

# An Association between Air Pollution and Daily Outpatient Visits for Respiratory Disease in a Heavy Industry Area

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## Abstract

In this work we used daily outpatient data from the Landseed Hospital in a heavily industrial area in northern Taiwan to study the associations between daily outpatient visits and air pollution in the context of a heavily polluted atmospheric environment in Chung-Li area during the period 2007–2011. We test the normality of each data set, control for the confounding factors, and calculate correlation coefficient between the outpatient visits and air pollution and meteorology, and use multiple linear regression analysis to seek significance of these associations. Our results show that temperature and relative humidity tend to be negatively associated with respiratory diseases. NO and NO<sub>2</sub> are two main air pollutants that are positively associated with respiratory diseases, followed by PM<sub>10</sub>, PM<sub>2.5</sub>, O<sub>3</sub>, CO, and SO<sub>2</sub>. Young outpatients (age 0–15 years) are most sensitive to changing air pollution and meteorology factors, followed by the eldest (age ≥66 years) and age 16–65 years of outpatients. Outpatients for COPD diseases are most sensitive to air pollution and meteorology factors, followed by allergic rhinitis, asthma, and pneumonia diseases. In the context of sex difference to air pollution and meteorological factors, male outpatients are more sensitive than female outpatients in the 16–65 age groups, while female outpatients are more sensitive than male outpatients in the young 0–15 age groups and in the eldest age groups. In total, female outpatients are more sensitive to air pollution and meteorological factors than male outpatients.

**Citation:** Wang K-Y, Chau T-T (2013) An Association between Air Pollution and Daily Outpatient Visits for Respiratory Disease in a Heavy Industry Area. PLoS ONE 8(10): e75220. doi:10.1371/journal.pone.0075220

**Editor:** Malcolm Gracie Semple, University of Liverpool, United Kingdom

**Received:** January 18, 2013; **Accepted:** August 14, 2013; **Published:** October 25, 2013

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**Funding:** This work was supported by National Central University-Landseed Hospital-100-A-004 and National Central University-Landseed Hospital-101-A-006. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

**Competing Interests:** The authors have declared that no competing interests exist.

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## Introduction

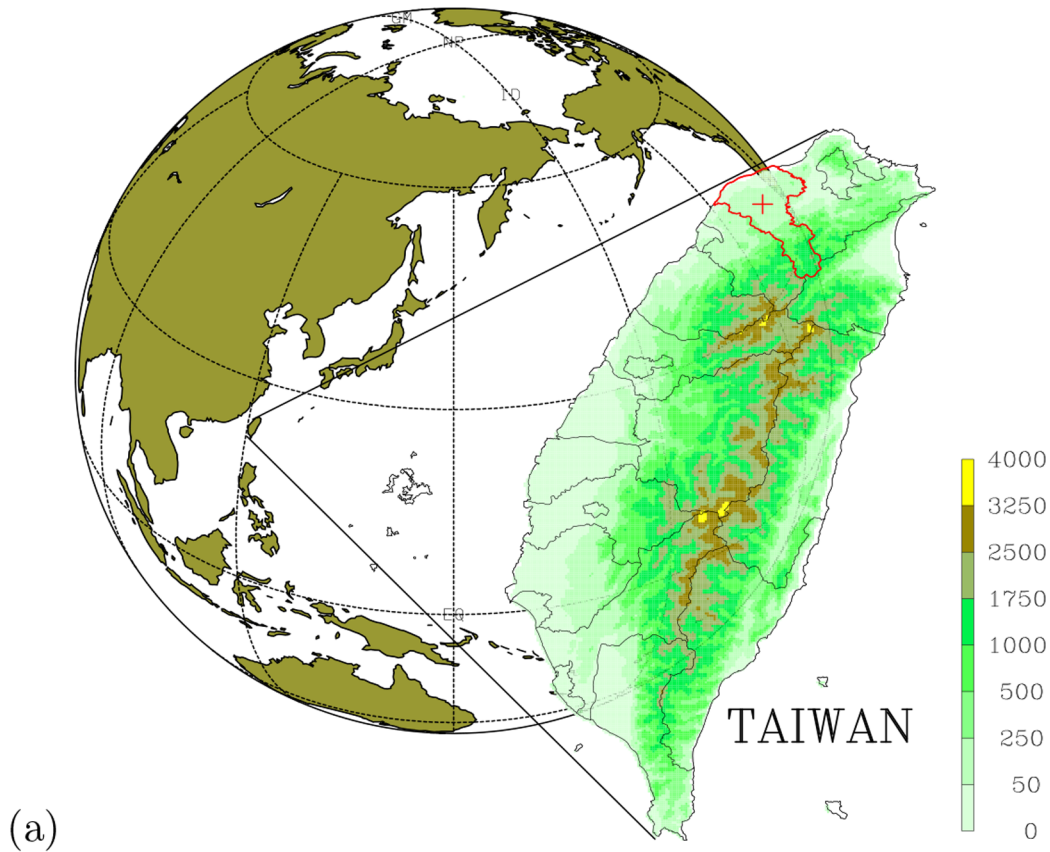
Taiwan contains high density of industrial factories using fossil fuel as a main source of energy to power Taiwan's economy [1]. As such, the air above Taiwan naturally contains heavy emissions from both industrial processes and mobile use every day. The air is polluted [2,3]. The industrial fruit is explicitly counted as the shining figures of significant gross industrial output every year. However, the air pollutants suspended in the air affect people who live in the county and the outcomes of polluted air on public health remains to be quantified. [4]. The cost of air pollution on human health needs to be counted as well so as to give a more balance picture of short-term fossil-fuel burning economy fruit with respect to the long-term impact on public health [5]. After all, the main motivation for the economy growth is for the long-term and sustainable welfare of the society. What will be the human health cost reflected in these waxing and waning of transient industrial figures?

Happily, Taiwan has a very good National Health Insurance (NHI) program for a high density population of 23 million [6,7]. The NHI is characterized by good accessibility (Taiwan citizen can see any doctor without referral, and may also go to any levels of hospitals directly), comprehensive coverage (cheap and abundant care), short waiting times, low cost, high coverage rate (99.6% of Taiwan population is covered by NHI in 2010), and a

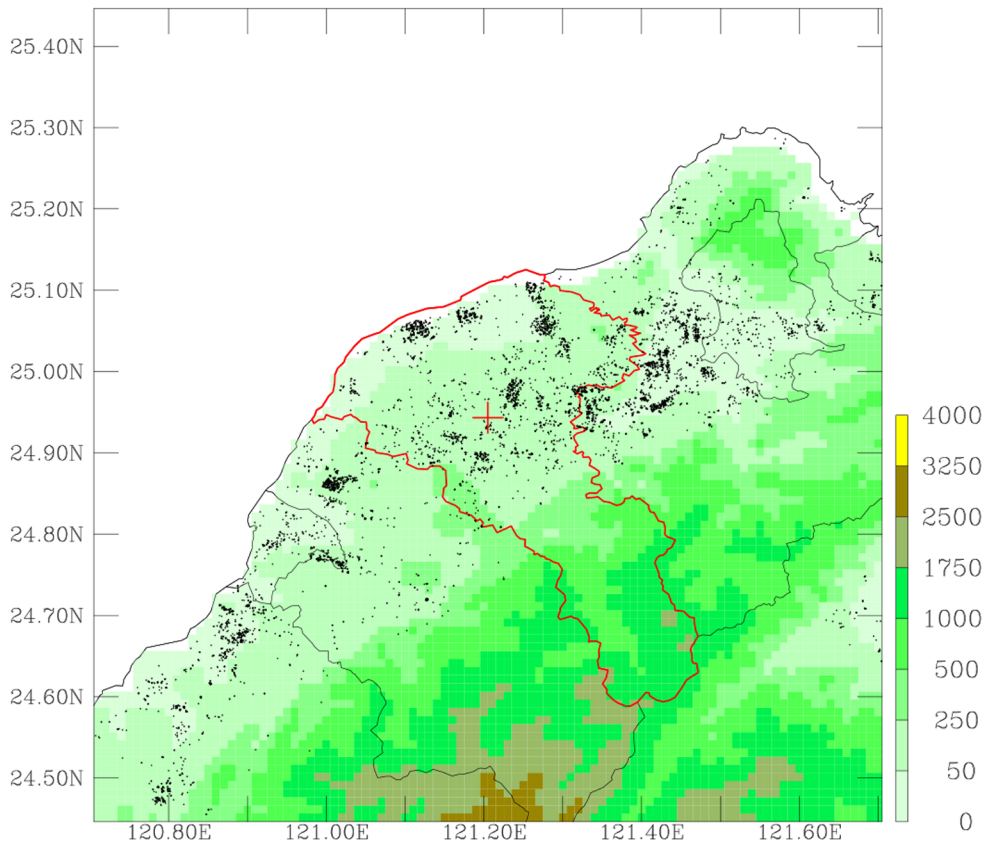
comprehensive and detailed nationwide NHI database that keeps every detailed record of the use of NHI [7,8]. NHI has contracted 92.1% of all hospitals and clinics in Taiwan in 2010 [9].

The NHI database enabled studies of association between air pollution and hospital admissions for cardiovascular disease [6], chronic obstructive pulmonary disease (COPD) [10], asthma [11], lower respiratory tract illness [12], and pneumonia [13]. In these works, NHI database provides quantified hospital admissions for above mentioned diseases, which were then analyzed against ambient air pollution levels obtained from a network of ambient air monitoring stations operated by Taiwan Environmental Protection Administration (EPA) [2]. People often get very ill to get admissions to hospitals. Mortality rate is another measure frequently used to quantify the impact of air pollution on public health [4]. Most of the time people visit hospitals to seek brief consultation and examination on their health. The results of these hospital outpatient visits are kept and comprising a large set of medical service records in NHI computer database [8]. This big data set reflects the status of the health of a population. As such, the use of outpatient data has become an important tool to understand the association between air pollution and public health [14,15,16,17,18].

Previous studies use NHI database to focus on the association between air pollution and hospital admissions. For example, to associate air pollution and hospital admissions for asthma during



(a)



(b)

**Figure 1. Geographical location of the study area.** (a) Location of the Landseed hospital (red cross) in Taiwan's Taoyuan County (area encircled with red solid line). (b) A high resolution map showing topography (shaded colors; in the unit of meter) in the northwestern Taiwan, Taoyuan County (area encircled with red solid line); the Landseed hospital (red cross), and significant industrial emission sources (black dots).  
doi:10.1371/journal.pone.0075220.g001

**Table 1.** Statistics for Tao-Yuan County (TYEPA, 2012; www.tyepb.gov.tw).

Population	2,010,000
Spatial Size	1,220.95 km <sup>2</sup>
Factories	10,412 (2,718 are under EPA 97 regulation)
Stacks	16,836
Total Factories in Taiwan	85,752 (Mar 2007; www.moeaidb.gov.tw)
Incinerators	21
Petro Stations	297 (Number 1 in Taiwan)
Industrial Areas	22 (No. 1 in Taiwan; 7 are major industrial areas)
Taiwans Top 500 Major Manufactures	More 1/3 in Tao-Yuan
Display Screen Manufactures	13 (Total 19 in Taiwan)
Industrial Productions	NTD 2.32 Trillions (USD 77 Billions)
	No. 1 in Taiwan; greater than Hsin-Chu Science Park
Mobile Vehicles	1,780,000
Total Mobile Vehicles in Taiwan	20,341,288 (Jan 2007; www.motc.gov.tw)

doi:10.1371/journal.pone.0075220.t001

the period 1996–2003 [11], and for cardiovascular disease during the period 1997–2001 [6] in Taipei; and to associate air pollution and hospital admissions for pneumonia in Kaohsiung during the period 1996–2004 [13]. A few studies reported association between daily outpatient visits and daily air pollution levels. For example, *Hwang and Chan* [12] used the NHI database to study effects of air pollution on daily clinic visits for lower respiratory tract illness in 50 townships in Taiwan during 1998. In this work we used outpatient data from a hospital in a heavily industrial area in northern Taiwan to study the association between daily outpatient visits and daily air pollution levels in the context of a heavily polluted atmospheric environment during the period 2007–2011.

**Data and Methods**

**Ethics Statement**

The statistics of daily hospital visits used in this work is openly published each year by the hospital [19,20,21,22]. Only the frequencies of visits for diseases are used in the study. No details of

patient’s personal information are involved in this work. As such, no ethics committee approving is needed. No written consent from patients, or from the next of kin, caretakers, or guardians on the behalf of minors/children parents are needed.

**1. Hospital Visit Data**

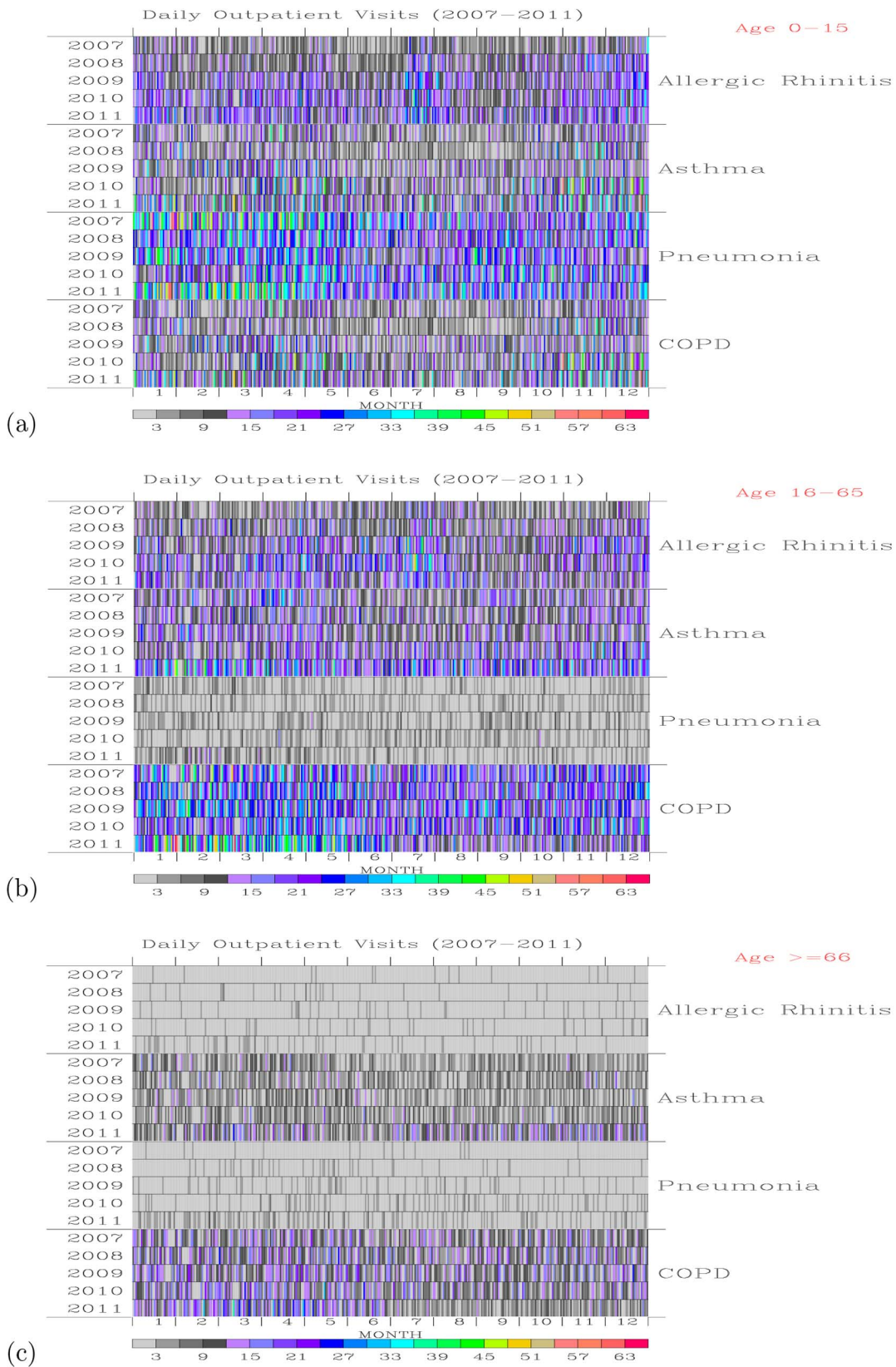
The Landseed hospital (121°12'18.36"E, 24°56'47.17"N) is located in the Taoyuan County, which is in northern Taiwan (Figure 1(a)). Taoyuan County is one of the top major industrial counties in Taiwan, contains several leading industrial figures. Table 1 shows a statistics for Taoyuan county, while the spatial distribution of point industrial emission sources is shown in Figure 1(b). Most of the outpatient visits to the Landseed hospital come from local community in Taoyuan County. About 60% of all visits are from nearby Chung-Li City and Ping-Jeng City, and more than 90% of daily outpatient visits are from Taoyuan County. The demographical nature of outpatients strongly indicates that the hospital is a local community hospital. Given the facts that Taoyuan County contains very heavy industrial production (Figure 1(a) and Table 1) and good records of ambient

