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Original Article

Title:

Ambient temperature and lung function in children with asthma in Australia

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Summary:

High ambient temperature is a risk factor for lung function of children with asthma in Australia.

ABSTRACT

Background: The association between ambient temperature and lung function in children with asthma is still uncertain.

Methods: A panel of 270 children (7−12 years) with asthma was recruited from six Australian cities. They performed three successive forced expiratory maneuvers twice daily for four weeks. The highest peak expiratory flow rate (PEF) and forced expiratory volume in one second (FEV_1) were stored for each session. Daily data were obtained on ambient temperature, relative humidity and air pollution, during the same period. Mixed models were used to examine the effects of temperature on lung function, controlling for individual characteristics and environmental factors.

Results: Ambient temperature was negatively related to both morning and evening PEF and FEV_1 for lag 0–3 days. In general, the effects of temperature were stronger in boys than in girls for evening PEF, while the effects were stronger in girls for evening FEV_1. Children with asthma living in southern cities were more sensitive to high temperature than those in the northern most city.

Conclusions: Higher ambient temperature is associated with lower lung function in children with asthma. Preventive health policies will be required for protecting children with asthma from the increasing frequency of high temperatures.

Keywords: Asthma, children, lung function, panel study, temperature

INTRODUCTION

Asthma is the most prevalent chronic disease among children and is of great public health concern. The prevalence of asthma among children in Australia is one of the highest in the world, affecting 16% of Australian children [1]. It is the leading cause of burden of disease in children aged 0–14 years in Australia, accounting for 17.9% of the total burden in boys and 18.6% in girls [2].

Genetic factors [3], environmental factors (e.g., air pollution) [4], and their interaction [5] are all important in the etiology and manifestations of asthma. Ambient temperature is a possible trigger for symptoms and disease exacerbation in people with asthma. It is widely accepted that average global ambient temperature is increasing and the frequency and intensity of high temperatures are increasing [6]. Many epidemiological studies have reported associations between changes in ambient temperature and increased risk of respiratory mortality [7] and morbidity [8], especially for vulnerable subgroups of the population, including children. A study conducted in London reported that a decrease in ambient temperature was associated with decline in lung function for patients with chronic obstructive pulmonary disease (COPD) [9]. However, few studies have investigated whether ambient temperature has short-term impacts on lung function in children with asthma in Australia.

The Australian Child Health and Air Pollution Study (ACHAPS) examined both the cumulative and short-term effects of environmental factors (e.g., ambient air pollution and temperature) on lung health in a representative national urban sample of children with asthma in Australia. Using data collected for the ACHAPS panel study, this analysis investigates the prospective day-to-day association between urban ambient temperature and lung function in a panel of primary school children with a history of asthma across Australia.

METHODS

Study sites

This study was conducted in six major Australian cities: Brisbane, Perth, Sydney, Adelaide, Canberra and Melbourne (Supplemental Material Figure S1 for the cities' location). A minimum of two air monitoring stations, with at least a five-year history of monitoring, were selected per city. Air monitoring stations were located so as to measure background concentrations of air pollutants rather than point sources of air pollutants. The study period for each location is described in Supplemental Material Table S1 and at (http://www.woolcock.org.au/LinkClick.aspx?fileticket=XHKmuklLev4%3D&tabid=36).

Data on ambient temperature, air pollution and relative humidity

Daily ambient levels of temperature and air pollution for 2007−2008 were obtained for each of the selected air monitoring stations. The measurements of interest for this panel study included daily 24-hour average, maximum and minimum temperature (°C), average ozone of the previous 8 hours for each hour of the day (8-hour moving average O_3, parts per billion, ppb) and daily 24-hour average nitrogen dioxide (NO_2).

We collected daily 24-hour average relative humidity from "Weather Underground" (http://www.wunderground.com/) for each city, as the data were incomplete at the monitoring stations.

