Air Pollution Levels Related to Peak Expiratory Flow Rates among Adult Asthmatics in Lampang, Thailand

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Abstract

Asthmatics may suffer harmful effects on their health due to air pollution. This study assesses the association between measured air pollution levels and peak expiratory flow rates (PEFR) among adults with asthma in Mae Moh district, Lampang, Thailand. The year-long study, resulting in 12,045 data points from 33 participants, was performed from November 2015 to October 2016. PEFR were compared against levels of CO, NO$_2$, O$_3$, SO$_2$, PM$_{2.5}$ and PM$_{10}$. A positive association between the daily mean concentration of NO$_2$ (lag 4) and PEFR on waking (morning PEFR): an increase of 1 ppb in NO$_2$ (lag 4) was associated an increase of 1.34 L min$^{-1}$ (95% Confidence interval (CI): 0.25, 2.44) in PEFR. Also, interaction between NO$_2$ (lag 4) and PM$_{10}$ (lag 6) was multiplicatively associated with decreased morning PEFR by -0.015 L min$^{-1}$ at 95% CI. NO$_2$ max (lag 2) and PM$_{10}$ max (lag 6) were associated negatively with coefficients of -0.07 and -0.013 at 95% CI, respectively. Furthermore, in morning PEFR, with PM$_{2.5}$ max included in the generalized estimating equation model, only NO$_2$ max (lag 2) and CO max (lag 6) associated negatively with coefficients of -0.08 and -1.71 at 95% CI, respectively. O$_3$ max (lag 3) and PM$_{2.5}$ max were positively related to evening PEFR with coefficients of 0.078 and 0.029 at 95% CI, respectively. The daily average PEFR and NO$_2$ (lag 4) associated positively with a coefficient of 0.15 at 95% CI, while SO$_2$ associated negatively with a coefficient of -0.47 at 95% CI. Conversely, NO$_2$ max (lag 2) associated negatively with a coefficient of -0.05 at 95% CI, while O$_3$ max (lag 3) associated positively with a coefficient of 0.06 at 95% CI. The findings indicated are that information regarding pollutants’ delayed effects and the negative effects of some pollutants on PEFR enable the forecasting of health effects and take serious actions to prevent those pollutants at their sources.

Keywords: Air pollution; Peak expiratory flow rates; Asthmatic patients; Mae Moh.
INTRODUCTION

Air pollution causes millions of premature deaths worldwide (Silva et al., 2016), and is linked to respiratory infections, heart disease, chronic obstructive pulmonary disease (COPD), stroke and lung cancer. It is associated with dyspnea, wheezing, coughing and asthma (World Health Organization, 2014; Kallawicha et al., 2018; Li et al., 2018) because of its identified impact on lung function (Lee et al., 2011; Arblex et al., 2012; Zhou et al., 2016; Chen et al., 2018).

The World Health Organization (WHO) estimated that in 2015, 383,000 deaths worldwide were due to asthma (WHO, 2017). Many studies have found that ambient air pollution causes adverse effects in asthmatic patients, for example, increased respiratory symptoms (Mann et al., 2010; Kelly and Fussell, 2011), worsened lung function (Aekpalakorn et al., 2003), and decreased peak expiratory flow rate (PEFR) (Wiwatanadate and Trakultivakorn, 2010; Zhou et al., 2016). PEFR, a spirometry parameter, is the maximum airflow rate accomplished during forced expiration following maximal inspiration (Ray et al., 1993; Quenier et al., 1997; Skladanowski et al., 2016). It is an especially useful measure for detecting airway obstruction early, when screening asthmatic patients and observing the effects of environmental and occupational exposure (Ray et al., 1993). Reduction in PEFR has been related to exposure to high concentrations of air pollutants, particularly among asthmatic patients (Hong et al., 2010; Wiwatanadate and Trakultivakorn, 2010; Wiwatanadate and Liwsrisakun, 2011; Yamazaki et al., 2011).

The Health Effects Institute (HEI) reported that particulate matter (PM) and ozone (O₃) are the worst threat toward good air quality in the Asian region (HEI, 2010). PM, a complex mixture of extremely small particles and liquid droplets consisting of organic chemicals, acids, and soil and dust particles (U.S. EPA, 2018), is designated as inhalable PM of aerodynamic diameter ≤ 10 µm (PM₁₀)
or PM of aerodynamic diameter $\leq 2.5\ \mu m$ (PM$_{2.5}$ or fine PM). Most PM occurs naturally in the environment, but increasing anthropogenic interferences in the environment have significantly increased the PM burden (Cha et al., 2019). Anthropogenic sources of PM include vehicular emissions and activities such as biomass burning, industrial processing, agricultural operations, and construction activities (Widiana et al., 2017; Deshmukh, et al., 2019; Hao et al., 2019; Hien et al., 2019; Hu et al., 2019; Liu et al., 2019; Shahid et al., 2019). PM emitted from natural sources and human activities includes carbon monoxide (CO), nitrogen dioxide (NO$_2$) and sulfur dioxide (SO$_2$).

In Thailand, high PM$_{10}$ concentrations contribute greatly to air pollution, which causes the country significant public health problems. In 2012, Saraburi Province, near Bangkok, recorded the highest PM$_{10}$ concentration in the country, owing to the stone milling and crushing activity carried out in the area, while areas in the north of the country had the second-highest concentration, due to its annual smog crisis linked to power plant emissions, post-harvest burning, forest fires, and vehicle exhaust fumes (Thepnuan et al., 2019). The problem has been worsening over time as concentrations of PM$_{10}$ have been increasing continually in every province of Thailand (PCD, 2013). In addition to forest fires, agricultural waste burning, vehicle exhaust emissions, construction work sites and industrial pollution, certain weather conditions are implicated: temperature inversions and little or no wind helps smog to settle and remain in one place. The northern provinces of Thailand, for example, Chiang Rai, Mae Hong Son and Tak, bordering Laos and/or Myanmar, also often suffer pollution that originates from those countries (PCD, 2013; Thepnuan et al., 2019). These diverse causes of smog in the northern provinces produce long- and short-term ill effects among the population. Experimental exposure to PM results in oxidative stress, airway hyper-responsiveness, and airway re-modeling, either alone or in combination with allergic sensitization (Stanek et al., 2011), while short-term exposure to ambient PM$_{2.5}$ and PM$_{10}$ in asthmatic children and adults has been associated with asthma
symptoms, especially in children with allergic sensitization (Mann et al., 2010; Meng et al., 2010). Long-term exposure to PM is associated with poorly controlled asthma and decrements in lung function in children and adults (Liu et al., 2009; Jacque et al., 2012). A study in northern Thailand during 2001 and 2002 found that 3.01% of 22-24 year-olds had asthma (Dejsomritrutai et al., 2006). The adverse environmental effects have not only damaged human physical and mental health, but also crops and livestock (Boonlong, 2011).

