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Air pollution, temperature and pediatric influenza in Brisbane, Australia

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ABSTRACT

Previous studies have demonstrated the importance of weather variables in influencing the incidence of influenza. However, the role of air pollution is often ignored in identifying the environmental drivers of influenza. This research aims to examine the impacts of air pollutants and temperature on the incidence of pediatric influenza in Brisbane, Australia. Lab-confirmed daily data on influenza counts among children aged 0–14 years in Brisbane from 2001 January 1st to 2008 December 31st were retrieved from Queensland Health. Daily data on maximum and minimum temperatures for the same period were supplied by the Australian Bureau of Meteorology. Winter was chosen as the main study season due to it having the highest pediatric influenza incidence. Four Poisson log-linear regression models, with daily pediatric seasonal influenza counts as the outcome, were used to examine the impacts of air pollutants (i.e., ozone (O_3), particulate matter ≤ 10 μm (PM_{10}) and nitrogen dioxide (NO_2)) and temperature (using a moving average of ten days for these variables) on pediatric influenza. The results show that mean temperature (Relative risk (RR): 0.86; 95% Confidence Interval (CI): 0.82–0.89) was negatively associated with pediatric seasonal influenza in Brisbane, and high concentrations of O_3 (RR: 1.28; 95% CI: 1.25–1.31) and PM_{10} (RR: 1.11; 95% CI: 1.10–1.13) were associated with more pediatric influenza cases. There was a significant interaction effect (RR: 0.94; 95% CI: 0.93–0.95) between PM_{10} and mean temperature on pediatric influenza. Adding the interaction term between mean temperature and PM_{10} substantially improved the model fit. This study provides evidence that PM_{10} needs to be taken into account when evaluating the temperature–influenza relationship. O_3 was also an important predictor, independent of temperature.

1. Introduction

Influenza is a serious public health problem, reported to be associated with approximately 250,000 to 500,000 deaths in the world annually (WHO, 2009). It is an important contributor to the burden of morbidity and mortality from respiratory diseases (Chow et al., 2006; Thompson et al., 2003, 2004). Influenza-related mortality and morbidity rates have not changed significantly over time (Thompson et al., 2003, 2004), even though an increasing number of vaccination campaigns have been implemented. Children, especially those aged under two years, are particularly vulnerable to influenza and its complications (WHO, 2009). Influenza is associated with a substantial number of outpatient visits and hospitalizations in children (Izurieta et al., 2000; Neuzil et al., 2000; Poehling et al., 2006). However, pediatric influenza is undertreated (Neuzil et al., 2000), despite the important role of children in the transmission of viruses (Glezen et al., 1978; Longini et al., 1982).

An increasing number of studies have explored the risk factors of influenza (Hu et al., 2012; Peng et al., 2012; Thiberville et al., 2012). The relationship between weather and influenza has only recently been examined in detail (Davis et al., 2012; Yang and Marr, 2011). Results suggest that influenza transmission is enhanced in the presence of cold and/or dry air (Lowen et al., 2007; Shaman and Kohn, 2009). Air pollutants, especially PM_{10} (Jaspers et al., 2005) and O_3 (Kesic et al., 2012), also play an important role in the transmission of influenza. Some researchers have found that there were interaction effects between temperature and PM_{10} on cardio-respiratory diseases (Ren et al., 2006) and mortality (Roberts, 2004). Low temperature and high PM_{10} concentration may interact to affect children's airways, and result in their much greater vulnerability to influenza (Ren et al., 2006). However, in previous studies, the role of interaction effect between temperature and PM_{10} on pediatric influenza has not been formally assessed.

Abbreviations: BIC, Bayesian information criterion; CI, confidence interval; RR, relative risk.

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Compared to adults, children are more likely to spend time outdoors, playing (Xu et al., 2012), which result in their greater exposure to both air pollution and high and low temperatures. Interaction effects represent the combined effects of variables on the outcome. When an interaction effect is present, the impact of one variable depends on the level of the other variable. In this study, we aimed to quantify the effects of temperature and air pollution on the incidence of lab-confirmed pediatric influenza (A and B) in Brisbane, Australia and to determine whether there was an interaction effect between temperature and concentration of PM_{10}.

