



Assessing the cold temperature effect on hospital visit by allergic rhinitis in Seoul, Korea

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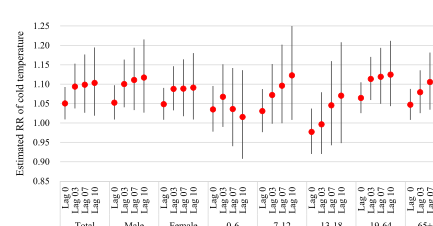
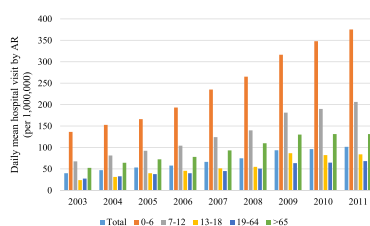
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HIGHLIGHTS

- Studies for assessing cold temperature effect on AR are scarce.
- Cold temperature effect on hospital visit by AR was assessed.
- Hospital visit by AR has steadily increased especially for the elderly population.
- We found cold temperature effect on AR and the strongest effect found in autumn season.
- More studies should be conducted for better understanding of temperature effect on AR.

GRAPHICAL ABSTRACT



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ABSTRACT

The association between temperature and health outcome has been studied in worldwide. However, studies for mild diseases such as AR, with high prevalence and considerable economic burden, are lacking compared to other relatively severe respiratory diseases. We aimed to assess the trend of hospital visit by AR and estimate the cold temperature effect on hospital visit by allergic rhinitis in Seoul, Korea, 2003–2011.

We fitted generalized additive model with quasi-poisson distribution, controlling for humidity, long-term trend, day of week, national holiday, and influenza epidemic. We estimated the cumulative cold temperature effect (10%, -1.7°C) referent to 7.9°C for the considered lag periods using distributed lag non-linear model: vary from the day of hospital visit to 10 days before. Stratified analysis by season was also conducted. To adjust for possible confounding effect of air pollutants, we additionally adjusted for PM_{10} , O_3 and NO_2 respectively.

Hospital visit counts and rates per 1,000,000 show increasing trend especially in elderly population (over 65 years). Hospital visit rate is higher in children population (age < 13 years). Statistically significant cold temperature effects were found in the total (1.094(95%CI: 1.037, 1.153)), male (1.100 (95%CI: 1.010, 1.163)), female (1.088 (95%CI: 1.059, 1.170)) and adult (1.113 (95%CI: 1.059, 1.170)) population with consideration of 3-day lag period. In the stratified analysis by the season, the strongest effect was shown in the autumn (Sep–Nov) season. Confounding effects by air pollutants were not found.

In this study, we found significant increasing trend of hospital visit by AR. This study provides suggestive evidence of cold temperature effect on hospital visit by AR. To reduce the growing burden of AR, it is important to find possible related environmental risk factors. More studies should be conducted for better understanding of temperature effect on AR.

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1. Introduction

Allergic rhinitis (AR), as one of the allergic respiratory diseases, has been an issue in public health area in both developed and developing countries due to their high prevalence and economic burden. According to the “WAO White Book on Allergy 2010”, about 10 to 30% of the adult population and as many as 40% of children are affected with AR. The World Health Organization have estimated that 400 million people in the world suffer from AR (Pawankar et al., 2011). Moreover, the prevalence of AR is still increasing (Pawankar et al., 2011).

In Korea, Seong et al. reported that prevalence of AR using nationwide survey increased in 2008 (25.07%) compared to 2005 (20.09%), and higher prevalence was observed in those younger than 10 years old (Seong et al., 2012). Another study that also used the nationwide study of Korean school children, estimated the prevalence to be 46.7% for ever having AR symptoms, to 42.2% for AR symptoms in the last 12 months and to 38.2% for doctor diagnosed AR (Y. Kim et al., 2015a). Rhee et al. investigated the prevalence of AR in the subjects aged ≥ 10 who participated in the Fifth Korean National Health and Nutritional Examination Survey in Korea (Rhee et al., 2014). The estimated prevalence of AR was $16.2\% \pm 1.0\%$ (Rhee et al., 2014). According to the annual report of National Health Insurance statistics in 2014, about 6.3 million people visited hospital for AR and paid >390 billion Korean Won (1 dollar is 1100 Korean Won) in medical expenses (Kim and Son, 2014). Another study have estimated the total economic burden of AR in 2010 to be \$273.92 million using National Health Insurance claims data (Kim et al., 2010).

AR is widely acknowledged as one of the major factor for asthma. Furthermore, higher prevalence (up to 95%) of AR in asthma patients and the theory of “one airway, one disease” (Grossman, 1997) may indicate the possibility of prevention or management of asthma or more severe respiratory diseases through a proper treatment or management of existing AR or respiratory symptoms. In that point of view, it is important to identify possible risk factors that can exacerbate current allergic respiratory symptoms.

To identify possible risk factors on AR, many studies across various disciplines were conducted. These studies mainly focused on indoor allergens such as residential chemical emissions, moisture/mold endotoxin, combustion products or genetic factors (Mendell, 2007; Dold et al., 1992; Mendell et al., 2011; Jaakkola et al., 2013). The association between temperature and health outcome has been widely studied across the worldwide and in light of climate change (Guo et al., 2014; Hajat and Haines, 2002; Miao et al., 2017). IPCC have projected that global warming will continue with increases in the frequency and intensity of extreme weather events. Studies investigating the association between temperature and health outcome are becoming more important now than ever. There are some clinical, epidemiological and biological evidences that suggest cold air can affect to respiratory symptoms (Koskela, 2007; Graudenz et al., 2007). Most of studies investigating cold temperature effects on respiratory diseases focused on general respiratory diseases (J00–J99), categories with similar diseases group (upper or lower respiratory diseases) (Carreras et al., 2015; Mäkinen et al., 2009) or severe diseases such as COPD or asthma (Fitzgerald et al., 2014; Zhang et al., 2014). However, despite evidences of possible mechanisms of cold temperature effect on allergic respiratory diseases, studies related to temperature effect on AR are scarce (Lee et al., 2003).

In this study, we aimed to look into the trend of hospital visit by AR for the period of 2003 to 2011 and to estimate the effect of cold temperature on hospital visit by AR with consideration for various lag structures in Seoul, Korea.

2. Material and methods

2.1. Study population

In this study, we targeted people who reside in Seoul. Seoul is the capital city of the Republic of Korea, and located at the center of the Korean Peninsula, with an area coverage of 605 km².

The Korean population is subjected to National Health Insurance Service operated by National Health Insurance Service (NHIS). According to the “Statistics in Health Insurance 2015”, the national insurance service system covers 97% of the Korean population and the other 3% are covered by the medical security system. Using this system, NHIS gathers hospital visit or hospitalization records through health insurance claim data and generates a massive national health insurance database.

Daily mean count of hospital visit by allergic rhinitis was extracted from the national health insurance database for the period of 2003 to 2011. To include all possible AR patients, we set the inclusion criteria to include those who were diagnosed with AR (ICD-10, J30) as primary or secondary cause. In general, hospital visit in tertiary medical institutions such as university hospitals are mostly scheduled visit, and since such visit might have different association with cold temperature, we excluded these visits in the calculation of daily mean count. To account for follow-up visits, we also excluded visits that occurred within a 30-day interval from the previous visit. Sex and age-specific (0–6, 7–12, 13–18, 19–64, 65+ years) hospital visit count was also calculated. The classification of children and adolescent (0–6, 7–12, 13–18 years) was made with consideration of Korean education system; individuals in the same age group might have higher chances of having similar exposure patterns.

2.2. Meteorological and air pollutants data

Hourly measured daily temperature and humidity in Seoul were obtained from the Meteorological Administration in the period of 2003 to 2011. Automated Synoptic Observing System (ASOS) is an equipment for measuring weather conditions, and this equipment was installed at the Jong-ro district, Seoul, in 1995. ASOS automatically measure temperature, humidity, and other weather conditions by every hour or by every 3 h. We calculated the daily mean temperature and humidity using hourly measured data.

Hourly measured ambient concentration of particles with diameter of 10 μm or less (also known as PM₁₀), ozone (O₃) and nitrogen dioxide (NO₂) were obtained from the National Institute of Environmental Research for the same period. Daily average value of PM₁₀ and NO₂ and maximum of 8-hour moving average within a day of O₃ was used as daily representative value.

2.3. Statistical analysis

To identify the monotonic trend of hospital visit by AR, we used Mann-Kendall test that commonly used non-parametric trend test to detect monotonic trend. Because the Mann-Kendall test is robust against serial dependency, seasonality, and departure from normality, we adopted this test to identify monotonic increase trend of hospital visit count by AR (Hirsch and Slack, 1984).

To estimate the cold temperature effect on hospital visit by AR, generalized additive model (GAM) with Quasi-Poisson distribution was used with consideration for long-term seasonal trend, humidity, day of week, national holiday, and influenza epidemic (Bhaskaran et al., 2013; Bell et al., 2004).

For the preliminary analysis, we analyzed the association between daily mean temperature and hospital visit by AR. The results indicate that the estimated relative risk (RR) of temperature showed increasing trend followed by decreasing trend for both an increase and decrease of temperature with referent to 7.9 °C (Supplementary Fig. A). Therefore, to estimate the cold temperature effect in the main analyses, we estimated the cumulative relative risks (RRs) of 10th percentile (−1.073 °C) of mean temperature referent to 7.9 °C with considered lag periods.