The northern province of Lampang ranks fourth in the most air-polluted provinces in Thailand, with an average maximum daily PM$_{10}$ of 237 µg m$^{-3}$, and an average that exceeds the standard level for 23 days a year (PCD, 2013). Within Lampang is Mae Moh district, located in a flat valley that is highly prone to temperature inversions, and also home to a coal-fired steam power plant. The Mae Moh Power Plant uses lignite mined from an open-pit (http://www.maemoh.egat.co.th). In 1992 and 1998, the Plant was involved in major environmental disputes, due to local villagers being exposed to sulfur dioxide released from the power plant, with further disputes since then. Thus, the main sources of air pollution in this area include power plant emissions, post-harvest burning, forest fires, and vehicle exhaust fumes. This study aimed to investigate the effects of air pollutants on daily PEFR in people suffering asthma living in Mae Moh district in Thailand. A longitudinal design of one year duration was used, with 33 participants, producing 12,045 person-days sample size, making this among the largest pollution-asthma panel studies ever carried out. Also, the use of time series analysis exposed the strongest lagged effect of each pollutant and on PEFR.

MATERIALS AND METHODS

Study design, setting, and participants
This study used a panel study design for obtaining a time series of repeated outcome measurements and exposures in a closed cohort of 33 adult sufferers of asthma. All 33 (1) had asthma as diagnosed by a physician, (2) experienced asthma symptoms during the past year, (3) were more than 15 years old, and (4) had lived in Mae Moh district for more than 1 year. In addition, all of the participants lived no further than 25 km from the Mae Moh air quality monitoring station, from which most air quality data was collected. The study protocol was approved by the Research Ethics Committee of the Faculty of Medicine, Chiang Mai University (CMU-REC No 270/2015). All of the participants signed an informed consent form before the study began. Data on participants was collected through structured interviews with the principal researcher and questionnaires requesting demographic characteristics, history of illnesses and allergies, and medication used. The participants additionally had a chest X-ray (CXR) and lung function test. The CXR showed no trace of cancer, empyema, emphysema or COPD for any of the 33 participants. All participants were non-smokers or had quit smoking more than one year earlier. Each participant was categorized for the severity of their asthma in accordance with the criteria of the U.S. National Heart, Lung and Blood Institute. (National Heart, Lung, and Blood Institute, 1997).

In orientation, participants were taught individually how to measure their own PEFR and asked to repeat the procedure to confirm that they could do it successfully. Each participant measured their PEFR 3 times and the highest and best value was recorded. The study commenced on 2nd November, 2015 and completed on 31st October, 2016. Every day during the study, each participant recorded their PEFR twice when they woke in the morning and before bed in the evening. The PEFR was measured using a mini-Wright peak flow meter (Clement Clarke International, Ltd, UK). Records of the participants were returned to the researcher at the end of each month, and the researcher also accessed data from participants’ hospital visits during the study period.
Measurements of air pollutants and meteorological data

Data for nitrogen dioxides (NO$_2$), ozone (O$_3$), sulfur dioxide (SO$_2$), (PM$_{2.5}$) and (PM$_{10}$) were collected from Mae Moh sub-district air monitoring station, and carbon monoxide (CO) data were collected from Sob-pad air quality monitoring station, both stations belonging to the Pollution Control Department, Thailand (PCD) (2013). At these automated air sampling monitoring stations the concentrations of each pollutant are monitored continuously and reported hourly. CO is analyzed technically using the non-dispersive infrared detection method, SO$_2$ by pararosaniline, NO$_2$ and O$_3$ by chemiluminescence, and PM$_{10}$ and PM$_{2.5}$ by the gravimetric method (Air Quality and Noise Management Bureau, PCD, Thailand, 2020). Daily average concentrations (0.00-24.00 o’clock) were computed, and the highest hourly concentration taken as the daily maximum. Meteorological data, including wind speed, temperature, global radiation, and rainfall quantity, were also collected from the PCD stations. Readings of pressure and relative humidity were taken from measurements at Lampang airport, which is approximately 30 km southwest of the study area (Lampang Meteorological Station). The meteorological and pollutant parameters were computed in the same way, except for pressure and relative humidity, which were based on the daily average and daily maximum data from the Lampang Meteorological Station.

Statistical analysis

Data on demographic background, and daily meteorological and air pollutant measurements were used to investigate the relationship between concentrations of air pollutants and PEFR by using the generalized estimating equation (GEE) model, which allowed this study to account for the within-
subject correlation of repeated measurements. All pollutant variables were recorded as a time series, and it was assumed that their effects were lagged (delayed). “Lag” means the delayed effect. The number means the number of days that the effect is delayed. For example, NO$_2$ (lag 4) means that the NO$_2$ data is the NO$_2$ level reported 4 days prior to the data it is being related to. The statistical software used in the analysis was the SPSS version 22 (IBM, Singapore).

The steps of analysis were as follows:

1) Separate univariate analysis of mean and maximum levels of the meteorological variables was performed (at lags of 0-6), with three separate measurements of PEFR; morning PEFR, evening PEFR, and daily average PEFR (morning PEFR + evening PEFR)/2, resulting in a total of three reported outcomes. 2) Each of the mean and maximum (max) pollutants (lags 0-6) were (univariately) analyzed separately with each outcome. The best lagged effect (i.e., the smallest $p$-value) was entered into the proceeding steps. 3) Demographic factors (gender, age, asthma severity, weight, and height) and day of the week were included in the model, together with the best lagged meteorological covariates for each outcome from the previous step. Those with a $p$-value < 0.25 were kept for further analysis (Wiwatanadate and Trakultivakorn, 2010). Selection of the 0.25 level was made by following the work of Bendel and Afifi (1977), which showed that use of a more conventional level (e.g., 0.05) often fails to identify variables that are considered important. Due to the autocorrelation nature of repeated measurements over time, this study produced plots of the autocorrelation functions (ACF) (Fig. 1) and partial autocorrelation functions (PACF) (Fig. 2) of all three PEFR outcomes, in order to visualize the characteristics of the correlation: there was an exponential decay pattern for all of the outcome variables, starting at lag 1, in both ACF and PACF plots, indicating that the appropriate structure was first-order autoregressive (StatSoft, Inc., 2007). An autocorrelation plot shows the value of the autocorrelation function on the vertical axis. It can range from $-1$ to $1$. The horizontal axis of
the plot shows the size of the lag between the elements of the time series. 4) All demographic data were applied to all meteorological variables for analysis of each outcome, with $p$ value $< 0.25$ from step 3 and the best lag of each pollutant from step 2. 5) If more than one pollutant was found to be statistically significant, the pollutants were chosen and adjusted with a demographic and meteorological variable. 6) The correlation structure with the smallest quasi-likelihood under the independence model criterion (QIC) was selected (Pan, 2001; Cui and Qian, 2007). 7) The parsimonious model was chosen by the lesser value of quasi-likelihood under the independence model criterion (QICC) (Pan, 2001; Cui and Qian, 2007).

