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Research Article

# Short-Term Exposure to Coarse Particles and Dyslipidemia Risk in Chengdu, China: A Time-Series Study

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**Abstract**

**Objectives:** Dyslipidemia, as a major risk factor for atherosclerotic cardiovascular disease (CVD), contributed to a large number of deaths. Ambient air pollution was recognized as a significant risk factor for dyslipidemia. We designed the study to explore how short-term exposure to ambient particulate matter, especially PM2.5-10, affected the incidence of dyslipidemia.

**Methods:** We used lipid data from 309,654 persons provided by the Medical Examination Center of Sichuan Provincial People's Hospital. Daily air pollutants and meteorological data derived from the nearest eight monitoring sites owned by the China Meteorological Administration. To evaluate the acute effects of ambient particulate matter on dyslipidemia in both the spatial and lag dimensions, we used a distributed lag non-linear model.

**Results:** We found that an increase of PM2.5-10 concentrations with an interquartile range (29.5 μg/m3) was positively associated with dyslipidemia with apparent lag effects cumulative effects at the lag of 0–7days. Furthermore, we discovered the unique role of PM2.5-10 on hypertriglyceridemia with a lag day of 1-3 days after adjusting the effect of PM2.5, and the cumulative impacts of PM2.5-10 peaked at a lag of 0–4 days (RR 1.045, 95%CI 1.005-1.087, p-value=0.05). Stratified analyses showed that younger, female or physically lighter individuals were potentially vulnerable groups.

**Conclusions:** Our study found that PM2.5-10 positively link with hypertriglyceridemia at lag days.

## ABBREVIATIONS

TC: Total Cholesterol; LDL-C: Low-density Lipoprotein Cholesterol; HDL: High-density Lipoprotein; TG: Triglycerides; CVD: Cardiovascular Disease; HyperLDL-C: Hyperbetalipoproteinemia; GBD: Global Burden of Disease Study; PM: Particulate Matter; HyperTC: Hypercholesterolemia; $NO_2$: Nitrogen Dioxide; $SO_2$: Sulfur Dioxide; $O_3$: Ozone; RH: Relative Humidity; DLNM: Distributed Lag Non-linear Model; GAM: Generalized Additive Model; ns: Natural Cubic Spline; Df: Degrees of Freedom; BMI: Body Mass Index; RR: Relative Risk; CI: Confidence Interval; IQR: Interquartile Range; WHO: World Health Organization; AQG; Air Quality Guideline; VLDL: Very-low-density Lipoproteins

## INTRODUCTION

Dyslipidemia, referring to the imbalance of lipids such as total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein (HDL), and triglycerides (TG), has been linked to a wide variety of adverse effects in cardiovascular disease (CVD)[1], pancreatitis [2] and non-alcoholic fatty liver disease [3]. Moreover, a large number of deaths attributed to dyslipidemia; for example, hyperbetalipoproteinemia (hyperLDL-C), a high risk for ischemic heart disease and ischemic stroke, contributed to about 4.40 million deaths globally in 2019, according to Global Burden of Disease Study (GBD) [4]. Changes in the prevalence of dyslipidemia show the same trend as socioeconomic development and are related to diet and unhealthy lifestyle habits [5]. As China's social environment has shifted and its economic volume has skyrocketed in decades, the prevalence of dyslipidemia has rapidly and substantially increased to more than 34% [6]. Furthermore, rapid economic expansion causes vital environmental challenges alongside health problems.

Ambient particulate matter (PM) pollution strongly linked to social and economic development. And it represents one of the risk exposures with the largest increase from 2010 to 2019 [7], and is widely acknowledged as a significant risk factor for human health. Earlier studies have shown that prolonged exposure to PM significantly increased the mortality risk alongside various diseases, especially for CVD [8]. Dyslipidemia might be one of the possible mediators that mediate the effect of PM on mortality, as earlier research has established a link that prolonged PM exposure increased the risk of dyslipidemia [9]. However, the increased daily mortality and CVD risk associated with short-term PM exposure have raised considerable concern in recent years [10]. We then wanted to explore whether there was any link between short-term exposure to PM and dyslipidemia. As previous studies have not yielded consistent results, we previously estimated the effect of short-term exposure to $PM_{2.5}$ (fine particles, diameter < 2.5 μm) on dyslipidemia where found that $PM_{2.5}$ enhanced the relative risk of hyperTC (hypercholesterolemia), hyperLDL-C and hypertriglyceridemia (hyperTG) by a substantial amount [11]. In this article, we look more at the short-term role of $PM_{2.5\text{-}10}$ (coarse particles, 2.5 μm < diameter < 10 μm).

Ambient particulate matter is a heterogeneous combination of solid and liquid particles floating in the air with two main components, $PM_{2.5}$ and $PM_{2.5\text{-}10,}$ differ in terms of the impact on human health because of their diversity in composition and differential deposition in the body. A systematic review by Brunekreef, B.et al. proposed that fine and coarse particles are two different types of contaminants that must be examined separately in epidemiologic and research investigations [12]. Nevertheless, the health impacts of $PM_{2.5\text{-}10}$ have received increased attention. The earlier studies discovered the unique role in $PM_{2.5\text{-}10}$ in human health, including the mortality, morbidity, prevalence, or hospital admissions for various diseases [13,14]. Many studies explored inconsistent results about the relationship between $PM_{2.5\text{-}10}$ and dyslipidemia. Few studies reported that $PM_{2.5\text{-}10}$ correlated to changes in TG [15,16]. However, a study in Korea found no association between $PM_{2.5\text{-}10}$ and lipid profiles [17].

Based on existing studies, the link between exposure to $PM_{2.5\text{-}10}$ and dyslipidemia dosed not elucidated clearly. Our study attempted to explore the impact of short-term PM exposure on dyslipidemia, precisely the effect of $PM_{2.5\text{-}10}$, among Chinese adults in both the spatial and lag dimensions. In addition, we investigated the possible moderating effects of age, gender, and BMI on these correlations.

## MATERIALS AND METHODS

### Data collections

**Lipids data:** The lipid data collected from the Medical Examination Center of Sichuan Provincial People's Hospital. Peripheral venous blood samples collected from 309,654 subjects aged 18-79year-old. These samples were collected by trained healthcare professionals using the automatic biochemical analyzer (Olympus AU5421, Japan) following an overnight fast, spanning the period from May 10, 2015, to May 10, 2017. The lipid data recorded after biochemical analysis of peripheral venous blood samples. Dyslipidemia is the occurrence of one or more of the following conditions: hypercholesterolemia (hyperTC, TC≥ 5.18 mmol/L), hyperbetalipoproteinemia (hyperLDL-C, LDL-C ≥ 3.4 mmol/L), hypoalphalipoproteinemia (hypoHDL-C, HDL-C ≤ 1.3 mmol/L) and hypertriglyceridemia (hyperTG, TG≥ 1.7 mmol/L), according to the National Lipid Association Recommendations[18]. The study did not need informed consent as the data were without any personal identifiable information. This study was approved by Sichuan Province Academy of Medical Sciences (Ethics Committee Approval Number: 2017-156).

