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Estimation of attributable risk and medical costs of major mental disorders associated with particulate matter exposures among children and adolescents in Republic of Korea, 2011-2019

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Estimation of attributable risk and medical costs of major mental disorders associated with particulate matter exposures among children and adolescents in Republic of Korea, 2011-2019

A Dissertation
Submitted to the Department of Public Health
at the Graduate School of Yonsei University
in partial fulfillment of the
requirements for the degree of
Doctor of Philosophy in Public Health

Yae Won Ha

December 2022

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This certifies that the Doctoral Dissertation

of Yae Won Ha is approved.

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December 2022

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ABSTRACT

Estimation of attributable risk and medical costs of major mental disorders associated with particulate matter exposures among children and adolescents in Republic of Korea, 2011-2019

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(Directed by Professor Changsoo Kim)

Background: Mental disorder has a lower mortality or fatality rate than other chronic diseases, while lost years due to disability are significant. In particular, among children and adolescents, if those who suffer from ADHD, ASD, and depression, the costs at the society or nation level as well as individuals, are considerable. Several studies reported that it was associated with mental disorders and exposure to air pollution. However, few studies have yet evaluated psychiatric disease burden due to air pollution among children and adolescents.

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Methods: We used time-series analysis to evaluate the association between exposure to air pollution and major mental disorders (ADHD, ASD and depression) among children and adolescents using NHIS data from 2011 to 2019. Also, we estimated disability-adjusted life years and population attributable fraction to air pollution. The total direct medical costs of each disorder (per 1patient) were calculated by COI method, and then total attributable cost was estimated by multiplying the costs by attributable number.

Results: It showed that it was associated with between exposure to air pollutants and major mental disorders-medical institutions visits except ozone (RRs in PM_{10} (per 10μg/m^3): 1.08, $PM_{2.5}$ (per 10μg/m^3): 1.09, respectively). The PAF in major mental disorders was estimated to 7.23~8.97% (PM_{10}) and 3.16~6.87% ($PM_{2.5}$). In addition, ADHD and depression showed an increase in both total medical costs and out-of-pocket costs due to particulate matter.

Conclusion: We found that it was associated with major mental disorders due to exposure to particulate matter, and among them, PM_{10} and $PM_{2.5}$ could be attributable about 7~9% and 3 ~ 7%, respectively. In addition, we found that total medical costs and out-of-pocket costs attributable to particulate matter in ADHD and depression. To the best of our knowledge, it is the first study to calculate the medical costs and attributable burden of major mental disorders associated with air pollution exposure in children and adolescents. Therefore, these results could be presented as a basis for lowering air quality standards.

Keywords: particulate matter, mental disorders, DALY, medical cost

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I. INTRODUCTION

1. Background

Air pollution is one of the emerging public health problems worldwide, and 7 million people are estimated to die prematurely because of exposure to air pollution.[1] Exposure to air pollution is known to be related to the incidence of respiratory and cardiovascular diseases as well as an increase in the risk of mortality. Recently, some health effects of mental illness such as schizophrenia, suicide, major depressive disorders, anxiety caused by exposure to air pollution have been reported.[2-4] Also, epidemiological studies have been reported the association between exposure to air pollution and mental disorders such as attention-deficit/hyperactivity disorder (ADHD), autism spectrum disorder (ASD), working memory loss, and anxiety symptoms in the infants, children, and adolescents who are more vulnerable to air pollution.[5-7]

Mental illness has a lower mortality or fatality rate than other chronic diseases, while lost years due to disability are significant. In addition, other than medical expenses, such as ADHD, ASD, and depression, the costs at the society or nation level as well as individuals, such as education, are significant. Therefore, reducing air pollution exposure, especially in children vulnerable to air pollution exposure, could reduce health burdens and costs. However, few studies have yet evaluated a psychiatric disease burden and cost due to air pollution among children and adolescents.

In this context, the aim of this study was to 1) evaluate the association between short-term exposure to air pollution and major mental disorders among children and

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adolescents, and 2) to estimate major mental disorders burden population attributable fraction to air pollution and mental disorders burden among children and adolescents.

2. Study objectives

We aimed to evaluate burden of major mental disorders due to air pollution in children and adolescents. Details of the study objectives are as follows:

(1) To evaluate the association between short-term exposure to outdoor air pollution including particulate matter <10 µm in aerodynamic diameter (PM_{10}), particulate matter <2.5 µm in aerodynamic diameter ($PM_{2.5}$), ozone (O_3), nitrogen dioxide (NO_2), sulfide dioxide (SO_2) and carbon monoxide (CO) and medical institutions visits for major mental disorders (ADHD, ASD, and depression) among children and adolescents who aged <19 in nationwide using National Health Insurance Service (NHIS) data from 2011 to 2019.

(2) To estimate these major mental disorders attributable to air pollution through attributable number (AN) and population attributable fraction (PAF).

(3) To evaluate health-related burden of major mental disorders by estimating disability-adjusted life years (DALYs), comprehensive indicator, considering mortality and morbidity.

(4) To calculate medical costs of major mental disorders.

(5) To estimate overall burden of major mental disorders due to air pollution in children and adolescents.

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II. LITERATURE REVIEW

1. Burden of mental disorders

Mental health conditions are one of the main causes of the social and economic burden of disease in the world. In recently, GBD 2019 estimated that 654.8 million cases and 970.1 million cases would be suffering from mental illness in 1990 and 2020, respectively in the world.[8] With mental health emerging as a major public health problem, the burden of mental illness has been also increasing in adolescents.

Attention deficit/hyperactivity disorder (ADHD), one of the mental disorders that develops in childhood, has distraction, hyperactivity, impulsiveness, and carelessness, and often persists into adulthood. According to the U.S. Centers for Disease Control and Prevention (CDC), about 9.8 % of people who aged 3 ~ 17 years were reported to have experience in diagnosed with ADHD in lifetime.[9] Also, the prevalence increased slightly from 5.7 % in 2012 to 6.8 % in 2018.[10] One study, which calculated the burden of 11 psychiatric diseases, burden of ADHD was the second highest at 39 % of all mental illnesses under the age of 10 in Korea.[11] Another study reported that 32,605 DALYs in 2012 (6.18 per 1,000 people) and economic burden of ADHD was U.S $47.55 million (0.004 % of Korean GDP).[12]

With ADHD, autism spectrum disorder (ASD) is one of the neurodevelopmental diseases that also develops in early period. In 2019, the disease burden caused by ASD was estimated to be around 43.07*105 DALYs worldwide, and it was found to increase every year.[13] One study examined prevalence and economic burden of ASD in Korea. The prevalence of ASD showed a trend of increasing from about 5.04 to 11.0 per 100,000 people over 8 years, and consistently total costs of ASD were rising from $2,700,596 to $9,645,503. [14] Other countries, also showed high economic burden in lifetime in one person with ASD ($2.2 million, and $2.4 million, respectively).[15] These two mental diseases have a relatively low fatality rate compared to other diseases, but they are a lot of burden not only on individuals but also on national level by causing disabilities due to the diseases.

Depression, one of the major mental problems that emerges among children and adolescents, is considered the second leading cause of disability worldwide.[8] According to this study, which calculated burden of 12 mental illnesses using data from 204 countries around the world. Depressive disorders accounts for a high proportion of all ages (Figure 1).

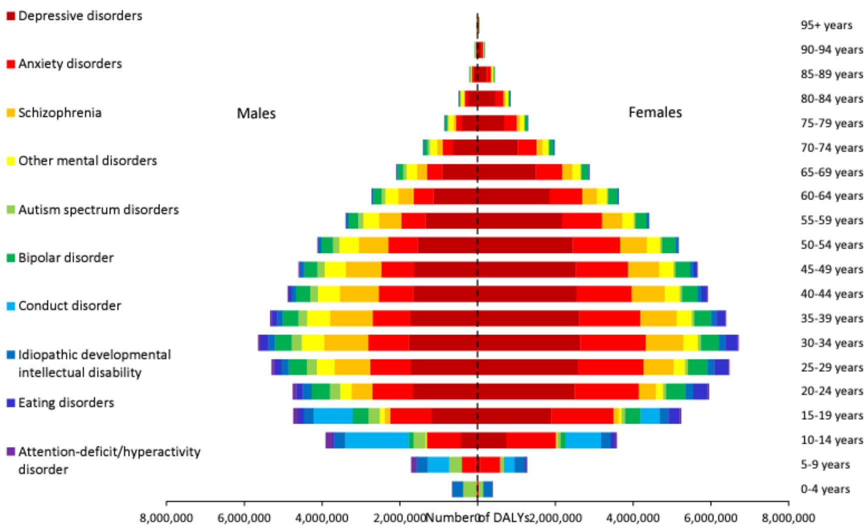

Figure 1. Global disability-adjusted life-years by mental disorder, sex, and age in 2019 [8]

In Korea, burden of depression ranked 10th in the leading causes, accounting for

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about 2.7 % in 2008. [16] Another study showed that the prevalence rate increased by about twice over 10 years, and increased with age.[17] In U.S., the prevalence of depression among aged 4 ~ 17 years increased by about three times from 1.8 % to 3.1 % (2012 to 2018).[10]

2. Risk of mental disorders due to exposure to air pollution in children and adolescents

Recently, a few studies reported the association between exposure to air pollution and mental disorders. [2, 18-21] In particular, some studies showed that exposure to air pollution increases risk of mental disorders in adolescents vulnerable to air pollution exposure.

ADHD

Many epidemiological studies reported that the association between risk of ADHD and exposure to air pollution. Markevych et al. reported that association between incidence of ADHD and exposure to PM_{10}, NO_2, and lower Normalized Difference Vegetation Index (NDVI).[22] Using insurance company data, about 66,800 people were followed up during about 10 to 14 years, and were evaluated exposure assessment by modeling based on their address (postal-code). During the study period, about 2,040 ADHD cases were reported, and showed that increased risk of PM_{10} (per 10 $\mu m/m^3$) was 1.97 and NO_2 (per 10 $\mu m/m^3$) was 1.32, respectively. Similarly, Thygesen et al. selected subjects through national registry data, and also confirmed ADHD diagnosis using Patient Register, Psychiatric Central Research Register.[6] Air pollution modeling was performed to evaluate annual NO_2 and $PM_{2.5}$ exposure. In Germany, two cohorts evaluated air pollution exposure to children. 10 and 15 years old were associated with an increase in $PM_{2.5}$ (10 years: 1.12, 95% CI:

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1.01; 1.23, 15 years: 1.11, 95% CI: 1.01; 1.22).[23] In Canada, using secondary data, Yuchi et al. investigated the incidence of ADHD and greenspace, $PM_{2.5}$, and NO_2 exposure during 7 years.[24] And in this study, during the follow-up, it found that there was the inverse relationship between greenspace and ADHD, and no significant relationship between exposure to $PM_{2.5}$, NO_2 and ADHD.

A longitudinal-study was conducted that four times 3-back d test to assess working-memory were performed by their parents who had school aged-children in Barcelona, and the scores decreased as traffic-related air pollutants (TRAP) concentration increased during about 3.5 years with mixed-linear models.[25] Recently, one study examined that relationship between ADHD-related medication use and green-space. [26] A total of 248,270 people aged 5 ~ 12 years were examined, categorized and analyzed according to the percentage of green space (area) defined as within 250 and 500 m of the subject's residence. The prevalence of medication usage significantly reduced about 3 % in people living in more green space than less green space within 250 m of the subjects' residence. In Korea, it was reported the association between short-term exposure to air pollution (PM_{10}, SO_2, NO_2) and hospital admission for ADHD. [27] This study examined at new hospitalization cases (ADHD) among aged 10 ~ 19 years nationwide from 2013 to 2015 using the NHIS data. In a single lag structure model, the RR of PM_{10}, NO_2, and SO_2 (per interquartile increase) was 1.12 (lag1, 95% CI: 1.05; 1.20), 1.47 (lag3, 95% CI: 1.25; 1.73), 1.27 (lag1, 95% CI: 1.14; 1.41), respectively. In addition, the risk was greater in aged 15 ~ 19 years than in aged 10-14 years, exposure to NO_2 and SO_2. Furthermore, a cross-sectional study showed that air pollution exposure and ADHD symptoms were related. Forns et al. investigated strengths and difficulties questionnaire (SDQ) scores in elementary school students aged 7 to 11 in Barcelona, and showed that positive association between exposure to air pollution (Elemental Carbon (EC), Black Carbon (BC), and

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NO_2) and some of SDQ scores to assess behavior. [28]

ASD

One study reported that $PM_{2.5}$ was associated with high risk of ASD using meta-analysis. [13] From 20 studies, pooled odds ratio (OR) was 1.62 (95% CI: 1.22; 2.15) during the first year after birth, and 3.13 (95% CI: 1.47; 6.67) during the second year after birth. Another meta-analysis study also showed that the association between long-term exposure to $PM_{2.5}$ and ASD. [29] The pooled RR was 1.68 (95% CI: 1.20; 2.34) through six studies.

In a cohort study conducted in Taiwan, long-term exposure to air pollutants and new ASD were evaluated under age of 3. [30] During 11 years, 49,073 children were diagnosed with ASD, and it showed that the risks of O_3 per 10 ppb, CO per 100 ppb, NO_2 per 10 ppb, and SO_2 per 1 ppb increase levels were associated with each air pollutants. However, it was not significant in PM_{10} levels. Also, another case-control study conducted in Ohio, and this reported an elevated risk in Q_3 per interquartile increase, first and 2nd year of life ozone and cumulative periods (OR range: 1.19-1.27) and 2nd, first year $PM_{2.5}$ and cumulative periods (OR range: 1.11-1.17). In China, case-control study was conducted and showed that PM (PM_1, $PM_{2.5}$, PM_{10}) is associated with increased risks of ASD during the first three years of life (OR: 1.86, 1.78, 1.68). [31] In Korea, it was reported that association between short-term exposure to air pollution ($PM_{2.5}$, NO_2, O_3) and ASD-related hospitalization. [22] This study examined at new hospitalization cases (ASD) among age 5 ~ 14 years nationwide from 2011 to 2015 using the NHIS data. The diagnosis of ASD was defined as the case of hospitalization with the following ICD-10 code; F84.0, F84.1, F84.5, F84.8, F84.9. In single lag structure model, the RR of $PM_{2.5}$, NO_2, and O_3 (per interquartile increase) was 1.17 (lag 1), 1.09 (lag 5), 1.27 (lag 4), respectively. In addition, the

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risk was greater in males than in females, exposure to $PM_{2.5}$.

Depression

Roberts et al. investigated that association between exposure to $PM_{2.5}$ and NO_2 and mental health using longitudinal study. [33] Adjusted for gender, ethnicity, region, social and economic status, family psychiatric history, and smoking status etc., exposure to air pollution at the age of 12 was associated with increased risk of depression at the age of 18, but was not at the age of 12. Recently, in San Francisco, one study examined the association between exposure to ozone and depression in teenagers. [34] In results, when they lived in high-ozone areas during four years, there was a significant increase in depression symptoms.

3. DALY of disease

Epidemiological studies have generally shown health effects by using indicators such as mortality, fatality, incidence, and prevalence, etc. However, as these indicators had limitations that could not simultaneously express the risk of death and the burden of injury, the development of a complex and comprehensive indicator began. One of the comprehensive indicators, disability-adjusted life years (DALY), was developed in early 1990 in the form of subtracting the burden of death and injury from full life expectancy. [35] Initially, it started as single study, but now global study performed by Institute for Health Metrics and Evaluation (IHME). By estimating more than 100 diseases of burden by age, sex, and region, the risk factors that contribute to a specific disease can be identified, and it can help select the risk factors and diseases that should be involved first in public health perspectives.

