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Long-term exposure to air pollution and the risk of suicide death: A population-based cohort study

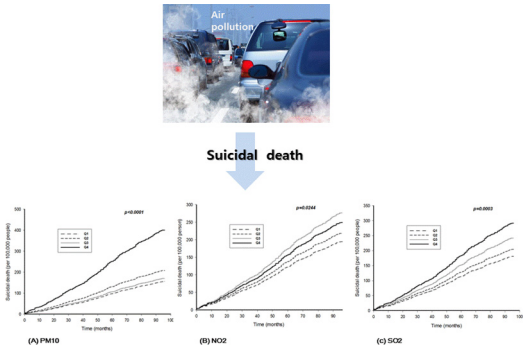
Jin-young Min [a], Hye-Jin Kim [b], Kyoung-bok Min [b,*]

[a] Institute of Health and Environment, Seoul National University, Seoul, Republic of Korea
[b] Department of Preventive Medicine, College of Medicine, Seoul National University, Seoul, Republic of Korea

HIGHLIGHTS

- Air pollution is associated with mental health problems.
- We investigated the risk of suicide death on exposure to air pollution.
- Adults exposed to high air pollution had an increased likelihood for suicide death.
- Adults having an underling disease and living in metropolitan areas were more susceptible to air pollution exposure.
- Air pollution may be a risk factor for completed suicide.

GRAPHICAL ABSTRACT



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ABSTRACT

Suicide is a major public health problem. Previous studies have reported a significant association between acute exposure to air pollution and suicide; little attention has been paid to the long-term effects of air pollution on risk of suicide. We investigated whether long-term exposure to particulate matter of ≤10 μm in diameter (PM_{10}), nitrogen dioxide (NO_2), and sulfur dioxide (SO_2) would be associated with a greater risk of death by suicide. The study sample comprised 265,749 adults enrolled in the National Health Insurance Service-National Sample Cohort (2002−2013) in South Korea. Suicide death was defined as per ICD-10 code. Data on air pollution exposure used nationwide monitoring data, and individual exposure levels were assigned using geographic information systems. Air pollution exposure was categorized as the interquartile range (IQR) and quartiles. Hazards ratios (HRs) were calculated for the occurrence of suicide death after adjusting for potential covariates. During the study period, 564 (0.2%) subjects died from suicide. Increases in IQR pollutants (7.5 μg/m^3 for PM_{10}, 11.8 ppb for NO_2, and 0.8 ppb for SO_2) significantly increased HR for suicide death [PM_{10}: HR = 3.09 (95% CI: 2.63–3.63); NO_2: HR = 1.33 (95% CI: 1.09–1.64); and SO_2: HR = 1.15 (95% CI: 1.07–1.24)]. Compared with the lowest level of air pollutants (Quartile 1), the risk of suicide significantly increased in the highest quartile level (Quartile 4) for PM_{10} (HR = 4.03; 95% CI: 2.97–5.47) and SO_2 (HR = 1.65; 95% CI: 1.29–2.11) and in the third quartile for NO_2 (HR = 1.52; 95% CI: 1.17–1.96). HRs for subjects with a physical or mental disorder were higher than that those for subjects without the disorder. Subjects living in metropolitan areas were more vulnerable to long-term PM_{10} exposure than those living in non-metropolitan areas. Long-term exposure to air pollution was associated with a significantly increased risk of suicide death. People having underlying diseases or living in metropolitan areas may be more susceptible to high air pollution exposure.

* Corresponding author at: Department of Preventive Medicine, Colleague of Medicine, Seoul National University, 103 Daehak-ro, Jongno-gu, Seoul 110-799, Republic of Korea.
E-mail address: minkb@snu.ac.kr (K. Min).

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1. Introduction

Suicide is a major public health problem around the world. An estimated 1.4% of deaths worldwide are a result of suicide, making it the 15th leading cause of death (World Health Organization, 2014). Suicide completion is not just a threat to personal life but also poses a substantial burden on individuals, families, and communities (World Health Organization, 2014). Suicidal behaviors are largely influenced by a variety of factors such as individual traits (i.e., poverty, impulsive aggression, and physical and mental health status), interpersonal conflict, and lack of social supports and networks (Sinyor et al., 2017; Turecki and Brent, 2016).

The possible association between environmental exposure to pollutants and suicide has recently become a concern (Sinyor et al., 2017). One important environmental exposure is air pollution (Bakian et al., 2015; Kim et al., 2010; Kim et al., 2015; Szyszkowicz, 2010; Yang et al., 2011). Historically, air pollution has been a significant contributor to the development of cardiovascular and respiratory illnesses and mortality (Brunekreef and Holgate, 2002; Hoek et al., 2013); emerging evidence also suggests the existence of air pollution-induced mental health problems (Lim et al., 2012; Min and Min, 2017; Oudin et al., 2016; Power et al., 2015; Sass et al., 2017). Exposure to particulate matter of ≤10 μg/m (PM_{10}), particulate matter of ≤2.5 μg/m ($PM_{2.5}$), nitrogen dioxide (NO_2), or ozone (O_3) was significantly associated with the prevalent symptoms of depression and anxiety as well as psychological distress (Lim et al., 2012; Power et al., 2015; Sass et al., 2017). Compared with children and adolescents living in areas with lower air pollution, those living in areas with higher air pollution were more likely to be diagnosed with childhood Attention Deficit Hyperactivity Disorder or to have a dispensed medication for a psychiatric disorder (Min and Min, 2017; Oudin et al., 2016).

Considering the close relationship between air pollution exposure and mental health, it is not surprising that previous studies found that high exposure to air pollutants is significantly associated with an increased risk of completed suicide (Bakian et al., 2015; Kim et al., 2010; Kim et al., 2015; Szyszkowicz, 2010; Yang et al., 2011). A study conducted in South Korea analyzed a total of 4341 suicide cases from data on suicides that occurred in seven metropolitan cities in 2004 (Kim et al., 2010). The authors found that exposures to PM_{10} on lag day 2 and $PM_{2.5}$ on lag day 1 were associated with maximum increases of 9.0% and 10.1% in suicide completion. A US-based study conducted by Bakian et al. (2015) identified a significant association between short-term exposure to air pollutants and suicide completed in Salt Lake County, Utah (Bakian et al., 2015). The adjusted odds for suicide death were 20% for NO_2 on lag day 3 and 5% for $PM_{2.5}$ on lag day 2. A recent Chinese study found a similar relationship between air pollution and suicide death (Lin et al., 2016). Additional studies have documented the seasonal variation (i.e., for summer and cold) in the association between air pollution and the risk of suicide (Szyszkowicz, 2010; Yang et al., 2011).Although most previous studies have demonstrated the short-term effect of air pollutants on completed suicide (Bakian et al., 2015; Kim et al., 2010; Kim et al., 2015; Yang et al., 2011), epidemiologic studies have suggested a potential effect of long-term air pollution on aspects of poor mental health in humans (Kim et al., 2016; Min and Min, 2017; Tzivian et al., 2015). Mice exposed to $PM_{2.5}$for 10 months showed depressed-like affective responses or cognitive impairment, through increased in circulating inflammatory markers or structural changes in hippocampus (Fonken et al., 2011). Based on this circumstantial evidence, examining the association between long-term exposure to air pollution and completed suicide may be a valuable contribution to extend findings from previous research.

