Effect of ambient temperature on incidence of tuberculosis and effect modification by meteorological factors in Jinan, China during 2012-2015: A time-series analysis

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KEYWORDS
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Abstract

Objective For assessing the nonlinearity and delayed effect of temperature on incidence of tuberculosis and effect modification by meteorology factors, daily data on meteorological factors, air pollutants and incidence were obtained in Jinan, China, from 2012 to 2015.

Methods A distributed lag non-linear model (DLNM) combined with quasi-Poisson regression model was employed to assess the associations. We further built a series of weather-stratified models to assess the effect modification by meteorological factors.

Results The correlation between tuberculosis cases and daily average temperature (Tmean) was negatively nonlinear with a delayed effect. At the current day (lag 0), the increase of Tmean decreased the risk of tuberculosis incidence; over lag 0-70 days, the decrease of low Tmean and the increase of the high Tmean both indicated the increased risk of TB. The cold temperature showed an immediate effect at the current day, with a harvesting effect in the following days. The effect modifications by relative humidity, wind speed and sunshine duration were observed.

Conclusion The cold effect accelerates the onset of potentially infected people in the short term. It is necessary to consider effect modification by meteorological factors in assessing temperature effects on incidence of tuberculosis. Which might shed light on the strategy of tuberculosis prevention and control.

Background

In the past decades, the prospect of continued global warming, climate change,
serious pollution and extreme weather events has concentrated attention on the harmful impacts of environment on public health. Many studies (Kunst et al., 1993, Shaposhnikov and Revich, 2018, Yu, 2009) have reported an increased mortality caused by high or low temperature. However, previous studies mainly focused on the relationships between meteorological factors and chronic diseases, such as respiratory diseases (RD) (Li Mengmeng et al., 2019), cardiovascular diseases (CVD) and myocardial infarction (Yang et al., 2017). With growing concerns about climate change, an increasing number of studies also began to focus on associations of weather variability with the fluctuations of infectious diseases and suggested that weather factors play an important role in infection incidences (Heaney et al., 2016), such as hand-foot-mouth disease (Tian et al., 2018), Zika virus infection (Chien et al., 2018) and diarrhea (Wang et al., 2019).

Worldwide, Tuberculosis (TB) is one of the top 10 causes of death and the leading cause from a single infectious agent (above HIV/AIDS). Millions of people continue to fall sick with TB each year. Two thirds of cases were in eight countries with the highest rates in India (27%), China (9%) and Indonesia (8%). China is not only the second largest country with the highest number of cases, but also one of the three countries with the largest numbers of multidrug-resistant and rifampicin-resistance (MDR/RR-TB) (13%). (World Health Organization, 2018) TB remains an ongoing intractable health challenge in China.

TB spread pattern is influenced by geographic and social factors, which indicated it is necessary to assess the impacts of temperature on TB in various regions. Seasonal fluctuations in TB notifications have been reported from a number of researches (Douglas et al., 1996, Naranbat et al., 2009, Willis et al., 2012), these studies also suggest delayed effects of environmental factors. Further, it has been
shown that the risk of TB has a correlation with climate and extreme heat or cold temperatures. (Beiranvand et al., 2016, Onozuka and Hagihara, 2015) Due to the diversity of temperature ranges and fluctuations, climate types, and economic environments in different regions, the relationships between temperature and TB in different regions should be studied and will provide important evidence also for other countries.

Moreover, a lot of studies in different regions put forward that other environmental factors can also exert an effect on TB incidence. For example, the areas with extra dry climate are high-risk regions of TB (Onozuka and Hagihara, 2015); the decrease of SD lead to an increased risk of TB (Koh et al., 2013); the TB incidence are positively associated with the WS (Li Q. et al., 2019, Rao et al., 2016). The meteorological and environmental factors are some of the central variables affecting the airborne transmission of pathogens. (Cole and Cook, 1998, Fernstrom and Goldblatt, 2013) Yet there have been only limited studies on effect modification by other meteorological factors on temperature effect on TB.

