

Association between air pollution and chronic rhinosinusitis: a nested case-control study using meteorological data and national health screening cohort data*

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Abstract

Background: Inconsistent results about the effect of air pollution on chronic rhinosinusitis (CRS) have been reported. This study aimed to evaluate the impact of meteorological conditions/air pollution on the prevalence of CRS in adult Koreans.

Methodology: The data from the Korean National Health Insurance Service-Health Screening Cohort from 2002 through 2015 were used. A CRS group (defined as ICD-10 codes J32, n=6159) was matched with a control group (n=24,636) in 1:4 ratios by age, sex, income, and region of residence. The meteorological conditions and air pollution data included the daily mean, highest, and lowest temperature (°C), daily temperature range (°C), relative humidity (%), ambient atmospheric pressure (hPa), sunshine duration (hr), and the rainfall (mm), SO₂ (ppm), NO₂ (ppm), O₃ (ppm), CO (ppm), and PM10 (µg/m³) levels before the CRS diagnosis. Crude and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for CRS were analyzed using logistic regression analyses.

Results: When the NO₂ level increased by 0.1 ppm, the odds for CRS increased 5.40 times, and when the CO level increased by 1 ppm and PM10 increased by 10 µg/m³, the odds for CRS decreased 0.75 times and 0.93 times, respectively. Other meteorological conditions, such as the mean/highest/lowest temperature, temperature range, rainfall and other air pollution, such as SO₂ and O₃, were not statistically significant. NO₂ for 90 days before the index date increased the risk of CRS in all subgroups, except for the nasal polyp and older age subgroups.

Conclusion: CRS is related to high concentrations of NO₂.

Key words: sinusitis, air pollution, meteorological concepts, nitrogen dioxide, population surveillance

Introduction

Air pollution is as a complex mixture whose effects are attributed to nitrogen dioxide (NO₂), sulfur dioxide (SO₂), carbon monoxide (CO), particulate matter (PM), or ozone (O₃). NO₂ is a common unwanted pollutant derived from the combustion of fossil fuels in stationary sources and motor vehicles; SO₂ is com-

monly generated from the burning of coal; CO is a gas formed during the incomplete combustion of carbon-containing fuels; and PM10 particles are derived from road dust, materials from vehicle brakes and tires, and construction activities such as crushing⁽¹⁾. NO₂ is toxic by itself, and its concentrations often correlate with those of other air pollutants. Nitrogen oxides (NO_x)

and volatile organic compounds (VOCs) are the main precursor pollutants for O_3 formation⁽²⁾.

Air pollution is associated with human health. Several studies have reported that air pollution leads to mortality and morbidity worldwide⁽³⁾. According to the Global Burden of Disease Study, ambient air pollution accounted for 11.3% of female deaths and 12.2% of male deaths globally and was the 4th leading contributor to attributable disability-adjusted life years (DALYs) in 2019⁽⁴⁾. Recently, a systematic review of epidemiological studies conducted in Korea examining the health effects of exposure to air pollution was reported⁽⁵⁾. A time series study showed that the mortality rate increases by 0.51% in the summer and 0.45% in the fall for each $10 \mu\text{g}/\text{m}^3$ increase in PM10 in South Korea⁽⁶⁾. Our previous studies have shown that air pollution is related to several diseases⁽⁷⁻¹⁰⁾.

Furthermore, climate plays important roles in affecting air quality because emission, transport, dilution, chemical transformation, and deposition of air pollutants can be influenced by meteorological variables such as temperature, humidity, wind speed and direction, and mixing height⁽²⁾. Several studies have indicated that climate change affects air pollution concentrations^(11,12). Higher temperatures promote chemical reactions leading to ozone and secondary particle formation⁽¹¹⁾. The concentration of air pollutants is negatively correlated with relative humidity but positively correlated with atmospheric pressure⁽¹³⁾. However, the levels of impact depend on the type of pollutants and vary across regions. Therefore, when analyzing the effect of air pollution on human health, it is necessary to consider not only air pollution but also meteorological conditions.

Studies have shown significant associations between air pollution and respiratory diseases, such chronic obstructive pulmonary disease⁽¹⁴⁾, asthma⁽¹⁵⁾, and allergic rhinitis⁽¹⁶⁾. Chronic rhinosinusitis (CRS) is a chronic inflammatory respiratory disease with a multifactorial etiology that includes genetic factors, comorbid medical diseases, and environmental factors⁽¹⁷⁾. Environmental factors known to cause CRS include air pollution, inhaled allergens, smoking, and infection^(18,19). Some recent studies have reported an association between air pollution and CRS, but the results are inconsistent. A cross-sectional study using the National Health Interview Survey in U.S. from 1997 to 2006 found that the standardized regression coefficients were 0.013 for PM, 0.026 for SO_2 , 0.026 for NO_2 , and 0.027 for CO, indicating that the prevalence of sinusitis is correlated with air quality⁽²⁰⁾. On the other hand, in a previous study in Germany, there was no correlation between the total CRS patient rates and air pollution (SO_2 , NO_2 , and total suspended PM) with $r = -0.025$, but there was a positive correlation between these variables only in the districts with above average air pollution levels⁽²¹⁾. A study conducted in Pittsburgh showed that a 1.89-fold increased risk in the proportion of patients with CRS without nasal polyps (CRSsNP) who required further surgery ($P=0.015$) for each unit increase

in PM2.5, but this association was not identified in patients with CRS with nasal polyps (CRSwNP) ($P=0.445$)⁽²²⁾.

The aim of this study was to evaluate the impact of meteorological conditions/air pollution on the prevalence of CRS with and without nasal polyps in adult Koreans. A better understanding of the relationship between air pollution and CRS will contribute to disease prevention.

Materials and methods

Ethics

The Ethics Committee of Hallym University (2019-10-022) permitted this study. Written informed consent was waived by the Institutional Review Board. All analyses adhered to the guidelines and regulations of the Ethics Committee of Hallym University.

Study population and participant selection

We have described the Korean National Health Insurance Service-Health Screening Cohort (NHIS-HEALS) and meteorological and air pollution data in the supplement (Supplementary File 1) and in our previous studies^(8,9,23).

Participants who were diagnosed with CRS were selected from 514,866 patients with 615,488,428 medical claim codes ($n = 8560$). To select CRS participants who were diagnosed first, we excluded CRS participants who were diagnosed from 2002 to 2003 ($n = 2395$). We included a control group of individuals who were not defined as having CRS from 2002 through 2015 among the mother population ($n = 506,306$). Control participants were removed if they had died before 2004 or had no records since 2004 ($n = 1518$). In addition, control participants were excluded if they were treated with J32 (chronic sinusitis) using ICD-10 codes once ($n = 123,135$). The CRS group was matched with the control group in 1:4 ratios by age, sex, income, and region of residence. Selection bias was minimized by selecting the control groups with random number order. For the CRS group, the index date was defined as the timepoint at which the patients were diagnosed with CRS. A random day during the 1-year period before the index date of the matched CRS group was defined as the index date for the control group. During the matching process, 357,017 control participants and 6 CRS participants were excluded. Finally, 6159 CRS participants were 1:4 matched with 24,636 control participants. Among the CRS participants, 2956 were treated for nasal polyps (ICD-10 codes: J33, CRSwNP), and the other 3203 were not (CRSsNP) (Figure 1).

We analyzed and compared meteorological data and air pollution data over a moving average of 1 month (30 days), 3 months (90 days), 6 months (180 days), and 1 year (365 days) before the index date between the CRS and control groups, the CRSwNP and control groups, and the CRSsNP and control groups, respectively.

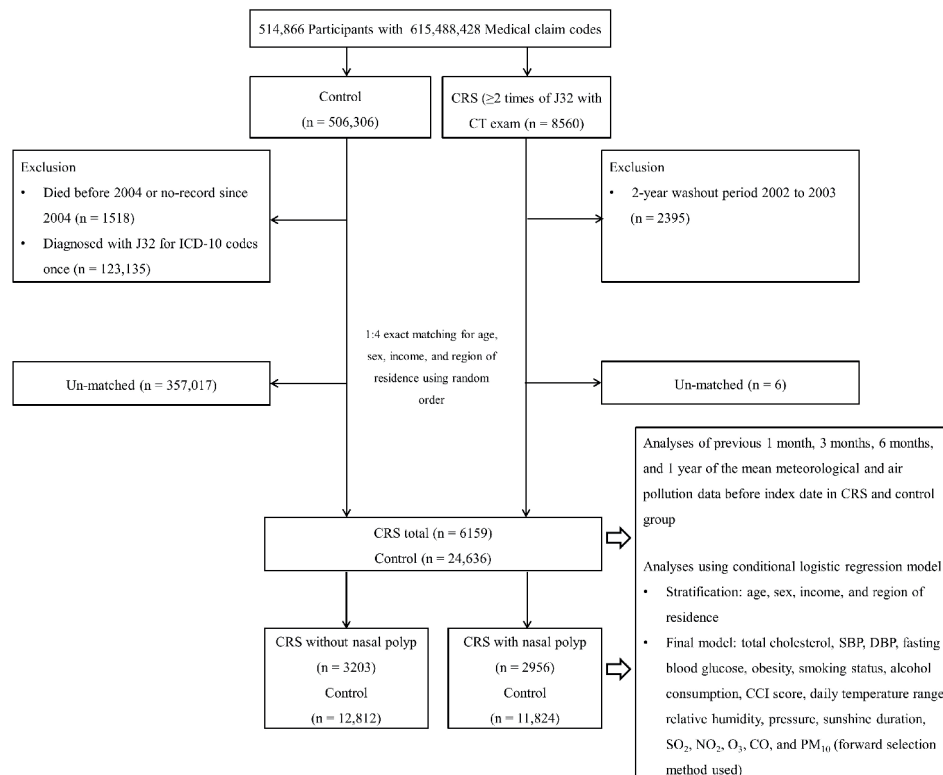


Figure 1. A schematic illustration of the participant selection process. Among 514,866 participants, 6159 of the CRS participants were matched with 24,636 of the control participants for age, sex, income, and region of residence. Then, the CRS and control groups were linked with the meteorological conditions and air pollution data before the index date.