**RESULTS**

*Demographic and asthma characteristics of the cohort*

The asthma severity classification according to the Global Initiative for Asthma (GINA) (2008) were categorized into 4 levels: intermittent, mild persistent, moderate persistent and severe persistent (Bateman *et al.*, 2008). **Table 1** presents descriptive statistics of the demographic and asthma characteristics of the cohort. After 4 participants withdrew from this study, 33 remained (11 males and 22 females). Their mean age was $49.4 \pm 10.0$ years, mean body weight $63.2 \pm 13.1$ kg and mean height $157.1 \pm 6.2$ cm, and their asthma severity was categorized as mild intermittent 13 (39.4%), mild persistent 11 (33.3%) and moderate persistent 9 (27.3%).

*Description of ambient pollutants*

Concentrations of NO$_2$, O$_3$, CO, SO$_2$, PM$_{10}$, and PM$_{2.5}$ were collected daily for the 365 days of the study. Due to monitoring equipment malfunction, records for NO$_2$, O$_3$ and CO were missing for 17
days (4.66%), 3 days (0.82%) and 2 days (0.55%), respectively. The daily average concentrations were 4.87 ppb, 1.28 ppb, 33.92 ppb, 49.09 µg m\(^{-3}\), 28.91 µg m\(^{-3}\) and 0.76 ppm for NO\(_2\), SO\(_2\), O\(_3\), PM\(_{10}\), PM\(_{2.5}\), and CO, respectively. The meteorological daily averages were 0.98 m/s for wind speed, 26.03°C for temperature, 72.40 % for relative humidity, 163.14 w/m\(^2\) for global radiation, 1,009.96 mbar for pressure and 0.14 mm for precipitation.

Daily mean and max pollutants and meteorological parameters are shown in Table 2. The daily average PM\(_{10}\) and PM\(_{2.5}\) concentration exceeded the Thai standard concentrations of 120 µg m\(^{-3}\) and 50 µg m\(^{-3}\) for 18 and 76 days, respectively.

Table 3(a) shows the correlation matrix of mean ambient air pollutants and mean meteorological parameters. The highest correlation of ambient air pollutants was that between PM\(_{10}\) and PM\(_{2.5}\), \(r = 0.981\).

Table 3(b) shows the correlation matrix of max ambient air pollutants and max meteorological parameters. The highest correlation of max ambient air pollutants was that between PM\(_{10}\) max and PM\(_{2.5}\) max, \(r = 0.918\).

**Association between daily average pollutant levels and PEFR**

**Morning PEFR**

A separate single-pollutant model was performed, and adjustments to each best-lagged pollutant made for gender, asthma severity, day of the week, age, weight, wind speed (lag 5), temperature (lag 1), global radiation (lag 4), pressure (lag 1) and rain quantity (lag 6). It was found that NO\(_2\) (lag 4) associated positively with morning PEFR, with a coefficient of 0.23 (95% CI: 0.03, 0.43). PM\(_{10}\) (lag 6) and CO (lag 6) associated negatively with morning PEFR, with coefficients of -0.05 (95% CI: -0.07,
-0.02) and -3.93 (95% CI: -7.43, -0.43), respectively. The multi-pollutant models were analyzed further with all possible combinations of pollutants from the single-pollutant model [excluding SO₂ (lag 4), O₃ (lag 3) and PM₂.₅ (lag 6)]. It was found that the ambient daily mean concentration of NO₂ (lag 4) associated positively with morning PEFR, with a coefficient of 1.34 (95% CI: 0.25, 2.44). This meant that an increase of 1 ppb in the daily mean ambient concentration of NO₂ (lag 4 concentration 4 days earlier) was associated with an increase in morning PEFR of 1.34 L min⁻¹. Meanwhile, NO₂ (lag 4) and PM₁₀ (lag 6) [NO₂ (lag 4)×PM₁₀ (lag 6)] associated negatively with a coefficient of -0.015 (95% CI: -0.030, -0.001). This meant that the interaction between the daily mean concentration of NO₂ (lag 4) and PM₁₀ (lag 6) associated multiplicatively with a decreased morning PEFR by -0.015 (95% CI: -0.030, -0.001) (Table 4).

Evening PEFR

Evening PEFR was analyzed using the single-pollutant model in the same manner as the method mentioned above. The results showed that there was no statistical significance.

Daily average PEFR

The single-pollutant model showed that NO₂ (lag 4) was statistically positively related to the daily average PEFR with a coefficient of 0.15 (95% CI: 0.02, 0.29), while SO₂ was statistically negatively related to the daily average PEFR with a coefficient of -0.52 (95% CI: -1.03, -0.02). The multi-pollutant model showed that NO₂ (lag 4) associated positively with PEFR with a coefficient of 0.15 (95% CI: 0.01, 0.29), while SO₂ associated negatively, with a coefficient of -0.47 (95% CI: -0.92, -0.01) (Table 5).

Association between daily maximum pollutant levels and PEFR
Morning PEFR

The single-pollutant model showed that PM$_{2.5}$ max (lag 4) related both statistically and positively to morning PEFR with a coefficient of 0.02 (95% CI: 0.001, 0.04). NO$_2$ max (lag 2), PM$_{10}$ max (lag 6) and CO max (lag 6) associated negatively with morning PEFR, with coefficients of -0.07 (95% CI: -0.13, -0.01), -0.02 (95% CI: -0.03, -0.01), and -1.68 (95% CI: -3.08, -0.27), respectively. Both PM$_{10}$ and PM$_{2.5}$ were significant, due to analysis of the single model. Analysis of the multi-pollutant model of morning PEFR was made separately for PM$_{2.5}$ and PM$_{10}$.