**Table 2.** List of PM<sub>10</sub>-based Multiple Linear Regression Models.

Model1	OP =	$\beta_0 + \beta_1 (PM_{10})$
Model2	OP =	$\beta_0 + \beta_1 (PM_{10}) + \beta_2 (PM_{2.5})$
Model3	OP =	$\beta_0 + \beta_1 (PM_{10}) + \beta_2 (PM_{2.5}) + \beta_3 (O_3)$
Model4	OP =	$\beta_0 + \beta_1 (PM_{10}) + \beta_2 (PM_{2.5}) + \beta_3 (O_3) + \beta_4 (CO)$
Model5	OP =	$\beta_0 + \beta_1 (PM_{10}) + \beta_2 (PM_{2.5}) + \beta_3 (O_3) + \beta_4 (CO) + \beta_5 (NO)$
Model6	OP =	$\beta_0 + \beta_1 (PM_{10}) + \beta_2 (PM_{2.5}) + \beta_3 (O_3) + \beta_4 (CO) + \beta_5 (NO) + \beta_6 (NO_2)$
Model7	OP =	$\beta_0 + \beta_1 (PM_{10}) + \beta_2 (PM_{2.5}) + \beta_3 (O_3) + \beta_4 (CO) + \beta_5 (NO) + \beta_6 (NO_2) + \beta_7 (SO_2)$
Model8	OP =	$\beta_0 + \beta_1 (PM_{10}) + \beta_2 (PM_{2.5}) + \beta_3 (O_3) + \beta_4 (CO) + \beta_5 (NO) + \beta_6 (NO_2) + \beta_7 (SO_2) + \beta_8 (TEMP)$
Model9	OP =	$\beta_0 + \beta_1 (PM_{10}) + \beta_2 (PM_{2.5}) + \beta_3 (O_3) + \beta_4 (CO) + \beta_5 (NO) + \beta_6 (NO_2) + \beta_7 (SO_2) + \beta_8 (TEMP) + \beta_9 (RAIN)$
Model10	OP =	$\beta_0 + \beta_1 (PM_{10}) + \beta_2 (PM_{2.5}) + \beta_3 (O_3) + \beta_4 (CO) + \beta_5 (NO) + \beta_6 (NO_2) + \beta_7 (SO_2) + \beta_8 (TEMP) + \beta_9 (RAIN) + \beta_{10} (WD)$
Model11	OP =	$\beta_0 + \beta_1 (PM_{10}) + \beta_2 (PM_{2.5}) + \beta_3 (O_3) + \beta_4 (CO) + \beta_5 (NO) + \beta_6 (NO_2) + \beta_7 (SO_2) + \beta_8 (TEMP) + \beta_9 (RAIN) + \beta_{10} (WD) + \beta_{11} (WS)$
Model12	OP =	$\beta_0 + \beta_1 (PM_{10}) + \beta_2 (PM_{2.5}) + \beta_3 (O_3) + \beta_4 (CO) + \beta_5 (NO) + \beta_6 (NO_2) + \beta_7 (SO_2) + \beta_8 (TEMP) + \beta_9 (RAIN) + \beta_{10} (WD) + \beta_{11} (WS) + \beta_{12} (RH)$

OP: outpatient visits; TEMP: temperature; RAIN: rainfall; WD: wind direction; WS: wind speed; RH: relative humidity.

doi:10.1371/journal.pone.0075220.t002



**Figure 2. Daily outpatient visits.** For the ages (a) 0–15, (b) 16–65, and (c) above 66 year-old group of people for each of the respiratory system diseases during the 2007–2011 period.  
doi:10.1371/journal.pone.0075220.g002

**Table 3.** List of Total Outpatient Visits According to Disease and Year.

Disease	2007	2008	2009	2010	2011
Allergic Rhinitis	5118	6803	8413	9041	9021
Asthma	7779	7475	7910	8988	12458
Pneumonia	7878	7036	7066	6989	9051
Chronic obstructive pulmonary disease	11061	11225	12159	12082	13076

doi:10.1371/journal.pone.0075220.t003

air monitoring data, the combination of local community outpatient visit data with air pollution monitoring data makes it ideal to look for the association between ambient air pollution and public health.

A list of International Classification of Diseases, 9th Revision (ICD-9), for respiratory system were selected from outpatient visit database for this work. There are four diseases from which data of daily outpatient visits were analyzed and their correlations with daily air pollutants and meteorology were calculated. These diseases are allergic rhinitis (477), asthma (493), pneumonia (480–486), and COPD (490–493).

The hospital contains very detailed records of daily outpatients for each of the disease category. These data extend the period 2007–2011. The daily outpatient data for each disease category are divided into three age groups: ages 0–15, 16–65, and above 66 years old. The divisions of age groups are similar to *Hajat et al.* [23], *Hajat et al.* [24], and *Jalaludin et al.* [18].

Let's denote  $x_{ijk}$  as a one-dimensional vector, representing a time series of daily outpatient numbers for each  $i$  disease category at each  $j$  age group and each  $k$  year. Hence, we can write  $x_{ijk}$  as following,

$$x_{ijk} = x(i,j,k) \tag{1}$$

$$i = \text{disease category} = 1, \dots, 4 \tag{2}$$

$$j = \text{age group} = 1, \dots, 3 \tag{3}$$

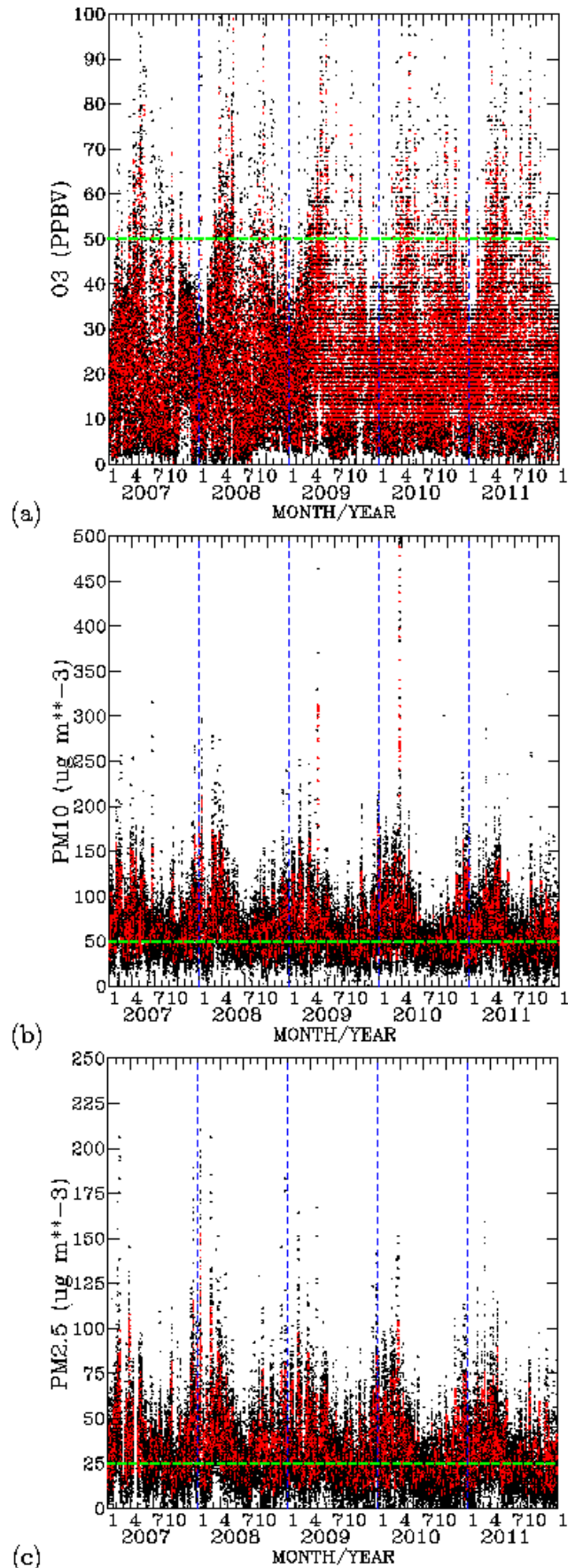
$$k = \text{year} = 2007, \dots, 2011 \tag{4}$$

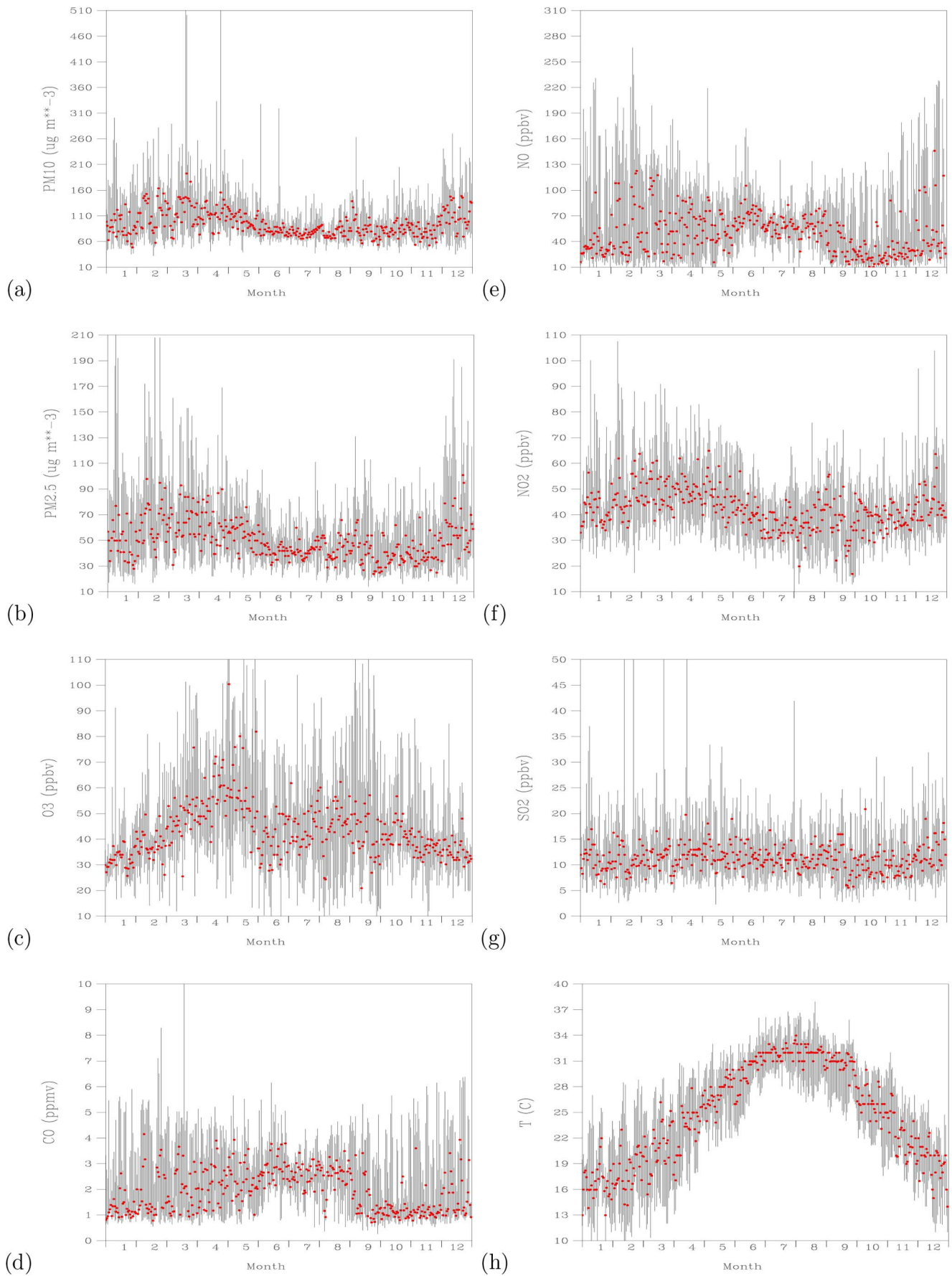
## 2. Ambient Air Pollution and Meteorological Data

In this work we use ambient air pollution and meteorological data obtained from Chung-Li station (close to the hospital), which is one of the more than 80 ambient air monitoring stations operated by Taiwan EPA [2,25]. This network of ambient air monitoring stations has started its current scale of operation since 1994. Each station reports hourly measurements of air pollutants

**Figure 3. Time-series plots of air pollutants.** (a)  $O_3$  (ppbv), (b)  $PM_{10}$  ( $\mu g m^{-3}$ ), and (c)  $PM_{2.5}$  ( $\mu g m^{-3}$ ) for the 2007–2011 period. Black dots indicate hourly data, while red dots indicate 8-hourly mean for  $O_3$ , and 24-hourly mean for  $PM_{10}$  and  $PM_{2.5}$ . Green dashed are pollutant levels according to the WHO guidelines.

doi:10.1371/journal.pone.0075220.g003





**Figure 4. Time-series plots of daily maximum (black lines) for the same Julian day of 2007–2011 period.** For (a) PM<sub>10</sub> ( $\mu\text{g m}^{-3}$ ), (b) PM<sub>2.5</sub> ( $\mu\text{g m}^{-3}$ ), (c) O<sub>3</sub> (ppbv), (d) CO (ppmv), (e) NO (ppbv), (f) NO<sub>2</sub> (ppbv), (g) SO<sub>2</sub> (ppbv), and (h) temperature ( $^{\circ}\text{C}$ ). Red dots indicate medium values for each Julian day.  
doi:10.1371/journal.pone.0075220.g004

and meteorology. A total of 12 observational variables from Chung-Li station are used in this work. These variables contain 7 main air pollutants (PM<sub>10</sub>, PM<sub>2.5</sub>, O<sub>3</sub>, CO, NO, NO<sub>2</sub>, and SO<sub>2</sub>) and 5 key meteorological observations (temperature, precipitation, wind direction, wind speed, and relative humidity). Let's denote  $y_{lk}$  as a vector for these air pollution and meteorological variables. Hence, we can write

$$y_{lk} = y(l, k) \quad (5)$$

$$l = \text{observational variables} = 1, \dots, 12 \quad (6)$$

$$k = \text{year} = 2007, \dots, 2011 \quad (7)$$

### 3. Test of Normality for Hospital, Air Pollution, and Meteorological Data

The daily hospital outpatient data is continuous in day, but the hospital does not provide regular outpatient service during weekends (Saturday and Sunday), and other public holidays (Lunar New Year, Moon Festival, Dragon Boat Festival, etc). As such, data that occurred during the public holidays are removed to prevent artificial bias (zero outpatient visits) introduced by these holidays (holiday effect) in the calculation of correlation coefficients. Air pollution and meteorological data during the public holidays are also removed accordingly to avoid holiday effect. We note that if the holiday effect not removed from the time-series data, the correlation coefficients exhibit (not shown here) overwhelmingly associations between the diseases and NO, NO<sub>2</sub>, CO, and SO<sub>2</sub>.

