larger when we used the simpler functional form (moving average)

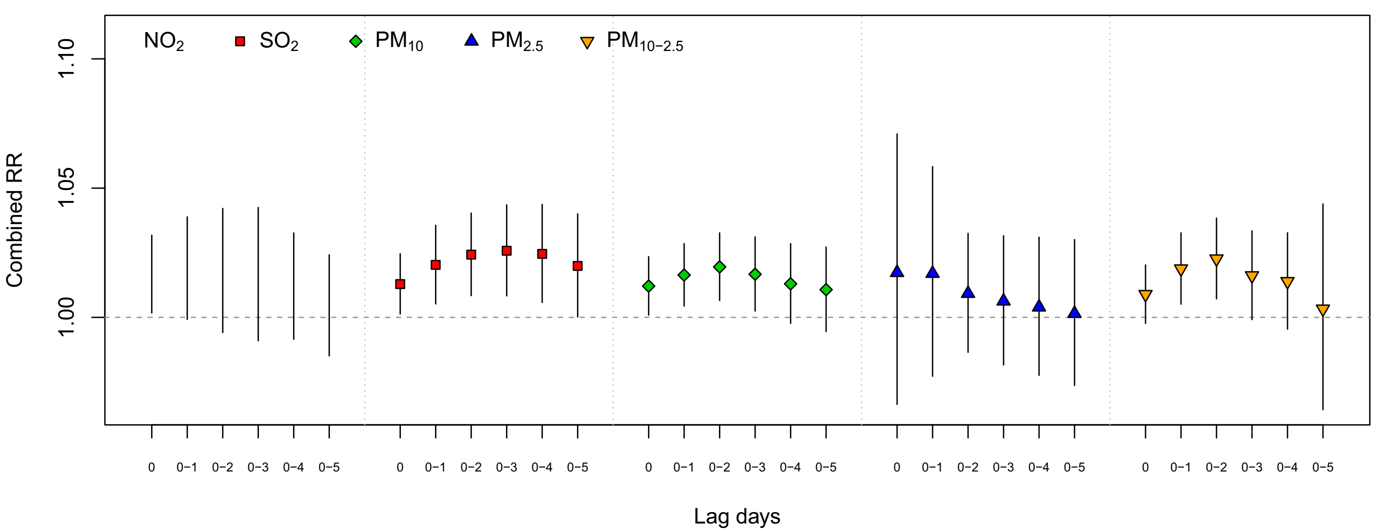

Figure 2. Lag structure of combined relative risks (RRs) and 95% confidence intervals of suicide per interquartile range increase in the concentration of nitrogen dioxide (NO_2), sulfur dioxide (SO_2), particulate matter with aerodynamic diameter ≤ 10 μm (PM_{10}), particulate matter with aerodynamic diameter ≤ 2.5 μm; ($PM_{2.5}$), and coarse particulate matter ($PM_{10-2.5}$) averaged across the cities after adjusting for potential confounders (i.e., ambient temperature, sunshine duration, day-of-week, public holiday, seasonality, and long-term time trend) in single-pollutant models.

