博士論文

Effects of short-term exposure to ambient particulate matter and temperature on lung function of school children in Dhaka, Bangladesh

（ダッカにおける大気中粒子状物質及び気温への短期曝露が
就学児童の肺機能に及ぼす影響）

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Abstract

Short-term exposure to ambient particulate matter (PM) and temperature plays a significant role in human health. The current study investigated the effects of short-term ambient PM and temperature on lung function in children and seasonal variation in these associations in Dhaka, Bangladesh. Additionally, this research explored the asthma prevalence in the study schools.

The study was conducted in three schools located in three cities inside and around Dhaka, Bangladesh, within 1km of existing continuous air-monitoring stations (CAMS). A cross-sectional questionnaire survey for all school children and a panel study of a subgroup of children (*n*=314) involving the repeated measurement of lung function was conducted in 2013. Linear mixed-effects models adjusted for potential confounders were used to examine the effect of the exposure variables on lung function.

In the panel of 314 children, short-term exposure to high ambient $PM_{2.5}$, large diurnal temperature range (DTR) and low ambient temperature were associated with a significant decrement in children's lung function. Our analysis also demonstrated significant seasonal

variation in these associations, as the estimated effects of high $PM_{2.5}$ on lung function measures were generally stronger in summer than in winter, while the estimated adverse effects of low daily mean temperature on lung function measures were only evident in winter. Although the magnitude of the effects varied between winter and summer, this study provides evidence that increase in $PM_{2.5}$, DTR and decrease in temperature are independent risk factor to the health of children.

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Abbreviations

ACF: Autocorrelation function
ATS: American Thoracic Society
BAPMAN: Bangladesh Air Pollution Management Project
BMD: Bangladesh Meteorological Department
CAMS: Continuous air monitoring station
CASE: Clean Air and Sustainability Project
CIs: Confidence intervals
CNG: Compressed natural gas
CMH: Cochran-Mantel-Haenszel
DTR: Diurnal temperature range
DoE: Department of Environment
ER: Emergency room
ERS: European Respiratory Society
FEV1: Forced expiratory volume within 1 second
FVC: Forced vital capacity
GDP: Gross domestic product
GIS: Geographic information system
icddr,b: International Centre for Diarrhoeal Disease Research, Bangladesh
IPCC: Intergovernmental panel on climate change
ISAAC: International Studies of Asthma and Allergies in Childhood
MPI: Multi-pollutant index
NAAQS: National ambient air quality standards
NILU: Norwegian Institute for Air Research
OR: Odds ratio
PEF: Peak expiratory flow
PEFR: Peak expiratory flow rate
PFT: Pulmonary function test
PM: Particulate matter
TSP: Total suspended particle
US: United States
US EPA: United States Environment Protection Agency
WHO: World Health Organization

Chapter 1: Introduction

1.1 Ambient air pollution and health

According to the World Health Organization (WHO), air pollution has become the world's single biggest environmental health risk. An estimated 3.7 million premature deaths occurred worldwide due to ambient air pollution in 2012 (1). Low and middle-income countries in the WHO's South-East Asia and Western Pacific Regions had the largest air pollution-related burden as 88% of these premature deaths occurred in countries in these regions.

1.1.1 Ambient particulate matter (PM) and health

Among the air pollutants, particulate matter (PM) affects more people than any other pollutant (2). As the most severe health effects of air pollution are attributed to PM, it also attracts particular interest among researchers and in the political sphere. The term "particulate matter" refers to the complex heterogeneous mixture of solid particles and/or droplets of variable size found in suspension in the air. Particulate matter consists of various components, both organic and inorganic particles, including dust, acids of nitrates and sulfates, organic chemicals, soot and metals. The chemical composition of PM may vary with regard to its major emission sources and atmospheric condition (3). According to the United States Environment Protection Agency (US EPA) (4), particle pollution can be categorized as

- "Inhalable coarse particles," larger than 2.5 micrometers and smaller than 10 micrometers in diameter , usually found near roads and in the vicinity of dust-producing industries. The PM_{10} (particles with a diameter of 10 micrometers or less) has been employed by the US EPA in setting the national ambient air quality standards (NAAQS) and also measured by most regulatory agencies (5).
- "Fine particles," 2.5 micrometers in diameter and smaller ($PM_{2.5}$), usually found in smoke and haze.

The health effects of short-term exposure to both coarse and fine particulate matter (PM) are well documented (6). Short-term exposure is usually defined as an exposure of less than 30 days. Many studies have demonstrated that short-term exposure to ambient particulate air pollution is associated with an increased risk of mortality for broadly defined cardiovascular or respiratory causes (7). Along with increased mortality, there is abundant evidence that short-term exposure to PM can cause increases in respiratory and cardiovascular morbidity, often measured as an increase in hospital admissions and emergency department visits (8).

1.1.2 Ambient PM and respiratory health

Respiratory health-related diseases and symptoms are one of the major contributors to ambient PM-related morbidity as both coarse and fine PM includes small inhalable particles that can penetrate the thoracic region of the respiratory system. Although the biological mechanism(s) linking inhalation to respiratory health effects has yet to established, particle-induced inflammatory responses mediated via oxidative stress may be important in this respect (9).

Epidemiological studies have shown that short-term exposure to ambient PM is associated with various types of respiratory health-related morbidity. Evidence has been found that increased PM is associated with increases in hospital admissions due to asthma (10, 11), emergency department visits (12, 13), aggravation of respiratory symptoms (14), and in pulmonary function decrement (15).

1.1.3 Ambient PM and respiratory health in children

Children are considered as being one of the groups most vulnerable to the adverse respiratory health-related effects of ambient air pollution (16). Children have a different response to exposure to air pollution as their immune system and lungs are not fully developed (11). The lung is not fully formed at birth and 80% of alveoli are formed after birth with changes in the lung continuing through adolescence (17). Children also have a larger lung surface area and inhale a higher volume of air per kilogram of body weight than adults (11). In addition, children have a higher exposure to air pollution because they spend more time outdoors and engage in a greater level of physical activity than adults (18). Thus, their air intake into the lungs is much greater than adults.

A large number of epidemiological studies have examined the respiratory health effects of ambient air pollution in children and demonstrated that children are at risk for adverse effects from acute exposure to particular matter. For example, the association between hospital admissions for childhood asthma and ambient PM_{10} and $PM_{2.5}$ was found to be significant, with an increase in the asthma admission rate of 3.67% (1.52-5.86) and 3.24% (0.93-5.60) in Hong Kong for an increase in the IQR of daily mean concentration of PM_{10} (33.4mg/m^3) and $PM_{2.5}$ (20.6mg/m^3), respectively (19).

1.1.4 Lung function measurement to evaluate respiratory health

Lung function is commonly used as a noninvasive measure of respiratory health as the lung function level is a predictor of future cardiorespiratory morbidity and mortality (20).

Spirometry is the most common type of pulmonary function test (PFT) to measure lung function. It measures the amount (volume) and/or speed (flow) of air that can be inhaled and exhaled. Common parameters measured by spirometry are forced vital capacity and forced expiratory volume. Forced vital capacity (FVC) is expressed in liter (L) and measures the total volume exhaled after a maximum inspiration. Forced expiratory volume within 1 second (FEV1) is a marker of airway obstruction. FEV1 is also expressed in liter (L), measuring the maximum volume that can be exhaled within 1 second. Other commonly used measures are peak expiratory flow (PEF) which is the maximal flow (or speed) achieved during the maximally forced expiration initiated at full inspiration. Lung function changes over the lifetime, steadily increasing from birth to early adulthood, culminating in a plateau phase in a person's mid-twenties and then decreases with age (21). Besides age, lung function is also influenced by gender, body height and size, health status, and race.

1.1.5 Effect of PM on the lung function of children in panel studies

Epidemiological studies have commonly used a "panel" design, a subtype of cohort study to evaluate the short-term effects of PM on lung function. In panel study, subjects are followed over a period of time at specific intervals. The key feature of the panel studies is the repeated measurement of the same subjects at different points in time. To obtain additional information, panel designs are often nested within cross-sectional studies (22).

Several panel studies have reported a short-term effect of PM on lung function in both asthmatic and non-asthmatic children (Table 1). Ward et al., (2004) performed a meta-analysis of worldwide panel studies published up until 2002 that reported the short-term effects of outdoor PM on children's peak expiratory flow (PEF) for both asthmatic and healthy children (23). They reported that most studies showed an adverse effect of particulate air pollution on PEF. Weinmayr et al., (2010) conducted a systematic review to quantify the short-term effects of ambient PM_{10} on the respiratory health of asthmatic children using panel studies published in 1990 to 2008 and found PM_{10} was inversely associated with PEF, although the result was not statistically significant (24). Li et al., (2012) reviewed the panel studies published between January 2000 to November 2011 on the effects of ambient air pollution on lung function in children (≤18years old) and found significant adverse effects of PM on lung function by synthesizing the data of the 20 articles which were available that examined lung function (22). Despite the heterogeneity of the study populations and exposure levels, these reviews provided strong support for the hypothesis that there are significant adverse effects of particulate matter on lung function in children.

1.2 Temperature and health

Weather and climate play a significant role in human health. It is now well accepted that climate change is occurring and occurring at a faster rate than ever before. In the past few decades' temperature increases at a faster rate than before and more warming is predicted for the next century. There was a 0.13°C increase in global mean temperature per decade from 1956 to 2005, compared to an increase of 0.07°C per decade between 1906 and 2005. The global mean temperature increased by 0.07°C per decade between 1906 and 2005, but by 0.13°C per decade from 1956 to 2005 (25). With the increasing average global temperature, the frequency and intensity of temperature extremes has also changed and it is anticipated that the average global temperature and the frequency of extreme weather events will increase more intensely in the 21st century (26).

The effects of ambient temperature on mortality and morbidity have been extensively studied and short-term exposure to both cold and hot temperature has been found to be associated with increased mortality and morbidity (27-30). For example, in the 1995 Chicago heat wave, it was estimated that 1,072 (11%) excess hospital admissions occurred among all age groups (31). The relative risk of hospital admissions due to asthma associated with cold temperature was 1.20 (95% CI, 1.01-1.41) for a 2 weeks average lag in Shanghai, China (32). In Tibet, increased hospital admission was associated with exposure to both hot and cold temperatures and high temperature was also associated with increased respiratory diseases (RR: 1.119, 95% CI: 1.01-1.24) at short lags (33). In Hong Kong, hospital admissions increased by 4.5% for every increase of 1 °C above 29 °C during the hot season and increased by 1.4% for every decrease of 1 °C within the 8.2-26.9 °C range during the cold season (34).

Studies have also focused on the effects of the diurnal temperature range (DTR) on health and reported that an increase in DTR adversely affects hospital admissions and deaths (35-37). DTR is considered as an important index of weather change (or weather variability) and calculated as the difference between the maximum and minimum temperatures within 1 day. In Beijing, China, a 1°C increase in the 8-day moving average of DTR was associated with an increase of

2.08% (95% CI: 0.88%–3.29%) in respiratory emergency room admissions (38). Although fewer studies exit that evaluate the effect of DTR than those evaluate daily temperature, there is growing evidence that DTR has significant adverse effect on mortality and morbidity, especially for cardiovascular and respiratory diseases (39).

1.2.1 Ambient temperature and respiratory health in children

Respiratory health-related hospitalization and emergency department visits are one of the main contributors to ambient temperature-induced morbidity (40, 41). For example, Lin et al. (2009) reported an increased count of respiratory diseases (2.7%; 95% CI: 1.3, 4.2) with a 1°C increase in temperature during the summer in New York City (41). Children are one of the most vulnerable groups to the effects of temperature extremes on respiratory diseases including asthma and there has been increasing interest in evaluating the effect of temperature on children's health (42, 43).

Epidemiological studies have reported the adverse effects of both hot and cold temperature on the respiratory health of the children. It was reported that hospital admissions for pediatric asthma were negatively associated with maximum temperature in Singapore (44). Hospital admissions for asthma were negatively correlated with monthly air temperature among children, especially for young children (age 0–4 years) in Athens, Greece (45). A study conducted in

Fukuoka, Japan also showed that within day temperature fluctuation was associated with an increased risk of emergency hospitalization due to asthma for children under 12 years old (46). Another study reported that both a rapid decrease in temperature within a 3-day period and higher temperature enhanced the risk of emergency visits for pediatric asthma in Tokyo, Japan (47). Hence, there has been a wide range of heterogeneity across these studies both in terms of the direction and magnitude of the results.

1.2.2 Ambient temperature and lung function in children

Previously, studies were carried out to investigate the effects of extreme cold temperature on lung function under experimental conditions, i.e., in an environmental chamber or breathing through a heat-exchanger system especially for patients with respiratory diseases (48, 49). Very few studies have focused on the effect of ambient temperature on lung function in children (Table 2). Understanding the temperature-induced change in lung function is important as it would help in providing greater knowledge of the effects of short-term temperature changes on respiratory health (22). Recently, a research group investigated the effect of ambient temperature on lung function in asthmatic children in Australia. These researchers reported that exposure to high ambient temperature and large DTR was associated with lower lung function in children with asthma (50, 51).

1.3 Climate and weather in Dhaka, Bangladesh

Bangladesh is a developing nation in south Asia. It is the world's eighth most populous country and one of the most densely populated countries with over 160 million people. It has a rapidly growing market-based economy with gross domestic product (GDP) growth of around 6% per annum.

According to the Bangladesh Meteorological Department (BMD), Bangladesh has a tropical monsoon climate with wide seasonal variations in rainfall, high temperatures, and high humidity. In the traditional Bengali calendar, the year consists of six seasons. However, meteorologically, the year in Bangladesh can be divided into four distinct seasons; pre-monsoon (March— May), monsoon (June—September), post-monsoon (October—November) and winter (December—February) (52).

Dhaka, the capital and also the largest city in Bangladesh is located in the center of the Bengal delta. Dhaka has an estimated population of more than 15 million people that makes it one of the largest cities in the world. Dhaka also has a typical tropical monsoon climate since the country is relatively flat, climate is homogenous across the entire country.

1.4 Air pollution in Dhaka, Bangladesh

The accelerating pace of economic development and the industrialization of Bangladesh has been accompanied by severe urban air pollution, which has made its capital city one of the most polluted cities in the world. As a result of this, a number of studies have focused on outdoor air pollution in Dhaka.

In a study conducted in 1999, the estimated concentration of particulate matter (PM) and black smoke exceeded both national and international standards in metropolitan Dhaka (53). From January 2003, the government of Bangladesh introduced some policy interventions including banning all two-stroke engines from the roads in Dhaka, banning old buses and promoting the use of compressed natural gas (CNG) for vehicles. An analysis of data from 2000 to 2004 resulted in the claim that the amount of fine particulate matter in the air was decreasing as a result of the government's policy interventions (54). However, even with a decreasing trend, the mean yearly values in this period were still much higher than the standards permitted by the United States Environmental Protection Agency (US EPA) as well as the Bangladesh national air quality standard for PM. The PM_{10} mass concentration was also much higher than the WHO annual average guideline value of 20 $\mu g/m^3$ and 24-h mean of 50 $\mu g/m^3$ (55). A number of recent studies have shown that the concentration of air pollutant in Dhaka city is still high (56). A recently developed multi-pollutant index (MPI) ranked Dhaka as having the worst air quality among the top 18 mega-cities of the world (57). The Norwegian Institute for Air Research (NILU) and the Clean Air and Sustainability Project (CASE) at the Department of Environment (DoE), Bangladesh, also recently reported high concentrations of some air pollutants ($PM_{2.5}$, PM_{10} ,NO_2 and SO_2) at most sites sampled in the Dhaka city area in a screening study conducted in 2011 (56).

There is distinct seasonal variation and some spatial variation in the concentration of air pollutants in Dhaka. One study measured the aerosol particle size distribution for Dhaka from January to April, 2006 and found significant seasonal differences when comparing winter and the pre-monsoon seasons, with the highest monthly value of particles observed in January and the lowest in April. Compared to the pre-monsoon season, aerosol particles were around 2 to 4 times higher in number in winter (58). Another study showed the temporal and spatial pattern of air quality by studying the fine and coarse PM concentrations measured at two air quality monitoring stations in Dhaka in 2000-2006. For both locations, a characteristic seasonal difference was observed for coarse PM as well as for the fine particles, with higher concentrations during winter. Average yearly PM concentrations were higher in the location that had a close proximity to major roadways than in the other location which was in a semi-residential area located at the Atomic Energy Centre, Dhaka Campus with relatively less traffic

(55).The BAPMAN study conducted in Dhaka city also reported spatial variation in air pollutants within Dhaka city (56).

The major source of fine PM in Dhaka is from motor vehicles and brick kiln emissions (59). Previous research has shown that vehicular emissions and emissions from brick kilns are the major contributors to air pollution in Dhaka especially in the dry season, while the contribution from emissions from metal smelters increases during the rainy season (60).

1.5 Asthma prevalence in Dhaka, Bangladesh

As yet, few studies have evaluated respiratory health-related diseases or the prevalence of asthma in Bangladesh for any location or age group. Among those that have, one study examined asthma prevalence among school children in Dhaka city (3 schools) and found that 16.4% of the children (13-16 years) had asthma when using the International Studies of Asthma and Allergies in Childhood (ISAAC) questionnaire (61). Another school-based cross-sectional study reported the asthma prevalence specifically for Dhaka district. This study was conducted in 2000 and reported that the lifetime (ever) and 12-month period (recent) prevalence of wheezing with 95% CIs were 13.8% (12.9-14.6) and 7.6% (6.9-8.2), respectively, using the ISAAC protocol for children (62).

Some additional evidence is available for children living in other places in Bangladesh. For example, one study examined the asthma prevalence for children aged 5-6 years old living in rural Bangladesh, where the observed prevalence of wheezing as determined by the ISAAC questionnaire was 16.1% (95% CI: 14.3%, 18.0%) (63). In a nationwide cross-sectional study conducted in 1999, the reported prevalence of asthma (wheezing in the last 12 months) was7.3% among children aged 5-14 years old (64). Even the most recent study available showing asthma prevalence in Dhaka is conducted in 2007; therefore, the current status of asthma prevalence for children in the Dhaka is largely unknown.

1.6 Rationale of the current study

In this study, we assessed the effect of short-term exposure to ambient PM and temperature on children's lung function. We selected school children as the study participants as children are especially vulnerable to the respiratory-related adverse effects of air pollutants. We used lung function measurement as it is the most common noninvasive method to determine a person's respiratory health condition.

Previous studies demonstrated that there are adverse effects of short-term exposure to ambient PM on lung function in children (Table 1). However, there were still several important data gaps that we wanted to address in this study.

- Firstly, we wanted to assess the associations discussed above in a developing country where there is increasing air pollution due to economic growth. From Table 1, it is clear that to date, the overwhelming majority of studies have been conducted in western countries. In a review of panel studies on children's lung function and respiratory symptoms, Le et al., (2012) also highlighted this fact and pointed to the need for such studies to be undertaken in developing nations as the greatest burden of disease due to air pollution is occurring in the developing world (22). Also, regional assessment of this association is important as there are substantial regional differences in PM concentration and composition (65) and epidemiological studies have shown that the levels and composition of particulate matter are directly linked to adverse effects on human health.
- Secondly, there was also a lack of research from regions with a tropical climate. Among the few worldwide studies conducted in places with such a climate, only 3 studies have been conducted in the tropical climate regions in Asia (Thailand and Bangladesh). Meteorological conditions such as wind, temperature, air turbulence, air pressure, rainfall, cloud cover and local climate can all affect air quality.