Variables

Independent variable

Daily mean temperature (°C), daily highest temperature (°C), daily lowest temperature (°C), daily temperature range (°C), relative humidity (%), ambient atmospheric pressure (hPa), sunshine duration (hr), rainfall (mm), SO₂ (ppm), NO₂ (ppm), O₃ (ppm), CO (ppm), and PM₁₀ (µg/m³) for moving averages of 1 month (30 days), 3 months (90 days), 6 months (180 days), and 1 year (365 days) before the index date were defined as the independent variables in our previous studies^(8,9).

Covariate

Age groups were divided into 5-year intervals: 40-44, 45-49, 50-54..., and 85+ years old (10 age groups). Income groups were classified into 5 classes (class 1 [lowest income]-5 [highest income]). The region of residence was grouped into urban and rural areas following our previous study⁽²⁴⁾. Tobacco smoking, alcohol consumption, and obesity using BMI (body mass index, kg/m²)⁽²⁵⁾ were categorized in the same way as in our study⁽²⁶⁾. Systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting blood glucose, and total cholesterol were measured. The Charlson Comorbidity Index (CCI) has been widely used to measure the disease burden using 17 comorbidities as the continuous variable (0 [no comorbidities] through 29 [multiple

comorbidities])⁽²⁷⁾.

Dependent variable

CRS was defined if the participants were treated with ICD-10 codes J32 (chronic sinusitis) ≥ 2 times and underwent head and neck CT evaluations (Claim codes: HA401-HA416, HA441-HA443, HA451-HA453, HA461-HA463, or HA471-HA473). Among the total CRS participants, CRSwNP was defined as those treated with ICD-10 codes J33 (nasal polyp) and CRSsNP as the remaining participants.

Statistical analyses

The general characteristics between the CRS and control group were compared using chi-squared test. The mean meteorological and air pollution data for 3 months (90 days) before the index date were compared using independent T-tests. Meteorological and air pollution data were compared with CRS total group, CRSwNP group, CRSsNP group and their respective control groups. To analyze the odds ratio (OR) with 95% confidence intervals (CI) of meteorological and air pollution data, crude (simple model; Tables S1, S2, and S3), model 1 (adjusted for total cholesterol, SBP, DBP, fasting blood glucose, obesity, smoking status, alcohol consumption, and CCI score; Tables S1, S2, and S3), and model 2 (adjusted for model 1 plus

Table 1. General characteristics of the participants.

Characteristics	Total participants		
	CRS total	Control	P-value
Age (years, n, %)			
40-44	233 (3.8)	932 (3.8)	
45-49	972 (15.8)	3,888 (15.8)	
50-54	1,338 (21.7)	5,352 (21.7)	
55-59	1,302 (21.1)	5,208 (21.1)	
60-64	983 (16.0)	3,932 (16.0)	1.000
65-69	713 (11.6)	2,852 (11.6)	
70-74	387 (6.3)	1,548 (6.3)	
75-79	170 (2.8)	680 (2.8)	
80-84	50 (0.8)	200 (0.8)	
≥ 85	11 (0.2)	44 (0.2)	
Sex (n, %)			
Male	3,784 (61.4)	15,136 (61.4)	1.000
Female	2,375 (38.6)	9,500 (38.6)	
Income (n, %)			
1 (lowest)	755 (12.3)	3,020 (12.3)	
2	727 (11.8)	2,908 (11.8)	
3	932 (15.1)	3,728 (15.1)	1.000
4	1,347 (21.9)	5,388 (21.9)	
5 (highest)	2,398 (38.9)	9,592 (38.9)	
Region of residence (n, %)			
Urban	2,851 (46.3)	11,404 (46.3)	1.000
Rural	3,308 (53.7)	13,232 (53.7)	
Obesity (BMI, kg/m², n, %)			
< 18.5 (underweight)	104 (1.7)	541 (2.2)	
≥ 18.5 to < 23 (normal)	2,001 (32.5)	8,517 (34.6)	
≥ 23 to < 25 (overweight)	1,830 (29.7)	6,860 (27.9)	0.001 ^a
≥ 25 to < 30 (obese I)	2,049 (33.3)	7,995 (32.5)	
≥ 30 (obese II)	175 (2.8)	723 (2.9)	
Smoking status (n, %)			
Nonsmoker	4,047 (65.7)	16,086 (65.3)	
Past smoker	902 (14.7)	2,996 (12.2)	<0.001 ^a
Current smoker	1,210 (19.7)	5,554 (22.5)	
Alcohol consumption (n, %)			
< 1 time a week	4,031 (65.5)	16,335 (66.3)	0.204
≥ 1 time a week	2,128 (34.6)	8,301 (33.7)	
Charlson comorbidity index (n, %)			
0	3,982 (64.7)	17,834 (72.4)	
1	1,007 (16.4)	3,066 (12.5)	
2	556 (9.0)	1,733 (7.0)	<0.001 ^a
3	272 (4.4)	815 (3.3)	
≥ 4	342 (5.6)	1,188 (4.8)	
Total cholesterol (mg/dL, mean, SD)	197.1 (37.2)	199.0 (37.6)	0.001 ^a
SBP (mmHg, mean, SD)	125.4 (16.1)	126.7 (16.9)	<0.001 ^a
DBP (mmHg, mean, SD)	78.4 (10.6)	79.0 (10.9)	<0.001 ^a
Fasting blood glucose (mg/dL, mean, SD)	99.5 (31.8)	100.6 (32.1)	0.015 ^a
Meteorological and air pollution data (mean, SD)			
Mean temperature for 90 days (°C)	11.6 (8.5)	12.9 (8.5)	<0.001 ^a
Highest temperature for 90 days (°C)	16.8 (8.4)	18.0 (8.3)	<0.001 ^a
Lowest temperature for 90 days (°C)	7.2 (8.9)	8.5 (8.9)	<0.001 ^a
Temperature range for 90 days (°C)	9.6 (1.8)	9.5 (1.8)	0.005 ^a
Relative humidity for 90 days (%)	64.4 (8.6)	65.4 (8.8)	<0.001 ^a
Ambient atmospheric pressure for 90 days (hPa)	1006.8 (7.1)	1006.1 (7.1)	<0.001 ^a
Sunshine duration for 90 days (hr)	5.9 (0.9)	5.9 (0.9)	<0.001 ^a
Rainfall for 90 days (mm)	8.2 (2.7)	8.6 (2.9)	<0.001 ^a
SO ₂ for 90 days (ppb)	5.5 (1.7)	5.4 (1.7)	<0.001 ^a
NO ₂ for 90 days (ppb)	24.9 (9.8)	24.1 (9.6)	<0.001 ^a
O ₃ for 90 days (ppb)	22.6 (8.1)	23.0 (7.9)	0.001 ^a
CO for 90 days (ppb)	559.8 (144.7)	552.7 (143.6)	0.001 ^a
PM10 for 90 days (µg/m ³)	54.3 (12.4)	53.7 (12.3)	0.002 ^a

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; ppb, parts per billion; SD, standard deviation. ^a Chi-square test or independent T-test. Significance at P < 0.05.

daily temperature range, relative humidity, pressure, sunshine duration, SO₂, NO₂, O₃, CO, and PM10 using the forward selection method) were calculated using conditional logistic regression. In these analyses, age, sex, income, and region of residence were stratified. In the analyses of 30 days, 90 days, 180 days, and 365 days of exposure, we selected 90 days as the main term. The

results of other days of exposure are displayed in supplemental files (Tables S4, S5, and S6).

For the subgroup analyses in the CRS total group, we divided the participants by age (< 60 years old and ≥ 60 years old), sex (males and females), income (low and high income), and region of residence (urban and rural). The results of subgroup analyses

Table 2. Adjusted odds ratios (95% confidence interval) of the meteorological and air pollution matter (mean of 90 days before the index date) for CRS total/with nasal polyp/without nasal polyp.