We then compute observed frequency distribution, which is calculated by binning daily data into 15 bin intervals for each year and for each data. The 15-bin intervals is empirically determined to give sufficient resolution of the data when testing data normality with respect to the continuous normal distribution.

Given an observed frequency distribution one can calculate its mean value and standard deviation. With a mean value and its standard deviation, one can calculate an expected frequency distribution of data if the data is normally distributed [26]. Finally, we can access the normality of observed data by testing the observed frequency distribution against its theoretical normal distribution using statistical methods (e.g. the Chi-square test) following *Press et al.* [26].

### 4. Correlation Coefficient Analysis

Given the outpatient vector  $x_n$  and variable vector  $y_n$ , we compute correlation coefficient following *Press et al.* [26]. A measure of significance of this correlation coefficient  $r$  is obtained by computing the Student's  $t$  probability  $P$  following *Press et al.* [26]. The small values of  $P$  indicates a significant correlation.

In addition, meteorological factors that might play a confounding role are separately considered as warm days (temperature above  $25^{\circ}\text{C}$ ) and cool days (temperature below  $25^{\circ}\text{C}$ ) in this work, following the method proposed by *Chang et al.* [6], *Cheng et al.* [13], and *Yang et al.* [11]. *Hwang and Chan* [12] also include temperature

as a confounding variable in their analysis. Since warm days are often associated with high relative humidity and cool days are often associated with low relative humidity [27], the stratification of days between warm and cool days also separates the effect of relative humidity from high to low.

### 5. Multiple Linear Regression Model Analysis

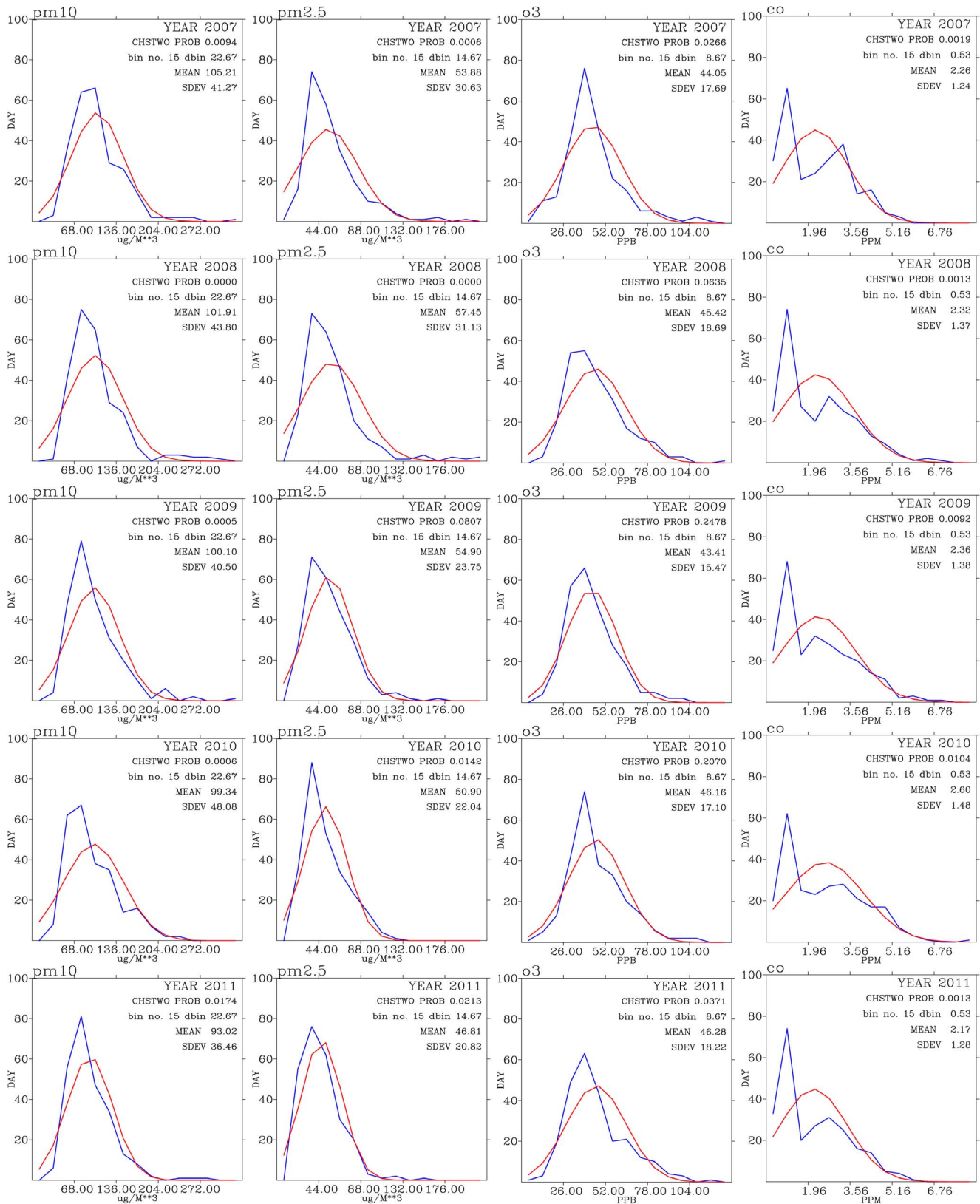
In this work we use multiple linear regression analysis to account for confounding effects when associating daily hospital visits for diseases with air pollutants and meteorological factors. Multiple linear regression analysis has been widely used to control for confounding factors when predicting dependent variables from independent variables [28,29,30,31,32,33,34].

We have developed multiple linear regression models for association analysis following the methods described in *Kleinbaum et al.* [35], which contains detailed mathematical formulas for the multiple linear regression models, equations to compute statistical significance of regression results, and a rich example data set that demonstrate the results from various multiple linear regression models. *Kleinbaum et al.* [35] use SAS package to carry out multiple linear regression computation. However, in order to facilitate the efficiency of processing large data set from medical and meteorological sources, it is necessary to build computational models from the methods described in *Kleinbaum et al.* [35].

The multiple linear regression models we have developed for this work have been carefully and successfully tested against data from *Kleinbaum et al.* [35]. We have run our models through data in Table 5.1, which shows observations on systolic blood pressure (SBP) and age for a sample of 30 individuals. We have compared our model results with edited SAS output for Table 5.1 in page 52 of *Kleinbaum et al.* [35]. We have also run our model through data shown in Table 8.1, containing a list of weight, height, and age of a random sample of 12 nutritionally deficient children. Our models were compared with a list of edited SAS output from 6 multiple regression models (shown in pages 124–126). Our detailed comparisons show consistent results between SAS calculations and our model calculations. These comparisons demonstrate our models are accurate when compared with the SAS package. We then use these multiple models to run through the medical and the meteorological data.

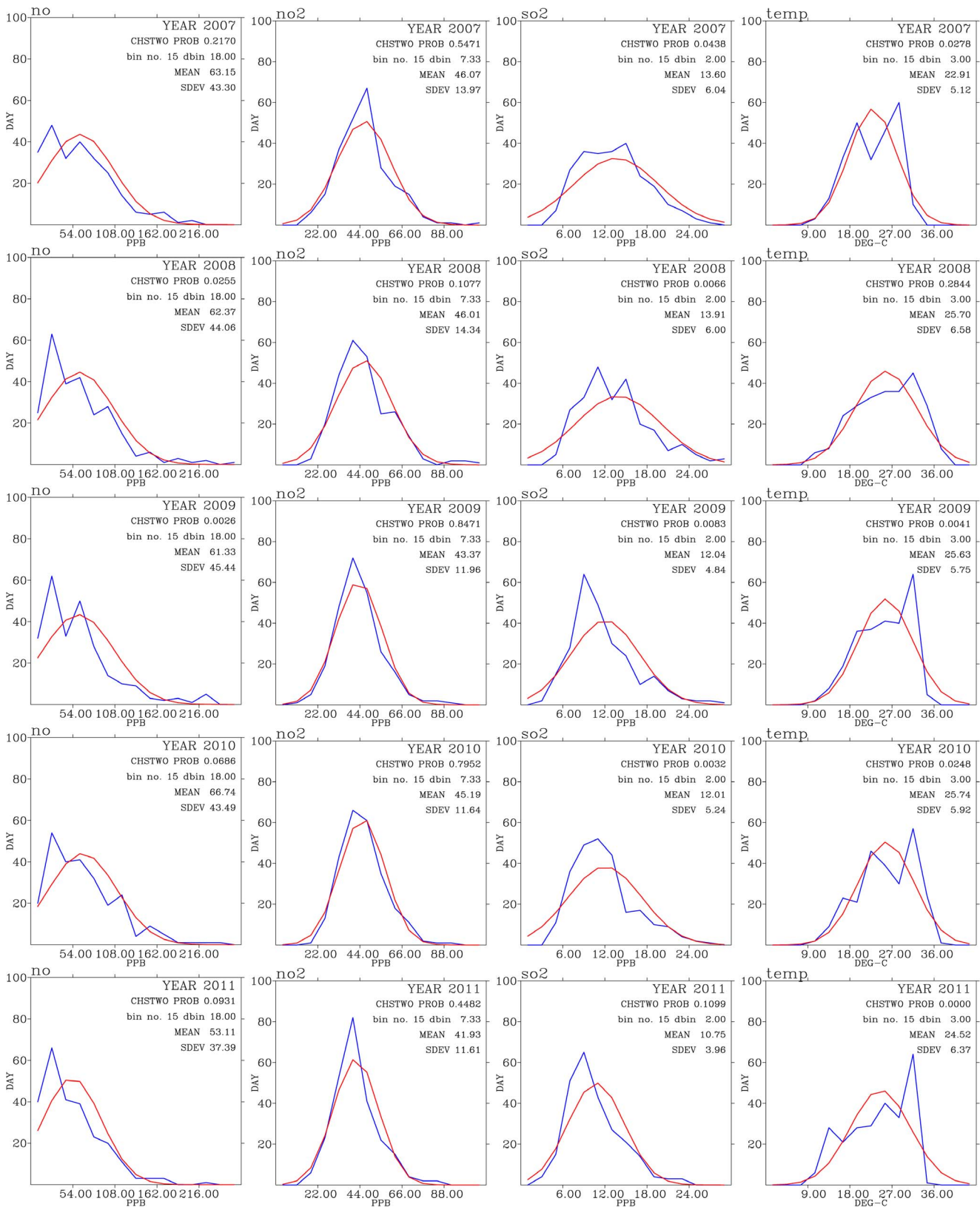
Table 2 shows a typical example of our multiple linear regression analysis. A list of PM<sub>10</sub>-based multiple linear regression models that were systematically used to run the medical and meteorological data. The purpose is to find the best model that associate air pollutant PM<sub>10</sub> with outpatient visits for each of respiratory diseases discussed in this work. Following *Kleinbaum et al.* [35], we use  $R^2$  and statistical significance level ( $P$  value) to select the best model for our analysis.

Table 2 shows a list of PM<sub>10</sub>-based model analysis. Similarly, we have systematically run twelve multiple linear regression models based on PM<sub>2.5</sub>, O<sub>3</sub>, CO, NO, NO<sub>2</sub>, SO<sub>2</sub>, temperature, rainfall, wind direction, wind speed, and relative humidity, respectively. As such, a total of 144 models were run for each of respiratory disease, in each year of 2007–2011, considering male and female outpatients separately, and for each of three age groups of outpatients (0–15, 16–65, and above 66 years). Hence, we have completed a total of 17,280 model analysis (4 respiratory diseases  $\times$  144 models/disease  $\times$  5 years  $\times$  2 sex groups/year/age group

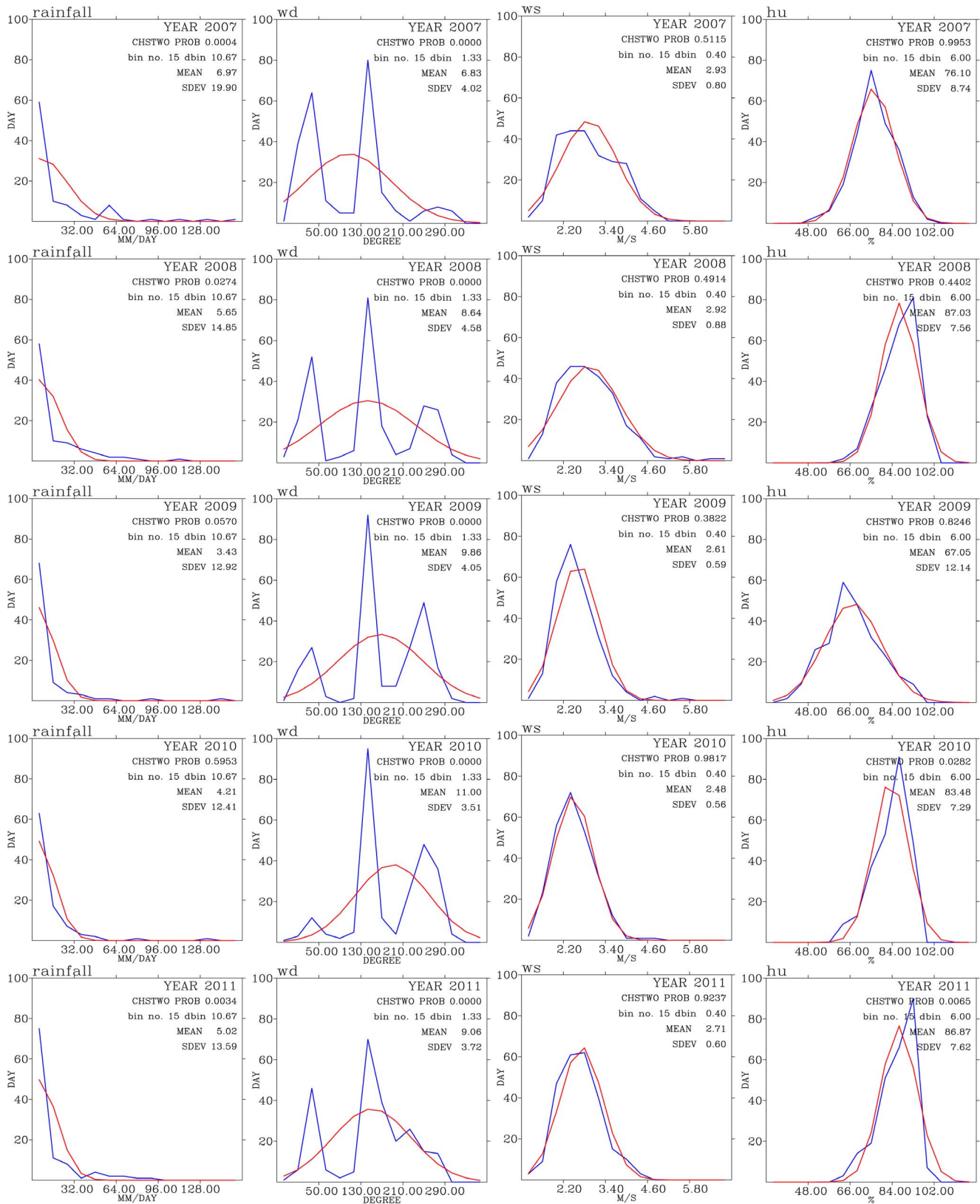


**Figure 5. Test of normal distribution for PM<sub>10</sub> (left panels), PM<sub>2.5</sub> (second from the left panels), O<sub>3</sub> (second from the right), and CO (right panels) for the years from 2007 (top row) to 2011 (bottom row).**  
doi:10.1371/journal.pone.0075220.g005