Dhaka is located in south Asia, has a tropical climate and has recently been shown to have a very high PM concentration, especially in winter. Only one study has reported on the short-term effects of PM on lung function for school children in Dhaka, and this was almost a decade ago in 2007 (61). This is why, it was important to now evaluate the effect of PM on lung function for the children in this area.

Compared to particulate matter, the effect of short-term ambient temperature on lung function remains largely unexplored in any population and region. As shown in the summary of the studies that have evaluated the short-term effects of ambient temperature on lung function (Table 2), only one research group has investigated the association between ambient temperature and lung function for children and that study was conducted for Australian asthmatic children. The relationship between ambient temperature and lung function for non-asthmatic children and any children in other regions has yet to be explored.

The effect of season on the association between particulate pollution and temperature-related exposures on lung function is also yet to be explored.

In previous studies, it was observed that season can modify the effect of air pollutants on mortality and respiratory morbidity (66, 67). In a systemic review and meta-analysis examining the short-term effects of PM_{10} on respiratory health for asthmatic and symptomatic children, Weinmayr et al., (2010) found that the estimated effect of PM_{10} on asthma was higher in the studies that were conducted in the summer (24). Examining the effect of season on the association between particulate matter and lung function is important as it will help to determine whether season has a modifying effect on the association between air pollutant and respiratory health-related mortality and morbidity. No study so far directly has examined the seasons' modifying effects on the association.

In the literature review, we found that there was a lack of background information, such as about the prevalence of asthma and respiratory syndromes for our study population. Therefore, to determine the prevalence of asthma and potential risk factors associated with it among our study participants, we also conducted a cross-sectional questionnaire survey.

1.7 Objectives

In summary, the objectives of the current study were

- To investigate the effects of short-term ambient PM and temperature on lung function in both asthmatic and non-asthmatic children in a school-based panel survey in Dhaka, Bangladesh.

- To examine the effect of season in these associations (short-term ambient PM and temperature on lung function).

- To determine the prevalence of asthma and potential risk factors associated with it in the study schools through the use of a cross-sectional questionnaire survey.

Chapter 2: Methods

2.1 Study setting and design

The study was conducted in three schools located in three cities inside and around Dhaka, Bangladesh. We conducted a cross-sectional questionnaire survey to determine the prevalence of asthma for all school children and then undertook a panel study to evaluate changes in lung function associated with exposure to ambient particulate matter and temperature for selected students. The cross-sectional survey was conducted during February-March, 2013. In the panel study for lung function measurement, children were followed up to 6 months from February to July, 2013.

2.2 Study site

Both studies were conducted in three schools located in three cities in and around Dhaka, Bangladesh. One school was located in the center of Dhaka city and the other two schools were in Gazipur and Narayangonj, which were two cities near Dhaka. The schools were selected based on the location of existing continuous air-monitoring stations (CAMS) operated by the Department of the Environment (DOE), Bangladesh. All the schools were within 1 km of the monitoring stations. The three selected schools were non-government school, the most common type of school for offering secondary education (Grade 6-10) in Bangladesh. According to the

Bangladesh Bureau of Education Information and Statistics (BANBEIS), non-government schools comprise the majority of schools providing have the highest share for offering the secondary education in Bangladesh (there were 317 government schools and 18439 non-government schools providing for secondary education in 2008).The GIS location of all schools is shown on the map (Figure 1).The names of the schools, the assigned codes for each school, and the corresponding city and monitoring station are presented in Table 3.

A map with the GIS location of each school and corresponding air-monitoring station with detailed characteristics is shown in Figure 2. It presents the characteristics of each area such as the distribution of major roads, water bodies, agricultural land and buildings in each location.

2.3 Study participants

2.3.1 Participants for the questionnaire survey

For the questionnaire survey, the study participants were all of the children studying in the three schools. In total, 1554 students participated in the study with a response rate of 73%. However, the actual response rate might have been much higher than the estimated response rate. Specifically, we calculated the response rate by using all students who were registered in the schools' register books as the denominator. But, many students were not actually attending school even though they had been admitted to school. The school authorities informed us that many students dropped out of school even after they had registered for the school year. However, as we conducted the questionnaire survey in the beginning of the school year, it was not possible for us to determine the actual number of students attending the three schools.

A package containing an information sheet and questionnaire was distributed to the children in their classrooms. The questionnaire asked about respiratory symptoms and illnesses, relevant environmental exposures and the family history of asthma. Students were requested to take the questionnaire home. Students in grades 1-8 were asked to give it to their parents to complete while students in grades 9-10 were requested to complete the questionnaire by themselves. All of the students were asked to return the questionnaires to their respective class teacher within 1 week.

2.3.2 Participants in the lung function test

For the lung function test panel study, children from grades 6-8 were enrolled from each school. We chose grade 6 as a starting point as children studying in classes below grade 6 might be too young to perform Spirometry properly and then, included students up to grade 8 to get an adequate number of asthmatic students. However, even though we did not get our desired number of asthmatic children from these grades we did not include students from higher grades as we wished to minimize the age range to avoid age dependent heterogeneity in lung function among participants. Two groups of children were selected: asthmatic and non-asthmatic.

In principle, all the children (approximately 40 in each school) with doctor-diagnosed asthma (or less if not available) and 80 children without asthma from grades 6-8 attending each of these schools were invited to take part in the panel study. The non-asthmatic children were selected by respective teachers of each school with purposive sampling. Approximately 80 non-asthmatic children were to be selected from each school, so one third of 80 non-asthmatic children were selected per grade in each school. In the classroom, children were seated in long benches, approximately 4 students per bench. The teacher picked up one or two children from each bench to select the expected number of participants predetermined by number of classes per grade and number of children per class. However, the actual number of children varied between the schools due to availability and feasibility. The study procedure was explained to these children. Information sheets with a detailed explanation of the study, an informed consent form and questionnaire were sent to the parents to inform them about the study and to obtain approval for their children's participation in this study. If they agreed, parents responded to the questionnaire and provided informed consent. After obtaining verbal agreement from the children and informed consent from their parents, 314 children in total (86 asthmatic and 228 non-asthmatics) were finally enrolled in the study from the three schools. Information on the GIS location of the participants from one school was collected and is shown in Figure 3.

2.4 Questionnaire assessment

The questionnaire had three parts.

The first part was concerned with the assessment of respiratory health. Children were examined using the International Study of Asthma and Allergies in Childhood (ISAAC) written questionnaire for asthma. In the ISAAC core questionnaire for asthma for children, questionnaires for 6/7 and 13/14 year olds are available. In this study, the questionnaire for 6/7 year olds was used for children in grades 1- 8, while the questionnaire for 13/14 year olds was used for children in grades 9-10.

We used a Bengali translation (national and local language) of the ISAAC questionnaire that was used in previous research (61). This ISAAC questionnaire had been translated into Bengali and back-translated in English by the previous research group. This questionnaire was additionally checked by a medical doctor who was a specialist in asthma in Bangladesh.

Current wheezing, ever wheezing and ever having had asthma were defined using the ISAAC questionnaire. Current wheezing was defined as wheezing symptoms in the past 12 months; ever wheezing was defined as wheezing symptoms at any point in the past; and ever asthma was defined as asthma symptoms at any point in the past (64).

The second part of the questionnaire asked questions about demographic characteristics and home environmental-related factors. This part contained questions about the participant's age, grade and sex as well as about family size, parental education and occupation, house type, cooking method used at home and water source. There were also questions regarding potential risk factors associated with respiratory health such as the number of smokers at home, the father's smoking status, pets (cat/dog) at home and use of mosquito coils.

The third part of the questionnaire inquired about the family history of asthma. It asked questions about parental and grandparental asthma status. In this part, a question that asked whether the participant had ever been diagnosed as asthmatic by a physician was also included.

2.5 Lung function measurement:

Lung function tests were carried out in February-March and June-July, 2013. Meteorologically, the month of February is in the winter season and March falls within the pre-monsoon season. June-July is the monsoon season in Bangladesh. However, to simplify matters in this study, February-March is classified as winter and June-July as summer.

We planned to carry out the lung function test once a week for 1 month in each season; eight times in total for each of the three schools. However, due to the occurrence of some unforeseen events such as strikes, national holidays and school events, we were unable to perform these tests as scheduled. The actual schedule of the test days is shown in Table 4.

Lung function was measured by spirometry, the most common kind of pulmonary function test (PFT) to measure lung function. It measures the amount (volume) and/or speed (flow) of air that can be inhaled and exhaled. Chestgraph (Model HI-105, Chest, Japan) was used for spirometry. The protocol for the lung function measurements was in accordance with American Thoracic Society and European respiratory Society (ATS/ERS) recommendations (68). Three to eight maneuvers were performed to comply with ATS acceptability and reproducibility criteria. This required each child to perform at least 3 FVC trials that were acceptable, and with at least two acceptable trials that were reproducible (difference $< 5\%$). The best trial of the three reproducible maneuvers was selected. Lung function measurements included the following parameters: forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1) and peak expiratory flow (PEF) derived from the best maneuver. Before starting the actual lung function tests, we carried out a practice session for study participants on a separate day. In that session, the lung function test procedure was explained and then, each of them performed a rehearsal test.

Anthropometric weight and height measurements were recorded for each participant before the beginning of the first lung function measurement.

2.6 Assessment of environmental exposure

Air pollution exposure data was obtained from the existing continuous air-monitoring stations (CAMS) operating under the "Clean Air and Sustainable Environment Project (CASE)" by the Department of the Environment (DoE), Ministry of Environment and Forests, Bangladesh.

Daily (24 h average) data for $PM_{2.5}$ and PM_{10} for the year 2013 was retrieved from four continuous air-monitoring stations (CAMS). As also mentioned above, each school is located within 1 km of a monitoring station and participants in each school were assigned to an exposure level from the nearest monitoring center (Figure1). There are two CAMS within 1 km of one school (RDH) inside metropolitan Dhaka. The average concentration of the two CAMS was calculated and used as the exposure level for the participants in that school. Meteorological data (daily ambient levels of average, maximum and minimum temperature and relative humidity) was provided by the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) and the Disaster Prevention Research Institute, University of Kyoto. The meteorological data was collected from one location in Dhaka city.

2.7 Statistical analysis

The basic characteristics of the participants were summarized using descriptive statistics. Spearmen rank correlation coefficients were determined between PM and the meteorological variables. We calculated odds ratios (OR) with 95% confidence intervals (CI) to assess the demographic and home environment-related risk factors that were associated with asthma (doctor-diagnosed). We used a Cochran-Mantel-Haenszel (CMH) test to calculate crude (unadjusted) ORs with 95% CIs while controlling for the effects of school. Logistic regression analysis was used to calculate ORs with 95% CIs with the model adjusted for age, sex, family size, parents' education level, number of smokers in the family, having a cat as a pet, fathers' occupation and school.

The short-term effect of ambient particulate matter (i.e., $PM_{2.5}$, PM_{10}) and temperature on lung function outcomes was studied using linear mixed-effects models. This model is applicable in studies where repeated measurements are made on the same subjects (e.g., panel studies) as in this study (69). Because of the autocorrelated nature of repeated measurements over time, the autocorrelation function (ACF) of the residuals was plotted while undertaking regression diagnostics. We ran two models, that is, one with both random intercepts and random slopes, and another with only random intercepts. As the models were not statistically different according to the maximum likelihood-based likelihood ratio tests (70), only the random intercepts were kept in the final model.

In this study, FVC, FEV1, PEF and the FEV1/FVC ratio were treated as the outcome variables. To account for the heterogeneity across participants, lung function parameters data were transformed into percentage deviation (%) variables except for the FEV1/FVC ratio. The median value for each participant over the study period was first subtracted from the absolute values of the outcome measurement, before being divided by the median and multiplied by 100 to obtain the percentage deviation (71).

In this study, we examined the short-term exposure effects of ambient PM and temperature separately. For PM, we used the daily mean concentration of $PM_{2.5}$ and PM_{10} measured at the nearest monitoring stations. To evaluate the effect of temperature, we carried out separate analyses for daily mean temperature (24-h average), and DTR as exposure variables. For all exposure variables, we tested models with multi-day moving averages (up to 3 days) to examine the potentially delayed response as reported in previous studies (69, 72). As all lung function tests were performed in the morning, the same-day (lag 0) PM effect was excluded because it was assumed to be negligible. We also excluded the same-day (lag 0) DTR effect for the same reason. DTR was calculated as the difference between the maximum and minimum temperatures within a day. When studying the effect of PM exposure, we adjusted the model for temperature exposure (i.e., daily mean and DTR), and vice versa.

We included a number of covariates to control for potential confounding effects. Personal characteristics such as age, height and weight were included to account for between-subject variability. Models were also adjusted for exposure to environmental tobacco smoke. The study period was adjusted using a categorical variable to account for seasonal variation. Schools were initially regarded as random effects, but a subsequent model with a fixed school effect indicated that there was no difference. Therefore, a school indicator variable was included to adjust for study location. We did not adjust for sex since two of the three schools were single gender schools. Time was considered a random effect that accounts for intra-individual correlated measurements. We also adjusted for relative humidity.

To assess the effect modification of season, a multiplicative interaction term for the exposure variable and season (indicator variable) was included along with the main effects. When the magnitude of the effect of an exposure on an outcome is differed or modified depending on the value of a third variable, that phenomenon is called effect modification (also called statistical interaction) and the third variable is called effect modifier (73). In epidemiological study, effect modification is commonly identified by stratification (i.e., by examining the association separately by effect modifier). We also performed stratified analyses by dichotomizing the winter and summer season. We then applied a multiple comparison by calculating the *p*-value for the difference in the estimates of the exposure effects between the winter and summer seasons (74).

Results are reported as estimated changes in percentage deviations (%) for FVC, FEV1, PEF and estimated changes in the FEV1/FVC ratio with 95% CI in lung function measures associated with a 20 μg/m^3 increase in PM, a 1^0 C decrease in mean temperature and a 1^0 C increase in DTR.

The statistical software package R version 3.1.0 (R Development Core Team, 2008), specifically the "nlme" package, was used to conduct the above mixed-effect regression analyses.

2.8 Ethics statement

The study protocol was approved by the "Research Ethics Committee at Graduate School of Medicine, the University of Tokyo". Permission was also obtained from the relevant school authorities. All subjects gave verbal permission. Written informed consent was obtained from the parent before their child participated in the lung function panel study.

Chapter 3: Results

3.1 Results of the cross-sectional questionnaire survey

Characteristics of the study population for all children and separately by school are presented in Table 5. In total, 1554 students aged between 5-18 years participated in the study. The age range of the students differed between the schools as each school had a different range of grades. Fifty-two percent of the study participants were girls.

Most of the participants' parents (91%) went to at least primary school. Fathers of these children usually had monthly paid jobs or ran businesses whereas most of their mothers were housewives. The majority of the childrens' families used natural gas as a fuel for cooking at home and had concrete or tin built houses. In half of the houses, there was at least one smoker and 43% of the fathers were smokers. Twenty-nine percent had kept a cat and 13% kept a dog as a pet at home in last 12 months. Thirty percent of the study participants had domestic animals at home. Most of the childrens' families used mosquito coil for more than 3 days a week.

Table 6 presents information about the distribution of asthma and respiratory health symptoms obtained from the questionnaire survey. Among the participating students, 12% had doctor-diagnosed asthma. In total, 19% reported having a wheeze and 14% reported that they had asthma at some point in their life. The prevalence figures for doctor-diagnosed asthma and respiratory symptoms obtained by using the ISAAC questionnaire were higher for students at RDH followed by NBA and KRS.

Crude and adjusted odds ratios (OR) with 95% confidence intervals (CI) were used to determine what factors were associated with having doctor-diagnosed asthma (Table7). Children whose parents had more than a primary school education had significantly higher odds of having asthma than children with less educated or illiterate parents. Having a father or any family member smoke was associated with significantly higher odds of having childhood asthma. In addition, children who had a cat as a pet in their household were significantly more likely to have asthma. No other demographic characteristics or home environmental-related factors were significantly associated with having doctor-diagnosed asthma.

3.2 Results of the panel study

3.2.1 Descriptive statistics of the panel study

The descriptive statistics of the participants of the panel survey are presented in Table 8. In total, 314 children participated in this study including 86 (27%) with doctor-diagnosed asthma. The mean age of the study children was 12 (range 9-16) years, while 54% of the participants were girls. The mean standing height and weight of the participants were 149 (±9) cm and 39 (±9) kg, respectively. In total, the participants provided 1546 daily observations for lung function measurements. The median values of their lung function parameters for all measurements were as follows: PEF 3.45 L/s, FEV1 1.90 L and FVC 2.25 L.

3.2.2 Environmental variables

Descriptive statistics for the weather variables and concentrations of air pollutants during the total study period (February 10-July 14) and by each study period in the different seasons are presented in Table 9. The mean level of $PM_{2.5}$ and PM_{10} was 88µg/m^3 and 153µg/m^3, respectively, during the total study period. PM concentration varied greatly between seasons, with higher mean values observed in winter than in summer. During winter, the level of $PM_{2.5}$ was between 63-215 µg/m^3, whereas in summer, it ranged between 12-43 µg/m^3. The mean temperature was 27 ^{0}C during the study period. Readings for the weather variables (temperature and relative humidity) were lower in winter than in summer as expected.

Spearman correlations for the environmental variables are presented in Table 10. Daily temperature, relative humidity and study period were negatively correlated with PM, whereas DTR was positively correlated with PM.

3.2.3 Association of particulate matter exposure and lung function

The estimated changes in lung function parameters in relation to an increase of 20 µg/m^3 in $PM_{2.5}$ for all children and separately for asthmatic and non-asthmatic children at different lag exposures, obtained from linear mixed-effect models are presented at Table11 and Figure 4. A 20 μg/m^3 increase on the previous day's $PM_{2.5}$ was associated with a significant decrease in all lung function parameters , with a change of −4.18% (95% CI, −5.70 to −2.65) for PEF, −2.04% (95% CI, −2.91 to −1.17) for FEV1, −0.64% (95% CI, −1.10 to −0.17) for FVC, and −0.015% (95% CI, −0.021 to −0.009) for FEV1/FVC. A significant negative correlation persisted for the cumulative previous 2 days lag for PEF and the FEV1/FVC ratio. Asthmatic children had slightly higher estimates than non-asthmatic children. However, the estimates for asthmatic and non-asthmatic children were generally not significantly different ($p > 0.05$; supplemental Table 3).

Lung function parameters were not significantly associated with PM_{10} for any group of children except for FVC (Table 12, Figure 5). FVC had a positive correlation with a 20 μg/m^3 increase in PM_{10} for the previous day (lag1) and previous cumulative 2 days lag.

3.2.4 Association of temperature exposure and lung function

For all participants, a 1^{0}C decrease in temperature had a consistent negative association with lung function parameters up to 3 days lag (Table 13 and Figure 6). For a 1^0 C decrease in daily mean temperature for the cumulative lag of the current and previous day, changes in lung function parameter were - 3.02% (95% CI, -1.69 to- 4.35) for PEF, -1.48% (95% CI, -0.75 to -

2.22) for FEV-1, 0.73% (95% CI, -0.33 to -1.13) for FVC, and -0.007% (95% CI,- 0.002 to -0.012) for FEV1/FVC. The estimated effects were generally higher for asthmatic children than non-asthmatics, although not statistically different ($p > 0.05$; supplemental Table 4).