**Air pollution and meteorological data:** Air pollutants and meteorological data collected from eight environmental monitoring stations in Chengdu (http://www.cnemc.cn) from May 10, 2015, to May 10, 2017. Air pollutants data included 24-hour mean concentrations of $PM_{2.5}$, $PM_{10}$ (diameter < 10 μm), nitrogen dioxide ($NO_2$), sulfur dioxide ($SO_2$), and 8-hour mean concentrations of ozone ($O_3$). Daily mean the concentration of $PM_{2.5\text{-}10}$ were calculated by subtracting the daily mean concentrations of $PM_{2.5}$ from $PM_{10}$. Meteorological data included daily average temperature (°C) and day-to-day average relative humidity (RH). In the study there was no missing data.

### Statistical analysis

Because distributed lag non-linear model (DLNM)[19], has been used to characterize relationships with both immediate and delayed impacts of environmental stressors, we applied a quasi-Poisson generalized additive model (GAM) with DLNM to estimate the influence of short-term PM exposure on the incidence of dyslipidemia, particularly in its lag dimension. First, the implementation of this model rests on the foundation of a cross-basis bi-dimensional function, one for the exposure-response relationship and the other for the lag-response relationship. We fitted exposure-response associations using linear functions for air pollutants and non-linear function for temperature [20]. We fitted lag-exposure associations using polynomials function with degree of 3 and set the maximum lag to 7 days, which were typically short [21]**.** Second, as our interest was in short-term associations, we controlled the long-term patterns and seasonality by fitted time using natural cubic spline (ns) with 7 degrees of freedom (df) /year. We fitted the effect of RH using ns with 3 df and weekend days were also taken into account since exposure levels may be varied on weekdays and weekends. In addition, to avoid collinearity, $PM_{10}$ and $NO_2$ were not included in this multi-pollutant model. We set two models to further explore through the distinctive role of $PM_{2.5\text{-}10}$. The models are crude model and the adjusted model. The study obtained from the crude model after adjusting the effect of $PM_{2.5}$. Furthermore, the data stratified by sex (females and males), age (<45 years; ≥45 years) and BMI (<24 kg/m$^2$; ≥24 kg/m$^2$) for further analysis. We reported RRs with the 95% confidence interval (CI) of associations as the changes of the incidence of dyslipidemia for an increment of an interquartile range (IQR) concentration in three size-specific PM.

We performed sensitivity analyses by altering the df from 5 to 9 df/per year and from 3 to 5 df in the ns function for Time and RH, respectively, to see if we sufficiently controlled for long-term and the humidity trends. R (version. 4.0.3) and dlnm package[22] applied to analyze statistics and perform visualization through this study. The significance level employed in this research was 0.05.

## RESULTS

### Descriptive statistics

Table 1 displays a summary of the air pollutants, meteorological factors, and subjects' profiles during the study period from 2015 to 2017. Daily mean values were 61.17μg/m$^3$ for $PM_{2.5}$, 102.47μg/m$^3$ for $PM_{10}$, 41.3μg/m$^3$ for $PM_{2.5-10}$, 53.61μg/m$^3$ for $NO_2$, 14.64μg/m$^3$ $SO_2$, and 92.99μg/m$^3$ for $O_3$. According to WHO global air quality guidelines, recommended short-term (24-hour) air quality guideline (AQG) levels were 15μg/m$^3$ for $PM_{2.5}$ and 45μg/m$^3$ for $PM_{10}$ (*WHO, 2022*). The daily mean levels of $PM_{2.5}$ and $PM_{10}$ were much higher than the AQG level. The daily mean temperature and relative humidity were 18.23±7.5°C and 77.2±11.61%, respectively. Our study population's mean age and BMI were 42.91±13.54 years old and 23.35±3.30 kg/m$^2$. The mean serum levels of LDL-C, HDL-C, TC, and TG were 2.80±0.79, 1.30±0.32, 4.76±0.92, and 1.69±1.51 mmol/L, respectively. Our study computed the Pearson correlations between variables, and the results presented in (Figure S1). The characteristics of subgroups are in [Table S1]. There was 309,654 samples, including 136,400 cases of females, 178,717 cases in the young group (age<45 years), and 184,161 cases with BMI<24 kg/m$^2$.

### Associations between air pollutants and dyslipidemias

The associations between three size-specific PM and dyslipidemias presented in (Figure S2) and [Table S2]. In single-day lag structures, the significant effects occurred to hyperLDL-C, hyper-TC, and hyperTG for $PM_{2.5}$, and hyperLDL-C, and hyperTG for $PM_{2.5-10}$. In cumulative lag structure, the significant effects occurred to hyperLDL-C, hyperTC, and hyper TG both for $PM_{2.5}$ and $PM_{2.5-10}$. We observed $PM_{10}$, influenced by $PM_{2.5}$ and $PM_{2.5-10}$, were significantly associated with hyperLDL-C, hyperTC, and hyperTG in both lag structures. The lagged and cumulative effects of $PM_{2.5-10}$ on dyslipidemia using the crude and adjusted models displayed in (Figure1) and [Table 2]. In the crude model, the risk of hyperLDL-C associated with $PM_{2.5-10}$ exposure at lag0 (RR 1.030, 95%CI 1.002-1.058, p-value=0.05), and the risk of hyperTG was statistically significant with $PM_{2.5-10}$ exposure at lag3(RR 1.009, 95%CI 1.001-1.017, p-value=0.05) and lag4 (RR 1.009, 95%CI 1.001-1.017, p-value=0.05). The cumulative effect of $PM_{2.5-10}$ exposure reached the maximum at a lag of 0–7 days for hyperLDL-C (RR 1.055, 95%CI 1.002-1.018, p-value=0.05), a lag of 0-6 days for hyperTC (RR 1.046, 95%CI 1.009-1.085, p-value=0.05) and a lag of 0-6 days hyperTG (RR 1.042, 95%CI 1.009-1.077, p-value=0.05), respectively. In the adjusted model, only the risk of hyperTG was associated with $PM_{2.5-10}$ exposure at lag1-3 and was higher than the risk without adjustment for $PM_{2.5}$. As the lag days increased, the risk of hyperTG rose first and then decreased, reaching a maximum at lag2 (RR 1.018, 95%CI 1.005-1.031, p-value=0.05). The cumulative effects of $PM_{2.5-10}$ peaked at a lag of 0–4 days (RR 1.049, 95%CI 1.009-1.090, p-value=0.05) [Table 2]. Results consistently showed that an IQR increase of $PM_{2.5-10}$ concentration (29.5 μg/m3) was positively associated with hyperTG with apparent lagged and cumulative effects.

In stratified analyses by sex, age, and BMI, Figure 2 describes the results of the subgroup analyses with per IQR increase in $PM_{2.5-10}$ exposure on hypertriglyceridemia in different groups. These associations were only significant among the subjects who were female, younger than 45 years old and with BMI<24 kg/m$^2$. For example, the risk effects of $PM_{2.5-10}$ with female were statistically significant at lag3 (RR 1.020, 95%CI 1.003-1.037, p-value=0.05) and lag4 (RR 1.017, 95%CI 1.001-1.033, p-value=0.05) and higher in the adjusted model at lag2 (RR 1.029, 95%CI 1.003-1.057, p-value=0.05) and lag3 (RR 1.023, 95%CI 1.000-1.0457, p-value=0.05) [Table S3].