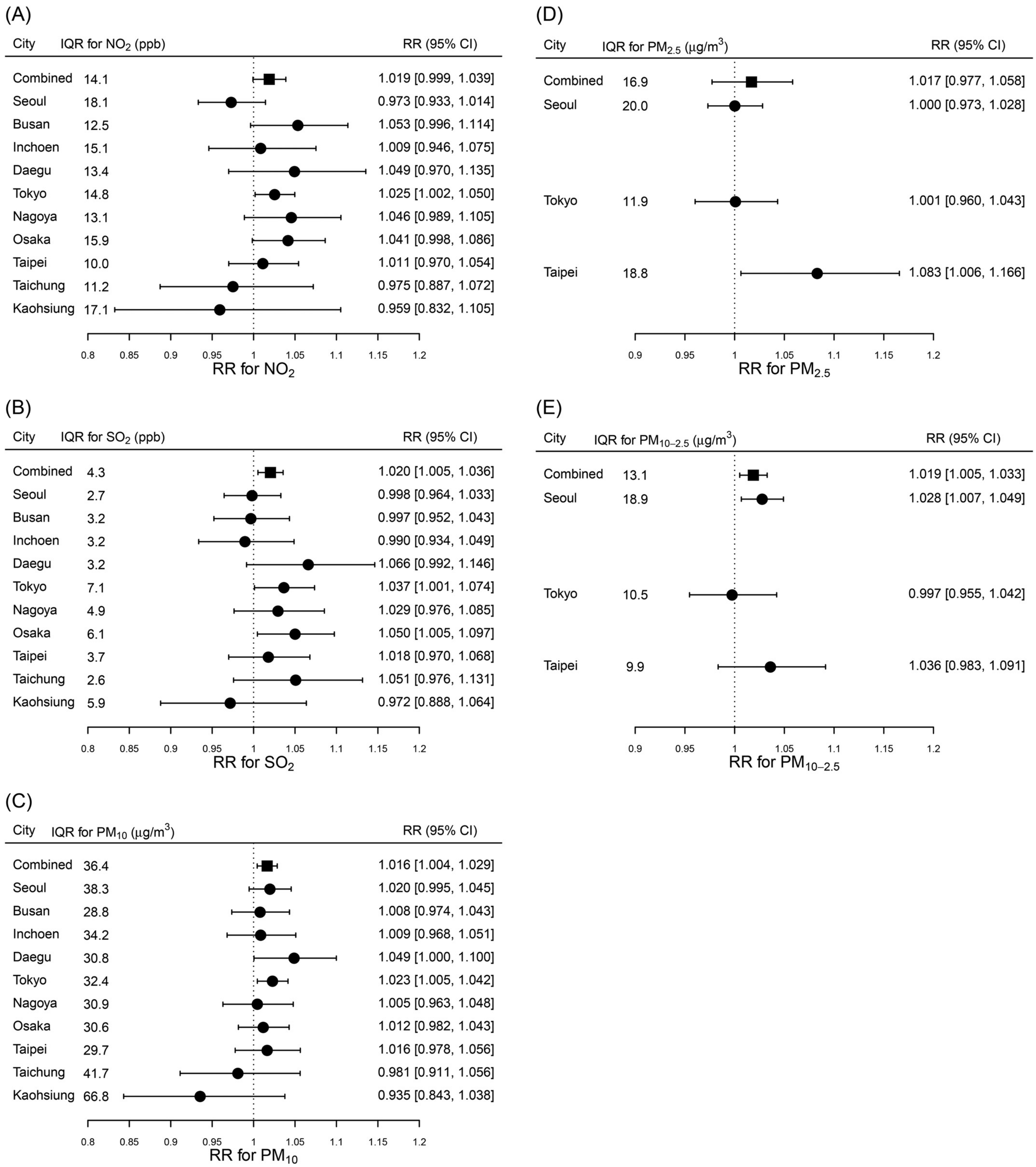

Figure 3. Interquartile range (IQR), combined and city-specific relative risks (RRs), and 95% confidence intervals of suicide per IQR increase in the average 0–1 d concentration of (*A*) nitrogen dioxide (NO_2), (*B*) sulfur dioxide (SO_2), (*C*) particulate matter with aerodynamic diameter ≤ 10 μm (PM_{10}), (*D*) particulate matter with aerodynamic diameter ≤ 2.5 μm ($PM_{2.5}$), and (*E*) coarse particulate matter ($PM_{10-2.5}$) after adjusting for potential confounders (i.e., ambient temperature, sunshine duration, day-of-week, public holiday, seasonality, and long-term time trend) in single-pollutant models.

of temperature and sunshine duration for adjustment instead of the distributed lag nonlinear models (see Figure S5). This finding implies that a simpler form of adjustment for weather variables may lead to bias in the estimates (Gasparrini 2016), and we relied on the latter approach in reporting our main results.

In other analyses, the effect estimates were fairly robust to the adjustment of additional weather variables (relative humidity, atmospheric pressure, and precipitation) (see Figure S6). The results showed no clear pattern of possible bias in the air pollution–suicide associations attributable to the longer stratum (see Figure S7),

Table 2. Combined relative risks and 95% confidence intervals in single- and two-pollutant models.

Primary exposure	Adjustment of another pollutant	RR^a (95% CI)
NO_2	No adjustment	1.019 (0.999, 1.039)
	SO_2	1.014 (0.990, 1.040)
	PM_{10}	1.015 (0.986, 1.045)
SO_2	No adjustment	1.020 (1.006, 1.035)
	NO_2	1.012 (0.995, 1.029)
	PM_{10}	1.014 (0.995, 1.034)
PM_{10}	No adjustment	1.016 (1.004, 1.029)
	NO_2	1.011 (0.995, 1.026)
	SO_2	1.014 (1.000, 1.029)
$PM_{2.5}$	No adjustment	1.017 (0.977 1.058)
	NO_2	1.022 (0.970, 1.078)
	SO_2	1.012 (0.986, 1.037)
$PM_{10-2.5}$	No adjustment	1.019 (1.005, 1.033)
	NO_2	1.020 (0.999, 1.043)
	SO_2	1.022 (1.007, 1.036)

Note: CI, confidence interval; NO_2, nitrogen dioxide; $PM_{2.5}$, particulate matter with aerodynamic diameter ≤2.5 μm; PM_{10}, particulate matter with aerodynamic diameter ≤10 μm; $PM_{10-2.5}$, coarse particulate matter; RR, relative risk; SO_2, sulfur dioxide. In single-pollutant models, a subset of data without any missing copollutants was used to ensure comparability.

