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Chemical components of respirable particulate matter associated with emergency hospital admissions for type 2 diabetes mellitus in Hong Kong

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ABSTRACT

Background: Epidemiological studies have shown that short-term exposure to particulate matter (PM) mass is associated with diabetes morbidity and mortality, although inconsistencies still exist. Variation of chemical components in PM may have contributed to these inconsistencies. We hypothesize that certain components of respirable particulate matter (PM_{10}), not simply PM_{10} mass, can exacerbate symptoms or cause acute complications for type 2 diabetes mellitus (T2DM).

Methods: We used a Poisson time-series model to examine the association between 17 chemical components of PM_{10} and daily emergency hospital admissions for T2DM among residents aged 65 years or above from January 1998 to December 2007 in Hong Kong. We estimated excess risk (ER%) for T2DM hospitalizations per interquartile range (IQR) increment in chemical component concentrations of days at lag_0 through lag_3, and the moving average of the same-day and previous-day (lag_{0-1}) in single-pollutant models. To further evaluate the independent effects of chemical components on T2DM, we controlled for PM_{10} mass, major PM_{10} chemical components, and gaseous pollutants in two-pollutant models.

Results: In the single-pollutant models, PM_{10} components associated with T2DM admissions include: elemental carbon, organic carbon, nitrate, and nickel. The ER% estimates per IQR increment at lag_{0-1} for these four components were 3.79% (1.63, 5.95), 3.74% (0.83, 6.64), 4.58% (2.17, 6.99), and 1.91% (0.43, 3.38), respectively. Risk estimates for nitrate and elemental carbon were robust to adjustment for co-pollutant concentrations.

Conclusions: Short-term exposure to some PM_{10} chemical components such as nitrate and elemental carbon increases the risk of acute complications or exacerbation of symptoms for the T2DM patients. These findings may have potential biological and policy implications.

1. Introduction

The global diabetes epidemic is becoming a serious threat to public health. The first WHO Global Report on Diabetes showed that the number of people living with diabetes almost quadrupled to 422 million in 2014 from 108 million in 1980 (World Health Organization, 2016). This number is projected to be 592 million in 2038 (International Diabetes Federation, 2013). Type 2 diabetes mellitus (T2DM) is a metabolic disorder characterized by high glucose levels in the blood caused by insulin resistance and relative insulin deficiency, accounting for >90% of all diabetes cases (American Diabetes Association, 2006).

The increase in diabetes prevalence in recent years may be primarily attributable to modern lifestyles including obesity, physical inactivity, and the growing aging population (Van Dieren et al., 2010). Both long-term (Anderson et al., 2012; Brook et al., 2013; Chen et al., 2016; Eze et al., 2014; Liu et al., 2016) and short-term exposure to (Goldberg et al., 2013; Kan et al., 2004) particulate matter (PM) have been linked to diabetes, although there are still inconsistencies among studies. For example, a 10 μg/m^3 increment in long-term fine particulate matter ($PM_{2.5}$) exposure was associated with 1.49 fold higher risk (95% CI, 1.37, 1.62) for diabetes-related mortality in the 1991 Canadian follow-up study (Brook et al., 2013), while the findings were negative in the American Cancer Society Cancer Prevention II study (Pope et al., 2004). Positive associations were reported for short-term PM_{10} exposure in Shanghai, China (Kan et al., 2004), but not in the ten metropolitan areas in the European Mediterranean region (Samoli et al., 2014).

The inconsistencies among previous studies might relate to numerous factors such as the population susceptibilities, diabetes prevalence,

Abbreviations: PM_{10}, particulate matter with aerodynamic diameter less than or equal to 10 μm; T2DM, type 2 diabetes mellitus; NO_2, nitrogen dioxide; SO_2, sulfur dioxide; O_3, ozone; ICD-9, ninth revision of the international classification of diseases; OC, organic carbon; EC, elemental carbon; NO_3^-, nitrate; SO_4^{2-}, sulfate; NH_4^+, ammonium; Ni, nickel; Na^+, sodium ion; K^+, potassium ion; Cl^-, chloride ion; Al, aluminum; As, arsenic; Ca, calcium; Cd, cadmium; Fe, iron; Mg, magnesium; Mn, manganese; Pb, lead.

