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Is short-term exposure to ambient fine particles associated with measles incidence in China? A multi-city study



Gongbo Chen^a, Wenyi Zhang^b, Shanshan Li^{a,c}, Gail Williams^a, Chao Liu^b, Geoffrey G. Morgan^d, Jouni J.K. Jaakkola^e, Yuming Guo^{a,c,*}

^a School of Public Health, University of Queensland, Brisbane, Australia

^b Center for Disease Surveillance & Research, Institute of Disease Control and Prevention, Academy of Military Medical Science, Beijing, China

^c Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia

^d University Centre for Rural Health, University of Sydney, Lismore, NSW, Australia

^e Center for Environmental and Respiratory Health Research, Institute of Health Sciences, University of Oulu, Oulu, Finland

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ABSTRACT

Background: China's rapid economic development has resulted in severe particulate matter (PM) air pollution and the control and prevention of infectious disease is an ongoing priority. This study examined the relationships between short-term exposure to ambient particles with aerodynamic diameter $\leq 2.5 \mu\text{m}$ (PM_{2.5}) and measles incidence in China.

Methods: Data on daily numbers of new measles cases and concentrations of ambient PM_{2.5} were collected from 21 cities in China during Oct 2013 and Dec 2014. Poisson regression was used to examine city-specific associations of PM_{2.5} and measles, with a constrained distributed lag model, after adjusting for seasonality, day of the week, and weather conditions. Then, the effects at the national scale were pooled with a random-effect meta-analysis.

Results: A $10 \mu\text{g}/\text{m}^3$ increase in PM_{2.5} at lag 1 day, lag 2 day and lag 3 day was significantly associated with increased measles incidence [relative risk (RR) and 95% confidence interval (CI) were 1.010 (1.003, 1.018), 1.010 (1.003, 1.016) and 1.006 (1.000, 1.012), respectively]. The cumulative relative risk of measles associated with PM_{2.5} at lag 1–3 days was 1.029 (95% CI: 1.010, 1.048). Stratified analyses by meteorological factors showed that the PM_{2.5} and measles associations were stronger on days with high temperature, low humidity, and high wind speed.

Conclusions: We provide new evidence that measles incidence is associated with exposure to ambient PM_{2.5} in China. Effective policies to reduce air pollution may also reduce measles incidence.

1. Introduction

Numerous studies conducted since 1990's have provided cumulative evidence of the adverse health effects of particulate air pollution (Dockery, 2009). A recent global assessment estimated that 2.9 million deaths and 69.7 million disability-adjusted life-years per year were attributed to ambient particulate matter (PM) pollution (Forouzanfar et al., 2015). PM consists of both solid and liquid particles from various sources and the toxicity of PM is determined by particle size, surface area and chemical composition (Nel, 2005). Compared with coarse particles, fine particles with aerodynamic diameter $\leq 2.5 \mu\text{m}$ (PM_{2.5}) are more toxic, as they are inhaled more deeply into the lungs with longer residency times (Pope and Dockery, 2006).

Measles is a highly contagious disease which can lead to serious health consequences including death (Sotir et al., 2016), with a fatality rate of between 3% and 15% in high-income countries (Choe et al., 2015). In spite of the ongoing WHO vaccination program to eradicate measles worldwide since the 1990's, measles is still re-emerging in high-income countries (Holzmann et al., 2016) and measles outbreaks are still observed in upper middle-income countries, like China (Zhang et al., 2016a).

To date, most studies have focused on the effects of PM on cardiovascular and respiratory disease (Arnold, 2014). However, studies in recent years have also reported associations between PM and infectious diseases (e.g., influenza, hemorrhagic fever with renal syndrome and Hand, Foot, and Mouth Disease) (Feng et al., 2016; Han

* Corresponding author at: Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC 3004, Australia.

E-mail address: yuming.guo@monash.edu (Y. Guo).

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et al., 2013; Huang et al., 2016; Jang et al., 2015). Inhalation transports PM deep into the lung and virus attached to particles may invade the lower part of respiratory tract directly and thus enhance the induction of infections (Sedlmaier et al., 2009).

With the rapid economic growth and urbanization, China is experiencing very high concentrations of PM (Brauer et al., 2012). There are very few large-scale studies evaluating the health effects of PM in China due to the limited availability of data on health and air pollution. Particularly, no previous study has examined the relationship between short-term exposure to PM_{2.5} and measles incidence in China. In this study, we examined the effects of PM_{2.5} exposure on the daily incidence of new cases of measles in 21 cities in China with daily data on both ambient PM_{2.5} and measles incidence.