The multi-pollutant model with all possible combinations of pollutants [excluding SO$_2$ max (lag 4), and O$_3$ max (lag 4)] from the single-pollutant model applied showed that NO$_2$ max (lag 2) and CO max (lag 6) were negatively related to morning PEFR with coefficients of -0.08 (95% CI: -0.14, -0.02) and -1.71 (95% CI: -3.11, -0.30), respectively (Table 6(a)).

NO$_2$ max (lag 2) and PM$_{10}$ max (lag 6) associated negatively with coefficients of -0.07 (95% CI: -0.13, -0.01) and -0.013 (95% CI: -0.024, -0.002), respectively (Table 6(b)).

Evening PEFR

The single pollutant model showed that O$_3$ max (lag 3) and PM$_{2.5}$ max associated positively with evening PEFR, with coefficients of 0.09 (95% CI: 0.04, 0.14) and 0.03 (95% CI: 0.01, 0.05), respectively. The multi-pollutant model, with all possible combinations of pollutants [excluding NO$_2$ max (lag 1), SO$_2$ max (lag 5), PM$_{10}$ max (lag 3), and CO max (lag 1)] from the single-pollutant model showed that both O$_3$ max (lag 3) and PM$_{2.5}$ max were positively associated to evening PEFR with coefficients of 0.098 (95% CI: 0.03, 0.127) and 0.029 (95% CI: 0.007, 0.051) (Table 7).

Daily average PEFR

The single pollutant model showed that NO$_2$ max (lag 2) associated negatively with daily average PEFR, with a coefficient of -0.05 (95% CI: -0.10, -0.01), while O$_3$ max (lag 3) associated positively
with daily average PEFR, with a coefficient of 0.05 (95% CI: 0.02, 0.08). The multi-pollutant model with all possible combinations of pollutants [excluding SO\(_2\) max (lag 4), PM\(_{10}\) max, PM\(_{2.5}\) max, and CO max] from the single-pollutant model showed that NO\(_2\) max (lag 2) was negatively related to daily average PEFR with a coefficient of -0.05 (95% CI: -0.10, -0.01), and O\(_3\) max (lag 3) was positively related to daily average PEFR with a coefficient of 0.06 (95% CI: 0.02, 0.09) (Table 8).

**DISCUSSION**

A negative relationship between pollutant level and PEFR allows for the possibility that the pollutant harms PEFR. It follows that a positive relationship between pollutant level and PEFR allows for the possibility that the pollutant improves PEFR. In this study, the following negative relationships were found: NO\(_2\) max (lag 2) was found to be related negatively with both morning and daily average PEFR, and SO\(_2\) was related negatively to daily average PEFR. PM\(_{10}\) max (lag 6) appeared to associate negatively with morning PEFR. Also, CO max (lag 6) was negatively associated with morning PEFR. Conversely, NO\(_2\) (lag 4) had a consistently positive association with morning and daily average PEFR and O\(_3\) max (lag 3) was found to relate positively to daily average PEFR.

When inhaled, NO\(_2\) penetrates to the trachea, bronchi, bronchiole, and alveoli and is an irritant to the mucosa of the eyes, nose, throat, and lower respiratory tract. It also increases bronchial reactivity and increases susceptibility to infections and allergens. It is considered a good marker of vehicular pollution (Arbrex *et al.*, 2013). The finding in the present study that NO\(_2\) (lag 4) had a consistently positive association with morning and daily average PEFR was at odds with its ‘pollutant’ status and was contradictory to the results of most other studies, which show an inverse association between NO\(_2\) and PEFR (Pekkanen *et al.*, 1997; Timonen and Pekkanen, 1997; Castro *et al.*, 2009; Qian *et al.*, 2009). Meanwhile, in some studies, no link has been found between NO\(_2\) and PEFR (van der Zee *et al.*, 2000;
Kwon et al., 2007; Amadeo et al., 2015). As in the present study, Wiwatanadate and Trakultivakorn (2010) found that NO2 (lag 5) associated positively with morning PEFR. Although NO2 (lag 4) in the present study was associated statistically, significantly and positively with morning and daily average PEFR, the interaction of NO2 (lag 4) and PM10 (lag 6) produced a significantly inverse effect on morning PEFR, with a coefficient of -0.015 (95% CI: -0.03, -0.001) (Table 4). Furthermore, our result showed that NO2 max (lag 2) had a significantly inverse association with morning and average PEFR. Specifically, a 1 ppb increase in NO2 max (lag 2) concentration with PM2.5 was associated with a morning PEFR decrease of 0.08 L min\(^{-1}\) (Table 6(a)), while a 1 ppb increase in NO2 max (lag 2) concentration with PM10 was associated with a morning PEFR decrease of 0.07 L min\(^{-1}\) (Table 6(b)). A 1 ppb increase in NO2 max (lag 2) concentration was associated with an average PEFR decrease of 0.05 L min\(^{-1}\) (Table 8). These results show that NO2 max (lag 2) had a significant inverse association with morning and daily average PEFR and indicate a potential harmful effect of this pollutant. It is possible that NO2 enhances lung function at very low doses, while high doses reduce lung function. Studies have tended to conclude that significant inverse association between air pollutants and PEFR exists at high pollutant concentrations (Wichmann and Heinrich, 1995), while no significant associations exist at low dose exposures (Kwon et al., 2007).

This study found that O3 max (lag 3) had a consistently positive association with daily average PEFR, and O3 appeared to be a protective factor in enhancing PEFR. It is known that some toxic agents can be beneficial to health at a low dose, such as bacterial endotoxins, which help to decrease the risk of asthma in children (Obihara et al., 2007; Sordillo et al., 2010), and lifelong exposure to farms may effectively reduce asthma risk in adults (Douwes et al., 2007). Regarding O3, the results in the present study are in agreement with a study in Brazil showing that a 10 µg m\(^{-3}\) increase in O3 (lag 1) enhanced morning PEFR by 0.2 L min\(^{-1}\) in asthmatic children (Castro et al., 2009). However, other studies have
found a negative association between the O₃ concentrations and lung function. O₃ is one of the most well-studied air pollutants, with initial speculation about health effects dating to the mid-nineteenth century (Rohr, 2018). O₃ exposure results in airway inflammation, airway hyper-responsiveness, and decrements in lung function in healthy and asthmatic adults (Seltzer et al., 1986). Altug et al. (2014) found a significant negative association between 1-week average O₃ and PEF in children without respiratory complaints. Schachter et al. (2016) evaluated asthmatic children in New York and found that O₃ was associated with decreased FEV₁ in summer. A panel study of Australian children, who had bronchial hyperactivity and asthma, revealed a significant inverse association between mean daytime O₃ and mean daily deviation PEFR (coefficient = -2.61 and p-value = 0.001) (Jajaludin et al., 2000).