In the current study, we hypothesized that long-term exposure to air pollution is associated with a higher risk of suicide. Using a representative cohort of South Koreans, we conducted a prospective population-based study with a 4-year baseline period (2002–2005) and an 8-year follow-up assessment (2006–2013) to examine the association between long-term exposure to airborne particulate and gaseous pollutants and death by suicide in adults. Considering that the health impact of air pollution differs depending on underlying diseases (Bateson and Schwartz, 2004; Mann et al., 2002; Peel et al., 2007), and air quality is different in urban and rural residential areas (Ahn, 2015; Strosnider et al., 2017), we further analyzed the association between air pollution and suicide by the presence of a physical or mental disease and residential areas.

2. Materials and methods

2.1. Data source and study population

The National Health Insurance Service (NHIS) in South Korea provides mandatory social insurance programs for the entire population through government subsidies. The NHIS is the source of nearly all medical data serviced in healthcare facilities including medical examinations and treatment, prescriptions, personal information, and diagnostic codes, as per the International Classification of Diseases (ICD).

The NHIS-National Sample Cohort (NHIS-NSC) is a population-based cohort extracted from the NHIS database (project number: NHIS-2016-2-0081). The NHIS-NSC was constructed by a stratified random sampling design using age, gender, income, residential area, and annual medical expenses to ensure representativeness of the South Korean population. A total of 1,025,340 subjects who account for approximately 2.2% of the total eligible population, comprised the cohort in 2002; these subjects were followed-up until 2013 (Lee et al., 2016).

From the NHIS-NSC, we initially included 746,816 subjects who were aged ≥20 years in 2002. We excluded adults who had incomplete data on address and income (n = 22,878); the remaining population consisted of 723,938 subjects. Of these, approximately 37% had completed at least one medical examination and questionnaires on health behaviors (i.e., exercise, smoking status, and alcohol consumption), and so 458,189 subjects were excluded for the current study. A total of 265,749 adults were included for the final analysis. The study protocol was approved by the Institutional Review Board of Seoul National University Hospital. Informed consent was exempted by the committee.

2.2. Variables

As the main outcome variable, suicide death was defined as "death arising from an act inflicted upon oneself with the intent to kill oneself". Death due to suicide was defined as ICD-10 codes X60-X84.

Demographic characteristics, health behaviors, and the presence of mental and physical diseases were gathered as baseline characteristics of the study population in 2002–2005. Demographic variables included age in 10-year increments (20–29, 30–39, 40–49, 50–59, 60–69, 70–79, or ≥80 years), sex (male or female), residential area (metropolitan or non-metropolitan), and household income relative to the median (<25%, 25–50%, 50–75%, or >75%). Body mass index (BMI) was calculated as an individuals' weight in kilograms divided by height in meters squared, and was categorized as a binary variable (<25.0 or ≥25.0 kg/m^2). Health behaviors included exercise (yes or no), smoking experiences [no (never smoked) or yes (previously or currently smoker)], and alcohol consumption (yes or no). Disease status was defined as having a physical or mental disease potentially affecting the risk of suicide (Bostwick and Pankratz, 2000; Bronisch and Wittchen, 1994; Juurlink et al., 2004; Palmer et al., 2005; Scott et al., 2010). Physical health status was based on the Charlson comorbidity index (CCI) developed by Quan et al. (2005), in which the score ≥ 1 was classified as the presence of physical diseases (Quan et al., 2005). Mental health problems were defined as psychological conditions including anxiety, depression, major affective disorder, and schizophrenia (Bostwick and Pankratz, 2000; Bronisch and Wittchen, 1994; Palmer et al., 2005). The presence of psychiatric conditions was diagnosed by family physicians or general practitioners and specialist physicians in a hospital or

clinic, and the ICD-10 code was as follows: anxiety (ICD-10: F40-F41), depression (ICD-10: F32-F33), major affective disorder (ICD-10: F34, F38, F39), and schizophrenia (ICD-10: F20). Meteorological data were obtained from the National Meteorological Office and included as the yearly mean values of temperature and precipitation.

2.3. Estimation of individual exposure to air pollutants

We obtained air pollution data [particulate matter ≤10 μm in diameter (PM_{10}), nitrogen dioxide (NO_2), and sulfur dioxide (SO_2)] from the National Ambient Air Monitoring Information System (NAMIS) (Korea Environment Corporation, 2017). The NAMIS provided daily air pollution data from community-based monitoring sites (267 sites in 2002) that were available in real-time through the organizations' website (Korea Environment Corporation, 2017). We downloaded the pollutant data for PM_{10}, NO_2, and SO_2 and calculated their annual mean levels from January 2002 to December 2012. We then computed the long-term average exposure levels of these pollutants over a specific period (i.e., until diagnosis of suicide death or end of the study period) for each individual.

Since data on air pollution levels were not available for all areas of South Korea, we applied the interpolation technique using geographic information systems (GIS) tools (Arc GIS Version 10.4, ESRI, Redlands, CA, USA) to estimate PM_{10}, NO_2, and SO_2 levels in unmonitored regions. All monitoring sites were integrated within the GIS, and the Kriging geo-statistical method was used for the spatial interpolation of air pollution data; this methodology has been widely used to assess the effect of air pollutants on health (Jerrett et al., 2005). Individual exposure levels to air pollutants were based on their addresses, and we matched the extracted regional levels of the pollutants with persons' administrative district codes. Furthermore, we recorded changes in an individual's residence during the study period; if a participant shifted to a new house, the individual exposure level to air pollution was based on the area in which the person had spent the longest time in a given year.