Table 14 and Figure 7 presents the estimated changes with 95% confidence intervals in lung function parameters associated with a 1^0 C increase in DTR at different exposure metrics. In general, DTR was negatively associated with lung function indices. FVC was significantly inversely associated with DTR at all lag exposures. For all children, the cumulative previous 2 days DTR was associated with significant decreases in PEF and FEV1, with changes of −2.41% (95% CI, −4.27 to −0.56) and −1.28% (95% CI, −2.33 to −0.24), respectively. In general, asthmatic children were more affected by a 1^0 C increase in DTR, although not statistically different ($p > 0.05$; supplemental Table 5).

3.2.5 Effect of season on the associations between exposure and lung function

The estimated changes with 95% confidence intervals in lung function parameter associated exposure variables stratified by season and *p*-value for multiple comparison for estimates between the seasons are presented in Table 15 to Table18. The analyses shown in Table 15 to Table 18 are based on the combined data for asthmatic and non-asthmatic children as in the preceding analyses we found no statistical difference in these two groups in the estimated effects for lung function parameters in relation to exposure variables.

In both seasons, lung function parameters (except for FVC) were negatively associated with a 20 μg/m^3 increase on the previous day and cumulative average of the previous 2 days $PM_{2.5}$. In summer, the negative effect of $PM_{2.5}$ on lung function parameters (except for FVC) was stronger than in winter (Figure 8). Specifically, for PEF, there was a - 4.17 (95% CI, -5.69 to -2.65) decrease in winter and -10.92 (95% CI, -15.73 to -6.12) decrease in summer for a 20 μg/m^3 increase in $PM_{2.5}$ on the previous day. The differences in estimates were statistically significant at the previous day and cumulative previous 2 days lag (p <0.05) (Table 15).

For PM_{10}, the estimated changes in lung function parameters were significantly different only at the previous day lag (Table16). In summer, the lung function parameters (except for FVC) were significantly negatively associated with a 20 μg/m^3 increase in previous day PM_{10}.

When stratified by season, lung function parameters were significantly negatively associated with a 1^0 C decrease in temperature only in winter (Table 17, Figure 10). In summer, although not statistically significant, PEF, FEV1 and FEV1/FVC showed an opposite pattern and had a positive association associated with current day mean temperature. However, FVC had a stronger negative association with temperature in summer than in winter.

Chapter 4: Discussion

4.1. Main findings of the study

The present study estimated the effects of short-term exposure to ambient $PM_{2.5}$, daily mean temperature and DTR on lung function in a panel of school children in Bangladesh, and found that higher exposure to $PM_{2.5}$ and larger DTR and lower temperature were primarily associated with a reduction in lung function parameters. Our analysis also demonstrated significant seasonal variation in these associations as the estimated effects of $PM_{2.5}$ on lung function measures were generally stronger in summer than in winter, and the estimated adverse effects of low daily mean temperature on lung function measures were only evident in winter.

4.2 Asthma prevalence in Dhaka

Our results suggest that asthma and wheezing could be a significant cause of morbidity among school children in Bangladesh. This school-based survey showed high prevalence of doctor-diagnosed asthma (12%) among the participating students. According to the ISAAC questionnaire, 19% reported to have wheeze and 14% reported to have asthma at any point of life.

Few previous studies have evaluated respiratory health-related diseases or the prevalence of asthma for children in Dhaka, Bangladesh. Among those that have, a study using ISAAC questionnaire examined asthma prevalence among school children in Dhaka city (3 schools) in 2006 and also found high prevalence of asthma (16.4% for the children of 13-16 years) (61). Another school-based cross-sectional study was conducted specifically for Dhaka district in 2000 and reported that the lifetime (ever) and 12-month period (recent) prevalence of wheezing were 13.8% and 7.6% respectively, using the ISAAC protocol for children (62). In a nationwide cross-sectional study conducted in 1999, the reported prevalence of asthma (wheezing in the last 12 months) according to ISAAC protocol for children was7.3% among children aged 5-14 years old (64). The studies conducted in recent years (2006 and this study) including this study showed higher prevalence of wheezing and asthma than the studies conducted in earlier years (2000 and 1999). Thus, it is possible that there is an increasing trend of asthma prevalence for the children living in Dhaka. However, there were few studies are that are available and the existing studies had different methodology and study design. More research is needed to explore the trend of asthma prevalence in Bangladesh.

4.3 Association of particulate matter and lung function

4.3.1 Effects of $PM_{2.5}$ on lung function

In this study, for a 20 μg/m^3 increase in $PM_{2.5}$ at lag 1, there was a 4.18% decrease in PEF and 2.04% decrease in FEV1 for all children. Our results for ambient $PM_{2.5}$ are consistent with previous studies showing inverse associations of $PM_{2.5}$ with lung function parameters among school children (75). Ahmad et al., (2007) reported a 30% decrease in PEF in school children in Dhaka when $PM_{2.5}$ increased from its lowest (18μg/m^3) to highest (233 μg/m^3) daily mean value (61). However, a comparison of the estimated magnitudes of our findings with those from other studies is limited by the difference in study designs, lung function measures, expression of lung function measures and statistical methods used.

There was a significant inverse association between $PM_{2.5}$ and lung function in both asthmatic and non-asthmatic children. In contrast to this, several previous studies showed that asthmatic children were more sensitive to the adverse effects of particulate matter (76-78). However, in accord with our results, in an earlier study among school children in Dhaka, Bangladesh, $PM_{2.5}$ also had an adverse effect on lung function in both asthmatic and non-asthmatic children (61). Similarly, in a group of primary school children in the UK, asthmatic children were not more susceptible to the effects of air pollution (79, 80). Thus, our results add to a growing body of evidence indicating that the lung function of both asthmatic and non-asthmatic children might be affected by $PM_{2.5}$. However, the magnitude of the effects may differ in vulnerable subgroups such as asthmatics.

In this study, we showed the changes in lung function measures for a 20 μg/m^3 increase in $PM_{2.5}$. We found that during the study period the daily concentrations of $PM_{2.5}$ reached a very high level in Dhaka, especially in the winter where the range of the concentrations (i.e., from 63-215 μg/m^3) often exceeded the Bangladesh standard of 65μg/ m^3 for $PM_{2.5}$ and *always* exceeded the WHO 24-hour mean standard of 25μg/m^3. If we converted the estimates for an interquartile (173 μg/m^3) increase in $PM_{2.5}$ for this study, a 2.04% decrease in FEV1 for a 20 μg/m^3 increase in $PM_{2.5}$ would produce a 17.6% decrease in FEV1 and a 4.18% decrease in the PEF effect estimate would produce a 36.7% decrease in PEF. Previously, a 10% decrement in FEV1 has been suggested as constituting a meaningful adverse effect (81). Thus, the high concentration of $PM_{2.5}$ could result in a large number of children with respiratory morbidity and pose a significant public health concern for Bangladesh.

Our results suggested that for $PM_{2.5}$, there was a stronger effect observed at short lag than for the cumulative longer lag effects on lung function measures, which was not consistent with findings in all earlier studies (80). However, as the character of PM can vary greatly among regions and over time, depending on pollution sources and the prevailing atmospheric conditions, such factors might help explain this variation in results.

4.3.2 Effects PM_{10} on lung function

This study demonstrated that there was no consistent effect of PM_{10} on lung function measures for any group of children in this region.

This contrasts with the results from several previous studies that have demonstrated the adverse effect of PM_{10} on lung function in children (77, 78, 82). In particular, an earlier study conducted among school children in Dhaka found a 40% decrease in PEF when PM_{10} increased from its lowest (38µg/m^3) to highest (385 µg/m^3) daily mean value which was higher than the effect on $PM_{2.5}$ (30%) in their study (61). Weinmayr et al., (2004) while undertaking a systematic review and meta-analysis, investigated the short-term effects of PM_{10} only on children with asthma or asthma-like symptoms and found that PM_{10} had a significant effect on peak expiratory flow (PEF) (a decrease of –0.082 L/ min per 10µg/m^3 in PM_{10}; 95% CI: –0.214, –0.050) (24).

However, as in our study, several studies also failed to show an association between ambient PM_{10} and lung function in children (83-85). Ward et al., (2004), in a systematic review and meta-analysis of the effects of particulate air pollution in panel studies of children worldwide, suggested that the adverse effect of $PM_{2.5}$ was greater than PM_{10} on PEF (23). Other epidemiological studies have shown that smaller particles, such as $PM_{2.5}$ are more harmful than larger particles, such as total suspended particles (TSP) or PM_{10} (86, 87). The possible explanation given for this fact is that fine particles penetrate deeper into the lungs and also generate more toxicity due to them having a different chemical composition than larger particles (23). The results of this study thus provide further evidence that is in accordance with the hypothesis that finer particles are more harmful for health.

4.3.3 Seasonal variation in the effect of PM on lung function

We revealed significant seasonal variation in the effects of both $PM_{2.5}$ and PM_{10} on lung function in this study, especially at short lag. Interestingly, lung function parameters (except for FVC) showed a stronger inverse association with $PM_{2.5}$ in summer than in winter, although the particulate pollution was much higher in winter compared to summer.

The effect of season in the association of particles and lung function has yet to be revealed. Recently, one study reported an interactive effect of $PM_{2.5}$ and temperature on lung function for adults in Beijing, China (88). According to its findings, the effects of $PM_{2.5}$ on lung function were generally stronger in the presence of high temperatures than in the presence of low temperatures. In accordance with this, we found a stronger negative effect of PM in summer when the temperature was higher than in winter.

In a meta-analysis of the short-term effects of PM_{10} in children with asthma or asthma-like symptoms, the estimated effect of PM_{10} on asthma was found to be higher in studies that were conducted in summer (24). Previous epidemiological studies that have investigated the effect of temperature in the association between particulate air pollution and mortality demonstrated that the effect of PM on mortality was higher during warmer days (66). To explain this, these authors suggested that summer pollution is qualitatively different to winter pollution due to the difference in O_3 levels and people's behavioral change due to the weather. In summer, O_3 levels are usually higher, and people also spent more time outside which may have ultimately caused higher exposure to air pollution than in winter. However, the reason for the difference in effects by season suggested in previous studies might not be applicable to the current study. For example, although there was no information about this population regarding its behavioral patterns, from our observations over a long period of time in this setting, we doubt that there are any large differences in behavioral patterns between seasons. More specifically, in contrast to some of the places where previous research has been undertaken, the winter in this region is not very cold which makes higher or lower exposures due to behavioral differences linked to seasonal variation in the weather unlikely. Unfortunately, we had no daily data for O_3 to adjust the statistical models and no previous study was available which showed the temporal variation in O_3 levels in Bangladesh.

In our study, the concentration of PM was much higher in winter than in summer even though, the effect of PM on lung function was higher in summer. One previous study conducted in Dhaka showed that the source of PM pollution varied between the seasons. It found that the major source of PM in winter was brick kilns while in the rainy reason it was metal smelters (59). This is important as previous studies showed that the biological effects of a particle are significantly determined by the physical and chemical nature of the particle (89). Thus, it is possible that the chemical nature of PM in this region was different between seasons due to differences in its source and that the composition of summer PM was more harmful in terms of its respiratory health effects.

4.4 Association of daily mean temperature and lung function

4.4.1 Effects of daily mean temperature on lung function

We found that for school children in Dhaka, lower daily mean temperature had a robust and consistent adverse effect on lung function measures. These associations were significant even after adjustment for PM and DTR. These effects lasted for 3 days.

In accordance with our findings, a very recent study found that low ambient temperature were associated with decrements in PEF values in a panel of children in Baotou, China (90). It found that lung function was negatively associated with a decrease in temperature where an estimated decrease of −1.28 (95% CI: −1.69, −0.88) L/min for PEF was associated with a 1°C decrease in daily mean temperature with lag 0–2 days exposure. However, the results of this study were not presented in the same way as we expressed our findings concerning lung function parameters (percent deviation from the personal median), thus, the magnitude of the estimates are not comparable. Moreover, in contrast to our findings, previous research has also reported that high temperature was associated with a decrement in lung function (50) and increased the risk of experiencing respiratory symptoms (72) for children with asthma in Australia. This difference might be caused by the difference in the climatic areas. People living in different geographic areas and climatic zones may have adapted to regional climatic conditions in different ways and thus have different response patterns to changes in the weather.

The association between temperature decrease and adverse effects on lung function can be explained by several possible mechanisms that have been examined in previous studies. For example, inhalation of cold air has previously been associated with bronchoconstriction (49). Low ambient temperature can also directly induce airway inflammatory changes via cytokine activation (91). Cold temperature (cold temperature obtained by packing of head and neck in towels soaked in ice-cold water) was found to increase pathological vasoconstriction in swimmers and scuba drivers and thus, can reduce lung capacity (92). In addition, previous research showed that airway cooling (exercise challenge test at 2–5 °C air) caused airflow limitation in asthmatic children (93).

In this study the effects of ambient temperature on lung function lasted for several days. Previous studies that showed an effect of ambient temperature on lung function in children found a similar lagged effect (51, 72). Additionally, previous epidemiological studies that have reported the effects of ambient temperature on morbidity and mortality found that the effects were generally stronger in the first few days and lasted for several days (27, 94).

4.4.2 Seasonal variation in the effects of daily mean temperature on lung function

In this study, there was a significant difference in the effects of temperature between seasons for PEF and EFV1, especially at short lag exposure. In general, the adverse effects of temperature were attenuated in summer except for FVC.

Little information exists about the seasonal variation of ambient temperature on lung function either for children or adults. As yet, few epidemiological studies have examined the effect of season on the association between ambient temperature and respiratory morbidity and those that have done this have emphasize the importance of the seasonal modification in this association. Specifically, one study showed significant seasonal modification in the association of daily average temperature and emergency department visits for asthma and showed that winter and summer had higher risk while spring had a lower one, associated with increasing temperature in North Carolina, in the United States (95). Another study in Oulu, Finland reported that the association between daily ambient temperature and emergency room visits for asthma attacks was opposite in direction when compared between the summer and winter (96).

4.5 Association of DTR and lung function

4.5.1 Effect of DTR on lung function

The results of this study also provide evidence for the adverse effect of DTR on the lung function of children living in a tropical region, a result seen previously for Australian asthmatic children. We also extended evidence that the larger DTR worsen the lung function for non-asthmatic children.

There was little prior information available on the effect of DTR on lung function in children. As mentioned earlier, the only study that evaluated this association which was conducted among children with asthma in Australia found a similar negative effect of DTR on PEF that lasted for 3 days. It estimated that the effect of a 5^0C increase in DTR range on PEF for a 1 day lag was -4.32 (-6.41 to -2.22) for girls and -1.98 (-4.01 to 0.05) for boys (51). In our study, the estimated change in PEF for a 1^0C increase in DTR for asthmatic children was -1.64 (95% CI: -2.93, -0.34) and -3.25 (95% CI: -5.27, -1.24) for lag day 1 and 2, respectively.

We found increase in DTR can cause a significant decrease in lung function. This is important as previous research has shown that DTR is significantly associated with elevated emergency room admissions for childhood asthma (37). Lim et al., (2012) also examined the effect of DTR on hospital admissions for asthma in Korea and found that 1°C increment of DTR was significantly associated with percent change of hospital admissions for asthma during 2003–2006 (percent change1.1 %; 95 % CI, 0.1–2.0%) (97). Lung function decrement is linked to the risk of hospitalization attributable to cardiovascular and respiratory diseases and overall health status and a decrease in lung function with increased DTR can cause an excess of respiratory morbidity.

In this study the estimated effects of DTR on lung function exhibited cumulative lag effects up to 3 days which is similar to in earlier studies. For instance, this finding is consistent with a previous study that evaluated a similar association for asthmatic Australian children (51). The association between DTR and respiratory morbidity was also found frequently in the first 1 to 3 days after exposure (98, 99).

Pathophysiological responses, such as bronchospasms and inflammatory changes in the respiratory epithelium at the tissue level in response to sudden temperature change have been suggested as possible biological mechanisms underlying the inverse association between DTR and respiratory health (100). In addition, previous research showed that a sudden temperature change in inhaled air could result in inflammatory nasal responses (101). For children, as a result of these pathophysiological responses, high DTR might cause additional environmental stress on the cardiopulmonary system (100) and lead to a decrement in lung function.

4.5.2 Seasonal variation in the effect of DTR on lung function

The seasonal variation of DTR on morbidity and mortality has been shown in various reports previously. In a systematic review on the impact of DTR on human health, it was suggested that DTR might be modified by season, while varied susceptibility among people in different seasons was mentioned as one of the possible reasons for this seasonal variation (100). For example, the effects of DTR on emergency room admissions for cardiovascular, respiratory, digestive, and genitourinary diseases were different across the four seasons (38). However, seasonal variation in the effect of DTR on lung function is largely unknown. We found at short lag, the estimated negative effect of DTR on most of the lung function parameters was smaller in summer than in winter. In accordance with our study, previous research showed that the effects of DTR were higher for cardiovascular diseases in Hong Kong and sudden infant death in Shanghai on cold days than warm days (36, 102). Another study conducted in Shanghai found that there was no significant increase in respiratory mortality on warm day (>23 °C), although the adverse effects of DTR on respiratory mortality were observed for all points in time (103).

The effects of extremely high or low DTR on health events were found to be stronger than those of moderate DTR (104). In Australia, the DTR effect on admissions for childhood asthma increased significantly only when the DTR was above 10^{0}C for children aged 0–14 years (37).

In our study, the mean DTR was larger in winter than in summer. The stronger effect of DTR in winter might also point to the fact that DTR effects only occur after a certain threshold. However, the acquisition of more evidence from future research is needed in this regard to better explain this phenomenon.

4.6 Limitations of the study

There are several limitations to the present study that should be taken into account when interpreting these results.

First, there was no data available pertaining to other potential pollutants such as O_3, NO_2 and SO_2 which meant that they could not be considered in the current study. As previous reports have showed an association between these pollutants and respiratory outcomes, especially for O_3 it is possible that our results might have been confounded by these unmeasured factors. However, previous articles that have examined multi pollutants, demonstrated that $PM_{2.5}$ had the strongest and most robust effects on lung function measures (69, 105).

In addition, the ambient temperature, relative humidity, and air pollution data was obtained from existing fixed monitoring stations rather than individual exposures, which may have led to measurement errors in exposure. There are a possibility of overestimation if the assigned exposure levels from a given monitoring station are lower than the actual individual exposure.

However, we found that most of our study participants lived very close to the air monitoring stations (Figure 3). Previous research has highlighted that temperatures are strongly correlated within cities and temperature measurement data obtained from fixed monitoring locations showed similar results compared to spatially resolved temperature data at estimating city-wide associations between temperature and mortality (106).

In this study, significant difference was observed in the effect of both PM and temperature on lung function by season. This difference may be due to the seasonal variation in temperature. This can also reflect the seasonal difference in other risk factors that interact with or mediate the effect of PM or temperature on lung function. However, we were unable to adjust for some confounders such as pollen, viral infection, mold, time spent outdoors which may vary by season in these associations due to lack of data.

Another limitation of this study was that we relied on the parents report for identifying the participants with doctor-diagnosed asthma rather than examination by a physician. This can lead to the misclassification of participants if there were any under or over reporting by the parents.

Moreover, throughout this study, the effects of the relative change in the temperature on lung function measures were presented in this study. However, we had done stratified analysis between the association of temperature and lung function by season. In this study, the two seasons; summer and winter represents different temperature range. (18-29^{0}C in winter vs 27-32^{0}C in summer). The analysis performed by season showed different magnitude of effect for 1^{0}C decrease in daily mean temperature (Table 17). Thus, it is possible that depending on the absolute temperature range, the effect of relative difference in temperature had different effect on lung function.