Study subjects

Schools within three kilometers (km) of selected air monitoring stations were identified. All children in school years three to five (aged 7−12 years) attending schools that had agreed to participate were then invited to participate in the cross-sectional study. In this part of the study, conducted in 2007−2008, parents completed a baseline questionnaire about the children's lung health and potential environmental factors related to asthma. Children with doctor-diagnosed asthma and symptoms of asthma within the preceding year, that is, with current asthma, and who lived within a three km radius of the corresponding air monitoring station were invited to take part in the panel study. A panel of 270 primary school children with a history of asthma formed the sample for this study. Each child provided four weeks of data. The study was conducted in Melbourne, Brisbane, Adelaide, Perth and Canberra during 2007 and in Sydney during 2008.

Lung function measurement

Each participant was provided with an electronic peak flow meter (Mini Wright Digital, MWD, Clement Clarke, Essex, UK) and asked to perform three successive forced expiratory maneuvers, before taking any inhaled medication, twice daily for four weeks. The highest peak expiratory flow rate (PEF, liters per minute, L/min) and forced expiratory volume in one second (FEV_1, liters, L) from these three successive measurements were automatically stored in the device with a date and time stamp. The children also recorded symptoms of asthma and medications taken in a diary every morning and evening.

Statistical analyses

A generalized additive mixed model (GAMM) was used to examine the effects of ambient temperature (daily 24-hour average, maximum and minimum) on PEF and FEV_1 (morning and evening values). Children's morning and evening PEF and FEV_1 were used as dependent variables. As both the morning and evening PEF and FEV_1 were normally distributed, the Gaussian family was used in the analyses. A natural cubic spline with three degrees of freedom for ambient temperatures was used to detect non-linearity of effects. Preliminary results (plots and model comparisons) suggested that associations could be modeled using a linear function without major loss of precision (Figure 1 as an example), and therefore a linear function was used in the final analyses.

Because children's sex, age, standing height and weight affect lung function, such factors were controlled for by inclusion in all models. In the basic models, ambient temperature, children's sex, age, standing height and weight were specified as fixed effects, while subject was included as a random effect, thus controlling for the effects of season and location. Because air pollution, relative humidity, city characteristics and medication use are potential confounders for the association between temperature and lung function, we introduced 3-day mean concentration of O_3, 3-day mean concentration of NO_2, 3-day mean of relative humidity, city and category of medication use into the regression models as fixed effects. We controlled only for O_3 and NO_2, because O_3 is strongly correlated with temperature and a previous study found NO_2 had a significant effect on children's lung function in Australia (http://www.woolcock.org.au/LinkClick.aspx?fileticket=XHKmuklLev4%3D&tabid=36).

As previous studies showed that effects of ambient temperature appeared not only on the same day, but also on several following days [10, 11], the lagged effects of ambient temperature for up to three days on children's PEF and FEV_1 were also examined.

The same model was used to assess the effects of ambient temperature on children's lung function stratified by sex. To describe whether children have adapted to their local climate, we also examined the effects of temperature (moving average lag 0–3) on lung function in five cities separately (Brisbane, Perth, Sydney, Adelaide and Melbourne). The number of participants was insufficient to fit GAMM in Canberra.

In general, children's lung function was more sensitive to daily maximum temperature than daily 24-hour average and minimum temperatures. The maximum temperature gave the highest effect estimates and best model fits (results not shown). Therefore, we used daily maximum temperature as the exposure metric in this study.

A number of sensitivity analyses were conducted to check the robustness of our findings and included: controlling for respiratory symptoms as a categorical variable; removing O_3, NO_2, relative humidity and medication use from the models one at a time to check for changes in the effect estimates; controlling for other air pollutants, for example, particulate matter less than 2.5 micrometers ($PM_{2.5}$) and sulfur dioxide (SO_2); and, including time and time squared into the models to control for learning effects.