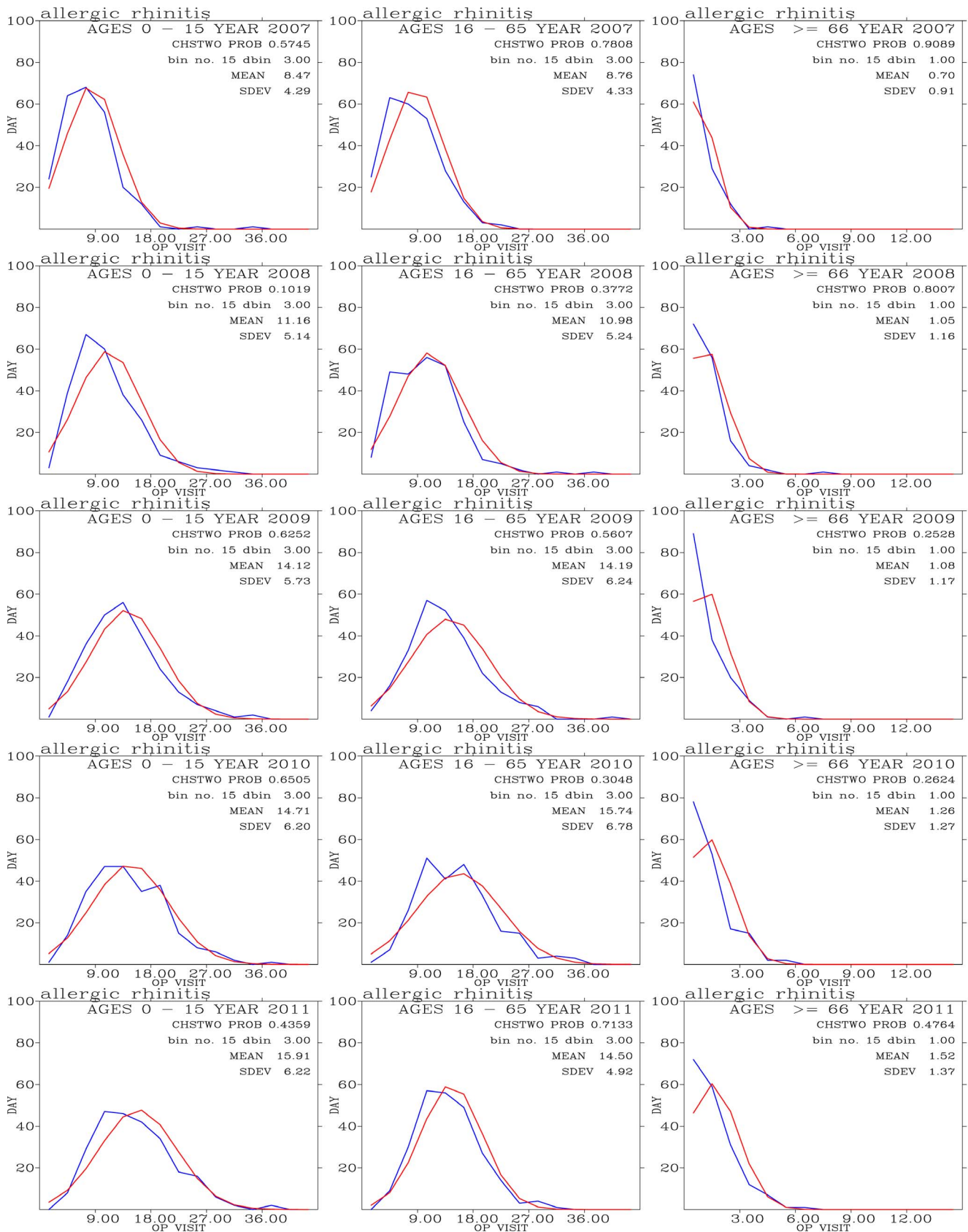




**Figure 6. Test of normal distribution for NO (left panels), NO2 (second from the left panels), SO2 (second from the right panels), and temperature (right panels) for years from 2007 (top row) to 2011 (bottom row).**  
doi:10.1371/journal.pone.0075220.g006

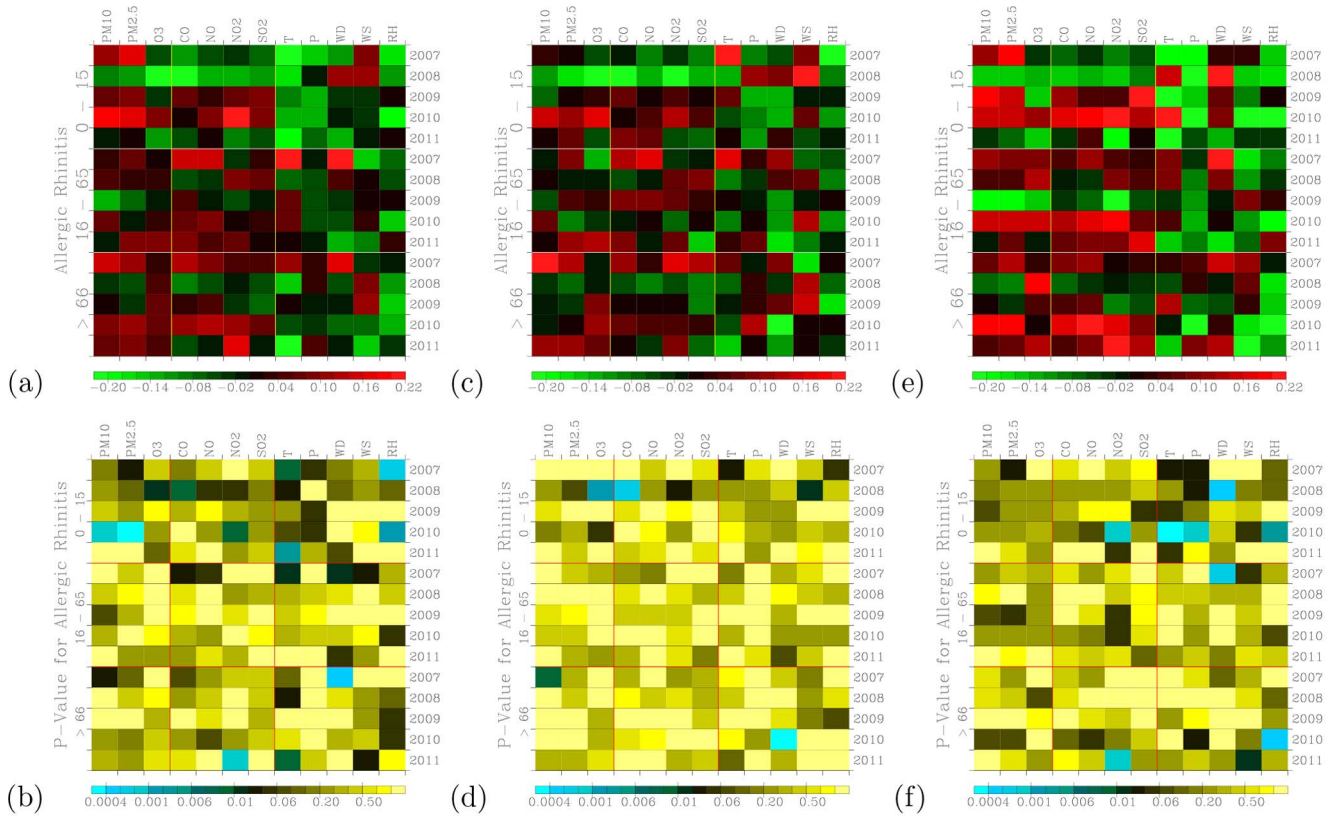


**Figure 7. Test of normal distribution for rainfall (left panels), wind direction (second from the left panels), wind speed (second from the right panels) and relative humidity (right panels) for years from 2007 (top row) to 2011 (bottom row).**  
doi:10.1371/journal.pone.0075220.g007



**Figure 8. Binned daily outpatient visits for allergic rhinitis (blues curves) and expected normal distribution (red curves) from years 2007 (top row) to 2011 (bottom row); and for outpatients with ages 0-15 (left panels), 16-65 (middle panels), and above 66 (right panels).**

doi:10.1371/journal.pone.0075220.g008



**Figure 9. Distribution of correlation coefficients when correlating hospital visits for allergic rhinitis with air pollutants and meteorology for three age groups during (a) the 2007–2011 periods. (c) The same as in (a) but to control for warm days (temperature above 25°C); and (e) to control for cold days (temperature below 25°C). Significance of correlation are shown in (b), (d), and (f).**  
doi:10.1371/journal.pone.0075220.g009

× 3 age groups/sex). The results that are statistically most significant are shown in the following section.

**Results**

**1. Daily Outpatients For Respiratory System Diseases During 2007–2011**

Figure 2 shows daily outpatient visits for the 0–15, 16–65, and above 66 year-old age group of people for each of the respiratory system diseases during the 2007–2011 period. For the age 0–15 group of outpatients (Figure 2a), most of the daily visits were for pneumonia disease, followed by allergic rhinitis, asthma, and COPD. Peak visits for pneumonia disease during January–April, while the period with low pneumonia outpatients occurred during summer months of June and July. For allergic rhinitis disease, more daily hospital visits occurred during late February to early May, July–August, and November–December than other months. The first and the last periods are normally associated with poor air quality [36], while the summer months of July August may be associated with high relative humidity.

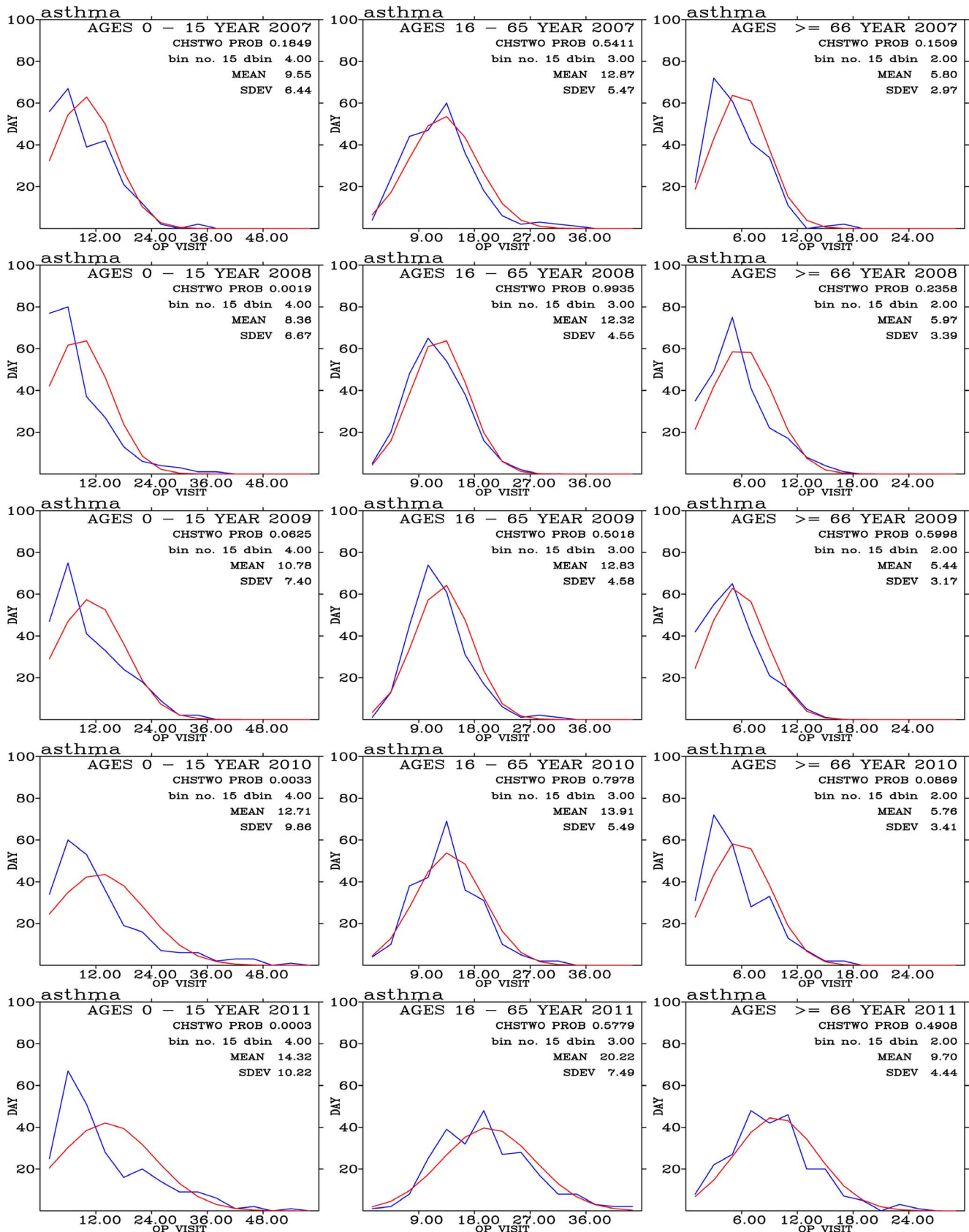
For the 16–65 age group outpatients (Figure 2b), most of the hospital visits were for COPD disease, followed by asthma and allergic rhinitis. Few visits were for pneumonia. For COPD outpatients, more visits occurred during winter to spring months than the summer months. For the group of outpatients with ages above 66, their visits are mainly associated with COPD and asthma (Figure 2c). Table 3 gives a summary of the total number of outpatient visits for each disease of the respiratory system during 2007–2011.

**2. Air Pollution and Meteorology During 2007–2011**

Time-series plots of hourly ambient air monitoring of O<sub>3</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub> at EPA Chung-Li station for the period 2007–2011 are shown in Figure 3. Also shown in the figure are the 8-hourly mean O<sub>3</sub>, 24-hourly mean PM<sub>10</sub>, and 24-hourly mean PM<sub>2.5</sub>. Elevated levels of hourly and 8-hourly mean O<sub>3</sub> mostly occurred during spring and summer seasons, Figure 3(a). Around 2% (2007), 4% (2008), 3% (2009), 3% (2010), and 4% (2011) of 8-hourly mean O<sub>3</sub> are higher than the World Health Organization (WHO) air quality guidelines for 8-hourly mean O<sub>3</sub> [37].