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As the research institution changed from WHO to IHME, the calculation method of DALY also changed (GBD 2019 Disease and Injuries Collaborators). First, it changed from the incidence-based approach to the prevalence-based approach. In previous approach, the loss caused by current disease was applied to the future. In other words, if the disease occurs at this time, future losses are also considered. However, it is a suitable method for evaluating burden of disease only for disease with a high incidence rate and low prevalence rate. On the other hand, the prevalence approach does not calculate the future value, considering only the current point. Second, GBD 2010 study (Global Laid of Disease Study) do not consider the discount rate and age weights. The discount rate is calculated in consideration of the future health years, and age weights is parameter considered under the assumption that the burden of disease varies according to age. Regarding this weight, GBD 2010 decided not to apply the weight reflecting on debates. The third is the method of change to estimate disability weights. Disability weights is a value representing the severity of more than 100 diseases from 0 to 1. This value was calculated by performing a Delphi survey on medical professionals (doctors, nurses or medical students) with abundant knowledge of existing diseases. However, there has been criticism that it has shown diversity in values depending on the background of countries, society, and economy, and does not reflect the preferences of the general population. In order to overcome this discrepancy, various methods such as time exchange method have been applied and survey for the general population also conducted in each country. On the other hand, studies applying the incidence-based approach or prevalence-based approach have been continuously conducted in Korea.[16, 36] Unlike GBD 2010, domestic studies used an incidence-based approach or hybrid approach (mixture of incidence and prevalence).

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III. MATERIAL AND METHODS

This study was based on nationwide in Korea. The study area of the study were 16 regions (7 metropolitan cities (Seoul, Busan, Incheon, Daegu, Gwangju, Daejeon, and Ulsan), and 9 provinces (Gyeonggi, Gangwon, Chungcheongbuk, Chungcheongnam, Jeollabuk, Jeollanam, Gyeongsangbuk, Gyeongsangnam, and Jeju), from 1 January 2011 to 31 December 2019.

1. Data Sources

1) National Health Insurance Service data (NHIS)

We used customized NHIS database, which is provided to researchers by constructing individual data set for each research purpose, from January 2011 to December 2019. This NHIS data covered about 97 % of Korea's population and included information on medical use (disease of International Classification of Disease (ICD)-10 code, hospitalization, prescription days, and medical practice), demographic variables (identification number, sex, birth year, death date, and residence address) as well as socio-economic variables (insurance premiums, and income). [37] All personally identifiable information was encrypted and provided the data to the researcher.

New major mental disorders of cases were defined as follows; the fastest medical institution visits among children and adolescents who aged <19 during the study period. We used the ICD-10 codes to identify mental disorders (Table 1). The code of each disorder was selected based on literatures. [27, 32, 38] To select only the subjects

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that occurred during the study period, we excluded if there were medical records before 2011. Then, we aggregated daily count with major mental disorders as a total.

Table 1. ICD-10 code for mental disorders

Major Mental disorders	**ICD-10 code**
Attention-deficit/hyperactivity disorder (ADHD)	F90.0
Autistic spectrum disorders (ASD)	F84.0, F84.1, F84.5, F84.8, F84.9
Depression (major depressive disorder)	F32 - F33

2) Air pollution data

Air pollution data including particulate matter <10 μm in aerodynamic diameter (PM_{10}), particulate matter <2.5 μm in aerodynamic diameter ($PM_{2.5}$), ozone (O_3), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and carbon monoxide (CO) was collected from the Air Korea site (http://m.airkorea.or.kr/main). In 2019, there were about 389 automatic monitoring stations nationwide, and hourly data was collected from this monitoring stations. We calculated hourly data as daily mean data and then re-calculated it as region-daily mean data by averaging. If there were several monitoring stations in each region, it was calculated by arithmetic mean. $PM_{2.5}$ data were collected and calculated from 2015 to 2019 because it was monitored nationwide from 2015.

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3) Meteorological data

Daily measured data of the meteorological variables, including temperature (°C), and relative humidity (%) were collected from the Korea National Meteorological Administration (https://www.data.kma/cmmm/main.do/). Then, we also calculated daily mean by regions with the same methods for air pollution data.

4) Statistics Korea

The mid-year population was obtained from the registered data, and calculated by region, age group (age < 5, 5 ~ 9, 10 ~ 14, 15 ~ 19), and sex from 2011 to 2019. [39] Mortality data (2019) provides the cause of death, the number of deaths by sex and age every year. [40] From this data, we calculated the number of deaths by age group, and sex caused by major mental disorders.

5) Korea Health Panel data (Version 1.7.3)

Average transportation costs were collected from the Korea Health Panel Survey of 201. 1 provided the Korea Institute for Health and Social Affairs & National Health Insurance Service. Average transportation costs of outpatient and inpatient for all mental disorders (ICD-10 codes: F00-F99) was calculated, there is no transportation cost for each disease (average outpatient transportation cost = 1248 KRW, inpatient cost = 10,358 KRW). Transportation costs during outpatient and inpatient were calculated under the assumption that parents were accompanied when visiting the medical institutions because the patients were under the age of 19. Transportation

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costs were only collected through data from in 2011, and calculated by multiplying the consumer price index (CPI) of the transportation in every year. Also, it was considered a round trip.

$Transportaion\ costs_{y+1} =$
$Average\ outpatient\ transportation\ cost_{y}$ X $Number\ of\ outpatient\ visits$ (or inpatient) X $CPI_{y+1}\ X\ 4$

- CPI_y: consumer price index in year y+1

2. Statistical Methods

1) Relative risk (RR)

We estimated the relative risk (RR) for each of 16 regions as overall RR through two step processes. First, we applied time-series analysis design to evaluate the association between short-term exposure to air pollution and medical institutions visits for major mental disorder (MD)s. Time-series analysis is a unit of time (day), and was used when both exposure and outcome change over time. It was known that it is useful to examine the association between short-term exposure to air pollution and health outcome .[41] We used over-dispersed generalized additive model (GAM).[42] The generalized additive model is a semi-parametric model that can be expressed in the form of the sum of linear and non-linear functions as it has the characteristic of being flexible.

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$$Log[E(Y_t)] = \alpha + \beta * air\ pollutant\ level_i + ns(date,\ df = 7/year)$$
$$+ ns(temperature_i,\ df = 6 * year)$$
$$+ ns(relative\ humidity_i,\ df = 3 * year) + day\ of\ week$$
$$+ holiday + log(offset)$$

- $E(Y_t)$: counts due to major mental disorders on day *i*
- exp (β): relative risk
- ns: natural spline
- df: degree of freedom
- offset: total population of each of the regions

We assumed a linear relationship between exposure and outcome (counts of medical institutions visits) and estimated the relative risk from the calculated beta (exp (β) = RR). Covariates such as time, weather variables (temperature, relative humidity), day of week, and holiday were considered. The date, time variable consisting of a series of numbers, was adjusted to control unmeasured long-term trends, and was inserted into the model as a function of spline with a degree of freedom (*df*) of 7 per year according to previous studies. [43, 44] Temperature and relative humidity were also inserted into the model as a function of spline with 6 *df*, consistent with previous studies, respectively. [43-45] In addition, day of the week and holiday known to affect medical institutions visits were added to the model as parametric variable. Total population of each region was also added as an offset term. Lag effect, which is the effect of concentration before exposure to air pollutants affecting health, was also considered. This conducted in single lag structure models (lag 0 ~ lag 14) and cumulative lag structure models (cumulative lag 1 ~ cumulative lag 14).

In the second stage, we analyzed using random-effects meta-analyses for pooled RRs by combining 16 region-specific RRs. Because the RRs of each region showed heterogeneity, we used random-effects model that can reflect heterogeneity between regions. Among the estimated pooled RRs, the longest statistically significant RR were selected and subsequent analyses were performed in cumulative lag models. [46, 47]

To identify group that are particularly vulnerable to air pollution exposure, we also performed additional analysis stratified by age group, sex, and specific mental disorders.

2) Population Attributable Fraction (PAF)

The population attributable fraction (PAF) (%) was calculated from attributable number (AN) and the total counts of medical institutions visits during study period. [47, 48]

$$AN = \sum_i^n (Baseline\ risk) * [\exp(\beta 0 * \Delta C_i) - 1]$$

$$PAF\ (\%) = \frac{Attributable\ number}{Total\ number} \mathrm{X}\ 100$$

- *AN*: total attributable number due to exposure to air pollutants above the reference concentration

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- *Baseline risk*: average counts at days with reference concentration
- *i*: days when air pollutant concentration is higher than the reference concentration
- β: coefficients extracted from GAM
- ΔC_i: the difference between air pollutant concentration and reference concentration
- *PAF*: population attributable fraction of major mental disorders
- *Total number*: total counts of major mental disorders during study period

We applied *WHO's air quality standards* 2005 (24-hour mean; 50 μg/m^3 for PM_{10}, 25 μg/m^3 for $PM_{2.5}$) and 2021 (24-hour mean; 45 μg/m^3 for PM_{10}, 15 μg/m^3 for $PM_{2.5}$) as the reference concentrations. [49, 50] Assuming that the reference concentration is the minimum exposure concentration, it could be said that the total number of medical institutions visits when the concentration is higher than the reference concentration is attributable to exposure to air pollution. In O3 and NO_2, it only calculated in 2005 and 2021 because there was no appropriate standard in 2005.

We further calculated population attributable fraction by increasing in the concentration of PM10, applying reference concentrations as the minimum level of PM10 (5.3 μg/m^3) in our data. Based on the equation, there is a possibility that population attributable fraction may increase, even if the reference concentration is lower than 50 μg/m^3.

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3) Disability-adjusted life years (DALY)

The disability-adjusted life years (DALY) is one of the indicators to measure burden of diseases by integrating death from disease and the occurrence of disability. It appears as the sum of years of life lost (YLL) and years of healthy life lost due to disability (YLD). [51]

$$\mathrm{DALY} = \mathrm{YLL} + \mathrm{YLD}$$

There are two approaches to estimating DALY: an incidence-based approach, and prevalence-based approach. Depending on the study design or the characteristics of the disease, it can be calculated by using one approach or both approaches. In our study design, we used an incidence-based approach because we could assume first incidence case by excluding people who visited medical institutions before study period through medical insurance data. We assumed that the burden of disease does not vary depending on age, and the discount rate was 3 %.

YLL is the premature death due to major MDs in this study, and was calculated from the following equation.

$$\mathrm{YLL} = \mathrm{N} \;\; \mathrm{X} \;\; \frac{1}{0.03} \;\; \mathrm{X} \;\; (1 - e^{-(0.03L)})$$

- *N*: the number of deaths
- *L*: life expectancy at age of death (years)

The number of deaths (N) refers to direct death by major mental disorders. This was defined as the case where major mental disorders and ICD-10 codes match in

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the cause of death data [40]. Number of deaths under the age of 19 were calculated by sex, and age group (age: 0 ~ 5, 5 ~ 9, 10 ~ 14, 15 ~ 19). Life expectancy (L) refers to the number of years that people belonging to that age survive on average, and life expectancy was also calculated by sex, and age group. [52]

YLD is the morbidity due to major MDs, and was calculated from the following equation.

$$\text{YLD} = I \ \text{X} \ DW \ \text{X} \ \frac{1}{0.03} \ \text{X} \ (1 - e^{-(0.03D)})$$

- *I*: the number of incidence cases
- *DW:* disability weight
- *D*: average duration of disease (years)

The average duration of disease refers to the period from the incidence of the disease to the cure. *Duration* was calculated from the difference between the first and last days of hospital visits by gender and age group and it was expressed as an annual average within the study period through the NHIS data. Disability weight was a value that expresses the degree of disability for a specific disease within the range of 0 (perfect health) to 1 (almost death). [53] Disability weights is generally priority between several diseases in a specific group, which can vary depending on national, social, and economic background. [54] Therefore, we obtained disability weight from recent literature that calculated disability weight by conducting a self-reported survey of medical experts in Korea. The disability weights were obtained in the same ICD-10 codes as in Table 1. In depression, it was divided into mild (0.551), moderate (0.756), and severe (0.838) depending on the severity of the disease. Therefore, to combined disability weights, disability weights was recalculated by applying the

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distribution of the health status of depression patients in Korea. [38] The equation was as follows.

$$DW_{combined} = (DW_{mild} \text{ X } P_{mild}) + (DW_{moderate} \text{ X } P_{moderate}) + (DW_{severe} \text{ X } P_{severe})$$

- *DW:* disability weight
- *P:* prevalence

We then calculated DALY attributed to PM_{10} and $PM_{2.5}$ by multiplying *DALY*PAF.*[55]

4) Medical costs

The medical costs were calculated from the following sequential equations.

- Total medical costs = direct medical costs + direct nonmedical costs
- Direct medical costs = outpatient medical cost + inpatient medical cost + uninsured medical cost (out-of-pocket cost) + pharmacy cost
- Direct nonmedical costs = transportation cost for hospital visits

Fist, direct medical costs included medication fees, insurance premiums, and pharmacy cost. The elements of direct medical expenses were calculated using the NHIS data, and calculated by sex and age for specific mental disorders. The drug cost for each disease was calculated on the assumption that the preferred primary treatment was taken at the maximum dose for about a year by subjects of each age. The weighted average price for each main ingredient and the medication information

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provided by Health Insurance Review and Assessment Service and Pharmaceutical Information Center.[56, 57]

In ADHD, methylphenidate and atomoxetine are used as pharmacotherapy in Korea, and the primary drugs used among them are methylphenidate, a 12-hour sustained release.[58] In ASD, there are currently no treatment for drug, and most of the pharmacotherapy proceeds in the form of antipsychotics that help improve comorbid symptoms such as depression, seizures, and insomnia. Usually used drugs as ASD-related pharmacotherapy are aripiprazole and risperidone approved by FDA (U.S. Food and Drug Administration), and SSRI (selective serotonin reuptake inhibitor) and ADHD treatments are also used to control some symptoms.[59] In the case of risperidone, it is not recommended to be used in Korea, therefore we calculated according to the usage of aripiprazole. In depression, monotherapy is considered as the first strategy.[60] It is recommended to use it in combination with other atypical antipsychotics when accompanied by psychotic symptoms, and to replace it with other antidepressants or add other drugs if the initial reaction is insufficient. According to a recently reported paper, out of a total of 2,272 cases of antidepressants, none are licensed for use under the age of 18, but most of them are prescribed as off-label, especially escitalopram (31.7%), fluoxetine (24.4%), sertraline (11.5%), paroxetine (7.5%), trazodone (4.7%), bupropion (4.6%), and imipramine (4.4%).[61] Also, in some cases, it was not recommended to children and adolescents, therefore we calculated as sertraline, imipramine the drugs presented.

Table 2. Drugs primarily used in children and adolescents and initial and maximum dosage by disease

Disorders	Generic name	Initial dose/1	Maximum

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		day	dose/1 day
Attention-deficit/hyperactivity disorder (ADHD)	**Methylphenidate**	18 mg	54 ~ 72 mg
	Atomoxetin	0.5 mg/kg ~ 40 mg	1.4 mg/kg or 100 mg
Autistic spectrum disorders (ASD)	**Aripiprazole**	5 ~ 10 mg	15 ~ 30 mg
	Risperidone	Above age 19	-
Depression (major depressive disorder)	Escitalopram	Above age 19	-
	Fluoxetine	Above age 19	-
	Sertraline	25 ~ 50 mg	200 mg
	Paroxetine	Above age 19	-
	Trazodone	Above age 19	400 ~ 600 mg
	Bupropion	Above age 19	-
	Imipramine	25 mg	25 ~ 300 mg

We then calculated the economic cost of total hospital admission expenses and out-of-pocket cost due to exposure to air pollution. [45]

$$AC_{ytotal} = AN_y * Cost_{ytotal}$$

$$AC_{ypocket} = AN_y * Cost_{ypocket}$$

- $Cost_{ytotal}$: total hospital admission expenses in year y (1 patient)
- $Cost_{ypocket}$: total hospital admission expenses in year y (1 patient)
- AN_y: total attributable number due to exposure to air pollutants above the reference concentration in year y

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- AC_{ytotal}: total direct medical costs in year y
- $AC_{ypocket}$: total out-of-pocket costs attributable to exceeding air pollution exposure in year y

3. Statistical Software

All descriptive statistics were performed using SAS version 9.4 (SAS Institute, Cary, NC). All time-series analyses were conducted using R '*mgcv*' package (version 1.8-40), and meta-analyses were conducted using R '*metafor*' package (version 3.8-1). A P-value < 0.05 was considered statistically significant.

4. Ethic Statement

This study was approved by the Institutional Review Board, Yonsei University Health System (IRB number: 4-2022-1199) and adhered to the tenets of the Declaration of Helsinki. The institutional review board waived the requirement for informed consent, as this was a retrospective study.