2.4. Statistical analysis

To estimate the effect of air pollutants on suicide death, long-term PM_{10}, NO_2, and SO_2 exposure levels from 2002 to the occurrence of suicide completion or end of the study period, as applicable, were scaled to the interquartile range (IQR) for each pollutant (7.5 $\mu g/m^3$ for PM_{10}, 11.8 ppb for NO_2, and 0.8 ppb for SO_2). Air pollutants were also categorized into quartiles with three cut-off points (25th, 50th, and 75th percentiles) for PM_{10} (Quartile 1, <51.25 $\mu g/m^3$; Quartile 2, 51.25–55.84 $\mu g/m^3$; Quartile 3, 55.84–58.73 $\mu g/m^3$; and Quartile 4, ≥58.73 $\mu g/m^3$), NO_2 (Quartile 1, <20.9 ppb; Quartile 2, 20.9–24.1 ppb; Quartile 3, 24.1–32.7 ppb; and Quartile 4, ≥32.7 ppb), and SO_2 (Quartile 1, <5.1 ppb; Quartile 2, 5.1–5.4 ppb; Quartile 3, 5.4–5.9 ppb; and Quartile 4, ≥5.9 ppb). We conducted Cox-proportional hazards regression for multivariable analysis of the occurrence of completed suicide by an IQR increase ($\mu g/m^3$ or ppb) of long-term exposure to PM_{10}, NO_2 and SO_2 from 2002 to suicide completion or end of the study period. We calculated hazard ratios (HRs) and 95% confidence intervals (CIs) for the outcome variable associated with each pollutant per increase in IQR. Additionally, HRs for each pollutant quartile level (Quartiles 2–4) were compared with Quartile 1 (reference group). The proportional hazards assumption for the model was confirmed. The Cox-proportional hazards regression model was adjusted for demographic variables (i.e., age, sex, residential area, and household income), health behaviors (i.e., exercise, smoking, and alcohol consumption), disease status (with or without a physical or mental disease), and metrological variables (i.e., temperature and precipitation). To investigate the modification effect on disease status, we classified the subjects into the two groups, with and without a physical or mental disease, and analyzed the association between air pollution and suicide death in each group. We further examined the association by stratifying residential areas as metropolitan and non-metropolitan. All analyses were performed using SAS 9.4 software (SAS Institute, Cary, NC, USA), and the statistical significance level was set at $\alpha = 0.05$.

3. Results

Table 1 shows the total population and the number and percentage of suicide death. Adults who died from suicide were more likely to be older, be male, live in non-metropolitan area, be in the lowest household income bracket, and have a low BMI. Adults who died from suicide were more likely to not exercise, to have never smoked, to drink alcohol, and to be having a disease status (in other words 'with a physical or mental disease').

Although correlations varied from pollutant to pollutant, there were significant positive correlations among each pollutant (Supplementary Table 1). The highest correlation levels were found between PM_{10} and NO_2 ($r = 0.68$, p-value ≤ 0.0001).

Table 2 indicates the comparison of mean air pollution (PM_{10}, NO_2, and SO_2) for subjects by suicide event and residential areas. Mean (SE) concentrations of air pollutants were 55.11 (0.01) $\mu g/m^3$ for PM_{10}, 25.64 (0.01) ppb for NO_2, and 5.55 (0.00) ppb for SO_2. IQR concentrations were 7.5 $\mu g/m^3$, for PM_{10}, 11.8 ppb for NO_2, and 0.8 ppb for SO_2. When we compared mean air pollution levels between subjects with and without suicide death during the follow-up period, PM_{10} and SO_2 levels were significantly higher for subjects who did not die by suicide compared to subjects who did die by suicide, whereas NO_2 levels did not differ between the two groups. Subjects living in metropolitan

Table 1
Characteristics of study population.

Characteristics	Total population	no. of suicide cases (%[a])	
Age (years)			
20–29	48,264	39	(0.08)
30–39	60,159	88	(0.15)
40–49	70,509	124	(0.18)
50–59	44,506	102	(0.23)
60–69	31,508	144	(0.46)
70–79	9584	57	(0.59)
≥80	1219	10	(0.82)
Sex			
Male	145,189	419	(0.29)
Female	120,560	145	(0.12)
Residential areas			
Metropolitan	123,399	236	(0.19)
Non-metropolitan	142,350	328	(0.23)
Household income relative to the median (%)			
Lowest (<25%)	84,718	214	(0.25)
25–50%	52,291	115	(0.22)
50–75%	60,562	118	(0.19)
Highest (>75%)	68,178	117	(0.17)
BMI (kg/m^2)			
<25	175,451	395	(0.23)
≥25	90,298	169	(0.19)
Exercise			
No	124,031	292	(0.24)
Yes	141,718	272	(0.19)
Smoking status			
Never	68,415	192	(0.28)
Current smoker	197,334	372	(0.19)
Alcohol consumption			
No	121,911	248	(0.20)
Yes	143,838	316	(0.22)
Disease status[b]			
No	192,077	299	(0.16)
Yes	73,672	265	(0.36)

BMI, body mass index; CCI, Charlson Comorbidity Index.

[a] % means percentage of suicide cases corresponding to each category in individual characteristics.

[b] Disease state means whether there is a physical or mental health problem. The CCI score of ≥1 or the presence of psychiatric conditions (i.e., anxiety, depression, major affective disorder, and schizophrenia) was considered to be having a disease status.

Table 2
Comparison of mean (SE) air pollution for subjects by suicide event and residential areas.

Air pollutants	Mean	SE	IQR	Suicide event					Residential areas				
				Subjects with suicide death		Subjects without suicide death		p-Value*	Subjects living in metropolitan		Subjects living in non-metropolitan		p-Value*
PM_{10} (μg/m^3)	55.11	(0.01)	7.48	55.11	(0.01)	57.01	(0.02)	<0.0001	55.35	(0.01)	55.15	(0.01)	<0.0001
NO_2 (ppb)	25.64	(0.01)	11.78	25.60	(0.01)	25.50	(0.02)	0.7032	28.00	(0.00)	23.80	(0.00)	<0.0001
SO_2 (ppb)	5.55	(0.00)	0.77	5.55	(0.00)	5.65	(0.00)	0.0064	5.69	(0.00)	5.46	(0.00)	<0.0001

SE, standard error; IQR, interquartile range.
* p-Value on *t*-test.

areas were exposed to significantly higher PM_{10}, NO_2, and SO_2 levels than those living in non-metropolitan areas (all p-value < 0.0001).