According to the studies estimating the ambient temperature effect on morbidity, delayed effects were taken into account from the date of the hospital visit to the visit for a period of up to one month (Ye et al., 2012). AR symptoms that are triggered by cold air can

appear after a relatively short period (from a few minutes to couple of hours after exposure) due to the immunologic responses (Greiner et al., 2011). However, because the general public perception is that AR is a relatively mild ailment and symptoms do not require immediate medical care, it could be possible that people may postpone their hospital visit. The preliminary analysis for the association between temperature and hospital visit for AR with consideration for 21 days of delayed effect showed that the effect of temperature was not seen after 10 days from the day of hospital visit (Supplementary Fig. B). Therefore, we considered various delayed effects of cold temperature: from the day of hospital visit to 3, 7, 10 days before the hospital visit. Distributed Lag Non-linear Model was used to consider both the non-linear effect of temperature and delayed effect (Gasparrini et al., 2010; Gasparrini, 2011). The degree of freedom for long term time trend, temperature, and lag function of temperature are chosen through various sensitivity analysis (from 3 to 9 degree of freedom for each variable (Supplemental Fig. C)).

The model for estimating the cold temperature effect is:

$$\text{Log}(E(Y)) = \alpha + S(\text{temperature}, df = 7, \text{lag}(0, 03, 07, 10, df = 5)) + \text{humidity} + S(\text{long-term time trend}, df = 7/\text{per year}) + D(\text{day of week}) + D(\text{public holiday}) + D(\text{influenza epidemic}) + \text{Air pollutant}$$

where

- $E(Y)$ is expected number of daily hospital visits by AR.
- Day of week, public holiday, and influenza epidemic were contained as dummy variables

- Considered lag of temperature: 0, 0–3, 0–7, 0–10
- Additional adjustment for air pollutants (PM_{10} , O_3 , NO_2)

In this study, we hypothesized that cold temperature effect on AR might vary by the season since behavioral patterns can be changed by season. Therefore, stratified analysis by season (spring: March–May, fall: September–November, and winter: December–February) were additionally conducted. As we aimed to estimate the cold temperature effect, we did not estimate the effect of temperature for the summer season. In the season-specific model, instead of cubic spline of time variable, indicator variable for year and cubic splines of day of year with 3 degree of freedom were used to consider long-term trend in each season. In addition, sex and age might also affect the association between temperature and AR, thus, stratified analysis by sex and age-group were also conducted.

Other pollutants such as PM_{10} , O_3 , and NO_2 are known as risk factor for respiratory diseases (Khafaie et al., 2016; Deng et al., 2016a; Lee et al., 2002; Takizawa, 2011; D'amato, 2002). To identify the possible confounding effect of air pollutants (PM_{10} , O_3 , NO_2), we added each air pollutant separately in the above model. All statistical analyses were conducted using R3.2.4.

3. Results

The trend of daily mean number of hospital visit by AR in total, sex, and age-specific groups during the period of 2003 to 2011 in Seoul are presented in Fig. 1. The number of hospital visit by AR showed an

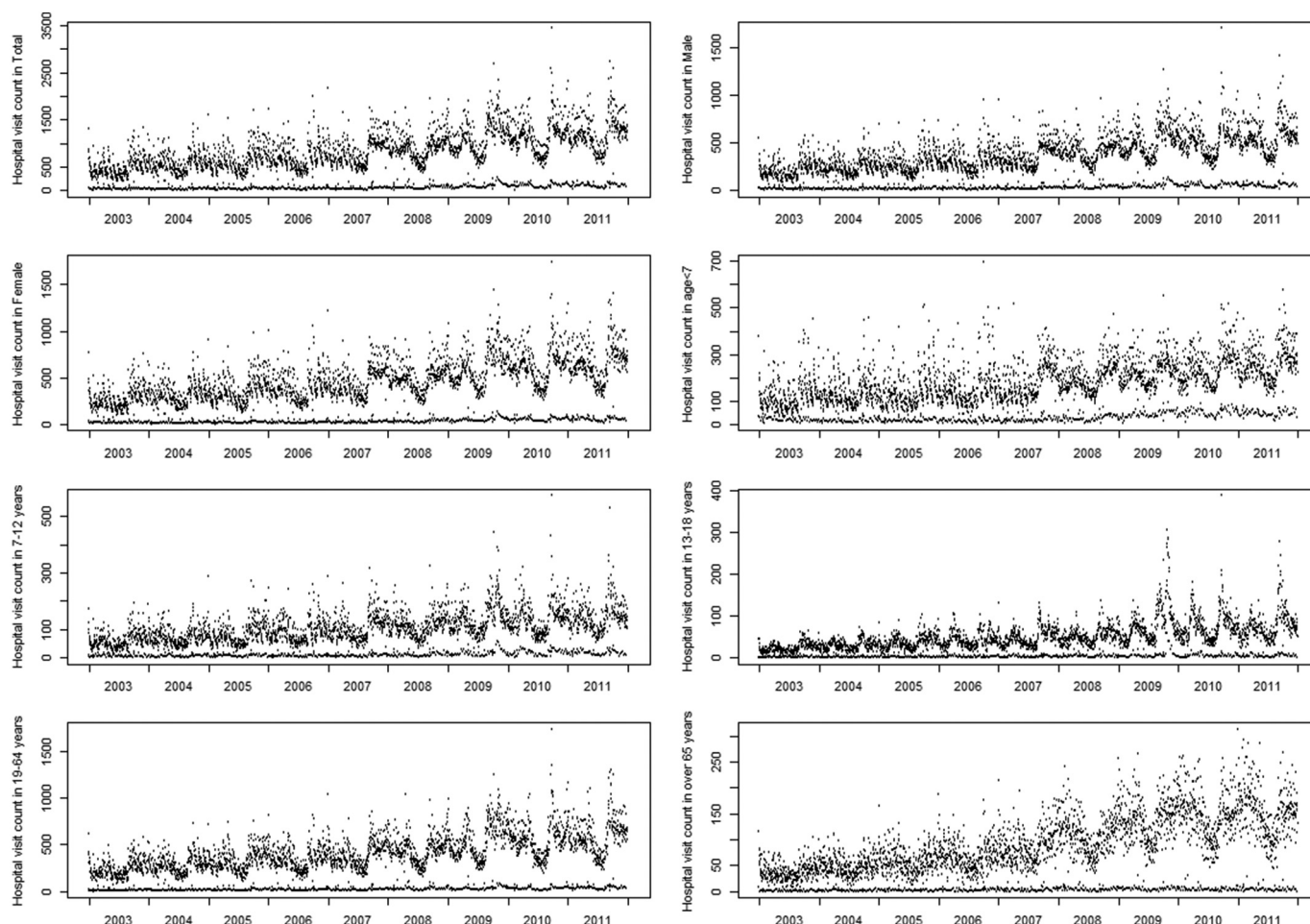


Fig. 1. The trend of daily counts of hospital visit by AR for the total, sex, and age-specific groups for the period of 2003 to 2011, in Seoul.

Table 1

Summary statistics for daily counts of hospital visit, meteorological and air pollutants variables in Seoul in the period of 2003 to 2011.

Year	Daily mean counts of hospital visit by AR ((mean (range)), person/day)							
	Total	Male	Female	0–6	7–12	13–18	19–64	>65
2003	408 (11, 1329)	181 (5, 573)	227 (6, 767)	107 (5, 452)	52 (0, 194)	19 (0, 65)	199 (1, 610)	31 (0, 115)
2004	479 (11, 1420)	213 (4, 654)	266 (4, 766)	115 (4, 457)	62 (1, 190)	24 (0, 73)	237 (3, 723)	41 (0, 111)
2005	542 (10, 1709)	242 (6, 728)	301 (4, 981)	119 (5, 510)	69 (0, 288)	31 (0, 104)	274 (3, 757)	48 (0, 164)
2006	588 (8, 2013)	263 (3, 951)	325 (5, 1062)	132 (1, 697)	77 (0, 259)	35 (0, 105)	289 (3, 816)	55 (0, 187)
2007	679 (12, 2174)	305 (7, 955)	374 (5, 1219)	155 (2, 516)	88 (1, 318)	40 (0, 132)	326 (4, 1043)	70 (0, 214)
2008	764 (21, 1944)	349 (10, 960)	415 (11, 984)	170 (3, 470)	95 (2, 327)	43 (0, 138)	367 (10, 1043)	89 (0, 242)
2009	955 (28, 2703)	435 (13, 1265)	519 (15, 1438)	197 (4, 550)	118 (4, 445)	67 (0, 306)	459 (10, 1249)	113 (0, 266)
2010	981 (19, 3444)	447 (9, 1701)	534 (10, 1743)	211 (10, 517)	118 (1, 574)	63 (0, 389)	468 (6, 1734)	120 (0, 262)
2011	1026 (36, 2753)	469 (16, 1417)	558 (12, 1409)	223 (16, 576)	121 (3, 530)	63 (0, 280)	494 (6, 1293)	125 (0, 313)
Total	713 (8, 3440)	322 (3, 1701)	390 (4, 1743)	159 (1, 697)	89 (0, 574)	43 (0, 389)	346 (1, 1734)	77 (0, 313)
P for trend	0.0002	0.0002	0.0002	0.0002	0.0003	0.0016	0.0002	0.0002

Meteorological variables (mean (range))		Air pollutants (mean (range))			
Temperature (°C)	Humidity (%)	PM ₁₀ (µg/m ³)	O ₃ (ppb)	NO ₂ (ppb)	
2003	12.86 (−12.76, 26.98)	64.60 (26.62, 95.79)	68.92 (11.68, 248.17)	23.83 (1.93, 75.81)	38.22 (14.96, 90.34)
2004	12.34 (−14.00, 30.43)	62.00 (27.79, 95.75)	60.67 (10.27, 289.50)	24.08 (2.51, 78.06)	36.85 (12.50, 77.23)
2005	12.12 (−10.30, 30.10)	60.65 (21.08, 93.37)	58.20 (10.84, 203.53)	29.85 (4.04, 97.00)	34.05 (12.49, 68.87)
2006	13.05 (−11.57, 29.60)	60.61 (23.95, 96.00)	59.37 (10.93, 869.12)	29.32 (2.56, 78.10)	36.03 (12.21, 65.99)
2007	13.27 (−6.49, 28.67)	62.24 (24.00, 92.91)	60.95 (11.43, 438.28)	30.09 (2.57, 107.11)	37.94 (12.85, 92.02)
2008	12.95 (−9.17, 30.04)	59.45 (19.41, 93.83)	54.97 (11.63, 311.62)	31.64 (3.19, 93.92)	37.68 (12.69, 82.15)
2009	12.94 (−10.76, 29.15)	62.10 (28.25, 93.66)	53.92 (8.96, 298.02)	34.88 (3.23, 98.46)	35.29 (12.88, 78.36)
2010	12.14 (−13.15, 29.23)	62.89 (25.66, 96.25)	49.03 (9.03, 216.03)	31.27 (2.24, 109.47)	33.55 (10.90, 71.71)
2011	12.07 (−14.56, 28.77)	59.53 (24.00, 93.08)	46.89 (5.04, 272.33)	30.95 (3.19, 92.41)	32.79 (9.07, 75.86)
Total	12.75 (−14.57, 30.43)	61.46 (19.42, 96.25)	56.98 (5.04, 869.12)	29.54 (1.93, 109.47)	1.84 (9.07, 92.02)

increasing trend with seasonal variation for the total and all of the subgroups.