In addition to meteorological factors, air pollution has also been linked to TB risk. The effects of carbon monoxide (CO) and particulate matter less than 2.5 μm in aerodynamic diameter (PM$_{2.5}$) on incidence of TB were significant. (Fernandes et al., 2017, Liu et al., 2018, Smith et al., 2016) However, many studies (Li Mengmeng et al., 2019, Onozuka and Hagihara, 2015) of ambient temperature and health outcome did not account for air pollutants, and in the previous review (Basu and Samet, 2002), it was not clear whether air pollutants acted as confounders, effect modifiers, or both. It is critical to control the effect of pollutants in models with ambient temperature, since they may often exert the influence on a daily basis (Basu, 2009). On the other hand, Jinan is a typical heavily polluted area, and the
relationship between cases of TB and pollutants have been determined in Jinan. Thus, the actual association between ambient temperature and incidence can be observed, only after controlling pollutants in the models.

Here, this study aimed to assess the effect of ambient temperature as well as delayed effect on TB based on the infectious disease surveillance data in Jinan by using distributed lag non-linear model (DLNM) controlling the effects of the pollutants affecting the infection of TB. Although almost all studies that examine the effects of air pollution and mortality have controlled for meteorological factors, control for air pollution in studies assessing the effects of temperature has been rare. Simultaneously, based on the relationship between $T_{\text{mean}}$ and incidence of TB, this study also investigated if the other meteorological factors modify the temperature-TB incidence relationship. It will help plan effective intervention strategies for the prevention and control of TB in similar populations and help public health professionals to make response.

Methods

Study area and population

Jinan is located in the Mideast of China (36°01’N to 37°32’N, 116°11’E to 117°44’E). It towards the south is Tai Mountain, whilst the north is bordered by the Yellow River. Belonged to the warm temperate continental climate, four seasons. The total area is 7,998 km$^2$, and the total population reaches 7.32 million. The male/female ratio of target population is 0.984. Fourteen percent of the total population is the elderly (65 years of age). In 2017, the density of population is 805 person/km$^2$. (Jinan Statistical Bureau, 2018) In recent years, Jinan’s annual average temperature has gradually increased and extreme weather events have occurred frequently with
extreme $T_{\text{max}}$ recorded 41.7 °C and extreme $T_{\text{min}}$ recorded -17 °C (Wang et al., 2016). In 2017, the number of high temperature (daily maximum temperature ≥ 35 °C) days reached 30, which was the most numerous days for nearly two decades. (Jinan Meteorological Bureau, 2018) At the same time, Jinan is a typical high-pollution city. At the beginning and end of each year, continuous haze appears in Jinan. (Jinan Meteorological Bureau, 2017, 2018)

Data collection

Daily TB cases counts data, from January 1, 2012 to December 31, 2015, were obtained from Jinan Municipal Center for Disease Control and Prevention (JMCDC), which has access to the Chinese National Notifiable Communicable Diseases Surveillance System. As a notifiable infectious disease in China, all cases of TB are required to be reported online within 24 hours after diagnosis in the hospital. The TB cases in the JMCDC database included all newly diagnosed active pulmonary TB cases.

Daily meteorological data including daily maximum ($T_{\text{max}}$), mean ($T_{\text{mean}}$), and minimum ($T_{\text{min}}$) temperature, mean relative humidity (RH), wind speed (WS), sunshine duration (SD), air pressure (PRESS) and daily amount of precipitation (PRCP) were collected from the China Meteorological Sharing Service System Network (http://cdc.cma.gov.cn/home.do) during the same period as the TB cases data.

Daily mean hourly air pollutants data (inhalable PM$_{2.5}$ and CO) were obtained from the Jinan Environmental Monitoring Center. The data was obtained from 14 fixed monitoring stations, spanning the entire region, including 11 sites located in urban areas and 3 sites located in suburban county areas. Daily average values of air pollution were used in this study and calculated the average from above 14 fixed
monitoring stations.

Statistical analysis

Firstly, a descriptive analysis was performed to describe the distribution of TB cases, meteorological factors and pollutants during the study period. The minimum, maximum, quartiles, mean and standard deviation were calculated. The associations of TB cases with meteorological factors and air pollutants were assessed by Pearson’s correlation test. Factors un-related to the incidence of TB were excluded in the model.