Another limitation was using the ISAAC questionnaire for 6/7 years old for all the children in grade 1-8. By doing so, many children who were 13/14 years or older were also included in this category. The basic difference between the ISSAC questionnaires for 6/7 and for 13/14 year olds is the former should be reported by parent of the participant, whereas the latter by the participant. However, there were two main reasons for using the ISAAC questionnaire for 6/7 year old children for children in school years up to grade 8. First, the complete questionnaire also had other parts besides ISAAC, such as questions about the family history of asthma and home-environment-related questions. In previous studies conducted in other countries (Brazil and Canada), parents' report was used to obtain information in this regard (i.e. family asthma history and home-environment) for children of 6-15 years old (69,107). Moreover, based on our previous experience in conducting questionnaire survey in this area, we assumed it would be difficult for the younger children to answer the questions about family history of asthma and home-environment. Due to the necessity of obtaining accurate information on these topics, we sent the whole questionnaire to the parents to complete and that is why, the ISAAC questionnaire designed for 6/7 year olds was used for children up to grade 8, where parents reported about their child's asthma symptoms. Secondly, in Bangladesh, the age range of the children in each grade was not fixed. Specifically, it was difficult for us to decide the exact grade from which we should start the questionnaire for 13/14 years old. To minimize the confusion, we used the questionnaire for 13/14 year olds from grade 9 or above only.

Lastly, this study was conducted in children only from non-government schools located within 1km of the CAMS inside and around Dhaka. This may limit out capacity to generalize the study findings to the general population of similar age group in Bangladesh.

However, children from non-government school should reflect the general population as 98% of the total schools are non-governmental for offering secondary education in Bangladesh (108). The remaining 2% are government schools. These non-government schools do not differ with the government schools in education curriculum and system. Moreover, Bangladesh government provides the 90% of the salaries of the teachers, cost for infrastructure development, education supplies and equipment in these non-government schools (108). Thus, it is unlikely that the choice of the school type limits our study participants to any particular subgroup. However, the study areas were predominantly urban and sub-urban area that is extremely densely populated and congested. Therefore it is difficult to generalize the results to children who live in rural areas and other smaller cities.

Chapter 5: Conclusion

The results of our study suggest that short-term ambient exposure to high $PM_{2.5}$, low temperature and large DTR are independent risk factors to the health of children. The observed high concentration of $PM_{2.5}$ and low temperature in winter could thus results in a large number of children with respiratory morbidity in Bangladesh. Additionally, our study provides novel insights of seasonal modification into the associations between environmental exposures (PM, temperature and DTR) and lung function for children. These results might be used to develop preventive measures and policies to protect the health of the children in Bangladesh.

Table 1 : Panel studies of ambient particulate matter and lung function in children

Region	Study period	Exposure	Lung function	Subject	Key findings	Study (Reference)
Oceania						
Sydney, Australia	1 February-31 December, 1994	PM_{10}	PEF	125 children with a history of wheeze (9.6 yrs)	PM_{10} was not associated with children's PEF.	Jalaludin et al., 2000 (82)
Christchurch, New Zealand	Winter 2004	PM from wood burning	PEF	93 male students including 26 asthmatics (12-18yrs)	For healthy school students, there was no significant effect of PM on lung function. Peak PM levels had small effects on asthmatic student's lung function	Epton et al., 2008 (75)
North America						
Utah Valley, US	Winter of 1990-1991	PM_{10}	PEF	39 asthmatic and 40 non-asthmatic children (9-11 yrs)	Relatively small but statistically significant ($p < 0.01$) negative associations between PEF and PM_{10} were observed for both the symptomatic and asymptomatic samples.	Pope and Dockery, 1992 (79)
US	1 June-31 August 1993	PM_{10}	PEF	846 asthmatic children (4-9 yrs)	Although not statistically significant, estimated effects of PM_{10} on morning %PEF were negative	Mortimer et al., 2002 (109)
Los Angeles, US	4 November 1999-23 January 2000	PM_{10}	PEF	22 Hispanic asthmatic children (10-16 yrs)	PM had an adverse effect on children's evening PEF, but not on their morning PEF	Delfino et al., 2003 (110)
Southern California, USA	August-October 1999 or April-June 2000	$PM_{2.5}$ PM_{10}	FEV_1	19 asthmatic children (9-17 yrs)	$PM_{2.5}$ and PM_{10} had a negative effect on FEV_1	Delfino et al., 2004 (81)
Seattle, US	1999-2002	$PM_{2.5}$ PM_{10}	FEV_1 PEF	17 asthmatic children (6- 12 yrs)	In children not receiving anti-inflammatory medication, same day exposures to $PM_{2.5}$ were associated with decrements in PEF, and FEV1	Trenga et al., 2006 (111)
Vancouver, Canada	1990-1991	PM_{10}	PEF	132 asthmatic and 74 non-asthmatic children (6-13 yrs)	Increases in PM_{10} were associated with reductions in PEF and asthmatic children were more susceptible to these effects than other children	Vedal et al., 1998 (77)
Windsor, Canada	11 October-11 December 2005	$PM_{2.5}$	FEV_1	182 asthmatic primary school children (9-14 yrs)	$PM_{2.5}$ decreased children's FEV_1 in a short time period, such as in a day	Dales et al., 2009 (104)

Table 1 : Continued

Region	Study period	Exposure	Lung function	Subject	Key findings	Study (Reference)
South America						
Rio de Janeiro, Brazil	6 weeks during May to October 2004	PM_{10}	PEF	118 school children (6-15 yrs)	PM_{10} was associated with decreased PEF in children	Castro et al., 2009 (107)
Mexico	April 1991 to February 1992	$PM_{2.5}$ PM_{10}	PEF	71 children (5-13 y of age) with mild asthma	Exposure to high PM reduced PEF in mildly asthmatic children	Romieu et al., 1996 (112)
Mexico	April 1991 to February 1992	PM_{10}	PEF	65 children (5-13 y of age) with mild asthma	The effects of PM_{10} on PEF were small, negative but not statistically significant	Romieu et al., 1997 (113)
Asia						
Tokyo, Japan	1 October-24 December 2000	Hourly and 24-hour: $PM_{2.5}$	PEF	17 severe asthmatic children (8-15yrs)	Increased concentrations of $PM_{2.5}$ were related to decreases in PEF among hospitalized severely asthmatic children	Yamazaki et al., 2011 (114)
Ashkelon, Israel	March-June 1999 and September-December 1999	$PM_{2.5}$ PM_{10}	PEF	285 asthmatic school children (10- 12 yrs)	$PM_{2.5}$ had significant effects on PEF in southern Israel	Peled et al., 2005 (115)
Mae Moh, Thailand	1 October 1997 -30 November 1997	PM_{10}	FVC, $FEF_{25-75\%}$, FEV1, PEF	83 asthmatic and 92 non asthmatic children (6-14 yrs)	For asthmatic children, a small negative association was found between PM_{10} and lung function. No association was found between air pollution and lung function in non-asthmatic children	Aekplakorn et al., 2003 (76)
Dhaka, Bangladesh	2007	$PM_{2.5}$ PM_{10}	PEF	120 asthmatic and 60 non-asthmatic (9-16 yrs)	For both asthmatic and non-asthmatic children, PEF 40% decreased when PM_{10} increased from its lowest to highest level (38 to 385 µg/m3) and a 30% decreased when $PM_{2.5}$ increased from its lowest to highest level (18 to 233 µg/m3)	Ahmad et al., 2007 (61)

Table 1 : Continued

Region	Study period	Exposure	Lung function	Subject	Key findings	Study (Reference)
Europe						
Birmingham and Sandwell, UK	13 January-10 March 1997 and 19 May -14 July 1997	$PM_{2.5}$ PM_{10}	PEF	162 asthmatic and non-asthmatic primary school children (9 yrs)	No consistent effect of $PM_{2.5}$ and PM_{10} on PEF	Ward et al., 2002 (78)
UK	1 November 1996 - 14 February 1997	PM_{10}	PEF	179 school children (7-13 yrs)	PM_{10} had an adverse effect on PEF	Peacock et al., 2003 (116)
Paris, France	1 April-30 June 1996	PM_{13}	PEF	82 asthmatic children (7-15 yrs)	PM_{10} was not associated with children's PEF.	Just et al., 2002 (83)
Paris, France	November 15 1992 to May 9 1993	PM_{13}	PEF	84 medically diagnosed asthmatic children	Slightly correlated with PEF in the subgroup of mild asthmatics with no inhaled steroid	Segala et al., 1998 (117)
Emilia-Romagna, Italy	February-May 1999	$PM_{2.5}$ TSP	PEF	118 asthma-like primary school children (6-11yrs)	No statistically significant effect of pollutants on PEF	Ranzi et al., 2004 (118)
Austria	September 2000-August 2001	PM_{1} $PM_{2.5}$ PM_{10}	FEV0.5, FEV1, FVC, PEF	163 primary schoolchildren (7-10yrs)	Particles had an adverse impact on most lung function parameters	Moshammer et al., 2006 (74)
Kuopio, Finland	March 13 to April 23, 1995	PM_{10} $PM_{2.5}$	PEF	49 children with chronic respiratory symptoms (8-13 yrs)	1-day lagged $PM_{2.5}$ was statistically significantly associated with morning PEF	Tittanen et al., 1999 (119)
14 centers in Europe	Winter of 1993/1994	PM_{10}	PEF	2,010 asthmatic children	No clear association between PM_{10} on morning and evening PEF	Roemer et al., 1998 (PEACE) (120)

Table 2 : Panel studies of ambient temperature and lung function in children

Region	Study period	Exposure	Lung function	Subject	Key findings	Study (Reference)
Australia	2007-2008	Maximum temperature	FEV1, PEF	270 asthmatic children (7-12yrs)	Ambient temperature was negatively related to both PEF and FEV1 for 0-3 days lag	Li et al., 2014 (50)
Australia	2007-2008	Diurnal temperature range (DTR)	PEF	270 asthmatic children (7-12yrs)	An increase in DTR induced a reduction in PEF and effects lasted for 3 days	Li et al., 2014 (51)

Table 3: Study schools, corresponding air monitoring stations and their location

Location (place)	School (Code)	GIS location of School	Continuous Air Monitoring Station (CAMS)	GIS location of CAMS
Dhaka	Rajdhani High School (RDH)	23°45'30.25"N 90°22'52.21"E	CAMS 1: Sangshad Bhaban	23°45'44.91"N 90°22'55.58"E
			CAMS 2: Farmgate	23°45'33.04"N 90°23'22.27"E
Gazipur	Kazi Rajia Sultana Girls School (KRS)	23°59'21.30"N 90°25'26.44"E	CAMS 4	23°59'38.79"N 90°25'20.24"E
Narayanganj	Narayangonj Bar Academy School (NBA)	23°37'36.00"N 90°30'22.05"E	CAMS 5	23°37'35.87"N 90°30'22.12"E

Table 4: Lung function test days by school

School (Location)	Winter (February-March, 2013)				Summer (June-July, 2013)		
	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
RDH (Dhaka)	11-Feb	19-Feb	26-Feb	18-Mar	27-Jun	4-Jul	
KRS (Gazipur)	10-Feb	23-Feb	2-Mar		18-Jun	26-Jun	2-Jul
NBA (Narayangonj)	13-Feb	20-Feb	27-Feb		1-Jul	7-Jul	14-Jul

Table 5: Descriptive statistics for the participants of the cross-sectional questionnaire survey

Characteristics	**Median (Range) or Number (%)**			
	Total (*n* =1554)	**RDH** (*n* =339)	**KRS** (*n* =273)	**NBA** (*n* =923)
Age (years)	13 (5-18)	13 (8-18)	13 (10-17)	13 (5- 18)
Gender				
Female	815 (52%)	154 (42%)	273 (100%)	388 (43%)
Male	739 (48%)	215 (58%)		524 (57%)
Family characteristics				
Family member (number)	5 (2-15)	5 (3-12)	5 (3-13)	5 (2-15)
Siblings (number)	2 (0-8)	2 (0-7)	2 (0-7)	2 (0-8)
Education				
Father				
Primary school	434 (28%)	71 (19%)	104 (39%)	259 (29%)
High school	534 (35%)	118 (32%)	75 (28%)	341 (38%)
College/University	422 (28%)	155 (42%)	41 (15%)	226 (25%)
No education	142 (9%)	24 (7%)	50 (19%)	68 (8%)
Mother				
Primary school	558 (36%)	104 (30%)	106 (40%)	343 (38%)
High school	543 (35%)	133 (36%)	83 (31%)	327 (36%)
College/University	270 (18%)	96 (26%)	15 (6%)	159 (18%)
No education	163 (9%)	28 (8%)	64 (24%)	71 (8%)
Occupation				
Father				
Monthly paid job	662 (44%)	202 (55%)	93 (35%)	367 (42%)
Business	593 (39%)	142 (39%)	112 (43%)	339 (38%)
Day laborer	209 (14%)	13 (4%)	34 (13%)	162 (18%)
Farmer	48 (3%)	9 (2%)	23 (9%)	16 (2%)
Mother				
Monthly paid job	176 (11%)	28 (8%)	78 (29%)	70 (5%)
Business	38 (2%)	17 (5%)	8 (3%)	13 (1%)
Day laborer	23 (1%)	2 (1%)	3 (1%)	18 (2%)
Housewife	1299 (85%)	320 (87%)	181 (67%)	798 (89%)

Table 5, continued

Characteristics	Total (n=1554)	RDH (n=339)	KRS (n=273)	NBA (n=923)
	Median (Range) or Number (%)			
Cooking method				
Gas	1328 (86%)	343 (93%)	174 (64%)	811 (90%)
Wood/Fire	181 (12%)	16 (4%)	88 (32%)	77 (8%)
Electricity	23 (1%)	2 (1%)	5 (2%)	16 (2%)
Other	12 (1%)	6 (2%)	4 (1%)	2 (0%)
House type				
Concrete	856 (56%)	267 (73%)	103 (38%)	486 (54%)
Tin	628 (41%)	94 (26%)	137 (51%)	437 (44%)
Wood/mud	30 (2%)	0	25 (9%)	5 (1%)
Other	22 (1%)	6 (2%)	3 (1%)	13 (1%)
Water source				
Tube well	323 (21%)	50 (14%)	101 (38%)	172 (19%)
Tap water	1060 (70%)	277(76%)	135 (51%)	648 (73%)
Other	140(9%)	37(10%)	31 (12%)	72 (8%)
Smoker at home				
Father	656 (43%)	156 (43%)	127 (48%)	373 (41%)
Any family member	783 (50%)	199 (50%)	137 (49%)	447 (49%)
Animal contact in past 12 months				
Cat as pet	441 (29%)	90 (25%)	98 (36%)	253 (28%)
Dog as pet	202 (13%)	18 (5%)	60 (22%)	124 (14%)
Domestic animal	453 (30%)	103 (28%)	116 (42%)	234 (26%)
Mosquito coil use in a week				
> 5 days or regularly	504 (33%)	75 (20%)	51 (19%)	378 (42%)
3 - 5 days	565 (37%)	141 (39%)	118 (44%)	306 (34%)
< 3 days	260 (13%)	94 (26%)	63 (24%)	103 (12%)
Never	197 (13%)	56 (15%)	35 (13%)	106 (12%)

Table 6: Distribution of asthma and respiratory symptoms among study participants from the cross-sectional questionnaire survey

Respiratory health end points	**No. [%]**			
	Total (*n* =1554)	**RDH** (*n* =339)	**KRS** (*n* =273)	**NBA** (*n* =923)
Doctor-diagnosed asthma	181 (12%)	49 (13%)	26 (10%)	106 (12%)
From ISAAC questionnaire				
Ever wheeze	285 (19%)	81 (23%)	43 (16%)	161 (18%)
Ever asthma	214 (14%)	59 (16%)	32 (12%)	123 (14%)
*Recent wheeze after sports	219 (14%)	65 (18%)	54 (20%)	100 (11%)
*Recent dry cough	349 (23%)	105 (29%)	60 (22%)	184 (21%)

*Symptoms occurred in last 12 months

Table 7: Crude and adjusted odds ratios (OR) for selected characteristics

	Total	Asthmatic	Non-asthmatic	Crude OR[a]	95%CI	Adjusted OR[b]	95%CI
Age (years)							
≥ 12	1201	135	1066	**1.00**		**1.00**	
< 12	291	41	250	**1.25**	(0.85 , 1.82)	**1.32**	(0.88 , 1.97)
Sex							
Female	808	85	723	**1.00**		**1.00**	
Male	722	96	626	**1.25**	(0.88 , 1.76)	**1.18**	(0.82 , 1.73)
Household size							
< 10	1425	168	1257	**1.00**		**1.00**	
≥ 10	58	5	53	**1.37**	(0.54 , 3.49)	**1.88**	(0.74 , 6.38)
Parents' education							
Primary or none	480	38	442	**1.00**		**1.00**	
High School	573	87	486	**2.07***	(1.38 , 3.10)	**2.38***	(1.54 , 3.74)
College / University	457	55	402	**1.48**	(0.94 , 2.33)	**1.90***	(1.16 , 3.14)
Father's occupation							
Monthly paid job	652	72	580	**1.00**		**1.00**	
Business	589	67	522	**1.06**	(0.75 , 1.52)	**1.02**	(0.71 , 1.48)
Day laborer	204	32	172	**1.52**	(0.95 , 2.43)	**1.61**	(0.96 , 2.68)
Farmer	47	6	41	**1.32**	(0.52 , 3.32)	**1.15**	(0.32 , 3.22)
Mother's occupation							
Monthly paid job	173	22	151	**1.00**		**1.00**	
Business	38	3	35	**0.52**	(0.14 , 1.95)	**0.46**	(0.10 , 1.53)
Day laborer	23	2	21	**0.63**	(0.14 , 2.84)	**0.61**	(0.09 , 2.40)
House wife	1283	153	1130	**0.83**	(0.51 , 1.37)	**0.80**	(0.48 , 1.38)

[a]Cochran-Mantel-Haenszel (CMH) test with continuity correction for school

[b]Adjusted for age, sex, family size, parent education level, no. of smokers in family, cat as pet, father's occupation and school

Table 7, continued

	Total	Asthmatic	Non-asthmatic	Crude OR[a]	95%CI	Adjusted OR[b]	95%CI
Cooking method							
Gas	1307	159	1148	**1.00**		**1.00**	
Wood/Fire	179	16	163	**0.80**	(0.46 , 1.40)	**0.74**	(0.40 , 1.31)
House type							
Concrete	846	100	746	**1.00**		**1.00**	
Tin	619	78	541	**1.13**	(0.82 , 1.57)	**1.05**	(0.73 , 1.49)
Wood/mud	30	2	28	**0.73**	(0.15 , 3.50)	**0.58**	(0.09 , 2.22)
Water source							
Tube well	317	38	279	**1.00**		**1.00**	
Tap water	1046	118	928	**0.88**	(0.59 , 1.31)	**0.98**	(0.6 , 1.52)
Smoking							
Father							
No	856	72	784	**1.00**		**1.00**	
Yes	652	108	544	**2.18***	(1.59 , 3.00)	**2.33***	(1.66 , 3.28)
Any family member							
None	768	68	700	**1.00**		**1.00**	
At least one	739	112	627	**1.85***	(1.34 , 2.55)	**1.98***	(1.41 , 2.80)
Animal contact							
Cat as pet							
No	1073	108	965	**1.00**		**1.00**	
Yes	437	71	366	**1.78***	(1.29 , 2.46)	**1.73***	(1.22 , 2.44)
Dog as pet							
No	1307	154	1153	**1.00**		**1.00**	
Yes	199	26	173	**1.20**	(0.76 , 1.89)	**1.22**	(0.75 , 1.94)
Domestic animal							
No	1056	126	930	**1.00**		**1.00**	
Yes	449	51	398	**0.97**	(0.68 , 1.37)	**0.92**	(0.63 , 1.33)
Mosquito coil use in a week							
< 3 days	448	60	388	**1.00**		**1.00**	
3-5 days	563	59	504	**0.75**	(0.51 , 1.11)	**0.72**	(0.47 , 1.09)
> 5 days	494	59	435	**0.93**	(0.62 , 1.37)	**0.83**	(0.54 , 1.27)