Summary statistics for hospital visit count, meteorological, and air pollutants variables are presented in Table 1. For the total study period, the daily mean hospital visit counts were 713 (8, 3440) for total, 322 (3, 1701) for male, 390 (4, 1743) for female, 159 (1, 697) for 0–6 years, 89 (0, 574) for 7–12 years, 43 (0, 389) for 13–18 years, 346 (1, 1734) for 19–64 years, and 77 (0, 313) for older than 64 years. Daily mean hospital visit count is roughly increased by 2.5 fold from 408 in 2003 to 1026 in 2011 for the total population. The largest increment of hospital visit was shown in elderly group with roughly a 4.0 fold increase from 31 in 2003 to 125 in 2011. The trend test of hospital visit count shows significant monotonic increase for total and for all of the subgroups. The mean temperature and humidity were 12.75 °C and 61.46 %, respectively. Mean temperature and humidity of each year were not significantly varied during the study period. Mean ambient concentration of PM₁₀ and NO₂ were 56.98 µg/m³ and 35.84 ppb, respectively, and

maximum of 8-hour moving average of O₃ was 29.54 ppb. The mean ambient concentration of PM₁₀ and NO₂ shows decreasing trend (from 68.92 µg/m³ in 2003 to 46.89 µg/m³ in 2011 for PM₁₀ and from 38.22 ppb in 2003 to 32.79 ppb in 2011 for NO₂), but O₃ showed increasing trend (from 23.83 ppb in 2003 to 30.95 ppb in 2011). The trend of mean temperature, relative humidity, and air pollutants (PM₁₀, NO₂, and O₃) were presented in the supplementary data (Fig. D).

Fig. 2 depicts the trend of hospital visit rate per 1,000,000 and the composition of AR patients by age-group and year. To calculate hospital visit rate, mid-year population of each year was used. Hospital visit rates per 1,000,000 have steadily increased over time for all age-group. Relatively higher increment hospital visit rate was observed in the 0–6 years population (from 40.25/1,000,000 in 2003 to 83.62/1,000,000 in 2011) followed by 7–12 years (from 15.46/1,000,000 in 2003 to 36.36/1,000,000 in 2011) and elderly population (from 5.79/1,000,000 in 2003 to 23.11/1,000,000 in 2011). Despite the increasing trend of hospital visit rates in the children population (0–12 years), the proportion of

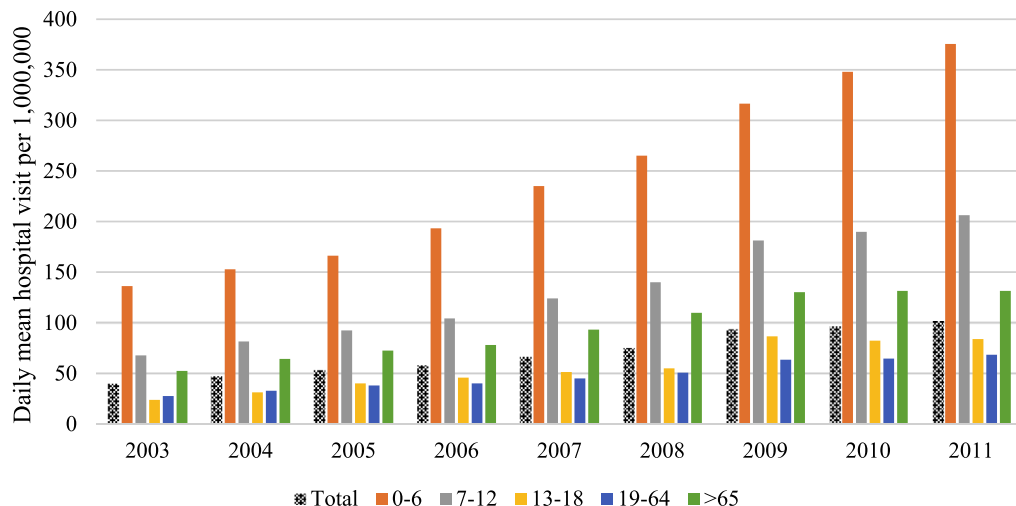


Fig. 2. The trend of hospital visit rates per 1,000,000 for AR in total and specific age-group for the period of 2003 to 2011 in Seoul.

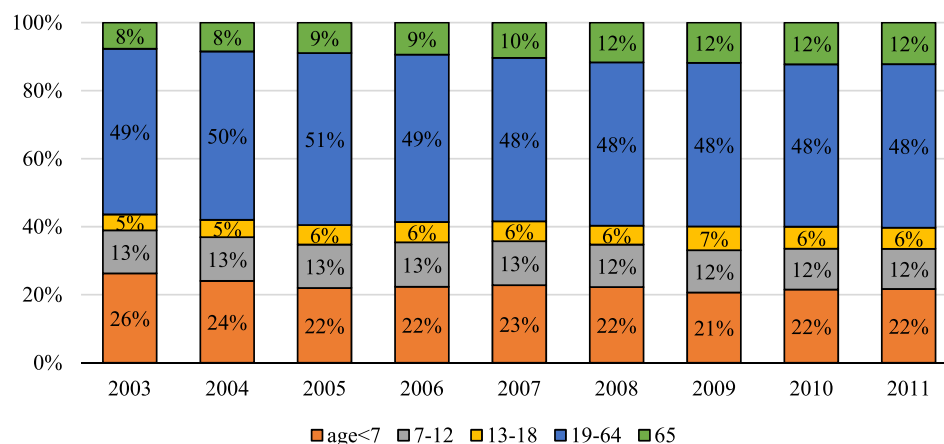


Fig. 3. The proportions of each age-group of hospital visit by AR in each year for the period of 2003 to 2011 in Seoul.

AR patients belonging to this population has decreased over time (from 26.28% in 2003 to 21.70% in 2011 for 0–6 years and from 12.66% in 2003 to 11.83 in 2011 for 7–12 years) (Fig. 3). Whereas the proportion of patients belonging to the elderly population (>64 years) has increased (from 7.07% in 2003 to 12.21% in 2011). For the 13–18 years group, the proportion of AR patients increased until 2009 (from 4.65% in 2003 to 7.01% in 2009) and then showed a decreasing pattern (6.00% in 2011). For 19–64 years, the proportion of AR patients are relatively stable than other age groups. The decreasing trend of AR patients proportion in children (0–12 years) and increasing trend in elderly (>64 years) might be explained by the aging phenomenon in Korea.

Summary statistics for daily hospital visit counts by AR, meteorological, and air pollutants variables for the whole study period and for the season specific periods are described in Table 2. The season-specific daily mean hospital visit counts were 727 (14, 2057) for spring, 887 (15, 3444) for autumn, and 733 (8, 2331) for winter season. In the autumn season, daily mean counts of hospital visits were greater than other two seasons in total and all subgroups. The season-specific mean temperature were 11.91 °C (−4.99, 25.15) for spring, 15.04 °C (−4.23, 27.00) for autumn, and −0.44 °C (−14.57, 12.24) for winter season. The humidity in spring and winter season were relatively lower than autumn. For air pollutants, the ambient concentration were lower in autumn season except for O₃. PM₁₀ and O₃ were higher in spring season and NO₂ was higher in winter season.

In Fig. 4, the estimated relative risks (RRs) of cold temperature at −1.073 °C with referent to 7.9 °C (10th percentile of mean temperature) are depicted with consideration for various lag structures by total and subgroup for the whole and season specific periods without adjustment of air pollutants. Significant cold effects were found

except for 0–6 and 13–18 years group. In total population, the RRs are stabilized after consideration of 3-days delayed effect (lag03, 1.094(95% CI: 1.037, 1.153)). Such a pattern of RRs was also found in male (1.100(95% CI: 1.010, 1.163)), female (1.088 (95% CI: 1.033, 1.146)), and the adult (19–64 years, 1.113 (95% CI: 1.059, 1.170)) population. For 0–6 years group, although it was not statistically significant, the greatest effect was found at a 3-days lag structure (lag03, 1.067(95% CI: 0.990, 1.151)) and showed decreasing pattern with increase of considered lag periods. For 7–12 and 13–18 years group, the estimated RRs showed increasing pattern with increases of considered lag periods (lag10, 1.122 (95% CI: 1.008, 1.250) for 7–12 years and 1.070 (95% CI: 0.948, 1.208) for 13–18 years). For elderly population, cold temperature effects were increased with increase of considered lag periods and showed greatest effect at the 7-days lag structure (lag07, 1.105 (95% CI: 1.008, 1.176)).