[a]Combined RRs of suicide per interquartile range (IQR) increase in the average 0–1 day concentration across the cities (14.1 ppb for NO_2, 4.3 ppb for SO_2, 36.4 $\mu g/m^3$ for PM_{10}, 16.9 $\mu g/m^3$ for $PM_{2.5}$, and 13.1 $\mu g/m^3$ for $PM_{10-2.5}$), after adjusting for potential confounders (i.e., ambient temperature, sunshine duration, day-of-week, public holiday, seasonality, and long-term time trend).

although their 95% CIs became wider in the narrower stratum, most likely because of a lack of control days matched to a case.

When including the days with extremely high PM concentrations in the Korean cities, the combined RRs for PM_{10}, $PM_{2.5}$, and $PM_{10-2.5}$ were generally weaker (see Figure S8). This finding suggests that the association with PM becomes attenuated at extreme levels.

Discussion

We found that higher levels of NO_2, SO_2, PM_{10}, and $PM_{10-2.5}$ were associated with increased risk of suicide in 10 large cities in three northeast Asian countries. These associations were found at shorter delayed exposure lasting a few days and were generally consistent across the cities. We also found weak evidence of effect modification by age group in some cities in the stratification analysis. Some of the associations in the single-pollutant model weakened after adjusting for a second pollutant.

Our findings from the single-pollutant model are in part consistent with previous epidemiological studies, which found that higher levels of air pollutants were associated with increased suicides. Lin et al. (2016) reported an association between suicide and higher levels of PM_{10}, NO_2, and SO_2 in a single-pollutant analysis for Guangzhou, China. Kim et al. (2010) reported associations between PM_{10} and $PM_{2.5}$ and suicide cases in a subpopulation with cardiovascular diseases in seven cities in South Korea. The latter study used data from 2004, and our study confirmed this evidence using a longer period of data and in the entire population. Another study, undertaken in Salt Lake County, Utah, also based on a single-pollutant model, reported positive associations between NO_2 and $PM_{2.5}$ levels and suicide but found no association for SO_2 or PM_{10} (Bakian et al. 2015). The associations for $PM_{2.5}$ reported by the previous studies in South Korea (Kim et al. 2010) and in the United States (Bakian et al. 2015) were based on single-lag estimates, but these associations weakened when including multiple lag days to estimate the effects of cumulative exposure. Similar to our findings, all the previous evidence of associations suggested short exposure periods lasting one day (current day) to an average of 0–3 d.

A previous study conducted in Tokyo reported little evidence for the association of NO_2, SO_2, $PM_{2.5}$, and suspended particulate matter with total suicides based on both the single- and two-pollutant models (Ng et al. 2016). Their finding of a lack of associations between air pollutants and total suicide is inconsistent with our significant findings from the single-pollutant model; this discrepancy may be due to the differences in the study design, such as the study period and the geographical boundary of Tokyo, which render the results not directly comparable. For example, we used data from central Tokyo, which is smaller than the metropolitan Tokyo in Ng et al. (2016). Our study period spanned 30 y (April 1979 to March 2009), whereas Ng et al. (2016) investigated a shorter and more recent period (from 2001 to 2011).

In our study, some of the air pollution–suicide associations from the single-pollutant model were attenuated after adjusting for a second pollutant. For example, the association for SO_2 was largely reduced after adjusting for NO_2 or for PM_{10}. These reductions may be due to high correlations among the pollutants. The mean values of Pearson's correlation coefficient across cities were 0.65 between NO_2 and SO_2, 0.64 between NO_2 and PM_{10}, and 0.60 between PM_{10} and SO_2 (see Table S2). A notable finding is that the association between PM_{10} and suicide remained significant after adjusting for SO_2, although we observed that the association for SO_2 decreased considerably after adjusting for PM_{10} or for NO_2. This finding suggests that SO_2 may act as a proxy for PM_{10} or for NO_2 in unadjusted models, and its effect on suicide should therefore be interpreted with caution. It is also noteworthy that the concentrations of SO_2 were generally low in our study area (ranging between 3.7 and 7.3 ppb, with the exception of Kaohsiung, where the concentration was 9.3 ppb) and have decreased over time in Japanese and Taiwanese cities (data not shown). The observed SO_2 levels were lower than those recommended by World Health Organization air quality guidelines (24-h mean of 20 $\mu g/m^3$; approximately 7.6 ppb) (Krzyzanowski and Cohen 2008; WHO 2006).