However, a study of children in northern France found that this association was not significant (Declercq et al., 2000). Dales et al. (2009) similarly found no significant associations for ozone concentration and FEV₁, and Samoli et al. (2017) followed 186 children for 5 weeks and found that personal ozone exposure was not associated with PEF.

SO₂ penetrates into upper airways, trachea, bronchi, and bronchioles, and affects the mucosa of the eyes, nose, throat, and respiratory tract. It causes cough and increases bronchial reactivity, facilitating bronchoconstriction (Arbex et al., 2012). In the present study, a mean daily increase of 1 ppb of SO₂ was associated with a decrease in daily average PEFR of 0.47 L min⁻¹. Once again, the literature offers other works that also reported a negative association (Qian et al. (2009) and Wiwatanadate and Trakultivakorn (2010)), and those that report no association between SO₂ and PEFR (Aekplakorn et al., 2003; Park et al., 2005; Uno et al., 2005; Canova et al., 2010). It is noteworthy that SO₂ appeared to have adverse effects on lung function in adult asthmatic patients in the present study even though the 24-h average levels of SO₂ never exceeded the standard value for Thailand of 120 ppb during the study period.
This study found that CO max (lag 6) associated negatively with morning PEFR, with a coefficient of -1.71 (95% CI: -3.1, -0.30) (Table 6(a)); a 1 ppm increase of daily ambient CO max concentration (lag 6) was associated with a decrease in morning PEFR of 1.71 L min\(^{-1}\). This result supports previous works: Park et al. (2005) found that in a panel of 64 asthmatic adults, CO associated negatively with PEFR variability and mean daily average PEFR; Penttinen et al. (2001) found that CO associated negatively with daily average, morning and evening PEFR in adult asthmatic patients; Canova et al. (2010) revealed that CO negatively associated with morning and evening PEFR (p=0.01-0.03) in adult asthmatic patients.

Regarding PM\(_{2.5}\) and PM\(_{10}\), epidemiological studies suggest that PM\(_{2.5}\) may exert greater toxicity than larger particles (Xing et al., 2016). Toxicological studies have demonstrated that PM exposure may impact respiratory health by inducing both lung inflammation and systemic inflammation (Li et al., 2017; Maciejczyk et al., 2018).

Various studies have found an association between PM\(_{2.5}\) concentrations and decreased lung functions (Li et al., 2017; Chen et al., 2019; Huang et al., 2019; Rohana et al., 2019) but this was not the case in this study, even when ambient PM\(_{2.5}\) levels frequently exceeded the US NAAQS during the study period. This was not surprising because the causal components and susceptible subgroups of particulate matter are not clear (Delfino et al., 2003). Also, the major sources of air pollution in this study were located in northern Thailand, where there are forest fires and open field burning, which is different from most other studies that relate air pollution to traffic (Wiwatanadate and Liwsrisaku, 2010). Regarding the positive association between O\(_3\) max (lag 3), PM\(_{2.5}\) max and evening PEFR, our study showed that 84% of participants used Budesonide meter dose inhaler (MDI) and Salbutamol MDI. These medications can attenuate the effects of air pollution and PEFR. Peters et al. (1997) found that medication use in asthmatics attenuated the associations between particulate air pollution and
PEFR. There may also be other uncontrolled factors affecting this association. PM\textsubscript{10} max (lag 6) associated negatively with morning PEFR, with a coefficient of -0.01 (95% CI: -0.024, -0.002). Specifically, a 1 µg m\textsuperscript{-3} increase in daily ambient PM\textsubscript{10} max concentration (lag 6) was associated with a decrease in morning PEFR of 0.01 L min\textsuperscript{-1}. These results support previous findings (Hoek \textit{et al.}, 1998; Qian \textit{et al.}, 2009; Wiwatanadate and Liwsrisakun, 2011; Missagia \textit{et al.}, 2018). Missagia \textit{et al.} (2018) studied 117 children and adolescents in a Brazilian public school and found that an increase of 14 µg m\textsuperscript{-3} in PM\textsubscript{10} associated with decreased morning PEFR by -1.04% (95% CI: -1.32; -0.77). Hoek \textit{et al.} (1998) analyzed and averaged data from five panel studies and reported an increase of 10 µg m\textsuperscript{-3} in PM\textsubscript{10} related to a decrease of 0.07% in mean PEFR\%. In the present study, no adverse effects were identified for PM\textsubscript{10} and evening PEFR. This may be because airway narrowing / symptoms felt on waking up were immediately recorded by participants (i.e., before taking any remedial action), whereas remedial actions (including self-medication) taken during the day may have alleviated or removed symptoms at the time of the ‘before bed’ PEFR (Pride, 1992; Timonen and Pekkanen, 1997). A systematic review by Ward and Ayres (2004) showed air pollution effects on children. It indicated that PM\textsubscript{2.5} produced more adverse effects than PM\textsubscript{10}, as an increase in PM\textsubscript{2.5} and PM\textsubscript{10} levels of 10 µg m\textsuperscript{-3} associated with a decrease in PEFR of -0.063 L min\textsuperscript{-1} (95% CI: -0.091; -0.034) and -0.012 L min\textsuperscript{-1} (95% CI: -0.017; -0.008), respectively. In contrast, the present study found that PM\textsubscript{10} produced more adverse effects than PM\textsubscript{2.5}.

The main implications of findings reported in this study are, first, that information regarding pollutants’ delayed effects will enable the forecasting of health effects and help the concerned health organizations to be prepared for patients in advance of likely increases in demand. Second, knowledge of the negative effects of some pollutants on PEFR will encourage health policy makers to take serious actions to prevent those pollutants at their sources.
**Limitation**

The use of a steroid inhaler (Budesonide MDI) and bronchodilator (Salbutamol MDI) by 84% of the participants in this study could weaken or confound the effects of the pollutants. This is because the use of anti-inflammatory medication could either intensify the effects of ambient pollutants on lung function (Lewis et al., 2005) or guard against the pro-inflammatory effects of air pollutants (Delfino et al., 2002). Peter et al. (1997) found that the use of medication in asthmatic patients diminished the association between particulate air pollution and PEFR. Also, existing resources for this study were inadequate for comprehensively taking into account several likely confounding factors such as aeroallergens and indoor air pollution (household dust, cooking fumes, second-hand smoke, or incense smoke) and indoor allergens from pets and working patterns and places. Furthermore, the concentrations of ambient pollutants might not represent the individual's exposure doses due to different physiology.