[a]Cochran-Mantel-Haenszel (CMH) test with continuity correction for school
[b]Adjusted for age, sex, family size, parent education level, no. of smokers in family, cat as pet, father's occupation and school

Table 8: Descriptive statistics for the participants (*n* =314) of the panel study

Characteristics	**Value**
Age (years) (mean[SD])	12 (1.6)
Gender (no. [%])	
Female	171 (54%)
Male	144 (46%)
Doctor diagnosed asthma (no. [%])	86 (27%)
Height (cm) (mean[SD])	149 (±9)
Weight (kg) (mean[SD])	39 (±9)
[a]Lung function (median [5th-95th percentile])	
PEF (L/s)	3.45 (1.61-6.13)
FEV1 (L)	1.90 (1.20-3.03)
FVC (L)	2.25 (1.56-3.34)
Family characteristics (median[range])	
Members	5 (2-13)
Siblings	2 (0-10)
Education(no. [%])	
Father	
Primary school	105 (34%)
High school	97 (31%)
College/University	71 (23%)
No education	40 (13%)
Mother	
Primary school	111 (35%)
High school	101 (32%)
College/University	47 (15%)
No education	54 (17%)

[a]Median[5th-95th percentile] of lung finction parameters for all measurements

Table 8, continued

Characteristics	Value
Occupation(no. [%])	
Father	
Monthly paid job	135 (45%)
Business	114 (38%)
Day laborer	47 (16%)
Farmer	7 (2%)
Mother	
Monthly paid job	45 (14%)
Business	11 (4%)
Day laborer	2 (1%)
Housewife	254 (81%)
House type (no. [%])	
Concrete	140 (45%)
Tin	160 (51%)
Wood/mud	9 (3%)
Cooking method (no. [%])	
Gas	269 (86%)
Wood/Fire	39 (12%)
Electricity	3 (11%)
Water source (no. [%])	
Tube well	68 (22%)
Tap water	227 (73%)
Smoker at home	
Father (no. [%])	150 (48%)
Family members (median[range])	1 (0-6)
Animal contact in past 12 months (no. [%])	
Cat as pet	58 (18%)
Dog as pet	30 (10%)
Domestic animal	78 (15%)
Mosquito coil use in a week (no. [%])	
> 5 days or regularly	69 (22%)
3 - 5 days	106 (34%)
< 3 days	70 (22%)
Never	68 (22%)

Table 9: Summary statistics for ambient particulate pollutants and weather variables

Environmental variable	Mean	Min	5th	25th	50th	75th	95th	Max
Total period (*n* = 155 days; Feb 10 - Jul 14)								
[a]$PM_{2.5}$ (µg/m^3)	88	12	14	23	97	196	205	215
[a]PM_{10} (µg/m^3)	153	34	41	54	154	246	338	384
Temperature (daily mean,°C)	27	18	22	25	27	29	30	32
Diurnal Temperature Range (°C)	8	2	4	5	8	10	11	12
Relative humidity (%)	61	30	34	44	63	78	87	91
Winter (*n* = 37 days; Feb 10 - Mar 18)								
[a]$PM_{2.5}$ (µg/m^3)	128	63	87	104	133	159	205	215
[a]PM_{10} (µg/m^3)	230	112	131	182	229	302	359	384
Temperature (daily mean,°C)	25	18	20	23	25	27	28	29
Relative humidity (%)	47	30	34	38	45	51	72	83
Summer (*n* = 27 days; Jun 18 - Jul 14)								
[a]$PM_{2.5}$ (µg/m^3)	21	12	13	17	21	28	38	43
[a]PM_{10} (µg/m^3)	54	34	37	45	51	58	88	117
Temperature (daily mean,°C)	29	27	27	28	29	30	30	32
Relative humidity (%)	79	64	72	75	78	82	88	91

[a]Daily mean calculated as 24h average for $PM_{2.5}$, PM_{10}

Table 10: Spearman rank correlation coefficients of environmental variables

	Study period*	Temperature	DTR	Relative Humidity	$PM_{2.5}$
Temperature	0.76				
DTR	-0.79	-0.45			
Relative humidity	0.79	0.40	-0.82		
$PM_{2.5}$	-0.86	-0.59	0.76	-0.83	
PM_{10}	-0.85	-0.52	0.79	-0.88	0.96

* Two study periods, winter and summer coded as 1 and 2, respectively

Table 11: Estimated changes with 95% confidence intervals in lung function parameters associated with a 20 μg/m^3 increase in $PM_{2.5}$ at different exposure metrics

Lung function parameters	Lag[a]	All children		Asthmatic children		Non-asthmatic children	
		Estimate	95%CI	**Estimate**	95%CI	**Estimate**	95%CI
PEF							
	L1	**-4.18**	(-5.70 , -2.65)	**-4.60**	(-6.41 , -2.79)	**-3.54**	(-5.14 , -1.94)
	L1_2	**-2.19**	(-3.93 , -0.46)	**-2.59**	(-4.55 , -0.63)	**-1.57**	(-3.34 , 0.21)
	L1_3	**-0.13**	(-2.26 , 2.00)	**-0.53**	(-2.80 , 1.74)	**0.43**	(-1.69 , 2.54)
FEV1							
	L1	**-2.04**	(-2.91 , -1.17)	**-2.25**	(-3.26 , -1.23)	**-1.89**	(-2.79 , -0.10)
	L1_2	**-0.52**	(-1.49 , 0.46)	**-0.68**	(-1.78 , 0.42)	**-0.37**	(-1.36 , 0.63)
	L1_3	**0.12**	(-1.04 , 1.29)	**-0.05**	(-1.32 , 1.22)	**0.31**	(-0.88 , 1.49)
FVC							
	L1	**-0.64**	(-1.10 , -0.17)	**-0.68**	(-1.23 , -0.14)	**-0.56**	(-1.04 , -0.08)
	L1_2	**0.38**	(-0.14 , 0.90)	**0.35**	(-0.24 , 0.93)	**0.44**	(-0.09 , 0.97)
	L1_3	**0.61**	(-0.02 , 1.25)	**0.60**	(-0.09 , 1.29)	**0.67**	(0.03 , 1.31)
FEV1/FVC							
	L1	**-0.015**	(-0.021 , -0.009)	**-0.015**	(-0.022 , -0.007)	**-0.014**	(-0.021 , -0.008)
	L1_2	**-0.011**	(-0.018 , -0.004)	**-0.011**	(-0.019 , -0.003)	**-0.011**	(-0.018 , -0.004)
	L1_3	**-0.009**	(-0.017 , 0.000)	**-0.008**	(-0.018 , 0.001)	**-0.008**	(-0.017 , 0.001)

Models adjusted for time trend, study period, school, age, weight, height, smoker in family, relative humidity, mean temperature and DTR

Lung function indices (PEF, FEV1, FVC) defined as percentage deviation from personal median

[a]Lag exposure of $PM_{2.5}$ (L1: day before lung function test, L1_2: cumulative average of previous 2 days before lung function test , L1_3: cumulative average of previous 3 days before lung function test)

Table 12: Estimated changes with 95% confidence intervals in lung function parameters associated with a 20 μg/m^3 increase in PM_{10} at different exposure metrics

Lung function parameters	Lag[a]	All children		Asthmatic children		Non-asthmatic children	
		Estimate	95%CI	Estimate	95%CI	Estimate	95%CI
PEF							
	L1	**-0.32**	(-1.15 , 0.52)	**-0.56**	(-1.54 , 0.42)	**-0.18**	(-1.05 , 0.68)
	L1_2	**0.36**	(-0.59 , 1.31)	**0.07**	(-1.02 , 1.16)	**0.52**	(-0.46 , 1.49)
	L1_3	**0.68**	(-0.24 , 1.60)	**0.42**	(-0.65 , 1.49)	**0.82**	(-0.12 , 1.77)
FEV1							
	L1	**-0.07**	(-0.55 , 0.41)	**-0.11**	(-0.67 , 0.44)	**-0.04**	(-0.53 , 0.46)
	L1_2	**0.26**	(-0.28 , 0.80)	**0.25**	(-0.37 , 0.87)	**0.29**	(-0.27 , 0.84)
	L1_3	**0.08**	(-0.46 , 0.61)	**0.06**	(-0.55 , 0.67)	**0.12**	(-0.42 , 0.66)
FVC							
	L1	**0.26**	(0.02 , 0.51)	**0.20**	(-0.09 , 0.48)	**0.28**	(0.03 , 0.54)
	L1_2	**0.44**	(0.16 , 0.71)	**0.40**	(0.08 , 0.71)	**0.45**	(0.17 , 0.73)
	L1_3	**0.22**	(-0.05 , 0.49)	**0.18**	(-0.14 , 0.49)	**0.23**	(-0.05 , 0.51)
FEV1/FVC							
	L1	**-0.003**	(-0.006 , 0.000)	**-0.003**	(-0.007 , 0.001)	**-0.003**	(-0.007 , 0.001)
	L1_2	**-0.002**	(-0.006 , 0.002)	**-0.002**	(-0.007 , 0.003)	**-0.002**	(-0.006 , 0.002)
	L1_3	**-0.002**	(-0.006 , 0.002)	**-0.002**	(-0.006 , 0.003)	**-0.002**	(-0.006 , 0.002)

Models adjusted for time trend, study period, school, age, weight, height, smoker in family, relative humidity, mean temperature and DTR

Lung function indices (PEF, FEV1, FVC) defined as percentage deviation from personal median

[a]Lag exposure of PM_{10} (L1: day before lung function test, L1_2: cumulative average of previous 2 days before lung function test, L1_3: cumulative average of previous 3 days before lung function test)

Table 13: Estimated changes with 95% confidence intervals in lung function parameters associated with a 1^0 C decrease in daily mean temperature at different exposure metrics

Lung function parameters	Lag[a]	All children		Asthmatic children		Non-asthmatic children	
		Estimate	95% CI	**Estimate**	95% CI	**Estimate**	95% CI
PEF							
	L0	**-2.19**	(-0.78 , -3.60)	**-2.31**	(-0.73 , -3.88)	**-1.69**	(-0.27 , -3.11)
	L0_1	**-3.02**	(-1.69 , -4.35)	**-3.00**	(-1.53 , -4.46)	**-2.48**	(-1.14 , -3.81)
	L0_2	**-3.24**	(-1.86 , -4.62)	**-3.03**	(-1.56 , -4.51)	**-2.48**	(-1.12 , -3.83)
	L0_3	**-3.32**	(-1.89 , -4.75)	**-3.24**	(-1.70 -4.79)	**-2.58**	(-1.17 , -4.00)
FEV1							
	L0	**-1.14**	(-0.36 , -1.92)	**-1.41**	(-0.53 , -2.28)	**-1.04**	(-0.25 , -1.84)
	L0_1	**-1.48**	(-0.75 , -2.22)	**-1.71**	(-0.89 , -2.53)	**-1.39**	(-0.63 , -2.15)
	L0_2	**-1.51**	(-0.75 , -2.28)	**-1.77**	(-0.92 , -2.61)	**-1.41**	(-0.63 , -2.20)
	L0_3	**-1.27**	(-0.47 , -2.07)	**-1.57**	(-0.69 , -2.46)	**-1.17**	(-0.35 , -1.98)
FVC							
	L0	**-0.79**	(-0.37 , -1.21)	**-0.75**	(-0.28 , -1.23)	**-0.74**	(-0.31 , -1.17)
	L0_1	**-0.73**	(-0.33 , -1.13)	**-0.71**	(-0.26 , -1.15)	**-0.68**	(-0.27 , -1.09)
	L0_2	**-0.53**	(-0.12 , -0.94)	**-0.54**	(-0.09 , -0.99)	**-0.47**	(-0.05 , -0.88)
	L0_3	**-0.22**	(0.21 , -0.65)	**-0.27**	(0.20 , -0.74)	**-0.16**	(0.27 , -0.60)
FEV1/FVC							
	L0	**-0.004**	(0.002 , -0.009)	**-0.005**	(0.001 , -0.011)	**-0.004**	(0.002 , -0.009)
	L0_1	**-0.007**	(-0.002 , -0.012)	**-0.008**	(-0.002 , -0.014)	**-0.007**	(-0.001 , -0.012)
	L0_2	**-0.009**	(-0.003 , -0.014)	**-0.010**	(-0.004 , -0.016)	**-0.008**	(-0.003 , -0.014)
	L0_3	**-0.009**	(-0.003 , -0.014)	**-0.010**	(-0.004 , -0.016)	**-0.008**	(-0.003 , -0.014)

Models adjusted for time trend, study period, school, age, weight, height, smoker in family, relative humidity, $PM_{2.5}$ and DTR

Lung function indices (PEF, FEV1, FVC) defined as percentage deviation from personal median

[a]Lag exposure of daily mean temperature (L0: same day of lung function test, L0_1: cumulative average of same day and day before lung function test, L0_2: cumulative average of same day and previous 2 days before lung function test, L1_3: cumulative average of same day and previous 3 days before lung function test)

Table 14: Estimated changes with 95% confidence intervals in lung function parameters associated with a 1^{0} C increase in DTR at different exposure metrics

Lung function parameters	Lag[a]	All children		Asthmatic children		Non-asthmatic children	
		Estimate	95%CI	Estimate	95%CI	Estimate	95%CI
PEF							
	L1	**-0.96**	(-2.06 , 0.13)	**-1.64**	(-2.93 , -0.34)	**-0.68**	(-1.82 , 0.45)
	L1_2	**-2.41**	(-4.27 , -0.56)	**-3.25**	(-5.27 , -1.24)	**-2.14**	(-4.03 , -0.26)
	L1_3	**-2.02**	(-4.37 , 0.33)	**-2.97**	(-5.48 , -0.46)	**-1.75**	(-4.13 , 0.63)
FEV1							
	L1	**-0.50**	(-1.11 , 0.11)	**-0.74**	(-1.47 , -0.01)	**-0.42**	(-1.06 , 0.21)
	L1_2	**-1.28**	(-2.33 , -0.24)	**-1.54**	(-2.67 , -0.41)	**-1.21**	(-2.26 , -0.15)
	L1_3	**-0.96**	(-2.27 , 0.36)	**-1.22**	(-2.62 , 0.18)	**-0.87**	(-2.20 , 0.47)
FVC							
	L1	**-0.37**	(-0.70 , -0.04)	**-0.42**	(-0.81 , -0.03)	**-0.36**	(-0.70 , -0.01)
	L1_2	**-1.21**	(-1.77 , -0.65)	**-1.21**	(-1.82 , -0.61)	**-1.21**	(-1.78 , -0.65)
	L1_3	**-1.30**	(-2.02 , -0.59)	**-1.30**	(-2.06 , -0.54)	**-1.31**	(-2.03 , -0.58)
FEV1/FVC							
	L1	**-0.002**	(-0.006 , 0.002)	**-0.003**	(-0.008 , 0.002)	**-0.002**	(-0.006 , 0.003)
	L1_2	**-0.001**	(-0.008 , 0.007)	**-0.002**	(-0.010 , 0.006)	**-0.001**	(-0.008 , 0.007)
	L1_3	**0.003**	(-0.007 , 0.013)	**0.002**	(-0.009 , 0.012)	**0.004**	(-0.006 , 0.014)

Models adjusted for time trend, study period, school, age, weight, height, smoker in family, relative humidity, daily mean temperature and $PM_{2.5}$

Lung function indices (PEF, FEV1, FVC) defined as percentage deviation from personal median

[a]Lag exposure of DTR (L1: day before lung function test, L1_2: cumulative average of previous 2 days before lung function test, L1_3: cumulative average of previous 3 days before lung function test)

Table 15: Estimated changes with 95% confidence intervals in lung function parameters associated with a 20 μg/m^3 increase in $PM_{2.5}$ at different exposure metrics by season

Lung function parameters	Lag[a]	Winter		Summer		*p*-value[b]
		Estimate	95% CI	Estimate	95% CI	
PEF						
	L1	**-4.17**	(-5.69 , -2.65)	**-10.92**	(-15.73 , -6.12)	**0.01**
	L1_2	**-2.16**	(-3.89 , -0.42)	**-8.12**	(-13.52 , -2.73)	**0.04**
	L1_3	**0.09**	(-2.05 , 2.24)	**-5.04**	(-10.70 , 0.62)	**0.10**
FEV1						
	L1	**-2.24**	(-3.07 , -1.41)	**-6.07**	(-8.79 , -3.36)	**0.01**
	L1_2	**-0.76**	(-1.71 , 0.20)	**-4.29**	(-7.35 , -1.23)	**0.03**
	L1_3	**0.00**	(-1.19 , 1.20)	**-3.07**	(-6.26 , 0.11)	**0.08**
FVC						
	L1	**-0.58**	(-1.05 , -0.12)	**0.95**	(-0.52 , 2.41)	**0.05**
	L1_2	**0.40**	(-0.12 , 0.91)	**2.18**	(0.54 , 3.82)	**0.04**
	L1_3	**0.57**	(-0.06 , 1.21)	**2.34**	(0.61 , 4.06)	**0.06**
FEV1/FVC						
	L1	**-0.015**	(-0.021 , -0.009)	**-0.053**	(-0.072 , -0.034)	<**0.01**
	L1_2	**-0.011**	(-0.018 , -0.004)	**-0.049**	(-0.070 , -0.028)	<**0.01**
	L1_3	**-0.007**	(-0.016 , 0.002)	**-0.041**	(-0.063 , -0.019)	<**0.01**

Models adjusted for time trend, study period, school, age, weight, height, smoker in family, relative humidity, mean temperature and DTR

Lung function indices (PEF, FEV1,FVC) defined as percentage deviation from personal median

[a]Lag exposure of $PM_{2.5}$ (L1: day before lung function test, L1_2: cumulative average of previous 2 days before lung function test, L1_3: cumulative average of previous 3 days before lung function test)

[b]Multiple comparison for estimates of $PM_{2.5}$ between winter and summer seasons

Table 16: Estimated changes with 95% confidence intervals in lung function parameters associated with a 20 μg/m^3 increase in PM_{10} at different exposure metrics by season