We observed a higher risk of suicide mortality associated with air pollution (NO_2, SO_2, and PM_{10}) in the young age group (10–24 y) than in the older age groups in some cities, although subsequently, the combined RRs provided weak evidence of an effect modification. A few previous studies have reported a similar tendency. Lin et al. (2016) reported higher risks for NO_2 and SO_2 in a population <65 y old in Guangzhou, China. Kim et al. (2010) reported a higher risk for PM_{10} in a population 36–64 y old in seven cities in South Korea. In Tokyo, there was evidence of an association for NO_2 in the population <30 y of age, although the association was not reported for the total population (Ng et al. 2016).

Mechanisms for why increases in air pollutants may be associated with suicide are unknown. Previous researchers have hypothesized that higher levels of air pollution induce proinflammatory cytokines that may lead to a neuroinflammatory effect on the brain (e.g., dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis and changes in neurotransmitter levels) by direct and indirect pathways and that these pathways, in turn, may be involved in the development of depression, suicidal behavior, or both (Bakian et al. 2015; Kim and Cho 2016; Ng et al. 2016). Some studies have suggested that air pollutants can reach the brain through multiple pathways and may cause neuroinflammation related to neurodegenerative diseases such as Parkinson disease (Block and Calderón-Garcidueñas 2009; Levesque et al. 2011). A cohort study has indicated potential links between oxidative stress, inflammation, and anxiety related to air pollution (Power et al. 2015). Previous evidence has mainly supported the chronic effect of air pollution on the brain, whereas our study demonstrates a short-term association between air pollution and suicide, suggesting that higher levels of air pollutants, playing a role as neurotoxins,