The season specific estimated RRs showed somewhat different estimates compared to whole study period. For the spring season, relatively greater effect was found compared to total period. However, for the younger population, we could not find statistically significant cold temperature effect. For the adult population, the estimated RR was stabilized when 3-days lag structure was considered (1.269 (95%CI: 1.118, 1.440)), while for the elderly population the estimated RRs were increased with increase of considered lag period and showed greatest effect at the 7-days lag structure (1.217 (95%CI: 1.014, 1.461)). For the autumn season, the estimated RR was increased with increasing of considered lag period for the total and all of subgroup. In the total population, the greatest effect was found in the model adjusting 10-days lag structure (lag10, 1.744 (95% CI: 1.301, 2.339)). For the winter season, estimated RRs were not statistically significant and even it showed

Table 2

Summary statistics for daily hospital visit counts by AR, meteorological, and air pollutants variables for the total and season specific period from 2003 to 2011 in Seoul.

		Total period	Spring	Autumn	Winter
		Mean (range)	Mean (range)	Mean (range)	Mean (range)
Total (person/day)		713 (8, 3440)	727 (14, 2057)	887 (15, 3444)	733 (8, 2331)
Gender (person/day)	Male	322 (3, 1701)	327 (7, 996)	402 (6, 1701)	327 (3, 1043)
	Female	390 (4, 1743)	395 (7, 1092)	486 (9, 1743)	406 (4, 1288)
Age (person/day)	age ≤ 6	159 (1, 697)	156 (3, 516)	200 (4, 697)	155 (2, 498)
	7 ≤ age < 13	89 (0, 574)	90 (1, 322)	115 (2, 574)	89 (0, 288)
	13 ≤ age < 19	43 (0, 389)	44 (0, 181)	61 (0, 389)	35 (0, 132)
	19 ≤ age < 65	346 (1, 1734)	349 (3, 1103)	429 (7, 1734)	367 (1, 1165)
	age ≥ 65	77 (0, 313)	82 (0, 285)	82 (0, 268)	87 (0, 313)
	Temperature (°C)	12.75 (−14.57, 30.43)	11.91 (−4.99, 25.15)	15.04 (−4.23, 27.00)	−0.44 (−14.57, 12.24)
Humidity (%)		61.46 (19.42, 96.25)	55.88 (19.42, 95.33)	62.32 (25.29, 95.79)	55.49 (27, 96.25)
PM ₁₀ (μg/m ³)		56.98 (5.04, 869.12)	69.89 (9.27, 869.12)	48.42 (5.04, 192.83)	64.38 (8.78, 298.02)
O ₃ (ppb)		29.54 (1.93, 109.47)	38.19 (2.57, 91.21)	23.52 (1.93, 71.60)	16.07 (2.24, 40.60)
NO ₂ (ppb)		35.84 (9.07, 92.02)	38.28 (12.21, 82.15)	35.46 (9.07, 90.02)	41.13 (14.21, 79.47)

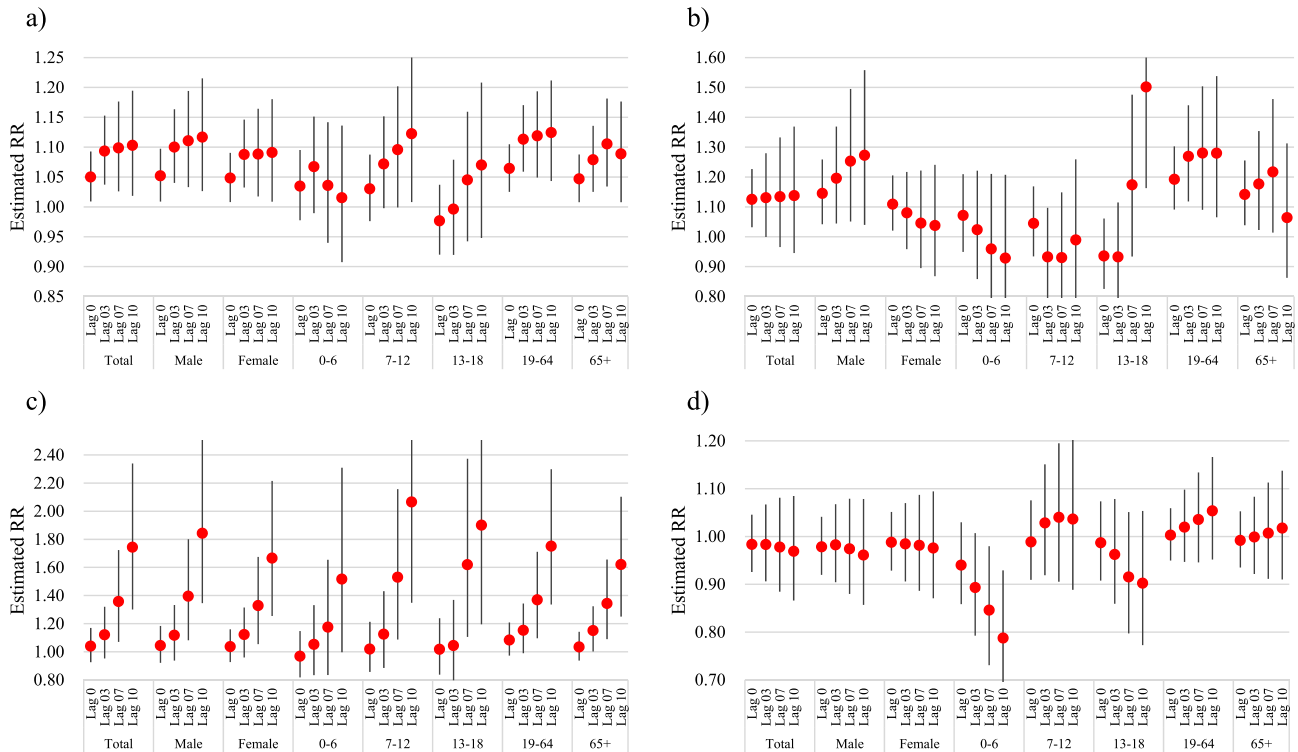


Fig. 4. The estimated relative risk of cold temperature at -1.703°C with reference to 7.933°C (10th percentile) without adjusting for air pollutants, a) during the whole, b) spring, c) autumn, and d) winter of study periods.

protective effect for the group < 7 years old. In the season specific analysis, the greatest and statistically significant effects of cold temperature on AR were found for the autumn season for total and all subgroup analysis.

To assess possible confounding effect by air pollutants (PM_{10} , O_3 and NO_2), we additionally adjusted an air pollutant in the model respectively. After adjusting for air pollutants, the estimated RRs were not significantly differed with estimates from unadjusted model (supplemental material Table A–D).

4. Discussion

In our study, we assessed the trend of hospital visit by AR, and we estimated cold temperature effect on hospital visit by AR using the national health insurance claim data for the 9 year period (2003–2011)

in Seoul, Korea. As a result, we found the increasing trend of daily mean hospital visit counts and rates per 1,000,000 over time and significant cold temperature effect especially at autumn season.

The number of hospital visit count showed significant increasing trend with seasonal variation during the 9-years study period (2003–2011). The largest increment of hospital visit by AR was found for the elderly population. The hospital visit rates per 1,000,000 have also increased over time, especially in the elderly population. In this population, visit rates by 2011 have roughly a 4-fold increased since 2003 (from 5.79/1,000,000 in 2003 to 23.11/1,000,000 in 2011). Moreover, the composition of elderly population in the total patient has increased over time (from 7.07% in 2003 to 12.21% in 2011). Relatively greater increases of hospital visit rate in the elderly population rather than other age groups might be partially explained by the aging phenomenon in Korea. The proportion of elderly population (age > 64) in

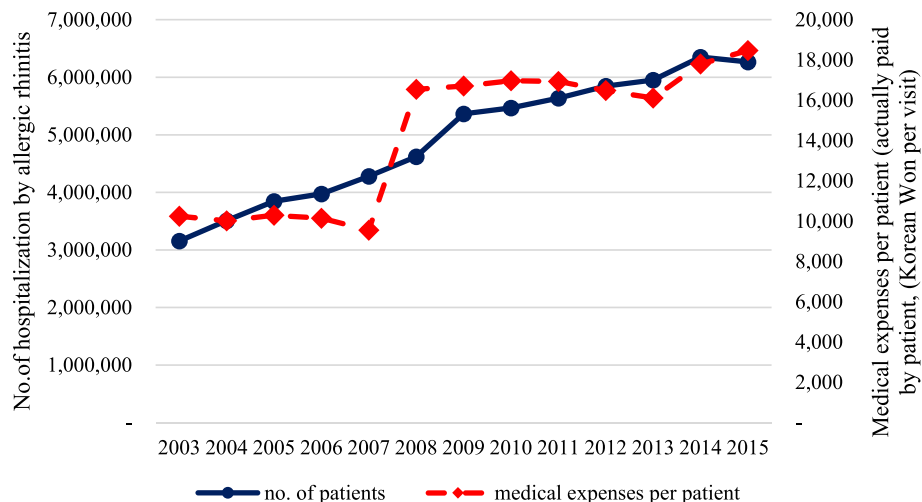


Fig. 5. Number of patients who visited hospital by allergic rhinitis and actually paid medical expenses by patient in Korea (Korean Won).

Seoul has increased from 5.86% from 2003 to 9.82% in 2011. With an expectation of increase in the elderly population by aging phenomenon, valid policies to reduce burden of AR should be implemented in the near future, especially for elderly population. For the younger population (age < 19), the higher hospital visit rate per 1,000,000 was found in the young children population (age < 7). In children population, it is not easy to distinguish between symptoms of AR and non-allergic rhinitis triggered by drug or viral infection (J.S. Kim et al., 2015b). Therefore, high chances of misdiagnosed of AR in children population might partially contribute to the higher hospital visit rates in this age group.

According to the 'Health Insurance Statistical Yearbook' for the period of 2003 to 2015, total number of person who visited hospital due to AR and actually paid medical expenses by patient per visit are steadily increased (Fig. 5). Nationally, in 2015, number of hospital visit patients have nearly doubled in the past 12 years. In our study, hospital visit counts in 2011 showed nearly a 2.5-fold increase in the past 9 years (from 2 to 4-fold increase in each age group). Although our results could not be directly compared with national data, increase of hospital visit rate in Seoul is relatively larger than national increment.