The associations of an IQR increase of $PM_{2.5-10}$ exposure with dyslipidemias were robust when we altered the dfs for calendar time (5–9 df/year) (Figure S3) and altered the dfs for RH (3-6 df) (Figure S4).

**Table 1**: Summary of the air pollutants, meteorological factors and subjects' profile

| Variables | Mean (SD) | Minimum | Percentile | | | Maximum |
|---|---|---|---|---|---|---|
| | | | 25th | 50th | 75th | |
| **Air pollutants** | | | | | | |
| $PM_{2.5}$(μg/m$^3$) | 61.17(40.36) | 8 | 34 | 50 | 77 | 313 |
| $PM_{10}$(μg/m$^3$) | 102.47(62.63) | 16 | 59 | 84 | 126 | 480 |
| $PM_{2.5-10}$(μg/m$^3$) | 41.3(25.42) | 5 | 23 | 34 | 52.25 | 183 |
| $NO_2$(μg/m$^3$) | 53.61(16.05) | 15 | 42 | 52 | 63 | 121 |
| $SO_2$(μg/m$^3$) | 14.64(5.49) | 5 | 11 | 14 | 18 | 38 |
| $O_3$(μg/m$^3$) | 92.99(55.25) | 6 | 50 | 82 | 133 | 293 |
| **Meteorological factors** | | | | | | |
| Mean temperature (°C) | 18.2(7.53) | 2 | 11 | 19 | 25 | 32 |
| Relative humidity (%) | 77.2(11.61) | 27 | 70 | 78 | 86 | 100 |
| **Subjects' profile** | | | | | | |
| Age | 42.91(13.54) | 18.00 | 32.00 | 42.00 | 52.00 | 79.00 |
| BMI (kg/m$^2$) | 23.35(3.30) | 13.07 | 20.96 | 23.18 | 25.46 | 48.44 |
| LDL-C (mmol/L) | 2.80(0.79) | 0.02 | 2.25 | 2.75 | 3.28 | 10.09 |
| TC (mmol/L) | 4.76(0.92) | 0.28 | 4.12 | 4.69 | 5.31 | 19.67 |
| TG (mmol/L) | 1.69(1.51) | 0.06 | 0.90 | 1.31 | 1.97 | 42.40 |
| HDL-C (mmol/L) | 1.30(0.32) | 0.07 | 1.07 | 1.27 | 1.50 | 4.42 |

## DISCUSSION

In this time-series investigation, we used DLNM to investigate the relationships between short-term exposure to size-specific particulate matters, including $PM_{2.5}$, $PM_{2.5-10}$, and $PM_{10}$, and the prevalence of dyslipidemia in a developing nation. According to our findings, an IQR rise in PM concentrations had lag and cumulative effects on hyperLDL-C, hyperTC, and hyperTG in lag0-7 days. Furthermore, we discovered the unique role of $PM_{2.5-10}$ on hyperTG, and stratified analyses showed that the risk of $PM_{2.5-10}$ exposure to hyperTG was generally higher among female, young and normal-weight participants.

**Table 2**: Relative risk (RR) and 95% confidence interval (CI) for dyslipidemia for an IQR increase (29.25 μg/m3) in concentrations of $PM_{2.5-10}$

| | The crude model | | The adjusted model | |
|---|---|---|---|---|
| | **Acute effects** | **Cumulative effects** | **Acute effects** | **Cumulative effects** |
| Hyper-LDL | | | | |
| Lag0 | **1.030 (1.002, 1.058)** | **1.030 (1.002, 1.058)** | 1.015 (0.972, 1.059) | 1.015 (0.972, 1.059) |
| Lag1 | 1.007 (0.994, 1.020) | **1.037 (1.003, 1.072)** | 1.007 (0.989, 1.026) | 1.022 (0.970, 1.077) |
| Lag2 | 0.997 (0.982, 1.012) | 1.034 (0.998, 1.071) | 1.004 (0.984, 1.024) | 1.026 (0.971, 1.084) |
| Lag3 | 0.995 (0.983, 1.008) | 1.029 (0.990, 1.069) | 1.003 (0.986, 1.020) | 1.029 (0.972, 1.090) |
| Lag4 | 0.999 (0.987, 1.011) | 1.028 (0.986, 1.072) | 1.003 (0.987, 1.019) | 1.032 (0.971, 1.096) |
| Lag5 | 1.005 (0.991, 1.019) | 1.033 (0.987, 1.081) | 1.001 (0.983, 1.020) | 1.033 (0.968, 1.102) |
| Lag6 | 1.010 (0.998, 1.022) | 1.044 (0.994, 1.096) | 0.997 (0.981, 1.013) | 1.030 (0.962, 1.102) |
| Lag7 | 1.011 (0.986, 1.037) | **1.055 (1.002, 1.111)** | 0.988 (0.953, 1.025) | 1.018 (0.952, 1.088) |
| Hyper-TC | | | | |
| Lag0 | 1.012 (0.992, 1.033) | 1.012 (0.992, 1.033) | 0.994 (0.963, 1.025) | 0.994 (0.963, 1.025) |
| Lag1 | 1.004 (0.994, 1.014) | 1.016 (0.992, 1.042) | 1.005 (0.991, 1.018) | 0.998 (0.961, 1.037) |
| Lag2 | 1.003 (0.992, 1.014) | 1.019 (0.993, 1.046) | 1.010 (0.996, 1.025) | 1.008 (0.969, 1.050) |
| Lag3 | 1.006 (0.996, 1.015) | 1.025 (0.996, 1.055) | 1.010 (0.998, 1.022) | 1.019 (0.977, 1.062) |
| Lag4 | 1.009 (1.000, 1.018) | **1.034 (1.003, 1.066)** | 1.006 (0.994, 1.018) | 1.025 (0.981, 1.070) |
| Lag5 | 1.009 (0.999, 1.020) | **1.043 (1.009, 1.079)** | 0.999 (0.985, 1.013) | 1.024 (0.977, 1.073) |
| Lag6 | 1.003 (0.994, 1.012) | **1.046 (1.009, 1.085)** | 0.989 (0.978, 1.001) | 1.013 (0.964, 1.064) |
| Lag7 | 0.987 (0.969, 1.006) | 1.033 (0.994, 1.074) | 0.979 (0.952, 1.006) | 0.992 (0.944, 1.042) |
| Hyper-TG | | | | |
| Lag0 | 1.003 (0.985, 1.022) | 1.003 (0.985, 1.022) | 0.999 (0.971, 1.027) | 0.999 (0.971, 1.027) |
| Lag1 | 1.005 (0.996, 1.014) | 1.009 (0.987, 1.031) | **1.015 (1.002, 1.027)** | 1.014 (0.979, 1.049) |
| Lag2 | 1.007 (0.997, 1.018) | 1.016 (0.992, 1.040) | **1.018 (1.005, 1.031)** | 1.032 (0.995, 1.070) |
| Lag3 | **1.009 (1.001, 1.017)** | 1.025 (0.999, 1.052) | **1.013 (1.002, 1.024)** | **1.045 (1.007, 1.085)** |
| Lag4 | **1.009 (1.001, 1.017)** | **1.034 (1.006, 1.063)** | 1.004 (0.993, 1.015) | **1.049 (1.009, 1.092)** |
| Lag5 | 1.007 (0.997, 1.016) | **1.041 (1.010, 1.073)** | 0.995 (0.983, 1.008) | **1.044 (1.000, 1.090)** |
| Lag6 | 1.001 (0.993, 1.009) | **1.042 (1.009, 1.077)** | 0.991 (0.980, 1.002) | 1.035 (0.989, 1.082) |
| Lag7 | 0.991 (0.974, 1.008) | 1.033 (0.997, 1.070) | 0.995 (0.971, 1.020) | 1.030 (0.985, 1.077) |
| Hypo-HDL | | | | |
| Lag0 | 0.991 (0.970, 1.012) | 0.991 (0.970, 1.012) | 1.001 (0.969, 1.035) | 1.001 (0.969, 1.035) |
| Lag1 | 0.997 (0.987, 1.007) | 0.988 (0.964, 1.013) | 0.990 (0.976, 1.005) | 0.991 (0.952, 1.032) |
| Lag2 | 0.999 (0.987, 1.010) | 0.986 (0.961, 1.013) | 0.987 (0.972, 1.003) | 0.979 (0.939, 1.021) |
| Lag3 | 0.997 (0.987, 1.007) | 0.983 (0.955, 1.012) | 0.990 (0.977, 1.003) | 0.969 (0.927, 1.013) |
| Lag4 | 0.994 (0.985, 1.003) | 0.978 (0.948, 1.009) | 0.995 (0.982, 1.008) | 0.964 (0.921, 1.010) |
| Lag5 | 0.993 (0.982, 1.004) | 0.971 (0.938, 1.004) | 0.999 (0.985, 1.015) | 0.964 (0.917, 1.013) |
| Lag6 | 0.994 (0.985, 1.003) | 0.965 (0.930, 1.002) | 1.000 (0.988, 1.013) | 0.964 (0.915, 1.016) |
| Lag7 | 1.000 (0.981, 1.020) | 0.965 (0.927, 1.005) | 0.994 (0.966, 1.023) | 0.958 (0.910, 1.010) |