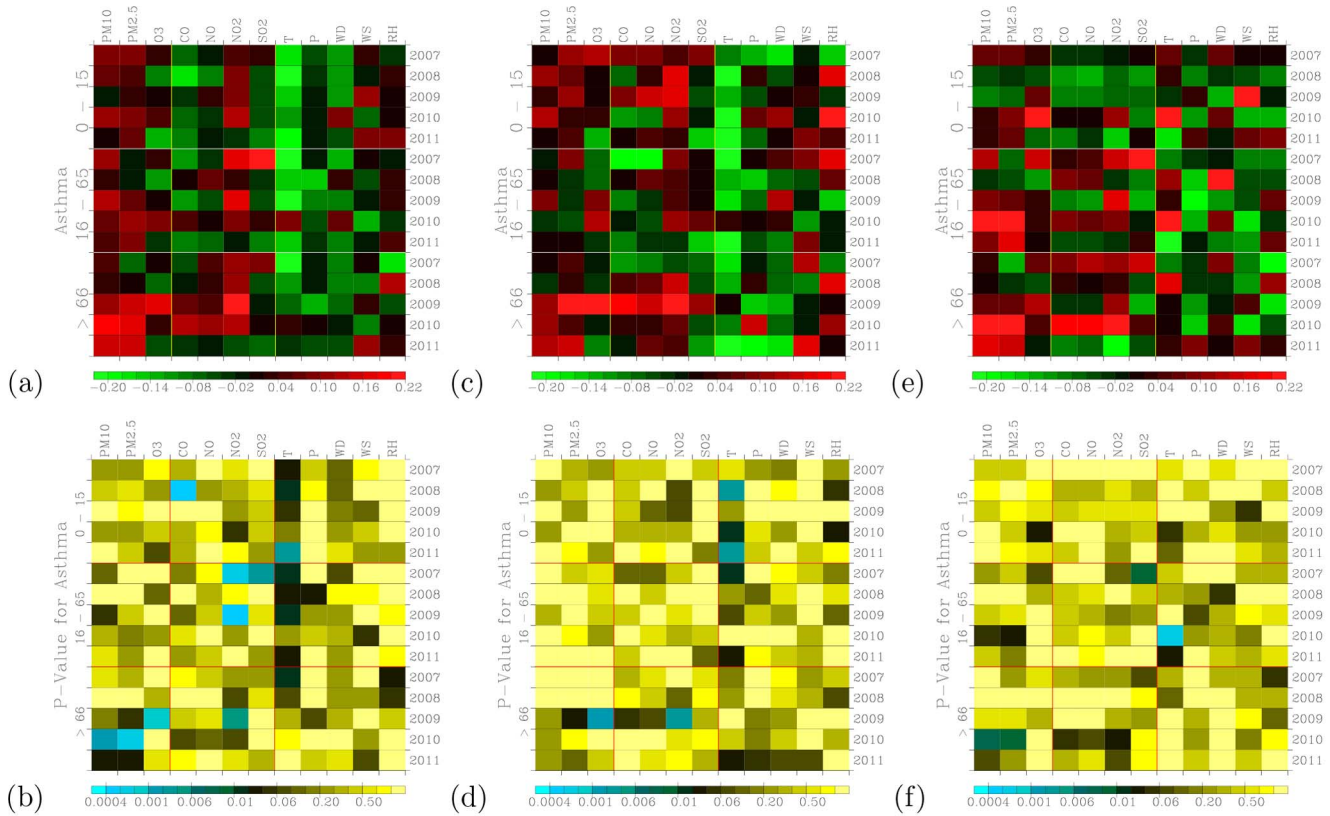
For PM<sub>10</sub>, Figure 3(b), both hourly and 24-hourly mean levels are mostly above the 24-hourly mean levels of 50 μg m<sup>-3</sup> recommended by WHO air quality guidelines for PM<sub>10</sub>. Around 68% (2007), 65% (2008), 61% (2009), 49% (2010), and 54% (2011) of 24-hourly PM<sub>10</sub> are higher than the WHO standard for PM<sub>10</sub>. For PM<sub>2.5</sub>, around 52% (2007), 57% (2008), 55% (2009), 39% (2010), and 44% (2011) of 24-hourly mean levels are above the 24-hourly mean levels of 25 μg m<sup>-3</sup> recommended by the WHO standard for PM<sub>2.5</sub>. Elevated levels of PM<sub>10</sub> and PM<sub>2.5</sub> frequently occurred during the winter, spring, and fall seasons. Summer is the only season when ambient levels of PM<sub>10</sub> and PM<sub>2.5</sub> are low. Taiwan is under the strong influence of the southerly Asian summer monsoon flow in the summer season. This monsoon flow brings clean tropical air to the entire county, resulting in a much reduced ambient air pollution in summer [36].

Figure 4 shows time-series plots of daily maximum values of PM<sub>10</sub>, PM<sub>2.5</sub>, O<sub>3</sub>, CO, NO, NO<sub>2</sub>, SO<sub>2</sub>, and temperature for the 2007–2011 period. Range of the daily maximum values for each variable during 2007–2011 are shown as vertical lines. Hence, the



**Figure 10. Binned daily outpatient visits for asthma (blues curves) and expected normal distribution (red curves) from years 2007 (top row) to 2011 (bottom row); and for outpatients with ages 0–15 (left panels), 16–65 (middle panels), and above 66 (right panels).**

doi:10.1371/journal.pone.0075220.g010



**Figure 11. Distribution of correlation coefficients when correlating hospital visits for asthma with air pollutants and meteorology for three age groups during (a) the 2007–2011 periods. (c) The same as in (a) but to control for warm days (temperature above 25 °C); and (e) to control for cold days (temperature below 25 °C). Significance of correlation are shown in (b), (d), and (f).**  
doi:10.1371/journal.pone.0075220.g011

longer the vertical lines, the larger the variations that had occurred in that day of the year. Daily maximum levels of PM<sub>10</sub> greater than 50  $\mu\text{g m}^{-3}$  (Figure 4(a)) and PM<sub>2.5</sub> greater than 25  $\mu\text{g m}^{-3}$  (Figure 4(b)) can overwhelmingly occur each day of the period 2007–2011. Daily maximum levels of O<sub>3</sub> higher than 50 ppbv mostly occurred during March–May and July–October months (Figure 4(c)). Except for the June–August months, daily maximum levels of CO (Figure 4(d)) and NO (Figure 4(e)) exhibit large variability. Daily maximum levels of NO<sub>2</sub> show clear seasonal cycle (Figure 4(f)). High levels of NO<sub>2</sub> occurred during the winter to spring seasons, followed by low levels of NO<sub>2</sub> in summer season. NO<sub>2</sub> levels rise again in the fall to winter seasons. Daily maximum levels of SO<sub>2</sub> show less clear seasonal cycle than NO<sub>2</sub> (Figure 4(g)). The medium values of daily maximum SO<sub>2</sub> are centered about 10 ppbv. Large variabilities of daily maximum SO<sub>2</sub> close to 20 ppbv frequently occurred all year round. Daily maximum temperatures follow the marching of the season, with high temperatures occurred during July–August and low temperatures occurred during January–February (Figure 4(f)). Temperatures in summer months show less variability than those occurred in the winter to spring months.

The observations show that the variations of daily maxima for CO and NO are smaller and the minimum concentrations for both species are higher during June–August months than during the rest of other months. Since the dominating flows during the June–August months are coming from the south directions [36], the persistently high minimum CO and NO levels indicate sustained contribution from local pollution sources. The ability to reach low CO and NO during the rest of other months indicate

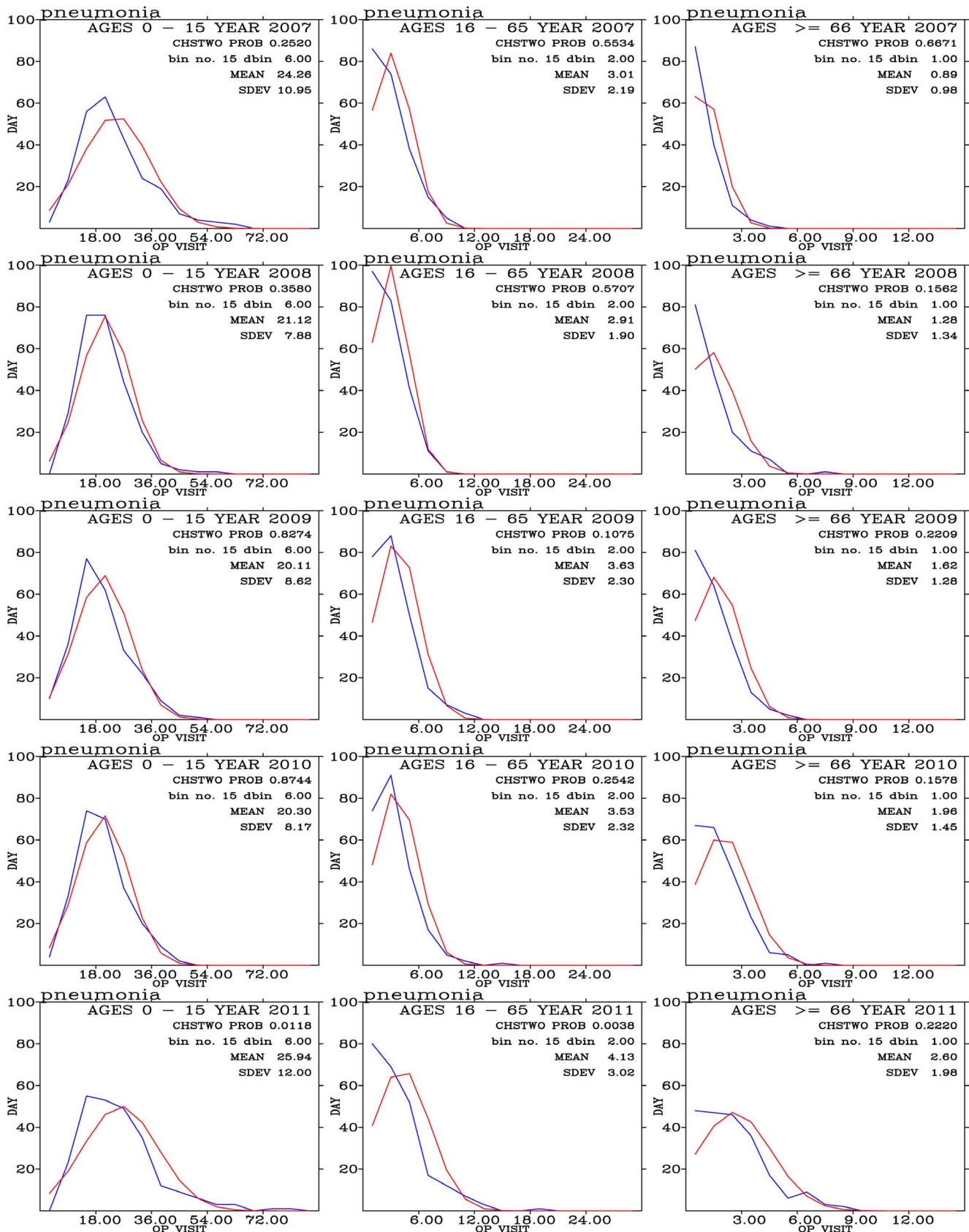
the effect of large-scale flows from the north directions to bring daily maximum CO and NO to low concentration.

### 3. Test of Normality for Air Pollutant and Meteorology Data

Figure 5, Figure 6, and Figure 7 shows test of normality for air pollutants and meteorological data for each year of the analysis period of this work. Except for CO, rainfall, and wind direction, the rest of the data exhibit patterns of normal distribution when binned data are compared with the expected normal distribution.

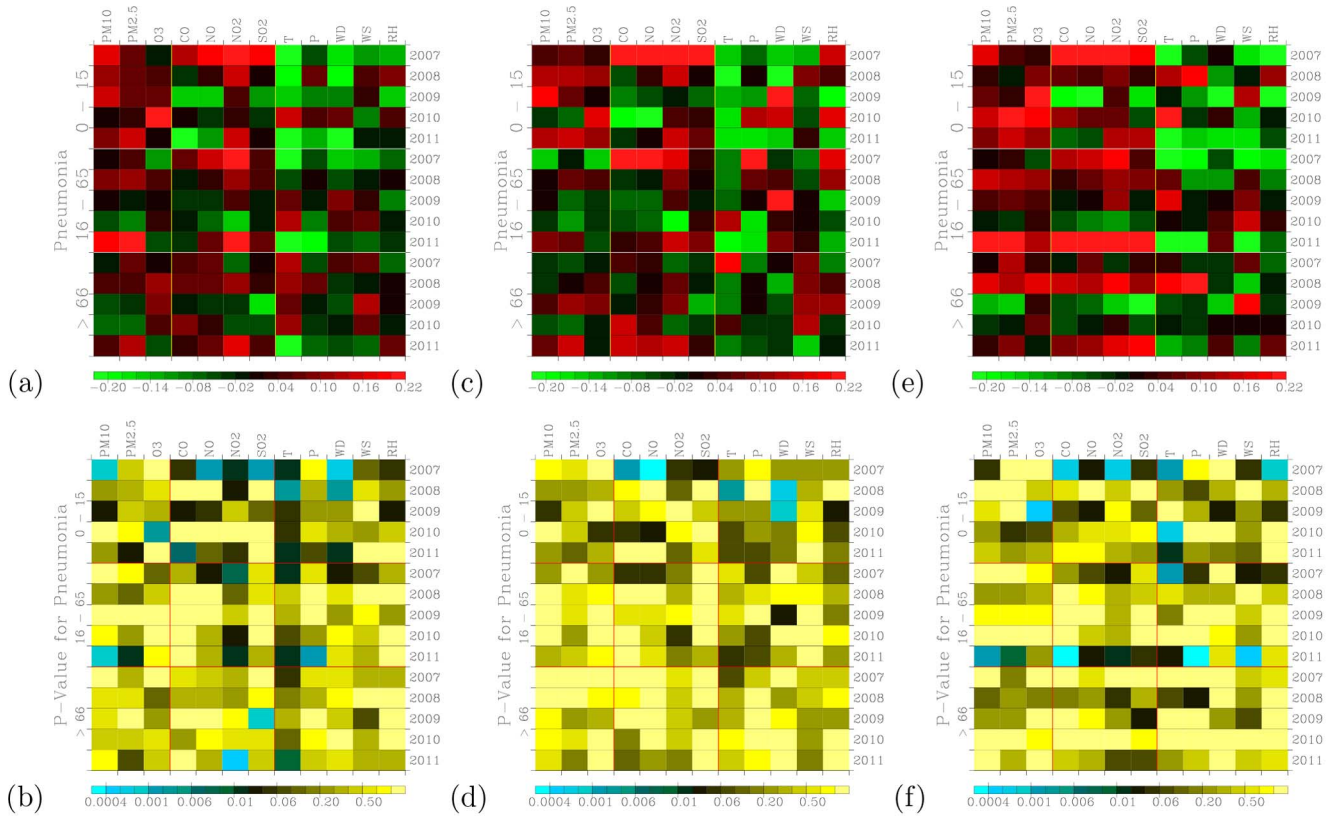
The mean values for PM<sub>10</sub> for these five years have decreased from 105  $\mu\text{g m}^{-3}$  in 2007 to 93  $\mu\text{g m}^{-3}$  in 2011. However, standard deviations of PM<sub>10</sub> varies between 36 and 41  $\mu\text{g m}^{-3}$ . This indicates that daily maximum PM<sub>10</sub> in most days of each year are much higher than those WHO guidelines. This is consistent with the time-series analysis shown in Figure 3(b). This result indicates that Taoyuan area frequently under the influence of processes (local emissions and/or non-local sources) that persistently sustain elevated levels of PM<sub>10</sub>.