Increases of AR prevalence have been reported from studies that were conducted in various countries (Patil et al., 2015; Björkstén et al., 2008; Sultész et al., 2017; De Marco et al., 2012; Bråbäck et al., 2004). It is speculated that climate changes and increases in greenhouse gases such as CO₂ might influence aeroallergens through distribution of plants and amount and season of pollen (Beggs, 2004). Pollen is a known major risk factor for AR. Kim et al. (2012) has investigated the trend of pollen counts in Seoul for the period of 1999 to 2009 and they found the increasing trend of pollen counts both tree and weed pollen count with the increasing trend of sensitization rates to pollen in children who suffered from allergic diseases (Kim et al., 2012). Another study has also investigated changes of aeroallergens sensitization in children from tertiary referral hospital in Seoul in 2000, 2005 and 2010, and they found significant increasing trend of sensitization rates to tree pollens, cat dander, and dog dander (Jung et al., 2014). Lee et al. (2011) has also found the increasing trend of sensitization rates to pollen allergens for all age groups who suffer from allergic diseases in Gyeonggi province, Korea (Lee et al., 2011). Such an increase in pollen count coupled with an increased sensitization rate to pollens or animal dander in Seoul, Korea, might partially explain the increasing trend of hospital visit by AR.

In addition to effect of aeroallergens such as pollen on respiratory allergic diseases, meteorological conditions are also suspected as a risk factor on onset or exacerbation of existing diseases (Hajat and Haines, 2002; Mäkinen et al., 2009; Fitzgerald et al., 2014). Although possible mechanisms about cold temperature effect on allergic respiratory diseases are suggested by some studies (Koskela, 2007; Graudenz et al., 2007), it is still unclear. In our study, the estimated cold temperature effect in the total population was 1.094 (lag03, 95% CI: 1.037, 1.153). In the total population, the estimated RRs stabilized when considering of 3-days delayed effect. However, within the younger population (0–6, 7–12 and 13–18 years), considerable difference in patterns of estimated RRs by various lag structure were detected. The younger population were categorized based on the Korean Education System (preschool children (0–6 years), elementary (7–12 years), and middle and high school (13–18 years)). Because the differences in educational activity or outdoor activity by the educational system, different exposure patterns by the system might partially explain the different cold temperature effect on hospital visit by AR.

In the stratified analysis by season, we found seasonally different cold temperature effect on AR. In the autumn season, statistically significant cold temperature effects were found with gradual increases of estimated risks with increment of considered lag periods. However, in the winter season, although it was not statistically significant, protective cold temperature effects were shown. The protective effect in winter season might be partially due to changes

of behavioral patterns in accordance with the change of season. Behavioral change can modify an exposure pattern to cold temperature. In the winter season, expected continuing of outdoor cold temperature will reduce outdoor activity and people may be more cautious in protecting their health status especially for someone who already has respiratory related symptoms. In the study of investigating association between cold spell and hospitalization by asthma, cold spell in winter season was significantly associated with decline of mean hospitalization by asthma (Fitzgerald et al., 2014). Behavioral changes during the winter cold spell such as adherence to medical guidelines and limiting exposure to cold temperature may prevent exacerbation of asthma (Fitzgerald et al., 2014). Therefore, behavioral changes with respect to changing weather conditions might partially explain the differences between cold temperature effects by the season. In a study that evaluated the effect of environmental factors affecting on the number of clinic consultations for non-allergic rhinitis in Japan, different meteorological factors were identified by the different seasons (Hoshino et al., 2015). In autumn season, mean temperature and mean vapor pressure were identified as major factors affecting non-allergic rhinitis, however, in spring-summer season temperature difference and air pollutants factors were identified (Hoshino et al., 2015). This result suggests the possibility that rhinitis symptoms may be triggered by different meteorological factors according to the season. This possibility might also partially explain the seasonal difference of cold temperature effect on AR in our study.

Air pollutants were identified as risk factors for increasing the risk of hospital visits or admissions for allergic respiratory diseases (Khafaie et al., 2016; Deng et al., 2016a; Lee et al., 2002; Takizawa, 2011; D'amato, 2002; Deng et al., 2016b). Since we aimed to investigate the cold temperature effect, we only considered air pollutants as potential confounder in our study. To identify the potential confounding effect by air pollutants, we additionally included air pollutants (PM₁₀, O₃, and NO₂) respectively in the model. After consideration of the each air pollutants, the estimated RRs were not considerably different compare to the estimates from unadjusted model. Even though our study result shows suggestive evidence of independent cold temperature effect on AR, cautious interpretation should be needed because various outdoor and/or indoor allergens that are related to cold temperature can be a symptom trigger of AR. Therefore, to identify independent temperature effect on AR, temperature related aeroallergen data should be obtained and additionally adjusted in the further analysis.

Our study have several limitations. First, despite the spatial variations of personal exposure to temperature, we used one monitoring station data as a surrogate for personal exposure to temperature or air pollutants. Therefore, measurement error for these variables were inevitable. However, temperature distribution is not likely to vary in a single city within a single day, the results of our study might not be substantially affected by the measurement error of temperature exposure. Furthermore, because personal exposure data were impossible to obtain such a long period (9-year) for all study subjects, the best way to estimate exposure was to use the data from monitoring station data. Second, in our study we only used the mean temperature as a daily representative value to estimate cold temperature effect. Temperature variability (DTR; diurnal temperature change) is a strong risk factor for admission due to respiratory infection (Carreras et al., 2015). Therefore, in a further analysis we should consider other temperature metrics such as intra or inter-daily temperature change as daily representative values to identify related meteorological factors attributable to burden of AR.

Nevertheless, our study have several strengths. Studies identifying the association between temperature and allergic respiratory diseases mainly have focused on the total respiratory diseases or relatively more severe diseases such as hospitalization by asthma. Therefore, studies investigating the association between AR and temperature are relatively sparse. Moreover, to the best of our knowledge, our study is the

first study investigating the association between AR and temperature in Seoul, Korea. More studies should be conducted to better understanding on temperature effect on allergic respiratory diseases.

5. Conclusion

In conclusion, we analyzed the trend of hospital visit by AR for the period of 2003 to 2011 in Seoul, Korea and estimated the cold temperature effect on hospital visit by AR with consideration of various lag structures. As a result, we found the increasing trend of hospital visit by AR especially in the elderly population and suggestive evidence of cold temperature effect on AR especially in autumn season.

AR has been an issue in public health area in both developed and developing countries due to their high prevalence and economic burden. In Korea, disease and economic burden of AR still increase. To reduce this increasing burden, more studies, which investigate the risk factors responsible to newly onset or triggering of AR, should be conducted. Those study results with our study's one will be used as evidentiary materials for establishing valid health or environmental policies to reduce health and economic burden of AR. In our study, as one of study for investing possible risk factor of AR, we provided the suggestive evidence of cold temperature effect. To provide more credible evidences about temperature effect on AR, further studies are needed.

Acknowledgement

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Declaration of interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.scitotenv.2018.03.166>.

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Appendix A. Supplementary Data

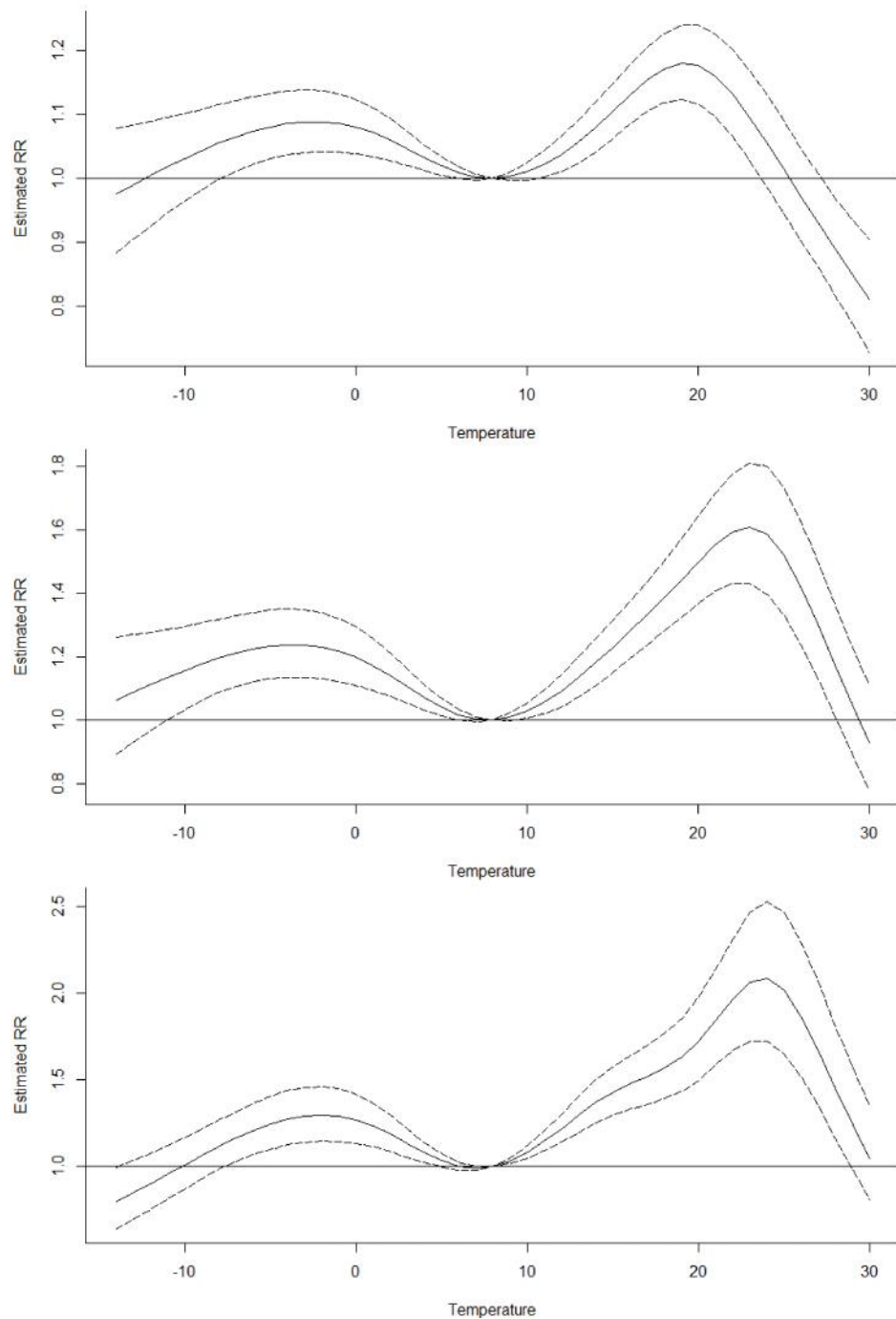


Figure A. Estimated relative risks of temperature on hospital visit by AR: a) no lag effect, b) 10 days, and c) 21 days lag effect.