**CONCLUSIONS**

In this study, SO$_2$, PM$_{10}$ max (lag 6) and NO$_2$ max (lag 2) exhibited a significant inverse association with PEFR. Also, interaction between NO$_2$ (lag 4) and PM$_{10}$ (lag 6) appeared to have significantly negative additive effects on PEFR. These pollutants, then, at the particular noted lags, potentially contributed to a reduction in participants’ PEFR in this study. Conversely, some pollutants had a positive association with PEFR, suggesting a benefit to PEFR of increased concentrations. NO$_2$ (lag 4) and O$_3$ max (lag 3) fell into this category. As discussed, it has been reported that low concentrations of a pollutant may be beneficial to PEFR and, also as discussed, other researchers have also found
positive as well as negative associations with PEFR for supposed ‘pollutants.’ Nonetheless, it is counterintuitive to expect a positive relationship between pollutant concentration and PEFR. Further investigation is suggested. It was also seen that each pollutant (and meteorological factor) did not necessarily have the same lagged effect on PEFR. The combination of NO\textsubscript{2} max (lag 2) with PM\textsubscript{10} max (lag 6), for example, associated significantly with decreased morning PEFR, suggesting that the effects on lung function of both pollutants take time to manifest.

ACKNOWLEDGMENTS

This study was funded by the Faculty of Medicine, Chiang Mai University and the Ministry of Science and Technology, Taiwan under Grant No. MOST 108-2221-E-041-003-MY3. The authors are very thankful for the real time air monitoring data from the Pollution Control Department, Thailand, and the Northern Meteorology Center, Thailand for its meteorological data. Special thanks go to all of the asthmatic patients who participated in this study. The authors declare no competing interest.
REFERENCES


Thailand.


Figure Captions

Fig. 1. Autocorrelation function plot of daily morning PEFR of 33 asthmatic patients in Mae Moh District, Lampang, Thailand.

Fig. 2. Partial autocorrelation function plot of daily morning PEFR of 33 asthmatic patients in Mae Moh district, Lampang, Thailand.
Fig. 1. Autocorrelation function plot of daily morning PEFR of 33 asthmatic patients in Mae Moh District, Lampang, Thailand.
Fig. 2. Partial autocorrelation function plot of daily morning PEFR of 33 asthmatic patients in Mae Moh district, Lampang, Thailand.
Table Captions

**Table 1.** Descriptive statistics of 33 asthmatic patients in Mae Moh District, Lampang, Thailand, 2 November 2015–31 October 2016.

**Table 2.** Daily meteorological and pollutant measurements; Daily max meteorological and max pollutant measurements in Mae Moh District, Lampang Thailand, 2 November 2015–30 November 2016.

**Table 3(a).** Correlation matrix of mean ambient air pollutants and mean meteorological parameters in Mae Moh District, Lampang, Thailand, 2 November 2015–31 October 2016.

**Table 3(b).** Correlation matrix of max ambient air pollutants and max meteorological parameters in Mae Moh District, Lampang, Thailand, 2 November 2015–31 October 2016.

**Table 4.** The multi-pollutant model of daily average $\text{NO}_2$ (lag 4), $\text{PM}_{10}$ (lag 6), $\text{CO}$ (lag 6), $\text{NO}_2$ (lag 4)$\times\text{PM}_{10}$ (lag 6) and morning PEFR.

**Table 5.** The multi-pollutant model of daily average $\text{NO}_2$ (lag 4), $\text{SO}_2$ and daily average PEFR.

**Table 6(a).** The multi-pollutant model of daily average $\text{NO}_2$ max (lag 2), $\text{PM}_{2.5}$ max (lag 4), $\text{CO}$ max (lag 6) and morning PEFR.

**Table 6(b).** The multi-pollutant model of daily average $\text{NO}_2$ max (lag 2), $\text{PM}_{10}$ max (lag 6), $\text{CO}$ max (lag 6), and morning PEFR.

**Table 7.** The multi-pollutant model of $\text{O}_3$ max (lag 3), $\text{PM}_{2.5}$ max and evening PEFR.
Table 8. The multi-pollutant model of daily average NO₂ max (lag 2), O₃ max (lag 3) and daily average PEFR.
Table 1. Descriptive statistics of 33 asthmatic patients in Mae Moh District, Lampang, Thailand, November 2015–31 October 2016.

<table>
<thead>
<tr>
<th>Demographic Data</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. male/female</td>
<td>11/22</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>49.4 (10.0)a</td>
</tr>
<tr>
<td>Mean weight (kg)</td>
<td>63.2 (13.1)a</td>
</tr>
<tr>
<td>Mean height (cm)</td>
<td>157.1 (6.2)a</td>
</tr>
<tr>
<td>Asthma severity (%)</td>
<td></td>
</tr>
<tr>
<td>Mild Intermittent</td>
<td>13 (39.4)b</td>
</tr>
<tr>
<td>Mild Persistent</td>
<td>11 (33.3)b</td>
</tr>
<tr>
<td>Moderate Persistent</td>
<td>9 (27.3)b</td>
</tr>
<tr>
<td>Severe Persistent</td>
<td>0</td>
</tr>
</tbody>
</table>

a. The number in parentheses is standard deviation.
b. The number in parentheses is the frequency of each category.
Table 2. Daily mean and daily max meteorological and pollutant measurements in Mae Moh District, Lampang Thailand, 2 November 2015 – 30 November 2016.