**Table S1**: General characteristics of subgroups

| Variables n (%) | Sex | | Age | | BMI | |
|---|---|---|---|---|---|---|
| | **Female** | **male** | **<45 years** | **≥45 years** | **<24 kg/m²** | **≥24 kg/m²** |
| Total | 136400(44.0) | 173254(56.0) | 178717(57.7) | 130937(42.3) | 184161(59.5) | 125493(40.5) |
| HyperLDL-C | 23469(36.1) | 41519(63.9) | 28153(43.3) | 36835(56.7) | 31139(47.9) | 33849(52.1) |
| HyperTC | 37503(40.9) | 54186(59.1) | 38386(41.9) | 53303(58.1) | 46434(50.6) | 45255(49.4) |
| HyperTG | 25936(25.2) | 76905(74.8) | 49821(48.4) | 53020(51.6) | 37512(36.5) | 65329(63.5) |
| HyperHDL-C | 44978(49.2) | 46450(50.8) | 52205(57.1) | 39223(42.9) | 42106(46.1) | 49322(53.9) |

**Table S2: Associations between an IQR increase of $PM_{2.5}$ (43μg/m³) and $PM_{10}$ (67μg/m³) concentrations and dyslipidemia**

| **$PM_{2.5}$** | | | | |
|---|---|---|---|---|
| **Lag days** | **Relative risk and 95% confidence interval** | | | |
| | **HyperLDL-C** | **HyperTC** | **HyperTG** | **HypoHDL-C** |
| Lagged effects | | | | |
| Lag0 | **1.037 (1.007,1.067)** | **1.025 (1.003, 1.047)** | 1.010 (0.991, 1.030) | 0.983 (0.961, 1.005) |
| Lag1 | 1.004 (0.990,1.018) | 1.001 (0.991, 1.011) | 0.996 (0.986, 1.005) | 1.006 (0.995, 1.016) |
| Lag2 | 0.991 (0.974,1.009) | 0.996 (0.983, 1.010) | 0.995 (0.983, 1.007) | 1.011 (0.997, 1.025) |
| Lag3 | 0.993 (0.979,1.007) | 1.003 (0.992, 1.013) | 1.003 (0.993, 1.012) | 1.005 (0.995, 1.016) |
| Lag4 | 1.002 (0.989,1.015) | **1.013 (1.003, 1.022)** | **1.012 (1.003, 1.021)** | 0.995 (0.986, 1.005) |
| Lag5 | 1.013 (0.997, 1.030) | **1.019 (1.007, 1.031)** | **1.016 (1.005, 1.027)** | 0.988 (0.976, 1.001) |
| Lag6 | **1.021 (1.007,1.034)** | **1.014 (1.005, 1.024)** | 1.008 (0.999, 1.018) | 0.991 (0.981, 1.001) |
| Lag7 | 1.018 (0.992,1.045) | 0.991 (0.972, 1.011) | 0.983 (0.966, 1.001) | 1.010 (0.990, 1.031) |
| Cumulative effects | | | | |
| Lag0 | **1.037 (1.007, 1.067)** | **1.025 (1.003, 1.047)** | 1.010 (0.991, 1.030) | 0.983 (0.961, 1.005) |
| Lag1 | **1.041 (1.008, 1.074)** | **1.026 (1.002, 1.051)** | 1.006 (0.984, 1.028) | 0.988 (0.965, 1.013) |
| Lag2 | 1.032 (0.998, 1.067) | 1.023 (0.998, 1.048) | 1.001 (0.979, 1.024) | 0.999 (0.974, 1.025) |
| Lag3 | 1.024 (0.987, 1.063) | 1.025 (0.997, 1.054) | 1.004 (0.979, 1.030) | 1.004 (0.976, 1.033) |
| Lag4 | 1.026 (0.985, 1.069) | **1.038 (1.007, 1.070)** | 1.016 (0.988, 1.044) | 1.000 (0.970, 1.031) |
| Lag5 | 1.040 (0.994, 1.088) | **1.058 (1.023, 1.094)** | **1.032 (1.001, 1.064)** | 0.988 (0.956, 1.022) |
| Lag6 | **1.062 (1.010, 1.116)** | **1.073 (1.034, 1.114)** | **1.041 (1.006, 1.077)** | 0.979 (0.943, 1.017) |
| Lag7 | **1.081 (1.026, 1.139)** | **1.064 (1.023, 1.106)** | 1.024 (0.987, 1.061) | 0.989 (0.950, 1.030) |
| **$PM_{10}$** | | | | |
| Lag days | Relative risk and 95% confidence interval | | | |
| | HyperLDL-C | HyperTC | HyperTG | HypoHDL-C |
| Lagged effects | | | | |
| Lag0 | **1.035 (1.007, 1.064)** | 1.020 (0.999, 1.042) | 1.007 (0.988, 1.026) | 0.986 (0.965, 1.007) |
| Lag1 | 1.006 (0.993, 1.019) | 1.003 (0.993, 1.013) | 1.000 (0.991, 1.009) | 1.002 (0.992, 1.012) |
| Lag2 | 0.994 (0.977, 1.011) | 1.000 (0.987, 1.013) | 1.001 (0.990, 1.013) | 1.006 (0.993, 1.019) |
| Lag3 | 0.994 (0.980, 1.008) | 1.005 (0.995, 1.015) | 1.007 (0.997, 1.016) | 1.002 (0.991, 1.012) |
| Lag4 | 1.001 (0.989, 1.014) | **1.013 (1.003, 1.022)** | **1.012 (1.003, 1.021)** | 0.995 (0.985, 1.004) |
| Lag5 | 1.011 (0.996, 1.027) | **1.017 (1.005, 1.028)** | **1.013 (1.003, 1.024)** | 0.990 (0.978, 1.002) |
| Lag6 | **1.018 (1.005, 1.031)** | **1.011 (1.001, 1.021)** | **1.006 (0.997, 1.015)** | 0.992 (0.982, 1.002) |
| Lag7 | 1.018 (0.992, 1.044) | 0.990 (0.971, 1.009) | 0.987 (0.970, 1.004) | 1.006 (0.986, 1.026) |
| Cumulative effects | | | | |
| Lag0 | **1.035 (1.007, 1.064)** | 1.020 (0.999, 1.042) | 1.007 (0.988, 1.026) | 0.986 (0.965, 1.007) |
| Lag1 | **1.042 (1.009, 1.075)** | 1.023 (0.999, 1.048) | 1.006 (0.985, 1.028) | 0.988 (0.964, 1.012) |
| Lag2 | **1.035 (1.001, 1.071)** | 1.023 (0.998, 1.049) | 1.008 (0.985, 1.031) | 0.993 (0.968, 1.019) |
| Lag3 | 1.029 (0.991, 1.069) | 1.028 (0.999, 1.058) | 1.014 (0.988, 1.041) | 0.995 (0.967, 1.024) |
| Lag4 | 1.030 (0.989, 1.074) | **1.041 (1.009, 1.073)** | 1.026 (0.998, 1.055) | 0.990 (0.959, 1.021) |
| Lag5 | 1.042 (0.995, 1.091) | **1.058 (1.023, 1.095)** | **1.040 (1.008, 1.072)** | 0.979 (0.946, 1.014) |
| Lag6 | **1.060 (1.008, 1.116)** | **1.070 (1.030, 1.111)** | **1.046 (1.011, 1.083)** | 0.971 (0.935, 1.009) |
| Lag7 | **1.079 (1.023, 1.139)** | **1.059 (1.017, 1.103)** | 1.032 (0.995, 1.071) | 0.977 (0.937, 1.018) |