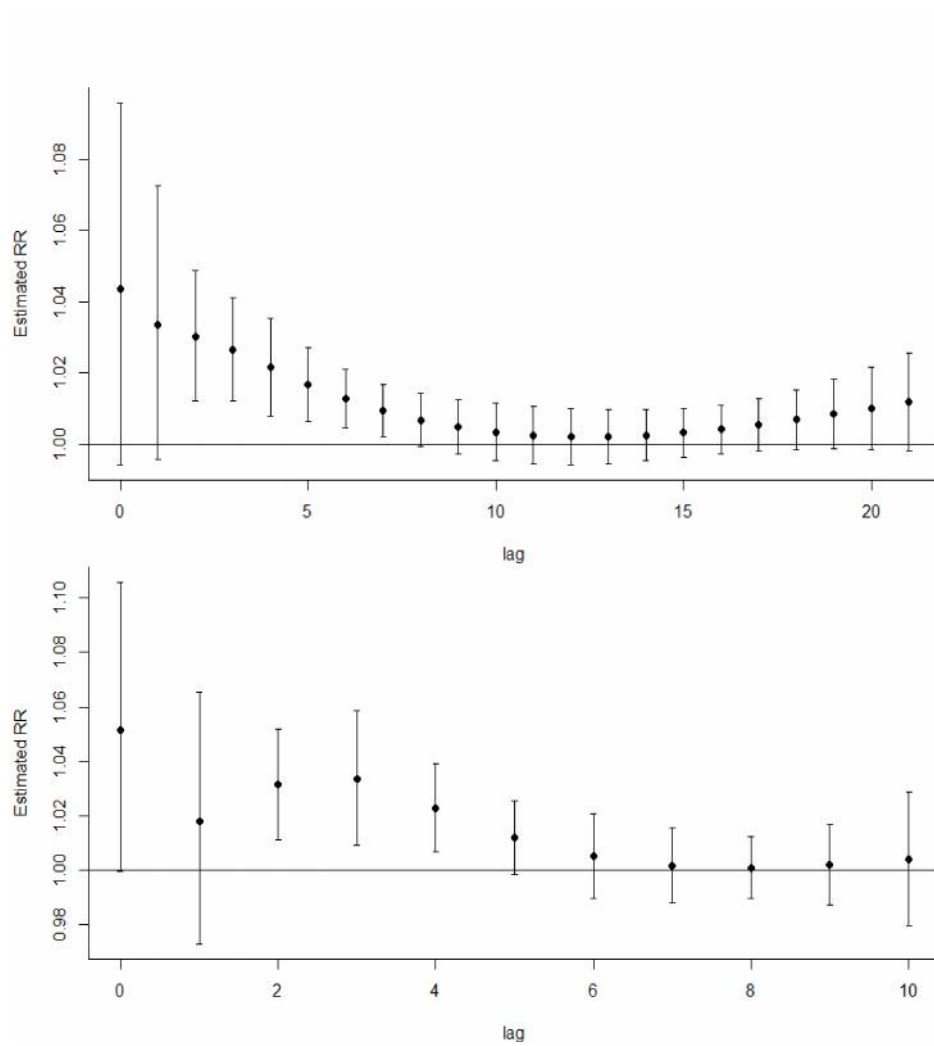
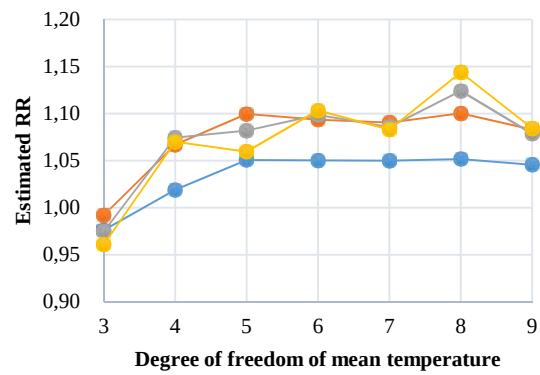
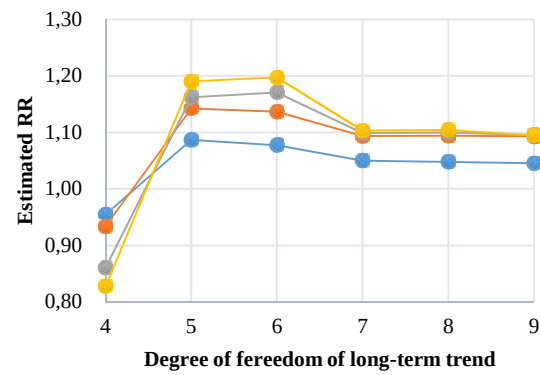


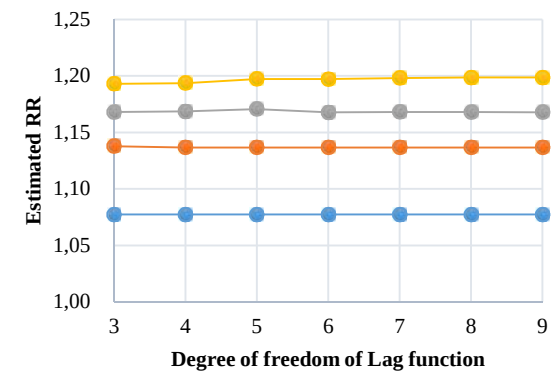
Figure B. Estimated relative risks of temperature for the considered lag period: a) for the 21 days and b) 10 days lag period before the hospital visit



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Figure C. The results of sensitivity analysis by varing a degree of freedom for each considered variables

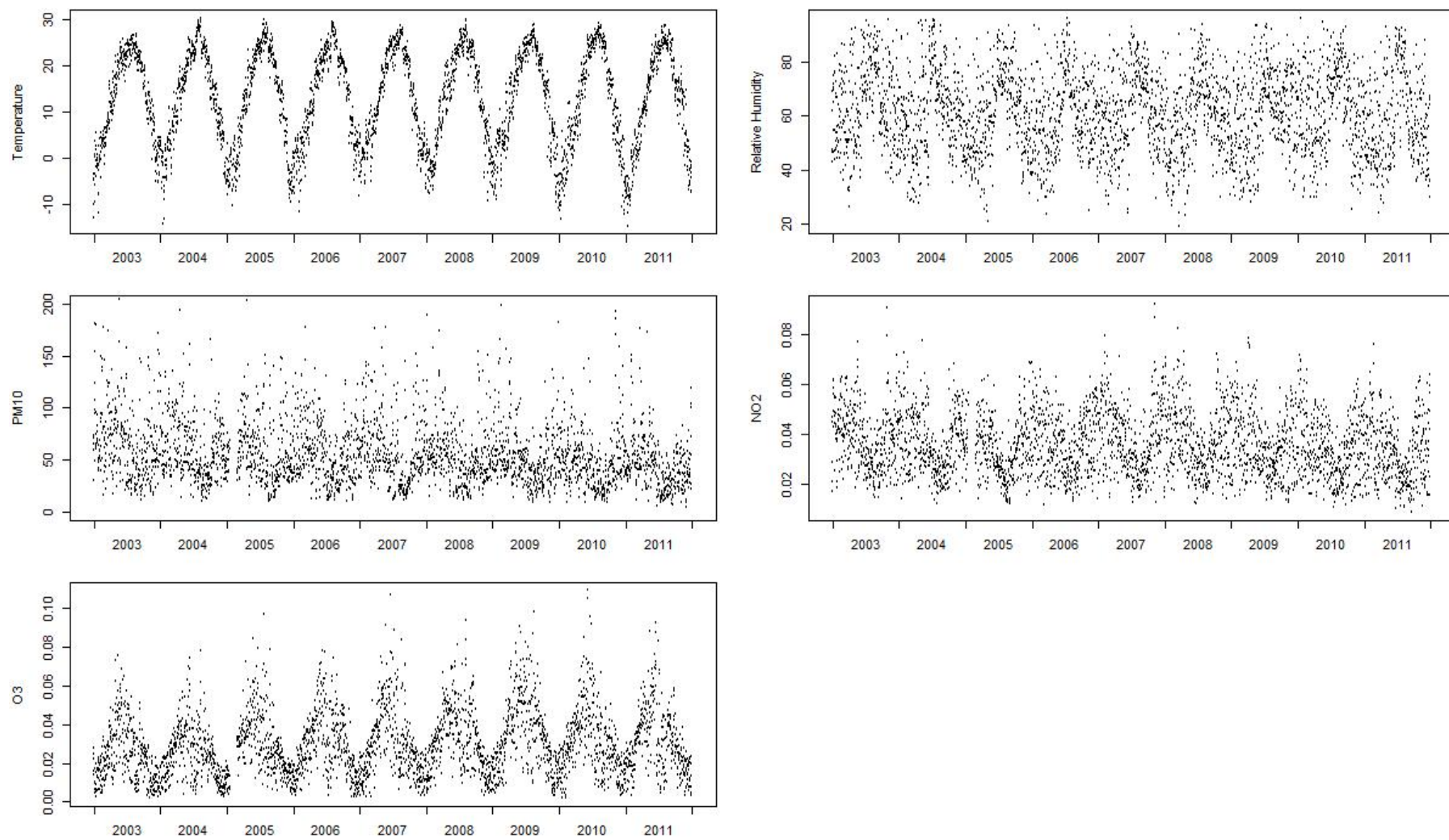


Figure D. The trend of mean temperature, relative humidity, and air pollutants (PM10, NO2, and O3) for the period of 2003 to 2011.