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sample size, exposure assessment, and statistical methods in controlling for confounders. Another key factor is that PM composition may vary from location to location because PM is a mixture of different components associated with particular local and regional sources of air pollution.

Emergency hospital admissions for diabetes are due to acute complications of diabetes (e.g., ketoacidosis, hyperosmolarity) and acute onset of chronic complications (e.g., renal manifestations and peripheral circulatory disorders) (Amaize and Mistry, 2016). Time-series analysis is well suited for evaluating short-term effects of time-varying exposures on health. In the present study, we aimed to identify which chemical components of PM_{10} (PM with a diameter < 10 μm) are associated with T2DM emergency hospitalizations using 10 years of daily time-series data from January 1, 1998 to December 31, 2007 in Hong Kong.

2. Materials and methods

2.1. Air pollution and meteorological data

The Hong Kong Environmental Protection Department (HKEPD) established the PM_{10} chemical speciation network to measure twenty-six PM_{10} chemical components, in addition to PM_{10} mass. PM_{10} samples were collected with quartz filters using High Volume PM_{10} samplers. The filters were analyzed for gravimetric mass, elements (e.g., nickel, aluminum) by inductively coupled plasma atomic emission spectroscopy (ICP-AES), ions (e.g., sulfate, nitrate) by ion chromatography (IC), and elemental carbon/organic carbon by a thermal/optical transmittance method (Yuan et al., 2013). During the study period, 24-hour PM_{10} sampling was carried out at six air quality monitoring stations, these six monitoring stations interspersed in different districts of Hong Kong, which included Yuen Long, Tsuen Wan, Sham Shui Po, Tung Chung, Central Western, and Kwun Tong, and were reported to well represent the general population exposure on a regular basis (Fig. S1) (Pun et al., 2014b). After excluding those chemical components that had a contamination issue or that had >25% of samples below the analytical detection limit or that had >25% of missing values, in the end a total of 17 chemical components were retained for data analysis. They were elemental carbon (EC), organic carbon (OC), nitrate (NO_3^-), sulfate (SO_4^{2-}), ammonium ion (NH_4^+), chloride ion (Cl^-), sodium ion (Na^+), potassium ion (K^+), aluminum (Al), arsenic (As), calcium (Ca), cadmium (Cd), iron (Fe), magnesium (Mg), manganese (Mn), nickel (Ni), and lead (Pb). Nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and ozone (O_3) were also monitored at the same day and the same monitoring stations with PM_{10} chemical components. Air pollutant concentrations generally had moderate-to-very high monitor-to-monitor correlations (Table S1). We also obtained daily mean temperature and relative humidity data from the Hong Kong Observatory for the same study period.

2.2. Type 2 diabetes mellitus hospitalizations

We computed daily counts of emergency hospital admissions for the elderly aged 65 years or older with the principal diagnosis of T2DM [International Classification of Diseases, 9th revision (ICD-9): 250.X0 and 250.X2, X = 0–9] recorded in the Hospital Authority Corporate Data Warehouse, which covers all publicly funded hospitals that provides 24-hour accident and emergency services and covers 90% of hospital beds for Hong Kong residents (Tian et al., 2016). The Accident and Emergency (A&E) Departments in all publicly funded hospitals of Hong Kong adopted a triage system to ensure that patients with more serious conditions were accorded higher priority in medical treatment (Ho, 2013). Patients who did not require emergency attendance would not be treated in A&E Department but rather transferred to public or private clinics. The diabetes patients included in the current study were those with acute complications or with acute symptoms related to chronic conditions.