Bold characters mean statistically significant ($P < 0.05$)

**Table S3**: Lagged effects of $PM_{2.5-10}$ on hypertriglyceridemia modified by sex (female, male), age (<45 years, ≥45 years) and BMI (<24 kg/m$^2$, ≥24 kg/m$^2$)

| Lag days | Relative risk and 95% confidence interval | | | | | |
|---|---|---|---|---|---|---|
| | Female | Male | Age<45 | Age≥45 | BMI<24 | BMI≥24 |
| Crude Model | | | | | | |
| Lag0 | 1.001 (0.965, 1.038) | 1.003 (0.988, 1.019) | 1.008 (0.984, 1.033) | 0.995 (0.977, 1.012) | 1.007 (0.979, 1.035) | 0.998 (0.985, 1.012) |
| Lag1 | 1.013 (0.995, 1.031) | 1.000 (0.993, 1.008) | 1.011 (0.999, 1.022) | 0.998 (0.990, 1.007) | 1.009 (0.995, 1.022) | 1.000 (0.993, 1.006) |
| Lag2 | 1.019 (0.999, 1.040) | 1.000 (0.991, 1.008) | 1.012 (0.998, 1.026) | 1.000 (0.991, 1.010) | 1.012 (0.996, 1.028) | 1.000 (0.993, 1.008) |
| Lag3 | **1.020 (1.003, 1.037)** | 1.001 (0.994, 1.008) | **1.012 (1.001, 1.024)** | 1.001 (0.993, 1.009) | **1.014 (1.001, 1.027)** | 1.001 (0.994, 1.007) |
| Lag4 | **1.017 (1.001, 1.033)** | 1.002 (0.995, 1.009) | 1.010 (0.999, 1.021) | 1.002 (0.994, 1.009) | **1.014 (1.002, 1.026)** | 1.001 (0.995, 1.006) |
| Lag5 | 1.010 (0.990, 1.029) | 1.002 (0.995, 1.010) | 1.005 (0.993, 1.018) | 1.003 (0.994, 1.012) | 1.009 (0.994, 1.024) | 1.001 (0.994, 1.008) |
| Lag6 | 1.000 (0.984, 1.016) | 1.001 (0.994, 1.008) | 0.997 (0.986, 1.008) | 1.005 (0.998, 1.013) | 0.997 (0.985, 1.010) | 1.003 (0.997, 1.009) |
| Lag7 | 0.988 (0.954, 1.023) | 0.996 (0.982, 1.011) | 0.984 (0.962, 1.008) | 1.010 (0.993, 1.026) | 0.978 (0.952, 1.004) | 1.006 (0.993, 1.019) |
| Adjusted Model | | | | | | |
| Lag0 | 0.996 (0.941, 1.053) | 0.994 (0.971, 1.018) | 1.004 (0.968, 1.043) | 0.993 (0.967, 1.020) | 0.986 (0.944, 1.029) | 0.989 (0.969, 1.010) |
| Lag1 | 1.022 (0.998, 1.048) | 1.004 (0.994, 1.014) | **1.029 (1.013, 1.046)** | 1.001 (0.989, 1.013) | 1.012 (0.993, 1.031) | 1.005 (0.996, 1.014) |
| Lag2 | **1.029 (1.003, 1.057)** | 1.006 (0.995, 1.018) | **1.032 (1.014, 1.050)** | 1.003 (0.990, 1.016) | **1.023 (1.002, 1.044)** | 1.007 (0.997, 1.017) |
| Lag3 | **1.023 (1.000, 1.046)** | 1.004 (0.995, 1.013) | **1.019 (1.005, 1.034)** | 1.001 (0.990, 1.012) | **1.021 (1.004, 1.039)** | 1.001 (0.993, 1.010) |
| Lag4 | 1.009 (0.987, 1.031) | 0.999 (0.990, 1.009) | 1.002 (0.987, 1.016) | 0.998 (0.988, 1.009) | 1.013 (0.996, 1.030) | 0.994 (0.986, 1.002) |
| Lag5 | 0.994 (0.968, 1.020) | 0.995 (0.985, 1.006) | 0.987 (0.970, 1.004) | 0.999 (0.987, 1.011) | 1.000 (0.980, 1.020) | 0.990 (0.981, 0.999) |
| Lag6 | 0.984 (0.963, 1.006) | 0.994 (0.985, 1.003) | 0.982 (0.968, 0.996) | 1.005 (0.995, 1.016) | 0.987 (0.970, 1.003) | 0.996 (0.988, 1.004) |
| Lag7 | 0.986 (0.938, 1.036) | 0.998 (0.978, 1.020) | 0.996 (0.964, 1.030) | 1.021 (0.996, 1.046) | 0.978 (0.941, 1.016) | 1.018 (1.000, 1.038) |