Table A. The estimated relative risk of cold temperature at -1.703 °C with referent to 7.933°C (10th percentile) with adjustment of air pollutants respectively in the total study period.

Population	Lags	Without adjustment			With PM			With NO ₂			With O ₃		
		RR	RR_Low	RR_High	RR	RR_Low	RR_High	RR	RR_Low	RR_High	RR	RR_Low	RR_High
Total	Lag 0	1.050	1.009	1.093	1.032	0.991	1.075	1.030	0.987	1.074	1.032	0.992	1.074
	Lag 03	1.094	1.037	1.153	1.068	1.012	1.127	1.065	1.008	1.124	1.068	1.012	1.126
	Lag 07	1.099	1.026	1.176	1.061	0.989	1.137	1.059	0.988	1.136	1.059	0.988	1.135
	Lag 10	1.103	1.019	1.195	1.050	0.968	1.140	1.051	0.968	1.141	1.048	0.966	1.137
Male	Lag 0	1.052	1.009	1.097	1.036	0.993	1.082	1.030	0.985	1.077	1.037	0.995	1.082
	Lag 03	1.100	1.040	1.163	1.081	1.021	1.144	1.076	1.015	1.140	1.081	1.021	1.143
	Lag 07	1.111	1.033	1.194	1.081	1.004	1.164	1.078	1.001	1.161	1.080	1.003	1.162
	Lag 10	1.117	1.026	1.215	1.076	0.987	1.174	1.076	0.986	1.174	1.074	0.985	1.171
Female	Lag 0	1.048	1.008	1.090	1.029	0.989	1.071	1.030	0.988	1.074	1.028	0.989	1.069
	Lag 03	1.088	1.033	1.146	1.058	1.004	1.116	1.056	1.001	1.114	1.057	1.003	1.114
	Lag 07	1.088	1.017	1.164	1.044	0.975	1.118	1.044	0.974	1.118	1.042	0.974	1.116
	Lag 10	1.091	1.009	1.180	1.029	0.950	1.116	1.031	0.951	1.117	1.027	0.948	1.113
0-6	Lag 0	1.035	0.978	1.095	1.032	0.973	1.094	1.018	0.958	1.083	1.025	0.968	1.086
	Lag 03	1.067	0.990	1.151	1.055	0.977	1.139	1.043	0.965	1.128	1.048	0.972	1.131
	Lag 07	1.036	0.940	1.142	1.013	0.919	1.118	1.004	0.910	1.108	1.005	0.912	1.107
	Lag 10	1.015	0.908	1.136	0.995	0.888	1.116	0.991	0.884	1.111	0.986	0.881	1.103
7-12	Lag 0	1.030	0.976	1.087	1.022	0.967	1.080	1.007	0.951	1.067	1.013	0.959	1.069
	Lag 03	1.072	0.998	1.152	1.055	0.981	1.135	1.046	0.972	1.126	1.047	0.975	1.126
	Lag 07	1.096	0.999	1.202	1.062	0.967	1.166	1.055	0.960	1.159	1.054	0.960	1.156
	Lag 10	1.122	1.008	1.250	1.074	0.963	1.198	1.072	0.961	1.196	1.068	0.958	1.191
13-18	Lag 0	0.977	0.920	1.037	0.965	0.908	1.024	0.969	0.910	1.032	0.950	0.895	1.008
	Lag 03	0.996	0.920	1.079	0.967	0.893	1.048	0.966	0.890	1.047	0.955	0.882	1.035
	Lag 07	1.045	0.942	1.159	0.986	0.888	1.095	0.986	0.888	1.096	0.974	0.878	1.081
	Lag 10	1.070	0.948	1.208	0.980	0.867	1.109	0.985	0.870	1.115	0.974	0.861	1.102
19-64	Lag 0	1.064	1.025	1.105	1.037	0.998	1.077	1.040	0.999	1.082	1.043	1.005	1.083
	Lag 03	1.113	1.059	1.170	1.076	1.023	1.132	1.077	1.023	1.133	1.081	1.028	1.136
	Lag 07	1.119	1.049	1.193	1.067	1.000	1.140	1.070	1.002	1.143	1.070	1.003	1.143
	Lag 10	1.124	1.043	1.212	1.056	0.978	1.141	1.060	0.981	1.145	1.056	0.978	1.141
65+	Lag 0	1.047	1.008	1.088	1.035	0.995	1.076	1.038	0.996	1.081	1.040	1.000	1.080
	Lag 03	1.079	1.025	1.136	1.065	1.011	1.122	1.065	1.010	1.124	1.068	1.015	1.125
	Lag 07	1.105	1.034	1.182	1.086	1.015	1.162	1.086	1.014	1.162	1.089	1.018	1.164
	Lag 10	1.089	1.008	1.176	1.055	0.974	1.141	1.054	0.974	1.142	1.057	0.976	1.143

Table B. The estimated relative risk of cold temperature at -1.703 °C with referent to 7.933°C (10th percentile) with adjustment of air pollutants respectively in the spring season.

Population	Lags	Without adjustment			With PM			With NO ₂			With O ₃		
		RR	RR_Low	RR_High	RR	RR_Low	RR_High	RR	RR_Low	RR_High	RR	RR_Low	RR_High
Total	Lag 0	1.125	1.032	1.227	1.117	1.023	1.219	1.093	0.996	1.199	1.124	1.031	1.226
	Lag 03	1.131	0.999	1.280	1.130	0.998	1.279	1.126	0.993	1.278	1.122	0.991	1.271
	Lag 07	1.134	0.966	1.333	1.135	0.966	1.333	1.127	0.957	1.327	1.122	0.954	1.319
	Lag 10	1.138	0.946	1.369	1.137	0.945	1.368	1.134	0.941	1.367	1.120	0.930	1.349
Male	Lag 0	1.145	1.042	1.259	1.136	1.032	1.250	1.098	0.992	1.216	1.143	1.040	1.257
	Lag 03	1.196	1.045	1.369	1.194	1.043	1.368	1.182	1.030	1.357	1.182	1.032	1.355
	Lag 07	1.253	1.051	1.495	1.253	1.051	1.495	1.236	1.033	1.477	1.232	1.032	1.472
	Lag 10	1.273	1.040	1.558	1.272	1.039	1.557	1.261	1.028	1.546	1.245	1.016	1.525
Female	Lag 0	1.109	1.021	1.205	1.102	1.013	1.198	1.089	0.995	1.191	1.109	1.020	1.205
	Lag 03	1.080	0.958	1.217	1.080	0.958	1.217	1.082	0.958	1.223	1.076	0.954	1.213
	Lag 07	1.046	0.895	1.222	1.046	0.895	1.222	1.045	0.893	1.224	1.039	0.888	1.215
	Lag 10	1.038	0.868	1.241	1.037	0.867	1.240	1.040	0.869	1.246	1.027	0.858	1.229
0-6	Lag 0	1.071	0.949	1.209	1.065	0.942	1.204	1.016	0.892	1.157	1.068	0.946	1.205
	Lag 03	1.024	0.858	1.221	1.024	0.858	1.222	0.999	0.834	1.196	1.012	0.848	1.209
	Lag 07	0.959	0.760	1.211	0.960	0.760	1.211	0.933	0.737	1.180	0.942	0.745	1.191
	Lag 10	0.929	0.714	1.208	0.928	0.714	1.207	0.909	0.697	1.185	0.900	0.692	1.171
7-12	Lag 0	1.045	0.934	1.169	1.054	0.941	1.180	1.002	0.888	1.130	1.046	0.935	1.170
	Lag 03	0.933	0.793	1.097	0.939	0.798	1.104	0.918	0.778	1.083	0.932	0.792	1.097
	Lag 07	0.930	0.753	1.149	0.932	0.755	1.151	0.916	0.740	1.135	0.928	0.750	1.148
	Lag 10	0.989	0.777	1.259	0.987	0.775	1.256	0.975	0.765	1.244	0.986	0.774	1.257
13-18	Lag 0	0.936	0.825	1.061	0.951	0.839	1.079	0.925	0.809	1.058	0.937	0.826	1.062
	Lag 03	0.932	0.780	1.115	0.941	0.788	1.125	0.928	0.774	1.114	0.931	0.778	1.114
	Lag 07	1.174	0.934	1.476	1.174	0.935	1.474	1.173	0.930	1.478	1.175	0.933	1.479
	Lag 10	1.502	1.163	1.940	1.490	1.155	1.924	1.492	1.153	1.931	1.509	1.166	1.952
19-64	Lag 0	1.192	1.091	1.302	1.173	1.073	1.282	1.172	1.066	1.289	1.191	1.090	1.301
	Lag 03	1.269	1.119	1.440	1.263	1.113	1.433	1.280	1.125	1.456	1.259	1.109	1.429
	Lag 07	1.280	1.090	1.504	1.279	1.089	1.502	1.287	1.094	1.515	1.265	1.076	1.487
	Lag 10	1.280	1.065	1.538	1.281	1.066	1.539	1.292	1.074	1.555	1.259	1.047	1.515
65+	Lag 0	1.142	1.039	1.255	1.129	1.026	1.243	1.107	0.999	1.226	1.140	1.037	1.254
	Lag 03	1.177	1.023	1.354	1.175	1.021	1.352	1.166	1.010	1.345	1.165	1.012	1.341
	Lag 07	1.217	1.014	1.461	1.217	1.014	1.461	1.200	0.997	1.444	1.201	0.999	1.444
	Lag 10	1.064	0.863	1.313	1.063	0.861	1.311	1.056	0.854	1.305	1.044	0.845	1.289

Table C. The estimated relative risk of cold temperature at -1.703 °C with referent to 7.933°C (10th percentile) with adjustment of air pollutants respectively in the autumn season.