2.3. Statistical analysis

PM_{10} samples were collected on average every-sixth-day on a distinct sampling schedule for each of the six monitoring stations, thus for one particular day, there may be zero or multiple samples taken from the whole territory. Collectively, 69% of the study days had speciation measurements from at least one station; there is not an obvious pattern for missing data occurrence in the time-series. To compute the territory-wide mean concentrations of PM_{10} chemical components, we applied a centering method to remove the station-specific influence on the measurements of each component. Details of the centering method were reported elsewhere (Katsouyanni et al., 1996; Pun et al., 2014a; Wong et al., 2001). Fig. S2 shows time-series plots of PM_{10} chemical components. All pollutant concentrations are expressed in $\mu g/m^3$ except for EC and OC, which are reported in μg carbon/m^3.

This was a time-series study, and we used generalized additive models to estimate associations between PM_{10} chemical components and emergency hospital admissions for T2DM. The same-day mean temperature ($Tmean_0$) was used to control for the immediate effect of temperature, while the moving average of lag 1–3 days ($Tmean_{1-3}$) was used to control for the delayed effects of temperature. Natural cubic splines with 8 degrees of freedom (*df*) per year were used to control for time trend and seasonality. We used natural cubic splines with 3 *df* for both $Tmean_0$ and $Tmean_{1-3}$ to account for the nonlinearity of temperature effect, and included them simultaneously in the model (Tian et al., 2014). We used natural cubic spline with 3 *df* to control for the same-day mean relative humidity (*rh*). We also adjusted for day of the week (*DOW*), public holidays (*Holiday*), and influenza epidemics (*influenza*) as dummy variables. Our model is shown as follows:

$$\begin{aligned}\log[EY] = \mu + \beta_1 COMP + ns(time, df = 8/\text{year} \times no.\text{of year}) \\ + ns(Tmean_0, df = 3) + ns(Tmean_{1-3}, df = 3) \\ + ns(rh, df = 3) + \beta_2 DOW + \beta_3\, influenza + \beta_4 Holiday\end{aligned} \quad (1)$$

where *COMP* represents PM_{10} chemical components, $ns(.)$ denotes natural cubic splines, and β_i indicates regression coefficients.

We first used single-pollutant models to examine the association of emergency hospitalizations for T2DM with each PM_{10} component on the same day (lag_0) and the previous 1–3 days (lag_1 to lag_3), and the moving average of same-day and previous-day (lag_{0-1}) while adjusting for time-varying confounders. For chemical components demonstrating statistically significant associations at lag_{0-1} in single-pollutant models, we further constructed two-pollutant models. We adjusted one at a time for PM_{10} mass, the major PM_{10} components (those contributing ≥4% to PM_{10} mass: EC, OC, SO_4^{2-}, NO_3^-, and NH_4^+), and gaseous pollutants (SO_2, NO_2, and O_3). Risk estimates were treated with caution when correlation between the two pollutants was ≥0.6 (Bell et al., 2014; Mostofsky et al., 2012; Tian et al., 2013). Besides that, we also included Ni which was significantly associated with diabetes hospitalizations in the single-pollutant models. For sensitivity analysis, we reanalyzed the time-series data using linear interpolation to fill in missing data for the days without data from any stations via the *na.approx* function in the R *zoo* package (Pun et al., 2015; Pun et al., 2014b).

The results were reported in terms of the percentage excess risk (ER%) increase in daily T2DM emergency hospitalizations for an interquartile range (IQR) increment of PM_{10} chemical components, and respective 95% confidence intervals (CI). All statistical significance tests were two-sided, and values of $p < 0.05$ were considered statistically significant. The data were analyzed using the statistical software R (version 3.1.2), and the "mgcv" (version 1.8–12) package.

3. Results

During the 10-year study period of 3652 days, we identified 40,150 T2DM emergency admissions (11.0 ± 3.8 admissions per day), with a mean age of 76 (range: 65–104) and female percentage 57.4%. Among these 3652 days, 2520 (~69%) days had non-missing values for PM_{10} chemical component concentrations. Table 1 shows summary statistics of emergency hospital admissions for T2DM, meteorological conditions, and concentrations of PM_{10} mass and its chemical components. The daily mean temperature and relative humidity were 23.6 °C and 78.0%, respectively. Gaseous pollutants concentrations were 59.9, 20.2, and 30.1 μg/m^3 for NO_2, SO_2, and O_3, respectively. The daily mean concentrations of PM_{10} was 55.7 μg/m^3, with EC, OC, NO_3^-, SO_4^{2-}, NH_4^+, and Ni accounting for 7.18%, 15.62%, 6.28%, 19.39%, 5.39%, and 0.01% of the PM_{10} mass, respectively.