Table 3 shows HRs for suicide death by PM_{10}, NO_2, and SO_2 levels. With an IQR increase in each pollutant, adjusted HRs were significant [PM_{10}: HR = 3.09 (95% CI: 2.63–3.63); NO_2: HRs = 1.33 (95% CI: 1.09–1.64); and SO_2: HRs = 1.15 (95% CI: 1.07–1.24)]. Compared to the lowest quartile of each air pollutant, subjects who were exposed to the highest quartile (Quartile 4) had a significantly higher risk of suicide death [PM_{10}: adjusted HR = 4.03 (95% CI: 2.97–5.47); NO_2: adjusted HRs = 1.36 (95% CI: 1.02–1.83); and SO_2: adjusted HR = 1.65 (95% CI: 1.29–2.11)]. Significant dose-response relationships were found in increases in air pollution quartiles (p for trend < 0.05). Kaplan-Meier survival curves (Supplementary Fig. 1) display that subjects living in an area with high air pollution had significantly higher probability of suicide death than those living in an area with low air pollution, in term of exposure to PM_{10} (p < 0.0001), NO_2 (p = 0.0163), or SO_2 (p = 0.0003).

Table 4 shows HRs for suicide death due to PM_{10}, NO_2, and SO_2 levels by the presence of a physical or mental disease. Subjects with a physical or mental disease exhibited more predominant effect on the association between air pollution and suicide than those without the disease. With an IQR increase in each pollutant, subjects with a physical or mental disease had significant adjusted HRs for suicide death [PM_{10}: HR = 3.27 (95% CI: 2.60–4.10); NO_2: HR = 1.39 (95% CI: 1.03–1.87); and SO_2: HR = 1.19 (95% CI: 1.07–1.33)], whereas those without the disease showed significance regarding PM_{10} exposure only (HR = 2.81; 95% CI: 2.26–3.49). Regarding comparisons of exposure to the quartile air pollution (Quartile 1 as a reference group), adults with a physical or mental disease showed significantly increased HRs in the high quartiles of PM_{10} (adjusted HR = 4.35; 95% CI: 2.79–6.79 in Quartile 4), NO_2 (adjusted HR = 1.85; 95% CI: 1.30–2.62 in Quartile 3), and SO_2 (adjusted HR = 1.70; 95% CI: 1.20–2.41 in Quartile 4) and exhibited a significant dose-response relationship between these pollutants and suicide risk (p for trend < 0.05). Conversely, subjects without a physical or mental disease showed a similar relationship, but showed lower HRs for suicide death [PM_{10}: adjusted HR = 3.21 (95% CI: 2.14–4.82) in Quartile 4; NO_2: adjusted HR = 1.42 (95% CI: 1.01–2.01) in Quartile 3; and SO_2: adjusted HR = 1.40 (95% CI: 1.01–1.94) in Quartile 4] than those with the disease. No significant dose-response relationships were established in the increases in the quartiles of NO_2 and SO_2 exposures.

Table 5 indicates HRs for suicide death due to PM_{10}, NO_2, and SO_2 levels in residential areas. Overall, subjects living in metropolitan areas had a higher likelihood of suicide death associated with air pollutants, except for SO_2, than those living in non-metropolitan areas. Subjects living in metropolitan areas had significant HRs for suicide death regarding an IQR increase of PM_{10} and NO_2 [PM_{10}: adjusted HR = 4.93 (95% CI: 3.83–6.35) and NO_2: adjusted HR = 1.89 (95% CI: 1.20–2.97)], but not SO_2. Similarly, compared with the lowest quartile (Quartile 1), except for SO_2, they showed significantly increased HRs in the highest quartile (Quartile 4): adjusted HR = 6.79 (95% CI: 4.14–11.12) for PM_{10} and adjusted HR = 1.72 (95% CI: 1.01–2.94) for NO_2. Conversely, subjects living in non-metropolitan areas were associated with significant HRs for completed suicide with increases in both IQR and the quartile air pollutants.

Table 3
HRs (95% CIs) for suicide by interquartile-range (IQR) increases and the quartiles of air pollutants.

Air pollutants	No. of suicide case/total population	Unadjusted model	Adjusted model[a]
PM_{10} (μg/m^3)			
IQR[b] increases		1.87 (1.64–2.13)	3.09 (2.63–3.63)
Quartiles			
Quartile 1 (<51.25)	98/62,495	Reference	Reference
Quartile 2 (51.25–55.84)	143/69,972	1.31 (1.01–1.69)	1.57 (1.19–2.05)
Quartile 3 (55.84–58.73)	97/67,111	0.92 (0.69–1.21)	1.64 (1.17–2.31)
Quartile 4 (≥58.73)	226/66,171	2.21 (1.74–2.80)	4.03 (2.97–5.47)
p for trend		<0.0001	<0.0001
NO_2 (ppb)			
IQR[b] increases		0.96 (0.83–1.12)	1.33 (1.09–1.64)
Quartiles			
Quartile 1 (<20.9)	147/69,302	Reference	Reference
Quartile 2 (20.9–24.1)	148/71,762	0.97 (0.77–1.22)	1.20 (0.94–1.52)
Quartile 3 (24.1–32.7)	146/61,444	1.12 (0.89–1.40)	1.52 (1.17–1.96)
Quartile 4 (≥32.7)	123/63,241	0.91 (0.71–1.15)	1.36 (1.02–1.83)
p for trend		0.3794	0.0163
SO_2 (ppb)			
IQR[b] increases		1.11 (1.03–1.19)	1.15 (1.07–1.24)
Quartiles			
Quartile 1 (<5.1)	117/64,460	Reference	Reference
Quartile 2 (5.1–5.4)	120/65,773	1.00 (0.78–1.29)	1.14 (0.87–1.50)
Quartile 3 (5.4–5.9)	148/68,316	1.19 (0.93–1.52)	1.36 (1.05–1.76)
Quartile 4 (≥5.9)	179/	1.48 (1.17–1.87)	1.65 (1.29–2.11)
p for trend		0.0014	0.0003

[a] Adjusted for age, sex, residential area, household income, MI, exercise, smoking status, alcohol consumption, disease status, temperature, and precipitation.
[b] IQR: 7.5 μg/m^3 for PM_{10}, 11.8 ppb for NO_2, and 0.8 ppb for SO_2.

4. Discussion

In a large, national cohort study of South Korean adults, we found that long-term exposure to air pollution was associated with an increased risk of death by suicide. With an IQR increase in air pollutant levels, the risk of suicide death was the highest in PM_{10}, at approximately 3-fold, and increased 1.3-fold with NO_2 exposure and 1.2-fold with SO_2 exposure. When we compared to subjects exposed to the lowest level of air pollutants, the risk of suicide death increased significantly in the highest quartile of PM_{10} (4-fold) and SO_2 (1.7-fold) and the third quartile of NO_2 (1.4-fold). Subjects diagnosed with a physical or mental disease exhibited greater HRs of suicide death associated with high air pollution than those without the disease. Moreover, the association between exposure to air pollutants (except for SO_2) and completed suicide was more predominant among subjects living in metropolitan areas than among those living in non-metropolitan areas.