Secondly, the effect of $T_{\text{mean}}$ on TB cases was estimated utilizing a distributed lag non-linear model (DLNM) with quasi-Poisson regression. DLNM, a flexible modelling framework, describes simultaneously the shape of the relationship along both the space of the predictor and the lag dimension of its occurrence. (Gasparrini et al., 2011). As potential confounders, long-term trend/seasonality (by using day of study), day of the week (DOW), public holiday (HOD), RH, WS, SD, CO and PM$_{2.5}$ were considered. Their effects were removed on by using smooth functions to calculate net effect of $T_{\text{mean}}$ on incidence of TB. (Hastie and Tibshirani, 1990) The degrees of freedom (df) of splines in different functions were automatically selected by Generalized Approximate Cross-Validation (GACV). The Pearson’s correlation test and collinearity diagnosis were used to analyze the correlation and collinearity between the various factors. Generally, when $|r_s| \geq 0.8$, it is considered that there is a strong correlation between factors; when the variance inflation factor (VIF) $\geq 10$, it is considered that there may be a serious collinearity between factors (D. Beaumont et al., 1981, Schroeder et al., 1990).

Instead of using a linear term, a cross matrix for the daily temperature was established to represent the non-linear and delayed effect. We selected a natural
cubic spline basis to model the non-linear effects using three df in the temperature space, and the polynomials with four degrees to examine the delayed effect. Model selection for lag structure was carried out by minimizing the GACV criteria; these lag structure (3, 4, 5, 6, 7, 8, 9, 10, 11, 12 weeks) corresponded to different GACV values (1.680, 1.677, 1.680, 1.667, 1.666, 1.673, 1.665, 1.655, 1.661, 1.661) during the modeling attempt. Referring to the previous study (Onozuka and Hagihara, 2015, Xiao et al., 2018) and GACV values, we set a maximum lag structure as 70 days (10 weeks) as it also is longer than the incubation period (4-8 weeks). We used mean value of $T_{\text{mean}}$ (15.0°C) as the reference to calculate the relative risks ($RR$s), and used the minimum, the 5\textsuperscript{th} and 25\textsuperscript{th} of percentiles temperature as the cold temperature effect and the maximum, the 95\textsuperscript{th} and 75\textsuperscript{th} of percentiles as the hot effect.

Thirdly, a weather-stratified DLNM was developed to quantify the effect modification by RH, WS and SD. We used this model to estimate the temperature effect for two meteorological factors strata: <50\textsuperscript{th} percentile and >50\textsuperscript{th} percentile. Meanwhile, in the research process, it was found that the effects of temperature ranging from the 25\textsuperscript{th} to 75\textsuperscript{th} quantile were basically not significant. We selected a double threshold function as basis to model the cold and hot temperature effects with the 25\textsuperscript{th} and 75\textsuperscript{th} quartiles as the cut-off points. We used the interval as a reference to estimate the cold temperature effect (the 5\textsuperscript{th} percentile) and hot temperature effect (the 95\textsuperscript{th} percentiles). Further, we also insert an interaction function of $T_{\text{mean}}$ with RH, WS or SD to identify whether the exists of effect modifications are due to chance. (Kamangar, 2012)

Sensitivity analyses
To check the robustness and validity of the main findings of this study, sensitivity analyses were performed by adjusting df of temperature (df = 2, 4, 5), fitting the models to TB cases at lag 0 and lag 0–70 days. Further, we also conducted sensitivity analyses by adjusting one environmental factor at a time or excluding all air pollution factors (PM$_{2.5}$, CO) or all meteorological factors (RH, WS, SD) from the model.

In this study, the relative risk (RR) and 95% confidence interval (95% CI) were used as the evaluation indexes of the effect. The analysis was performed by Stata software (version 15.0) and packages (splines, DLNM, mgcv) of R statistical software (version 3.5.2). Statistical significance was set at $P < 0.05$.

**Results**

**Descriptive analysis**

During the study period January 1, 2012 to December 31, 2015, 15,010 cases of TB were notified in the study area, and the 5$^{th}$, 25$^{th}$, 75$^{th}$ and 95$^{th}$ percentiles of daily $T_{\text{mean}}$ were -1.8°C, 5.2°C, 24.0°C and 29.0°C. Table 1 presents descriptive statistics for TB cases, pollutants and meteorological factors in Jinan, respectively. The time-series distributions of TB and $T_{\text{mean}}$ were shown in Fig. 1, demonstrating a seasonal trend for the series. The minimum of $T_{\text{mean}}$ gradually increased from 2012 to 2015, and the cases of TB fluctuated slightly with more cases occurring in spring and fall.