Fig. 1 shows the ER (%) of T2DM emergency hospitalizations per IQR increment in the concentrations of PM_{10} chemical components using single-pollutant models. PM_{10} mass was associated with emergency hospital admissions for T2DM at lag_2 with ER (%) of 2.42 (95% confidence interval (CI), 0.30, 4.53) per IQR (41.5 μg/m^3). EC, OC, NO_3^-, Ni, and K^+ were all significantly associated with T2DM hospitalizations at certain lags from lag_0 to lag_3. Based on previous studies in Hong Kong (Wong et al., 2008), we used lag_{0-1} as a priori lag structure and found EC, OC, NO_3^-, and Ni were all associated with emergency hospital admissions for T2DM (Fig. 1). With one IQR increment in pollution level at lag_{0-1}, the ER (%) of T2DM emergency admissions for EC, OC, NO_3^-, and Ni were 3.79 (1.63, 5.95), 3.74 (0.83, 6.64), 4.58 (2.17, 6.99), and 1.91 (0.43, 3.38), respectively.

We observed relatively high correlations ($r > 0.8$) of PM_{10} mass with OC and Mn. We observed high correlations ($r > 0.8$) of Fe with Al, Ca, and Mn, of Pb with K^+, and of NH_4^+ with SO_4^{2-} (Table 2).

In the two-pollutant models, we further controlled for co-pollutants to examine the independent effects of chemical components for EC, OC, NO_3^-, and Ni. However, cautions should be taken when interpreting the results due to the high correlations between pairs of certain components. For example, it is possible that the non-statistically significant risk estimate of OC after adjustment for PM_{10} mass, NO_3^-, or NO_2 may relate to over-adjustment. In general, the associations of EC and NO_3^- with T2DM hospitalizations were robust to co-pollutant adjustment, while the risk estimates for Ni and OC lost statistical significance in the two-pollutant models (Fig. 2). When linear interpolation was used to fill in missing values for the concentrations of chemical components, the risk estimates for the chemical components did not change substantially (Fig. S3).

4. Discussion

We examined the effects of PM_{10} chemical components on the emergency hospital admissions for T2DM among residents aged 65 years or above in Hong Kong from 1998 to 2007. This was one of the few studies in the literature to explore the association between chemical components and emergency T2DM hospitalizations. EC, OC, NO_3^-, and Ni in PM_{10} were linked to increased risks of T2DM emergency admissions. The associations of EC and NO_3^- with T2DM hospitalizations were robust to co-pollutant adjustment.

4.1. Association between PM mass and diabetes mellitus

We identified 8 studies examining the associations between short-term PM mass and diabetes mellitus mortality or hospital admission (Table S2). Most of the studies found positive association of PM mass with diabetes mellitus mortality or hospital admissions, but the current study found no positive associations, in line with the multicity study conducted in the European Mediterranean region (Samoli et al., 2014).

4.2. Association between PM components and diabetes mellitus

We identified only one earlier study on the associations between PM_{10} chemical components and emergency hospital admissions for diabetes, which was conducted in the 26 U.S. communities (Zanobetti et al., 2009). This study reported that $PM_{2.5}$ higher in EC and OC were associated with lower rates of diabetes admissions whereas the $PM_{2.5}$ higher in SO_4^{2-} and As were associated with higher rates of diabetes. In our current study, the number of daily emergency hospital admissions for T2DM was positively associated with NO_3^- and EC, but not with SO_4^{2-}

Table 1
Summary statistics of emergency hospital admissions, meteorological conditions, and concentrations of PM_{10} and its chemical components in Hong Kong, China, 1998–2007.