2. Materials and methods

2.1. Data collection

Lab-confirmed daily data on the number of influenza cases among children aged 0–14 years in Brisbane from 2001 January 1st to 2008 December 31st were obtained from Queensland Health (QH). Under the provisions of the Public Health Act (2005), all laboratory-confirmed cases of influenza in pathology laboratories are required to be notified to QH, regardless of whether the test request was from the public or private health sector (Queensland Health, 2005). Data reported to QH include the onset date and place of onset of the notified cases of influenza infection, serotype, birth date and sex of the patients and laboratory test date. Daily data on maximum and minimum temperatures in Brisbane for the same period were retrieved from the Australian Bureau of Meteorology. The Queensland Department of Environment and Heritage Protection supplied the data on daily average particular matter ≤ 10 μm (PM_{10}) (μg/m^3), daily average nitrogen dioxide (NO_2) (μg/m^3) and daily average ozone (O_3) (ppb).

2.2. Statistical analyses

To detect whether the data were over-dispersed in the Poisson setting, we fitted negative binomial, quasi-Poisson and Poisson models, and found the Poisson model had the best model fit. Winter was the season with the highest incidence of pediatric influenza, and therefore we selected the winter data for analysis. Variance inflation factor analysis was performed to determine the possible effects of collinearity. A Poisson log-linear regression, with daily influenza count as outcome variable, was used to examine the impacts of mean temperature and air pollutants on pediatric influenza in Brisbane. The incubation period of pediatric influenza was taken into account (Weinstein et al., 2003) and thus mean temperature, O_3, PM_{10} and NO_2, calculated using a moving average of ten days (Tsuchihashi et al., 2011), were considered as exposure variables.

$$Y_t \sim Poisson(\mu_t)$$
$$\mathrm{Log}(\mu_t) = \alpha + \beta_1 T_t + \beta_2 \mathrm{PM}_{10t} + \beta_3 O_{3t} + \beta_4 NO_{2t} + \beta_5 T_t * \mathrm{PM}_{10}$$

where t is the day of the observation; Y_t is the observed daily childhood influenza on day t; α is the model intercept; T_t is the ten days' moving average mean temperature; PM_{10t} is the ten days' moving average PM_{10}; O_{3t} is the ten days' moving average O_3, NO_{2t} is the ten days' moving average NO_2 and $T_t * PM_{10}$ is the interaction term of mean temperature and PM_{10}. Models were built sequentially. Firstly, we explored the association between pediatric influenza and mean temperature (Model I). Secondly, we assessed the association between pediatric influenza and air pollutants, including O_3, PM_{10} and NO_2 (Model II). Thirdly, we entered both mean temperature and air pollutants into the model (Model III). Based on the results of Model III, we added an interaction term between temperature and PM_{10} into the model (Model IV). The models were assessed using the Bayesian information criterion (BIC). All data analysis was performed using the software Statistical Package for the Social Science version 19 (SPSS, Inc., Chicago, IL, USA).

3. Results

There were 2922 lab-confirmed cases of pediatric influenza during the study period. Summary statistics for daily pediatric influenza cases, mean temperature and air pollutants in winter are given in Table 1. The average number of daily pediatric influenza cases was 2.0. The mean value of daily mean temperature was 15.9 °C. The mean values of O_3, PM_{10} and NO_2 were 15.3 ppb, 18.4 μg/m^3 and 11.1 μg/m^3. Fig. 1 shows the time-series distributions of daily pediatric influenza, mean temperature, PM_{10}, O_3 and NO_2 from 2001 to 2008 in winter (1st June–31st August) of Brisbane.

Table 2 shows the Spearman correlation between mean temperature and air pollutants. There were negative correlations between pediatric influenza incidence and mean temperature, and positive correlations between pediatric influenza incidence and O_3 and PM_{10}. Additionally, there were negative correlations between mean temperature and air pollutant concentrations (O_3 ($r = -0.092$, $P < 0.05$), PM_{10} ($r = -0.127$, $P < 0.01$) and NO_2 ($r = -0.075$, $P < 0.01$)).