To the best of our knowledge, this is the first study to consider the association between long-term air pollution and suicide death. However, our results are in line with the results of prior studies that

Table 4
HRs (95% CIs) for suicide by interquartile-range (IQR) increases and the quartiles of air pollutants by the presence of physical or mental disease.

Air pollutants	With a physical or mental disease[a] (n = 73,672)				Without a physical or mental disease (n = 192,077)			
	Unadjusted model		Adjusted model[b]		Unadjusted model		Adjusted model[b]	
PM_{10} (μg/m^3)								
IQR[c] increases	2.16	(1.78–2.62)	3.27	(2.60–4.10)	1.87	(1.56–1.24)	2.81	(2.26–3.49)
Quartiles								
Quartile 1 (<51.25)	Reference		Reference		Reference		Reference	
Quartile 2 (51.25–55.84)	1.55	(1.06–2.26)	1.67	(1.13–2.45)	1.20	(0.84–1.71)	1.33	(0.93–1.91)
Quartile 3 (55.84–58.73)	1.06	(0.69–1.63)	1.78	(1.08–2.92)	1.07	(0.75–1.55)	1.75	(1.13–2.70)
Quartile 4 (≥58.73)	2.73	(1.91–3.91)	4.35	(2.79–6.79)	1.97	(1.42–2.37)	3.21	(2.14–4.82)
p for trend	<0.0001		<0.0001		<0.0001		<0.0001	
NO_2 (ppb)								
IQR[c] increases	0.99	(0.79–1.25)	1.39	(1.03–1.87)	1.01	(0.82–1.25)	1.30	(0.99–1.72)
Quartiles								
Quartile 1 (<20.9)	Reference		Reference		Reference		Reference	
Quartile 2 (20.9–24.1)	0.87	(0.62–1.22)	1.20	(0.72–1.45)	1.01	(0.74–1.39)	1.15	(0.84–1.59)
Quartile 3 (24.1–32.7)	1.36	(0.99–1.88)	1.85	(1.30–2.62)	1.16	(0.85–1.59)	1.42	(1.01–2.01)
Quartile 4 (≥32.7)	0.89	(0.61–1.28)	1.42	(0.92–2.20)	0.91	(0.66–1.27)	1.22	(0.82–1.81)
p for trend	0.0305		0.0023		0.5367		0.2504	
SO_2 (ppb)								
IQR[c] increases	1.14	(1.03–1.27)	1.19	(1.07–1.33)	1.09	(0.98–1.20)	1.10	(0.99–1.21)
Quartiles								
Quartile 1 (<5.1)	Reference		Reference		Reference		Reference	
Quartile 2 (5.1–5.4)	0.85	(0.58–1.25)	0.93	(0.62–1.39)	1.08	(0.77–1.51)	1.17	(0.82–1.66)
Quartile 3 (5.4–5.9)	1.18	(0.83–1.69)	1.30	(0.90–1.87)	1.02	(0.73–1.43)	1.10	(0.78–1.56)
Quartile 4 (≥5.9)	1.55	(1.11–2.17)	1.70	(1.20–2.41)	1.36	(0.99–1.87)	1.40	(1.01–1.94)
p for trend	0.0046		0.0002		0.1673		0.1941	

[a] With a physical or mental disease includes participants with disease status of 'yes'. Disease status was defined as the CCI scores ≥ 1 or the presence of psychiatric conditions (i.e., anxiety, depression, major affective disorder, and schizophrenia).
[b] Adjusted for age, sex, residential area, household income, MI, exercise, smoking status, alcohol consumption, disease status, temperature, and precipitation.
[c] IQR:7.5 μg/m^3 for PM_{10}, 11.8 ppb for NO_2, and 0.8 ppb for SO_2.

examined the acute effect of air pollution on completed suicide (Bakian et al., 2015; Kim et al., 2010; Lin et al., 2016; Yang et al., 2011). In these studies, although the concentration and composition of air pollutants and population-level features (i.e., age and race) vary across countries, the researchers have consistently demonstrated a significantly increased risk of suicide associated with high concentrations of particulate

Table 5
HRs (95% CIs) for suicide by interquartile-range (IQR) increases and the quartiles of air pollutants by residential areas (metropolitan vs. non-metropolitan).

Air pollutants	Metropolitan areas (n = 123,399)				Non-metropolitan areas (n = 142,350)			
	Unadjusted model		Adjusted model[a]		Unadjusted model		Adjusted model[a]	
PM_{10} (μg/m^3)								
IQR[b] increases	2.62	(2.09–3.29)	4.93	(3.83–6.35)	1.72	(1.56–1.24)	2.95	(2.39–3.65)
Quartiles								
Quartile 1 (<51.25)	Reference		Reference		Reference		Reference	
Quartile 2 (51.25–55.84)	0.85	(0.67–1.09)	0.86	(0.54–1.37)	1.50	(1.26–1.79)	2.46	(1.72–3.54)
Quartile 3 (55.84–58.73)	0.59	(0.47–0.75)	1.59	(0.92–2.74)	1.17	(0.95–1.44)	3.10	(1.93–4.98)
Quartile 4 (≥58.73)	3.15	(2.58–3.85)	6.79	(4.14–11.12)	1.94	(1.64–2.29)	4.33	(2.79–6.71)
p for trend	<0.0001		<0.0001		<0.0001		<0.0001	
NO_2 (ppb)								
IQR[b] increases	1.08	(0.84–1.39)	1.89	(1.20–2.97)	1.05	(0.85–1.31)	1.45	(1.13–1.87)
Quartiles								
Quartile 1 (<20.9)	Reference		Reference		Reference		Reference	
Quartile 2 (20.9–24.1)	0.95	(0.74–1.23)	0.89	(0.56–1.43)	1.05	(0.90–1.22)	1.32	(0.99–1.77)
Quartile 3 (24.1–32.7)	1.13	(0.89–1.44)	1.48	(0.91–2.39)	1.13	(0.97–1.32)	1.76	(1.27–2.43)
Quartile 4 (≥32.7)	1.09	(0.86–1.38)	1.72	(1.01–2.94)	0.88	(0.73–1.06)	1.45	(0.97–2.18)
p for trend	0.3030		0.0532		0.0900		0.0083	
SO_2 (ppb)								
IQR[b] increases	1.05	(0.96–1.18)	1.04	(0.94–1.15)	1.28	(0.98–1.20)	1.31	(1.17–1.47)
Quartiles								
Quartile 1 (<5.1)	Reference		Reference		Reference		Reference	
Quartile 2 (5.1–5.4)	1.01	(0.81–1.25)	1.12	(0.73–1.73)	0.98	(0.82–1.16)	1.19	(0.83–1.69)
Quartile 3 (5.4–5.9)	0.94	(0.75–1.17)	1.22	(0.80–1.85)	1.00	(0.85–1.17)	1.44	(1.04–2.00)
Quartile 4 (≥5.9)	1.41	(1.15–1.73)	1.31	(0.87–1.96)	1.44	(1.23–1.68)	1.88	(1.37–2.57)
p for trend	0.0001		0.5933		<0.0001		0.0005	

[a] Adjusted for age, sex, household income, MI, exercise, smoking status, alcohol consumption, disease status, temperature, and precipitation.
[b] IQR:7.5 μg/m^3 for PM_{10}, 11.8 ppb for NO_2, and 0.8 ppb for SO_2.

and gaseous air pollutants (Bakian et al., 2015; Kim et al., 2010; Lin et al., 2016; Yang et al., 2011). Thus, based on the existing evidence, our findings, which suggest an association between long-term exposure and risk of suicide, may be expected.