**Correlation analysis and collinearity diagnosis between TB cases and environmental factors**

An additional table exhibits the matrix of Pearson correlations between TB cases and other variables [see Additional file 1]. TB was positive correlated with $T_{\text{mean}}$, $T_{\text{max}}$, $T_{\text{min}}$, SD and WS, and negative correlated with PM$_{2.5}$, CO, PRESS and RH ($P < 0.05$). No statistical association was found between the TB cases and PRCP ($P >$
0.05). However, there was a strong negative correlation between PRESS and $T_{\text{mean}}$ ($r_s = -0.87$), and hence collinearity might exist. Variable PRCP and PRESS were excluded from the model. Through collinearity diagnosis, it was found that the VIF values of all factors in the model were $< 5$, so there was no severe collinearity, and the model was established.

The relationships between $T_{\text{mean}}$ and TB cases

Fig. 2 illustrates the three-dimensional graph of a nonlinear relationship between $T_{\text{mean}}$ and TB cases, with reference at 15.0°C. Fig. 3 presents the lag-response relationships between different $T_{\text{mean}}$ levels (minimum, the 5th, 25th, 75th and 95th percentiles and maximum temperature) and incidence. The effect of the minimum temperature led to the high risk in TB incidence at lag 0 and the second incidence peak at the lag 57. The $-1.8$ °C also presented a similar trend. The effect of the 25th percentile of $T_{\text{mean}}$ remained insignificant and the risk of the 75th percentile fluctuated slightly. The 95th percentile peaked after lag 14 and had no significance in the following days.

Fig.4 shows the effect and cumulative effect of temperature after different lag days. Low temperature increased the RR of TB incidence at the lag 0. The overall cumulative effect showed a U-shape; however, effects had considerable statistical variability reflected by large confidence intervals due to a small number of maximum and minimum $T_{\text{mean}}$ days. More specifically, relative to 15.0°C, the colder temperature showed a lower risk after lag 21 and lag 0-42 days. After lag 63, the risk of TB incidence increased with the decrease of $T_{\text{mean}}$, and the cumulative risk of 10.1°C was 0.90 (95% CI: 0.81, 1.00) and of 25.2°C was 1.18 (95% CI: 1.02, 1.37) after lag 0-63 days.
The effect modification by meteorological factors

Combined the effects at the cold temperature (the 5th percentile of $T_{mean}$) compared with the 25th percentile and the hot temperature (the 95th percentile of $T_{mean}$) compared with the 75th percentile, are presented in Fig. 5. High RH increased the risk of TB in hot temperature situation after lag 21 and in cold temperature situation after lag 70, respectively. In addition, low WS increased the risk for temperature effect at different lag period; and high WS decreased the risk in hot temperature at lag 49. Furthermore, low SD increased the risk in cold temperature situation at lag 21. By verifying the interaction terms, the interactions of RH ($P = 0.001$), WS ($P = 0.004$) and SD ($P = 0.02$) with $T_{mean}$ were significant, respectively.

Sensitivity analyses
An additional table contains details of the results from the sensitivity analyses [see Additional file 2]. When we changed df (2, 4, 5 df) for the temperature space in the DLNM, the estimated changes were slightly smaller. Adjusting for meteorological factors slightly changed the overall cumulative $RR$s, whereas adjusting for air pollution gave slightly larger in cold effect but still did not change substantially. Our sensitivity analyses suggested that the results were not dependent on modeling assumptions.

Discussion
We examined the effects of ambient temperature on TB cases in Jinan, one of the so-called four “ovens” with serious air pollution in mid-eastern China, during 2012 to 2015.

Our results of a negative and non-linear relationship between ambient temperature
and notified cases of TB infection are consistent with research carried out in other
countries with different weather conditions (Onozuka and Hagihara, 2015, Rao et
al., 2016, Xiao et al., 2018). We also found that the risk of TB incidence was greatly
affected by extreme temperature on the current day. On the other hand, the overall
cumulative effect showed trends for increased risks for decline of cold temperature
and increase of hot temperature.

Many investigators (Liao et al., 2012, Onozuka and Hagihara, 2015, Rao et al., 2016)
have reported the delayed effect in the relationship between TB and cold or hot
effect. Our study also confirmed that the delayed effect existed. The peak of cold
effect appeared earlier than that of hot effect, which is comparable to the results of
a study (Onozuka and Hagihara, 2015) conducted in Japan. In contrast to this
study’s findings, however, the results in the Japan study showed that high
temperature effects were generally constant at lag periods of up to 12 weeks,
whereas the effects in low temperature ranges were persistent over shorter lag
periods and diminished over time. This may be due to the warm climate in Japan, so
the 5th percentile temperature (5.4 °C) in the Japan study was only equivalent to the
25th percentile in our study. Yuanyuan Xiao (Xiao et al., 2018) found that average
temperature was inversely associated with TB incidence at a lag period of 2 months.
Similarly, we found that T_{mean} under 15°C was also negatively associated with TB at
lag 63, but hot effect was not significant.