2. Materials

2.1. Data collection

2.1.1. Measles data

Daily numbers of incident cases of measles for 21 cities between 28th Oct 2013 and 31st Dec 2014 were obtained from the China Information System for Disease Control and Prevention (CISDCP). China has established the large internet-based communicable disease reporting system covering the entire nation since 2004 which addressed the delays and under-reporting of communicable diseases (Wang et al., 2007). As measles is on the list of notified disease in China (Class B) (Wang et al., 2008), all hospitals and clinics within the National Notifiable Disease Reporting System are mandated to report each confirmed measles case which is diagnosed by subsequent routine laboratory examination (Ma et al., 2014). In this study, all measles cases were confirmed by both epidemiological linkage or clinical criteria and laboratory testing.

2.1.2. Ground PM_{2.5} measurement and weather conditions

Daily ground-level PM_{2.5} monitoring data during the same period as the measles data were obtained from China National Environmental Monitoring Center (CNEMC) administered by China Ministry of Environmental Protection. The monitoring data provided by CNEMC reflect the general background concentration of urban air pollution in Chinese cities. Details about ground measurements of PM_{2.5} were reported elsewhere (Cao et al., 2011; Zhou et al., 2014). Meteorological data for the 21 cities during the study period were obtained from the China Meteorological Data Sharing Service System of China Meteorological Administration (<http://data.cma.gov.cn>). Daily data on temperature (°C), relative humidity (%) and wind speed (km/h) were used for analysis.

2.2. Statistical analysis

The PM_{2.5}-measles association was examined by a two-stage analytic method with data on PM_{2.5}, count of incident measles cases and weather conditions in 21 cities in China using an approach previously described by Gasparrini et al. (Gasparrini et al., 2012, 2015; Guo et al., 2014). In the first stage, a time series model was used to estimate the city-specific PM_{2.5}-measles association, and in the second stage, these associations were pooled at the national level with a random-effect meta-analysis.

2.2.1. First stage of analysis

The City-specific PM_{2.5}-measles associations were examined with a time series Poisson regression model allowing for over-dispersion. A natural cubic spline with 7 degrees of freedom per year for time was used to control for the long-term trend and seasonality and a category variable was included in the model to control for the effect of day of the week (Peng et al., 2006). The delayed effects of meteorological factors (e.g., temperature, relative humidity and wind speed) were also controlled for with a seven-day moving average of each meteorological variable and a natural cubic spline with 4 degrees of freedom (Guo et al., 2013). To model the delayed effects of PM_{2.5}, a constrained distributed lag model (CDLM) was fitted for PM_{2.5} using natural cubic splines with three degrees of freedom (Gasparrini, 2014). To evaluate the potential modifying effects of PM_{2.5} on measles by meteorological factors, stratified analyses were performed by tertiles of 0–7 days' moving average of temperature, relative humidity and wind speed (as categorical variables) in each city during the study period (Atkinson et al., 1999; Chen et al., 2017).

2.2.2. Second stage of analysis

In the second stage, a meta-analysis was conducted to pool the city-specific PM_{2.5}-measles associations into a country-level effect estimate. The random-effects meta-analysis was fitted by maximum likelihood estimation to examine both within and between city variations regarding effect estimates (Gasparrini et al., 2012; Jackson et al., 2011). The pooled effect-estimates of PM_{2.5} on measles were expressed as relative risks (RR) with a 10 µg/m³ unit increase in PM_{2.5} and corresponding 95% confidence intervals (CI) were also calculated.

Sensitivity analyses were also performed for city-specific models to test the robustness of results. The lag days were changed to 15 days for PM_{2.5} to check whether the use of 7 lag days was sufficient to model its effects on measles. Precipitation was also included in the analysis. In addition, degrees of freedom for meteorological variables (3–6 df) and for time of the year (6–10 df) were modified. The stratified analyses with quartiles of meteorological variables were also performed and the results were compared with those using tertiles of meteorological variables. R software (version 3.2.2, R Development Core Team 2009) was used for all data analysis with “dnlm” and “mvmeta” packages.