The possible biological explanation on the observed association between air pollution and completed suicide has not been clarified. The most common understanding is that exposure to ambient particles and gaseous pollutants through respiratory or nasal inhalation activates pro-inflammatory cytokines, leading to systemic and neuronal inflammation and subsequent oxidative stress (Calderon-Garciduenas et al., 2008; Genc et al., 2012; Ji et al., 2015; Li et al., 2011; Yao et al., 2015). In experimental models, systematic inflammation and oxidative stress induced depression and anxiety-like behaviors (de Oliveira et al., 2007; Patki et al., 2013). These results are consistent with those of human studies, where increased inflammatory and oxidative stress markers were observed in subjects with depression and anxiety (i.e., mental health illnesses associated with a high risk of suicide) (Raison and Miller, 2011; Salim, 2014; Vogelzangs et al., 2013). Providing more direct evidence, high levels of various inflammatory cytokines (i.e., interleukin (IL) 2, IL-6, IL-8, and tumor necrosis factor α) have been found in suicide attempters or subjects with suicidal ideation (Serafini et al., 2013). In addition to systemic inflammation/oxidative stress, the possible association between hippocampal neurogenesis, neurotrophic factors, and major depression may be addressed in a biological context. Importantly, environmental insults (i.e., neurogenic or psychogenic stressors or certain immune insults) and major depression have been associated with structural alterations in the brain such as a loss of dendritic spines and synapses, a reduced dendritic arborization together with diminished glial cells in the hippocampus (Serafini et al., 2014). Both central monoamines and brain-derived neurotrophic factors are involved in the modulation of hippocampal progenitor proliferation and cell survival (Serafini et al., 2014). Therefore, it is biologically plausible that air pollution induces systematic inflammation/oxidative stress or impairs hippocampal neurogenesis and neurotrophic factor expression, leading pollutants to play a causative role in the occurrence of psychological problems or suicide attempts.

Importantly, subjects with a preexisting disease were more susceptible to air pollution exposure. With increases in IQR and quartiles of air pollutants, subjects with a physical or mental disease showed higher HRs for suicide death than those without the disease. In case of quartiles of PM_{10}, the likelihood for suicide death was increased by 36% in subjects diagnosed with a physical or mental disease [HR: 4.35 vs. HR: 3.21]. Consistent with this observation, previous studies have noticed risk elevation of adverse health outcomes in individuals with comorbidities (Bateson and Schwartz, 2004; Mann et al., 2002; Peel et al., 2007). Chronic conditions including diabetes, hypertension, congestive heart failure, and conduction disorders substantially increase the risk of morbidity and mortality associated with exposure to particulate and gaseous air pollutants (Bateson and Schwartz, 2004; Mann et al., 2002; Peel et al., 2007). Regarding completed suicide, Kim et al. (2010) found that an increase in PM_{10} was significantly associated with an increased suicide risk; the risk was particularly exacerbated in subjects with a cardiovascular disease (Kim et al., 2010). Many studies have produced evidence that suicide occurs as a result of physical or mental disease (Bostwick and Pankratz, 2000; Bronisch and Wittchen, 1994; Juurlink et al., 2004; Palmer et al., 2005; Scott et al., 2010) and that exposure to air pollutants affects developing or aggravating chronic diseases (Brunekreef and Holgate, 2002; Hoek et al., 2013; Kampa and Castanas, 2008). Taken together, our findings and those reported in previous studies suggest that the association between air pollution and risk of completed suicide is likely mediated by physical and mental health conditions.

Of notable is that we observed differences between subjects living in metropolitan and non-metropolitan areas regarding the association between air pollution and suicide death. Except for SO_2 exposure, HRs for suicide death were higher than for subjects living in metropolitan areas than for those living in non-metropolitan areas. Our findings support those of some previous studies on the different regional effect of air pollution on health outcomes (Priftis et al., 2007; Public Health England, 2014; Tian et al., 2015). Generally, traffic-related pollutants such as PM_{10} and NO_2 exhibit high levels in metropolitan areas, mainly due to the continuous rise in traffic (Ranjeet, 2008). SO_2 levels reflect not only road traffic but also fuel combustion from industrial facilities and residential wood combustion. Such regional variations in pollutants may be attributed to differences in the air pollution-related health problems, herein completed suicide. However, because there are several other factors (i.e., living conditions, social and medical benefits, lifestyle, and contents of pollutants) shaping metropolitan and non-metropolitan areas, further studies are necessary to confirm the reported association between air pollution and suicide death and to determine whether this association is mediated by the residential area.

Several study limitations need to be considered. An important limitation is the methodology used to assess air pollution. In epidemiologic studies, particular concern is placed on minimizing exposure misclassification at unmonitored locations and improving individual exposure estimates. To overcome such challenges, several previous studies have used GIS spatial analysis (Liao et al., 2006; Tsai et al., 2009). We similarly performed GIS with the Kriging interpolation method, which is an advanced geostatistical procedure to estimate an unknown value as a weighted average from the nearest sampling points. Nevertheless, we cannot rule out a level of uncertainty involved in the exposure assessment of air pollution. Furthermore, we used the representative, population-based cohort of the NHIS-NSC, but excluded more than half of the original sample due to lack of confounding variables, mainly medical health examinations with questionnaires on health behaviors. As shown in Supplementary Table 2, there was a significant demographic difference between the excluded and included participants of this study. Compared with latter, the former people were more likely to be young (20–29 years) or old (≥70 years) adults, to be female, to live in metropolitan areas, or to have a lower income (Quartile 1). Although the general health examination in South Korea focuses on employees and ordinary people, it is mandatory for employees; thus, the excluded population exhibited the characteristics such as being young or very old, being females, and having a relatively low income. Therefore, the results from a set of participants with certain characteristics cannot be generalized to the entire target population. Caution should be taken to apply our findings to other study settings. In addition, the NHIS-NSC was not specifically designed to investigate the association between air pollution and completed suicide; not all potential confounding variables (i.e., previous experience of suicidal behaviors, marital status, and occupation) were fully available for the current study. Finally, although the existing studies have demonstrated a different association between air pollution and suicide risk regarding specific periods of the year, such as the early summer in Taiwan (Yang et al., 2011) or cold season in Canada (Szyszkowicz, 2010), our study did not investigate the air pollution effect on suicide by seasonality. Thus, future research including factors such as personal exposure monitoring, seasonality, and unmeasured confounding variables is warranted to clarify the observed association between chronic exposure to air pollution and risk of suicide death.