The difference in lag effects as our results of DLNMs suggested would be also
related to some characteristics, and some researchers have provided this context
for interpreting our results. Fares (Fares, 2011) manifested that lower temperature
during winter may induce the susceptibility to respiratory epithelium infection. The
fluctuation in weather temperature during winter may also act on the respiratory epithelium by slowing mucociliary clearance and inhibiting phagocytosis, causing pathophysiological responses, which then lead to increase the susceptibility to infection. (Mourtzoukou and Falagas, 2007) In addition, in winter in Jinan, the citywide coal-burning heating exacerbates smog, which would increase the number of carriers that can spread pathogens (Fernstrom and Goldblatt, 2013); Liu (Liu et al., 2018) provided the evidence that heavy pollution is positively correlated with TB incidence. Furthermore, Naranbat (Naranbat et al., 2009) hypothesized that temperature may change the indoor time people spend. China is a populous country, people gather, and close door and windows during the winter, and the crowded indoor environment is also a risk factor for infectious diseases.

We found some evidence of harvesting effect in our study; there was an incidence deficit for the minimum and the 5th percentile $T_{\text{mean}}$ at the lag about 3 weeks. We speculate that the harvesting effect would support the mechanism of temperature influencing the incidence risk. In particular, it may be that presents in extreme cold temperature only hasten the TB incidences of individuals in a small, frail, infected subset of the population who will attack even in the absence of extreme cold effect. A possible reason is extreme cold air attacks the body’s respiratory and immune systems, speeding up the onset of TB to infected people. In contrast, the hot effect on the respiratory system are less direct. (Roberts and Switzer, 2004) However, meteorological factors may play an important role. Our findings showed that low RH decreased the risk of TB for temperature which was different from Yingjie Zhang’s research (Zhang et al., 2019). In cold temperature situation, the increased RH may create a suitable environment for the growth and reproduction of
tuberculosis. Our study also suggested that low WS could increase the effect of low $T_{\text{mean}}$ on TB at the current day and at lag 70. The higher WS could accelerate ventilation, dilute the concentration of bacteria and help reduce the risk of becoming infected. Although another study (Li Q. et al., 2019) indicated that areas with stronger wind speeds tend to have a higher infection risk, our study findings were supported by the findings of Kai Cao (Cao et al., 2016). As has been found in a few other studies (Cao et al., 2016, Koh et al., 2013, Rao et al., 2016), the low SD would raise the risk of TB. Our findings showed that the low level of SD positively modified on cold temperature effect. We speculate that this result would be also related to some view point indicated by these studies (Nnoaham and Clarke, 2008, Wilkinson et al., 2000) on TB that low serum vitamin D levels were associated with higher risk of active tuberculosis. The low SD would affect the absorption of vitamin D for public. However, there was still a lack of validation of biological mechanisms of vitamin D on TB, which should be a further direction.

A study limitation is the use of data on temperature and air pollution from fixed monitoring sites rather than measuring individual exposure, which would bring about measurement errors because individual exposure temperature may be not entirely identify with outdoor average temperature. Secondly, cold effect and hot effect was calculated by comparing the 5th to the 25th percentile and the 95th to the 75th percentile temperatures. This accounted for the effect of cold and hot temperature to some extent. But the reason for this way is that the study population is not sensitive to $T_{\text{mean}}$ ranging from the 25th to the 75th percentile, there may be inappropriateness when extrapolating calculating method to an unequal population or other diseases. In addition, we only used data from Jinan to
examine the effects of temperature on TB so the findings may not be generalizable to other areas.

Conclusions
The tuberculosis incidence in Jinan was found to be nonlinear and negative related with temperature, with a harvesting effect for cold temperature. Findings of this study add to the evidence that high temperatures have slower delayed effects on TB incidence while low temperatures appear to exhibit higher effects. Considering effect modification by RH, WS and SD in assessing temperature effects on TB incidence may be essential. These findings may have important implications for public health officials to control and prevent the TB risk of exposure to ambient temperature. Meanwhile, the public are also suggested to keep clear life environment, ventilate usually and supplement Vitamin D. Exploring the influencing factor and mechanism of TB can shed light on future TB control programs in China and even other country.