Means of PM<sub>2.5</sub> levels decrease from 53–57  $\mu\text{g m}^{-3}$  during 2007–2008 to 46  $\mu\text{g m}^{-3}$  in 2011. The standard deviations for PM<sub>2.5</sub> has also decreased from around 30  $\mu\text{g m}^{-3}$  in 2007 to 20  $\mu\text{g m}^{-3}$  in 2011. This indicates that about 68% of days in 2007 show daily maximum PM<sub>2.5</sub> varies between 26 and 66  $\mu\text{g m}^{-3}$  [50]. Most of the days in Taoyuan are having levels of PM<sub>2.5</sub> above WHO guidelines (see also Figure 3(c)). The mean values for NO, NO<sub>2</sub>, and SO<sub>2</sub> all show decreasing trends during the 2007–



**Figure 12. Binned daily outpatient visits for pneumonia (blues curves) and expected normal distribution (red curves) from years 2007 (top row) to 2011 (bottom row); and for outpatients with ages 0–15 (left panels), 16–65 (middle panels), and above 66 (right panels).**

doi:10.1371/journal.pone.0075220.g012



**Figure 13. Distribution of correlation coefficients when correlating hospital visits for pneumonia with air pollutants and meteorology for three age groups during (a) the 2007–2011 periods. (c) The same as in (a) but to control for warm days (temperature above 25°C); and (e) to control for cold days (temperature below 25°C). Significance of correlation are shown in (b), (d), and (f).**  
doi:10.1371/journal.pone.0075220.g013

2011 period (Figure 6), while the mean values for O<sub>3</sub> has slightly increased, from 44 ppbv in 2007 to 46 ppbv in 2011.

These analyses consistently show signs of decrease in primary pollutants while slightly increase in the secondary pollutant O<sub>3</sub> in the air. This could indicate the reduction in local industrial activities either by their relocation to other countries or by the effectiveness of more stringent emission control policies.

The wind directions show three modes of peak frequency distribution centered around 40°, 140°, and 270° directions. The highest frequency distribution of wind direction come from around 140° directions, indicating southerly winds. This is an indication of winds mostly occur during summer monsoon season when winds were from the south directions. The wind directions centered around 270° representing westerly winds, which normally occur during the day-time period when the sea breeze prevailed over the Taoyuan area (Figure 1(b)). The winds coming from around the 40° directions representing the prevailing northerly winds which occur mostly during the late fall, winter, and early spring seasons.

#### 4. Attributing Disease’s Environmental Effect: Test of Outpatient Normal Distribution and Correlation Coefficient Analysis

**4.1. Allergic Rhinitis.** Figure 8 shows frequency distribution of outpatient visits for allergic rhinitis and comparison with expected normal distribution. Outpatients for this disease concentrate on people with ages 0–15 and 16–65. The mean values of outpatient visits shows slightly increase trend during the 5-year

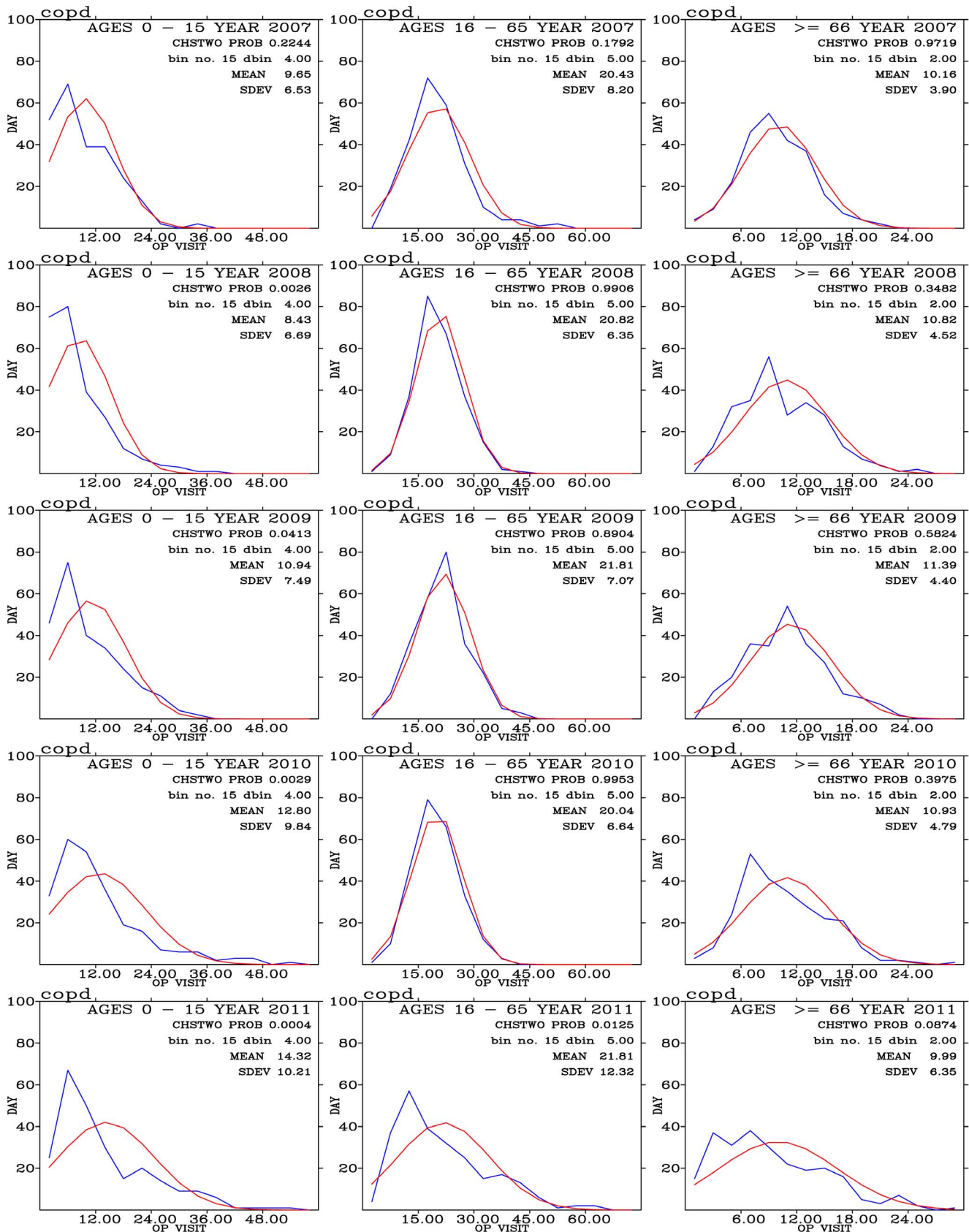
period. The outpatient visits shows close resemblance to the expected frequency distribution from normal distribution.

Figure 9(a) shows distribution of correlation coefficients when correlating hospital visits for allergic rhinitis with air pollutants and meteorology for three age groups during the 2007–2011 periods. Figure 9(b) shows a measure of significance for the correlation coefficients calculated in Figure 9(a). The small values in Figure 9(b) indicate significant correlation [26].

The 0–15 age group of outpatients for allergic rhinitis are mostly and positively correlated with PM<sub>10</sub> and PM<sub>2.5</sub>. Temperature shows significantly negative correlations for this young age group of outpatients. Temperatures do not exhibit a clear association with both the 16–65 and above 66 age groups of outpatients. Air pollutants such as PM<sub>10</sub>, PM<sub>2.5</sub>, O<sub>3</sub>, CO, NO, NO<sub>2</sub>, and SO<sub>2</sub> tend to show positive correlations with visits for allergic rhinitis when compared with meteorological factors. These pollutants have been shown to be related to allergic rhinitis [17].

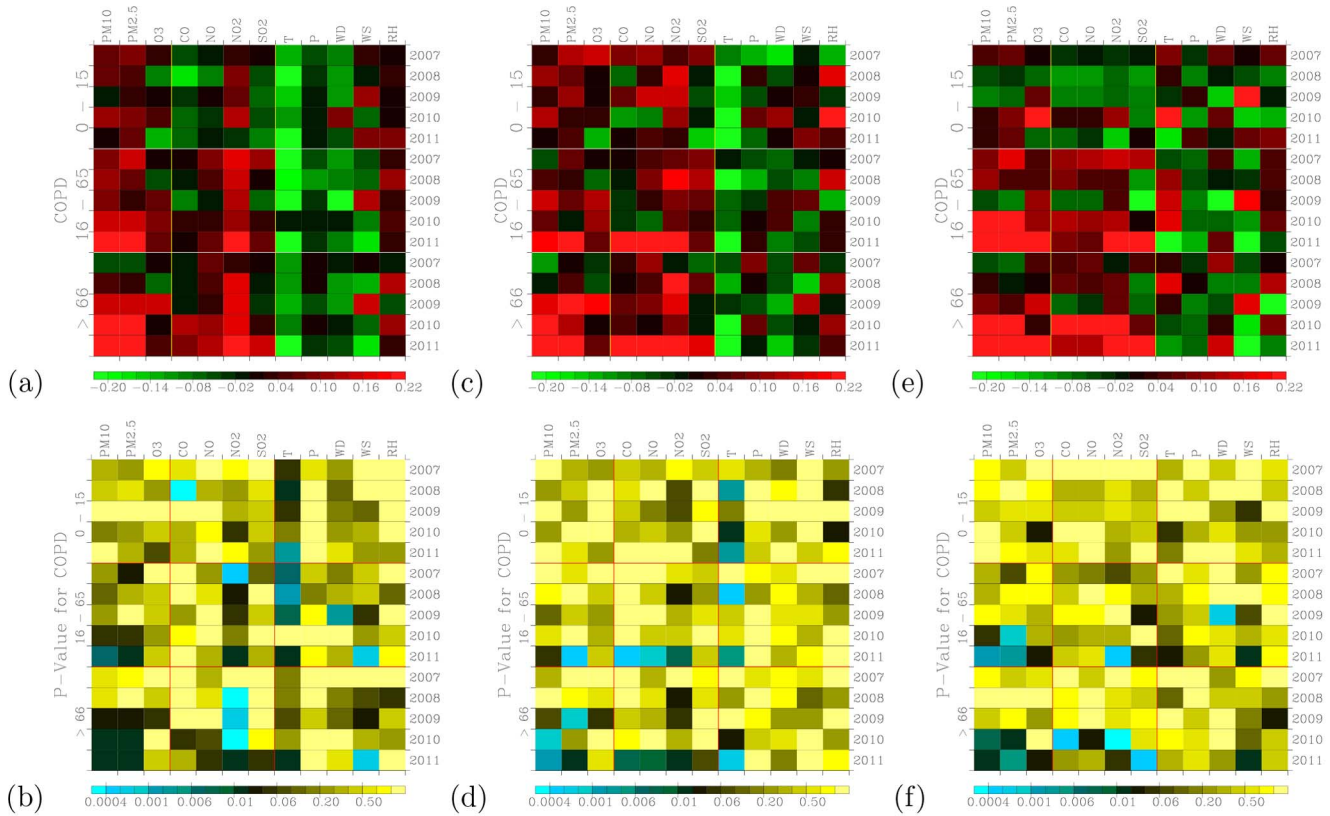
When controlled for temperature effect, both cool (Figure 9(c)) and warm (Figure 9(e)) days also exhibit positive correlation coefficients. However, the correlation coefficients during cool days are more pronounced and higher than those during warm days. Also the significance of correlation occurred during the cool days (Figure 9(f)) are stronger than those during the warm days (Figure 9(d)). This could indicate low temperatures can act to exacerbate the symptoms allergic rhinitis. Distribution of correlation coefficients during cool days (Figure 9(e)) are more pronounced than the effects of temperature were not controlled (Figure 9(a)). Hence, there is a confounding effect of temperature when





**Figure 14. Binned daily outpatient visits for COPD (blues curves) and expected normal distribution (red curves) from years 2007 (top row) to 2011 (bottom row); and for outpatients with ages 0-15 (left panels), 16-65 (middle panels), and above 66 (right panels).**

doi:10.1371/journal.pone.0075220.g014



**Figure 15. Distribution of correlation coefficients when correlating hospital visits for (a) COPD with air pollutants and meteorology for three age groups during the 2007–2011 periods. (c) The same as in (a) but to control for warm days (temperature above 25°C); and (e) to control for cold days (temperature below 25°C). Significance of correlation are shown in (b), (d), and (f).**  
doi:10.1371/journal.pone.0075220.g015

correlating daily outpatient visits for allergic rhinitis with air pollution levels.

Hajat *et al.* [23] found strong association between 4-day lag SO<sub>2</sub> and O<sub>3</sub> measurements and the number of consultations for allergic rhinitis in London. PM<sub>10</sub> and PM<sub>2.5</sub> are less significant in associating with the allergic rhinitis following Hajat *et al.* [2001]. On the other hand, Wong *et al.* [38] found significant and positive association between PM<sub>10</sub> and upper respiratory tract infections, while Wong *et al.* [2006] showed significant association between first visits for upper respiratory tract infections and an increase in the concentrations of NO<sub>2</sub>, O<sub>3</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub> in Hong Kong.

We note that positive correlations may not exit through all 5 years. For example, allergic rhinitis with PM<sub>10</sub> in 2008 are negative while the rest of other four years are positive for the age 0–15 group of outpatients (Figure 9(a)). The majority of the correlation coefficients are positive.

**4.2. Asthma.** Frequency distribution of daily outpatient visits for asthma is shown in Figure 10. These daily outpatient distribution shows remarkably close resemblance to the expected normal distribution in ages 16–65 and above 66 groups of people. The largest group of outpatients is from the 16–65 age group of people. Significant increases in the mean values of daily outpatient visits are seen in people with ages 16–65 and above 66.

Air pollutants such as PM<sub>10</sub>, PM<sub>2.5</sub>, and NO<sub>2</sub> exhibit positive correlations with the daily outpatient visits for asthma (Figure 11(a)). These correlations are very significant (Figure 11(b)), especially for outpatients with age above 66 years old. Our findings of strong and significant correlations between asthma and PM<sub>10</sub> and PM<sub>2.5</sub> are consistent with Schwartz *et al.* [39]

and Sheppard *et al.* [40]. Both studies showed the daily counts of emergency room visits persons under age 65 and non-elderly were significantly associated with PM<sub>10</sub> on the previous day in Seattle. Sunyer *et al.* [41] found daily admissions for asthma in adults increased significantly with increasing ambient levels of NO<sub>2</sub> in four European cities. McConnell *et al.* [42] found positive associations between air pollutants (PM<sub>10</sub> and NO<sub>2</sub>) and bronchitic symptoms in Southern California children with asthma. On the other hand, decrease in particulate air pollution were associated with decrease in asthma and bronchitis admissions of children [43] and mortality rates [44].

Outpatients for asthma disease negatively correlated with temperature and these correlations are significant. This result is consistent with Whittemore and Korn [45], who showed more asthma attacks on cool days in the Los Angeles area. Asthma outpatients also show negative correlations with wind direction. This indicates westerly winds tend to have lower asthma outpatients, while easterly winds tend to have higher number of asthma outpatients. Easterly winds are associated with winds from the ocean directions, while easterly winds are associated with winds from inland directions. More industrial factories and transportation vehicles are located from inland directions than from ocean directions.