Characteristics	Adjusted odds ratio (95% confidence interval)					
	CRS total		CRS with nasal polyp		CRS without nasal polyp	
	Final model ^{b, c}	P-value	Final model ^{b, c}	P-value	Final model ^{b, c}	P-value
Mean temperature for 90 days (°C)						
Highest temperature for 90 days (°C)						
Lowest temperature for 90 days (°C)						
Temperature range for 90 days (°C)	0.97 (0.94-0.99)	0.018 ^a				
Relative humidity for 90 days (%)	0.99 (0.98-0.99)	<0.001 ^a	0.99 (0.98-1.00)	0.001 ^a	0.99 (0.98-1.00)	0.002 ^a
Ambient atmospheric pressure for 90 days (hPa)	1.01 (1.00-1.01)	<0.001 ^a			1.01 (1.01-1.02)	0.001 ^a
Sunshine duration for 90 days (hr)	1.09 (1.04-1.14)	<0.001 ^a	1.11 (1.04-1.18)	0.002 ^a		
Rainfall for 90 days (mm)						
SO ₂ for 90 days (0.01 ppm)						
NO ₂ for 90 days (0.1 ppm)	5.40 (3.28-8.89)	<0.001 ^a			13.39 (6.17-29.09)	<0.001 ^a
O ₃ for 90 days (0.01 ppm)			0.80 (0.75-0.87)	<0.001 ^a	1.16 (1.07-1.25)	<0.001 ^a
CO for 90 days (ppm)	0.75 (0.57-0.99)	0.041 ^a	0.50 (0.34-0.74)	0.001 ^a		
PM10 for 90 days (10 µg/m ³)	0.93 (0.90-0.97)	<0.001 ^a			0.92 (0.88-0.96)	<0.001 ^a

CCI, Charlson comorbidity index; CRS, chronic rhinosinusitis; SBP, systolic blood pressure; DBP, diastolic blood pressure. ^a Conditional logistic regression model, Significance at $P < 0.05$. ^b Stratified model for age, sex, income, and region of residence. ^c A final model was adjusted for total cholesterol, SBP, DBP, fasting blood glucose, obesity, smoking status, alcohol consumption, CCI score, temperature range, relative humidity, ambient atmospheric pressure, sunshine duration, SO₂, NO₂, O₃, CO, and PM10 using the forward selection method.

regarding other days of exposure are displayed in the supplemental files (Tables S7, S8, and S9).

Two-tailed analyses were performed, and significance was defined as P values less than 0.05. SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) was used for statistical analyses.

Results

The general characteristics of the participants are presented in Table 1. Age, sex, income, and region of residence were exactly matched between the CRS and control groups. All the mean meteorological and air pollution data (mean, highest, and lowest temperature, temperature range, relative humidity, ambient atmospheric pressure, sunshine duration, rainfall, SO₂, NO₂, O₃, CO, and PM10) for 90 days before the index date showed significant differences between the CRS and control groups (all $P < 0.05$). The adjusted odds ratios (aORs) for CRS were 0.97 in the temperature range (95% CI=0.94–0.99, $P=0.018$), 0.99 in relative humidity (95% CI=0.98–0.99, $P<0.001$), 1.01 in ambient atmospheric pressure (95% CI=1.00–1.01, $P<0.001$), and 1.09 in sunshine duration (95% CI=1.04–1.14, $P<0.001$) during the 90 days before the index date (Table 2). When the NO₂ level increased by 0.1

ppm, the odds for CRS increased 5.40 times (95% CI=3.28–8.89, $P<0.001$) and when the CO level increased by 1 ppm and PM10 increased by 10 µg/m³, the odds for CRS decreased 0.75 times (95% CI=0.57–0.99, $P=0.041$) and 0.93 times (95% CI=0.90–0.97, $P<0.001$), respectively (Table 2). Mean, highest, and lowest temperatures, rainfall, SO₂, and O₃ did not show a significant difference.

Subgroup analyses according to the presence of nasal polyps are shown in Table 2. In the CRSwNP group, there was a significant positive association with sunshine duration for 90 days (aOR=1.11, 95% CI=1.04–1.18, $P=0.002$) and a negative association with relative humidity (aOR=0.99 95% CI=0.98–1.00, $P=0.001$), O₃ (aOR=0.80, 95% CI=0.75–0.87, $P<0.001$) and CO (aOR=0.50, 95% CI=0.34–0.74, $P=0.001$). In the CRSsNP group, there was a significant positive association with ambient atmospheric pressure (aOR=1.01, 95% CI=1.01–1.02, $P=0.001$), NO₂ (aOR=13.39, 95% CI=6.17–29.09, $P<0.001$), O₃ (aOR=1.16, 95% CI=1.07–1.25, $P<0.001$) and a significant negative association with relative humidity (aOR=0.99, 95% CI=0.98–1.00, $P=0.002$) and PM10 (aOR=0.92, 95% CI=0.88–0.96, $P<0.001$).

Figure 2 and Table S10 show the results of subgroup analyses

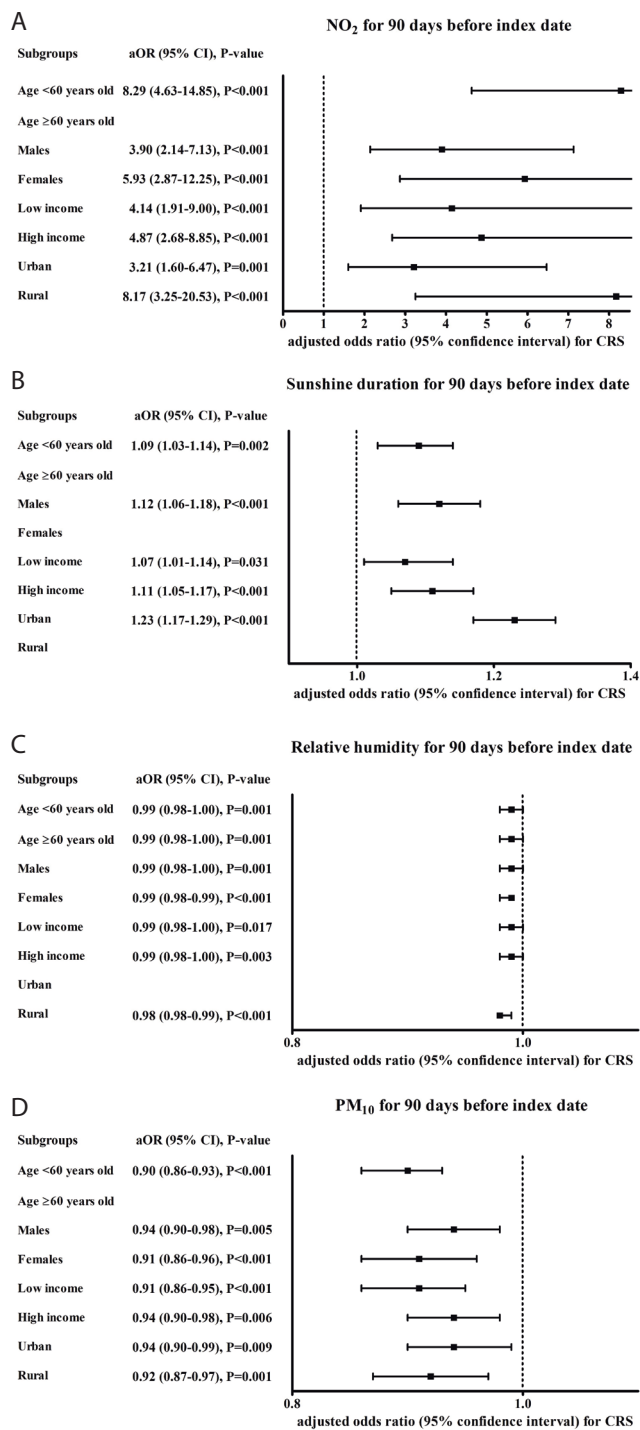


Figure 2. Subgroup analyses according to age, sex, income, and region of residence. Adjusted odds ratios (95% confidence interval) of the meteorological and air pollution (mean of 90 days before the index date) for CRS group compared with the control group.

according to age, sex, income, and region of residence. NO₂ for 90 days before the index date increased the risk of CRS in all subgroups, except the older age subgroup. Sunshine duration for 90 days before the index date increased the risk of CRS in the younger age, male sex, low income, high income, and urban

subgroups. Relative humidity for 90 days before the index date decreased the risk of CRS in all subgroups, except in urban areas. PM₁₀ for 90 days before the index date also decreased the risk of CRS in all subgroups, except in the older age subgroup.

Discussion

This study showed a positive association for NO₂ in the CRS total and CRSsNP groups. All age, sex, income, and region of residence subgroups (except for those 60 years or older) showed consistent findings for NO₂. Since the prevalence of CRS in the older age group was lower than that in the younger age group, the statistical power may not have reached the significance. Relative humidity for 90 days was negatively associated with CRS regardless of the presence of nasal polyps. However, other meteorological conditions, such as the mean/highest/lowest temperatures, temperature range, ambient atmospheric pressure, sunshine duration, rainfall and other air pollution factors, such as NO₂, O₃, CO, and PM₁₀, showed inconsistent results according to the included variables.