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IV. RESULTS

1. Descriptive statistics

The total number of medical institutions visits for major mental disorders was 367,357 during the whole study period. The daily mean (standard deviation, SD) number of major MDs was 7.0 (9.7) (Table 3). The daily mean number of ADHD, ASD, depression was 3.5 (5.1), 1.8 (3.0), 1.7 (2.8), respectively. The daily mean number of MD was higher in male than female (male: 5.1, female: 1.8).

Table 3. Summary statistics on daily average of mental disorders, 2011-2019

	Mean± SD	**Inter quartile range**	**Median (Min, Max)**
Major mental disorders (n)	7.0±9.7	8	4 (0, 73)
ADHD	3.5 ± 5.1	5	2 (0, 41)
ASD	1.8 ± 3.0	2	1 (0, 25)
Depression	1.7 ± 2.9	2	1 (0, 33)
Age group			
0 ~ 4	0.4±0.9	0	0 (0, 8)
5 ~ 9	2.2±3.1	3	1 (0, 26)
10 ~ 14	2.6±4.0	3	1 (0, 36)
15 ~ 19	1.8±3.4	2	0 (0, 37)
Sex			
Male	5.1±7.4	6	3 (0, 61)
Female	1.8±2.8	3	1 (0, 28)

Abbreviation, n: number; SD: Standard Deviation; ADHD: attention-deficit/hyperactivity disorder; ASD: autism spectrum disorder

The daily average concentration levels of PM_{10}, $PM_{2.5}$, SO_2, O_3, NO_2, and CO were

44.5 μg/m^3, 24.5 μg/m^3, 0.005 ppm, 0.028 ppm, 0.02 ppm, and respectively. The annual average concentration levels of PM_{10}, $PM_{2.5}$, NO_2 decreased from 2011 to 2019 (Appendix Table 2). The PM_{10} concentration was stable from 47.9 (31.6) in 2011 to 2015 and then decreased to 40.2 (21.7) in 2019. $PM_{2.5}$ concentration decreased from 26.4 (14.8) in 2015 to 22.3 (14.9) in 2019. The maximum concentration levels of PM_{10} and $PM_{2.5}$ was 626.4 μg/m^3, 140.6 μg/m^3. These concentrations were much higher compared to WHO air quality guideline standard 2005 (24 hour: PM_{10} (50), $PM_{2.5}$ (25), WHO, 2006).

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Table 4. Summary statistics on average of daily, air pollutants concentrations, and meteorological variables, 2011-2019

	Mean± SD	**Min**	**25 Percentile**	**50 Percentile**	**75 Percentile**	**Max**
Air pollutants						
PM_{10} (μg/m^3)	44.5±24.2	5.3	28.7	39.7	54.6	626.4
$PM_{2.5}$ (μg/m^3)	24.5±13.8	0.3	14.4	21.5	30.8	140.6
O_3 (ppm)	0.028±0.012	0.001	0.019	0.027	0.036	0.10
NO_2 (ppm)	0.02±0.01	0.001	0.01	0.02	0.03	0.08
SO_2 (ppm)	0.005±0.002	0.0002	0.003	0.004	0.006	0.03
CO (ppm)	0.5±0.1	0.076	0.37	0.45	0.56	2.1
Meteorological variables						
Temperature (℃)	13.5±9.9	-15.0	5.1	14.6	22.0	33.7
Relative humidity (%)	66.8±15.6	11.3	56.0	68.0	78.3	100

Abbreviation, n: number; SD: Standard Deviation; PM10: particulate matter <10 μm in aerodynamic diameter; PM2.5: particulate matter <2.5 μm in aerodynamic diameter; O3: ozone; NO2: nitrogen dioxide; SO2: sulfide dioxide; CO: carbon monoxide

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2. Relative risk of medical institutions visits for major mental disorders among children and adolescents associated with air pollutants

1) Single lag models

Table 5 showed the association between short-term exposure to air pollutant and medical institutions visits for major MDs according to different lag (lag 0 ~ lag 14) in single lag structure models. In PM_{10}, it was statistically significant at lag 0, lag 1, and lag 14. In $PM_{2.5}$, it was only statistically significant at lag 1 (RR per 10 μg/m^3 increase: 1.031, 95% CI: 1.005; 1.058). In NO_2, it was significant at lag 0, lag 1, lag 5, lag 6, lag 7, lag 8, lag 13, and lag 14. In SO_2, it was significant in lag 0, lag 1, and lag 14. In O_3, it was significant at lag 2, lag 3, lag 4, lag 10, lag 11, and lag 12. In CO, it was significant at lag 0, lag 1, lag 7, and lag 14.

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Table 5. Relative risks in medical institutions visits for major mental disorders among children and adolescents associated with air pollutant along different single lag structures models.

	PM_{10} (per 10 μg/m^3)		**$PM_{2.5}$ (per 10 μg/m^3)**		**NO_2 (per 1ppb)**		**SO_2 (per 1ppb)**		**O_3 (per 1ppb)**		**CO (per 1ppb)**	
	RR	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**
lag0	1.074*	(1.050;1.099)	1.025	(0.969;1.080)	1.088*	(1.073;1.102)	1.159*	(1.106;1.212)	0.942	(0.932;0.953)	1.0017*	(1.0012;1.0022)
lag1	1.021*	(1.008;1.033)	1.031*	(1.005;1.058)	1.009*	(1.005;1.013)	1.024*	(1.001;1.047)	1.000	(0.997;1.004)	1.0005*	(1.0003;1.0007)
lag2	0.997	(0.985;1.009)	1.026	(0.998;1.053)	0.979	(0.973;0.984)	0.968	(0.944;0.992)	1.022*	(1.019;1.026)	0.9999	(0.9997;1.0002)
lag3	0.991	(0.980;1.003)	1.013	(0.987;1.040)	0.976	(0.970;0.982)	0.960	(0.938;0.982)	1.022*	(1.019;1.025)	0.9998	(0.9996;1.000)
lag4	0.996	(0.986;1.006)	0.998	(0.977;1.018)	0.989	(0.985;0.993)	0.976	(0.958;0.994)	1.010*	(1.008;1.013)	0.9998	(0.9996;1.000)
lag5	1.003	(0.994;1.012)	0.983	(0.964;1.002)	1.004*	(1.001;1.007)	0.998	(0.981;1.015)	0.996	(0.993;0.998)	1.0000	(0.9998;1.0001)
lag6	1.008	(0.998;1.018)	0.973	(0.952;0.993)	1.015*	(1.012;1.018)	1.016	(0.994;1.038)	0.985	(0.982;0.988)	1.0001	(0.9999;1.0003)
lag7	1.008	(0.998;1.019)	0.967	(0.946;0.989)	1.018*	(1.014;1.021)	1.019	(0.995;1.044)	0.981	(0.978;0.984)	1.0001*	(1.000;1.0003)
lag8	1.003	(0.993;1.013)	0.966	(0.946;0.987)	1.012*	(1.009;1.015)	1.005	(0.986;1.024)	0.985	(0.983;0.988)	1.0001	(0.9999;1.0002)
lag9	0.992	(0.983;1.002)	0.971	(0.951;0.990)	0.999	(0.996;1.002)	0.980	(0.964;0.997)	0.996	(0.994;0.999)	0.9999	(0.9998;1.0001)
lag10	0.981	(0.971;0.991)	0.978	(0.957;0.999)	0.982	(0.977;0.987)	0.952	(0.932;0.971)	1.011*	(1.008;1.013)	0.9997	(0.9996;0.9999)
lag11	0.973	(0.961;0.985)	0.985	(0.960;1.010)	0.970	(0.963;0.977)	0.930	(0.902;0.957)	1.021*	(1.018;1.024)	0.9996	(0.9994;0.9998)
lag12	0.976	(0.964;0.988)	0.989	(0.964;1.015)	0.980	(0.975;0.985)	0.942	(0.920;0.965)	1.020*	(1.016;1.023)	0.9996	(0.9994;0.9998)
lag13	0.999	(0.988;1.011)	0.986	(0.961;1.010)	1.017*	(1.013;1.021)	1.003	(0.981;1.026)	0.994	(0.991;0.998)	0.9999	(0.9997;1.0001)

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lag14	1.056*	(1.030;1.082)	0.967	(0.907;1.027)	1.124*	(1.097;1.151)	1.156*	(1.069;1.243)	0.932	(0.923;0.941)	1.0007*	(1.0002;1.0013)

Abbreviation, RR: Relative risk, CI: Confidence Interval; *p <0.05; significant

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2) Cumulative lag models

Table 6 showed the association between short-term exposure to air pollutant and medical institutions visits for major mental disorders according to different lag (cumulative lag 1 ~ cumulative lag 14) in cumulative lag structure models. In PM_{10}, it showed significant association at cumulative lag 1 ~ cumulative lag 10, and showed the largest at cumulative lag 1 (RR per 10 $\mu g/m^3$ increase: 1.095, 95% CI: 1.061; 1.128). In $PM_{2.5}$, it showed only significant association at cumulative lag 3 (RR per 10 $\mu g/m^3$ increase: 1.094, 95% CI: 1.005; 1.184). In NO_2, it showed significant association at cumulative lag 1 ~ cumulative lag 14, and the largest effect at cumulative lag 14 (RR per 1 ppb: 1.142, 95% CI: 1.113; 1.171). In SO_2, it showed significant association at cumulative lag 1~ cumulative lag 3, cumulative lag 7 ~ cumulative lag 8, and the largest at cumulative lag 1 (RR per 1 ppb: 1.179, 95% CI: 1.117; 1.241). In CO, there was significant association at cumulative lag 1 ~ cumulative lag 10. However, in O_3, there was no significant at cumulative lag model.

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Table 6. Relative risks of medical institutions visits for major mental disorders among children and adolescents associated with air pollutant along different cumulative lag structures models.

	PM_{10} (per 10 μg/m^3)		$PM_{2.5}$ (per 10 μg/m^3)		NO_2 (per 1ppb)		SO_2 (per 1ppb)		O_3 (per 1ppb)		CO (per 1ppb)	
	RR	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**
cum1	**1.095***	**(1.061;1.128)**	1.056	(0.981;1.132)	1.090*	(1.077;1.104)	**1.179***	**(1.117;1.241)**	0.943	(0.930;0.956)	**1.0022***	**(1.0016;1.0028)**
cum2	1.091*	(1.053;1.129)	1.082	(0.999;1.165)	1.068*	(1.055;1.082)	1.147*	(1.076;1.218)	0.965	(0.952;0.979)	1.0022*	(1.0014;1.0029)
cum 3	1.082*	(1.040;1.124)	**1.094***	**(1.005;1.184)**	1.048*	(1.033;1.063)	1.106*	(1.027;1.184)	0.987	(0.974;1.000)	1.0019*	(1.0011;1.0027)
cum 4	1.078*	(1.032;1.124)	1.092	(0.996;1.188)	1.038*	(1.021;1.054)	1.080	(0.995;1.166)	0.997	(0.984;1.010)	1.0017*	(1.0009;1.0026)
cum 5	1.080*	(1.030;1.130)	1.076	(0.974;1.177)	1.042*	(1.024;1.060)	1.077	(0.985;1.169)	0.993	(0.980;1.007)	1.0017*	(1.0008;1.0026)
cum 6	1.088*	(1.034;1.141)	1.049	(0.941;1.156)	1.057*	(1.038;1.076)	1.092	(0.993;1.190)	0.978	(0.964;0.992)	1.0018*	(1.0008;1.0027)
cum 7	1.095*	(1.037;13153)	1.016	(0.902;1.131)	1.075*	(1.054;1.095)	1.110*	(1.005;1.215)	0.959	(0.943;0.975)	1.0019*	(1.0008;1.0029)
cum 8	1.097*	(1.035;1.160)	0.983	(0.861;1.105)	1.087*	(1.065;1.108)	1.116*	(1.004;1.229)	0.944	(0.927;0.961)	1.0019*	(1.0008;1.0030)
cum 9	1.090*	(1.023;1.156)	0.954	(0.825;1.084)	1.086*	(1.063;1.109)	1.097	(0.978;1.216)	0.941	(0.923;0.959)	1.0018*	(1.0007;1.0030)
cum 10	1.070*	(1.000;1.141)	0.933	(0.799;1.068)	1.070*	(1.046;1.094)	1.048	(0.924;1.173)	0.951	(0.932;0.970)	1.0016*	(1.0003;1.0028)
cum11	1.044	(0.970;1.117)	0.920	(0.780;1.060)	1.045*	(1.020;1.070)	0.979	(0.849;1.109)	0.972	(0.953;0.992)	1.0011	(0.9999;1.0020)
cum12	1.020	(0.943;1.098)	0.911	(0.764;1.057)	1.026*	(1.000;1.053)	0.920	(0.783;1.056)	0.992	(0.971;1.013)	1.0007	(0.9994;1.002)
cum13	1.019	(0.938;1.101)	0.897	(0.745;1.049)	1.043*	(1.016;1.071)	0.926	(0.783;1.069)	0.986	(0.964;1.008)	1.0006	(0.9994;1.002)

cum14	1.072	(0.985;1.158)	0.864	(0.703;1.025)	**1.142***	**(1.113;1.171)**	1.086	(0.933;1.239)	0.917	(0.894;0.940)	1.0014	(0.9999;1.0029)

Abbreviation, RR: Relative risk, CI: Confidence Interval, cum: cumulative lag, *p <0.05; significant

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3) Subgroup - Age group

For age group, the association between exposure to different air pollutants and medical institutions visits for major MDs was shown (Table 7). In PM_{10}, the RR was the largest in age 10 ~ 14 group (RR: 1.093, 95% CI: 1.039; 1.148), and the smallest in age <5 group (RR: 1.065, 95% CI: 0.963; 1.167), but not statistically significant. In NO_2 and CO, it was statistically significant in all age groups.

Table 7. Association between exposure to air pollutants and medical institutions visits by age group

Age group	Relative Risk and 95% Confidence Interval			
	Age < 5	**5 ~ 9**	**10 ~ 14**	**15~19**
PM_{10} at cumulative lag 3	1.065 (0.963; 1.167)	1.072* (1.015; 1.129)	1.093* (1.039; 1.148)	1.068* (1.006; 1.113)
$PM_{2.5}$ at cumulative lag 3	0.972 (0.686; 1.259)	1.063 (0.936; 1.190)	1.125* (1.011; 1.239)	1.083 (0.957; 1.209)
NO_2 at cumulative lag 3	1.089* (1.055; 1.123)	1.040* (1.020; 1.060)	1.050* (1.031; 1.069)	1.045* (1.023; 1.067)
SO_2 at cumulative lag 3	0.973 (0.796; 1.151)	1.063 (0.958; 1.167)	1.150* (1.046; 1.254)	1.164* (1.036; 1.292)
O_3 at cumulative lag 3	0.948 (0.921; 0.976)	0.985 (0.966; 1.003)	0.985 (0.968; 1.001)	0.995 (0.978; 1.013)
CO at cumulative lag 3	1.002* (1.0003; 1.004)	1.002* (1.0007; 1.003)	1.002* (1.001; 1.003)	1.001* (1.000; 1.003)

*p <0.05; significant

4) Subgroup - Sex

For sex, the association between exposure to air pollutants and medical institutions

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visits for major MDs was statistically significant in PM_{10}, NO_2, SO_2 and CO. Except for PM_{10} and O_3, the effect was greater in female than in male (Table 8). The difference between sex was not significant in all air pollutants (no effect modification).

Table 8. Association between exposure to air pollutants and medical institutions visits by sex

Sex	RR and 95% Confidence Interval		p value for interaction
	Male	Female	
PM_{10} at cumulative lag 3	1.079* (1.034; 1.123)	1.098* (1.038; 1.158)	0.389
$PM_{2.5}$ at cumulative lag 3	1.077 (0.980; 1.174)	1.150 (0.9995; 1.301)	0.263
NO_2 at cumulative lag 3	1.044* (1.028; 1.060)	1.056* (1.035; 1.077)	0.100
SO_2 at cumulative lag 3	1.085* (1.002; 1.169)	1.170* (1.054; 1.286)	0.068
O_3 at cumulative lag 3	0.985 (0.970; 1.000)	0.991 (0.975; 1.008)	1
CO at cumulative lag 3	1.0019* (1.0011; 1.0027)	1.0020* (1.0008; 1.0031)	0.827

Abbreviation, RR: Relative risk, *p <0.05; significant

5) Subgroup - Specific mental disorders

For specific mental disorders, ADHD was positive association between exposure to air pollutants and medical institutions visits except SO_2 and O_3 (Table 9). In ASD and depression, it showed the association between exposure to air pollutants and medical institutions visits except $PM_{2.5}$ and O_3.