Variable	No. of days	Mean (SD)	Percent of PM_{10} mass	Percentile			IQR
				25th	50th	75th	
Emergency hospital admissions (counts)							
T2DM	3652	11.0 (3.8)	–	9	11	13	5
Meteorological conditions							
Temperature, °C	3652	23.6 (4.9)	–	19.7	24.8	27.8	8.1
Relative humidity, %	3652	78.0 (10.0)	–	73.5	79.1	84.7	11.2
Pollutant concentration, μg/m^3							
NO_2	2497	59.9 (24.7)	–	42.6	59.0	75.0	32.4
SO_2	2499	20.2 (16.1)	–	9.8	16.0	25.2	15.5
O_3	2497	30.1 (20.3)	–	15.0	25.4	40.0	25.0
PM_{10}	2520	55.7 (30.8)	100.00	31.9	50.1	73.4	41.5
SO_4^{2-}	2520	10.8 (7.0)	19.39	5.4	9.6	14.3	8.9
OC	2511	8.7 (5.6)	15.62	4.5	7.4	11.5	7.0
EC	2511	4.0 (1.8)	7.18	2.9	3.8	4.9	2.0
NO_3^-	2520	3.5 (3.1)	6.28	1.5	2.5	4.8	3.3
NH_4^+	2520	3.0 (2.6)	5.39	1.0	2.5	4.4	3.3
Na^+	2520	1.5 (1.0)	2.69	0.8	1.3	2.0	1.2
Cl^-	2520	0.9 (1.1)	1.62	0.3	0.6	1.2	0.9
Ca	2520	0.8 (0.6)	1.44	0.4	0.6	1.0	0.6
K^+	2520	0.6 (0.6)	1.08	0.2	0.4	0.9	0.7
Fe	2520	0.5 (0.4)	0.90	0.3	0.4	0.7	0.4
Al	2520	0.3 (0.3)	0.54	0.1	0.2	0.3	0.2
Mg	2520	0.3 (0.2)	0.54	0.2	0.2	0.3	0.2
Pb	2520	0.07 (0.07)	0.13	0.02	0.04	0.10	0.08
Mn	2520	0.02 (0.02)	0.04	0.01	0.02	0.03	0.02
As	2520	0.005 (0.006)	0.01	0.001	0.003	0.007	0.006
Ni	2520	0.006 (0.006)	0.01	0.002	0.004	0.007	0.005
Cd	2520	0.002 (0.003)	0	0	0.001	0.003	0.002

Abbreviations: IQR, interquartile range; SD, standard deviation; T2DM, type 2 diabetes mellitus; NO_2, nitrogen dioxide; SO_2, sulfur dioxide; O_3, ozone; EC, elemental carbon; OC, organic carbon; NO_3^-, nitrate; SO_4^{2-}, sulfate; NH_4^+, ammonium; Na^+, sodium ion; K^+, potassium ion; Cl^-, chloride ion; Al, aluminum; As, arsenic, Ca, calcium; Cd, cadmium; Fe, iron; Mg, magnesium; Mn, manganese; Ni, nickel.