We found a positive association between NO₂ and CRS in the fully adjusted model including other air pollutants. Consistent with this result, a cross-sectional study using the National Health Interview Survey 1997–2006 reported that NO₂ levels are correlated with the prevalence of sinusitis (standardized B=0.026, P<0.001)⁽²⁰⁾. These results suggest that NO₂ has a more independent effect on CRS. In this study, there was a significant positive association between CRS and SO₂/CO/PM₁₀ in model 1 (OR=1.64 of SO₂; OR=1.45 of CO; OR=1.04 of PM₁₀; Table S1), but their relationship was changed to a negative correlation or a null value after controlling for other air pollutants (OR=a null value of SO₂; OR=0.75 of CO; OR=0.93 of PM₁₀). A previous study in China showed that the effects of SO₂ and CO on CRS decreased and became nonsignificant when adjusting for NO₂, supporting that NO₂ plays a more independent effect on CRS outpatient cases⁽²⁸⁾. Nevertheless, this significant association between NO₂ and CRS was not seen in only the CRSwNP group. Consistent with our results, a previous study in U.S. also reported that disease and symptom severity were significantly influenced by air pollutant levels only in CRSsNP patients⁽²²⁾. Thus, air pollutants may play a role in CRSsNP, highlighting the role of environmental factors in differential disease expression. However, further investigations are required to address the different roles of air pollution in disease phenotypes.

Potential risk factors for CRS have included anatomical factors, mucociliary impairment, osteitis⁽²⁹⁾, biofilms, superantigen effects, immune dysfunctions, impaired epithelial barrier⁽³⁰⁾, genetic factors⁽³¹⁾, and environmental factors⁽³²⁾. Environmental factors play a crucial role in the pathogenesis of various airway diseases because airway diseases including CRS are associated with the response of airway epithelial cells to the exposure of inhaled allergens, irritants, viruses and bacteria, and air pollu-

tants⁽³³⁾. Recently, the role of the microbiome in the pathogenesis of CRS has shown increased interest. Imbalance or dysbiosis of the microbiome may cause nasal inflammation⁽³⁴⁾.

The mechanism of association between air pollutant exposure and CRS may be due to several factors, including epithelial barrier disruption, ciliary dysfunction, induction of chronic inflammation, and alteration of the nasal microbiome. The sinonasal airway epithelium acts as the first physical barrier to inhaled air pollutant exposure. Air pollutants may cause airway epithelial cell injury⁽³⁵⁾. Defects of the epithelial barrier with decreased expression of tight junction proteins have been demonstrated in the pathogenesis of CRS⁽³⁶⁾, leading to the development of the epithelial barrier hypothesis. Additionally, inhalation of NO₂ causes airway inflammation and decreases immune function^(37, 38). Epithelial cells release proinflammatory cytokines following exposure to air pollutants, and these circulating inflammatory cytokines maintain systemic inflammation. A previous study showed a positive association with increasing serum interleukin-6 concentration (geometric mean 1.20, 95% CI=1.1–1.3, P=0.001) per quartile increase in NO₂ exposure⁽³⁹⁾. Furthermore, exposure of the nasal microbiota community to air pollutants can change the composition of the bacterial community to an unstable state, resulting in an inability to maintain physiological crosstalk with the host and, altering the immune status^(40, 41). An in vivo and in vitro study showed that air pollution alters *Staphylococcus aureus* and *Streptococcus pneumoniae* biofilm formation, antibiotic tolerance, and bacterial colonization⁽⁴²⁾. Increased PM10 was determined to be negatively associated with CRS. Contrary to our finding, in a study using the Korea National Health and Nutrition Examination Survey 2009, the PM10 concentrations showed a positive association with the risk of CRS (aOR = 1.22, 95% CI = 1.02 – 1.46)⁽⁴³⁾. However, those researchers calculated the OR adjusting for only age, sex, and region. In our study, in model 1 without adjusting for the other air pollutants, we found a positive association between PM10 and CRS (aOR = 1.04). However, in model 2 adjusting for the other air pollutants, the association was changed to a negative result (aOR = 0.93). In a recent Chinese study, the effects of SO₂, CO, and PM10 on CRS outpatients decreased and became nonsignificant after adjusting for other pollutants⁽²⁸⁾. Furthermore, in an in vitro study using human sinonasal epithelial cells, exposure to diesel PM did not affect ciliary beat frequency, transepithelial electrical resistance, or cytokine release⁽⁴⁴⁾. However, more well-controlled epidemiologic studies are needed to elucidate this association between PM and CRS.

The relative humidity was found to be negatively associated with CRS, although it is difficult to interpret whether this is a meaningful result because the OR of humidity for CRS is nearly 1.0. However, to our knowledge, the association of meteorolo-

gical conditions with CRS has not been previously discussed. An experimental study showed that the inhalation of dry air impairs mucociliary clearance, innate antiviral defense, and tissue repair⁽⁴⁵⁾, findings that support our results.

There are some limitations of this study. First, the exposure level to air pollution of each participant was not known. However, we matched the CRS and control groups for region of residence. Second, fewer participants lived in urban areas than in rural areas. However, a previous epidemiological study in Korea showed no difference between rural and urban areas with regard to the prevalence of CRS⁽⁴⁶⁾. Third, we had no data on the severity, control status, response to CRS treatment, and whether surgery was performed. Based on these factors, further studies are needed to evaluate the association between air pollution and CRS. Despite these limitations, the strength of the present study was that patients who were diagnosed based on ICD-10 codes for CRS and underwent CT were selected from a nationwide cohort population. Because Korea has a National Health Insurance system that covers almost the entire population and access to medical care is very easy, this study using the data of NHIS-HEALS may have a low risk of selection bias.

Conclusion

This study showed that CRS is related to high concentrations of NO₂. The relative humidity is negatively associated with CRS regardless of the presence of nasal polyps.

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None.

Authorship contribution

Concept and design: MWP, BP, HGC. Acquisition, analysis, or interpretation of the data: JHW, CM, HJJ. Drafting of the manuscript: JHW, HJJ. Critical revision of the manuscript for important intellectual content: MWP, BP, HGC. Statistical analysis: CM, HGC. Obtained funding: HGC. Administrative, technical, or material support: MWP, BP. Supervision: HGC. All authors: review and approval of the final manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.

Financial disclosure

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SUPPLEMENTARY MATERIAL

Table S1. Crude and adjusted odds ratios (95% confidence interval) of the meteorological and air pollution matter (mean of 30 days before the index date) for CRS.

Characteristics	Odds ratio for CRS total (95% CI)					
	Crude ^b	P-value	Model 1 ^{b, c}	P-value	Model 2 ^{b, d}	P-value
Mean temperature for 90 days (°C)	0.98 (0.98-0.99)	<0.001 ^a	0.98 (0.98-0.99)	<0.001 ^a		
Highest temperature for 90 days (°C)	0.98 (0.98-0.99)	<0.001 ^a	0.98 (0.98-0.99)	<0.001 ^a		
Lowest temperature for 90 days (°C)	0.98 (0.98-0.99)	<0.001 ^a	0.98 (0.98-0.99)	<0.001 ^a		
Temperature range for 90 days (°C)	1.04 (1.02-1.06)	<0.001 ^a	1.04 (1.02-1.06)	<0.001 ^a	0.97 (0.94-0.99)	0.018 ^a
Relative humidity for 90 days (%)	0.99 (0.98-0.99)	<0.001 ^a	0.99 (0.98-0.99)	<0.001 ^a	0.99 (0.98-0.99)	<0.001 ^a
Ambient atmospheric pressure for 90 days (hPa)	1.02 (1.01-1.02)	<0.001 ^a	1.02 (1.01-1.02)	<0.001 ^a	1.01 (1.00-1.01)	<0.001 ^a
Sunshine duration for 90 days (hr)	1.11 (1.08-1.15)	<0.001 ^a	1.11 (1.07-1.14)	<0.001 ^a	1.09 (1.04-1.14)	<0.001 ^a
Rainfall for 90 days (mm)	0.95 (0.94-0.96)	<0.001 ^a	0.95 (0.94-0.96)	<0.001 ^a		
SO ₂ for 90 days (0.01 ppm)	1.62 (1.36-1.92)	<0.001 ^a	1.64 (1.38-1.94)	<0.001 ^a		
NO ₂ for 90 days (0.1 ppm)	3.83 (2.70-5.41)	<0.001 ^a	4.00 (2.82-5.67)	<0.001 ^a	5.40 (3.28-8.89)	<0.001 ^a
O ₃ for 90 days (0.01 ppm)	0.93 (0.90-0.97)	<0.001 ^a	0.93 (0.89-0.96)	<0.001 ^a		
CO for 90 days (ppm)	1.41 (1.16-1.71)	0.001 ^a	1.45 (1.19-1.76)	<0.001 ^a	0.75 (0.57-0.99)	0.041 ^a
PM10 for 90 days (10 µg/m ³)	0.98 (0.98-0.99)	<0.001 ^a	1.04 (1.02-1.06)	0.001 ^a	0.93 (0.90-0.97)	<0.001 ^a

CCI, Charlson comorbidity index; CRS, chronic rhinosinusitis; SBP, systolic blood pressure; DBP, diastolic blood pressure. ^a Conditional logistic regression model, Significance at $P < 0.05$. ^b Stratified model for age, sex, income, and region of residence. ^c Model 1 was adjusted for total cholesterol, SBP, DBP, fasting blood glucose, obesity, smoking status, alcohol consumption, and CCI score. ^d Model 2 was adjusted for total cholesterol, SBP, DBP, fasting blood glucose, obesity, smoking status, alcohol consumption, CCI score, temperature range, relative humidity, ambient atmospheric pressure, sunshine duration, SO₂, NO₂, O₃, CO, and PM10 using the forward selection method.