In conclusion, we found that long-term PM_{10}, NO_2, and SO_2 exposure was associated with an increased risk of suicide death in South Korean adults; our study results extended the prior findings of an acute effect of air pollution on the risk of suicide. Furthermore, we found that adults diagnosed with underlying diseases or living in metropolitan areas were at a greater risk for suicide death associated with air pollutants, particularly with long-term to PM_{10} exposure. With substantial concerns regarding air pollution-induced adverse health effects, much effort has been made to ameliorate air pollution levels, but the exact safe levels of the pollutants are difficult to state. In particular, as shown in the present study, the suspected health risk due to air pollution may be enhanced in specific population groups (i.e., those with an underlying disease or those living in urban areas). In turn, it is necessary to evaluate the change in concentrations of air pollutants as well as the degree of

health damage, and to take measures to reduce or prevent health damage, focusing on vulnerable groups. Mental health clinicians can incorporate this perspective and administer effective treatment to subjects at risk for suicide or to those with high air pollution exposure.

Financial interests

The authors declare they have no actual or potential competing financial interests.

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Competing interests

The authors declare that they have no competing interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2018.02.011.

References

Ahn, J.Y., 2015. Spatial analysis of air pollution data based on linked micromap plots in Korea. International Conference on Circuits and Systems (CAS).
Bakian, A.V., Huber, R.S., Coon, H., Gray, D., Wilson, P., McMahon, W.M., et al., 2015. Acute air pollution exposure and risk of suicide completion. Am. J. Epidemiol. 181, 295–303.
Bateson, T.F., Schwartz, J., 2004. Who is sensitive to the effects of particulate air pollution on mortality? A case-crossover analysis of effect modifiers. Epidemiology 15, 143–149.
Bostwick, J.M., Pankratz, V.S., 2000. Affective disorders and suicide risk: a reexamination. Am. J. Psychiatry 157, 1925–1932.
Bronisch, T., Wittchen, H.U., 1994. Suicidal ideation and suicide attempts: comorbidity with depression, anxiety disorders, and substance abuse disorder. Eur. Arch. Psychiatry Clin. Neurosci. 244, 93–98.
Brunekreef, B., Holgate, S.T., 2002. Air pollution and health. Lancet 360, 1233–1242.
Calderon-Garciduenas, L., Solt, A.C., Henriquez-Roldan, C., Torres-Jardon, R., Nuse, B., Herritt, L., et al., 2008. Long-term air pollution exposure is associated with neuroinflammation, an altered innate immune response, disruption of the blood-brain barrier, ultrafine particulate deposition, and accumulation of amyloid beta-42 and alpha-synuclein in children and young adults. Toxicol. Pathol. 36, 289–310.
Fonken, L.K., Xu, X., Weil, Z.M., Chen, G., Sun, Q., Rajagopalan, S., et al., 2011. Air pollution impairs cognition, provokes depressive-like behaviors and alters hippocampal cytokine expression and morphology. Mol. Psychiatry 16, 987–995 (973).
Genc, S., Zadeoglulari, Z., Fuss, S.H., Genc, K., 2012. The adverse effects of air pollution on the nervous system. J. Toxicol. 2012, 782462.
Hoek, G., Krishnan, R.M., Beelen, R., Peters, A., Ostro, B., Brunekreef, B., et al., 2013. Long-term air pollution exposure and cardio-respiratory mortality: a review. Environ. Health 12, 43.
Jerrett, M., Arain, A., Kanaroglou, P., Beckerman, B., Potoglou, D., Sahsuvaroglu, T., et al., 2005. A review and evaluation of intraurban air pollution exposure models. J. Expo. Anal. Environ. Epidemiol. 15, 185–204.
Ji, X., Han, M., Yun, Y., Li, G., Sang, N., 2015. Acute nitrogen dioxide (NO_2) exposure enhances airway inflammation via modulating Th1/Th2 differentiation and activating JAK-STAT pathway. Chemosphere 120, 722–728.
Juurlink, D.N., Herrmann, N., Szalai, J.P., Kopp, A., Redelmeier, D.A., 2004. Medical illness and the risk of suicide in the elderly. Arch. Intern. Med. 164, 1179–1184.
Kampa, M., Castanas, E., 2008. Human health effects of air pollution. Environ. Pollut. 151, 362–367.
Kim, C., Jung, S.H., Kang, D.R., Kim, H.C., Moon, K.T., Hur, N.W., et al., 2010. Ambient particulate matter as a risk factor for suicide. Am. J. Psychiatry 167, 1100–1107.
Kim, Y., Myung, W., Won, H.H., Shim, S., Jeon, H.J., Choi, J., et al., 2015. Association between air pollution and suicide in South Korea: a nationwide study. PLoS One 10, e0117929.
Kim, K.N., Lim, Y.H., Bae, H.J., Kim, M., Jung, K., Hong, Y.C., 2016. Long-term fine particulate matter exposure and major depressive disorder in a community-based urban cohort. Environ. Health Perspect. 124, 1547–1553.
Korea Environment Corporation, 2017. Air Korea. http://www.airkorea.or.kr/index, Accessed date: 25 April 2017.
Lee, J., Lee, J.S., Park, S.H., Shin, S.A., Kim, K., 2016. Cohort profile: the National Health Insurance Service-National Sample Cohort (NHIS-NSC), South Korea. Int. J. Epidemiol.
Li, H., Han, M., Guo, L., Li, G., Sang, N., 2011. Oxidative stress, endothelial dysfunction and inflammatory response in rat heart to NO(2) inhalation exposure. Chemosphere 82, 1589–1596.
Liao, D., Peuquet, D.J., Duan, Y., Whitsel, E.A., Dou, J., Smith, R.L., et al., 2006. GIS approaches for the estimation of residential-level ambient PM concentrations. Environ. Health Perspect. 114, 1374–1380.
Lim, Y.H., Kim, H., Kim, J.H., Bae, S., Park, H.Y., Hong, Y.C., 2012. Air pollution and symptoms of depression in elderly adults. Environ. Health Perspect. 120, 1023–1028.