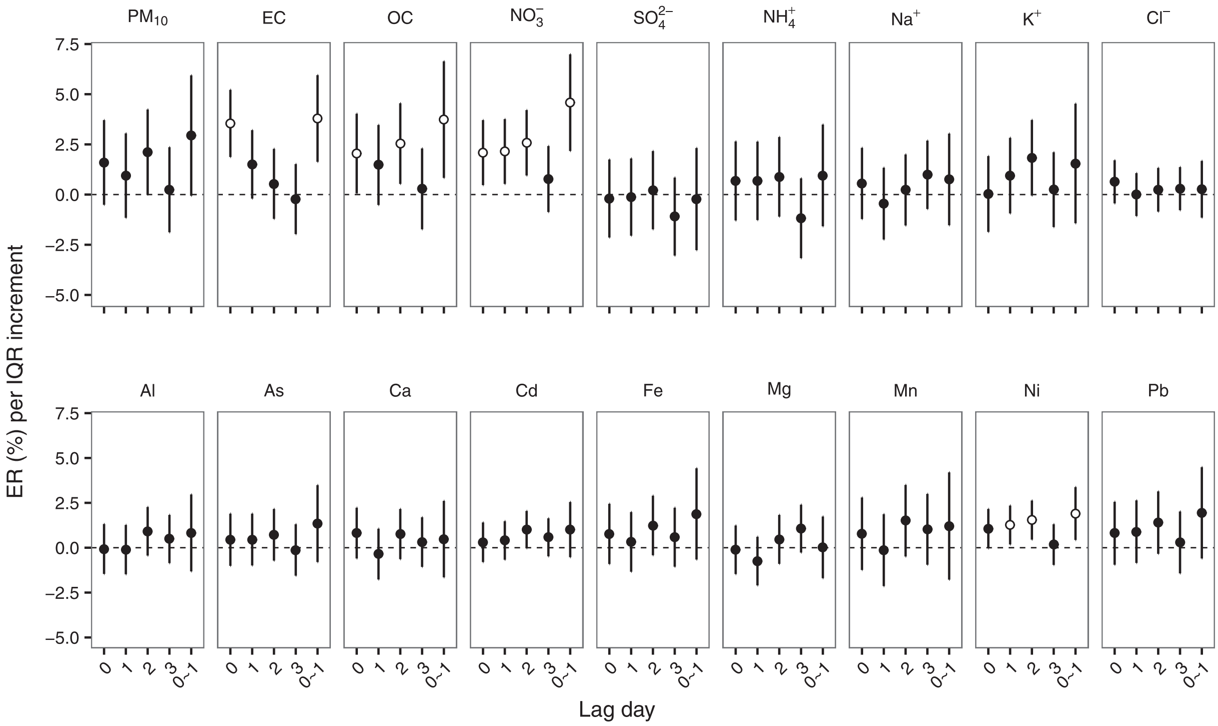

Fig. 1. Percentage excess risk (ER %) of emergency hospital admission for type 2 diabetes mellitus per interquartile range (IQR) increment in the concentrations of respirable particulate matter (PM_{10}) and its chemical components on single-days (the lag_0 through lag_3, and the moving average of lag_{0-1}) in the single-pollutant models adjusted for meteorological factors, time trends, public holiday, day of the week, and influenza epidemic, Hong Kong, China, 1998–2007. Filled circle indicates that the risk estimate is not statistically significant while hollow circle indicates it is statistically significant. EC, elemental carbon; OC, organic carbon; NO_3^-, nitrate; SO_4^{2-}, sulfate; NH_4^+, ammonium; Na^+, sodium ion; K^+, potassium ion; Cl^-, chloride ion; Al, aluminum; As, arsenic, Ca, calcium; Cd, cadmium; Fe, iron; Mg, magnesium; Mn, manganese; Ni, nickel; Pb, lead.

or As. Disparities in findings might be attributable to differences in sample size (e.g., daily average counts of emergency hospital admissions for diabetes, and the number of years of the time-series), study population (e.g., population susceptibility), and air pollution characteristics (e.g., air pollutant concentrations and PM composition). The multicity study in America (Zanobetti et al., 2009) used the proportion of chemical components to $PM_{2.5}$ mass to investigate the modification of the $PM_{2.5}$ mass association by $PM_{2.5}$ composition, so the effect estimates could not be quantitatively compared with ours, which explored directly the component effect on type 2 diabetes mellitus.

4.3. Biological mechanisms

There is evidence that exposure to short-term PM can alter endothelial function (Schneider et al., 2008), increase fasting glucose (Chen et al., 2016), and trigger systemic inflammation (Gurgueira et al., 2002;

Table 2
Pearson correlation of air pollutants.