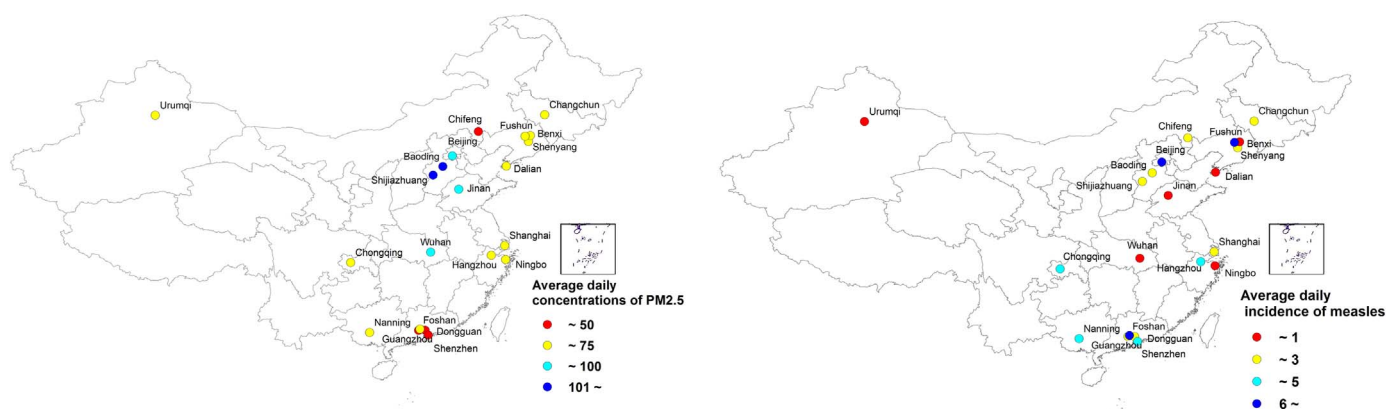


Fig. 1. Average daily concentrations of PM_{2.5} (µg/m³) and incidence of measles (average number per day) in 21 cities of China.

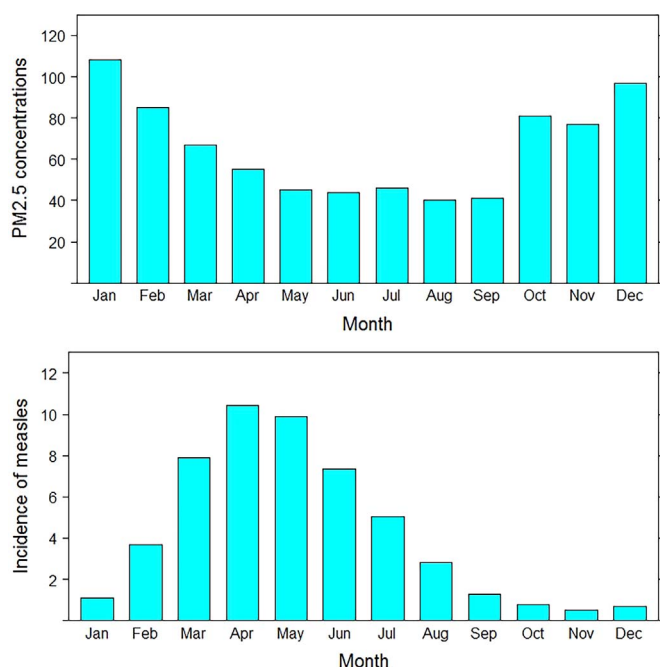


Fig. 2. Monthly average concentrations of PM_{2.5} (µg/m³) and incidence of measles (numbers per day) for all 21 cities.

3. Results

The average daily concentrations of ambient PM_{2.5} and incidence of measles in 21 cities during the study period were shown in Fig. 1. Cities with high levels of PM_{2.5} (> 101 µg/m³) were located in north of China including Baoding and Shijiazhuang. The highest concentrations of PM_{2.5} were observed in Baoding, Hebei Province (131.6 µg/m³). While cities showing low levels of PM_{2.5} (< 50 µg/m³) were located in south of China except for Chifeng, for example Shenzhen and Dongguan. Among all cities, Shenzhen in Guangdong Province had the lowest level of PM_{2.5} (36.3 µg/m³).

In total, 34,309 incident cases of measles were identified during the study period. The highest average daily numbers of measles occurred in Beijing and Guanzhou (n = 22 and 19, respectively). For the rest of the cities, daily numbers of measles were under 6. Cities with low daily numbers (n < 1) of measles were mainly located in eastern coastal areas of China, among which Jinan in Shandong Province had the lowest daily number of measles (n = 0.6).