Lung function parameters	Lag[a]	Winter		Summer		*p*-value[b]
		Estimate	95% CI	Estimate	95% CI	
PEF						
	L1	**-0.32**	(-1.15 , 0.52)	**-4.75**	(-7.92 , -1.57)	**0.01**
	L1_2	**0.43**	(-0.54 , 1.40)	**-0.85**	(-3.62 , 1.92)	**0.40**
	L1_3	**0.74**	(-0.23 , 1.71)	**0.04**	(-2.89 , 2.97)	**0.67**
FEV1						
	L1	**-0.07**	(-0.55 , 0.40)	**-1.83**	(-3.59 , -0.06)	**0.06**
	L1_2	**0.29**	(-0.26 , 0.84)	**-0.31**	(-1.84 , 1.22)	**0.48**
	L1_3	**0.10**	(-0.46 , 0.65)	**0.05**	(-1.56 , 1.66)	**0.96**
FVC						
	L1	**0.26**	(0.02 , 0.51)	**1.26**	(0.29 , 2.23)	**0.05**
	L1_2	**0.40**	(0.12 , 0.68)	**1.01**	(0.17 , 1.85)	**0.18**
	L1_3	**0.16**	(-0.13 , 0.44)	**0.82**	(-0.07 , 1.70)	**0.16**
FEV1/FVC						
	L1	**-0.003**	(-0.006 , 0.001)	**-0.022**	(-0.034 , -0.010)	<**0.01**
	L1_2	**-0.002**	(-0.006 , 0.002)	**-0.011**	(-0.022 , -0.001)	**0.11**
	L1_3	**-0.001**	(-0.005 , 0.003)	**-0.007**	(-0.018 , 0.004)	**0.35**

Models adjusted for time trend, study period, school, age, weight, height, smoker in family, relative humidity, mean temperature and DTR

Lung function indices (PEF, FEV1,FVC) defined as percentage deviation from personal median

[a]Lag exposure of PM_{10} (L1: day before lung function test, L1_2: cumulative average of previous 2 days before lung function test , L1_3: cumulative average of previous 3 days before lung function test)

[b]Multiple comparison for estimates of PM_{10} between winter and summer seasons

Table 17: Estimated changes with 95% confidence intervals in lung function parameters associated with a 1^0 C decrease in daily mean temperature at different exposure metrics by season

Lung function parameters	**Lag**[a]	**Winter**		**Summer**		***p*-value**[b]
		Estimate	95%CI	**Estimate**	95%CI	
PEF						
	L0	**-3.09**	(-1.61 , -4.56)	**2.43**	(5.17 , -0.31)	**<0.01**
	L0_1	**-3.17**	(-1.83 , -4.51)	**-0.99**	(1.66 , -3.64)	**0.15**
	L0_2	**-3.47**	(-2.08 , -4.86)	**-0.95**	(1.59 , -3.49)	**0.09**
	L0_3	**-3.73**	(-2.21 , -5.24)	**-1.72**	(0.81 , -4.25)	**0.18**
FEV1						
	L0	**-1.58**	(-0.77 , -2.40)	**1.11**	(2.62 , -0.41)	**<0.01**
	L0_1	**-1.58**	(-0.83 , -2.32)	**-0.30**	(1.17 , -1.76)	**0.13**
	L0_2	**-1.61**	(-0.83 , -2.39)	**-0.55**	(0.87 , -1.96)	**0.20**
	L0_3	**-1.34**	(-0.48 , -2.19)	**-1.03**	(0.39 , -2.45)	**0.73**
FVC						
	L0	**-0.66**	(-0.22 , -1.10)	**-1.27**	(-0.42 , -2.12)	**0.22**
	L0_1	**-0.66**	(-0.25 , -1.06)	**-1.57**	(-0.73 , -2.40)	**0.05**
	L0_2	**-0.42**	(-0.01 , -0.84)	**-1.29**	(-0.51 , -2.07)	**0.05**
	L0_3	**0.07**	(0.52 , -0.39)	**-1.23**	(-0.46 , -1.99)	**<0.01**
FEV1/FVC						
	L0	**-0.008**	(-0.002 , -0.013)	**0.017**	(0.028 , 0.006)	**<0.01**
	L0_1	**-0.008**	(-0.003 , -0.013)	**0.007**	(0.018 , -0.003)	**0.01**
	L0_2	**-0.010**	(-0.004 , -0.015)	**0.004**	(0.014 , -0.006)	**0.02**
	L0_3	**-0.011**	(-0.006 , -0.017)	**0.001**	(0.011 , -0.009)	**0.03**

Models adjusted for time trend, study period, school, age, weight, height, smoker in family, relative humidity, $PM_{2.5}$ and DTR

Lung function indices (PEF, FEV1, FVC) defined as percentage deviation from personal median

[a]Lag exposure of daily mean temperature (L0: same day of lung function test, L0_1: cumulative average of same day and day before lung function test, L0_2: cumulative average of same day and previous 2 days before lung function test, L1_3: cumulative average of same day and previous 3 days before lung function test)

[b]Multiple comparison for estimates of mean temperature between winter and summer seasons

Table 18: Estimated changes with 95% confidence intervals in lung function parameters associated with a 1^0 C increase in DTR at different exposure metrics by season

Lung function parameters	Lag[a]	Winter		Summer		*p*-value[b]
		Estimate	95%CI	Estimate	95%CI	
PEF						
	L1	**-1.80**	(-2.93 , -0.67)	**0.81**	(-1.05 , 2.67)	**0.02**
	L1_2	**-2.66**	(-4.62 , -0.70)	**-3.43**	(-5.79 , -1.06)	**0.64**
	L1_3	**-2.30**	(-4.82 , 0.21)	**-3.22**	(-6.18 , -0.26)	**0.66**
FEV1						
	L1	**-0.62**	(-1.26 , 0.03)	**0.03**	(-1.01 , 1.06)	**0.31**
	L1_2	**-1.26**	(-2.34 , -0.18)	**-1.35**	(-2.70 , 0.00)	**0.92**
	L1_3	**-1.09**	(-2.46 , 0.27)	**-0.61**	(-2.28 , 1.06)	**0.67**
FVC						
	L1	**-0.51**	(-0.85 , -0.16)	**0.28**	(-0.29 , 0.85)	**0.02**
	L1_2	**-1.46**	(-2.04 , -0.88)	**-0.56**	(-1.28 , 0.15)	**0.06**
	L1_3	**-1.64**	(-2.39 , -0.90)	**-0.48**	(-1.37 , 0.40)	**0.05**
FEV1/FVC						
	L1	**-0.002**	(-0.007 , 0.002)	**-0.001**	(-0.009 , 0.006)	**0.85**
	L1_2	**0.001**	(-0.007 , 0.009)	**-0.006**	(-0.015 , 0.004)	**0.31**
	L1_3	**0.005**	(-0.005 , 0.015)	**-0.001**	(-0.013 , 0.011)	**0.44**

Models adjusted for time trend, study period, school, age, weight, height, smoker in family, relative humidity, daily mean temperature and $PM_{2.5}$

Lung function indices (PEF, FEV1, FVC) defined as percentage deviation from personal median

[a]Lag exposure of DTR (L1: day before lung function test, L1_2: cumulative average of previous 2 days before lung function test, L1_3: cumulative average of previous 3 days before lung function test)

[b]Multiple comparison for estimates of diurnal temperature between winter and summer seasons

Figures

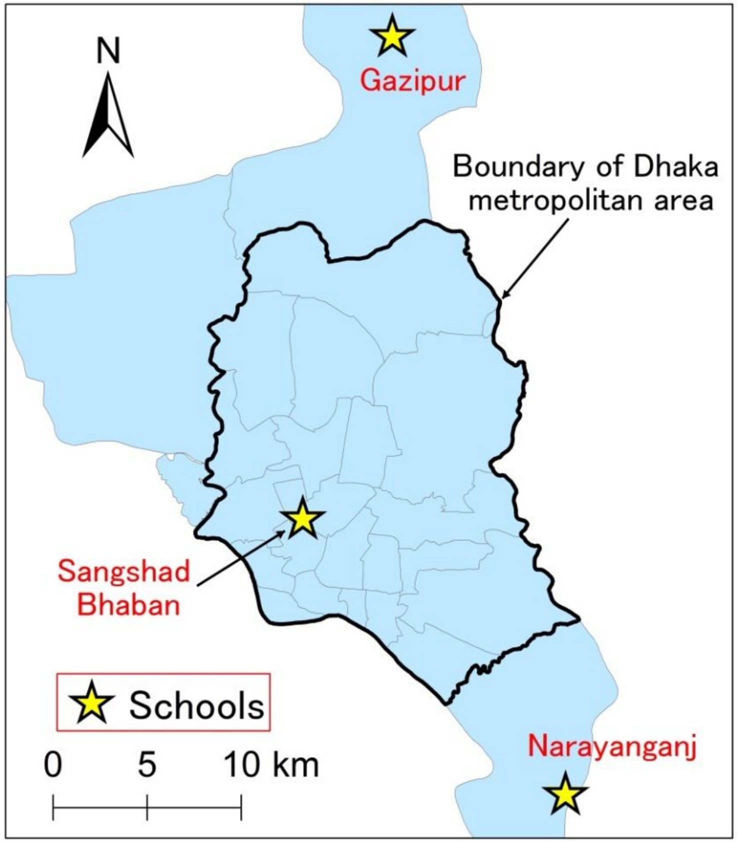

Figure 1: GIS location of all schools

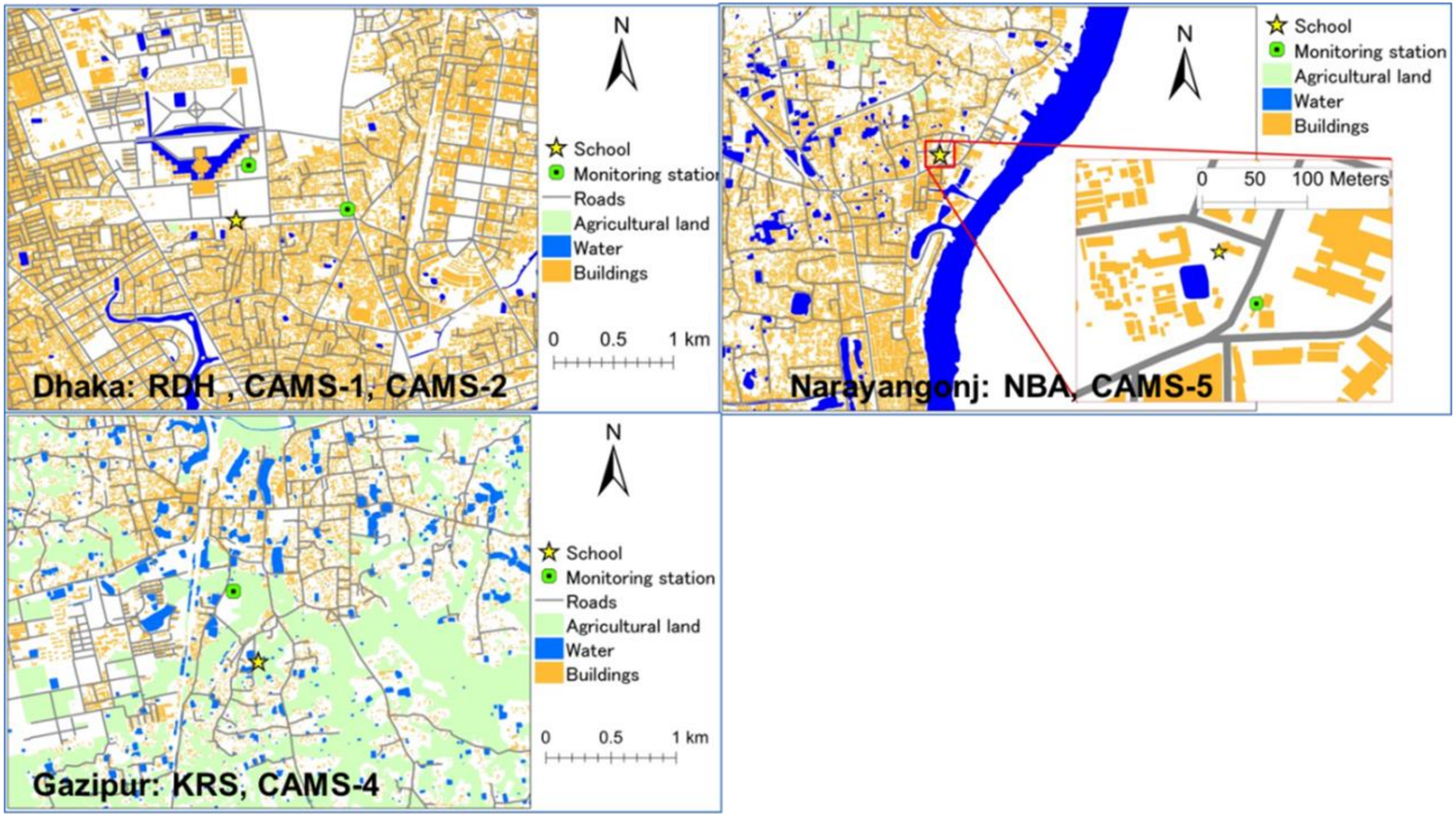

Figure 2: GIS location of the schools and corresponding continuous air-monitoring stations (CAMS)

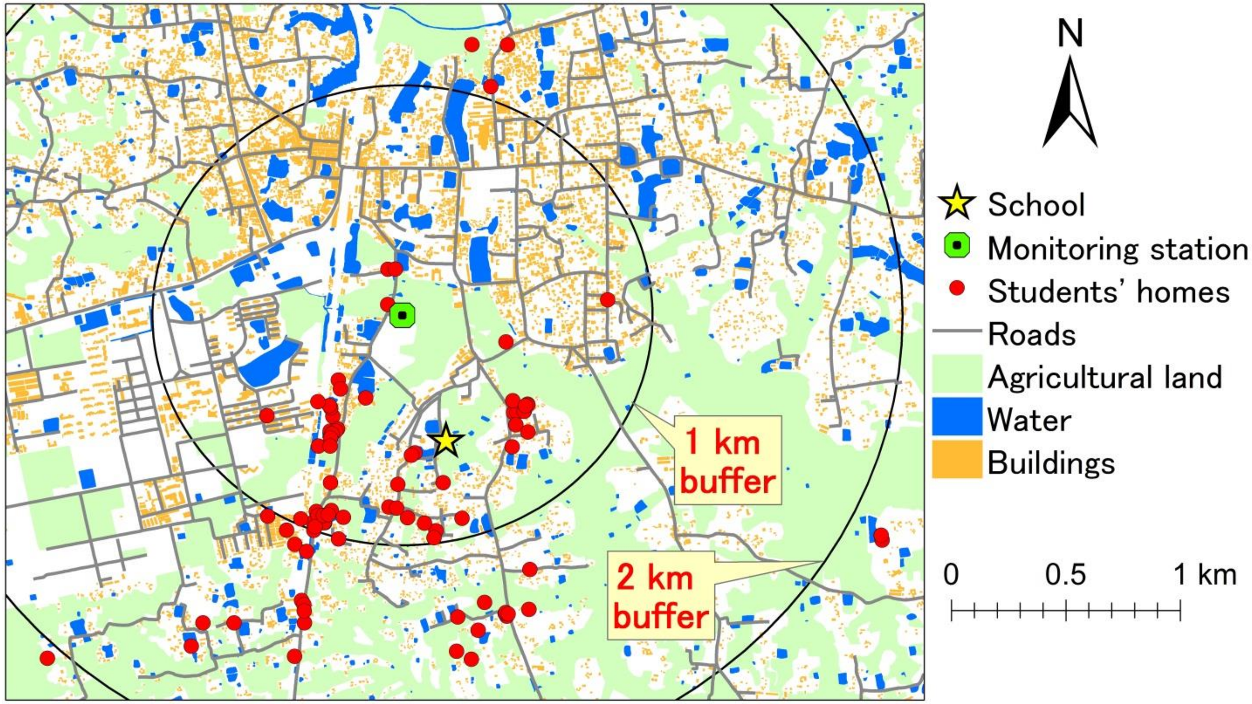

Figure 3: GIS location of the participants of one school (KRS, Gazipur)

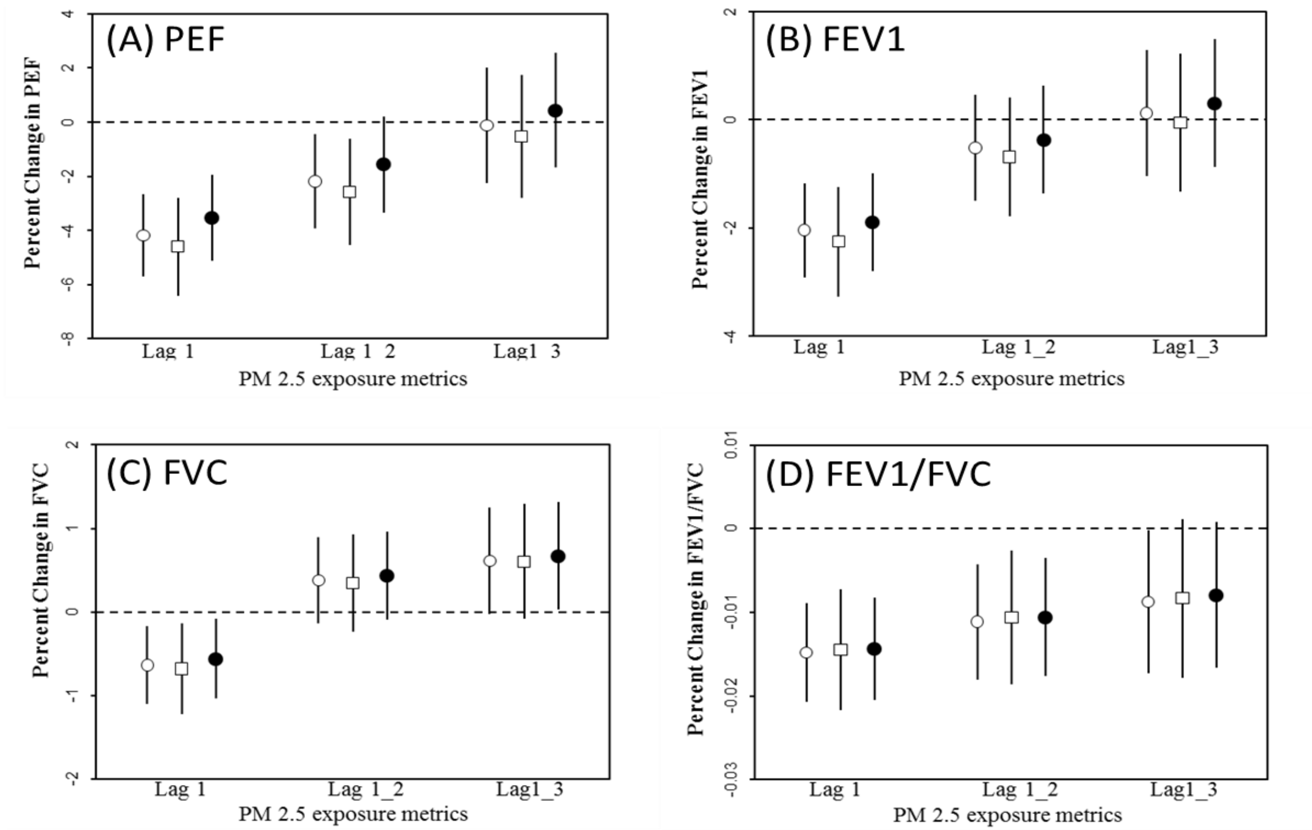

Figure 4: Percent changes and 95% confidence intervals in (A) PEF (B) FEV1 (C) FVC and (D) FEV1/FVC of all children, asthmatic and non-asthmatic children, in association with a 20μg/m^3 increase in $PM_{2.5}$ at different lag exposures. Models adjusted for time trend, study period, school, age, weight, height, smoker in family, relative humidity, daily mean and DTR. Lung function indices (PEF, FEV1, and FVC) defined as percentage deviation from personal median. Lag exposure of $PM_{2.5}$ (L1: day before lung function test, L1_2: cumulative average of previous 2 days before lung function test, L1_3: cumulative average of previous 3 days before lung function test). ○ Hollow circles: all children, □ hollow squares: asthmatic children and ● solid circles: non-asthmatic children.