Table 9. Association between exposure to air pollutants and medical institutions visits by specific mental disorders

Disorders	RR and 95% Confidence Interval			p value for interaction		
	ADHD	ASD	Depression	ADHD vs ASD	ADHD vs Depression	ASD vs Depression
PM_{10} at cumulative lag 3	1.071* (1.023;1.118)	1.097* (1.040;1.154)	1.080* (1.021;1.139)	0.117	0.631	0.053

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$PM_{2.5}$ at cumulative lag 3	1.094* (1.003;1.184)	1.035 (0.916;1.155)	1.106 (0.998;1.214)	0.171	0.713	0.013
NO_2 at cumulative lag 3	1.039* (1.022;1.055)	1.066* (1.045;1.086)	1.043* (1.023;1.063)	<0.001	0.475	<0.001
SO_2 at cumulative lag 3	1.086 (0.997;1.175)	1.130* (1.024;1.236)	1.132* (1.014;1.250)	0.176	0.294	0.947
O_3 at cumulative lag 3	0.988 (0.974;1.002)	0.968 (0.952;0.984)	1.000 (0.982;1.018)	<0.001	<0.001	0.037
CO at cumulative lag 3	1.002* (1.0007;1.0025)	1.002* (1.001;1.004)	1.002* (1.000;1.003)	0.001	0.865	0.054

Abbreviation, RR: Relative risk, ADHD: Attention-deficit hypertensive disorder, ASD: Autism Spectrum disorder, *p <0.05; significant

3. Attributable number and population attributable fraction of medical institutions visits associated with major mental disorders due to exposure to air pollution

Table 10 showed the attributable number and population attributable fraction attributable air pollution using the WHO air quality guidelines 2005 and 2021. From 2011 to 2019, about 26,557 cases were found to be caused by PM_{10} exposure, which accounted for about 7.23 % of all major MDs with WHO air quality guidelines 2005. About 11,624 cases were caused by $PM_{2.5}$ exposure in 2015-2019, and it accounted for about 3.16 % of all major MDs. Applying 2021 standards, 32,949 and 25,254 cases were found to be caused by PM_{10} and $PM_{2.5}$ exposure, which accounted for about 8.97, 6.87 % of all major MDs in 2015-2019, respectively.

Table 10. Attributable number and population attributable fraction (%) of major

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mental disorders- medical institutions visits due to air pollution, 2011-2019

Air pollution	Reference concentration	Attributable number	Population attributable fraction (%)
PM_{10}	50 μg/m^3	26557 (10747; 61297)	7.23 (2.93; 16.69)
	45 μg/m^3	32949 (13584; 72956)	8.97 (3.70; 19.86)
$PM_{2.5}$	25 μg/m^3	11624 (575; 24723)	3.16 (0.16; 6.73)
	15 μg/m^3	25254 (1248; 53710)	6.87 (0.34; 14.62)

In specific mental disorders, applying 50 μg/m^3 as the reference concentration, the population attributable fraction (%) of ADHD, ASD, and depression due to PM_{10} was 5.81 % (95% CI: 1.60; 14.31), 18.14 % (5.68; 65.27), and 14.11 % (2.95; 46.56), respectively. Likewise, applying 45 μg/m^3 as the reference concentration, that of three diseases was 7.29 %, 22.29 %, 17.56 %, respectively. The PAF of three diseases due to $PM_{2.5}$ was not statistically significant except for ADHD.

Table 11. Attributable number and population attributable fraction (%) of medical institutions visits by specific mental disorders, 2011-2019

Disease	Air pollution	Reference concentration	AN	PAF (%)
ADHD	**PM_{10}**	50 μg/m^3	8506 (2338; 10889)	5.81 (1.60; 14.31)
		45 μg/m^3	10640 (2967; 25137)	7.29 (2.03; 17.22)
	$PM_{2.5}$	25 μg/m^3	4804 (142; 10276)	3.29 (0.10; 7.04)
		15 μg/m^3	10392 (306; 22241)	7.12 (0.21; 15.23)
ASD	**PM_{10}**	50 μg/m^3	13856 (4342; 49862)	18.14 (5.68; 65.27)

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		45 μg/m^3	17029 (5490; 57493)	22.29 (7.19; 75.25)
	$PM_{2.5}$	25 μg/m^3	1735 (-3775; 8416)	2.27 (-4.94; 11.02)
		15 μg/m^3	3748 (-8125; 18219)	4.91 (-10.64; 23.85)
Depression	**PM_{10}**	50 μg/m^3	10087 (2108; 33283)	14.11 (2.95; 46.56)
		45 μg/m^3	12554 (2676; 39074)	17.56 (3.74; 54.66)
	$PM_{2.5}$	25 μg/m^3	5479 (-104; 12263)	0.08 (-0.001; 0.17)
		15 μg/m^3	11855 (-225; 26539)	16.58 (-0.32; 37.12)

Abbreviation, AN: Attributable number; PAF: Population attributable fraction; ADHD: attention-deficit/hyperactivity disorder; ASD: autism spectrum disorder

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4. YLL of medical institutions visits for major mental disorders

Table 12 showed the estimated YLL. According to mortality data, the number of deaths by age group, sex was calculated as 0 because there were no direct deaths from ADHD, ASD, and depression in children and adolescents under the age of 19 (Table 12).

Table 12. Years of life lost for major mental disorders under age of 19 in Korea, 2011-2019

Age group	Number of deaths		Life expectancy (years)		YLL
	Male	Female	Male	Female	
Total	0	0	74.3	80.3	0
0 ~ 4	0	0	79.9	85.9	0
5 ~ 9	0	0	75.6	81.6	0
10 ~ 14	0	0	70.6	76.6	0
15 ~ 19	0	0	65.6	71.6	0

Abbreviation, YLL: Years of life lost

5. YLD of medical institutions visits for major mental disorders

During the study period, in ADHD, the number of incidence cases (incidence rates per 100,000) under the age of 19 in the nationwide was 1,504 (13.2 %) and 3,312 (36.6 %) in 2011 and 2019, respectively, and increased by about 20%. By age group, it showed a rapid increase except for 0 ~ 4 years old, and by sex, male was about 3 ~ 4 times higher than female.

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Table 13. Trends of the incidence cases and rates of attention-deficit/hyperactivity disorder (per 100,000 population) by age group, sex during 2011-2019

	2011	2012	2013	2014	2015	2016	2017	2018	2019
Total	1504 (13.2)	1697 (15.3)	1880 (17.4)	1942 (18.4)	2037 (19.8)	2296 (23.0)	2573 (26.6)	2844 (30.4)	3312 (36.6)
Age group									
0~4	60 (2.6)	45 (1.9)	41 (1.8)	25 (1.1)	31 (1.4)	34 (1.6)	29 (1.4)	40 (2.0)	60 (3.3)
5~9	623 (26.5)	736 (31.4)	813 (35.1)	853 (37.3)	917 (39.5)	1049 (44.8)	1066 (45.7)	1013 (43.9)	999 (43.5)
10~14	637 (20.3)	699 (23.7)	742 (26.5)	759 (28.6)	743 (30.4)	814 (34.9)	1016 (43.5)	1257 (54.5)	1635 (71.8)
15~19	184 (5.2)	217 (6.2)	284 (8.3)	305 (9.2)	346 (10.7)	399 (12.8)	462 (15.7)	534 (19.1)	618 (23.4)
Sex									
Male	1212 (20.4)	1384 (23.9)	1528 (27.1)	1585 (29.0)	1629 (30.6)	1836 (35.5)	2067 (41.3)	2274 (47.1)	2619 (56.2)
Female	292 (5.4)	313 (5.9)	352 (6.8)	357 (7.0)	408 (8.2)	460 (9.5)	506 (10.8)	570 (12.6)	693 (15.8)

The incidence cases of ASD were 646 (5.7 %) and 982 (10.9 %) in 2011 and 2019, respectively, and it doubled during the study period. The incidence rates were higher in younger ages (0 ~ 9 years old) than older ages (10 ~ 19 years old) and increased in all age groups during 9 years. By sex, the incidence rates in male were about four times higher than that of female, and both genders doubled over nine years.

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Table 14. Trends of the incidence cases and rates of autism spectrum disorder (per 100,000 population) by age group, sex during 2011-2019

	2011	2012	2013	2014	2015	2016	2017	2018	2019
Total	646 (5.7)	676 (6.1)	694 (6.4)	674 (6.4)	696 (6.8)	729 (7.3)	801 (8.3)	880 (9.4)	982 (10.9)
Age group									
0~4	235 (10.1)	226 (9.8)	223 (9.7)	168 (7.4)	166 (7.4)	196 (9.0)	194 (9.4)	242 (12.4)	229 (12.6)
5~9	164 (7.0)	184 (7.9)	190 (8.2)	239 (10.4)	257 (11.1)	242 (10.3)	268 (11.5)	295 (12.8)	350 (15.2)
10~14	134 (4.3)	154 (5.2)	158 (5.6)	139 (5.2)	133 (5.4)	142 (6.1)	172 (7.4)	189 (8.2)	237 (10.4)
15~19	113 (3.2)	112 (3.2)	123 (3.6)	128 (3.9)	140 (4.3)	149 (4.8)	167 (5.7)	154 (5.5)	166 (6.3)
Sex									
Male	512 (8.6)	543 (9.4)	555 (9.8)	533 (9.7)	559 (10.5)	571 (11.1)	628 (12.6)	708 (14.7)	804 (17.2)
Female	134 (2.5)	133 (2.5)	139 (2.7)	141 (2.8)	137 (2.8)	158 (3.3)	173 (3.7)	172 (3.8)	178 (4.1)

The incidence cases of depression were 938 (8.3 %) and 2,543 (28.1 %) in 2011 and 2019, respectively. It showed a rapid increase in the age of 10 ~ 19 and similar incidence rates in male and female.

Table 15. Trends of the incidence cases and rates of depression (per 100,000 population) by age group, sex during 2011-2019

	2011	2012	2013	2014	2015	2016	2017	2018	2019

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Total	938 (8.3)	902 (8.1)	919 (8.5)	950 (9.0)	1050 (10.2)	1342 (13.4)	1622 (16.8)	2077 (22.2)	2543 (28.1)
Age group									
0~4	7 (0.3)	14 (0.6)	12 (0.5)	8 (0.4)	9 (0.4)	16 (0.7)	15 (0.7)	21 (1.1)	18 (1.0)
5~9	106 (4.5)	129 (5.5)	147 (6.3)	176 (7.7)	212 (9.1)	235 (10.0)	276 (11.8)	241 (10.5)	240 (10.5)
10~14	309 (9.9)	318 (10.8)	342 (12.2)	314 (11.8)	312 (12.7)	397 (17.0)	518 (22.2)	747 (32.4)	939 (41.2)
15~19	516 (14.5)	441 (12.7)	418 (12.2)	452 (13.6)	517 (15.9)	694 (22.3)	813 (27.7)	1068 (38.3)	1346 (51.0)
Sex									
Male	578 (9.7)	535 (9.2)	551 (9.8)	531 (9.7)	602 (11.3)	768 (14.9)	946 (18.9)	1094 (22.7)	1328 (28.5)
Female	360 (6.6)	367 (6.9)	368 (7.1)	419 (8.3)	448 (9.1)	574 (11.9)	676 (14.5)	983 (21.7)	1215 (27.8)

YLD due to ADHD showed a steady increase from 2011 to 2019 (In 2011: 438.7 YLDs per 100,000 / 2019: 1218.5 YLDs per 100,000) (Table 16). It increased about three times over nine years, and by age group, 5 ~ 14 years accounted for the majority. Also, YLD of male were about three to four times higher than that of female.

Table 16. Years lived with disability (per 100,000) due to attention-deficit/hyperactivity disorder in Koreans under aged 19, 2011-2019

	2011	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**
Total	438.7	507.4	576.4	611.6	658.9	764.1	884.8	1011.0	1218.5
Age group									
0~4	53.0	50.8	36.1	22.1	24.9	46.4	27.3	40.5	83.7

5~9	875.4	1038.1	1161.4	1231.9	1306.8	1482.9	1513.7	1458.6	1443.3
10~14	675.7	787.9	880.9	951.8	1010.6	1160.3	1449.6	1814.9	2389.5
15~19	172.1	206.9	276.5	305.6	354.5	425.4	522.9	636.7	778.2
Sex									
Male	676.9	793.7	900.6	961.4	1017.6	1181.4	1375.1	1566.0	1868.5
Female	177.7	194.6	224.1	233.7	272.8	316.6	359.6	418.0	525.5

YLD due to ASD also showed increase from 2011 to 2019 (In 2011: 188.1 YLDs per 100,000 / 2019: 359.8 YLDs per 100,000) (Table 17). The YLD of male were 285.7 and 570.3 in 2011 and 2019, respectively, showing a significant increase.

Table 17. Years lived with disability (per 100,000) due to autism spectrum disorders in Koreans under aged 19, 2011-2019

	2011	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**
Total	188.1	201.6	212.0	211.4	224.0	241.6	273.8	311.1	359.8
Age group									
0~4	313.8	309.2	309.6	230.5	233.5	279.8	285.5	368.1	387.9
5~9	229.6	258.6	269.0	341.2	361.3	340.6	376.6	422.3	502.9
10~14	142.4	173.8	187.6	174.4	180.8	202.3	245.1	272.8	346.3
15~19	106.1	107.0	120.0	128.5	143.6	159.1	189.2	183.9	209.3
Sex									

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Male	285.7	310.8	326.1	322.4	347.4	366.1	415.8	484.8	570.3
Female	80.9	82.2	87.9	91.3	91.1	108.0	121.1	125.5	134.6

YLD due to depression also showed a significant increase during nine years (In 2011: 271.4 YLDs per 100,000 / 2019: 919.9 YLDs per 100,000) (Table 18). It increased by about three times during the study period, and 935.1 and 902 were found in male and female, respectively.

Table 18. Years lived with disability (per 100,000) due to depression in Koreans under aged 19, 2011-2019

	2011	2012	2013	2014	2015	2016	2017	2018	2019
Total	271.4	265.9	277.5	292.8	332.4	438.1	547.2	723.3	919.9
Age group									
0~4	0.6	2.8	12.2	4.9	4.6	18.4	19.3	14.3	14.3
5~9	145.6	176.9	204.5	240.2	292.3	323.6	381.8	342.4	338.5
10~14	323.4	351.9	398.1	387.5	417.1	558.9	729.3	1061.9	1352.3
15~19	479.9	416.2	402.9	444.4	518.7	723.3	900.3	1252.0	1666.3
Sex									
Male	320.1	303.4	321.3	317.5	371.6	488.1	622.4	745.8	935.1
Female	218.0	224.7	229.4	265.1	287.3	381.9	463.2	702.8	902.5

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6. DALY of medical institutions visits for major mental disorders

As DALYs of all three diseases increased during study period, DALYs due to major mental disorders gradually increased (In 2011: 898.2 DALYs per 100,000 / 2019: 2498.2 DALYs per 100,000) (Table 19). For age group, it increased nearly four times in the 10 ~ 19 years old group, and by sex, it increased about three times.

Table 19. Disability-adjusted life-year (per 100,000) due to major mental disorders in Koreans under aged 19, 2011-2019

	2011	2012	2013	2014	2015	2016	2017	2018	2019
Total	898.2	974.9	1065.9	1115.8	1215.3	1443.8	1705.8	2045.4	2498.2
Age group									
0~4	367.4	362.8	357.9	257.5	263	344.6	332.1	422.9	485.9
5~9	1250.6	1473.6	1634.9	1813.3	1960.4	2147.1	2272.1	2223.3	2284.7
10~14	1141.5	1313.6	1466.6	1513.7	1608.5	1921.5	2424	3149.6	4088.1
15~19	758.1	730.1	799.4	878.5	1016.8	1307.8	1612.4	2072.6	2653.8
Sex									
Male	1282.7	1407.9	1548	1601.3	1736.6	2035.6	2413.3	2796.6	3373.9
Female	476.6	501.5	541.4	590.1	651.2	806.5	943.9	1246.3	1562.6

DALYs due to ADHD showed a steady increase from 2011 to 2019 (In 2011: 438.7 DALYs per 100,000 / 2019: 1218.5 DALYs per 100,000) (Table 20). Also, DALYs of male were about three to four times higher than that of female.