Fig. 2 presents the scatter plots of relationships between pediatric influenza, mean temperature, O_3 and PM_{10}, also revealing that there was a negative relationship between pediatric influenza and mean temperature. The relationships between pediatric influenza and the air pollutants (O_3 and PM_{10}) were positive.

Table 3 shows the associations of mean temperature and air pollutant concentrations with influenza incidence. The results showed that temperature at moving average of ten days (Model I) was statistically significantly associated with influenza incidence. Additionally, O_3 and PM_{10} (Model II) were significantly associated with influenza. Model III comprised mean temperature and air pollutants as exposures, showing that mean temperature (RR: 0.86; 95% CI: 0.82–0.89), O_3 (RR: 1.28; 95% CI: 1.25–1.31) and PM_{10} (RR: 1.11; 95% CI: 1.10–1.13) were significantly associated with influenza. Model IV, adding an interaction term between mean temperature and PM_{10} in model III, found that O_3 (RR: 1.26; 95% CI: 1.23–1.29) was significantly associated with influenza and that there was a significant interaction effect between mean temperature and PM_{10} (RR: 0.94; 95% CI: 0.93–0.95; main effects, mean temperature RR: 0.77; 95% CI: 0.67–0.92; and PM_{10} RR: 1.06; 95% CI: 1.05–1.07) on pediatric influenza. The BICs of the four models clearly reveal that the model with the interaction effect provided a much better fit to the data than the other models.

4. Discussion

This study found that, in Brisbane, temperature, O_3, and PM_{10} were significantly associated with pediatric influenza and that there was a significant interaction effect between PM_{10} and temperature. Taking air pollutants into account when modeling the association between temperature and pediatric influenza could substantially improve the accuracy of models.

In temperate areas, children, especially infants, are more likely to be attacked by influenza during the epidemic season (Neuzil et al., 2000). Pediatric influenza has caused great socioeconomic burdens in some regions (Chiu et al., 2012). Further, children play an

Table 1
Summary statistics for daily temperature, air pollution, and lab-confirmed pediatric seasonal influenza in winter (June–August) of Brisbane, Australia, from 2001 to 2008.

Variables	Mean	SD	Min	Percentile			Max
				25	50	75	
Mean temperature (°C)	15.9	1.8	10.7	14.7	15.9	17.1	20.8
O_3 (ppb)	15.3	4.6	3.2	11.9	15.1	18.6	30.7
PM_{10} (μg/m^3)	18.4	7.7	3.2	13.3	17.3	22.1	101.7
NO_2 (μg/m^3)	11.1	3.9	1.3	8.7	11.1	13.8	25.0
Influenza	2.0	3.8	0	0	1	2	28