<table>
<thead>
<tr>
<th>Exposure</th>
<th>No.</th>
<th>Min/Max</th>
<th>Mean ± S.D.</th>
<th>90&lt;sup&gt;th&lt;/sup&gt; percentile</th>
<th>Exposure</th>
<th>No.</th>
<th>Min/Max</th>
<th>Mean ± S.D.</th>
<th>90&lt;sup&gt;th&lt;/sup&gt; percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td>WS</td>
<td>365</td>
<td>.38/2.22</td>
<td>.98 (.39)</td>
<td>1.49</td>
<td>WS</td>
<td>365</td>
<td>0.80/ 4.20</td>
<td>2.08/11.50</td>
<td>3.1</td>
</tr>
<tr>
<td>Temp</td>
<td>365</td>
<td>9.11/34.94</td>
<td>26.03 (3.63)</td>
<td>30.73</td>
<td>Temp</td>
<td>365</td>
<td>10.10/ 41.80</td>
<td>31.83/4.34</td>
<td>38.5</td>
</tr>
<tr>
<td>RH</td>
<td>365</td>
<td>43.25/95.13</td>
<td>72.40 (11.67)</td>
<td>85.88</td>
<td>RH</td>
<td>365</td>
<td>63.00/ 99.00</td>
<td>91.95/23.92</td>
<td>98</td>
</tr>
<tr>
<td>GR</td>
<td>365</td>
<td>2.63/292.47</td>
<td>163.14 (46.55)</td>
<td>223.29</td>
<td>GR</td>
<td>365</td>
<td>21.00/ 940.00</td>
<td>690.18/63.04</td>
<td>860</td>
</tr>
<tr>
<td>Press</td>
<td>365</td>
<td>1000.56/1024.26</td>
<td>1009.96 (4.24)</td>
<td>1015.95</td>
<td>Pressure</td>
<td>365</td>
<td>1002.60/ 1027.10</td>
<td>1012.71/44.51</td>
<td>1018.37</td>
</tr>
<tr>
<td>RQ</td>
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<td>.00/2.82</td>
<td>.14 (.39)</td>
<td>0.5</td>
<td>RQ</td>
<td>365</td>
<td>0.00/ 67.60</td>
<td>3.38/0.65</td>
<td>12</td>
</tr>
<tr>
<td>NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>348</td>
<td>.74/29.55</td>
<td>4.87 (3.31)</td>
<td>9.26</td>
<td>NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>348</td>
<td>3.00/91.00</td>
<td>13.16/0.72</td>
<td>27</td>
</tr>
<tr>
<td>SO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>365</td>
<td>.00/6.14</td>
<td>1.28 (1.05)</td>
<td>2.52</td>
<td>SO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>365</td>
<td>.00/ 34.00</td>
<td>3.56/4.20</td>
<td>7</td>
</tr>
<tr>
<td>O&lt;sub&gt;3&lt;/sub&gt;</td>
<td>362</td>
<td>12.04/77.41</td>
<td>33.92 (16.53)</td>
<td>61.96</td>
<td>O&lt;sub&gt;3&lt;/sub&gt;</td>
<td>362</td>
<td>18.00/ 131.00</td>
<td>52.64/7.76</td>
<td>88</td>
</tr>
<tr>
<td>PM&lt;sub&gt;10&lt;/sub&gt;</td>
<td>365</td>
<td>9.46/188.71</td>
<td>49.09 (35.34)</td>
<td>101.54</td>
<td>PM&lt;sub&gt;10&lt;/sub&gt;</td>
<td>365</td>
<td>17.00/ 443.00</td>
<td>84.91/161.76</td>
<td>177</td>
</tr>
<tr>
<td>PM&lt;sub&gt;2.5&lt;/sub&gt;</td>
<td>365</td>
<td>5.00/155.96</td>
<td>28.91 (26.12)</td>
<td>67.92</td>
<td>PM&lt;sub&gt;2.5&lt;/sub&gt;</td>
<td>365</td>
<td>9.00/ 407.00</td>
<td>49.92/4.45</td>
<td>108</td>
</tr>
<tr>
<td>CO</td>
<td>363</td>
<td>.30/2.08</td>
<td>.76 (.38)</td>
<td>1.4</td>
<td>CO</td>
<td>363</td>
<td>0.35/ 3.53</td>
<td>1.12/9.14</td>
<td>2.18</td>
</tr>
</tbody>
</table>

NO<sub>2</sub>: nitrogen dioxide (ppb), SO<sub>2</sub>: sulfur dioxide (ppb), O<sub>3</sub>: ozone (ppb). PM<sub>10</sub>: particulate matter with a 50% cut-off of aerodynamic diameter ≤10 µm (µg m<sup>-3</sup>). PM<sub>2.5</sub>: particulate matter with a 50% cut-off of aerodynamic diameter ≤2.5 µm (µg m<sup>-3</sup>). CO: carbon monoxide (ppm), WS: wind speed (m s<sup>-1</sup>), Temp: temperature (°C), RH: relative humidity, GR: global radiation (w m<sup>-2</sup>), Press: pressure (mbar), RQ: rain quantity (mm).
Table 3.

**Table 3(a).** Correlation matrix of mean ambient air pollutants and mean meteorological parameters in Mae Moh District, Lampang, Thailand, 2 November 2015–31 October 2016.

<table>
<thead>
<tr>
<th>Mean</th>
<th>NO₂</th>
<th>SO₂</th>
<th>O₃</th>
<th>PM₁₀</th>
<th>PM₂.₅</th>
<th>CO</th>
<th>WS</th>
<th>Temp</th>
<th>RH</th>
<th>GR</th>
<th>Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>SO₂</td>
<td></td>
<td>.509**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>O₃</td>
<td>.488**</td>
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<td>.237**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM₁₀</td>
<td>.588**</td>
<td>.308**</td>
<td>.881**</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM₂.₅</td>
<td>.582**</td>
<td>.308**</td>
<td>.881**</td>
<td>.981**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CO</td>
<td>.499**</td>
<td>.282**</td>
<td>.755**</td>
<td>.821**</td>
<td>.829**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>WS</td>
<td>-.022*</td>
<td>-.065**</td>
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<td>.368**</td>
<td>.360**</td>
<td>.313**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Temp</td>
<td>-.231**</td>
<td>-.283**</td>
<td>.348**</td>
<td>.275**</td>
<td>.275**</td>
<td>.059**</td>
<td>.491**</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>RH</td>
<td>-.346**</td>
<td>-.152**</td>
<td>-.842**</td>
<td>-.735**</td>
<td>-.728**</td>
<td>-.539**</td>
<td>-.619**</td>
<td>-.595**</td>
<td></td>
<td></td>
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<tr>
<td>GR</td>
<td>.156**</td>
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<td>.485**</td>
<td>.475**</td>
<td>.313**</td>
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<td>.608**</td>
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<td>.170**</td>
<td>.128**</td>
<td>.137**</td>
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<td>.073**</td>
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<tr>
<td>RQ</td>
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<td>-.260**</td>
<td>-.254**</td>
<td>-.237**</td>
<td>-.204**</td>
<td>-.168**</td>
<td>.388**</td>
<td>-.333**</td>
<td>-.078**</td>
</tr>
</tbody>
</table>


**.** Correlation is significant at the 0.05 level (2-tailed).

**.** Correlation is significant at the 0.01 level (2-tailed).
Table 3(b). Correlation matrix of max ambient air pollutants and max meteorological parameters in Mae Moh District, Lampang, Thailand, 2 November 2015–31 October 2016.