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Table 20. Disability-adjusted life-year (per 100,000) due to attention-deficit/hyperactivity disorder in Koreans under aged 19, 2011-2019

	2011	2012	2013	2014	2015	2016	2017	2018	2019
Total	438.7	507.4	576.4	611.6	658.9	764.1	884.8	1011.0	1218.5
Age group									
0~4	53.0	50.8	36.1	22.1	24.9	46.4	27.3	40.5	83.7
5~9	875.4	1038.1	1161.4	1231.9	1306.8	1482.9	1513.7	1458.6	1443.3
10~14	675.7	787.9	880.9	951.8	1010.6	1160.3	1449.6	1814.9	2389.5
15~19	172.1	206.9	276.5	305.6	354.5	425.4	522.9	636.7	778.2
Sex									
Male	676.9	793.7	900.6	961.4	1017.6	1181.4	1375.1	1566.0	1868.5
Female	177.7	194.6	224.1	233.7	272.8	316.6	359.6	418.0	525.5

DALYs due to ASD also showed increase from 2011 to 2019 (In 2011: 188.1 DALYs per 100,000 / 2019: 359.8 DALYs per 100,000) (Table 21). The DALY of male were 285.7 and 570.3 in 2011 and 2019, respectively, showing a significant increase.

Table 21. Disability-adjusted life-year (per 100,000) due to autism spectrum disorders in Koreans under aged 19, 2011-2019

	2011	2012	2013	2014	2015	2016	2017	2018	2019
Total	188.1	201.6	212.0	211.4	224.0	241.6	273.8	311.1	359.8

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Age group									
0~4	313.8	309.2	309.6	230.5	233.5	279.8	285.5	368.1	387.9
5~9	229.6	258.6	269.0	341.2	361.3	340.6	376.6	422.3	502.9
10~14	142.4	173.8	187.6	174.4	180.8	202.3	245.1	272.8	346.3
15~19	106.1	107.0	120.0	128.5	143.6	159.1	189.2	183.9	209.3
Sex									
Male	285.7	310.8	326.1	322.4	347.4	366.1	415.8	484.8	570.3
Female	80.9	82.2	87.9	91.3	91.1	108.0	121.1	125.5	134.6

DALYs due to depression also showed a significant increase during nine years (In 2011: 271.4 DALYs per 100,000 / 2019: 919.9 DALYs per 100,000) (Table 22). It increased by about three times during the study period, and 935.1 DALYs and 902 DALYs were found in male and female, respectively.

Table 22. Disability-adjusted life-year due to depression in Koreans under aged 19, 2011-2019

	2011	2012	2013	2014	2015	2016	2017	2018	2019
Total	271.4	265.9	277.5	292.8	332.4	438.1	547.2	723.3	919.9
Age group									
0~4	0.6	2.8	12.2	4.9	4.6	18.4	19.3	14.3	14.3
5~9	145.6	176.9	204.5	240.2	292.3	323.6	381.8	342.4	338.5

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10~14	323.4	351.9	398.1	387.5	417.1	558.9	729.3	1061.9	1352.3
15~19	479.9	416.2	402.9	444.4	518.7	723.3	900.3	1252.0	1666.3
Sex									
Male	320.1	303.4	321.3	317.5	371.6	488.1	622.4	745.8	935.1
Female	218.0	224.7	229.4	265.1	287.3	381.9	463.2	702.8	902.5

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7. Attributable DALY for particulate matter

Attributable DALY for particulate matter (*DALY*PAF*) showed an increase from 2011 to 2019 when each PAF was applied (Table 23).

Table 23. Attributable DALYs (per 100,000) due to major mental disorders in Koreans under aged 19, 2011-2019

		Reference concentration	2011	2012	2013	2014	2015	2016	2017	2018	2019
Air pollution	PM_{10}	50 μg/m^3	65	70	77	81	88	104	123	148	181
		45 μg/m^3	81	87	96	100	109	130	153	183	224
	$PM_{2.5}$	25 μg/m^3	-	-	-	-	38	46	54	65	79
		15 μg/m^3	-	-	-	-	137	165	184	196	238

8. Costs of medical institutions visits for major mental disorders

The number of outpatient visits and inpatient admission (per 1 patient) for each disease was as follows. In ADHD, the number of outpatient visits (1 patient) rose slightly from about 7.9 to 9.6 during 9 years, and inpatient admissions ranged from 1.4 to 1.8 (Table 24).

Table 24. Outpatient visits and inpatient admissions of attention deficit hyperactivity disorder

		2011	2012	2013	2014	2015	2016	2017	2018	2019
Outpatient	Number of outpatient visits (per 1 patient)	7.9	8.5	8.5	8.6	8.7	9.3	9.5	9.7	9.6
Inpatient	Number of inpatient admissions (per 1 patient)	1.4	1.3	1.9	1.4	1.6	1.7	1.9	1.8	1.4

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	Hospital days (per 1 inpatient admissions)	31	46	41	48	31	41	30	37	59

In ASD, the number of outpatient visits (1 patient) rose also from about 9.9 to 11.2 during the study period, and hospitalization days (per 1 inpatient admission) were the least among the three diseases. (Table 25).

Table 25. Outpatient visits and inpatient admissions of autism spectrum disorders

		2011	2012	2013	2014	2015	2016	2017	2018	2019
Outpatient	Number of outpatient visits (per 1 patient)	9.9	16.7	15.5	15.3	15.1	14.3	12.4	12.3	11.2
Inpatient	Number of inpatient admissions (per 1 patient)	2.4	7.6	6.5	6.4	6.4	4.4	5.7	6.0	4.1
	Hospital days (per 1 inpatient admissions)	9	8	9	8	9	15	10	8	8

In depression, hospital days (per 1 inpatient admissions) ranged from 31 to 53 (Table 26).

Table 26. Outpatient visits and inpatient admissions of depression

		2011	2012	2013	2014	2015	2016	2017	2018	2019
Outpatient	Number of outpatient visits (per 1 patient)	5.7	6.5	7.0	6.7	6.6	7.0	7.1	8.0	7.9
Inpatient	Number of inpatient admissions	1.3	1.2	1.5	1.3	1.2	1.3	1.4	1.6	1.4

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(per 1 patient)									
Hospital days (per 1 inpatient admissions)	41	45	35	31	35	35	53	31	42

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Direct medical expenses, direct non-medical expenses, and total medical costs for each disease were as follows. The total medical costs per 1 patient (in ADHD) increased to 7,323,836 KRW and 11,785,362 KRW in 2011 and 2019, respectively. Similarly, the results of ASD and depression showed an increasing pattern during study period. Also, the proportion of outpatient costs in the total medical costs tended to increase in all diseases.

Table 27. Medical costs of attention deficit hyperactivity disorder (per 1 patient) from 2011 to 2019

	Year	2011	2012	2013	2014	2015	2016	2017	2018	2019
Direct medical costs	Outpatient medical cost	4,497,895 (0.61)	3,211,069 (0.57)	2,739,941 (0.54)	2,914,028 (0.52)	4,183,675 (0.61)	5,328,898 (0.66)	3,236,852 (0.55)	6,096,005 (0.70)	8,490,691 (0.72)
	Inpatient medical cost	579,944 (0.08)	678,813 (0.12)	568,816 (0.11)	547,471 (0.10)	632,858 (0.09)	629,470 (0.08)	626,072 (0.11)	683,449 (0.08)	769,350 (0.07)
	Drug prescription cost	1,254,688 (0.17)	1,234,613 (0.22)	1,234,613 (0.25)	1,234,613 (0.22)	1,234,613 (0.18)	1,232,605 (0.15)	1,230,598 (0.21)	1,230,598 (0.14)	1,212,530 (0.10)
Out of pocket cost	Outpatient medical cost	722,010 (0.10)	256,913 (0.05)	203,307 (0.04)	629,777 (0.11)	519,921 (0.08)	597,182 (0.07)	470,692 (0.08)	452,264 (0.05)	1,011,509 (0.09)
	Inpatient medical cost	171,865 (0.02)	176,530 (0.03)	157,179 (0.03)	156,763 (0.03)	174,118 (0.03)	181,714 (0.02)	180,632 (0.03)	169,079 (0.02)	184,028 (0.02)
Direct nonmedical cost	Transportation cost for hospital visits	97,434 (0.01)	98,391 (0.02)	125,406 (0.02)	105,809 (0.02)	115,832 (0.02)	124,567 (0.02)	137,079 (0.02)	135,633 (0.02)	117,254 (0.01)
Total direct costs		7,323,836	5,656,329	5,029,261	5,588,460	6,861,016	8,094,436	5,881,925	8,767,027	11,785,362

Unit: KRW

Table 28. Medical costs of autism spectrum disorders (per 1 patient) from 2011 to 2019

	Year	2011	2012	2013	2014	2015	2016	2017	2018	2019

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Direct medical costs	Outpatient medical cost	6,770,976 (0.50)	8,651,328 (0.57)	7,664,445 (0.48)	7,506,783 (0.53)	8,093,096 (0.57)	9,494,236 (0.60)	6,526,968 (0.53)	13,540,162 (0.69)	10,441,041 (0.68)
	Inpatient medical cost	2,104,059 (0.15)	2,890,418 (0.12)	2,976,557 (0.19)	2,686,947 (0.19)	2,940,057 (0.21)	2,747,942 (0.17)	2,772,175 (0.22)	2,750,032 (0.14)	2,191,464 (0.14)
	Drug prescription cost	3,142,650 (0.23)	2,895,180 (0.22)	2,895,180 (0.18)	1,884,495 (0.13)	1,375,320 (0.10)	1,358,895 (0.09)	1,314,000 (0.11)	1,306,335 (0.07)	1,246,110 (0.08)
Out of pocket cost	Outpatient medical cost	930,867 (0.07)	1,334,748 (0.05)	1,345,544 (0.08)	1,010,933 (0.07)	825,330 (0.06)	1,442,031 (0.09)	944,460 (0.08)	1,175,445 (0.06)	885,410 (0.06)
	Inpatient medical cost	537,676 (0.04)	743,783 (0.03)	821,209 (0.05)	731,112 (0.05)	619,004 (0.04)	578,091 (0.04)	495,788 (0.04)	463,028 (0.02)	372,303 (0.02)
Direct nonmedical cost	Transportation cost for hospital visits	148,849 (0.01)	406,949 (0.02)	358,866 (0.02)	358,052 (0.03)	359,526 (0.03)	270,426 (0.02)	323,914 (0.03)	341,851 (0.02)	249,937 (0.02)
Total direct costs		13,635,076	16,922,406	16,061,801	14,178,322	14,212,333	15,891,621	12,377,304	19,576,854	15,386,265

Unit: KRW

Table 29. Medical costs of depression (per 1 patient) from 2011 to 2019

Year	2011	2012	2013	2014	2015	2016	2017	2018	2019

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Direct medical costs	Outpatient medical cost	4,735,244 (0.71)	6,027,334 (0.78)	1,790,463 (0.41)	2,870,264 (0.68)	3,590,070 (0.70)	3,796,185 (0.73)	3,481,094 (0.69)	3,529,492 (0.68)	7,803,298 (0.77)
	Inpatient medical cost	477,812 (0.07)	507,038 (0.07)	1,609,005 (0.36)	522,689 (0.12)	532,033 (0.10)	589,731 (0.11)	608,963 (0.12)	710,911 (0.14)	812,998 (0.08)
	Drug prescription cost	216,445 (0.03)	151,840 (0.02)	151,840 (0.03)	151,840 (0.04)	151,110 (0.03)	147,825 (0.03)	141,255 (0.03)	140,160 (0.03)	133,590 (0.01)
Out of pocket cost	Outpatient medical cost	1,023,551 (0.15)	774,097 (0.10)	215,767 (0.05)	453,017 (0.11)	602,464 (0.12)	400,450 (0.08)	528,394 (0.11)	475,590 (0.09)	1,062,913 (0.11)
	Inpatient medical cost	159,097 (0.02)	167,009 (0.02)	544,662 (0.12)	157,713 (0.04)	148,633 (0.03)	183,844 (0.04)	168,773 (0.03)	183,040 (0.04)	177,318 (0.02)
Direct nonmedical cost	Transportation cost for hospital visits	82,311 (0.01)	83,957 (0.01)	100,500 (0.02)	91,524 (0.02)	87,269 (0.02)	94,663 (0.02)	101,548 (0.02)	117,138 (0.02)	107,862 (0.01)
Total direct costs		6,694,461	7,711,275	4,412,237	4,247,048	5,111,580	5,212,698	5,030,027	5,156,332	10,097,978

Unit: KRW

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As a result of calculating the cost by exposure to PM_{10} by attributable number, although ASD showed a decrease pattern in out-of-pocket costs due to particulate matter, ADHD and depression showed an increase in both total medical costs and out-of-pocket costs due to particulate matter.

Table 30. Attributable total medical costs and out-of-pocket costs of specific mental disorders due to PM_{10} and $PM_{2.5}$ during 2011-2019

		WHO's air quality guideline 2005				WHO's air quality guideline 2021			
		PM_{10}		$PM_{2.5}$		PM_{10}		$PM_{2.5}$	
Disease	**Year**	AC_{total}	AC_{pocket}	AC_{total}	AC_{pocket}	AC_{total}	AC_{pocket}	AC_{total}	AC_{pocket}
ADHD	2011	6,091 (1,443; 17,743)	860 (203; 2,504)	-	-	6,091 (1,444; 17,743)	1,016 (248; 2,859)	-	-
	2012	2,782 (846; 4,961)	235 (72; 420)	-	-	3,623 (1,101; 6,482)	306 (93; 548)	-	-
	2013	3,712 (1,104;6,811)	295 (88; 540)	-	-	4,666 (1,390; 8,569)	370 (110; 680)	-	-
	2014	4,832 (1,414;9,031)	809 (290; 1,856)	-	-	5,922 (1,733; 11,083)	992 (290;1,856)	-	-
	2015	8,629 (1,743;41,378)	990 (200; 4,746)	4,520 (133; 9,518)	518 (15; 1,092)	10,087 (2,142;45,680)	1,157 (246; 5,239)	9,639 (284;20,483)	1,106 (33;2,349)
	2016	6,486 (1,934; 11,966)	703 (210; 1,296)	6,127 (187; 12,563)	664 (20;1,361)	8,457 (2,531; 15,547)	916 (274; 1,684)	14,310 (431; 29,799)	1,550 (47; 3,228)
	2017	4,329 (1,284; 8,043)	554 (164; 1,028)	4,992 (148; 10,498)	638 (19; 1,342)	5,730 (1,711; 10,584)	733 (219; 1,353)	11,033 (326; 23,359)	1,411 (41; 2,987)
	2018	7,690 (2,331;13,833)	596 (181; 1,073)	8,419 (248; 17,814)	653 (19; 1,382)	9,860 (2,980;17,790)	765 (231;1,380)	17,590 (521;37,543)	1,364 (40; 2,912)

