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The impact of ambient fine particles on influenza transmission and the modification effects of temperature in China: A multi-city study

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ABSTRACT

Background: There is good evidence that air pollution is a risk factor for adverse respiratory and vascular health outcomes. However, data are limited as to whether ambient fine particles contribute to the transmission of influenza and if so, how the association is modified by weather conditions.
Objectives: We examined the relationship between ambient $PM_{2.5}$ and influenza incidence at the national level in China and explored the associations at different temperatures.
Methods: Daily data on concentrations of particulate matter with aerodynamic diameter < 2.5 μm ($PM_{2.5}$) and influenza incidence counts were collected in 47 Chinese cities. A Poisson regression model was used to estimate the city-specific $PM_{2.5}$-influenza association, after controlling for potential confounders. Then, a random-effect meta-analysis was used to pool the effects at national level. In addition, stratified analyses were performed to examine modification effects of ambient temperature.
Results: For single lag models, the highest effect of ambient $PM_{2.5}$ on influenza incidence appeared at lag day 2, with relative risk (RR) of 1.015 (95% confidence interval (CI): 1.004, 1.025) associated with a 10 μg/m^3 increase in $PM_{2.5}$. For moving average lag models, the significant association was found at lag 2–3 days, with RR of 1.020 (95% CI: 1.006, 1.034). The RR of influenza transmission associated with $PM_{2.5}$ was higher for cold compared with hot days. Overall, 10.7% of incident influenza cases may result from exposure to ambient $PM_{2.5}$.
Conclusions: Ambient $PM_{2.5}$ may increase the risk of exposure to influenza in China especially on cooler days. Control measures to reduce $PM_{2.5}$ concentrations could potentially also be of benefit in lowering the risk of exposure and subsequent transmission of influenza in China.

1. Introduction

Coinciding with China's rapid economic development and urbanization, air pollution has become a severe problem, and poses a major threat to the health of the Chinese population. Recent estimates suggest that annually air pollution in China kills >1.5 million people each year, about 17% of the nation's annual deaths (Rohde and Muller, 2015). One component of air pollution, in particular, is of increasing concern to public health experts; compared to other components, ambient particulate matter with aerodynamic diameter < 2.5 μm ($PM_{2.5}$) is able to penetrate deep into the lung and into the circulatory system (S Feng et al., 2016). Exposure to $PM_{2.5}$ is associated with a wide range of diseases including cardiovascular and respiratory disease (Arnold, 2014). In 2013, the Global Burden of Disease group estimated that exposure to ambient $PM_{2.5}$ to be the 12th leading risk factor for the global burden of disease and responsible for 2.9 million deaths and 69.7 million disability adjusted life-years, worldwide (Forouzanfar et al., 2015).

Despite substantial reductions in the burden of communicable disease in China over the past two decades, it remains a leading cause of death in the country (Wang et al., 2008). Of particular concern, both nationally and globally, is the increasing threat posed by emerging infectious diseases (e.g., severe acute respiratory syndrome [SARS] and the highly pathogenic avian influenza [*HPAI*]) in the Chinese population, both of which pose a significant public health threat (Wang et al., 2008). Few studies have examined the possible effect of ambient $PM_{2.5}$ concentrations on risk of communicable disease in China, but those that have reported a positive association between ambient

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$PM_{2.5}$ and localised transmission of influenza (C. Feng et al., 2016; Huang et al., 2016; Liang et al., 2014). However, until now there has been no large-scale examination of the association due to past unavailability of $PM_{2.5}$ data and incident cases of influenza at the national level. Neither has there been any detailed exploration of the possible effect of temperature on the transmissibility by ambient $PM_{2.5}$ of the influenza virus. In this study, we collected daily data on ambient $PM_{2.5}$ levels, weather conditions and influenza incidence from 47 cities in China in order to reliably determine the association between $PM_{2.5}$ and influenza incidence and the potential modification effects of ambient temperature on the relationship.

2. Materials

2.1. Data collection

2.1.1. Influenza data

Daily data of influenza cases for 47 cities in China from September 9, 2013 to December 31, 2014 were obtained from the China Information System for Disease Control and Prevention (CISDCP). China has established a web-based notifiable infectious disease management system linked with health administrative datasets, the disease control institution and the medical and health institutions at five levels: township, county (district), prefecture, province and national (Wang et al., 2008). Influenza cases were defined according to Technical guides for prevention and control of influenza issued by China Ministry of Health (http://www.moh.gov.cn/zwgkzt/s9491/200802/38820.shtml): sudden onset of fever ≥38 °C, cough or sore throat, and absence of other diagnoses. As influenza is a notifiable disease (Class C), sentinel hospitals are required to collect nasopharyngeal swabs for each identified case which are subsequently sent to designated laboratories for virus isolation and further identification and results are submitted online within 24 h (Liang et al., 2014; Shu et al., 2010).