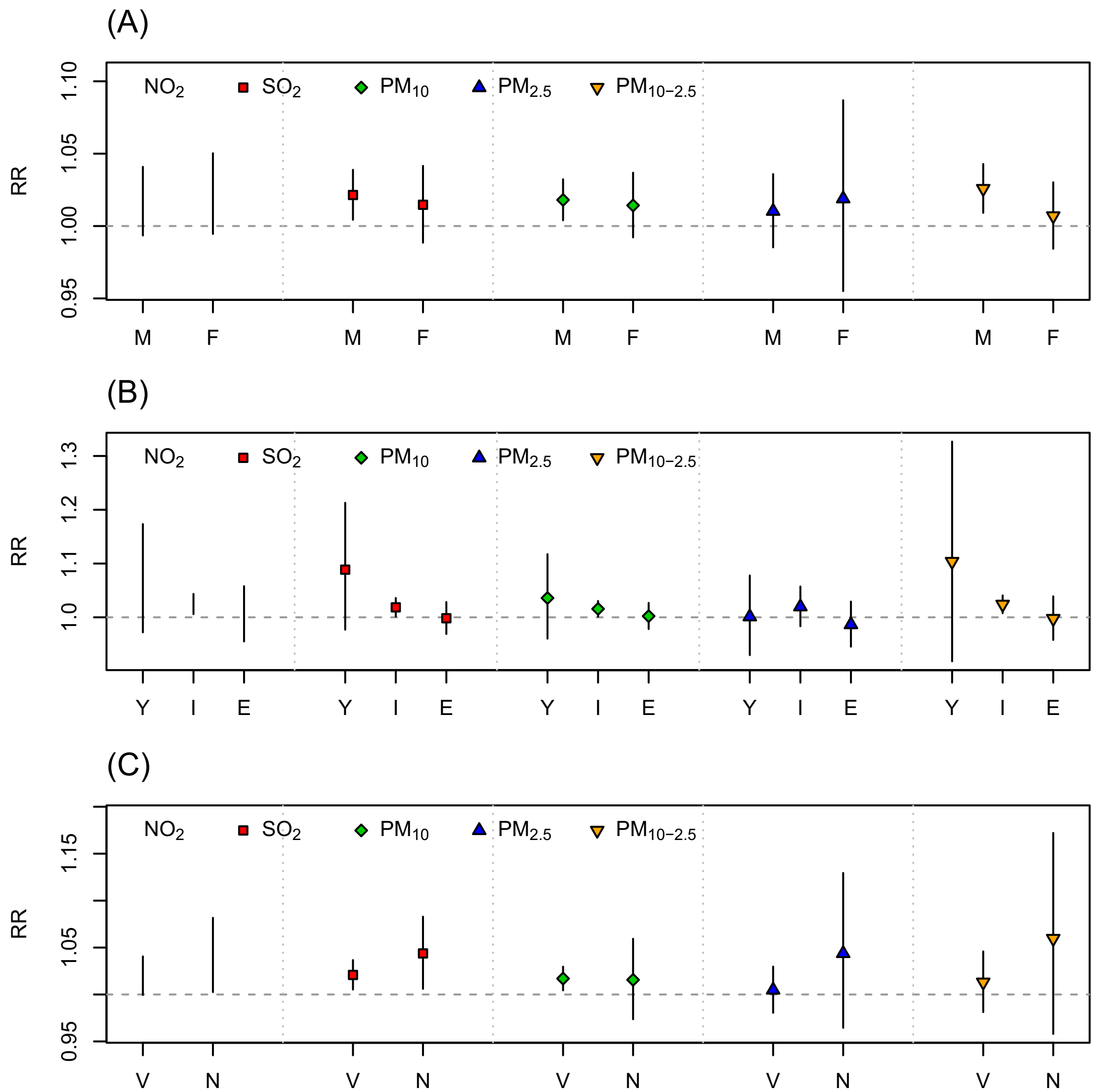

Figure 4. Combined relative risks (RRs) and 95% confidence intervals of suicide stratified by (*A*) sex (M, males; F, females), (*B*) age groups (Y, 10–24 y; I, 25–64 y; E, ≥65 years), and (*C*) method of suicide (V, violent suicide; N, nonviolent suicide) per interquartile range increase in the average 0–1 d concentration of nitrogen dioxide (NO_2), sulfur dioxide (SO_2), particulate matter with aerodynamic diameter ≤10 μm; (PM_{10}), particulate matter with aerodynamic diameter ≤2.5 μm ($PM_{2.5}$), and coarse particulate matter ($PM_{10-2.5}$) after adjusting for potential confounders (i.e., ambient temperature, sunshine duration, day-of-week, public holiday, seasonality, and long-term time trend) in single-pollutant models.

might provoke predisposed susceptible people to die by suicide. However, this supposition is premature and lacks support because suicide is a complex behavior linked to a number of psychosocial factors. Further research evaluating the neurophysiological response to air pollutants is needed to help understand the impact of air pollution on suicide.

One of our sensitivity analyses comparing two different approaches to control for temperature and sunshine duration showed that the effect estimates for the air pollution–suicide association were consistently higher in models that employed moving averages of the variables for adjustment, as opposed to the distributed lag nonlinear model. Our results suggest the importance of appropriate adjustment for weather factors, particularly temperature, in air pollution–suicide studies. This issue has been described in a simulation study by Gasparrini (2016), which suggested more flexible approaches. Because the temperature–suicide association was positive and strong in our study, the use of moving averages might have led to overestimation of the air pollution–suicide association. However, this should be evaluated further in a controlled setting.

This study has several limitations. First, it is possible that we did not consider other unmeasured time-varying factors that may be associated with suicide, and these remained as residual confounders. However, as we adjusted for day-of-week, seasonality, and long-term time trend using the time-stratified case-crossover design, such confounding may be negligible because it is unlikely that those factors change within a stratum. Second, suicide data may be underreported by misclassification, such that the cause of death is recorded as undetermined or accidental (Chan et al. 2015; Chang et al. 2010). However, such misclassification has become less likely in recent years. In Korea, death statistics have become more accurate because multisource databases are linked (Chan et al. 2015). Japan has had few misclassified suicide statistics over at least the past two decades (Chan et al. 2015). In addition, there is no reason to believe that the underreported cases have biased our findings substantially because the extent of misclassification is not likely to be associated with exposure levels (air pollution). Third, we used ambient air pollutant level as a surrogate for individual-level exposure. This measurement error, known as Berkson's error, could cause more uncertainty for the estimated association, but little or no bias (Armstrong 1998). Finally, we assumed that the association is constant over time, but it may vary over time. It would be interesting to investigate whether a time-varying association exists in future studies using more flexible statistical approaches.

Conclusion

Our study suggests that higher levels of air pollution may be associated with suicide. These findings contribute to a better understanding of suicide associated with environmental factors. Further study is required to identify the underlying mechanisms for the short-term association between air pollution and suicide.

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