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	2019	10,672 (3,152; 19,783)	1,218 (360; 2,258)	12,295 (346; 27,972)	1,404 (39; 3,193)	13,688 (4,063; 25,323)	1,563 (464; 2,891)	25,626 (733; 56,960)	2,925 (84; 6,503)
ASD	2011	20,863 (5,324; 81,408)	2,549 (651;9948)	-	-	24,192 (6,417;91,094)	2,956 (784; 11,132)	-	-
	2012	11,160 (4,317; 19,071)	1,607 (621; 2,746)	-	-	14,567 (5,616;24976)	2,097 (809; 3,596)	-	-
	2013	16,000 (6,010;28,372)	2,561 (962; 4,542)	-	-	20,128 (7,540;35,722)	3,222 (1,207;5,718)	-	-
	2014	14,282 (5,362;25311)	2,060 (773; 3,651)	-	-	17,957 (6,733; 31,872)	2,590 (971; 4,597)	-	-
	2015	40,463 (7,149;338,658)	4,710 (832;39,419)	-	-	45,640 (8,666;368,878)	5,312 (1,009;42,937)	-	-
	2016	17,779 (6,660; 32,012)	2,641 (989; 4,755)	-	-	23,144 (8,700;41,454)	3,438 (1,292; 6,157)	-	-
	2017	13,122 (4,881;23,859)	1,781 (662;3,238)	-	-	17,318 (6,486; 31,213)	2,350 (880; 4,236)	-	-
	2018	24,180 (9,270;41,763)	2,251 (863;3,889)	-	-	31,061 (11,874;53,822)	2,892 (1,106; 5,012)	-	-
	2019	20,567 (7,643; 37,095)	1,864 (693; 3,362)	-	-	26,354 (9,825; 47,366)	2,388 (890; 4,292)	-	-
Depression	2011	6,415 (1,110;24,924)	1,397 (242;5,429)	-	-	7,535 (1,350; 28,088)	1,641 (294;6,118)	-	-
	2012	4,147 (1,000;7,800)	584 (141;1,098)	-	-	5,407 (1,299;10,208)	761 (183;1,437)	-	-
	2013	3,335 (781;6,505)	714 (167;1,393)	-	-	4,192 (980;8,188)	898 (210;1,753)	-	-
	2014	4,204 (964;8,403)	724 (166;1,448)	-	-	5,156 (1,181;10,318)	888 (204;1,778)	-	-

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2015	8,011 (1,100;63,750)	1,408 (193;11,205)	-	-	9,248 (1,354;69,615)	1,626 (238;12,236)	-	-
2016	4,698 (1,101;9,272)	605 (142;1,195)	-	-	6,124 (1,439;12,025)	789 (186;1,550)	-	-
2017	4,137 (963;8,241)	682 (159;1,358)	-	-	5,473 (1,282;10,808)	902 (211;1,781)	-	-
2018	4,814 (1,150;9,154)	724 (173;1,376)	-	-	6,179 (1,472;11,787)	929 (221;1,772)	-	-
2019	10,259 (2,381;20,328)	1,454 (337;2,881)	-	-	13,159 (3,064;25,981)	1,865 (434;3,683)	-	-

ACtotal: Total costs of attributable; ACpocket: total out-of-pocket costs of attributable, Unit: 1000,000 KRW

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V. DISCUSSION

This study is the first attempt to evaluate overall burden of major mental disorders due to exposure to short-term air pollution in children and adolescents in Korea. It showed that it was associated with between exposure to air pollutants and major mental disorders-medical institutions visits except ozone The population attributable fraction was estimated to 7.23 ~ 8.97 % (PM_{10}) and 3.16 ~ 6.87 % ($PM_{2.5}$). ADHD and depression showed an increase in both total medical costs and out-of-pocket costs due to particulate matter.

This study, the overall risk of mental disorders (RR) due to short-term exposure for air pollutants was higher than previous studies at $PM_{2.5}$. A study reported that there is associated with emergency room hospitalization for mental disorders in Seoul and $PM_{2.5}$ using NHIS data from 2003 to 2013. [19] In this study, the relative risk of hospital admission due to $PM_{2.5}$ was 1.008. By specific mental disorders, the relative risks of ADHD due to exposure to air pollution were lower than those of other studies. Park et al. reported that the relative risk (per interquartile) of ADHD-related hospitalization due to exposure to PM_{10}, NO_2, and SO_2 as 1.17, 1.68, 1.29, respectively. [27] Since this study only considered ADHD-related hospitalization indicating severe symptoms of ADHD, it may be considered to show a difference from our results regarding both outpatient and inpatient. In our study, ASD showed different results depending on the air pollutants, there was no positive association between exposure to $PM_{2.5}$, O_3 and ASD. Previous studies showed mixed finding in the association between ASD and $PM_{2.5}$, O_3 exposure. Kim et al. 2022 evaluated hospitalization of ASD, and reported that the relative risks of ASD-related hospitalization for ages 5 ~ 14 were 1.17, 1.09, and 1.03, respectively, at $PM_{2.5}$, NO_2, and O_3 levels. [32] According to a study that examined the association between ASD

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and O_3 exposure, including maternal exposure, the OR of O_3 per interquartile increase ranged from 1.19 to 1.27. [63] Also, in a case-control study conducted in California, it showed that the OR of O_3 (per 11.54 ppb increase) was 1.12 in children diagnosed with ASD. [64] However, in a recently conducted meta-analysis study, including prenatal exposure, there was no association between O_3 exposure and ASD. [65]

Our study showed that there was a positive association between exposure to air pollution and depression except for $PM_{2.5}$ and O_3. Few studies have evaluated depression caused by short-term air pollution exposure in children and adolescents. Roberts et al. investigated that association between exposure to $PM_{2.5}$ and NO_2 and mental health using longitudinal study. [33] Exposure to air pollution at the age of 12 was associated with increased risk of depression at the age of 18, but was not at the age of 12. In San Francisco, one study examined the association between exposure to O_3 and depression in teenagers. [34] In results, when they lived in high-ozone areas during four years, there was a significant increase in depression symptoms.

There were few studies that the attributable fraction due to mental disorders associated with particulate matter. One study evaluated the association with hospitalization for overall mental disorders among all ages, as well as depression due to short-term exposure to PM_{10} and $PM_{2.5}$ in multi-city in China.[44] The attributable fraction (AF) of overall mental disorders (ICD -10 codes; F00-F99) due to PM_{10} was 9.17 % using WHO's air quality guideline 2005. In $PM_{2.5}$, the AF of overall mental disorders was 9.53 %.

The population attributable fraction (PAF) was calculated as the prevalence of the population exposed to the risk and the relative risk. However, if the reference concentrations set to 50 $\mu g/m^3$, it is divided into unexposed and exposed people

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based on 50 μg/m^3. Based on the equation, there is a possibility that population attributable fraction may increase, even if the reference concentration is lower than 50 μg/m^3. Therefore, we additionally calculated PAF by increasing the concentration of PM10, dividing the PM10 concentration by 0 ~ 25 μg/m^3, 25 ~ 50 μg/m^3, and 50 μg/m^3 or more. The PM10 concentration was 0 ~ 25 μg/m^3, 25 ~ 50 μg/m^3, and 50 μg/m^3 or higher, the PAF was calculated as 1.95%, 14.46%, and 23.86%, respectively (Appendix figure 10). We found that the increase in PAF as the concentration of the particulate matter increased.

According to a study that calculated DALY (per 100,000) of diseases related to mental and drug use, there were people under the age of 19 as follows; childhood behavioral disorders including ADHD, conduct disorder - male: 607, female: 222, pervasive development disorder including Autism, Asperger's syndrome - male: 98, female: 17, unipolar depressive disorders including major depressive disorders, dysthymia - male: 281, female: 394. [66] Hong et al. reported that YLDs (per 1,000) of total ADHD (under 19 years of age) was 32605, and 9471 in 0-9 years old and 23134 in 10 ~ 19 years old. [12] Other study that evaluated YLD of major depressive disorder in 2018, in male and female, and these results were lower YLDs than our results except for depression for female. [38] Compared to other studies, our study showed higher DALY except for depression for female. YLD calculated from various factors such as disability weights, duration of the disease, incidence rate, prevalence rate, and difference may have occurred from them. Also, the disability weights of ADHD (0.249) and ASD (0.510) are one value and the condition of the disease is expressed, whereas depression is divided into three categories: mild (0.551), moderate (0.756), and severe (0.838). Since the severity of the disease was mainly evaluated by experts, there was no information about pharmacy per patient. Therefore, we obtained the combined weights by applying the distribution of the severity in the depression from the recently published literature.

Attributable DALY for particulate matter (*DALY*PAF*) showed 181 ~ 224 in 2019 (PM_{10}) and 79 ~ 238 ($PM_{2.5}$). Through this result, it could be suggested that particulate matter may be attributable to mental disorders. Although we didn't take into account other factors like genetic and environmental factors that could cause mental disorders, air pollution is one of modifiable risk factors, suggesting that the prevention of mental disorders may be possible by reducing air pollution exposure. Specifically, several studies have reported that depression is especially directly related to suicide. Therefore, more management is needed for depression in adolescence, where adolescent emotions are sensitive.

Previous studies showed that children and adolescents with mental disorders may incur additional costs as well as medical expenses. Hong et al. examined that direct medical costs, direct non-medical costs for ADHD in 2012. [12] This study showed that the caregiver's cost accounted for more than 80% of the direct non-medical expenses ($ U.S. 9,091,483 in 2012). It has been shown that the burden on family members, including individuals, is high as well as in terms of medical expenses. Also, in ADHD and ASD, non-drug treatment like such as applied behavior analysis, conductive education as well as drug therapy is mainly performed at the same time. In Korea, play therapy is uninsured, but the cost could not be estimated because there was no information. Recently, it has been reported that education costs are significantly higher in ASD patients than non-ASD patients. [67]

Biological mechanism for specific mental disorders due to exposure to air pollution has not yet been identified. However, according to previous studies, the process of the particulate matter moving to the brain is well known to pass through the BBB (blood-brain barrier) through breathing and then to the brain. Recently, a pathway has been reported in which particulate matter enters the olfactory nerve through the olfactory epithelium and is directly transmitted to the brain without passing through BBB. [68,69] As a result, neuroinflammation occurs due to exposure to air pollution. Neuroinflammation means that the central nervous system such as brain, nerve is inflamed by exposure to external factors, including particulate matter. [70] And it causes air pollutants to promote the secretion of cytokine inflammatory factors, such as IL-1, and interferon-γ in the brain. Further research on specific mental disorders is needed in the future.

This study has some limitations. First, we did not consider the season effect that could affect mental disorders. However, some studies reported seasonal effects in the risk of mental disorders due to exposure to air pollution, but these results were not inconsistent. [47, 71] Further research on seasonal effects in the relationship between air pollution and mental disorders is needed. Second, there was a possibility of misclassification of exposure by measured monitoring data as a proxy for exposure. However, in this case, it is generally reported that *Berkson type error* occurs, and *this error* rather goes in the direction of reducing the association. [72] Third, we only use the outdoor air pollution exposure, not reflecting the actual exposure characteristics of an individual, which varies spending the time outside or doing activities. Fourth, we didn't take into account the additional costs (e.g., education costs) that may arise from mental illness, because of no available information. Several studies reported that ADHD and ASD were burdened with medical expenses, but additional costs such as special education costs were incurred because behavioral therapy, a non-drug treatment method, is generally combined with drug treatment. Fifth, there is a possibility that pharmacy costs are underestimated. Some drugs (like trazodone) for antidepressants have not been approved for those under the age of 19 in Korea because the clinical efficacy has not been evaluated sufficiently, but it was known to be prescribed at the judgment of off-the-label from the psychiatrist. According to the Texas children's medication algorithm project, the use of drugs is suggested step by step according to the patient's response, primarily recommending the use of a single drug. [73] Briefly, in the first stage, SSRI (Selective Serotonin Reuptake Inhibitor), is recommended in the second stage, and when the drug is not effective, another type of drug is used, or a combination of drugs is recommended. In addition, ADHD, ASD, and depression are generally accompanied by psychiatric diseases other than one symptom. Therefore, various drugs can be used depending on the patient. Therefore, it was calculated by assuming that the primary treatment reported in Korea was used first, and that the maximum dose was taken for one year.

The strengths of this study are as follows. This is the first study to evaluate the burden of major mental disorders for children and adolescents, vulnerable to particulate matter. In particular, we quantitatively estimated the burden of mental diseases, which accounted for a high proportion of children and adolescents. Second, most of the previous studies examined the association between short-term exposure to air pollution and mental disorder due to hospitalization of all ages. However, we evaluated both outpatient and inpatient. In particular, as shown in the results, it showed that the number of outpatient visits are much higher than that of inpatient visits in the major mental disorders (ADHD, ASD, depression) of children and adolescents. In addition, the economic burden of outpatient treatment is greater than the that of inpatient admission, unlike other diseases. Therefore, there is a possibility that burden of major mental disorders associated with short-term air pollution exposure may be underestimated in children and adolescents. Similarly, if all ages are included, more attention is paid to dementia and schizophrenia, which have a high prevalence in adults.

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VI. CONCLUSION

This study evaluated the medical institutions visits of major mental disorders due to short-term air pollution exposure among children and adolescents in nationwide except ozone. We found that it was associated with major mental disorders due to exposure to particulate matter, and among them, PM10 and PM2.5 could be attributable about 7~9% and 3 ~ 7%, respectively. In addition, we found that total medical costs and out-of-pocket costs attributable to particulate matter in ADHD and depression. To the best of our knowledge, it is the first study to calculate the medical costs and attributable burden of major mental disorders associated with air pollution exposure in children and adolescents. Therefore, the results of this study can be presented as a basis for lowering air quality standards.

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APPENDICES

Appendix Table 1. Total population (under age of 19) by regions, 2011-2019

Region	2011	2012	2013	2014	2015	2016	2017	2018	2019
Seoul	2040165	1972496	1904547	1838505	1769089	1695519	1623118	1545489	1482264
Busan	694822	672756	651430	630536	612730	592297	568776	547587	526561
Incheon	567466	551211	533850	515620	497705	481163	462799	444625	425510
Daegu	646204	636733	624197	610024	596288	581003	561488	543625	525651
Gwangju	380975	372523	363048	352827	340705	328561	315680	303164	290950
Daejeon	370050	363092	355910	344858	330013	317992	303223	289034	275008
Ulsan	281985	276157	269391	262920	256199	248633	239335	229903	221104
Gyonggi	2915316	2877725	2832378	2777854	2730973	2690625	2637136	2594752	2540452
Gangwon	329414	321237	312466	303490	294348	284782	273672	262724	253355
Chungcheongbuk	357043	349022	340628	331705	321947	313340	303032	293372	283642
Chungcheongnam	471440	447339	441430	433477	426450	419565	412335	402575	390093
Jeollabuk	422230	412149	401650	389766	377637	364993	350773	334788	319555
Jeollanam	410672	400209	389591	378153	368099	356630	342874	328745	314691
Gyongsangbuk	556768	542981	528851	513848	500721	486930	469847	452708	435932
Gyeongsangnam	768091	752576	735521	719151	702154	683138	664317	642539	619457
Jeju	144333	143025	141861	140865	140496	139999	138983	137438	134413

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Appendix Table 2. Annual average concentrations of air pollutants* during 2011-2019

Year	PM_{10} (μg/m^3)	$PM_{2.5}$ (μg/m^3)	NO_2 (ppm)	SO_2 (ppm)	O_3 (ppm)	CO (ppm)
2011	47.92±31.57	-	0.021±0.01	0.005±0.002	0.025±0.112	0.49±0.20
2012	43.21±20.20	-	0.020±0.01	0.005±0.003	0.027±0.011	0.50±0.19
2013	46.75±23.27	-	0.021±0.01	0.005±0.003	0.027±0.011	0.51±0.21
2014	46.64±24.97	-	0.021±0.01	0.005±0.002	0.028±0.013	0.50±0.19
2015	46.09±27.67	26.40±14.75	0.020±0.009	0.005±0.002	0.028±0.012	0.50±0.19
2016	44.76±21.45	25.50±12.28	0.020±0.009	0.004±0.002	0.029±0.012	0.48±0.15
2017	43.21±20.85	24.25±12.75	0.019±0.009	0.004±0.002	0.030±0.013	0.47±0.16
2018	40.57±21.73	22.68±13.54	0.018±0.010	0.004±0.002	0.029±0.012	0.45±0.16
2019	40.20±21.66	22.58±14.93	0.018±0.009	0.003±0.001	0.031±0.013	0.45±0.15

*Mean±Standard deviation

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Appendix Table 3. Pearson correlation coefficients between air pollutants and meteorological variables in Korea, during 2011-2019

	PM_{10}	$PM_{2.5}$	NO_2	SO_2	O_3	CO	Temperature	Humidity
PM_{10}	1							
$PM_{2.5}$	0.81*	1						
NO_2	0.46*	0.53*	1					
SO_2	0.43*	0.38*	0.53*	1				
O_3	0.11*	0.02*	-0.44*	-0.13*	1			
CO	0.54*	0.68*	0.70*	0.55*	-0.37*	1		
Temperature	-0.21*	-0.22*	-0.37*	-0.25*	0.39*	-0.48*	1	
Humidity	-0.24*	-0.08*	-0.20*	-0.19*	-0.14*	-0.07*	0.44*	1