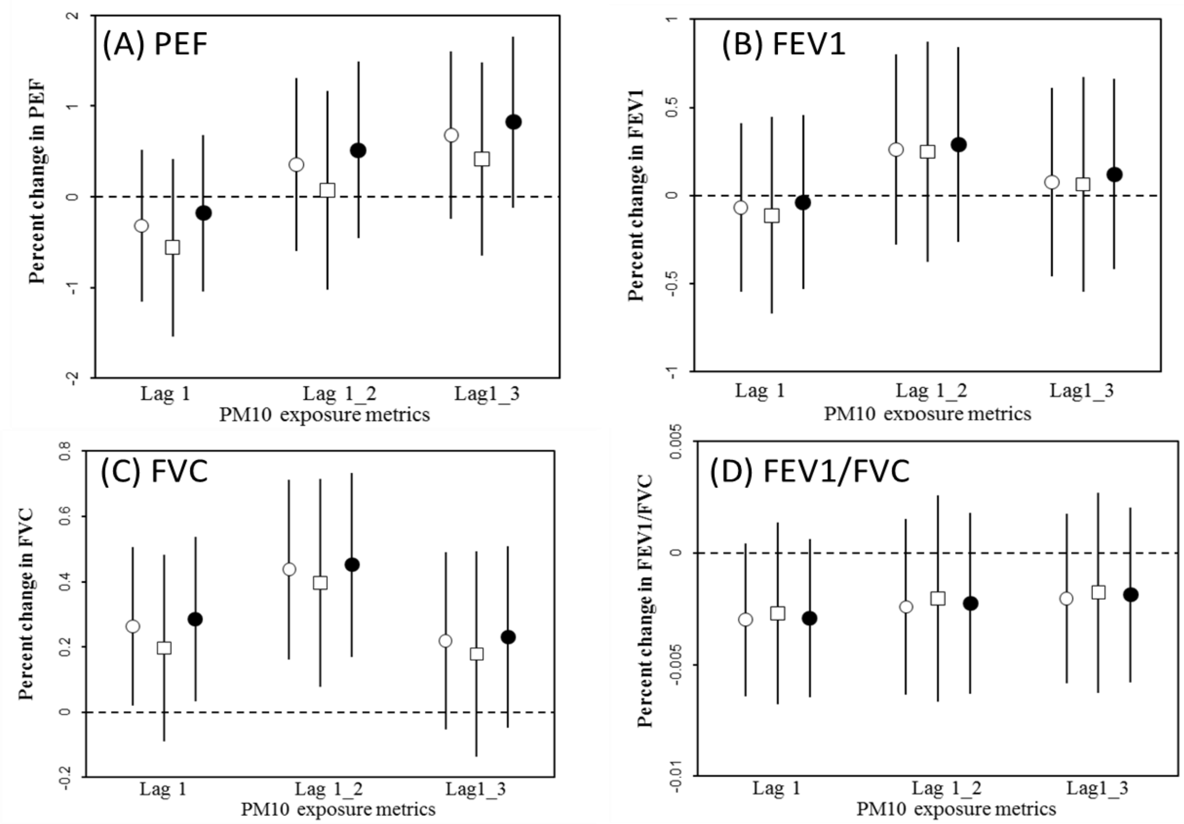

Figure 5: Percent changes and 95% confidence intervals in (A) PEF (B) FEV1 (C) FVC and (D) FEV1/FVC of all children, asthmatic and non-asthmatic children, in association with a 20μg/m^3 increase in PM_{10} at different lag exposures. Models adjusted for time trend, study period, school, age, weight, height, smoker in family, relative humidity, daily mean and DTR. Lung function indices (PEF, FEV1, and FVC) defined as percentage deviation from personal median. Lag exposure of $PM_{2.5}$ (L1: day before lung function test, L1_2: cumulative average of previous 2 days before lung function test, L1_3: cumulative average of previous 3 days before lung function test). ○ Hollow circles: all children, □ hollow squares: asthmatic children and ● solid circles: non-asthmatic children.

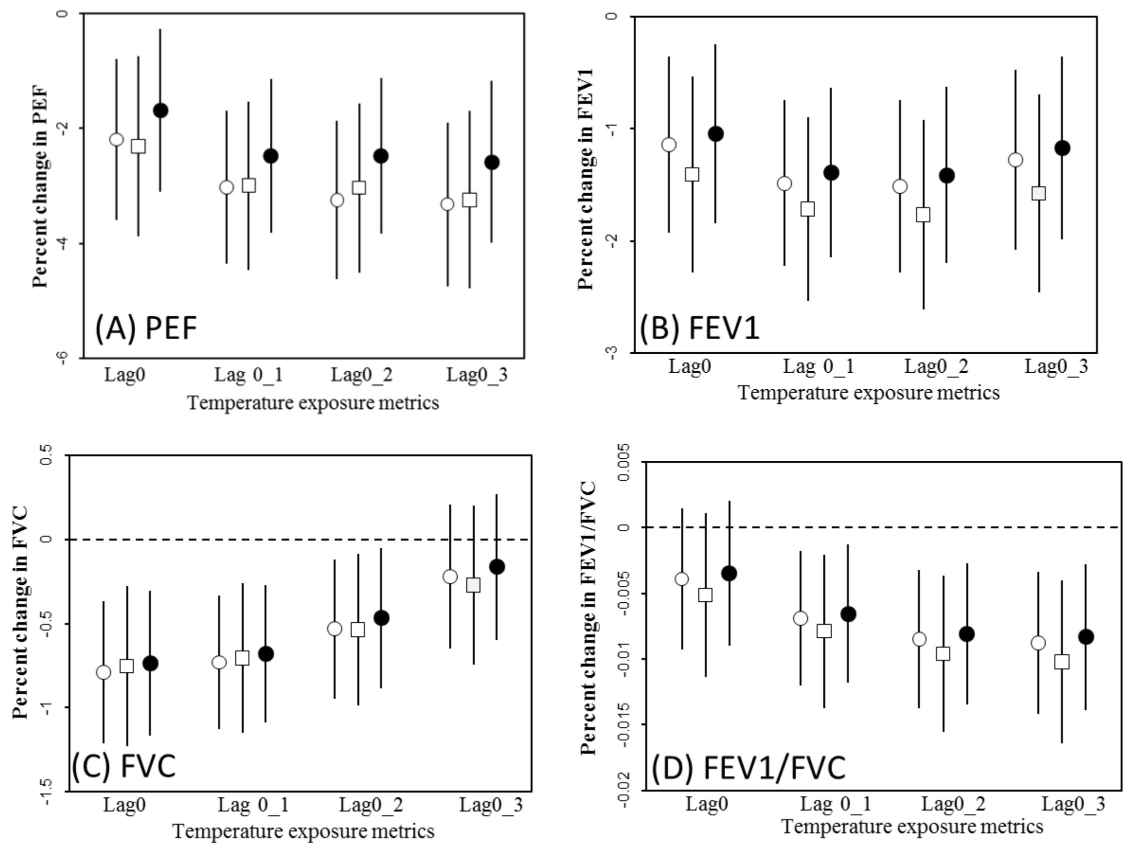

Figure 6: Percent changes and 95% confidence intervals in (A) PEF (B) FEV1 (C) FVC and (D) FEV1/FVC of all children, asthmatic and non-asthmatic children, in association with a 1^0C decrease in daily mean temperature at different lag exposures. Models adjusted for time trend, study period, school, age, weight, height, smoker in family, relative humidity, $PM_{2.5}$ and DTR. Lung function indices (PEF, FEV1, and FVC) defined as percentage deviation from personal median. Lag exposure of daily mean temperature (L0: same day of lung function test, L0_1: cumulative average of same day and day before lung function test, L0_2: cumulative average of same day and previous 2 days before the test, L1_3: cumulative average of same day and previous 3 days before the test). ○ Hollow circles: all children, □ hollow squares: asthmatic children and ● solid circles: non-asthmatic children.

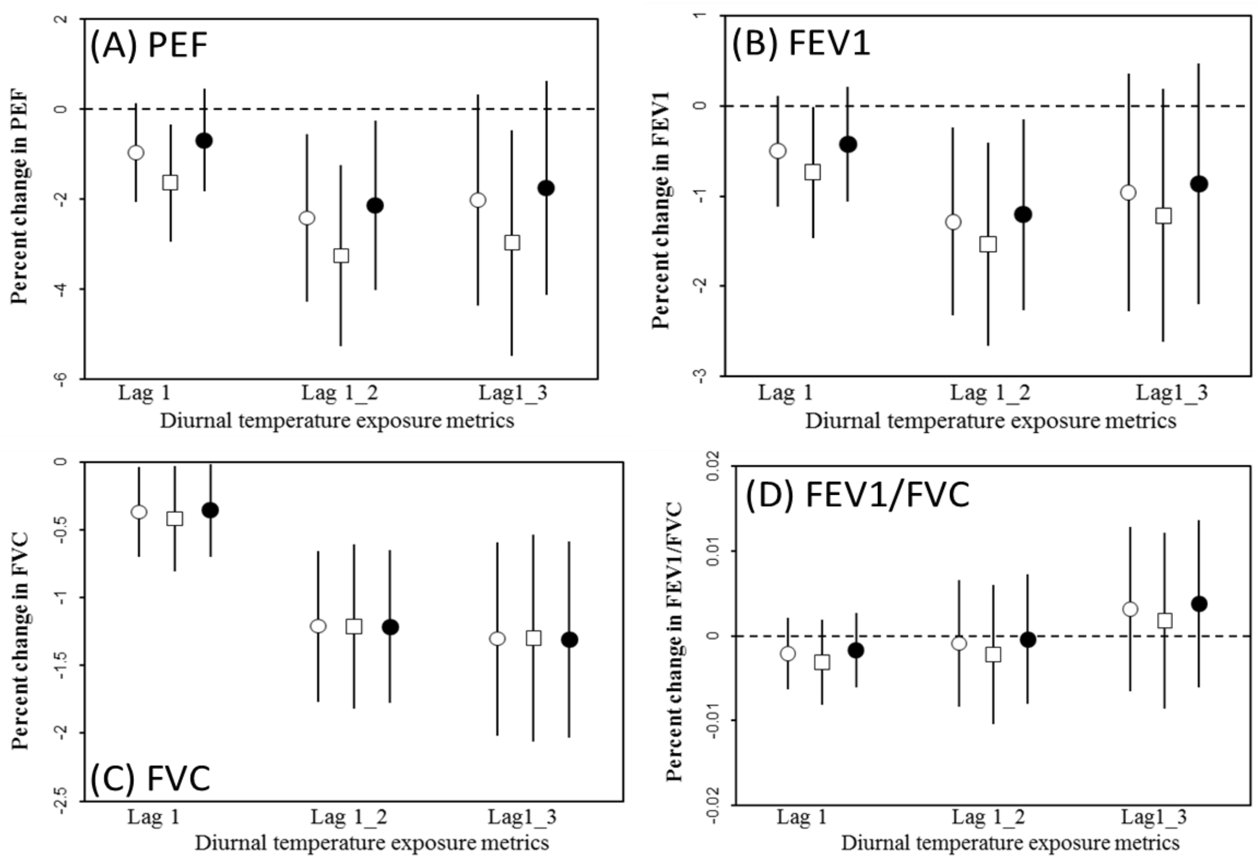

Figure 7: Percent changes and 95% confidence intervals in (A) PEF (B) FEV1 (C) FVC and (D) FEV1/FVC of all children, asthmatic and non-asthmatic children, in association with a 1^{0}C increase in DTR at different lag exposures. Models adjusted for time trend, study period, school, age, weight, height, smoker in family, relative humidity, $PM_{2.5}$ and daily mean temperature. Lung function indices (PEF, FEV1, and FVC) defined as percentage deviation from personal median. Lag exposure of DTR (L1: day before lung function test, L1_2: cumulative average of previous 2 days before the test, L1_3: cumulative average of previous 3 days before the test). ○ Hollow circles: all children, □ hollow squares: asthmatic children and ● solid circles: non-asthmatic children.

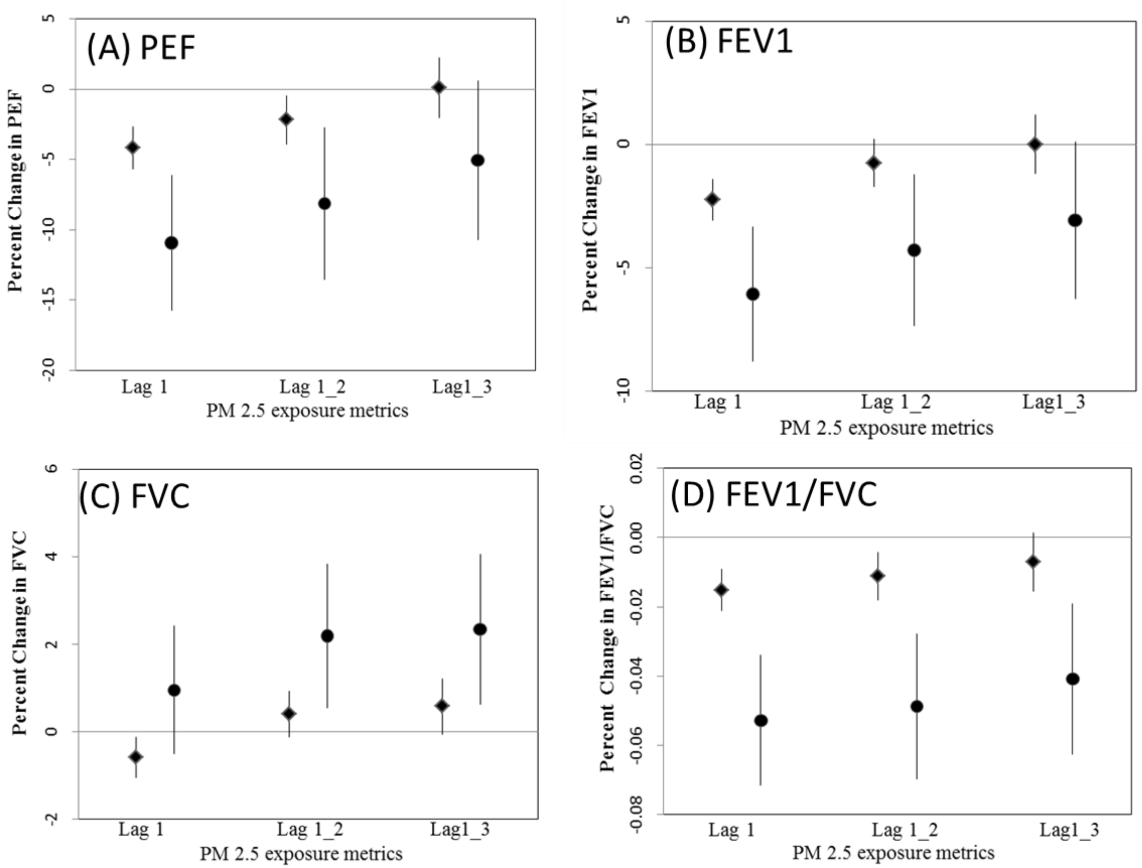

Figure 8: Percent changes and 95% confidence intervals in (A) PEF (B) FEV1 (C) FVC and (D) FEV1/FVC with a 20μg/m^3 increase in $PM_{2.5}$ at different exposure metrics by season. Models adjusted for time trend, study period, school, age, weight, height, smoker in family, relative humidity, daily mean and DTR. Lung function indices (PEF, FEV1, and FVC) defined as percentage deviation from personal median. Lag exposure of $PM_{2.5}$ (L1: day before lung function test, L1_2: cumulative average of previous 2 days before the test, L1_3: cumulative average of previous 3 days before the test). ◆ Solid squares represent winter and ● solid circles represent summer.

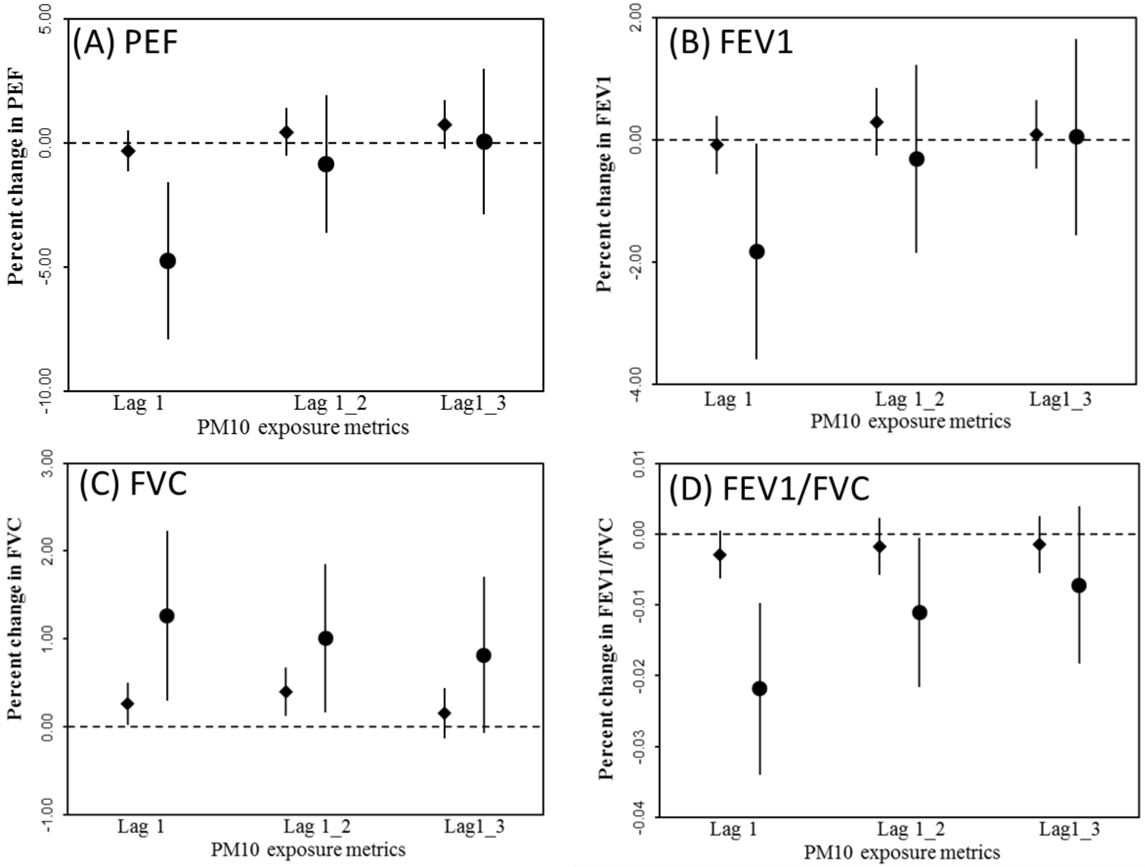

Figure 9: Percent changes and 95% confidence intervals in (A) PEF (B) FEV1 (C) FVC and (D) FEV1/FVC with a 20µg/m^3 increase in PM_{10} at different exposure metrics by season. Models adjusted for time trend, study period, school, age, weight, height, smoker in family, relative humidity, daily mean and DTR. Lung function indices (PEF, FEV1, and FVC) defined as percentage deviation from personal median. Lag exposure of PM_{10} (L1: day before lung function test, L1_2: cumulative average of previous 2 days before the test, L1_3: cumulative average of previous 3 days before the test). ◆ Solid squares represent winter and ● solid circles represent summer.