2.1.2. Ground $PM_{2.5}$ measurements

Ambient $PM_{2.5}$ concentrations were measured during the same time period as influenza data at 76 stations (Fig. S1 in Appendix) of the China Atmosphere Watch Network (CAWNET) administered by the China Meteorological Administration in 47 cities. Hourly $PM_{2.5}$ concentrations were measured using GRIMM EDM 180 environmental dust monitors. Further details regarding methods of measurements and the monitoring instruments used have been previously reported (Wang et al., 2015). To link $PM_{2.5}$ data with daily influenza case data, hourly $PM_{2.5}$ concentrations (C_{hour}) were converted to daily $PM_{2.5}$ concentrations ($C_{daily} = \sum_1^{24} C_{hour}/24$). City-level average concentrations were calculated if there were two or more stations in one city.

2.1.3. Meteorological data

Daily meteorological data were obtained from the China Meteorological Data sharing service system of the China Meteorological Administration (http://data.cma.gov.cn). Daily temperature, relative humidity, atmospheric pressure, wind speed, and hours of sunshine, were collected from 70 weather stations in 47 cities during the same period as the data for $PM_{2.5}$ and influenza incidence. The average value for each meteorological variable was calculated if there were two or more weather stations within a city.

2.2. Statistical analysis

The $PM_{2.5}$-influenza association was assessed using a two-stage analytic approach which has been widely applied in previous studies (Gasparrini, Armstrong, and Kenward, 2012; Gasparrini et al., 2015; Guo et al., 2014). In the first stage, the city-specific $PM_{2.5}$–influenza association was examined and in the second stage, a random effect meta-analysis was used to pool the associations at the country level.

2.2.1. First stage of analysis (city-specific associations)

A time series Poisson regression model was used to examine city-specific estimates allowing for over-dispersed case counts. Seasonality was controlled for using a natural cubic spline with seven degrees of freedom for time per year. A categorical variable was used to control for the confounding effect of day of the week. As weather conditions are associated with health outcomes and the impact can last for several days (Guo, Barnett, Pan, Yu, and Tong, 2011; Peng, Dominici, and Louis, 2006), we controlled for the potential confounding effects of five meteorological variables (daily mean temperature, relative humidity, air pressure, wind speed, and hours of sunshine) with moving average of the current day and the previous seven days using a natural cubic spline with three degrees of freedom for each of parameters (Guo et al., 2013).

To understand the characteristics of the lag associations between $PM_{2.5}$ and incident influenza, the associations were examined using a single lag model (from lag 0 to lag 7), and moving average lag model, separately. The city-specific effect estimates of influenza associated with a 10 μg/m^3 increase in $PM_{2.5}$ were calculated. To examine whether ambient temperature modified the associations between $PM_{2.5}$ and influenza, a stratified analysis was conducted according to daily temperature (for cold days, moderate cold days, moderate hot days, and hot days), by including an interactive term between $PM_{2.5}$ and temperature levels (as a categorical variable) in the city-specific regression model. The cold days, moderate cold days, moderate hot days, and hot days were classified by the quartile of 0–7 days' moving average of temperature in each city during the study period. To further examine statistical significance of different effects of $PM_{2.5}$ for temperature subgroups, a meta-regression was conducted with the effect estimates of stratum-level analyses as dependent variable and categorical variable of daily temperature as dependent variable (Li et al., 2016).

2.2.2. Second stage of analysis

A meta-analysis was used to pool the city-specific effect estimates obtained from the first-stage model. The meta-analysis was fitted using a random effect model by maximum likelihood, to obtain the national pooled estimates for each lag type, respectively. The $PM_{2.5}$-influenza associations were expressed as the relative risk (RR) and 95% confidence interval (CI) of influenza associated with a 10 μg/m^3 increase in $PM_{2.5}$.

2.2.3. Computation of the population attributable fraction of influenza due to ambient $PM_{2.5}$

Considering the modified effects of ambient temperature on $PM_{2.5}$-incident influenza associations, the attributable fractions were calculated by pooled effect estimates (β) and $PM_{2.5}$ concentrations for each temperature strata according to the formulas reported by Evans et al. (2013). We used the following model to assess the daily influenza cases attributed to $PM_{2.5}$ for each city:

$$\text{AIi} = \text{Influenza}_i \times [(\text{RR}_\text{i} - 1)/\text{RR}_\text{i}]$$

where 'i' is the day of the incident case of influenza; 'AI' is the number of incident influenza cases attributed to $PM_{2.5}$ on day 'i'; and 'Influenza$_i$' is the observed influenza cases on day 'i'; the RR is calculated by exp.(β) × moving average concentration of $PM_{2.5}$ on day 'i-i_1' and day 'i-i_2' accounting for the effects of $PM_{2.5}$ at lag i_1-i_2 days; β is pooled effect estimate for different temperature stratum in corresponding to temperature on day 'i'. 95% CI of pooled β were used to calculate the 95% CI of attributable fraction with the above equation.

The overall population attributable fraction was assessed by dividing the sum of all city-specific attributable cases by the total number of incident cases. In addition, the attributable fractions were also calculated for each temperature stratum.

Sensitivity analyses were performed on the parameters for the city-specific model to test the robustness of our results. We varied the number of lag days to 15 days for meteorological variables, to examine