*p-value< 0.05; significant

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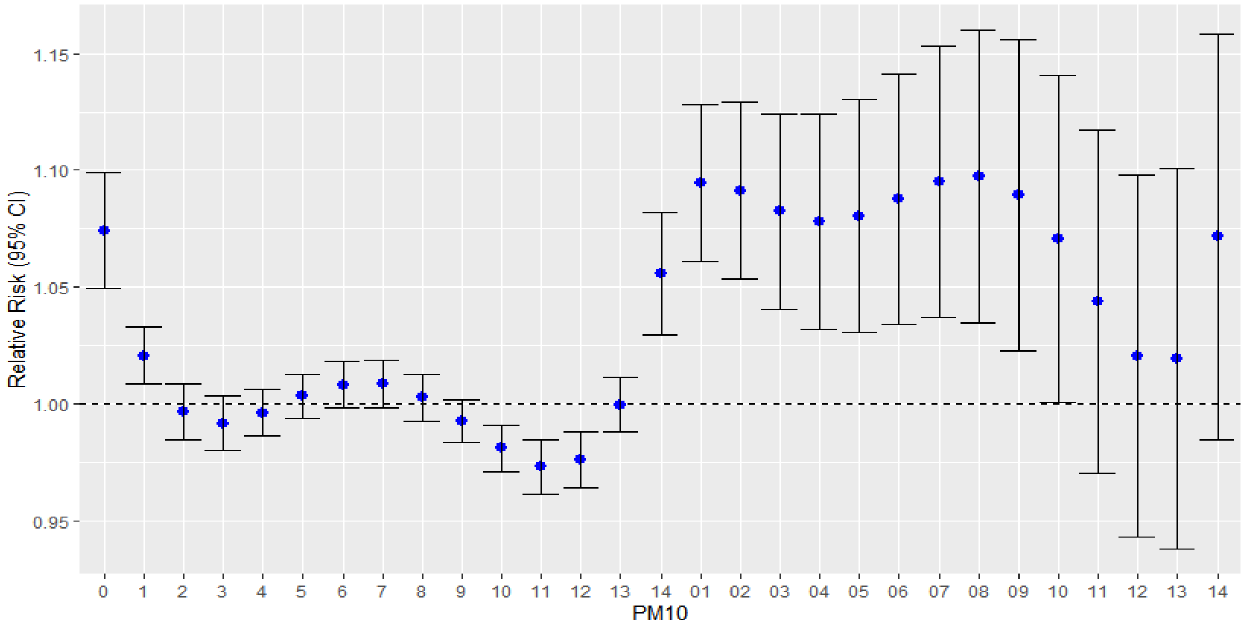

Appendix figure 1. Relative risk (95% Confidence Interval) of PM_{10} (per 10 μg/m^3) in the different lag model

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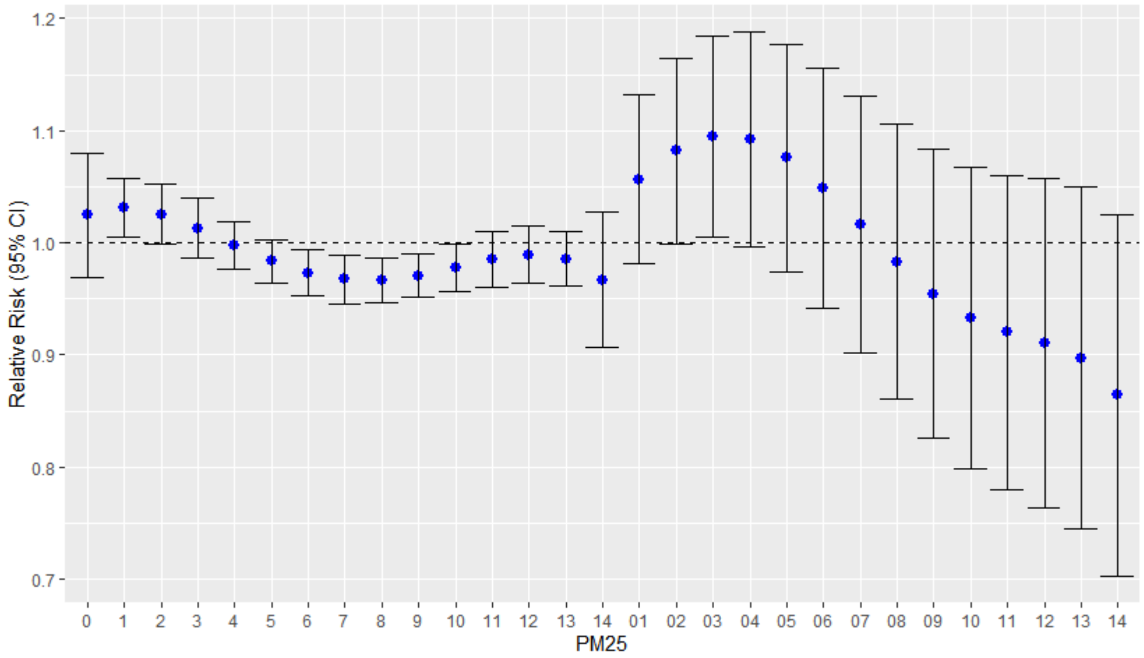

Appendix figure 2. Relative risk (95% Confidence Interval) of $PM_{2.5}$ (per 10 μg/m^3) in the different lag model

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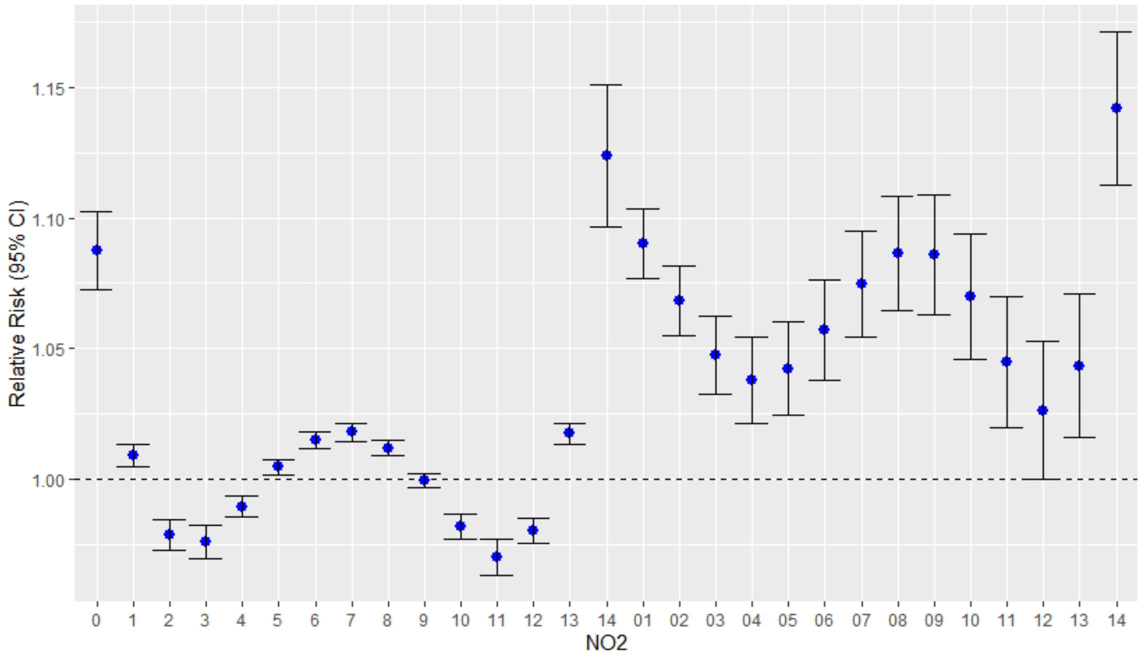

Appendix figure 3. Relative risk (95% Confidence Interval) of NO_2 (per 1ppb) in the different lag model

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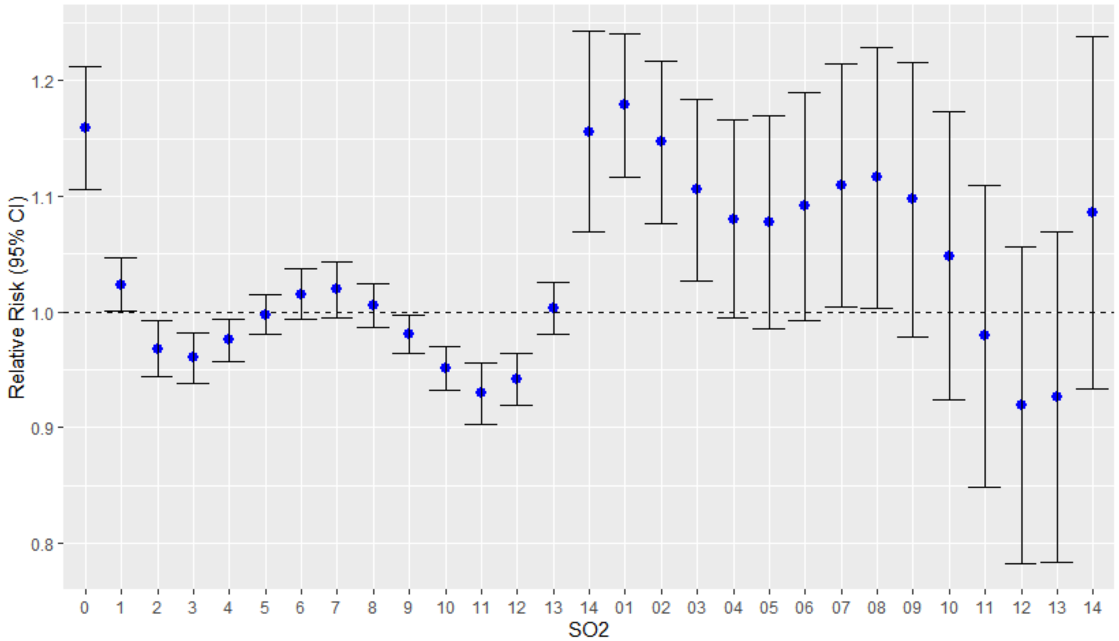

Appendix figure 4. Relative risk (95% Confidence Interval) of SO_2 (per 1ppb) in the different lag model

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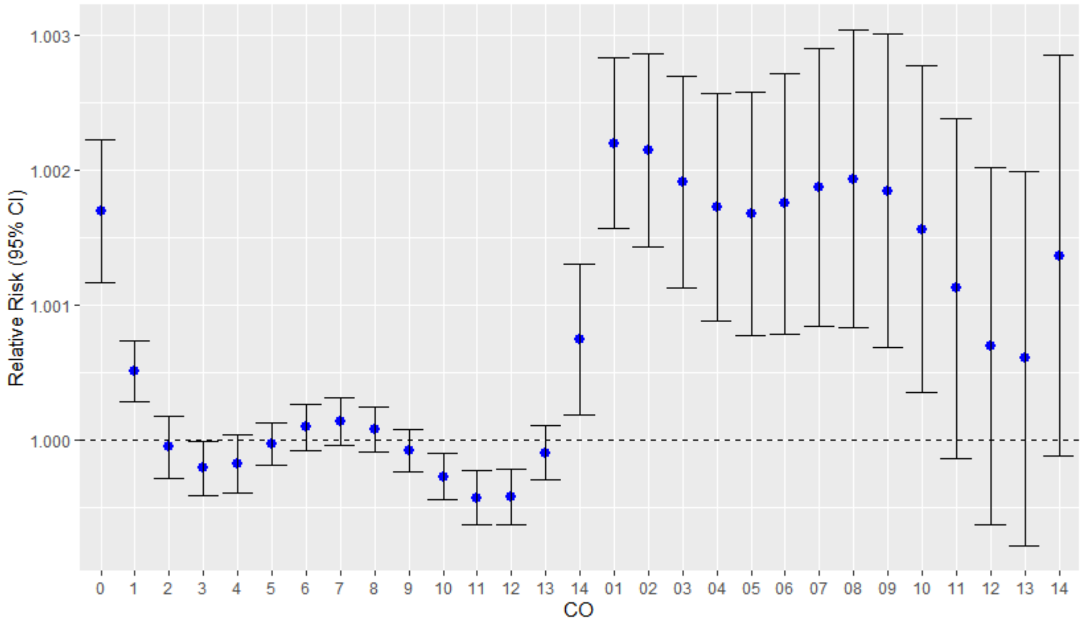

Appendix figure 5. Relative risk (95% Confidence Interval) of CO (per 1ppb) in the different lag model

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Appendix Table 4. Relative risks of medical institutions visit for major mental disorders for single-pollutant and two pollutant models.

	PM_{10}	**$PM_{2.5}$**	**NO_2**	**SO_2**	**O_3**	**CO**
Single pollutant	1.082* (1.040; 1.124)	1.094* (1.005; 1.184)	1.048* (1.033; 1.063)	1.106* (1.027; 1.184)	0.987 (0.974; 1.000)	1.0019* (1.0011; 1.0027)
+PM10	-	0.965 (0.863; 1.067)	1.034* (1.017; 1.052)	1.000 (0.910; 1.089)	1.006 (0.991; 1.020)	1.007 (0.9997; 1.0012)
+PM25	1.094* (1.043; 1.146)	-	1.045* (1.028; 1.061)	1.056 (0.967; 1.142)	1.009 (0.994; 1.024)	1.0016* (1.0005; 1.0027)
+NO2	0.914 (0.865; 0.963)	0.830 (0.736; 0.925)	-	0.675 (0.583; 0.767)	1.021* (1.009; 1.034)	0.995 (0.994; 0.996)
+SO2	1.052* (1.000; 1.104)	1.054 (0.962; 1.146)	1.041* (1.024; 1.059)	-	1.012 (0.997; 1.027)	1.0007 (0.9996; 1.0017)
+O3	1.130* (1.084; 1.176)	1.184* (1.092; 1.277)	1.029* (1.013; 1.045)	1.068 (0.984; 1.152)	-	1.0017* (1.0009; 1.0026)
+CO	1.040* (0.988; 1.091)	0.988 (0.891;1.086)	1.071* (1.051; 1.091)	0.984 (0.889; 1.078)	1.009 (0.995; 1.024)	-

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Appendix Table 5. Trends of the average duration (day) in attention-deficit hypertensive disorder by age group, sex during 2011-2019

	2011	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**
Total	170	176	183	185	186	192	197	199	201
Age group									
0~4	32	51	31	31	26	75	29	30	48
5~9	152	156	163	157	160	171	175	183	179
10~14	199	199	208	217	218	221	220	216	219
15~19	177	192	195	196	203	199	209	203	204
Sex									
Male	174	181	188	186	193	196	202	205	207
Female	152	151	159	181	161	178	178	178	180

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Appendix Table 6. Trends of the average duration (day) in autism spectrum disorders by age group, sex during 2011-2019

	2011	2012	2013	2014	2015	2016	2017	2018	2019
Total	161	163	161	161	157	164	158	161	168
Age group									
0~4	90	100	104	94	100	92	80	74	87
5~9	142	145	137	130	128	153	139	154	153
10~14	249	221	213	228	209	211	198	210	218
15~19	231	237	237	237	228	233	237	249	241
Sex									
Male	168	169	167	167	160	168	165	162	162
Female	133	136	139	139	143	149	131	155	164

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Appendix Table 7. Trends of the average duration (day) in depression by age group, sex during 2011-2019

	2011	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**
Total	142	132	132	123	123	127	128	126	132
Age group									
0~4	2	5	40	18	14	47	53	17	19
5~9	114	110	113	92	107	115	116	135	119
10~14	138	129	128	135	133	143	141	136	138
15~19	152	144	145	128	126	123	125	132	132
Sex									
Male	143	139	142	134	140	140	144	147	140
Female	140	122	118	109	101	109	107	117	123