Abbreviations
TB
tuberculosis
PM$_{2.5}$
particulate matter less than 2.5 μm in aerodynamic diameter
$T_{\text{mean}}$
daily average temperature
$T_{\text{max}}$
daily maximum temperature
$T_{\text{min}}$

daily minimum temperature

DLNM
distributed lag non-linear model

RH
relative humidity

WS
wind speed

SD
sunshine duration

PRCP
precipitation

PRESS
air pressure

Declarations

Ethics approval and consent to participate

Not applicable. Our study did not involve human trials. Newly diagnosed active pulmonary TB cases counts data were obtained from the Chinese National Notifiable Communicable Diseases Surveillance System. The system is a real-time network monitoring system for 37 statutory infectious diseases built by the Chinese Center for Disease Control and Prevention (CDC). Shuigao Jin has given an introduction to the system (Jin et al., 2006)

Consent for publication

Not applicable
Availability of data and material

The data that support the findings of this study are available from Jinan Municipal Center for Disease Control and Prevention (JMCDC) but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available.

Competing interests

The authors declare that they have no competing interests.

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Authors’ contributions

RY: Conceptualization, Software, Formal Analysis, Writing—Original Draft
LC: Investigation, Data Curation, Funding Acquisition
JZ: Investigation, Validation, Funding Acquisition
MW: Investigation, Data Curation
CJ: Conceptualization, Methodology, Formal Analysis, Supervision
SR: Supervision, Data Curation, Funding Acquisition
All authors read and approved the final
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Table

**Table. 1** Summary of daily environmental variables and incidence of TB in Jinan city, 2012–2015
| Variables | Minimum | Percentile | Maximum |
|-----------|---------|------------|---------|
|          | 25th    | 50th       | 75th    |          |
| Pollutants (μg/m³) |         |            |         |          |
| PM₂.₅    | 15      | 59         | 83      | 118      | 443      | 97 ± 58 |
| CO       | 465     | 990        | 1238    | 1631     | 6555     | 1408    |
| Meteorological Factor |         |            |         |          |
| Daily T<sub>mean</sub> (°C) | -9.4    | 5.2        | 16.9    | 24.0      | 33.8     | 15.0 ± 9 |
| Daily T<sub>max</sub> (°C) | -5.4    | 9.7        | 22.3    | 29.4      | 39.9     | 19.9 ± 8 |
| Daily T<sub>mix</sub> (°C) | -12.9   | 1.3        | 12.2    | 20.0      | 30.8     | 10.8 ± 8 |
| Daily RH (%) | 14      | 41         | 55      | 70        | 100      | 56 ± 5  |
| Daily SD (h) | 0.00    | 3.20       | 7.00    | 9.00      | 13.30    | 6.15 ± 4 |
| Daily WS (m/s) | 0.2     | 1.8        | 2.3     | 3.0       | 8.4      | 2.5 ± 1 |
| Daily PRESS (hPa) | 975.7   | 988.7      | 996.7   | 1003.6    | 1021.8   | 996.5   |
| Daily PRCP (mm) | 0.00    | 0.00       | 0.00    | 0.00      | 600.00   | 4.43 ± 2 |
| Case      | TB      | 0          | 2       | 4         | 7        | 26       | 5 ± 4   |

PM<sub>₂.₅</sub> fine particulate matter with an aerodynamic diameter of < 2.5 μm, CO carbon monoxide, T<sub>mean</sub> daily average temperature, T<sub>max</sub> daily maximum temperature, T<sub>min</sub> daily minimum temperature, RH relative humidity, SD sunshine duration, WS wind speed, PRESS pressure, PRCP daily amount of precipitation, TB case of TB

**Figures**
Figure 1

Daily time series of number of tuberculosis cases and daily average temperature
Figure 2

Relative risk of incidence of tuberculosis by daily average temperature (℃) and d

Figure 3

The effects of daily average temperature (℃) on incidence of tuberculosis along c
Pooled relative risks of TB incidence by daily average temperature over (A) lag 0, (B) lag 21, (C) lag 42, (D) lag 63.

Effect modification of the association between daily average temperature (°C) and tuberculosis.

Supplementary Files

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