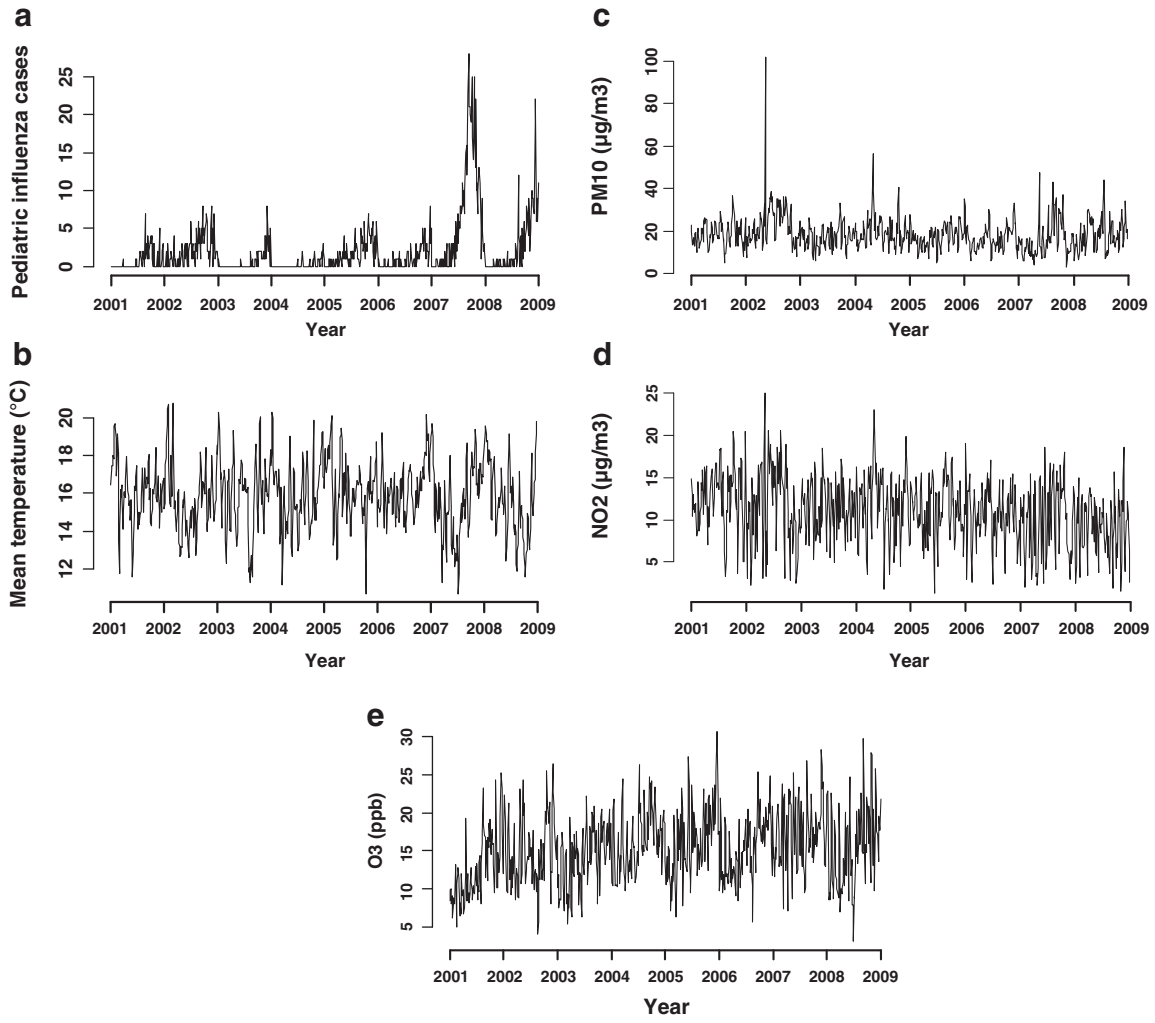

Fig. 1. a. Time-series distribution of pediatric influenza in winter (June–August) of Brisbane, Australia, from 2001 to 2008. b. Time-series distribution of mean temperature in winter (June–August) of Brisbane, Australia, from 2001 to 2008. c. Time-series distribution of PM_{10} in winter (June–August) of Brisbane, Australia, from 2001 to 2008. d. Time-series distribution of NO_2 in winter (June–August) of Brisbane, Australia, from 2001 to 2008. e. Time-series distribution of O_3 in winter (June–August) of Brisbane, Australia, from 2001 to 2008.

important role in the transmission of influenza, because school-age children are the major channel through which influenza virus is spread to households (Lipsitch and Viboud, 2009; Lofgren et al., 2007; Perio et al., 2012). Vaccination is an effective way to prevent influenza, but the vaccination rates among children are far from satisfactory because of fear, misconceptions and mistrust (Bhat-Schelbert et al., 2012). Regarding the current situation of pediatric influenza, it is particularly important to identify host and environmental risk factors for developing state-of-the-art early warning systems. This study stands out from previous studies by highlighting the role of air pollution in the relationship between temperature and pediatric influenza.