Table S2. Crude and adjusted odds ratios (95% confidence interval) of the meteorological and air pollution matter (mean of 30 days before the index date) for CRS with nasal polyp.

Characteristics	Odds ratio for CRS total (95% CI)					
	Crude ^b	P-value	Model 1 ^{b, c}	P-value	Model 2 ^{b, d}	P-value
Mean temperature for 90 days (°C)	0.98 (0.98-0.99)	<0.001 ^a	0.98 (0.98-0.99)	<0.001 ^a		
Highest temperature for 90 days (°C)	0.98 (0.98-0.99)	<0.001 ^a	0.98 (0.98-0.99)	<0.001 ^a		
Lowest temperature for 90 days (°C)	0.98 (0.98-0.99)	<0.001 ^a	0.98 (0.98-0.99)	<0.001 ^a		
Temperature range for 90 days (°C)	1.03 (1.01-1.06)	0.023 ^a	1.03 (1.01-1.06)	0.022 ^a		
Relative humidity for 90 days (%)	0.99 (0.98-0.99)	<0.001 ^a	0.99 (0.98-0.99)	<0.001 ^a	0.99 (0.98-1.00)	0.001 ^a
Ambient atmospheric pressure for 90 days (hPa)	1.02 (1.01-1.02)	<0.001 ^a	1.02 (1.01-1.02)	<0.001 ^a		
Sunshine duration for 90 days (hr)	1.10 (1.05-1.15)	<0.001 ^a	1.10 (1.05-1.15)	<0.001 ^a	1.11 (1.04-1.18)	0.002 ^a
Rainfall for 90 days (mm)	0.94 (0.93-0.96)	<0.001 ^a	0.94 (0.93-0.96)	<0.001 ^a		
SO ₂ for 90 days (0.01 ppm)	1.47 (1.16-1.88)	0.002 ^a	1.50 (1.17-1.91)	0.001 ^a		
NO ₂ for 90 days (0.1 ppm)	2.41 (1.46-3.98)	0.001 ^a	2.47 (1.49-4.08)	<0.001 ^a		
O ₃ for 90 days (0.01 ppm)	0.90 (0.85-0.95)	<0.001 ^a	0.90 (0.85-0.95)	<0.001 ^a	0.80 (0.75-0.87)	<0.001 ^a
CO for 90 days (ppm)	1.28 (0.97-1.69)	0.079	1.31 (0.99-1.73)	0.056	0.50 (0.34-0.74)	0.001 ^a
PM10 for 90 days (10 µg/m ³)	1.01 (0.98-1.04)	0.606	1.01 (0.98-1.05)	0.522		

CCI, Charlson comorbidity index; CRS, chronic rhinosinusitis; SBP, systolic blood pressure; DBP, diastolic blood pressure. ^a Conditional logistic regression model, Significance at P < 0.05. ^b Stratified model for age, sex, income, and region of residence. ^c Model 1 was adjusted for total cholesterol, SBP, DBP, fasting blood glucose, obesity, smoking status, alcohol consumption, and CCI score. ^d Model 2 was adjusted for total cholesterol, SBP, DBP, fasting blood glucose, obesity, smoking status, alcohol consumption, CCI score, temperature range, relative humidity, ambient atmospheric pressure, sunshine duration, SO₂, NO₂, O₃, CO, and PM10 using the forward selection method.

Table S3. Crude and adjusted odds ratios (95% confidence interval) of the meteorological and air pollution matter (mean of 90 days before the index date) for CRS without nasal polyp.

Characteristics	Odds ratio for CRS total (95% CI)					
	Crude ^b	P-value	Model 1 ^{b, c}	P-value	Model 2 ^{b, d}	P-value
Mean temperature for 90 days (°C)	0.98 (0.98-0.99)	<0.001 ^a	0.98 (0.98-0.99)	<0.001 ^a		
Highest temperature for 90 days (°C)	0.98 (0.98-0.99)	<0.001 ^a	0.98 (0.98-0.99)	<0.001 ^a		
Lowest temperature for 90 days (°C)	0.98 (0.98-0.99)	<0.001 ^a	0.98 (0.98-0.99)	<0.001 ^a		
Temperature range for 90 days (°C)	1.04 (1.01-1.07)	0.006 ^a	1.04 (1.01-1.06)	0.015 ^a		
Relative humidity for 90 days (%)	0.98 (0.98-0.99)	<0.001 ^a	0.98 (0.98-0.99)	<0.001 ^a	0.99 (0.98-1.00)	0.002 ^a
Ambient atmospheric pressure for 90 days (hPa)	1.02 (1.01-1.02)	<0.001 ^a	1.02 (1.01-1.02)	<0.001 ^a	1.01 (1.01-1.02)	0.001 ^a
Sunshine duration for 90 days (hr)	1.12 (1.07-1.17)	<0.001 ^a	1.11 (1.07-1.16)	<0.001 ^a		
Rainfall for 90 days (mm)	0.95 (0.94-0.97)	<0.001 ^a	0.95 (0.94-0.97)	<0.001 ^a		
SO ₂ for 90 days (0.01 ppm)	1.77 (1.40-2.25)	<0.001 ^a	1.79 (1.40-2.27)	<0.001 ^a		
NO ₂ for 90 days (0.1 ppm)	5.87 (3.63-9.51)	<0.001 ^a	6.16 (3.79-9.99)	<0.001 ^a	13.39 (6.17-29.09)	<0.001 ^a
O ₃ for 90 days (0.01 ppm)	0.96 (0.91-1.01)	0.113	0.95 (0.91-1.01)	0.076	1.16 (1.07-1.25)	<0.001 ^a
CO for 90 days (ppm)	1.56 (1.18-2.05)	0.002 ^a	1.60 (1.21-2.11)	0.001 ^a		
PM10 for 90 days (10 µg/m ³)	1.06 (1.03-1.10)	<0.001 ^a	1.07 (1.03-1.10)	<0.001 ^a	0.92 (0.88-0.96)	<0.001 ^a

CCI, Charlson comorbidity index; CRS, chronic rhinosinusitis; SBP, systolic blood pressure; DBP, diastolic blood pressure. ^a Conditional logistic regression model, Significance at $P < 0.05$. ^b Stratified model for age, sex, income, and region of residence. ^c Model 1 was adjusted for total cholesterol, SBP, DBP, fasting blood glucose, obesity, smoking status, alcohol consumption, and CCI score. ^d Model 2 was adjusted for total cholesterol, SBP, DBP, fasting blood glucose, obesity, smoking status, alcohol consumption, CCI score, temperature range, relative humidity, ambient atmospheric pressure, sunshine duration, SO₂, NO₂, O₃, CO, and PM10 using the forward selection method.

Table S4. Crude and adjusted odds ratios (95% confidence interval) of the meteorological and air pollution matter (mean of 30 days before the index date) for CRS.

Characteristics	Odds ratio for CRS total (95% CI)					
	Crude ^b	P-value	Model 1 ^{b, c}	P-value	Model 2 ^{b, d}	P-value
Mean temperature for 30 days (°C)	0.99 (0.98-0.99)	<0.001 ^a	0.99 (0.98-0.99)	<0.001 ^a		
Highest temperature for 30 days (°C)	0.99 (0.98-0.99)	<0.001 ^a	0.99 (0.98-0.99)	<0.001 ^a		
Lowest temperature for 30 days (°C)	0.99 (0.98-0.99)	<0.001 ^a	0.99 (0.98-0.99)	<0.001 ^a		
Temperature range for 30 days (°C)	1.03 (1.01-1.04)	0.001 ^a	1.03 (1.01-1.04)	0.001 ^a		
Relative humidity for 30 days (%)	0.99 (0.98-0.99)	<0.001 ^a	0.99 (0.98-0.99)	<0.001 ^a	0.99 (0.99-0.99)	<0.001 ^a
Ambient atmospheric pressure for 30 days (hPa)	1.01 (1.01-1.02)	<0.001 ^a	1.01 (1.01-1.02)	<0.001 ^a		
Sunshine duration for 30 days (hr)	1.07 (1.05-1.09)	<0.001 ^a	1.07 (1.05-1.09)	<0.001 ^a		
Rainfall for 30 days (mm)	0.97 (0.97-0.98)	<0.001 ^a	0.97 (0.97-0.98)	<0.001 ^a		
SO ₂ for 90 days (0.01 ppm)	1.56 (1.34-1.81)	<0.001 ^a	1.58 (1.35-1.84)	<0.001 ^a	1.43 (1.16-1.77)	0.001 ^a
NO ₂ for 90 days (0.1 ppm)	3.05 (2.21-4.21)	<0.001 ^a	3.16 (2.29-4.37)	<0.001 ^a	2.82 (1.88-4.22)	<0.001 ^a
O ₃ for 90 days (0.01 ppm)	1.00 (0.97-1.03)	0.891	0.99 (0.96-1.03)	0.726		
CO for 90 days (ppm)	1.25 (1.05-1.49)	0.014 ^a	1.28 (1.07-1.53)	0.007*	0.54 (0.41-0.70)	<0.001 ^a
PM10 for 90 days (10 µg/m ³)	1.04 (1.02-1.06)	<0.001 ^a	1.05 (1.03-1.07)	<0.001*		