	EC	OC	NO_3^-	Ni	SO_4^{2-}	NH_4^+	Na^+	K^+	Cl^-	Al	As	Ca	Cd	Fe	Mg	Mn	Pb	PM_{10}	NO_2	SO_2	O_3
EC	1.00																			
OC	0.39	1.00																		
NO_3^-	0.30	0.69	1.00																	
Ni	0.31	0.40	0.37	1.00																
SO_4^{2-}	0.22	0.64	0.53	0.43	1.00															
NH_4^+	0.25	0.72	0.67	0.48	0.93	1.00														
Na^+	−0.12	−0.17	0.22	−0.05	0.09	−0.03	1.00													
K^+	0.31	0.82	0.61	0.28	0.67	0.69	−0.12	1.00												
Cl^-	0.02	0.03	0.34	−0.01	−0.05	0.00	0.63	0.05	1.00											
Al	0.21	0.53	0.49	0.23	0.48	0.42	0.05	0.61	0.12	1.00										
As	0.29	0.73	0.51	0.40	0.69	0.73	−0.16	0.79	−0.01	0.54	1.00									
Ca	0.28	0.59	0.50	0.23	0.44	0.39	0.02	0.63	0.14	0.91	0.55	1.00								
Cd	0.26	0.60	0.45	0.28	0.50	0.53	−0.14	0.66	0.01	0.46	0.64	0.50	1.00							
Fe	0.32	0.67	0.58	0.31	0.58	0.54	0.00	0.69	0.10	0.93	0.64	0.93	0.55	1.00						
Mg	0.02	0.13	0.40	0.04	0.27	0.14	0.65	0.22	0.51	0.68	0.13	0.64	0.14	0.61	1.00					
Mn	0.30	0.72	0.59	0.30	0.68	0.66	−0.04	0.79	0.05	0.84	0.74	0.83	0.62	0.91	0.48	1.00				
Pb	0.33	0.80	0.59	0.34	0.68	0.71	−0.16	0.89	0.01	0.58	0.83	0.62	0.71	0.69	0.17	0.79	1.00			
PM_{10}	0.41	0.87	0.78	0.44	0.83	0.85	0.07	0.84	0.15	0.74	0.77	0.75	0.64	0.84	0.45	0.87	0.83	1.00		
NO_2	0.48	0.75	0.59	0.42	0.56	0.60	−0.08	0.56	−0.06	0.45	0.52	0.49	0.44	0.58	0.18	0.57	0.59	0.72	1.00	
SO_2	0.42	0.46	0.31	0.63	0.39	0.43	−0.14	0.32	−0.06	0.27	0.47	0.30	0.30	0.35	−0.02	0.34	0.39	0.45	0.47	1.00	
O_3	−0.11	0.17	0.11	0.06	0.52	0.37	0.20	0.32	−0.12	0.38	0.31	0.30	0.23	0.36	0.35	0.42	0.30	0.39	0.11	−0.06	1.00

Abbreviations: EC, elemental carbon; OC, organic carbon; NO_3^-, nitrate; SO_4^{2-}, sulfate; NH_4^+, ammonium; Na^+, sodium ion; K^+, potassium ion; Cl^-, chloride ion; Al, aluminum; As, arsenic, Ca, calcium; Cd, cadmium; Fe, iron; Mg, magnesium; Mn, manganese; Ni, nickel; Pb, lead; NO_2, nitrogen dioxide; SO_2, sulfur dioxide; O_3, ozone.