All statistical analyses were performed using R software. The "mgcv" package was used to conduct GAMM. In all analyses, the first three days of lung function recordings were excluded to minimize any learning effects. Final results are presented as the estimated changes in lung function associated with a 5°C increase in ambient temperature, with the

95% confidence interval (95% CI). *P*-value of <0.05 was declared as statistically significant.

RESULTS

Two hundreds and seventy primary school children with asthma were recruited, 46% of whom were girls. The children ranged in age from 7 to 12 years and had a mean ± standard deviation (SD) standing height and weight of 141±9.47 centimeters (cm) and 38.0±10.6 kilograms (kg), respectively. As expected, evening PEF and FEV_1 values were slightly higher than morning values (Table 1). Fourteen children took asthma medication every day and 127 children took no medication during the study period (Supplemental Material Figure S2). Individual characteristics were similar in the six cities, but exposure levels varied by city (Supplemental Material Table S2). All PEF and FEV_1 were positively correlated (Supplemental Material Table S3).

Table 2 presents the summary statistics for different metrics of ambient temperature, 8-hour moving average O_3, daily 24-hour average NO_2 and relative humidity during the panel study period. Mean observed daily 24-hour average, maximum and minimum ambient temperature were 15°C, 20°C and 10°C, respectively. The mean values for 8-hour moving average O_3, daily 24-hour average NO_2 and relative humidity were 25.3ppb, 9.89μg/m^3 and 71.0% respectively. Minimum, daily 24-hour average and maximum temperatures and 8-hour moving average O_3 were positively correlated (Supplemental Material Table S4), but they were negatively correlated with daily 24-hour average NO_2 and relative humidity (Supplemental Material Table S4).

Table 3 shows the associations between daily maximum temperature and morning and evening PEF and FEV_1 in asthmatic children from Australia. For all participants, daily maximum temperature was negatively associated with both morning and evening PEF and FEV_1 with a lag of one, two or three days. In girls, there was no significant association between daily maximum temperature and evening PEF at any lags. In general, the effects of daily maximum temperature on evening FEV_1 were stronger in girls than in boys, while the effects were stronger in boys for evening PEF.

Table 4 shows the effects of daily maximum temperature (moving average lag 0–3) on PEF and FEV_1 in five cities of Australia. The effects of temperature on children's lung function vary by city. In general, such effects were greater in southern cities (Perth, Sydney, Adelaide and Melbourne) than the relatively northern city (Brisbane). Melbourne had highest effects of temperature on lung function. For example, for evening FEV_1, a 5°C increase in daily maximum temperature (moving average lag 0–3) was associated with a decline of 90.1mL (95% CI: 30.1 mL, 150mL) in Melbourne and 6.86mL (95% CI: 71.2 mL, 84.9mL) in Brisbane.

When children's respiratory symptoms were included into the models as a categorical variable, the results were similar to our main findings (Supplemental Material Tables S5). In other sensitivity analyses, the effect estimates were unchanged when O_3, NO_2, relative humidity and medication use were removed from the models (results not shown). The results were also very similar to the main findings when either other air pollutants ($PM_{2.5}$ and SO_2) were controlled for or time and time squared were added to control for any learning effects (results not shown).

DISCUSSION

The principal findings of this study are that ambient temperature had adverse effects on the lung function of children with asthma and that the effects were apparent even when temperature was lagged by up to three days. Increases in ambient temperature were consistently associated with decrements in both PEF and FEV_1 in both boys and girls. The effects of temperature on children's lung function were higher in southern Australian cities than those in the northern most city.

Previous studies have found that reduced lung function is associated with mortality and morbidity from cardiovascular and respiratory diseases [12, 13]. There is also evidence that lung function is a good predictor of human health [14]. The finding that increased ambient temperature is associated with a reduction in lung function in children with asthma may have long term implications for morbidity and mortality.