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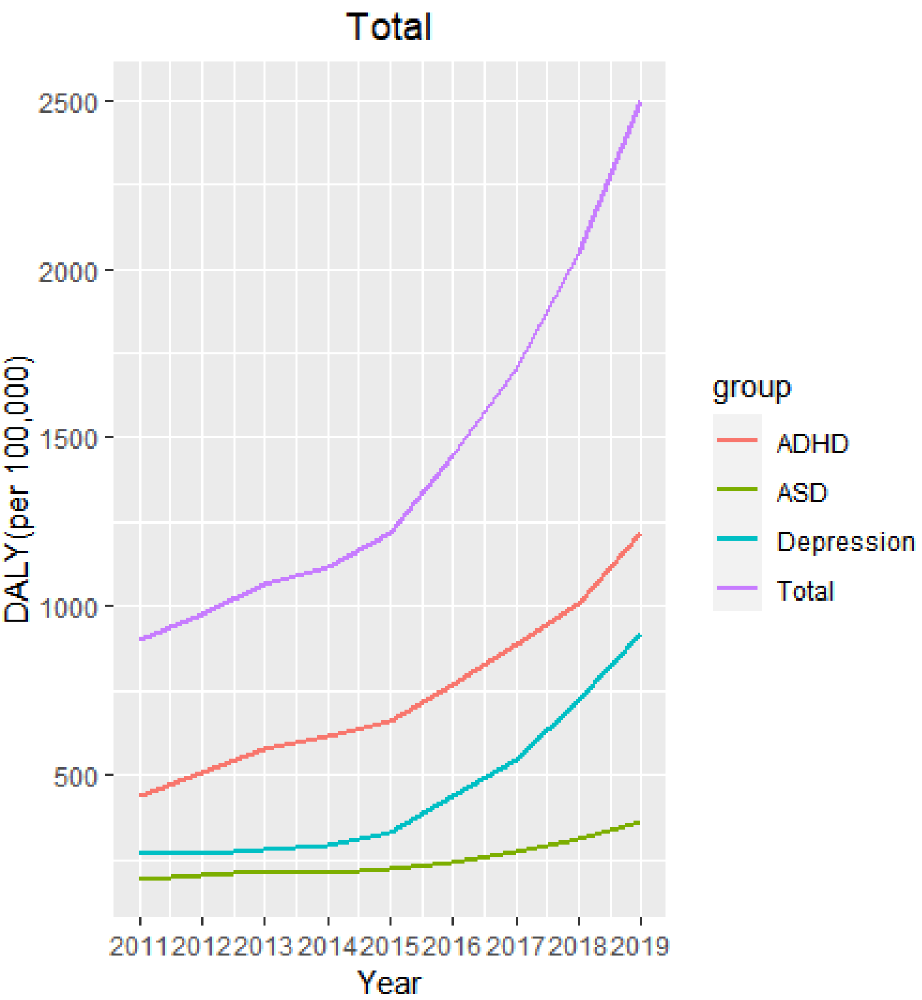

Appendix figure 6. Trends of disability-adjusted life years (total)

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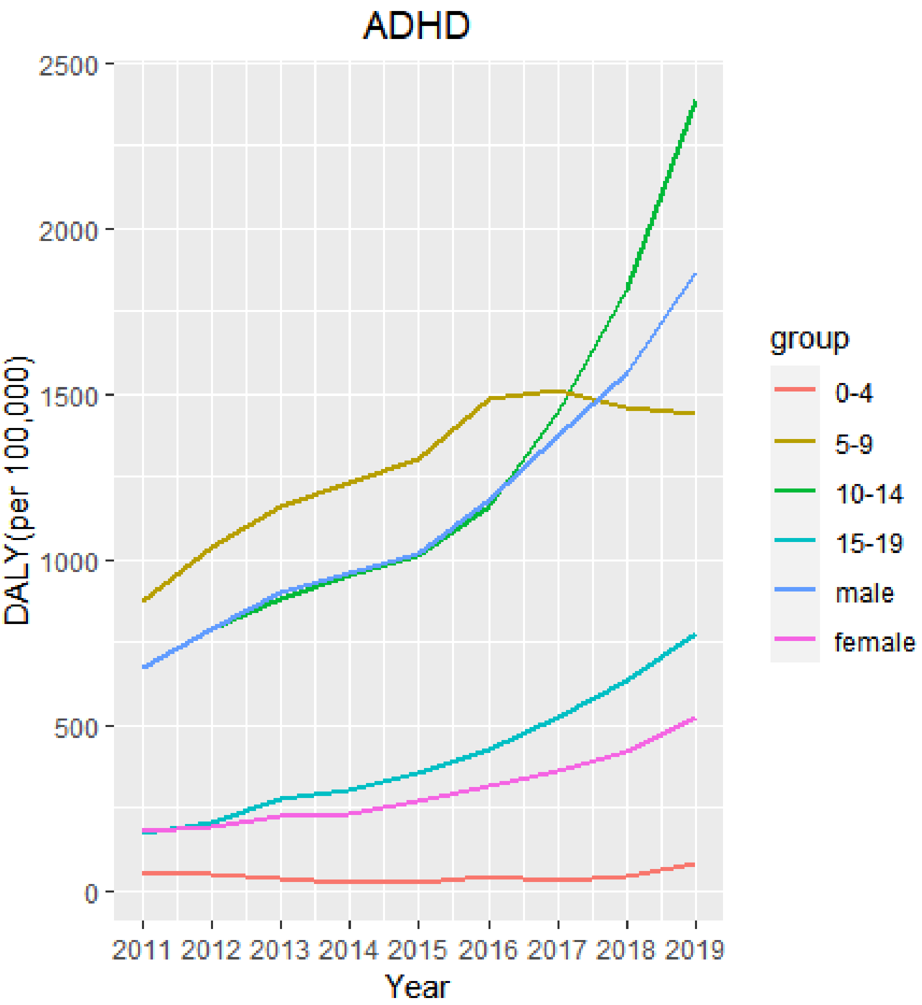

Appendix figure 7. Trends of disability-adjusted life years (ADHD)

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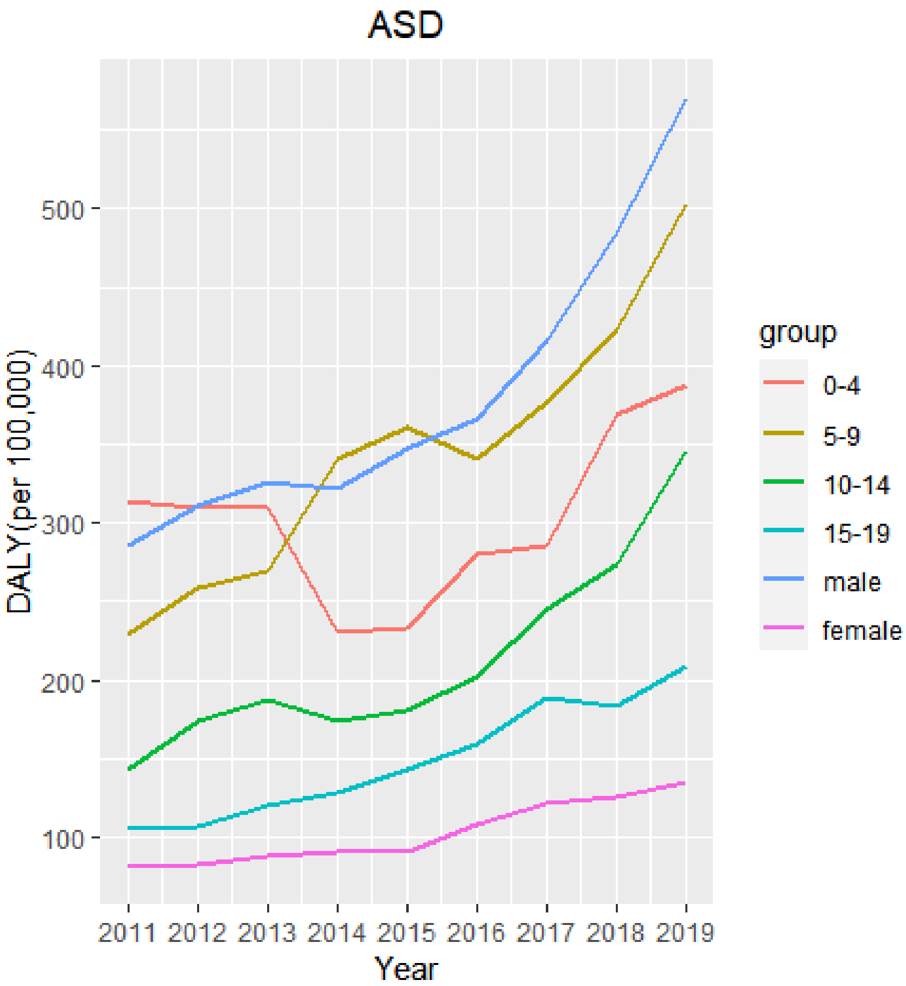

Appendix figure 8. Trends of disability-adjusted life years (ASD)

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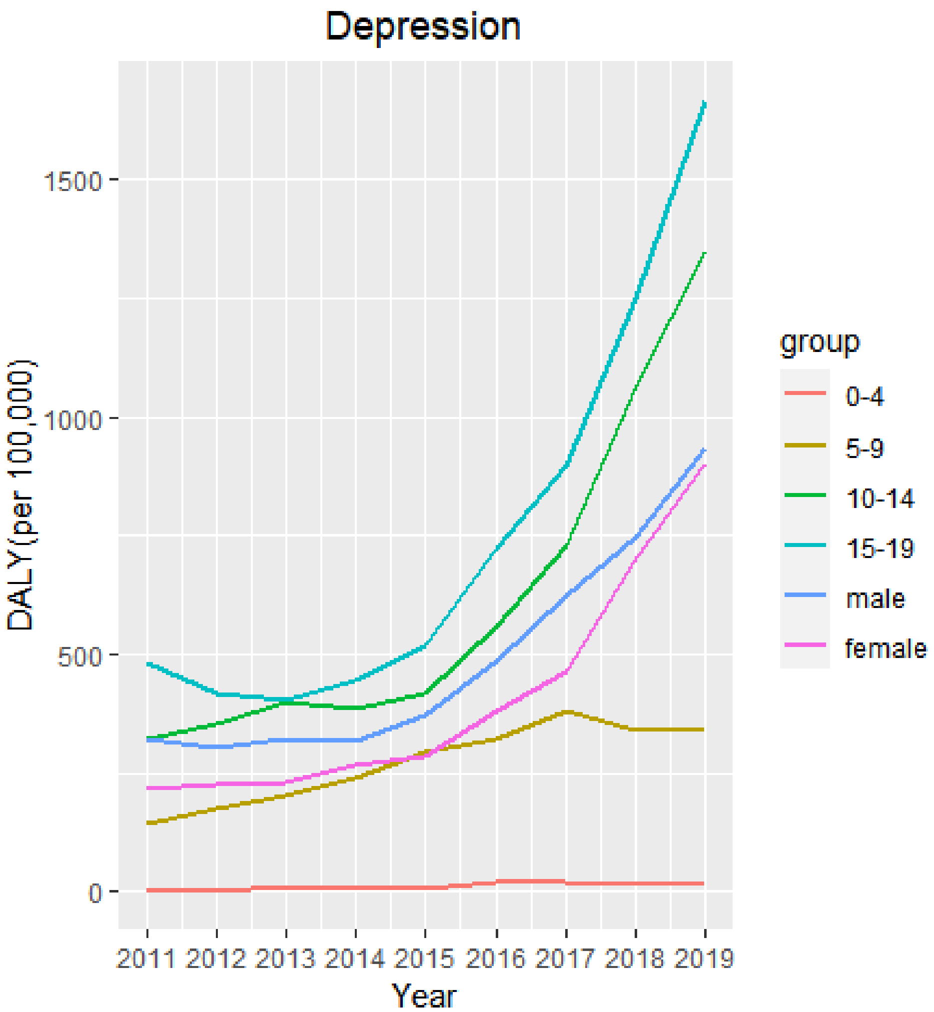

Appendix figure 9. Trends of disability-adjusted life years (depression)

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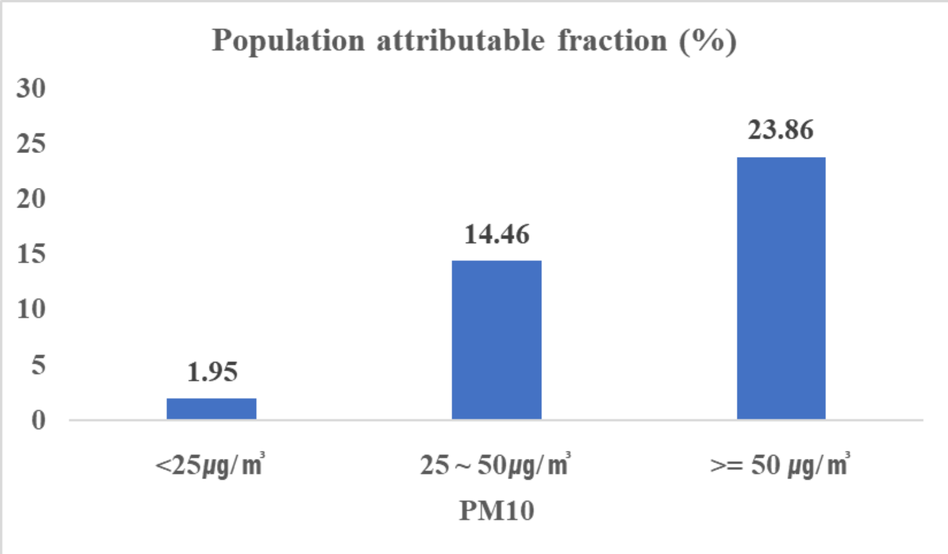

Appendix figure 10. Populatioin attributable fraction associated with PM10 with reference concentration (5.3 ㎍/㎥)

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ABSTRACT (IN KOREAN)

소아청소년에서 정신과적질환에 대한

미세먼지 노출의 기여위험도 및 의료비용 추정

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서론: 정신질환은 다른 만성질환에 비해 사망률이나 치사율이 낮은 반면, 장애로 인한 손실년수가 상당하다. 또한 ADHD, ASD, 우울증을 가진 개인뿐만 아니라 사회나 국가 차원의 비용이 상당하다. 최근 대기오염 노출과 정신과질환 간의 연관성을 보고한 역학연구들이 종종 있으나, 소아청소년의 대기오염 감소로 인한 정신질환 부담과 비용 감소를 평가한 연구는 아직 거의 없다.

방법: 2011 년부터 2019 년까지 국민건강보험공단데이터를 사용하여 소아청소년의 대기오염에 대한 단기 노출과 주요 정신장애(ADHD, ASD, 우울증) 간의 연관성을 평가하기 위해 시계열 분석을 사용했다. 또한 정신질환 부담에 기인하는 대기오염 노출(DALY*PAF)을 추정하였다. 각 정신질환의 총 비용은 COI 방법으로 계산한 다음 비용에 기여분위수(AN)를 곱하여 귀책 비용(AC)을 추정하였다.

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결과: PM_{10}(10μg/m3 증가당), $PM_{2.5}$(10μg/m3 증가당), NO2(1ppb 증가당), SO2(1ppb 증가당), CO(1ppb 증가당)에 대한 노출로 인한 주요 정신질환-병원 이용률의 상대적 위험은 각각 1.082, 1.094, 1.106, 1.0019 로 나타났다. 주요 정신과질환에서 미세먼지 노출로 인한 기여분율은 7.23 ~ 8.97% (PM_{10}), 3.16 ~ 6.87% ($PM_{2.5}$)로 나타났으며, 주요 정신과질환 부담에서 미세먼지 노출이 기인하는 (DALY*PAF)는 연구기간동안 점진적인 증가를 보였다. ADHD 와 우울증은 미세먼지로 인한 총 의료비와 현금지급 비용 모두 증가한 것으로 나타났다.

결론: 국내 소아청소년의 대기오염 노출로 인한 주요 정신질환의 의료이용에 관한 직접의료비 및 기여부담을 평가하였다. 이 결과는, 소아청소년의 대기오염 노출과 관련된 주요 정신질환의 의료 비용과 귀책 부담을 계산한 연구로, 대기질 기준을 낮추는 근거로 제시될 수 있을 것으로 사료된다.

핵심되는 말: 대기오염, 소아청소년, 정신과질환, 장애보정년수, 비용