Bold characters mean statistically significant ($P < 0.05$)

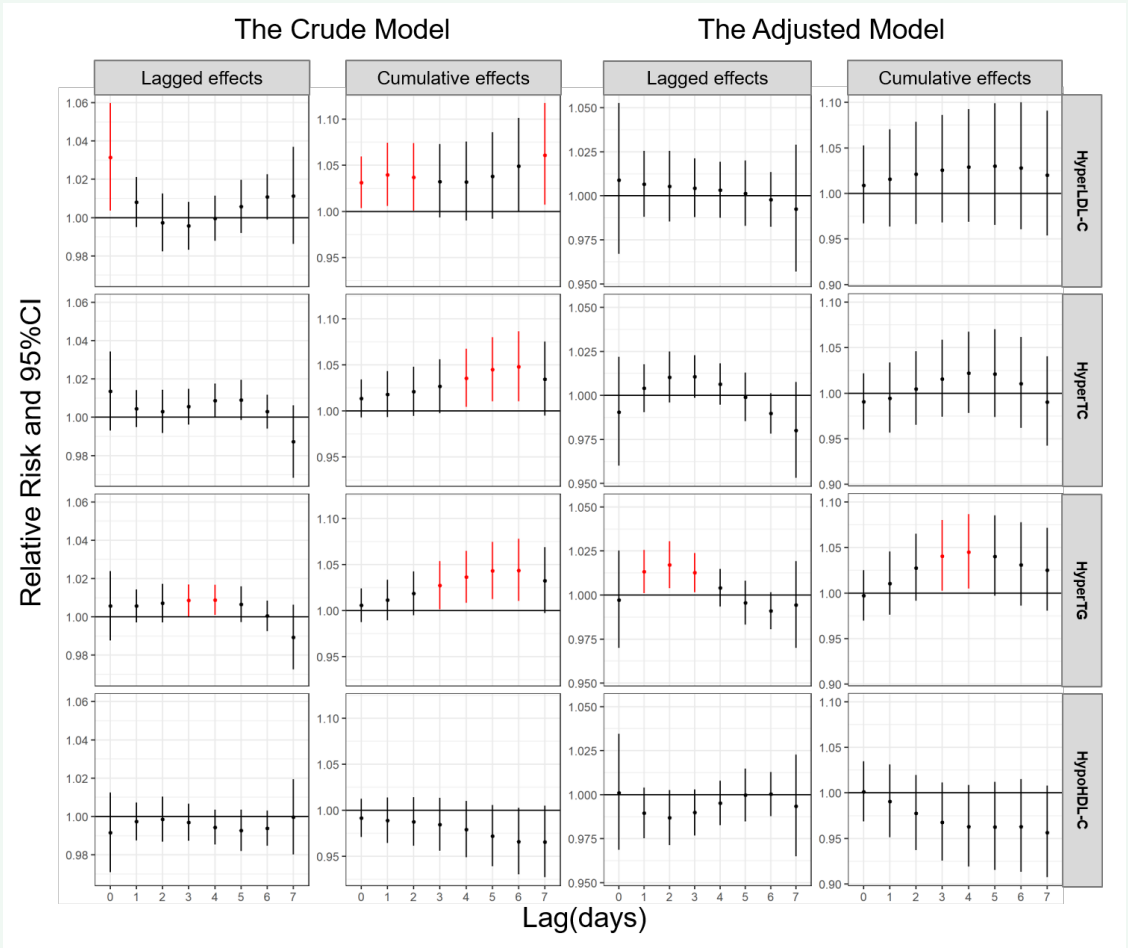


**Figure 1** Associations between an IQR increase of $PM_{2.5-10}$ concentration (29.5 μg/m$^3$) and dyslipidemia

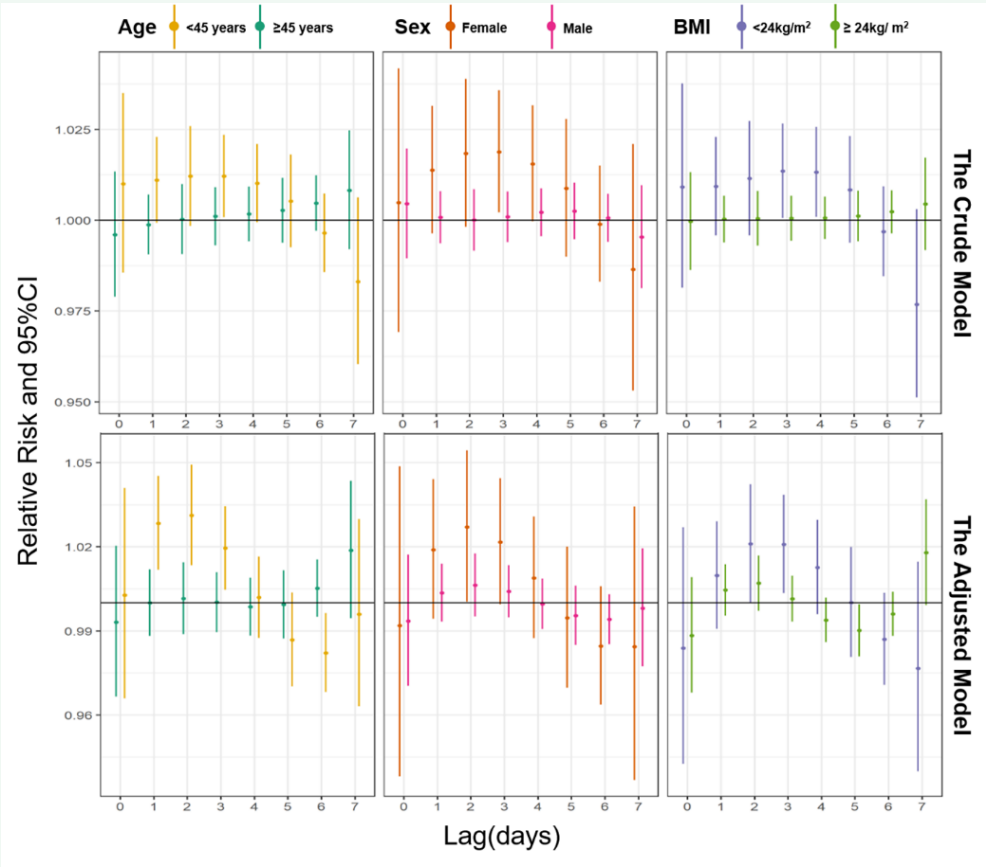


**Figure 2** Associations between an IQR increase of PM2.5-10 concentration (29.5 μg/m$^3$) and hypertriglyceridemia stratified by age, sex, and BMI