Fig. 2 shows the average daily concentrations of PM_{2.5} and daily number of measles in different months. The highest level of PM_{2.5} was observed in January (108.4 µg/m³) while the lowest was observed in August (40.5 µg/m³). Substantial differences were seen in daily numbers of measles between different months. Average daily number of measles was highest in April, whereas lowest in November (n = 10 and 1, respectively).

Fig. 3 shows the pooled effect estimates of PM_{2.5} on measles for lag days (lag 0 day to lag 7 day) obtained from the random-effects meta-analysis. PM_{2.5} was significantly associated with measles at lag 1 day, lag 2 day and lag 3 day [RR and 95% CI were 1.010 (1.003, 1.018), 1.010 (1.003, 1.016) and 1.006 (1.000, 1.012), respectively]. Thus, the pooled effect estimates of for a three-day cumulative PM_{2.5} exposure on measles at lag 1–3 days were further evaluated. Strong effects (RR > 1.080) were observed in cities including Hangzhou, Urumqi, Ningbo and Dongguan (Fig. 4). Overall, meta-analysis analysis shows that nationwide measles incidence was significantly associated with an increase of 10 µg/m³ in PM_{2.5} at lag 1–3 days (pooled RR: 1.029, 95% CI: 1.010, 1.048).

Table 1 shows the pooled effects estimates of PM_{2.5} on measles at lag 1–3 days stratified by temperature, relative humidity and wind

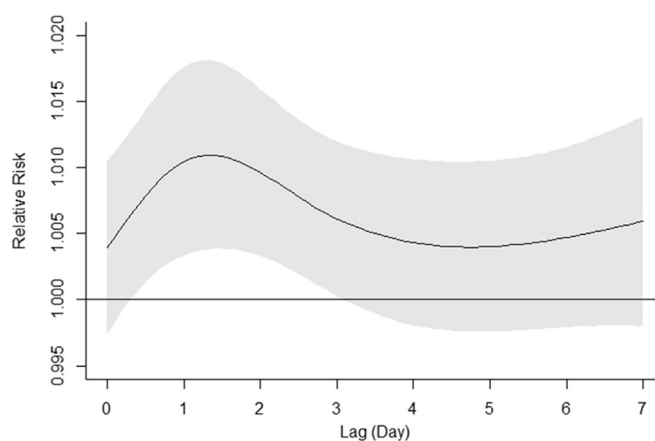


Fig. 3. The association between incidence of measles and an increase of 10 µg/m³ in PM_{2.5} at lags of 0–7 days. The black line indicates mean relative risk and the grey area indicates 95% confidence interval.

speed, which were divided into three levels (high, medium and low) according to tertiles of each meteorological variable. Strong and significant associations at lag 1–3 days between PM_{2.5} and measles were observed for days with high temperature (pooled RR: 1.027, 95% CI: 1.004, 1.051). Also stronger effects of PM_{2.5} on measles at lag 1–3 days were observed for days with low relative humidity (pooled RR: 1.027, 95% CI: 1.005, 1.050) and high wind speed (pooled RR: 1.024, 95% CI: 1.010, 1.038). Detailed results for each city are shown in Figs. S1S3 in the Appendix.

Our findings were robust to a range of sensitivity analyses including changing the maximum lag days to 15 days for PM_{2.5}, modifying the degrees of freedom for meteorological variables (3–6 df) and for time per year (6–10 df) or adjusting for the effects of precipitation. The results for PM_{2.5}-measles association with longer maximum lag times are shown in Figs. S4–S5 in the Appendix. In addition, stratified analysis with tertiles of meteorological variables showed more robust results and better model performance than those with quartiles of meteorological variables (Table S1–S3 in the Appendix).

4. Discussion

With the establishment of reporting system for infectious diseases and high coverage of immunization system, the incidence of measles in China has dropped dramatically since the 1970s (Ma et al., 2011; Wang et al., 2008). However, challenges remained as new genotypes of measles virus were identified and measles outbreaks were observed in some local areas and among particular population groups (Zhang et al., 2016a, 2010, 2016b). To the best of our knowledge, this is the first study to examine the effect of ambient PM_{2.5} on incidence of measles using data on incident cases of measles and ground monitoring of PM_{2.5} in 21 cities of China. We found the incidence of measles was statistically significantly associated with ambient PM_{2.5} across lag 1–3 days. Stratified analyses show that stronger effects were observed for days with high temperature, days with low humidity, and day with high wind speed.