For asthma, age 0–15 group of outpatients shows more prevailing positive correlations with PM<sub>10</sub>, PM<sub>2.5</sub>, O<sub>3</sub>, CO, NO, and NO<sub>2</sub> during warm days (Figure 11(c)) than during cold days (Figure 11(e)) when positive correlations are mostly associated with PM<sub>10</sub>, PM<sub>2.5</sub>, and O<sub>3</sub>. On the other hand, age 16–65 group of outpatients show pronounced positive correlations with all

**Table 4.** List of PM<sub>10</sub>-based Regression Coefficients, F value, R<sup>2</sup>, and P Value.

Sex	$\beta_1(\text{PM}_{10})$	$\beta_2(\text{PM}_{2.5})$	$\beta_3(\text{O}_3)$	$\beta_4(\text{CO})$	$\beta_5(\text{NO})$	$\beta_6(\text{NO}_2)$	$\beta_7(\text{SO}_2)$		
	$\beta_8(\text{TEMP})$	$\beta_9(\text{RAIN})$	$\beta_{10}(\text{WD})$	$\beta_{11}(\text{WS})$	$\beta_{12}(\text{RH})$	F-value	R <sup>2</sup>	P-value	
<i>Age Group 0–15 Years: Allergic Rhinitis; 2010; Male Outpatients</i>									
Model1	0.0051					1.98			
							0.01	0.1608	
Model2	0.0050	−0.0007				0.99			
							0.01	0.3736	
Model3	0.0052	−0.0014	0.0054			0.77			
							0.01	0.5110	
Model4	0.0037	−0.0049	0.0031	0.2948		1.73			
							0.03	0.1433	
Model5	0.0035	−0.0042	0.0025	0.3464	0.0017	1.39			
							0.03	0.2283	
Model6	0.0053	−0.0011	0.0056	0.3707	0.0015	−0.0299			
						1.78	0.04	0.1028	
Model7	0.0052	0.0003	0.0059	0.3914	0.0012	−0.0291	−0.0153		
						1.56	0.04	0.1482	
Model8	0.0037	0.0084	−0.0038	−0.0956	0.0051	−0.032	−0.0282		
	0.1385					3.01	0.09	0.0031	
Model9	0.0032	0.0081	0.0046	−0.1138	0.0054	0.002	−0.0322		
	0.1402	−0.0076				2.78	0.10	0.0040	
Model10	0.0027	0.0065	−0.0044	−0.1044	0.0043	−0.0008	−0.0269		
	0.0984	−0.0093	0.834			2.83	0.11	0.0024	
Model11	0.0034	0.0054	−0.0045	−0.1462	0.0045	−0.0064	−0.0292		
	0.0947	−0.0088	0.0752	−0.2501		2.67	0.11	0.0030	
Model12	0.0019	0.0071	−0.0121	−0.1463	0.0034	−0.0052	−0.0367		
	0.1029	−0.0014	0.0760	−0.3452	−0.0428	2.83	0.13	0.0012	

doi:10.1371/journal.pone.0075220.t004

pollutants during cool days than during days. For outpatients above age 65, occurrence of positive correlation coefficients during both warm and cold cool days are similar.

These results indicate that temperature can play a delicate effect on asthma outpatients. Cool days appear to reduce the effect of air pollutants on asthma symptoms for age 0–15 of outpatients, while effect of air pollutants enhanced during warm days. For older outpatients, age 16–65, effect of air pollutants on asthma symptoms are all enhanced during cool days than during warm days. For the eldest outpatients, age about 66, temperature effects are less clear when comparing cool with warm days. The appearance of highly correlated coefficients also exhibit high levels of significance, Figures 11(d) and 11(f). These results also indicate the confounding effects of temperatures on the association of daily asthma outpatients with air pollution levels.

**4.3. Pneumonia.** Frequency distribution of outpatients for pneumonia disease are shown in Figure 12 for three age group of people during the 2007–2011 period. Most outpatients for pneumonia concentrate on the 0–15 year-old people. The frequency distribution of these outpatients exhibit a good agreement with the expected normal distribution.

Pneumonia outpatients are positively correlated with PM<sub>10</sub>, PM<sub>2.5</sub>, O<sub>3</sub>, and NO<sub>2</sub> for age 0–15 group of outpatients (Figure 13(a)). High values of the these positive correlation coefficients often associated with low P-values (Figure 13(b)),

indicating that the correlations are significant. These results are consistent with previous findings. For example, *Penna and Duchade* [46] found a statistically significant association between the average annual levels of particulates and infant mortality from pneumonia. *Schwartz* [47] found causal association between the increasing particulate air pollution and increase in mortality rates from COPD and pneumonia. In a study of air pollution and infant mortality in Mexico City, *Loomis et al.* [48] showed that NO<sub>2</sub> and O<sub>3</sub> are also associated with the infant mortality, but not as consistently as with particulate air pollution.

For pneumonia, cool days (Figure 13(e)) generally exhibit a strong effect on the distribution of air pollutant correlated coefficients than during warm days (Figure 13(c)) and during all days (Figure 13(a)). For the youngest pneumonia outpatients (age 0–15), effects of PM<sub>10</sub>, PM<sub>2.5</sub>, and O<sub>3</sub> show strongly positive correlation coefficients. Effects of CO, NO, NO<sub>2</sub>, and SO<sub>2</sub> correlated coefficients are higher during the cool days than during the warm days. These correlations are significant (Figures 13(d) and 13(f)) and similar during cool and warm days. For the older outpatients (ages 16–65, and above 66), effects of air pollutants are significantly enhanced during the cool days than during the warm days.

Our results show the confounding effects of temperature are quite complicated. Effects of PM<sub>10</sub>, PM<sub>2.5</sub>, and O<sub>3</sub> on pneumonia outpatients are less sensitive to temperature for the youngest group

**Table 5.** Multiple Linear Regression Analysis of Allergic Rhinitis Outpatient Visits: Regression Coefficients, *F* value, *R*<sup>2</sup>, and *P* Value.

Sex	$\beta_1(\text{PM}_{10})$	$\beta_2(\text{PM}_{2.5})$	$\beta_3(\text{O}_3)$	$\beta_4(\text{CO})$	$\beta_5(\text{NO})$	$\beta_6(\text{NO}_2)$	$\beta_7(\text{SO}_2)$	<i>F</i> -value	<i>R</i> <sup>2</sup>	<i>P</i> -value
	$\beta_8(\text{TEMP})$	$\beta_9(\text{RAIN})$	$\beta_{10}(\text{WD})$	$\beta_{11}(\text{WS})$	$\beta_{12}(\text{RH})$					
<i>Age Group 0–15 Years: Allergic Rhinitis</i>										
2007										
male	–0.0000	0.0144	–0.0039	–0.3585	0.0061	–0.0109	–0.0480			
	–0.1231	–0.0201	0.0545	0.0843	–0.0396	2.97	0.13			0.0014
2008										
Male	–0.009	0.0047	–0.0362	–0.9378	0.0175	0.0215	0.0586			
	–0.0535	0.0088	0.1703	0.0081	–0.0830	3.63	0.15			0.0001
2010										
Male	0.0061	–0.0008	–0.0043	–1.1157	0.0225	0.1039	–0.0532			
	0.0574	0.0438	–0.1619	0.6995	–0.0535	2.47	0.11			0.0046
Female	0.0130	–0.0188	0.0045	–0.2243	0.0161	0.0468	–0.0944			
	–0.0766	–0.0311	0.0340	0.1682	–0.0404	3.29	0.14			0.0002
<i>Age Group 16–65 Years: Allergic Rhinitis</i>										
2007										
Male	0.0019	0.0071	–0.0121	–0.1463	0.0034	–0.0052	–0.0367			
	0.1029	–0.0014	0.0760	–0.3452	–0.0428	2.83	0.13			0.0012
<i>Age Group ≥ 65 Years: Allergic Rhinitis</i>										
2011										
female	0.0005	0.0000	0.0063	0.0115	–0.0012	0.0010	–0.0187			
	–0.0375	0.0044	–0.0223	–0.3737	–0.0086	2.50	0.11			0.0042

doi:10.1371/journal.pone.0075220.t005

of people but sensitive to other two older groups. Effects of CO, NO, NO<sub>2</sub>, and SO<sub>2</sub> are all sensitive to temperatures for all three age groups of outpatients.

**4.4. COPD.** Figure 14 shows frequency distribution of outpatient visits for COPD. The observed frequency distribution of outpatient visits are close to theoretical normal distribution for ages 16–65 and above 66 group of outpatients.

Outpatient visits for COPD shows overwhelmingly negative correlation with temperature (Figure 15(a)), and these correlations are very significant for three age groups of outpatients. Positive correlations are seen for PM<sub>10</sub>, PM<sub>2.5</sub>, and NO<sub>2</sub>. These correlations are very significant (Figure 15(b)). Positive correlations also seen for O<sub>3</sub> and NO but are not as persistently presented as for particulate air pollution and NO<sub>2</sub>. Previous works have shown positive association between particulate air pollution and COPD [47,49].

For COPD, the youngest outpatients (age 0–15) are more correlated with air pollutants during the warm days (Figure 15(c)) than during the cool days (Figure 15(e)). However, for the other two older group of outpatients (ages 16–65, and above 66), both warm days and cool days show similar distribution of correlation coefficients. COPD are mostly correlated with air pollutants for the oldest outpatients (above 66) and these correlations are significant (Figures 15(d) and 15(f)).

### 5. Multiple Linear Regression Model Analysis

As shown in Table 2, a list of twelve multiple linear regression models were used to find best association between outpatient visits and air pollutants and meteorological factors. Table 4 shows a list of typical results when PM<sub>10</sub>-based models were run one by one through the 0–15 age group of male outpatients for allergic rhinitis disease in 2010. These results show that complex models produces

statistically significant results (as seen from *F* value, *R*<sup>2</sup>, and *P* value) compared with simple models. Regression results are similar when PM<sub>10</sub>, PM<sub>2.5</sub>, and O<sub>3</sub> are three major independent variables. Inclusion of CO as an additional independent model variable increase *R*<sup>2</sup>, followed by inclusion of another independent model variable NO<sub>2</sub>. The most significant increase in *R*<sup>2</sup> occurs when temperature is included as an independent variable in the model. Addition of relative humidity, rainfall, and winds also increase *R*<sup>2</sup> and the statistical significance of our model analysis. Similar results consistently occur when run multiple linear regression models were run through other disease, age group of outpatients, air pollutants, and meteorological factors. These multiple linear regression results are also consistent with the confounding effects of temperature from correlation coefficient analysis shown in the previous section.

Table 5 shows multiple linear regression analysis of daily outpatients for allergic rhinitis. Our 12-parameter multiple linear regression models shows that the 0–15 age group of male outpatient visits are statistically significant in the 2007 (*P*=0.0014), 2008 (*P*=0.0001), and 2010 (*P*=0.0046) data. NO is the main pollutant and wind speeds is the main meteorological factor that are persistently and positively associated with the increase of outpatient visits. Relative humidity is persistently and negatively associated with the outpatient visits. Low relative humidity predicts higher outpatient visits than high relative humidity. For the female outpatients, only the 2010 data showing statistically significant association (*P*=0.0002). Positive associations occur with PM<sub>10</sub>, O<sub>3</sub>, NO, NO<sub>2</sub>, and wind speeds. Negative associations occur with temperature and relative humidity.

For the 16–65 age group of outpatients, multiple linear regression model shows only results for male outpatients in the 2007 data are statistically significant (*P*=0.0012). In this case,

**Table 6.** Multiple Linear Regression Analysis of Asthma Outpatient Visits Regression Coefficients, *F* value, *R*<sup>2</sup>, and *P* Value.

Sex	$\beta_1(\text{PM}_{10})$	$\beta_2(\text{PM}_{2.5})$	$\beta_3(\text{O}_3)$	$\beta_4(\text{CO})$	$\beta_5(\text{NO})$	$\beta_6(\text{NO}_2)$	$\beta_7(\text{SO}_2)$	<i>F</i> -value	<i>R</i> <sup>2</sup>	<i>P</i> -value
	$\beta_8(\text{TEMP})$	$\beta_9(\text{RAIN})$	$\beta_{10}(\text{WD})$	$\beta_{11}(\text{WS})$	$\beta_{12}(\text{RH})$					
<i>Age Group 0–15 Years: Asthma</i>										
2008										
male	−0.0081	0.0062	−0.0206	−0.5042	0.0021	0.0727	−0.0601			
	−0.1523	−0.0239	0.0321	0.1445	−0.0221	2.76	0.12			0.0015
female	0.0058	−0.0060	−0.0039	−0.6655	0.0088	0.0283	−0.0627			
	−0.0724	0.0049	−0.0661	−0.6085	−0.0066	3.03	0.13			0.0005
<i>Age Group 16–65 Years: Asthma</i>										
2007										
Male	−0.0039	−0.0048	0.0019	−0.5143	0.0073	0.0093	0.1561			
	−0.1279	−0.0100	−0.0054	0.0547	0.0281	3.57	0.15			0.0001
2009										
male	0.0088	−0.0196	−0.0039	−0.1584	0.0035	0.0386	−0.0590			
	−0.0883	−0.0266	−0.0385	−0.6217	−0.0075	2.65	0.12			0.0024
female	0.0161	−0.0223	−0.0065	−0.4537	−0.0003	0.0830	−0.0815			
	0.0120	−0.0141	−0.0188	0.4914	0.0181	2.16	0.10			0.0144
2011										
female	0.0219	0.0000	0.0269	−0.1364	0.0190	−0.0300	−0.0559			
	−0.3124	−0.0115	−0.0740	−1.2689	−0.0007	4.41	0.18			<0.0001
<i>Age Group ≥ 66 Years: Asthma</i>										
2007										
male	−0.0035	−0.0098	−0.0012	−0.3204	0.0144	−0.0005	0.0186			
	−0.1591	−0.0087	0.0711	0.0971	−0.0272	3.46	0.15			0.0001
2008										
male	−0.0061	0.0006	−0.0124	−0.4596	0.0054	0.0436	−0.0681			
	0.0053	−0.0002	−0.0406	−0.2538	0.0348	2.27	0.10			0.0095
2009										
male	−0.0071	0.0043	0.0127	0.1547	−0.0018	0.0579	−0.0893			
	−0.0085	−0.0144	−0.0001	0.4906	0.0021	2.07	0.09			0.0197
2011										
female	0.0150	−0.0000	0.0001	0.0939	0.0085	−0.0091	−0.0231			
	−0.1084	−0.0107	−0.0163	−0.0868	−0.0195	3.28	0.14			0.0002

doi:10.1371/journal.pone.0075220.t006

PM<sub>10</sub>, PM<sub>2.5</sub>, NO, and temperature positively predicts the increase of outpatient visits. Rainfall rates and relative humidity are negatively associated with outpatient visits.

For outpatients with ages greater than 66, statistically significant association between outpatient visits and air pollutants and meteorological factors occur mostly in the 2011 data for female outpatients (*P*=0.0042). Positive increase in air pollutants PM<sub>10</sub>, O<sub>3</sub>, CO, and NO<sub>2</sub> are associated with increase in outpatient visits. Temperature and relative humidity are negatively associated with the outpatient visits.

Table 6 shows multiple linear regression analysis of outpatient visits for asthma. For the 0–15 age group of both male and female outpatients, statistically significant associations occur only in the 2008 data (*P*=0.0015 for male, and *P*=0.0005 for female). Air pollutants NO and NO<sub>2</sub> are positively associated with both male and female outpatient visits. Temperature and relative humidity are negatively associated with outpatient visits. Male outpatient visits are also positively associated with PM<sub>2.5</sub> concentrations,

while female outpatient visits are positively associated with PM<sub>10</sub> concentrations.