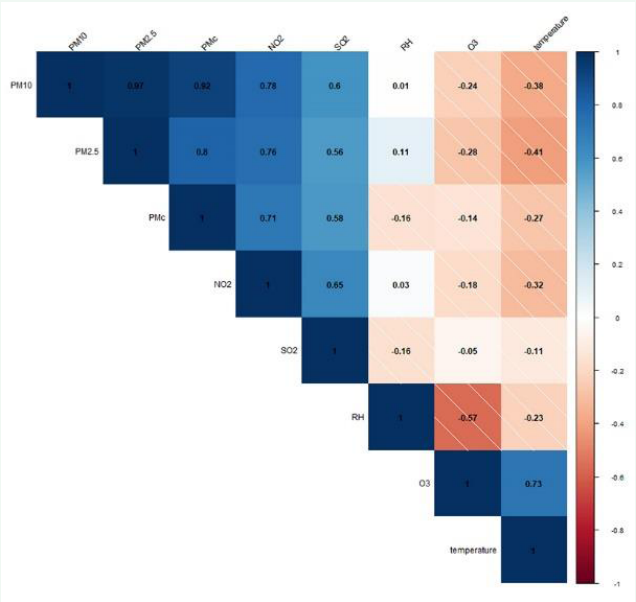


**Figure S1** Pearson correlations between air pollutants and meteorological factors

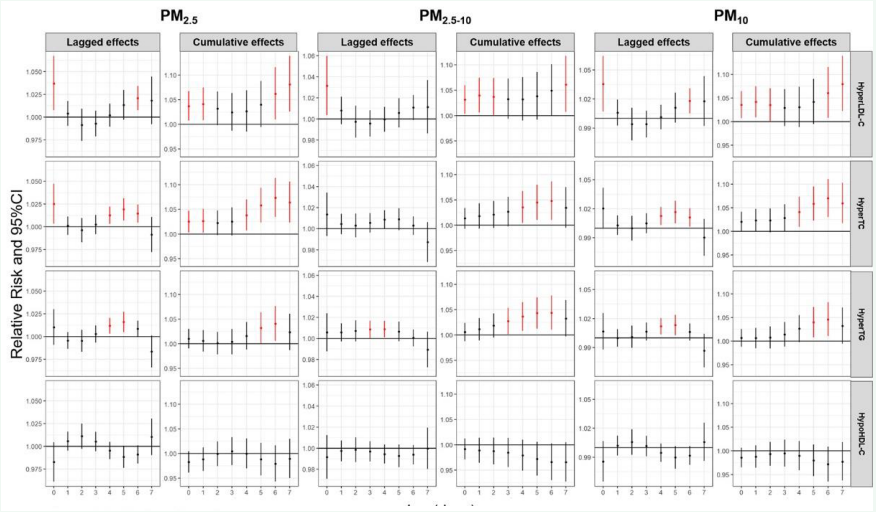


**Figure S2** Lagged and cumulative effects of $PM_{2.5}$, $PM_{2.5-10}$ and $PM_{10}$ on dyslipidemia

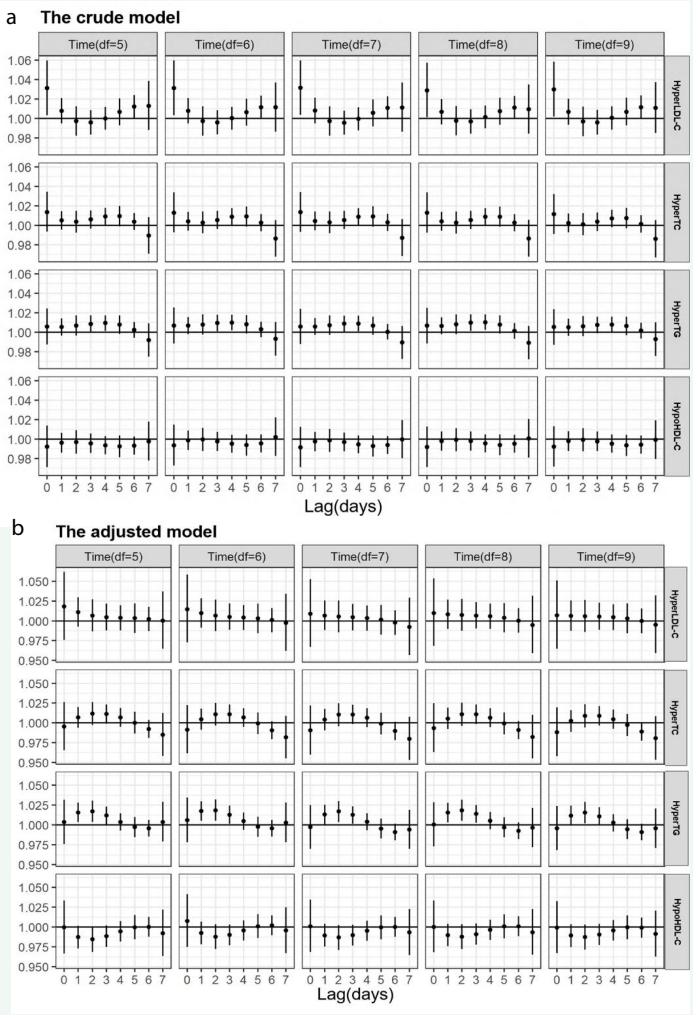


**Figure S3** **(a)**: Association between $PM_{2.5-10}$ and dyslipidemia when altering the degrees of freedom (5-9 df/year) for Time using the crude model. **(b)**: Association between $PM_{2.5-10}$ and dyslipidemia when altering the degrees of freedom (5-9 df/year) for Time using the adjusted model

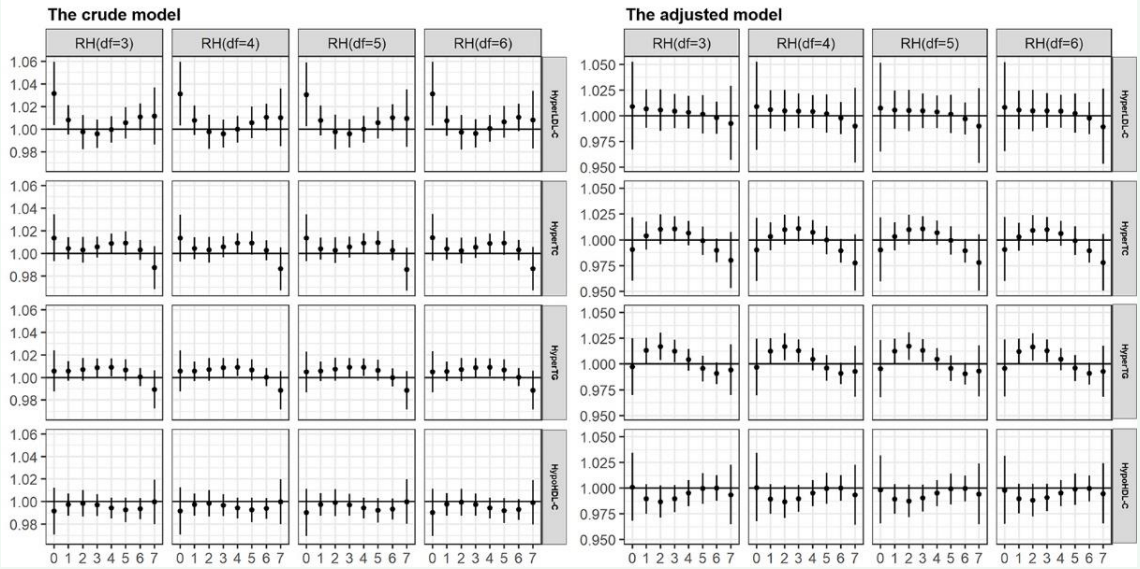


**Figure S4** Association between air $PM_{2.5-10}$ and dyslipidemia when altering the degrees of freedom (3-6 df/year) for RH