<table>
<thead>
<tr>
<th>Max</th>
<th>NO₂</th>
<th>SO₂</th>
<th>O₃</th>
<th>PM₁₀</th>
<th>PM₂.₅</th>
<th>CO</th>
<th>WS</th>
<th>Temp</th>
<th>RH</th>
<th>GR</th>
<th>Pressure</th>
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<td></td>
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<tr>
<td>O₃</td>
<td>.464**</td>
<td></td>
<td>.269**</td>
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<td></td>
<td></td>
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<td></td>
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<tr>
<td>PM₁₀</td>
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<td>.186**</td>
<td>.830**</td>
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<td>PM₂.₅</td>
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<td>.462**</td>
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<td>.429**</td>
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<td>-.416**</td>
<td>-.718**</td>
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<td>-.215**</td>
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<td>.181**</td>
<td>-.247**</td>
<td>-.092**</td>
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</table>


** Correlation is significant at the 0.01 level (2-tailed).
* Correlation is significant at the 0.05 level (2-tailed).
Table 4. The multi-pollutant model of daily average NO$_2$ (lag 4), PM$_{10}$ (lag 6), CO (lag 6), NO$_2$ (lag 4)×PM$_{10}$ (lag 6) and morning PEFR.

<table>
<thead>
<tr>
<th>morning PEFR</th>
<th>NO$_2$ (lag 4)</th>
<th>PM$_{10}$ (lag 6)</th>
<th>CO (lag 6)</th>
<th>NO$<em>2$ (lag 4)×PM$</em>{10}$ (lag 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β (95% CI)</td>
<td>p-value</td>
<td>β (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td></td>
<td>1.34 0.25</td>
<td>2.44 0.02</td>
<td>0.02 -0.08</td>
<td>0.12 0.66</td>
</tr>
<tr>
<td></td>
<td>-0.34 -9.53</td>
<td>8.85 0.94</td>
<td>-0.023 -0.030</td>
<td>-0.001 0.04</td>
</tr>
</tbody>
</table>

Adjusted for gender, severity of asthma, day of the week, age, weight, wind speed (lag 5), temperature (lag 1), global radiation (lag 4) and rain quantity (lag 6).

Table 5. The multi-pollutant model of daily average NO$_2$ (lag 4), SO$_2$ and daily average PEFR.

<table>
<thead>
<tr>
<th>Daily average PEFR</th>
<th>NO$_2$ (lag 4)</th>
<th>SO$_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>PEFR</td>
<td>0.15 0.01</td>
<td>0.29 0.03</td>
</tr>
</tbody>
</table>

Adjusted for gender, severity of asthma, day of the week, age, weight, wind speed (lag 5), temperature (lag 1), global radiation (lag 4), pressure (lag 1) and rain quantity (lag 2).
Table 6(a). The multi-pollutant model of daily average NO$_2$ max (lag 2), PM$_{2.5}$ max (lag 4), CO max (lag 6) and morning PEFR.

<table>
<thead>
<tr>
<th>NO$_2$ max (lag 2)</th>
<th>PM$_{2.5}$ max (lag 4)</th>
<th>CO max (lag 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta$ (95% CI)</td>
<td>$P$-value</td>
<td>$\beta$ (95% CI)</td>
</tr>
<tr>
<td>-0.08 (-0.14 to -0.02)</td>
<td>0.01</td>
<td>0.016 (-0.003 to 0.036)</td>
</tr>
</tbody>
</table>

Adjusted for gender, asthma severity, day of the week, age, weight, wind speed max (lag 6), temperature max (lag 4), relative humidity max (lag 1), global radiation max (lag 4), pressure max (lag 1) and rain quantity max (lag 6).

Table 6(b). The multi-pollutant model of daily average NO$_2$ max (lag 2), PM$_{10}$ max (lag 6), CO max (lag 6), and morning PEFR.

<table>
<thead>
<tr>
<th>NO$_2$ max (lag 2)</th>
<th>PM$_{10}$ max (lag 6)</th>
<th>CO max (lag 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta$ (95% CI)</td>
<td>$p$-value</td>
<td>$\beta$ (95% CI)</td>
</tr>
<tr>
<td>-0.07 (-0.13 to -0.01)</td>
<td>0.02</td>
<td>-0.01 (-0.024 to -0.002)</td>
</tr>
</tbody>
</table>

Adjusted for gender, asthma severity, day of the week, age, weight, wind speed max (lag 6), temperature max (lag 4), relative humidity max (lag 1), pressure max (lag 1) and rain quantity max (lag 6).
Table 7. The multi−pollutant model of O₃ max (lag 3), PM₂.₅ max and evening PEFR.

<table>
<thead>
<tr>
<th></th>
<th>O₃ max (lag 3)</th>
<th></th>
<th>PM₂.₅ max</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>β</td>
<td>(95% CI)</td>
<td>p-value</td>
<td>β</td>
<td>(95% CI)</td>
</tr>
<tr>
<td>0.078</td>
<td>0.03</td>
<td>0.127</td>
<td>0.029</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Adjusted for gender, asthma severity, age, weight, global radiation max (lag 1), pressure max (lag 1) and rain quantity max (lag 5).

Table 8. The multi−pollutant model of daily average NO₂ max (lag 2), O₃ max (lag 3) and daily average PEFR.

<table>
<thead>
<tr>
<th></th>
<th>NO₂ max (lag 2)</th>
<th></th>
<th>O₃ max (lag 3)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>β</td>
<td>(95% CI)</td>
<td>p-value</td>
<td>β</td>
<td>(95% CI)</td>
</tr>
<tr>
<td>-0.05</td>
<td>-0.10</td>
<td>-0.01</td>
<td>0.06</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Adjusted for gender, asthma severity, day of the week, age, weight, wind speed max (lag 6), temperature max (lag 4) and pressure max (lag 1).