The results of this study are consistent with previous studies on ambient temperature and human's lung function. Mann et al. found that, in summer, increases in ambient temperature were associated with reduced PEF and increased frequency of respiratory tract infection [15]. An American cohort study reported that warmer temperatures were associated with lower FEV_1 in cystic fibrosis patients [16]. Hales et al. found that warmer temperatures were associated with increased prevalence of asthma in adults [17].

There are very few studies examining the possible mechanisms for the association between temperature increases and the adverse effects on lung function. A possible explanation is that high temperatures are associated with higher levels of allergen exposure which is a potential environmental trigger of asthma [17]. Higher temperatures are also associated with airway drying, which may trigger bronchoconstriction [18]. Our results suggest that further studies are needed to assess the possible mechanisms for the associations between temperature and lung function.

This study found that the effects of ambient temperature on lung function appeared on the days following exposure (lag effects). This is consistent with the observations from many studies which have reported that effects of ambient temperature on mortality and morbidity last several days. The relationships were often observed to be acute and short-term with the strongest effects recorded in the first 1–3 days following exposure [10, 11]. Understanding this lagged effect is very important when developing preventive health and risk management policies for high temperature days.

This study revealed that boys exhibited greater susceptibility to high temperature than girls for evening PEF, while girls were more sensitive to high temperature than boys for evening FEV_1. However, these differences might be explained by chance, as they were not statistically significant (interaction test results not shown). So far, no consistent results have been reported in the literature regarding differential temperature risks by sex. Some studies found that male were sensitive to high temperatures while female were more vulnerable to lower temperatures [19], whereas others have found no differences between the sensitivity of men and women to cold or hot weather [20, 21]. Further detailed studies are needed to explore these sex differences.

We found that the effects of ambient temperature on children's lung function varied in different Australian cities. Children with asthma living in southern cities were more vulnerable to high temperature than those in the northern city. Melbourne should pay more attention to the effects of high temperature on children's lung function. Our results are consistent with the fact that mortality reaches its minimum at higher temperatures in hotter regions than in colder places [22, 23]. It may be that people acclimatize to their local climatic through physiological adaptation to slowly increasing temperatures [24]. Previous studies found that local conditions, such as social, economic, demographic factors and characteristics of infrastructure may modify the effects of ambient temperatures on human health [25]. Intensity of urban heat islands, social isolation, access to air conditioning and housing characteristics are also modifiers for temperature-health relationship [26]. However, when socio-economic indexes for areas of Australia were included in the models, effects were unchanged (results not shown).

The finding that high temperature has a significant impact on lung function of children with asthma may have clinically important implications. In particular, in population terms, even a small decline in average lung function may have important impacts at the extreme ends of the distribution [27]. Meanwhile, asthma is the most common chronic disease among children in Australia. The most recent data suggested that one in six Australian children have diagnosed asthma [1]. Therefore, a large group of children are susceptible to adverse effects of ambient temperature.

To the best of our knowledge, this is the first panel study to examine the short-term effects of ambient temperature on lung function in school children with asthma. It employed an Australian national sample with a relatively large sample size (N=270) to examine the effects of ambient temperature on both PEF and FEV_1. Morning and evening lung function were measured twice daily for four weeks, which contributed to the reliability of this study along with the use of different metrics of ambient temperature, examination of lag effects, and assessment of the effects by sex and location. We controlled for other pollutants as potential confounders of temperature effects, because a number of studies have reported that air pollution is a risk factor for decreased lung function and it may induce childhood asthma [28]. The findings may have implications in promoting capacity building for preventing health problems related to temperature increase.