Similar to previous studies (Davis et al., 2012; Tang et al., 2010), we found lower temperatures to be associated with influenza from the regression results. The time-series figure (Fig. 1) showed that the timing of low temperature and high influenza cases was very consistent (except for year 2002). Generally, there does not appear to be much temperature variability in the cold season across the study period. The temperature in years 2002, 2007 and 2008 was slightly colder than other years, and the influenza cases in two of these three years (2007 and 2008) were much higher. It has been postulated that low temperature drives the spread of influenza by increasing contact rates in the population, lengthening the survival of the virus, and affecting host immunity (Tamerius et al., 2011). In this study, O_3 was found to be associated with pediatric influenza. Several studies have documented the positive relationship between O_3 and influenza (Jakab and Bassett, 1990; Spannhake et al., 2002). O_3 exposure significantly increases adhesion of polymorphonuclear leukocytes to human tracheal epithelial cells (Tosi et al., 1994). Kesic et al. has found that exposure to O_3 disrupts the protease/antiprotease balance found in the human airway, contributing to increased influenza infection (Kesic et al., 2012). The results of this study also suggest that PM_{10} may play a role in the occurrence of pediatric influenza. The transmission of influenza virus is dependent

Table 2
Spearman's correlation between daily pediatric seasonal influenza, weather variables and air pollutants in winter (June–August) of Brisbane, Australia, from 2001 to 2008.

	Influenza	Mean temperature	O_3	PM_{10}	NO_2
Influenza	1.00				
Mean temperature	−0.17**	1.00			
O_3	0.21**	−0.092*	1.00		
PM_{10}	0.40**	−0.127**	−0.064	1.00	
NO_2	−0.016	−0.075*	−0.421	0.623**	1.00

Weather variables and air pollutants were used in moving average of 10 days.
** $P < 0.01$.
* $P < 0.05$.