Lin, G.Z., Li, L., Song, Y.F., Zhou, Y.X., Shen, S.Q., Ou, C.Q., 2016. The impact of ambient air pollution on suicide mortality: a case-crossover study in Guangzhou, China. Environ. Health 15, 90.
Mann, J.K., Tager, I.B., Lurmann, F., Segal, M., Quesenberry Jr., C.P., Lugg, M.M., et al., 2002. Air pollution and hospital admissions for ischemic heart disease in persons with congestive heart failure or arrhythmia. Environ. Health Perspect. 110, 1247–1252.
Min, J.Y., Min, K.B., 2017. Exposure to ambient PM10 and NO_2 and the incidence of attention-deficit hyperactivity disorder in childhood. Environ. Int. 99, 221–227.
de Oliveira, M.R., Silvestrin, R.B., Mello, E.S.T., Moreira, J.C., 2007. Oxidative stress in the hippocampus, anxiety-like behavior and decreased locomotory and exploratory activity of adult rats: effects of sub acute vitamin a supplementation at therapeutic doses. Neurotoxicology 28, 1191–1199.
Oudin, A., Bråbäck, L., Åström, D.O., Strömgren, M., Forsberg, B., 2016. Association between neighbourhood air pollution concentrations and dispensed medication for psychiatric disorders in a large longitudinal cohort of Swedish children and adolescents. BMJ Open 6, e010004.
Palmer, B.A., Pankratz, V.S., Bostwick, J.M., 2005. The lifetime risk of suicide in schizophrenia: a reexamination. Arch. Gen. Psychiatry 62, 247–253.
Patki, G., Solanki, N., Atrooz, F., Allam, F., Salim, S., 2013. Depression, anxiety-like behavior and memory impairment are associated with increased oxidative stress and inflammation in a rat model of social stress. Brain Res. 1539, 73–86.
Peel, J.L., Metzger, K.B., Klein, M., Flanders, W.D., Mulholland, J.A., Tolbert, P.E., 2007. Ambient air pollution and cardiovascular emergency department visits in potentially sensitive groups. Am. J. Epidemiol. 165, 625–633.
Power, M.C., Kioumourtzoglou, M.A., Hart, J.E., Okereke, O.I., Laden, F., Weisskopf, M.G., 2015. The relation between past exposure to fine particulate air pollution and prevalent anxiety: observational cohort study. BMJ 350, h1111.
Priftis, K.N., Anthracopoulos, M.B., Paliatsos, A.G., Tzavelas, G., Nikolaou-Papanagiotou, A., Douridas, P., et al., 2007. Different effects of urban and rural environments in the respiratory status of Greek schoolchildren. Respir. Med. 101, 98–106.
Public Health England, 2014. Estimating local mortality burdens associated with particulate air pollution. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/332854/PHE_CRCE_010.pdf, Accessed date: 20 December 2017.
Quan, H., Sundararajan, V., Halfon, P., Fong, A., Burnand, B., Luthi, J.C., et al., 2005. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med. Care 43, 1130–1139.
Raison, C.L., Miller, A.H., 2011. Is depression an inflammatory disorder? Curr. Psychiatry Rep. 13, 467–475.
Ranjeet, S., 2008. World Atlas of Atmospheric Pollution. Anthem Press.
Salim, S., 2014. Oxidative stress and psychological disorders. Curr. Neuropharmacol. 12, 140–147.
Sass, V., Kravitz-Wirtz, N., Karceski, S.M., Hajat, A., Crowder, K., Takeuchi, D., 2017. The effects of air pollution on individual psychological distress. Health Place 48, 72–79.
Scott, K.M., Hwang, I., Chiu, W.T., Kessler, R.C., Sampson, N.A., Angermeyer, M., et al., 2010. Chronic physical conditions and their association with first onset of suicidal behavior in the world mental health surveys. Psychosom. Med. 72, 712–719.
Serafini, G., Pompili, M., Elena Seretti, M., Stefani, H., Palermo, M., Coryell, W., et al., 2013. The role of inflammatory cytokines in suicidal behavior: a systematic review. Eur. Neuropsychopharmacol. 23, 1672–1686.
Serafini, G., Hayley, S., Pompili, M., Dwivedi, Y., Brahmachari, G., Girardi, P., Amore, M., 2014. Hippocampal neurogenesis, neurotrophic factors and depression: possible therapeutic targets? CNS Neurol. Disord. Drug Targets 13, 1708–1721.
Sinyor, M., Tse, R., Pirkis, J., 2017. Global trends in suicide epidemiology. Curr. Opin. Psychiatry 30, 1–6.
Strosnider, H., Kennedy, C., Monti, M., Yip, F., 2017. Rural and urban differences in air quality, 2008–2012, and community drinking water quality, 2010–2015 - United States. MMWR Surveill. Summ. 66, 1–10.
Szyszkowicz, M., 2010. Ambient sulfur dioxide and female ED visits for depression. Air Qual. Atmos. Health 4, 259–262.
Tian, T., Chen, Y., Zhu, J., Liu, P., 2015. Effect of air pollution and rural-urban difference on mental health of the elderly in China. Iran J. Public Health 44, 1084–1094.
Tsai, K.T., Lin, M.D., Chen, Y.H., 2009. Noise mapping in urban environments: a Taiwan study. Appl. Acoust. 70, 964–972.
Turecki, G., Brent, D.A., 2016. Suicide and suicidal behaviour. Lancet 387, 1227–1239.
Tzivian, L., Winkler, A., Dlugaj, M., Schikowski, T., Vossoughi, M., Fuks, K., et al., 2015. Effect of long-term outdoor air pollution and noise on cognitive and psychological functions in adults. Int. J. Hyg. Environ. Health 218, 1–11.
Vogelzangs, N., Beekman, A.T., de Jonge, P., Penninx, B.W., 2013. Anxiety disorders and inflammation in a large adult cohort. Transl. Psychiatry 3, e249.
World Health Organization, 2014. WHO mental health: suicide prevention. http://www.who.int/mental_health/suicide-prevention/en/, Accessed date: 28 April 2017.
Yang, A.C., Tsai, S.J., Huang, N.E., 2011. Decomposing the association of completed suicide with air pollution, weather, and unemployment data at different time scales. J. Affect. Disord. 129, 275–281.
Yao, G., Yue, H., Yun, Y., Sang, N., 2015. Chronic SO_2 inhalation above environmental standard impairs neuronal behavior and represses glutamate receptor gene expression and memory-related kinase activation via neuroinflammation in rats. Environ. Res. 137, 85–93.