A limitation of this study was that it only included urban children, and therefore we cannot generalize the results to children who live in rural areas. Additionally, the information on ambient temperature, relative humidity and air pollution was from fixed monitoring sites rather than individual exposures, which may lead to measurement errors in exposures. The estimated effects might be overestimated if exposure levels at the given monitoring site are in the lower range of population exposure. However, temperature measurements at fixed monitoring sites have been shown to be equally good at estimating city-wide associations between temperature and mortality compared to spatially resolved temperatures [30], because temperatures show little spatial variation within cities. We used the current day's maximum temperature as the principal exposure to assess effects on morning lung function, which may lead to measurement errors. However, because daily 24-hour average, maximum and minimum temperatures are very strongly correlated (Supplemental Material Table S4) and daily maximum temperature was the best predictor in this study, maximum temperature was the most appropriate exposure. The study lacked data on effects during summer as measurements were carried out only in school terms. We have used a non-linear function to examine whether the effects of temperature on lung function were non-linear, but a consistent linear relationship was found for both PEF and FEV_1. We have not examined or controlled for the effects of aero-allergens such as pollens in this study, as we didn't measure these factors in the study period.

CONCLUSIONS

This study suggests that increased ambient temperature adversely affected both PEF and FEV_1 in Australian school children with asthma. The effects lasted for several days. For evening PEF, boys were more sensitive to ambient temperature than girls, while girls were more vulnerable than boys for evening FEV_1. The results indicate that the increasing frequency of high temperatures might be a risk to the health of children with asthma.

Ethics statement:

The study protocol was approved by the Universities of Queensland and Sydney, Departments of Education in the Australian Capital Territory, New South Wales, Queensland, South Australia, Victoria, and Western Australia. Ethics approval was also obtained from the Catholic Education Office of Victoria to perform the study at selected Victorian Catholic primary schools. All subjects and parents or guardians gave written informed consent before participation in the study.

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Competing financial interests declaration:

The authors declare no competing financial interests.

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Table 1 Selected demographics and outcomes summary of study participants (270 primary school children with asthma) in Australia.

Index	All (N=270)		Female (n=123)		Male (n=147)	
	Mean ± SD	**Range**	**Mean ± SD**	**Range**	**Mean ± SD**	**Range**
Age (years)	10.0±1.20	7.50–12.8	10.1 ±1.20	7.50–12.3	9.97±1.18	7.79–12.8
Standing height (cm)	141±9.47	117–170	142±9.85	117–170	140±9.02	121–169
Weight (kg)	38.0±10.6	21.0–84.0	39.0±10.9	21.0–78.0	37.3±10.2	22.0–84.0
Morning PEF (L/min)	257±64.5	70.0–545	262±68.2	70.0–515	253±61.1	70.0–545
Evening PEF (L/min)	266±64.2	65.0–605	270±65.2	65.0–520	262±63.2	70.0–605
Morning FEV_1 (L)	1.81±0.47	0.60–4.35	1.73±0.46	0.60–3.40	1.87±0.47	0.60–4.35
Evening FEV_1 (L)	1.84±0.48	0.65–4.45	1.76±0.47	0.65–3.45	1.90±0.49	0.70–4.45

Abbreviations: cm: centimeter; FEV_1: forced expiratory volume in one second; kg: kilogram; L: liters; L/min: liters per minute; PEF: peak expiratory flow; SD: standard deviation.

Table 2 Descriptive statistics for selected daily exposure measurements during study period (four weeks of 2007–2008) in Australia.

Exposures	Mean ± SD	Median	IQR	Range
24-hour average temperature (°C)	15.1±4.66	15.1	11.8–17.6	4.27–31.0
Maximum temperature (°C)	20.0±5.76	19.4	15.4–23.5	9.50–39.9
Minimum temperature (°C)	10.5±4.35	10.5	7.30–13.6	0.10–24.1
8-hour moving average O_3 (ppb)	25.3±8.63	24.6	19.9–30.0	0.88–65.9
24-hour average NO_2 (μg/m^3)	9.89±6.27	8.91	5.26–13.2	0.05–35.4
Relative humidity (%)	71.0±13.1	73.0	63.0–80.0	32.0–94.1

Abbreviations: 8-hour moving average O_3: average ozone of the previous 8 hours for each hour of the day; IQR: inter-quartile range; NO_2: nitrogen dioxide; ppb: parts per billion; SD: standard deviation; μg/m^3: micrograms per cubic meter.