To date, very few studies have focused on the effect of air pollution on transmission of measles. A study conducted in a Korean city reported a negative, non-significant association between incidence of measles and PM_{2.5} (r = −0.261) (Jang et al., 2015). The inconsistency between the Korean study and our findings may be due to: 1) the present study estimated the lagged effects of PM_{2.5} and took into account a wide range of potential confounders; 2) the present findings were based on a larger data set with greater statistical power than the Korean study; 3) potential behavioural and health services access difference between China and Korea (Eggleston and Hsieh, 2004; Zhang et al., 2005). Previous studies have reported significant associations between

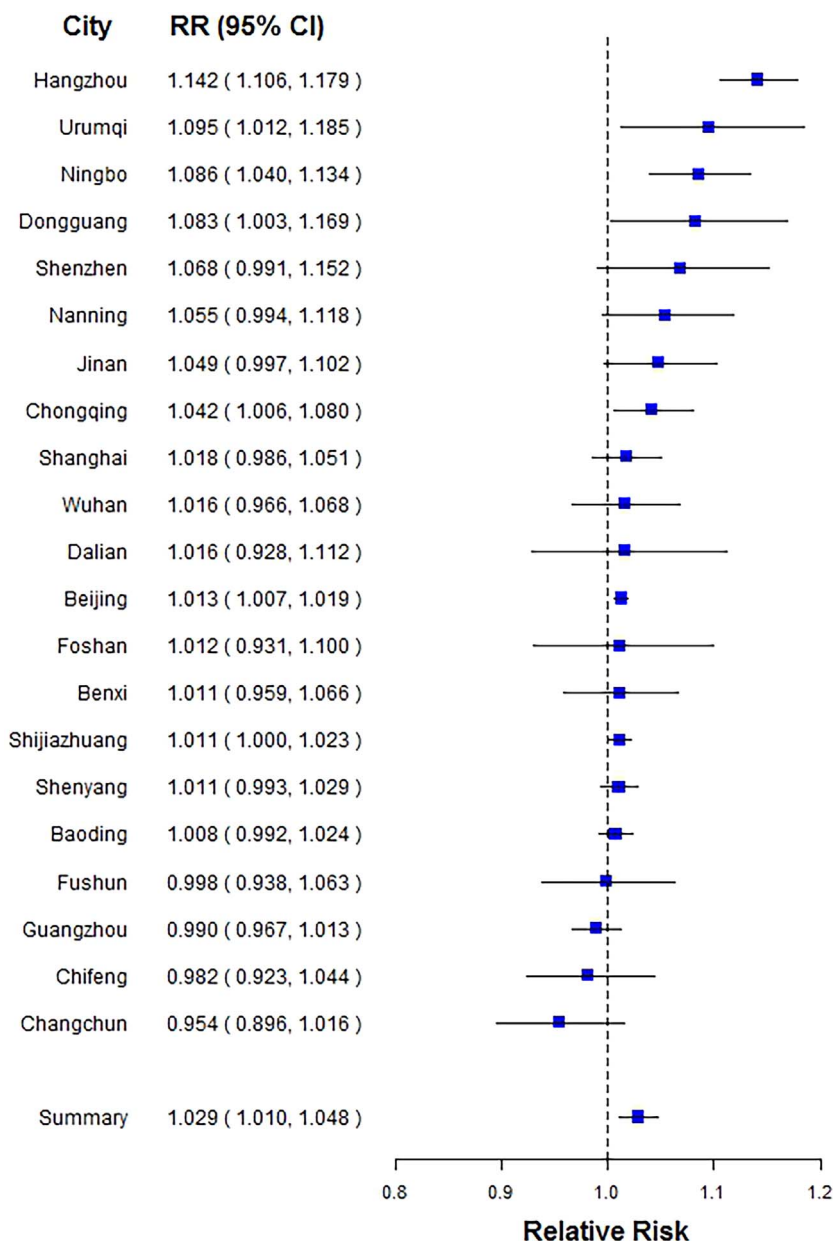


Fig. 4. The cumulative relative risks of measles incidence associated with an increase of 10 µg/m³ in PM_{2.5} over lags of 1–3 days.

Table 1

The association between cumulative exposure to PM_{2.5} and incidence of measles. Pooled-effect estimates (RR) and 95% confidence intervals (CI) were calculated for a unit increase of 10 µg/m³ in PM_{2.5} overall lags of 1–3 days and stratified by meteorological factors.