Previous studies have associated lipid levels and dyslipidemia with PM exposure. Long-term exposure to $PM_{2.5}$ has been associated with elevated TC, LDL-C, TG, and reduced HDL[23]. Regarding short-term exposure, several studies suggested that LDL-C, TC, and TG increased after exposure to a high level of $PM_{2.5}$[24], consistent with our previous findings [11]. $PM_{10}$ act similarly to $PM_{2.5}$[25], partly because of the large proportion of $PM_{2.5}$ in $PM_{10}$ mass concentration [26]. The association between $PM_{2.5-10}$ and blood lipids first proposed in a panel study published in 2007, which showed that $PM_{2.5-10}$ is associated with increased serum TG in adults with asthma [15]. After that, a Chinese study found a significant correlation between long-term exposure to $PM_{2.5-10}$ and the level of TG [16]. However, a research in Korea indicated no definitive link between $PM_{2.5-10}$ exposure and lipid profile alterations [17]. Nevertheless, up to date, no more studies have explored the association between $PM_{2.5-10}$ and dyslipidemia onsets, which restricted us from directly comparing our results with others.

This study explored the lagged effects of PM on dyslipidemia. We found that $PM_{2.5}$ and $PM_{2.5-10}$ had different impacts on dyslipidemia, and the effects of $PM_{10}$ were mixed by both $PM_{2.5}$ and $PM_{2.5-10}$. We took a further step to investigate the effects of $PM_{2.5-10}$ to reveal the unique role of $PM_{2.5-10}$. Like mentioned above, the exposure of $PM_{2.5}$ was strongly related to serum lipid levels and dyslipidemia. As a result, the impacts of $PM_{2.5-10}$ were likely to confound with $PM_{2.5}$ levels. We controlled the effect of $PM_{2.5}$ and found that significant risks for hyperTG with an IQR increase of $PM_{2.5-10}$ (29.5 μg/m3) that were noticed at lag1-3 and for cumulative effects, reached the maximum at a lag of 0–4 days (RR 1.049, 95%CI 1.009-1.092, p-value = 0.05). Even in the adjusted model, a large part of the effect of $PM_{2.5-10}$ offset due to colinearity between $PM_{2.5}$ and $PM_{2.5-10}$, yet the higher risk suggested that the effect of $PM_{2.5-10}$ on hyper-TG was still robust. These results are consistent with previous studies and more likely being an independent $PM_{2.5-10}$ exposure.

The biochemical processes underlying the relationship between air pollutants and lipid metabolism are widely unknown. A number of biological routes have been suggested and shown that the impaired lipid metabolism seems related to oxidative, systemic inflammation [27], and DNA methylation [28], and the release of inflammatory factors can affect lipid metabolism [29]. On the other hand PM are tiny enough to pass through the respiratory tract and settle in the tracheobronchial tree, respiratory bronchioles, and alveoli, where gas exchange placed [30]. This might also explain why PM exposure has such a high cumulative impact. The potential mechanism of the unique effect on $PM_{2.5-10}$ on hypertriglyceridemia may be related to its specific composition, especially endotoxin. Endotoxin-rich $PM_{2.5-10}$ had a massive inflammatory potential and appeared more active than $PM_{2.5}$[31], and endotoxin was associated with increases in serum triglycerides primarily by stimulating hepatic triglycerides production and very-low-density lipoproteins (VLDL) secretion [32].

In stratified analyses, the association between $PM_{2.5-10}$ and hypertriglyceridemia modified by age, sex and weight. We found that the lag effect of $PM_{2.5-10}$ has a vital impact on dyslipidemia only in people under 45 years old, which might be related to more outdoor activities and more air pollutant inhalation for younger people. Females were more sensitive to the effects of $PM_{2.5-10}$. This gender gap could be due to estrogen. According to Huo et al. air pollution can operate as a probable xenoestrogen by causing reactive oxygen and oxidative stress, which can affect serum lipid levels [33]. Meanwhile, the overweight people were less vulnerable to the adverse effects caused by $PM_{2.5-10}$, which was likely due to obesity's association with chronic low-grade

inflammation [34], and may be more tolerant of the inflammatory effects of short-term $PM_{2.5-10}$ exposure. To describe the correlation between age, sex, and weight in changing air pollution and dyslipidemia, there is limited and inconsistent epidemiological evidence, therefore additional research is needed.

This study has some strengths. Firstly, this is the first study to estimate lag and cumulative effects of exposure to three specific-size PM on dyslipidemia, including over 30 million samples from hospitals in China, by using distributed lag non-linear model (DLNM). Secondly, compared with the previous cross-sectional studies, this time series study may provide a more generalizable result because some factors (including diet, smoking, alcohol consumption which do not change from day to day) did not have an impact on our outcome. Finally, we discovered that short-term exposure to $PM_{2.5-10}$ raised the likelihood of hypertriglyceridemia substantially after adjusting the effect of $PM_{2.5}$, which concluded that $PM_{2.5-10}$ did have its unique role in increasing the risk of dyslipidemia.

Our research has a few limitations. Firstly, daily average $PM_{2.5-10}$ concentrations obtained by subtracting $PM_{2.5}$ from $PM_{10}$, like earlier research. This findings might result in more exposure misclassification of $PM_{2.5-10}$ than $PM_{2.5}$ or $PM_{10}$, as a decreased capacity to detect severe $PM_{2.5-10}$ consequences. Secondly, while utilizing the mean of the nine-site monitoring stations in Chengdu to reflect population exposure is a typical practice, it can lead to exposure measurement errors, which understate the consequences of air pollution. Finally, our data are based on only one city, Chengdu, and further multiple center studies are required to improve the generalizability of the results.

## CONCLUSIONS

Our time-series study found the significant delayed effects of short-term PM exposure on dyslipidemia rates by using DLNM. $PM_{2.5-10}$ originally reported to be strongly positively linked with hypertriglyceridemia at lag days, both with and without adjustment for $PM_{2.5}$. Additionally, our study likely explains part of the rise in daily mortality that linked to air pollutants and serve as a reminder to policymakers to pay attention to the identification and control of coarse particulate matter, as well as the care of vulnerable populations, including younger, female, and physically lighter individuals.

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### Ethics statement

No informed consent was obtained in our study because any personally identifiable information was scrambled to protect privacy and the researchers were blinded to patient identities. This study was approved by Sichuan Province Academy of Medical Sciences (Ethics Committee Approval Number: 2017-156).

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