Population	Lags	Without adjustment			With PM			With NO ₂			With O ₃		
		RR	RR_Low	RR_High	RR	RR_Low	RR_High	RR	RR_Low	RR_High	RR	RR_Low	RR_High
Total	Lag 0	1.040	0.926	1.169	1.043	0.927	1.174	1.047	0.928	1.180	1.042	0.928	1.171
	Lag 03	1.121	0.952	1.320	1.123	0.952	1.325	1.123	0.952	1.326	1.123	0.954	1.321
	Lag 07	1.358	1.070	1.724	1.358	1.069	1.725	1.361	1.071	1.729	1.377	1.085	1.748
	Lag 10	1.744	1.301	2.339	1.744	1.300	2.339	1.745	1.300	2.342	1.749	1.305	2.344
Male	Lag 0	1.044	0.921	1.184	1.048	0.923	1.190	1.048	0.921	1.192	1.046	0.923	1.186
	Lag 03	1.118	0.938	1.333	1.122	0.939	1.340	1.118	0.935	1.337	1.120	0.939	1.335
	Lag 07	1.395	1.081	1.801	1.395	1.080	1.802	1.395	1.080	1.802	1.412	1.094	1.824
	Lag 10	1.844	1.346	2.525	1.843	1.345	2.526	1.840	1.342	2.523	1.848	1.350	2.530
Female	Lag 0	1.037	0.926	1.160	1.039	0.927	1.164	1.045	0.931	1.174	1.039	0.928	1.162
	Lag 03	1.123	0.959	1.315	1.124	0.959	1.319	1.128	0.961	1.323	1.125	0.961	1.316
	Lag 07	1.329	1.054	1.674	1.328	1.053	1.675	1.333	1.057	1.682	1.349	1.070	1.700
	Lag 10	1.667	1.254	2.215	1.666	1.253	2.215	1.670	1.256	2.222	1.672	1.259	2.220
0-6	Lag 0	0.968	0.817	1.148	0.989	0.833	1.173	0.994	0.835	1.183	0.968	0.817	1.147
	Lag 03	1.053	0.833	1.332	1.081	0.853	1.370	1.076	0.848	1.365	1.054	0.834	1.333
	Lag 07	1.175	0.834	1.655	1.189	0.843	1.677	1.189	0.843	1.676	1.189	0.844	1.676
	Lag 10	1.517	0.997	2.309	1.524	1.001	2.323	1.528	1.003	2.329	1.518	0.998	2.310
7-12	Lag 0	1.020	0.857	1.213	1.036	0.869	1.235	1.018	0.852	1.217	1.023	0.860	1.217
	Lag 03	1.125	0.885	1.431	1.152	0.904	1.469	1.126	0.882	1.436	1.128	0.888	1.434
	Lag 07	1.531	1.087	2.157	1.544	1.095	2.178	1.526	1.082	2.152	1.563	1.109	2.202
	Lag 10	2.066	1.349	3.166	2.080	1.356	3.189	2.057	1.341	3.155	2.076	1.356	3.180
13-18	Lag 0	1.018	0.837	1.238	1.035	0.849	1.262	1.034	0.845	1.265	1.018	0.837	1.238
	Lag 03	1.045	0.797	1.369	1.077	0.820	1.416	1.062	0.807	1.397	1.044	0.797	1.369
	Lag 07	1.620	1.105	2.374	1.639	1.117	2.404	1.632	1.112	2.394	1.620	1.104	2.377
	Lag 10	1.901	1.195	3.025	1.904	1.196	3.032	1.913	1.202	3.047	1.905	1.197	3.033
19-64	Lag 0	1.084	0.972	1.209	1.073	0.961	1.198	1.083	0.968	1.212	1.086	0.974	1.211
	Lag 03	1.153	0.989	1.343	1.136	0.973	1.326	1.147	0.982	1.339	1.155	0.992	1.345
	Lag 07	1.369	1.096	1.711	1.359	1.087	1.698	1.369	1.094	1.712	1.393	1.114	1.740
	Lag 10	1.752	1.336	2.298	1.742	1.328	2.285	1.748	1.331	2.295	1.757	1.341	2.304
65+	Lag 0	1.034	0.937	1.141	1.023	0.926	1.130	1.026	0.926	1.136	1.035	0.938	1.142
	Lag 03	1.151	1.002	1.323	1.133	0.984	1.304	1.137	0.987	1.310	1.152	1.002	1.324
	Lag 07	1.344	1.090	1.656	1.329	1.078	1.639	1.335	1.082	1.647	1.349	1.094	1.663
	Lag 10	1.621	1.250	2.102	1.610	1.242	2.089	1.605	1.237	2.084	1.622	1.251	2.104

Table D. The estimated relative risk of cold temperature at -1.703 °C with referent to 7.933°C (10th percentile) with adjustment of air pollutants respectively in the winter season.

Population	Lags	Without adjustment			With PM			With NO ₂			With O ₃		
		RR	RR_Low	RR_High	RR	RR_Low	RR_High	RR	RR_Low	RR_High	RR	RR_Low	RR_High
Total	Lag 0	0.984	0.925	1.046	0.984	0.925	1.046	0.972	0.913	1.035	0.977	0.920	1.039
	Lag 03	0.983	0.906	1.067	0.983	0.906	1.067	0.979	0.903	1.062	0.984	0.908	1.067
	Lag 07	0.978	0.885	1.081	0.978	0.885	1.081	0.983	0.891	1.085	0.978	0.886	1.080
	Lag 10	0.969	0.866	1.085	0.969	0.866	1.085	0.980	0.877	1.094	0.970	0.868	1.084
Male	Lag 0	0.978	0.920	1.041	0.980	0.921	1.042	1.043	0.927	1.174	0.973	0.915	1.035
	Lag 03	0.983	0.904	1.068	0.989	0.912	1.074	1.123	0.952	1.325	0.985	0.907	1.069
	Lag 07	0.974	0.880	1.079	0.984	0.890	1.088	1.358	1.069	1.725	0.975	0.881	1.078
	Lag 10	0.961	0.857	1.078	0.976	0.871	1.092	1.744	1.300	2.339	0.963	0.860	1.078
Female	Lag 0	0.988	0.929	1.051	0.987	0.928	1.050	0.980	0.921	1.042	0.981	0.922	1.044
	Lag 03	0.984	0.906	1.070	0.990	0.912	1.075	0.989	0.912	1.074	0.984	0.906	1.069
	Lag 07	0.982	0.886	1.087	0.992	0.897	1.097	0.984	0.890	1.088	0.982	0.887	1.086
	Lag 10	0.976	0.871	1.094	0.989	0.884	1.108	0.976	0.871	1.092	0.976	0.872	1.093
0-6	Lag 0	0.940	0.858	1.030	0.944	0.862	1.034	0.987	0.928	1.050	0.938	0.856	1.028
	Lag 03	0.893	0.792	1.007	0.903	0.802	1.017	0.990	0.912	1.075	0.899	0.797	1.013
	Lag 07	0.846	0.731	0.979	0.860	0.743	0.994	0.992	0.897	1.097	0.850	0.735	0.984
	Lag 10	0.788	0.668	0.929	0.803	0.682	0.945	0.989	0.884	1.108	0.791	0.671	0.933
7-12	Lag 0	0.989	0.909	1.076	0.992	0.913	1.078	0.944	0.862	1.034	0.978	0.900	1.063
	Lag 03	1.028	0.919	1.151	1.044	0.935	1.165	0.903	0.802	1.017	1.033	0.925	1.154
	Lag 07	1.040	0.906	1.195	1.051	0.918	1.203	0.860	0.743	0.994	1.037	0.905	1.188
	Lag 10	1.037	0.888	1.210	1.046	0.900	1.217	0.803	0.682	0.945	1.033	0.888	1.201
13-18	Lag 0	0.987	0.908	1.073	0.983	0.904	1.069	0.992	0.913	1.078	0.973	0.894	1.058
	Lag 03	0.962	0.859	1.078	0.962	0.859	1.077	1.044	0.935	1.165	0.953	0.851	1.068
	Lag 07	0.915	0.797	1.051	0.918	0.800	1.053	1.051	0.918	1.203	0.904	0.788	1.038
	Lag 10	0.902	0.773	1.053	0.908	0.779	1.060	1.046	0.900	1.217	0.893	0.766	1.042
19-64	Lag 0	1.003	0.950	1.059	1.001	0.948	1.057	0.983	0.904	1.069	0.995	0.942	1.051
	Lag 03	1.020	0.947	1.098	1.022	0.950	1.100	0.962	0.859	1.077	1.016	0.944	1.094
	Lag 07	1.036	0.946	1.134	1.044	0.954	1.142	0.918	0.800	1.053	1.033	0.944	1.131
	Lag 10	1.054	0.952	1.166	1.067	0.965	1.180	0.908	0.779	1.060	1.052	0.951	1.164
65+	Lag 0	0.992	0.935	1.053	0.996	0.938	1.057	1.001	0.948	1.057	0.991	0.934	1.052
	Lag 03	0.999	0.922	1.083	1.008	0.930	1.093	1.022	0.950	1.100	1.006	0.928	1.091
	Lag 07	1.007	0.911	1.113	1.022	0.926	1.129	1.044	0.954	1.142	1.018	0.921	1.124
	Lag 10	1.018	0.910	1.138	1.036	0.928	1.158	1.067	0.965	1.180	1.029	0.920	1.149