For the elder group of male outpatients (16–65 years old), statistically significant associations occur in 2007 (*P*=0.0001) and 2009 (*P*=0.0024). In these two years of data, both NO and NO<sub>2</sub> shows persistently positive while temperature shows persistently negative association with outpatient visits. For the female outpatients, statistically significant associations occur in the 2009 (*P*=0.0144) and 2011 (*P*≤0.0001) data. PM<sub>10</sub> is the most significant factor that is persistently and positively associated with female outpatient visits.

For the eldest group of outpatients, statistically significant associations for male outpatients occur in the data of 2007 (*P*=0.0001), 2008 (*P*=0.0095), and 2009 (*P*=0.0197). No pollutants show persistently positive associations with male outpatient visits. For the female outpatients, statistically significant association occur in the 2011 data (*P*=0.0002). Air pollutants PM<sub>10</sub>, O<sub>3</sub>, CO, and NO are positively associated with outpatient

**Table 7.** Multiple Linear Regression Analysis of Pneumonia Outpatient Visits Regression Coefficients, *F* value, *R*<sup>2</sup>, and *P* Value.

Sex	$\beta_1(\text{PM}_{10})$	$\beta_2(\text{PM}_{2.5})$	$\beta_3(\text{O}_3)$	$\beta_4(\text{CO})$	$\beta_5(\text{NO})$	$\beta_6(\text{NO}_2)$	$\beta_7(\text{SO}_2)$	<i>F</i> -value	<i>R</i> <sup>2</sup>	<i>P</i> -value
	$\beta_8(\text{TEMP})$	$\beta_9(\text{RAIN})$	$\beta_{10}(\text{WD})$	$\beta_{11}(\text{WS})$	$\beta_{12}(\text{RH})$					
<i>Age Group 0–15 Years: Pneumonia</i>										
2007										
male	0.0084	−0.0232	−0.0108	0.8772	0.0094	−0.0120	0.1196			
	−0.5691	−0.0096	0.0415	−0.4870	−0.0301	5.59	0.22			<0.0001
female	0.0045	−0.0179	−0.0167	1.0369	−0.0034	−0.0015	0.0209			
	−0.4374	0.0126	−0.0295	−0.5496	−0.1042	3.99	0.17			<0.0001
2009										
male	0.0294	−0.0275	−0.0028	−0.0945	−0.0127	0.0317	−0.2386			
	−0.0998	−0.0126	−0.1883	−0.4633	−0.0628	2.94	0.13			0.0008
female	0.0240	−0.0181	−0.0134	−0.2471	0.0102	0.0414	−0.0975			
	−0.0694	−0.0146	−0.0756	−0.5318	−0.0763	2.67	0.12			0.0022
2011										
male	−0.0022	−0.0000	0.0535	−1.5489	0.0402	0.0135	0.1126			
	−0.3419	−0.0389	−0.3596	−2.0619	−0.0283	5.83	0.23			<0.0001
female	0.0032	−0.0000	0.0584	−0.6388	−0.0009	−0.0223	0.0266			
	−0.4399	−0.0604	−0.2782	−1.9063	−0.0325	9.66	0.33			<0.0001
<i>Age Group 16–65 Years: Pneumonia</i>										
2007										
male	−0.0099	0.0057	−0.0072	0.1920	−0.0012	0.0176	0.0018			
	−0.0859	−0.0034	0.0099	−0.0949	−0.0049	3.58	0.16			0.0001
female	−0.0013	−0.0043	−0.0122	−0.0286	0.0018	0.0083	−0.0126			
	−0.0555	−0.0028	−0.0104	−0.2840	−0.0271	2.45	0.11			0.0051
2011										
male	0.0045	0.0000	−0.0028	−0.3053	0.0080	0.0117	0.0074			
	−0.0648	−0.0182	0.0230	−0.0491	0.0063	3.04	0.13			0.0005
female	0.0018	0.0000	0.0004	0.1477	0.0058	0.0220	−0.0376			
	−0.1375	−0.0157	0.0401	−0.0271	−0.0260	6.18	0.24			<0.0001

doi:10.1371/journal.pone.0075220.t007

visits, while temperature and relative humidity are negatively associated with outpatient visits.

Table 7 shows multiple linear regression analysis of outpatient visits for pneumonia. For the age 0–15 group of male outpatients, statistically significant associations occur in the data of 2007 ( $P \leq 0.0001$ ), 2009 ( $P = 0.0008$ ), and 2011 ( $P \leq 0.0001$ ). Temperature and relative humidity exhibit persistently negative association with outpatient visits. For female outpatient, statistically significant associations occur in the 2007 ( $P \leq 0.0001$ ), 2009 ( $P = 0.0022$ ), and 2011 ( $P \leq 0.0001$ ) data.  $\text{PM}_{10}$  is the main pollutant that is persistently and positively associated with female outpatient visits. Temperatures and relative humidity are persistently and negatively associated with female outpatient visits.

For the age 16–65 group of outpatients, statistically significant associations for male outpatients occur in the data of 2007 ( $P = 0.0001$ ) and 2011 ( $P = 0.0005$ ). Air pollutants  $\text{NO}_2$  and  $\text{SO}_2$  show persistently positive associations with male outpatient visits. Temperatures are negatively associated with male outpatient visits. For the female outpatients, statistically significant association occur in the 2007 ( $P = 0.0051$ ) and 2011 ( $P \leq 0.0001$ ) data. Air pollutants CO, NO, and  $\text{NO}_2$  are positively associated with outpatient visits, while temperature and relative humidity are negatively associated with outpatient visits. For the eldest group of outpatients, no

statistically significant associations are found for outpatient visits during the 2007–2011 data.

Table 8 shows multiple linear regression analysis of associations of outpatient visits for COPD with respect to air pollutants and meteorological factors. Statistically significant association for the age 0–15 group of male outpatients occur only in the 2008 data ( $P = 0.0013$ ). In this case,  $\text{PM}_{2.5}$ , NO and  $\text{NO}_2$  are positively while temperature and relative humidity are negatively associated with outpatient visits. Statistically significant associations for female outpatients also occur only in the 2008 data ( $P = 0.0007$ ). Female COPD outpatients are positively associated with  $\text{PM}_{10}$ , NO, and  $\text{NO}_2$ ; and negatively associated with temperature and relative humidity.

For the age 16–65 group of male outpatients, statistically significant associations occur in the 2007 ( $P = 0.0120$ ), 2008 ( $P = 0.0116$ ), 2009 ( $P = 0.0088$ ), and 2011 ( $P = 0.0056$ ). In these four years of data, COPD male outpatients are persistently and positively associated with  $\text{PM}_{10}$ . For female COPD outpatients, statistically significant associations occur in the 2009 ( $P = 0.0014$ ) and 2011 ( $P \leq 0.0001$ ) data.  $\text{PM}_{10}$ ,  $\text{O}_3$ , NO, and relative humidity are positively associated with female COPD outpatient visits.

For the eldest group of male outpatients (age greater than 66 years old), statistically significant associations occur only in the

**Table 8.** Multiple Linear Regression Analysis of COPD Outpatient Visits Regression Coefficients, *F* value, *R*<sup>2</sup>, and *P* Value.

Sex	$\beta_1(\text{PM}_{10})$	$\beta_2(\text{PM}_{2.5})$	$\beta_3(\text{O}_3)$	$\beta_4(\text{CO})$	$\beta_5(\text{NO})$	$\beta_6(\text{NO}_2)$	$\beta_7(\text{SO}_2)$	<i>F</i> -value	<i>R</i> <sup>2</sup>	<i>P</i> -value
	$\beta_8(\text{TEMP})$	$\beta_9(\text{RAIN})$	$\beta_{10}(\text{WD})$	$\beta_{11}(\text{WS})$	$\beta_{12}(\text{RH})$					
<i>Age Group 0–15 Years: COPD</i>										
2008										
male	−0.0079	0.0053	−0.0221	−0.5171	0.0019	0.0755	−0.0631			
	−0.1512	−0.0231	0.0317	0.1388	−0.0210	2.82	0.12			0.0013
female	0.0059	−0.0064	−0.0042	−0.6612	0.0091	0.0299	−0.0638			
	−0.0704	0.0055	−0.0644	−0.6309	−0.0075	2.97	0.13			0.0007
<i>Age Group 16–65 Years: COPD</i>										
2007										
male	0.0167	0.0030	0.0425	−1.4398	0.0228	0.0590	0.0863			
	0.0688	−0.0236	0.0489	0.0075	0.1220	2.21	0.10			0.0120
2008										
male	0.0237	−0.0422	−0.0388	−0.4829	0.0065	0.0969	−0.0591			
	0.0243	−0.0412	−0.0228	−0.0512	0.0374	2.22	0.10			0.0116
2009										
male	0.0099	−0.0325	0.0017	−0.1240	0.0032	0.0853	−0.0886			
	−0.0958	−0.0217	−0.1388	0.2359	−0.0222	2.29	0.10			0.0088
female	0.0250	−0.0514	0.0260	−0.7680	0.0194	0.0899	−0.0951			
	0.0065	−0.0195	−0.0727	1.3777	0.0340	2.78	0.12			0.0014
2011										
male	0.0095	−0.0000	0.0336	0.3874	−0.0102	−0.0060	−0.1294			
	−0.2667	−0.0248	−0.0140	−1.5874	−0.0040	2.42	0.11			0.0056
female	0.0305	0.0000	0.0320	−0.1361	0.0202	−0.0001	−0.1247			
	−0.3681	−0.0008	0.0194	−1.2646	0.0115	3.78	0.16			<0.0001
<i>Age Group ≥ 65 Years: COPD</i>										
2008										
male	−0.0112	0.0060	−0.0206	−0.8232	0.0129	0.0635	−0.0550			
	0.0149	−0.0087	−0.0757	−0.4737	0.0335	2.22	0.10			0.0116
2010										
female	0.0086	0.0137	−0.0022	0.3628	−0.0045	0.0006	−0.0399			
	−0.0599	0.0034	0.0160	−0.2328	0.0185	3.45	0.15			0.0001
2011										
female	0.0182	0.0000	−0.0028	0.2111	0.0068	0.0210	−0.0641			
	−0.1424	−0.0027	0.0364	−0.0093	−0.0240	4.37	0.18			<0.0001

doi:10.1371/journal.pone.0075220.t008

2008 (*P* = 0.0116) data. In this case, PM<sub>2.5</sub>, NO, NO<sub>2</sub>, temperature, and relative humidity are positively associated with outpatient visits. For female outpatients, statistically significant associations occur in the 2010 (*P* = 0.0001) and 2011 (*P* ≤ 0.0001) data. In these two years of data, female COPD outpatients are positively associated with PM<sub>10</sub>, CO, and NO<sub>2</sub>. Temperatures are negatively associated with these outpatient visits.

**Summary**

Taiwan contains high density of industrial factories, polluted air, and a comprehensive National Health Insurance program that covers population and contracted 92.1% of all hospitals and clinics in Taiwan. In this work we used outpatient data from a hospital in a heavily industrial area in Taiwan to study the association between public health and air pollution in the context of a heavily

polluted atmospheric environment during the period 2007–2011. We used hospital visit data from the Landseed Hospital, and air pollution and meteorological data from EPA to study the association between air pollution levels, meteorology, and hospital visit frequency for the period 2007–2011 over Chung-Li area. We test the normality of each data set, control for the confounding factors, and calculate correlation coefficient between the outpatient visits and air pollution and meteorology, and use multiple linear regression analysis to seek significance of these associations.

Table 9 shows a summary of list of main pollutants and meteorological factors that are statistically significant in associating with the respiratory diseases from multiple linear regression analysis. Temperature and relative humidity tend to be negatively associated with respiratory diseases. NO and NO<sub>2</sub> are two main air pollutants that are positively associated with respiratory diseases, followed by PM<sub>10</sub>, PM<sub>2.5</sub>, O<sub>3</sub>, CO, and SO<sub>2</sub>. Young

**Table 9.** Summary of Multiple Linear Regression Analysis of Outpatient Visits for Respiratory Diseases.

	Allergic Rhinitis	Asthma	Pneumonia	COPD
<b>0–15 Age Group</b>				
male	+: NO, WS –: RH	+: PM <sub>2.5</sub> , NO, NO <sub>2</sub> –: T, RH	–: T, RH	+: PM <sub>2.5</sub> , NO, NO <sub>2</sub> –: T, RH
female	+: PM <sub>10</sub> , O <sub>3</sub> , NO, NO <sub>2</sub> –: T, RH	+: PM <sub>10</sub> , NO, NO <sub>2</sub> –: T, RH	+: PM <sub>10</sub> –: T, RH	+: PM <sub>10</sub> , NO, NO <sub>2</sub> –: T, RH
<b>16–65 Age Group</b>				
male	+: PM <sub>10</sub> , PM <sub>2.5</sub> , NO, T –: RH	+: NO, NO <sub>2</sub> –: T	+: NO <sub>2</sub> , SO <sub>2</sub> –: T	+: PM <sub>10</sub>
female		+ PM <sub>10</sub>	+: CO, NO, NO <sub>2</sub> –: T, RH	+: PM <sub>10</sub> , O <sub>3</sub> , NO
<b>≥ 66 Age Group</b>				
male				+: PM <sub>2.5</sub> , NO, NO <sub>2</sub> + T, RH
female	+: PM <sub>10</sub> , O <sub>3</sub> , CO, NO <sub>2</sub> –: T, RH	+: PM <sub>10</sub> , O <sub>3</sub> , CO, NO –: T, RH		+: PM <sub>10</sub> , CO, NO <sub>2</sub> –: T

+ means positive association; – means negative association; T: temperature; RH: relative humidity; WS: wind speed.

doi:10.1371/journal.pone.0075220.t009

outpatients (age 0–15 years) are most sensitive to changing air pollution and meteorology factors, followed by the eldest (age ≥ 66 years) and age 16–65 years of outpatients. Outpatients for COPD diseases are most sensitive to air pollution and meteorology factors, followed by allergic rhinitis, asthma, and pneumonia diseases. In the context of sex difference to air pollution and meteorological factors, male outpatients are more sensitive than female outpatients in the 16–65 age groups, while female outpatients are more sensitive than male outpatients in the young 0–15 age groups and in the eldest age groups. In total, female outpatients are more sensitive to air pollution and meteorological factors than male outpatients.

## Acknowledgments

We thank Taiwan EPA for making ambient air monitoring data openly accessible for research (<http://www.epa.gov.tw>); and Yi-Fang Chi, Tai-Fu

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Huang, Tsung-Yi Hsieh, and Chia-Chun Hsu for help in processing the air pollution, meteorology, and NHI data. Thanks also to Tien-Mu Hsiao and Chuan-Fa Hsieh for very inspirational discussions. We are very grateful for Leonard A. Barrie at the Cyprus Institute for reading the early version of the manuscript and sent us very useful comments. We are very grateful to Kleinbaum *et al.* [2008] and its predecessor versions (1988 and 1998) for very detailed description on methods of multiple linear regression analysis. We thank the reviewer's comments that greatly improved the clarity of this paper.

## Author Contributions

Conceived and designed the experiments: KYW TTC. Performed the experiments: KYW. Analyzed the data: KYW TTC. Contributed reagents/materials/analysis tools: KYW. Wrote the paper: KYW.



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