CCI, Charlson comorbidity index; CRS, chronic rhinosinusitis; SBP, systolic blood pressure; DBP, diastolic blood pressure. ^a Conditional logistic regression model, Significance at $P < 0.05$. ^b Stratified model for age, sex, income, and region of residence. ^c Model 1 was adjusted for total cholesterol, SBP, DBP, fasting blood glucose, obesity, smoking status, alcohol consumption, and CCI score. ^d Model 2 was adjusted for total cholesterol, SBP, DBP, fasting blood glucose, obesity, smoking status, alcohol consumption, CCI score, temperature range, relative humidity, ambient atmospheric pressure, sunshine duration, SO₂, NO₂, O₃, CO, and PM10 using the forward selection method.

Table S5. Crude and adjusted odds ratios (95% confidence interval) of the meteorological and air pollution matter (mean of 180 days before the index date) for CRS.

Characteristics	Odds ratio for CRS total (95% CI)					
	Crude ^b	P-value	Model 1 ^{b, c}	P-value	Model 2 ^{b, d}	P-value
Mean temperature for 180 days (°C)	0.98 (0.98-0.99)	<0.001 ^a	0.98 (0.98-0.99)	<0.001 ^a		
Highest temperature for 180 days (°C)	0.98 (0.98-0.99)	<0.001 ^a	0.98 (0.98-0.99)	<0.001 ^a		
Lowest temperature for 180 days (°C)	0.99 (0.98-0.99)	<0.001 ^a	0.99 (0.98-0.99)	<0.001 ^a		
Temperature range for 180 days (°C)	1.01 (0.98-1.04)	0.468	1.01 (0.98-1.03)	0.611		
Relative humidity for 180 days (%)	0.99 (0.99-0.99)	<0.001 ^a	0.99 (0.99-1.00)	<0.001 ^a		
Ambient atmospheric pressure for 180 days (hPa)	1.02 (1.01-1.02)	<0.001 ^a	1.02 (1.01-1.02)	<0.001 ^a		
Sunshine duration for 180 days (hr)	1.12 (1.07-1.17)	<0.001 ^a	1.11 (1.07-1.16)	<0.001 ^a	1.23 (1.17-1.29)	<0.001 ^a
Rainfall for 180 days (mm)	0.94 (0.93-0.95)	<0.001 ^a	0.94 (0.93-0.96)	<0.001 ^a		
SO ₂ for 90 days (0.01 ppm)	1.34 (1.09-1.64)	0.005 ^a	1.35 (1.10-1.66)	0.004 ^a	1.52 (1.17-1.98)	0.002 ^a
NO ₂ for 90 days (0.1 ppm)	2.84 (1.96-4.13)	<0.001 ^a	2.97 (2.04-4.32)	<0.001 ^a	5.10 (2.77-9.41)	<0.001 ^a
O ₃ for 90 days (0.01 ppm)	0.86 (0.82-0.90)	<0.001 ^a	0.85 (0.81-0.89)	<0.001 ^a	0.78 (0.73-0.84)	<0.001 ^a
CO for 90 days (ppm)	1.06 (0.84-1.34)	0.650	1.09 (0.86-1.38)	0.490	0.45 (0.31-0.63)	<0.001 ^a
PM10 for 90 days (10 µg/m ³)	0.97 (0.94-1.00)	0.049 ^a	0.98 (0.95-1.00)	0.098	0.86 (0.83-0.90)	<0.001 ^a

CCI, Charlson comorbidity index; CRS, chronic rhinosinusitis; SBP, systolic blood pressure; DBP, diastolic blood pressure. ^a Conditional logistic regression model, Significance at $P < 0.05$. ^b Stratified model for age, sex, income, and region of residence. ^c Model 1 was adjusted for total cholesterol, SBP, DBP, fasting blood glucose, obesity, smoking status, alcohol consumption, and CCI score. ^d Model 2 was adjusted for total cholesterol, SBP, DBP, fasting blood glucose, obesity, smoking status, alcohol consumption, CCI score, temperature range, relative humidity, ambient atmospheric pressure, sunshine duration, SO₂, NO₂, O₃, CO, and PM10 using the forward selection method.

Table S6. Crude and adjusted odds ratios (95% confidence interval) of the meteorological and air pollution matter (mean of 365 days before the index date) for CRS.

Characteristics	Odds ratio for CRS total (95% CI)					
	Crude ^b	P-value	Model 1 ^{b, c}	P-value	Model 2 ^{b, d}	P-value
Mean temperature for 365 days (°C)	1.02 (0.99-1.04)	0.190	1.02 (0.99-1.04)	0.238		
Highest temperature for 365 days (°C)	1.01 (0.99-1.04)	0.361	1.01 (0.98-1.04)	0.472		
Lowest temperature for 365 days (°C)	1.02 (0.99-1.04)	0.147	1.02 (0.99-1.04)	0.165		
Temperature range for 365 days (°C)	0.99 (0.96-1.02)	0.368	0.98 (0.95-1.02)	0.290		
Relative humidity for 365 days (%)	1.00 (0.99-1.01)	0.801	1.00 (0.99-1.01)	0.827	1.01 (1.00-1.02)	0.008 ^a
Ambient atmospheric pressure for 365 days (hPa)	1.00 (0.99-1.01)	0.831	1.00 (0.99-1.01)	0.820	0.99 (0.99-1.00)	<0.001 ^a
Sunshine duration for 365 days (hr)	1.17 (1.10-1.23)	<0.001 ^a	1.16 (1.10-1.22)	<0.001 ^a	1.20 (1.13-1.28)	<0.001 ^a
Rainfall for 365 days (mm)	1.00 (0.97-1.03)	0.877	1.00 (0.97-1.03)	0.913		
SO ₂ for 90 days (0.01 ppm)	0.99 (0.76-1.29)	0.926	1.02 (0.78-1.34)	0.866		
NO ₂ for 90 days (0.1 ppm)	2.31 (1.55-3.44)	<0.00 ^a	2.45 (1.64-3.66)	<0.001 ^a	2.07 (1.25-3.44)	0.005 ^a
O ₃ for 90 days (0.01 ppm)	0.98 (0.92-1.05)	0.631	0.97 (0.91-1.04)	0.402		
CO for 90 days (ppm)	0.44 (0.32-0.59)	<0.001 ^a	0.46 (0.34-0.63)	<0.001 ^a	0.61 (0.42-0.87)	0.007 ^a
PM10 for 90 days (10 µg/m ³)	0.97 (0.94-1.01)	0.124	0.98 (0.94-1.02)	0.318		

CCI, Charlson comorbidity index; CRS, chronic rhinosinusitis; SBP, systolic blood pressure; DBP, diastolic blood pressure. ^a Conditional logistic regression model, Significance at $P < 0.05$. ^b Stratified model for age, sex, income, and region of residence. ^c Model 1 was adjusted for total cholesterol, SBP, DBP, fasting blood glucose, obesity, smoking status, alcohol consumption, and CCI score. ^d Model 2 was adjusted for total cholesterol, SBP, DBP, fasting blood glucose, obesity, smoking status, alcohol consumption, CCI score, temperature range, relative humidity, ambient atmospheric pressure, sunshine duration, SO₂, NO₂, O₃, CO, and PM10 using the forward selection method.

Table S7. Subgroup analyses of crude and adjusted odds ratios (95% confidence interval) of the meteorological and air pollution matter (mean of 30 days before the index date) for total CRS according to age, sex, income, and region of residence.