Variable	RR (95% CI)		
	Low ^a	Medium ^a	High ^a
Temperature	1.012 (1.007, 1.016)	1.019 (0.999, 1.040)	1.027 (1.004, 1.051)
Relative humidity	1.027 (1.005, 1.050)	1.006 (0.990, 1.023)	1.022 (1.007, 1.038)
Wind speed	1.022 (1.003, 1.041)	1.009 (0.989, 1.030)	1.024 (1.010, 1.038)

^a Low, medium and high indicate three strata of meteorological variables (minimum to the first tertile, the first to the second tertile, the second tertile to maximum, respectively).

ambient particulate air pollution and other infectious diseases, including hemorrhagic fever and influenza (Han et al., 2013; Liang et al., 2014).

There are several potential mechanisms for the PM_{2.5}-measles association. Measles viruses attached to ambient particles may be transported over long distances under favourable weather conditions, for example dust storm days (Chen et al., 2010). Measles is a highly infectious diseases among children and exposure to air pollution makes children's airways more vulnerable to respiratory infections (Brugha and Grigg, 2014). There is experimental evidence that the lung defence mechanism against virus particles (mucociliary clearance, particle transport and detoxification) is weakened by exposure to air pollutants (Chauhan, 2003). Exposure to ambient particles can trigger the antioxidant defence which may further cause mutations in genetic expression and make individuals more sensitive to respiratory infection (Nel, 2005). In addition, meteorological factors influence both PM_{2.5} concentrations and measles transmission. For example, ambient temperature has effects on fuel usage and ambient chemical reactions which are relevant to concentrations of PM_{2.5} and humidity affects removal of

aerosol particles by wet scavenging (Kulshrestha et al., 2009). Also, both ambient temperature and humidity influence the survival of measles virus (Yang et al., 2014). Thus considering PM_{2.5} and weather conditions together can better prevent and control measles transmission. Compared to cities in northern China including Changchun, Chifeng and Fushun, stronger PM_{2.5}-measles associations and more obvious modification effects of meteorological variables were observed in coastal cities in south-eastern China, for example, Hangzhou, Ningbo and Dongguan. The spatial variations might be associated with different local climate in these areas that southern China is characterized with warmer weather (Yang et al., 2014), and there are more travellers in coastal areas of China which is also linked with measles transmission (Sotir et al., 2016).

Due to rapid economic development and industrialization, China is experiencing severe ambient air pollution, especially in some megacities including Beijing, Shanghai and Guangzhou (Chan and Yao, 2008). Severe air pollution and hazy weather occur frequently in China and may be associated with the transmission and re-emergent outbreak of measles. Also, the rapid urbanization in China coincides with large population movements from rural to urban regions facilitating measles transmission and outbreaks of measles (Sotir et al., 2016; Wang et al., 2008). Government should develop effective policies to reduce air pollution which could also potentially reduce the transmission of measles in China. Considering the lagged effects of ambient PM_{2.5} on measles transmission, the government and relevant departments should prevent the potential outbreak of measles after several days' exposure to PM_{2.5} pollution. The surveillance system should be improved by reducing reaction time and by reducing underreporting cases, and coverage of immunization of measles should be increased especially for school-age children (Ma et al., 2011). People should reduce outdoor activities in hazy days and relevant equipment, such as personal masks, are in need for outdoor workers to protect themselves from severe air pollution (Zhou et al., 2015). Our findings could also be used to forecast the outbreak of measles in the future.

This is the first study to evaluate the effects of short-term exposure to PM_{2.5} on the incidence of measles. Robust and reliable results at the national scale were obtained with a meta-analysis for results from 21 cities of China. A wide range of potential confounders were taken into account and the results were further verified by a series of sensitivity analyses. However, this study also has several limitations. There might be under-reported cases of measles in the reporting system, as cases of measles may also be identified by hospitals or clinics out of the surveillance system. As with most air pollution time series studies we used PM_{2.5} data from fixed monitoring stations to assess individual exposure, which might make the effect estimates towards to null. Apart from meteorological variables, other factors might be associated with transmission of measles that were not included in our analysis due to unavailability of data, e.g., access to vaccine and socioeconomic factors (Marin et al., 2006; Steingart et al., 1999).

5. Conclusion

The results of this study provide evidence that the incidence of measles is associated with short-term exposure to ambient PM_{2.5} in China. We recommend future studies assess the effects of air pollution on measles transmission to further investigate the association we have identified. The potential effect of ambient PM_{2.5} on measles incidence should be considered when developing strategies for control and prevention of measles.

Competing financial interests

The authors declare they have no actual or potential competing financial interests.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.envres.2017.03.046.

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