Table 3 Mixed model estimates of changes in lung function with every 5°C increase in daily maximum temperature at different lags among 270 children with asthma in Australia. [a]

	Lag [b]	Coefficient (95% CI)		
		All	Female	Male
Morning PEF (L/min)	**0**	–2.42 (–4.19, –0.65)**	–3.48 (–6.08, –0.88)**	–1.38 (–3.80, 1.04)
	1	–2.80 (–4.55, –1.05)**	–2.42 (–4.98, 0.14)	–3.08 (–5.48, –0.68)*
	2	–3.00 (–4.74, –1.26)**	–2.59 (–5.12, –0.05)*	–3.27 (–5.67, –0.87)**
	3	–1.59 (–3.29, 0.11)	–1.62 (–4.09, 0.85)	–1.46 (–3.80, 0.88)
Evening PEF (L/min)	**0**	–0.85 (–2.70, 1.00)	–0.26 (–2.89, 2.36)	–1.31 (–3.93, 1.31)
	1	–1.04 (–2.86, 0.78)	1.15 (–1.43, 3.74)	–2.88 (–5.45, –0.32)*
	2	–1.45 (–3.22, 0.32)	–0.52 (–3.01, 1.97)	–2.14 (–4.66, 0.38)
	3	–2.33 (–4.09, –0.56)**	–0.27 (–2.74, 2.19)	–4.14 (–6.66, –1.61)**
Morning FEV_1 (mL)	**0**	–9.39 (–24.7, 5.88)	–16.0 (–36.8, 4.80)	–2.97 (–25.0, 19.1)
	1	–18.1 (–33.0, –3.16)*	–7.06 (–27.4, 13.3)	–26.6 (–48.2, –5.01)*
	2	–26.9 (–41.6, –12.1)**	–24.4 (–44.4, –4.34)*	–29.1 (–50.5, –7.73)**
	3	–19.0 (–33.6, –4.33)*	–30.3 (–50.4, –10.3)**	–8.83 (–29.9, 12.2)
Evening FEV_1 (mL)	**0**	–4.40 (–22.6, 13.8)	–14.1 (–38.6, 10.5)	2.29 (–24.3, 28.9)
	1	–27.8 (–45.7, –9.99)**	–37.8 (–61.8, –13.7)**	–19.0 (–45.1, 7.18)
	2	–39.7 (–57.6, –21.9)**	–64.9 (–88.8, –40.9)**	–16.7 (–43.0, 9.56)
	3	–38.5 (–56.2, –20.7)**	–48.0 (–71.5, –24.5)**	–29.0 (–55.5, –2.46)*

[a] All models controlled for children's sex, age, standing height, weight, 3-day mean concentration of O_3, 3-day mean concentration of NO_2, 3-day mean of relative humidity, city and medication use as fixed effects.
[b] Lag 0 of temperature: exposure of current day's temperature; lag 1 of temperature: exposure of temperature on the day before; lag 2 of temperature: exposure of temperature on two days before; lag 3 of temperature: exposure of temperature on three days before.
* $p<0.05$, ** $p<0.01$.

Abbreviations: 95% CI: 95% confidence interval; FEV_1: forced expiratory volume in one second; L: liters; L/min: liters per minute; mL: milliliter; O_3: ozone; NO_2: nitrogen dioxide; PEF: peak expiratory flow.