Characteristics	Odds ratio for total CRS (95% CI)	
	Model 2 ^{b, c}	P-value
Age < 60 years old (n = 19,225)		
Relative humidity for 30 days (%)	0.99 (0.98-0.99)	<0.001 ^a
SO ₂ for 30 days (0.01 ppm)	1.44 (1.09-1.90)	0.011 ^a
NO ₂ for 30 days (0.1 ppm)	5.14 (2.82-9.39)	<0.001 ^a
O ₃ for 30 days (0.01 ppm)	1.06 (1.00-1.13)	0.044
CO for 30 days (ppm)	0.69 (0.47-1.00)	0.048 ^a
PM10 for 30 days (10 µg/m3)	0.95 (0.92-0.99)	0.007 ^a
Age ≥ 60 years old (n = 11,570)		
Relative humidity for 30 days (%)	0.99 (0.98-0.99)	<0.001 ^a
SO ₂ for 30 days (0.01 ppm)	1.48 (1.03-2.12)	0.033 ^a
NO ₂ for 30 days (0.1 ppm)	2.63 (1.32-5.23)	0.006 ^a
CO for 30 days (ppm)	0.48 (0.30-0.76)	0.002 ^a
Males (n = 18,920)		
Relative humidity for 30 days (%)	0.99 (0.98-0.99)	<0.001 ^a
SO ₂ for 30 days (0.01 ppm)	1.53 (1.17-2.01)	0.002 ^a
NO ₂ for 30 days (0.1 ppm)	2.76 (1.64-4.67)	<0.001 ^a
CO for 30 days (ppm)	0.52 (0.37-0.73)	<0.001 ^a
Females (n = 11,875)		
Relative humidity for 30 days (%)	0.99 (0.98-0.99)	<0.001 ^a
NO ₂ for 30 days (0.1 ppm)	2.87 (1.52-5.41)	0.001 ^a
CO for 30 days (ppm)	0.67 (0.46-0.96)	0.030 ^a
Low income (n = 12,070)		
Relative humidity for 30 days (%)	0.99 (0.98-0.99)	<0.001 ^a
High income (n = 18,725)		
Relative humidity for 30 days (%)	0.99 (0.99-0.99)	<0.001 ^a
SO ₂ for 30 days (0.01 ppm)	1.50 (1.14-1.98)	0.004 ^a
NO ₂ for 30 days (0.1 ppm)	3.34 (2.00-5.60)	<0.001 ^a
CO for 30 days (ppm)	0.52 (0.37-0.74)	<0.001 ^a
Urban (n = 14,255)		
Ambient atmospheric pressure for 30 days (hPa)	0.99 (0.99-1.00)	0.004 ^a
Sunshine duration for 30 days (hr)	1.06 (1.02-1.10)	0.002 ^a
NO ₂ for 30 days (0.1 ppm)	2.23 (1.38-3.60)	0.001 ^a
Rural (n = 16,540)		
Temperature range for 30 days (°C)	0.97 (0.94-1.00)	0.023 ^a
Relative humidity for 30 days (%)	0.99 (0.98-0.99)	<0.001 ^a
SO ₂ for 30 days (0.01 ppm)	2.24 (1.59-3.16)	<0.001 ^a
NO ₂ for 30 days (0.1 ppm)	4.52 (2.24-9.11)	<0.001 ^a
CO for 30 days (ppm)	0.27 (0.18-0.41)	<0.001 ^a

CCI, Charlson comorbidity index; CRS, chronic rhinosinusitis; SBP, systolic blood pressure; DBP, diastolic blood pressure. ^a Conditional logistic regression model, Significance at P < 0.05. ^b Stratified model for age, sex, income, and region of residence. ^c Model 2 was adjusted for total cholesterol, SBP, DBP, fasting blood glucose, obesity, smoking status, alcohol consumption, CCI score, temperature range, relative humidity, ambient atmospheric pressure, sunshine duration, SO₂, NO₂, O₃, CO, and PM10 using the forward selection method.

Table S8. Subgroup analyses of crude and adjusted odds ratios (95% confidence interval) of the meteorological and air pollution matter (mean of 180 days before the index date) for CRS according to age, sex, income, and region of residence.

Characteristics	Odds ratio for total CRS (95% CI)	
	Model 2 ^{b, c}	P-value
Age < 60 years old (n = 19,225)		
Sunshine duration for 180 days (hr)	1.22 (1.15-1.30)	<0.001 ^a
SO ₂ for 180 days (0.01 ppm)	1.46 (1.05-2.03)	0.024 ^a
NO ₂ for 180 days (0.1 ppm)	9.28 (4.21-20.44)	<0.001 ^a
O ₃ for 180 days (0.01 ppm)	0.81 (0.74-0.89)	<0.001 ^a
CO for 180 days (ppm)	0.47 (0.31-0.72)	0.001 ^a
PM10 for 180 days (10 µg/m ³)	0.84 (0.79-0.89)	<0.001 ^a
Age ≥ 60 years old (n = 11,570)		
Sunshine duration for 180 days (hr)	1.25 (1.15-1.35)	<0.001 ^a
O ₃ for 180 days (0.01 ppm)	0.74 (0.66-0.83)	<0.001 ^a
CO for 180 days (ppm)	0.53 (0.30-0.92)	0.025 [*]
PM10 for 180 days (10 µg/m ³)	0.93 (0.88-0.99)	0.017 [*]
Males (n = 18,920)		
Temperature range for 180 days (°C)	0.94 (0.90-0.98)	0.002 ^a
Sunshine duration for 180 days (hr)	1.28 (1.20-1.37)	<0.001 ^a
NO ₂ for 180 days (0.1 ppm)	3.29 (1.49-7.24)	0.003 ^a
O ₃ for 180 days (0.01 ppm)	0.81 (0.74-0.88)	<0.001 ^a
PM10 for 180 days (10 µg/m ³)	0.88 (0.84-0.93)	<0.001 ^a
Females (n = 11,875)		
Sunshine duration for 180 days (hr)	1.24 (1.15-1.34)	<0.001 ^a
NO ₂ for 180 days (0.1 ppm)	6.15 (2.29-16.49)	<0.001 ^a
O ₃ for 180 days (0.01 ppm)	0.76 (0.68-0.86)	<0.001 ^a
CO for 180 days (ppm)	0.45 (0.27-0.76)	0.003 ^a
PM10 for 180 days (10 µg/m ³)	0.87 (0.82-0.93)	<0.001 ^a
Low income (n = 12,070)		
Sunshine duration for 180 days (hr)	1.23 (1.14-1.33)	<0.001 ^a
NO ₂ for 180 days (0.1 ppm)	4.18 (1.54-11.36)	0.005 ^a
O ₃ for 180 days (0.01 ppm)	0.81 (0.72-0.90)	<0.001 ^a
CO for 180 days (ppm)	0.56 (0.33-0.93)	0.024 ^a
PM10 for 180 days (10 µg/m ³)	0.87 (0.82-0.94)	<0.001 ^a
High income (n = 18,725)		
Sunshine duration for 180 days (hr)	1.23 (1.15-1.30)	<0.001 [*]
SO ₂ for 180 days (0.01 ppm)	1.55 (1.10-2.18)	0.012 ^a
NO ₂ for 180 days (0.1 ppm)	5.46 (2.51-11.86)	<0.001 ^a
O ₃ for 180 days (0.01 ppm)	0.77 (0.70-0.84)	<0.001 ^a
CO for 180 days (ppm)	0.44 (0.28-0.70)	<0.001 ^a
PM10 for 180 days (10 µg/m ³)	0.87 (0.82-0.91)	<0.001 ^a
Urban (n = 14,255)		
Temperature range for 180 days (°C)	0.94 (0.89-0.98)	0.006 ^a
Sunshine duration for 180 days (hr)	1.45 (1.35-1.55)	<0.001 ^a
SO ₂ for 180 days (0.01 ppm)	0.54 (0.34-0.85)	0.008 ^a
O ₃ for 180 days (0.01 ppm)	0.63 (0.57-0.69)	<0.001 ^a
PM10 for 180 days (10 µg/m ³)	0.91 (0.86-0.95)	<0.001 ^a

Characteristics	Odds ratio for total CRS (95% CI)	
	Model 2 ^{b,c}	P-value
Rural (n = 16,540)		
Relative humidity for 180 days (%)	0.98 (0.97-0.99)	<0.001 ^a
SO ₂ for 180 days (0.01 ppm)	3.44 (2.25-5.25)	<0.001 ^a
NO ₂ for 180 days (0.1 ppm)	7.55 (2.38-23.94)	0.001 ^a
O ₃ for 180 days (0.01 ppm)	0.84 (0.76-0.93)	0.001 ^a
CO for 180 days (ppm)	0.14 (0.08-0.26)	<0.001 ^a
PM10 for 180 days (10 µg/m ³)	0.87 (0.81-0.93)	<0.001 ^a

CCI, Charlson comorbidity index; CRS, chronic rhinosinusitis; SBP, systolic blood pressure; DBP, diastolic blood pressure. ^a Conditional logistic regression model, Significance at P < 0.05. ^b Stratified model for age, sex, income, and region of residence. ^c Model 2 was adjusted for total cholesterol, SBP, DBP, fasting blood glucose, obesity, smoking status, alcohol consumption, CCI score, temperature range, relative humidity, ambient atmospheric pressure, sunshine duration, SO₂, NO₂, O₃, CO, and PM10 using the forward selection method.

Table S9. Subgroup analyses of crude and adjusted odds ratios (95% confidence interval) of the meteorological and air pollution matter (mean of 365 days before the index date) for CRS according to age, sex, income, and region of residence.