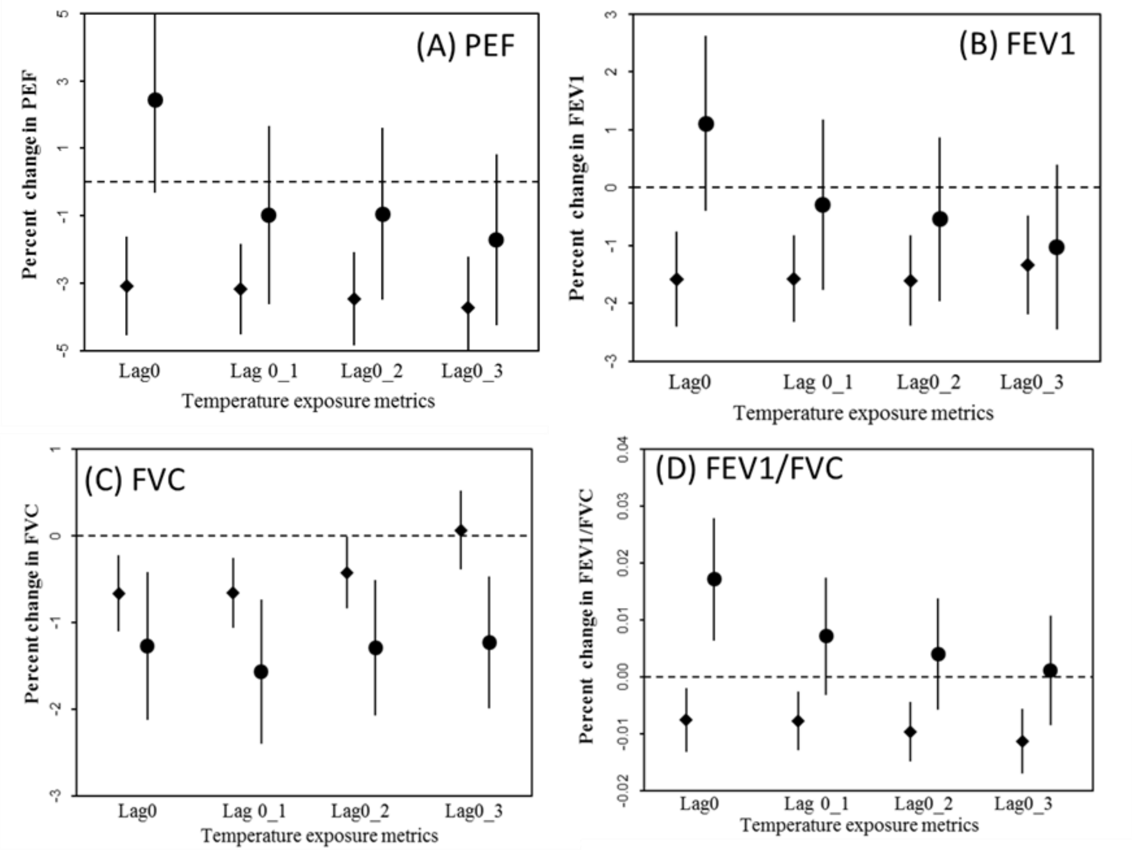

Figure 10: Percent changes and 95% confidence intervals in (A) PEF (B) FEV1 (C) FVC and (D) FEV1/FVC with a 1^0C decrease in daily mean temperature at different exposure metrics by season. Models adjusted for time trend, study period, school, age, weight, height, smoker in family, relative humidity and DTR. Lung function indices (PEF, FEV1, and FVC) defined as percentage deviation from personal median. Lag exposure of daily mean temperature (L0: same day of lung function test, L0_1: cumulative average of same day and day before lung function test, L0_2: cumulative average of same day and previous 2 days before the test, L1_3: cumulative average of same day and previous 3 days before the test). ◆ Solid squares represent winter and ● solid circles represent summer.

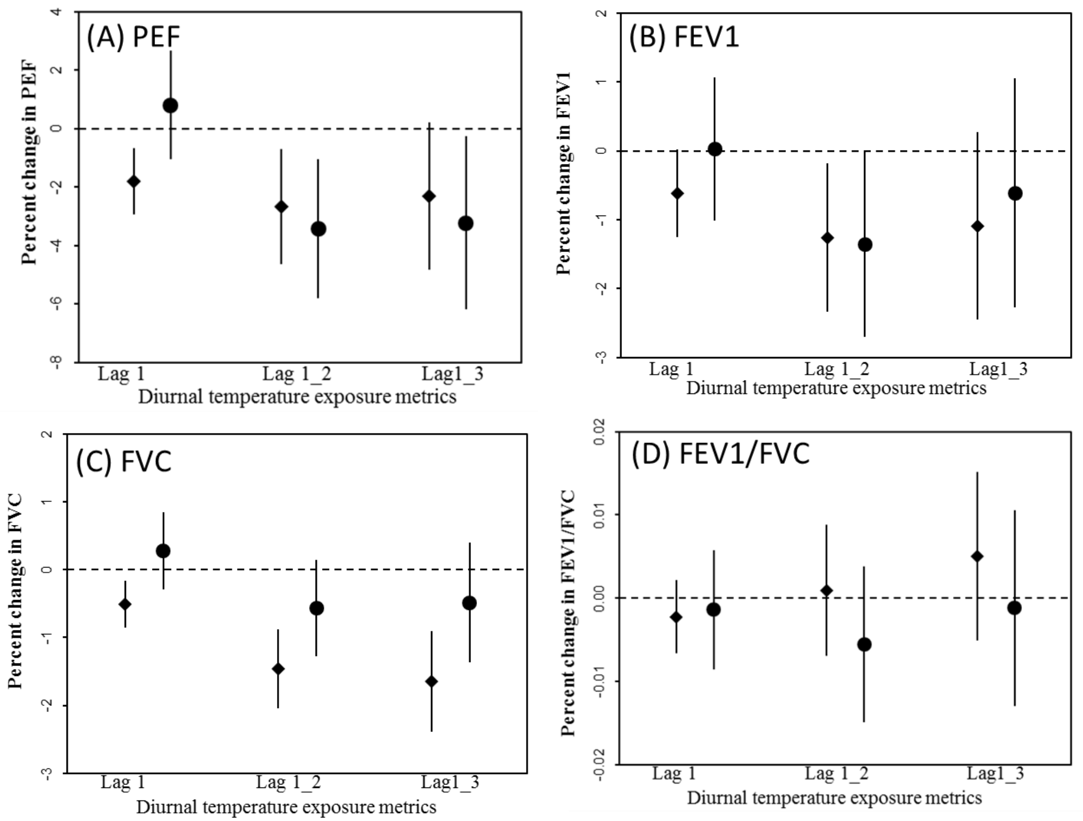

Figure 11: Percent changes and 95% confidence intervals in (A) PEF (B) FEV1 (C) FVC and (D) FEV1/FVC with a 1^0C increase in DTR at different exposure metrics by season. Models adjusted for time trend, study period, school, age, weight, height, smoker in family, relative humidity, daily mean temperature. Lung function indices (PEF, FEV1, and FVC) defined as percentage deviation from personal median. Lag exposure of daily mean temperature (L0: same day of lung function test, L0_1: cumulative average of same day and day before lung function test, L0_2: cumulative average of same day and previous 2 days before the test, L1_3: cumulative average of same day and previous 3 days before the test). ◆ Solid squares represent winter and ● solid circles represent summer.

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Supplemental materials

Supplemental Table 1: A summary of the particulate matter (PM) standards and guideline values

Pollutant	Averaging period	[a]Bangladesh (Standards)	[b]WHO (Guidelines)	[c]US-EPA (Standards)
PM_{10}	24-hour	150	50	[d]150
($\mu g/m^3$)	1-year	50	20	-
$PM_{2.5}$	24-hour	65	25	[e]35
($\mu g/m^3$)	1-year	15	10	[f]12

[a]Bangladesh National Ambient Air Quality Standards

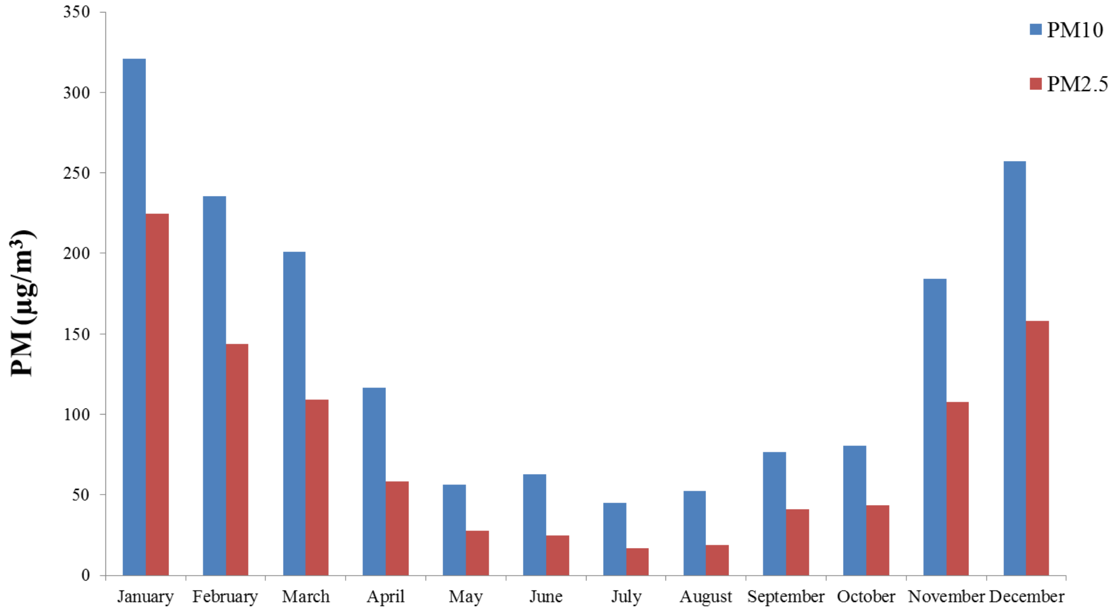
[b]World Health Organization (WHO) air quality guidelines (AQG)

[c]United States Environment Protection Agency (US-EPA) Standards

[d]Not to be exceeded more than once per year on average over 3 years

[e]98th percentile, averaged over 3 years

[f]Annual mean, averaged over 3 years



Supplemental Figure1: Monthly averaged PM of four continuous air monitoring stations (CAMS) in 2013

Supplemental Table 2: Values of exposure variables on lung function (LF) test day

Season	School	LF test day	PM2.5 (μg/m^3)	PM10 (μg/m^3)	Tmean ^{0}C	RH (%)
Winter	KRS	10-Feb	152	261	22	43
	RDH	11-Feb	128	192	22	46
	NBA	13-Feb	170	341	23	43
	RDH	19-Feb	93	166	21	56
	NBA	20-Feb	135	252	22	50
	KRS	23-Feb	160	250	25	47
	RDH	26-Feb	76	128	25	42
	NBA	27-Feb	180	336	25	44
	KRS	2-Mar	128	235	24	38
	RDH	18-Mar	71	130	26	41
Summer	KRS	18-Jun	60	115	32	64
	KRS	26-Jun	20	32	28	84
	RDH	27-Jun	15	43	29	83
	NBA	1-Jul	25	73	29	81
	KRS	2-Jul	33	59	29	78
	RDH	4-Jul	19	52	28	86
	NBA	7-Jul	18	76	29	77
	NBA	14-Jul	13	43	28	80

Supplemental Table 3 : Estimated changes with 95% confidence intervals in lung function parameters associated with a 20 μg/m^3 increase in $PM_{2.5}$ at different exposure metrics by asthma diagnosis

Lung function parameters	Lag[a]	Asthmatic children		Non-asthmatic children		*p*-value[b]
		Estimate	95%CI	Estimate	95%CI	
PEF						
	L1	**-4.60**	(-6.41 , -2.79)	**-3.54**	(-5.14 , -1.94)	0.40
	L1_2	**-2.59**	(-4.55 , -0.63)	**-1.57**	(-3.34 , 0.21)	0.46
	L1_3	**-0.53**	(-2.80 , 1.74)	**0.43**	(-1.69 , 2.54)	0.56
FEV1						
	L1	**-2.25**	(-3.26 , -1.23)	**-1.89**	(-2.79 , -0.10)	0.62
	L1_2	**-0.68**	(-1.78 , 0.42)	**-0.37**	(-1.36 , 0.63)	0.69
	L1_3	**-0.05**	(-1.32 , 1.22)	**0.31**	(-0.88 , 1.49)	0.70
FVC						
	L1	**-0.68**	(-1.23 , -0.14)	**-0.56**	(-1.04 , -0.08)	0.76
	L1_2	**0.35**	(-0.24 , 0.93)	**0.44**	(-0.09 , 0.97)	0.83
	L1_3	**0.60**	(-0.09 , 1.29)	**0.67**	(0.03 , 1.31)	0.89
FEV1/FVC						
	L1	**-0.015**	(-0.022 , -0.007)	**-0.014**	(-0.021 , -0.008)	0.98
	L1_2	**-0.011**	(-0.019 , -0.003)	**-0.011**	(-0.018 , -0.004)	0.99
	L1_3	**-0.008**	(-0.018 , 0.001)	**-0.008**	(-0.017 , 0.001)	0.96

Models adjusted for time trend, study period, school, age, weight, height, smoker in family, relative humidity, mean temperature and DTR

Lung function indices (PEF, FEV1, FVC) defined as percentage deviation from personal median

[a]Lag exposure of $PM_{2.5}$ (L1: day before lung function test, L1_2: cumulative average of previous 2 days before lung function test , L1_3: cumulative average of previous 3 days before lung function test)

[b]Multiple comparison for estimates of $PM_{2.5}$ between asthmatic and non-asthmatic children

Supplemental Table 4: Estimated changes with 95% confidence intervals in lung function parameters associated with a 1^0 C decrease in daily mean temperature at different exposure metrics by asthma

Lung function parameters	Lag[a]	Asthmatic children		Non-asthmatic children		*p*-value[b]
		Estimate	95% CI	Estimate	95% CI	
PEF						
	L0	**-2.31**	(-0.73 , -3.88)	**-1.69**	(-0.27 , -3.11)	0.58
	L0_1	**-3.00**	(-1.53 , -4.46)	**-2.48**	(-1.14 , -3.81)	0.62
	L0_2	**-3.03**	(-1.56 , -4.51)	**-2.48**	(-1.12 , -3.83)	0.60
	L0_3	**-3.24**	(-1.70 -4.79)	**-2.58**	(-1.17 , -4.00)	0.55
FEV1						
	L0	**-1.41**	(-0.53 , -2.28)	**-1.04**	(-0.25 , -1.84)	0.56
	L0_1	**-1.71**	(-0.89 , -2.53)	**-1.39**	(-0.63 , -2.15)	0.58
	L0_2	**-1.77**	(-0.92 , -2.61)	**-1.41**	(-0.63 , -2.20)	0.56
	L0_3	**-1.57**	(-0.69 , -2.46)	**-1.17**	(-0.35 , -1.98)	0.52
FVC						
	L0	**-0.75**	(-0.28 , -1.23)	**-0.74**	(-0.31 , -1.17)	0.96
	L0_1	**-0.71**	(-0.26 , -1.15)	**-0.68**	(-0.27 , -1.09)	0.94
	L0_2	**-0.54**	(-0.09 , -0.99)	**-0.47**	(-0.05 , -0.88)	0.84
	L0_3	**-0.27**	(0.20 , -0.74)	**-0.16**	(0.27 , -0.60)	0.75
FEV1/FVC						
	L0	**-0.005**	(0.001 , -0.011)	**-0.004**	(0.002 , -0.009)	0.71
	L0_1	**-0.008**	(-0.002 , -0.014)	**-0.007**	(-0.001 , -0.012)	0.75
	L0_2	**-0.010**	(-0.004 , -0.016)	**-0.008**	(-0.003 , -0.014)	0.73
	L0_3	**-0.010**	(-0.004 , -0.016)	**-0.008**	(-0.003 , -0.014)	0.67

Models adjusted for time trend, study period, school, age, weight, height, smoker in family, relative humidity, $PM_{2.5}$ and DTR

Lung function indices (PEF, FEV1, FVC) defined as percentage deviation from personal median

[a]Lag exposure of daily mean temperature (L0: same day of lung function test, L0_1: cumulative average of same day and day before lung function test, L0_2: cumulative average of same day and previous 2 days before lung function test, L1_3: cumulative

[b]Multiple comparison for estimates of mean temperature between asthmatic and non-asthmatic children

Supplemental Table 5: Estimated changes with 95% confidence intervals in lung function parameters associated with a 1^0 C increase in DTR at different exposure metrics by asthma diagnosis

Lung function parameters	Lag[a]	Asthmatic children		Non-asthmatic children		*p*-value[b]
		Estimate	95%CI	**Estimate**	95%CI	
PEF						
	L1	**-1.64**	(-2.93 , -0.34)	**-0.68**	(-1.82 , 0.45)	**0.67**
	L1_2	**-3.25**	(-5.27 , -1.24)	**-2.14**	(-4.03 , -0.26)	**1.17**
	L1_3	**-2.97**	(-5.48 , -0.46)	**-1.75**	(-4.13 , 0.63)	**0.54**
FEV1						
	L1	**-0.74**	(-1.47 , -0.01)	**-0.42**	(-1.06 , 0.21)	**0.84**
	L1_2	**-1.54**	(-2.67 , -0.41)	**-1.21**	(-2.26 , -0.15)	**1.10**
	L1_3	**-1.22**	(-2.62 , 0.18)	**-0.87**	(-2.20 , 0.47)	**0.65**
FVC						
	L1	**-0.42**	(-0.81 , -0.03)	**-0.36**	(-0.70 , -0.01)	**1.01**
	L1_2	**-1.21**	(-1.82 , -0.61)	**-1.21**	(-1.78 , -0.65)	**1.34**
	L1_3	**-1.30**	(-2.06 , -0.54)	**-1.31**	(-2.03 , -0.58)	**1.32**
FEV1/FVC						
	L1	**-0.0031**	(-0.0082 , 0.0019)	**-0.0017**	(-0.0061 , 0.0026)	**1.00**
	L1_2	**-0.0022**	(-0.0104 , 0.0059)	**-0.0004**	(-0.0081 , 0.0072)	**0.99**
	L1_3	**0.0018**	(-0.0086 , 0.0121)	**0.0037**	(-0.0061 , 0.0136)	**0.99**

Models adjusted for time trend, study period, school, age, weight, height, smoker in family, relative humidity, daily mean temperature and $PM_{2.5}$

Lung function indices (PEF, FEV1, FVC) defined as percentage deviation from personal median

[a]Lag exposure of DTR (L1: day before lung function test, L1_2: cumulative average of previous 2 days before lung function test, L1_3: cumulative average of previous 3 days before lung function test)

[b]Multiple comparison for estimates of diurnal temperature between asthmatic and non-asthmatic children