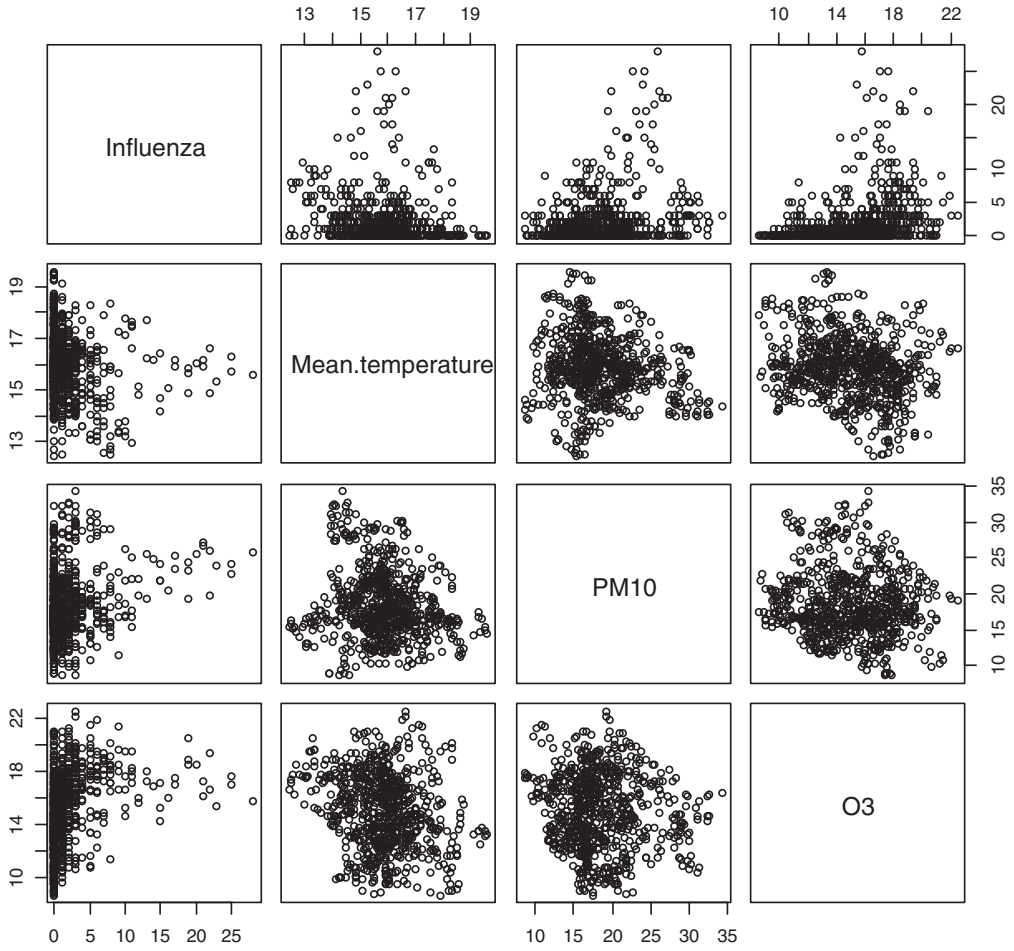

Fig. 2. The pairwise plot of pediatric influenza, mean temperature, PM_{10} and O_3 in winter (June–August) of Brisbane, Australia, from 2001 to 2008. All variables were used in moving average of 10 days.

on short-distance dispersion of droplets. Hammond et al. reported that PM_{10} could provide condensation nuclei for the virus droplets and thus facilitate the spread of influenza viruses (Hammond et al., 1989).

Table 3
Poisson regression of pediatric influenza with weather variables and air pollutants.

	RR[a]	95% CI	BIC
Model I			4235.35
Mean temperature	0.79	0.76–0.83	
Model II			3492.77
O_3	1.27	1.24–1.30	
PM_{10}	1.12	1.10–1.13	
NO_2	1.00	0.96–1.04	
Model III			3450.02
Mean temperature	0.86	0.82–0.89	
O_3	1.28	1.25–1.31	
PM_{10}	1.11	1.10–1.13	
NO_2	1.00	0.96–1.04	
Model IV			3297.62
Mean temperature	0.77	0.67–0.92	
O_3	1.26	1.23–1.29	
PM_{10}	1.06	1.05–1.07	
NO_2	1.01	0.97–1.04	
Mean temperature * PM_{10}	0.94	0.93–0.95	

All exploratory variables were used in moving average of 10 days. The significance of bold in the table refers to the variables with $P < 0.05$.

[a] Relative risk.

Temperature and air pollution are often significantly correlated, and they sometimes interact to affect human health (Ren et al., 2006). Interestingly, we found a significant interaction effect of PM_{10} and temperature on pediatric influenza, which is biologically plausible. Exposure to high PM_{10} concentration has been widely recognized as a threat to children's respiratory systems (Hoek et al., 2012; Weinmayr et al., 2010). PM_{10} exposure has been reported to affect airways through inhalation, including the upper airways, bronchioles, and alveoli (Gordon, 2003; Jeffery, 1999). Low temperature can trigger viral infection in the airway (Yuksel et al., 1996). Thus, low temperature and high concentration of PM_{10} may interact to synergistically affect children's airways, and result in their greater susceptibility to influenza virus.

This study has two major strengths. To the best of our knowledge, this is the first study to examine the interaction effect between PM_{10} and temperature on pediatric influenza. An additional benefit of the study is that, in using a ten-day moving average for mean temperature and air pollutants, the findings indicate that these variables could be used as part of a pediatric influenza early warning system. The effectiveness of such systems depends on a sufficient lag between the exposure variable and the outcome, and for there to be a sufficiently accurate signal in the exposure variable in terms of predicting the disease outcome. Several weaknesses should be acknowledged. First, this is a one-city study, and more work needs to be done to ascertain how generalizable our results are to other regions. Second, no prediction was done in this study. This is an area for future research and prediction studies will be implemented once a longer

time series is obtained. Third, this is an ecological study, and therefore some biases due to exposure misclassification are inevitable.

This study has found the important role of PM_{10} in the relationship between temperature and pediatric influenza, which may shed a new light for future risk prediction studies, and also for understanding the environmental drivers of influenza.

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