Table 4 Mixed model estimates of changes in lung function with every 5°C increase in maximum temperature (moving average lag0–3) among children with asthma, in five cities of Australia. Cities are ordered by latitude (north to south for Brisbane to Melbourne). [a]

City	Coefficient (95% CI)			
	Morning PEF (L/min)	Evening PEF (L/min)	Morning FEV_1 (mL)	Evening FEV_1 (mL)
Brisbane	–1.48 (–4.94, 1.98)	–3.98 (–15.3, 7.33)	–21.5 (–96.8, 53.9)	–6.86 (–84.9, 71.2)
Perth	–9.68 (–19.9, 0.52)	1.12 (–17.9, 20.1)	–48.0 (–181, 86.0)	–39.3 (–276, 198)
Sydney	–11.4 (–18.2, –4.54)**	–6.56 (–14.1, 0.93)	–73.5 (–139, –8.17)*	–9.84 (–91.4, 71.8)
Adelaide	–14.2 (–29.8, 1.32)	0.28 (–5.10, 5.65)	–9.75 (–63.6, 44.1)	–8.88 (–58.6, 40.9)
Melbourne	–9.20 (–14.6, –3.85)**	–5.18 (–10.4, 0.06)	–69.2 (–121, –17.2)**	–90.1 (–150, –30.1)**

[a] All models controlled for children's sex, age, standing height, weight, 3-day mean concentration of O_3, 3-day mean concentration of NO_2, 3-day mean of relative humidity and medication use as fixed effects.
* $p<0.05$, ** $p<0.01$.

Abbreviations: 95% CI: 95% confidence interval; FEV_1: forced expiratory volume in one second; L: liters; L/min: liters per minute; mL: milliliter; O_3: ozone; NO_2: nitrogen dioxide; PEF: peak expiratory flow.

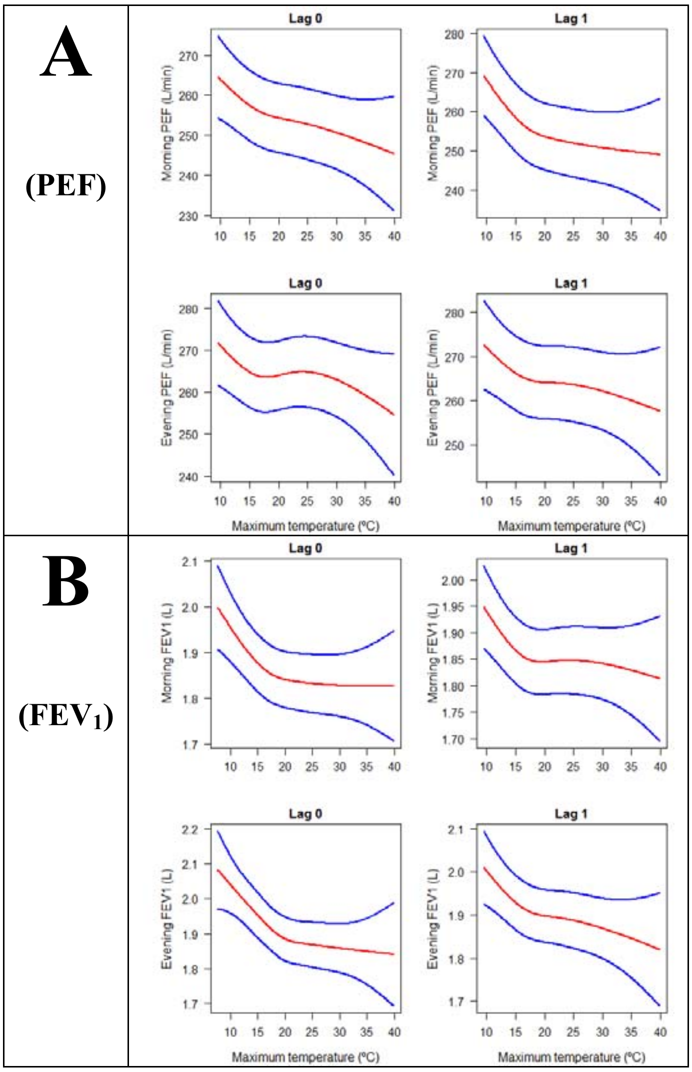

Figure 1 Relationship between daily maximum temperature and peak expiratory flow (A) and forced expiratory volume in one second (B) on the current and previous day, with three degrees of freedom natural cubic spline for daily maximum temperature.