Characteristics	Odds ratio for total CRS (95% CI)	
	Model 2 ^{b,c}	P-value
Age < 60 years old (n = 19,225)		
Relative humidity for 365 days (%)	1.03 (1.01-1.04)	<0.001 ^a
Ambient atmospheric pressure for 365 days (hPa)	0.99 (0.99-0.99)	<0.001 ^a
Sunshine duration for 365 days (hr)	1.27 (1.17-1.37)	<0.001 ^a
NO ₂ for 365 days (0.1 ppm)	40.84 (18.65-89.40)	<0.001 ^a
CO for 365 days (ppm)	0.27 (0.17-0.43)	<0.001 ^a
PM10 for 365 days (10 µg/m ³)	0.87 (0.81-0.94)	<0.001 ^a
Age ≥ 60 years old (n = 11,570)		
Relative humidity for 365 days (%)	1.02 (1.01-1.04)	0.009 ^a
Ambient atmospheric pressure for 365 days (hPa)	0.99 (0.98-1.00)	0.021 ^a
Sunshine duration for 365 days (hr)	1.26 (1.12-1.42)	<0.001 ^a
NO ₂ for 365 days (0.1 ppm)	5.82 (1.66-20.38)	0.006 ^a
CO for 365 days (ppm)	0.23 (0.11-0.49)	<0.001 ^a
Males (n = 18,920)		
Relative humidity for 365 days (%)	1.02 (1.01-1.04)	<0.001 ^a
Ambient atmospheric pressure for 365 days (hPa)	0.99 (0.99-0.99)	<0.001 ^a
Sunshine duration for 365 days (hr)	1.29 (1.19-1.39)	<0.001 ^a
NO ₂ for 365 days (0.1 ppm)	20.21 (9.39-43.47)	<0.001 ^a
CO for 365 days (ppm)	0.23 (0.14-0.38)	<0.001 ^a
PM10 for 365 days (10 µg/m ³)	0.92 (0.86-0.99)	0.026 ^a
Females (n = 11,875)		
Relative humidity for 365 days (%)	1.03 (1.01-1.04)	0.003 ^a
Ambient atmospheric pressure for 365 days (hPa)	0.99 (0.98-1.00)	0.015 ^a
Sunshine duration for 365 days (hr)	1.21 (1.08-1.36)	0.001 ^a
NO ₂ for 365 days (0.1 ppm)	15.42 (4.34-54.87)	<0.001 ^a
CO for 365 days (ppm)	0.26 (0.13-0.51)	<0.001 ^a

Characteristics	Odds ratio for total CRS (95% CI)	
	Model 2 ^{b, c}	P-value
Low income (n = 12,070)		
Relative humidity for 365 days (%)	1.02 (1.01-1.04)	0.003 ^a
Ambient atmospheric pressure for 365 days (hPa)	0.99 (0.99-0.99)	<0.001 ^a
Sunshine duration for 365 days (hr)	1.23 (1.11-1.36)	<0.001 ^a
NO ₂ for 365 days (0.1 ppm)	25.80 (9.72-68.50)	<0.001 ^a
CO for 365 days (ppm)	0.23 (0.13-0.42)	<0.001 ^a
PM10 for 365 days (10 µg/m ³)	0.88 (0.80-0.96)	0.005 ^a
High income (n = 18,725)		
Relative humidity for 365 days (%)	1.02 (1.01-1.04)	<0.001 ^a
Ambient atmospheric pressure for 365 days (hPa)	0.99 (0.99-0.99)	<0.001 ^a
Sunshine duration for 365 days (hr)	1.29 (1.19-1.39)	<0.001 ^a
NO ₂ for 365 days (0.1 ppm)	15.04 (8.01-28.26)	<0.001 ^a
CO for 365 days (ppm)	0.23 (0.14-0.36)	<0.001 ^a
Rural (n = 16,540)		
Ambient atmospheric pressure for 365 days (hPa)	0.99 (0.99-1.00)	<0.001 ^a
Sunshine duration for 365 days (hr)	1.15 (1.04-1.28)	0.007 ^a
SO ₂ for 365 days (0.01 ppm)	2.95 (1.85-4.69)	<0.001 ^a
NO ₂ for 365 days (0.1 ppm)	8.29 (3.96-17.34)	<0.001 ^a
CO for 365 days (ppm)	0.09 (0.05-0.15)	<0.001 ^a

CCI, Charlson comorbidity index; CRS, chronic rhinosinusitis; SBP, systolic blood pressure; DBP, diastolic blood pressure. ^a Conditional logistic regression model, Significance at $P < 0.05$. ^b Stratified model for age, sex, income, and region of residence. ^c Model 2 was adjusted for total cholesterol, SBP, DBP, fasting blood glucose, obesity, smoking status, alcohol consumption, CCI score, temperature range, relative humidity, ambient atmospheric pressure, sunshine duration, SO₂, NO₂, O₃, CO, and PM10 using the forward selection method.

Table S10. Subgroup analyses of crude and adjusted odds ratios (95% confidence interval) of the meteorological and air pollution matter (mean of 90 days before the index date) for CRS according to age, sex, income, and region of residence.

Characteristics	Odds ratio for total CRS (95% CI)	
	Model 2 ^{b, c}	P-value
Age < 60 years old (n = 19,225)		
Relative humidity for 90 days (%)	0.99 (0.98-1.00)	0.001 ^a
Sunshine duration for 90 days (hr)	1.09 (1.03-1.14)	0.002 ^a
NO ₂ for 90 days (0.1 ppm)	8.29 (4.63-14.85)	<0.001 ^a
PM10 for 90 days (10 µg/m ³)	0.90 (0.86-0.93)	<0.001 ^a
Age ≥ 60 years old (n = 11,570)		
Relative humidity for 90 days (%)	0.99 (0.98-1.00)	0.001 ^a
Ambient atmospheric pressure for 90 days (hPa)	1.01 (1.00-1.02)	0.002 ^a
Males (n = 18,920)		
Temperature range for 90 days (°C)	0.95 (0.92-0.98)	0.038 ^a
Relative humidity for 90 days (%)	0.99 (0.98-1.00)	0.001 ^a
Ambient atmospheric pressure for 90 days (hPa)	1.01 (1.00-1.01)	0.011 ^a
Sunshine duration for 90 days (hr)	1.12 (1.06-1.18)	<0.001 ^a
NO ₂ for 90 days (0.1 ppm)	3.90 (2.14-7.13)	<0.001 ^a
PM10 for 90 days (10 µg/m ³)	0.94 (0.90-0.98)	0.005 ^a

Characteristics	Odds ratio for total CRS (95% CI)	
	Model 2 ^{b,c}	P-value
Females (n = 11,875)		
Relative humidity for 90 days (%)	0.99 (0.98-0.99)	<0.001 ^a
NO ₂ for 90 days (0.1 ppm)	5.93 (2.87-12.25)	<0.001 ^a
PM10 for 90 days (10 µg/m ³)	0.91 (0.86-0.96)	<0.001 ^a
Low income (n = 12,070)		
Relative humidity for 90 days (%)	0.99 (0.98-1.00)	0.017 ^a
Sunshine duration for 90 days (hr)	1.07 (1.01-1.14)	0.031 ^a
NO ₂ for 90 days (0.1 ppm)	4.14 (1.91-9.00)	<0.001 ^a
PM10 for 90 days (10 µg/m ³)	0.91 (0.86-0.95)	<0.001 ^a
High income (n = 18,725)		
Temperature range for 90 days (°C)	0.95 (0.92-0.98)	0.003 ^a
Relative humidity for 90 days (%)	0.99 (0.98-1.00)	0.003 ^a
Ambient atmospheric pressure for 90 days (hPa)	1.01 (1.00-1.01)	0.011 ^a
Sunshine duration for 90 days (hr)	1.11 (1.05-1.17)	<0.001 ^a
NO ₂ for 90 days (0.1 ppm)	4.87 (2.68-8.85)	<0.001 ^a
PM10 for 90 days (10 µg/m ³)	0.94 (0.90-0.98)	0.006 ^a
Urban (n = 14,255)		
Sunshine duration for 90 days (hr)	1.23 (1.17-1.29)	<0.001 ^a
NO ₂ for 90 days (0.1 ppm)	3.21 (1.60-6.47)	0.001 ^a
O ₃ for 90 days (0.01 ppm)	0.84 (0.78-0.91)	<0.001 ^a
PM10 for 90 days (10 µg/m ³)	0.94 (0.90-0.99)	0.009 ^a
Rural (n = 16,540)		
Relative humidity for 90 days (%)	0.98 (0.98-0.99)	<0.001 ^a
SO ₂ for 90 days (0.01 ppm)	2.60 (1.78-3.79)	<0.001 ^a
NO ₂ for 90 days (0.1 ppm)	8.17 (3.25-20.53)	<0.001 ^a
CO for 90 days (ppm)	0.25 (0.16-0.39)	<0.001 ^a
PM10 for 90 days (10 µg/m ³)	0.92 (0.87-0.97)	0.001 ^a

CCI, Charlson comorbidity index; CRS, chronic rhinosinusitis; SBP, systolic blood pressure; DBP, diastolic blood pressure. ^a Conditional logistic regression model, Significance at P < 0.05. ^b Stratified model for age, sex, income, and region of residence. ^c Model 2 was adjusted for total cholesterol, SBP, DBP, fasting blood glucose, obesity, smoking status, alcohol consumption, CCI score, temperature range, relative humidity, ambient atmospheric pressure, sunshine duration, SO₂, NO₂, O₃, CO, and PM10 using the forward selection method.