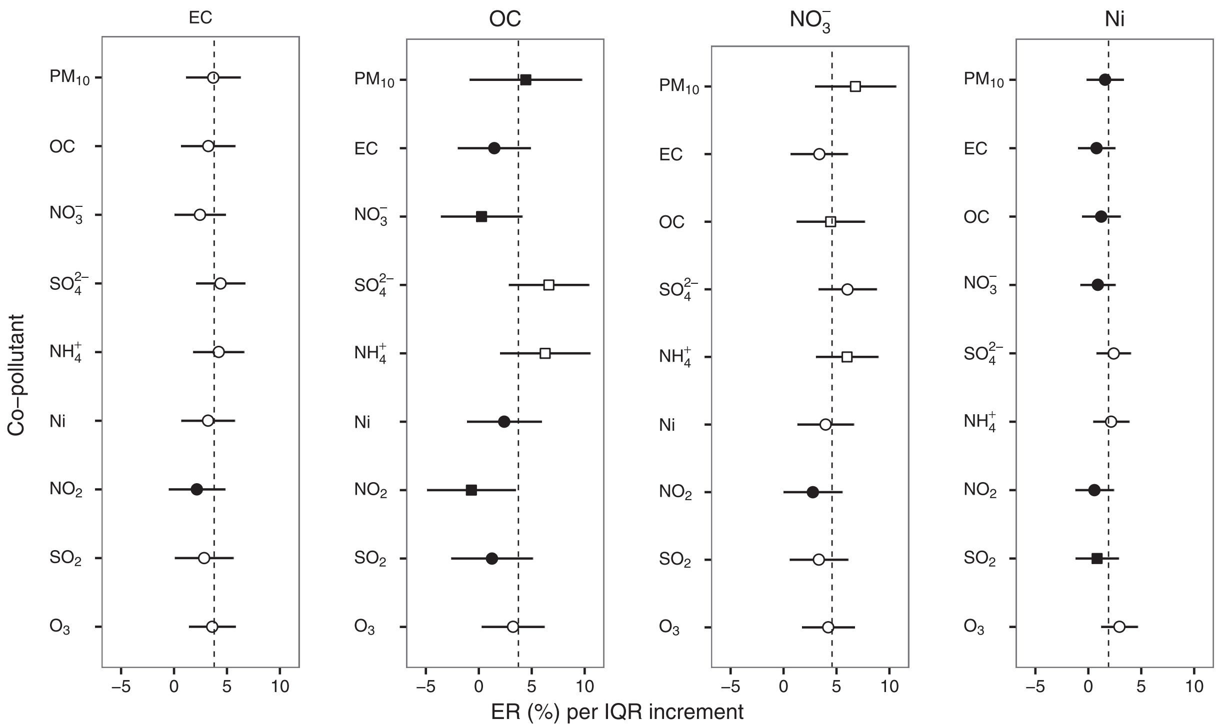

Fig. 2. Percentage excess risk (ER %) of emergency hospital admission for type 2 diabetes mellitus per interquartile range (IQR) increment in the concentrations of 2-day moving average (current day and previous day, lag_{0-1}) of daily respirable particulate matter (PM_{10}) and its chemical components with additional adjustment for co-pollutant in the two-pollutant models. Circle indicates that correlation between the second pollutant and the first is <0.6 in the two-pollutant models while square denotes the correlation is ≥0.6. Filled circle or square represents the risk estimate is not statistically significant while hollow circle or square indicates it is statistically significant. The vertical dash line denotes the point estimate of the chemical components in the single-pollutant models. EC, elemental carbon; OC, organic carbon; NO_3^-, nitrate; SO_4^{2-}, sulfate; NH_4^+, ammonium; Na^+, sodium ion; K^+, potassium ion; Cl^-, chloride ion; Al, aluminum; As, arsenic, Ca, calcium; Cd, cadmium; Fe, iron; Mg, magnesium; Mn, manganese; Ni, nickel; Pb, lead; NO_2, nitrogen dioxide; SO_2, sulfur dioxide; O_3, ozone.

Sun et al., 2013), and therefore may increase insulin resistance (Sun et al., 2009). Thus, it is biologically plausible that the number of hospitalizations for diabetes could be elevated on days with higher PM pollution.

EC and OC are mainly from combustion-related source, such as local gasoline and diesel vehicle exhausts, and regional industrial and agricultural combustion (Pun et al., 2015). Exposure to EC and OC has a potential to increase oxidative stress, which is considered to be a major risk factor for both the onset and progress of T2DM (Rains and Jain, 2011) and its associated complications, such as endothelial dysfunction, systemic inflammation, and dyslipidemia (Rajagopalan and Brook, 2012). One in vitro experimental study found that lipid peroxidation in BEAS-2B cells was associated with EC and OC when human bronchial epithelial BEAS-2B cells were exposed to particle extracts at 100 μg/ml for 8 h (Huang et al., 2002). Epidemiological studies generally support pro-inflammatory effects of EC and OC. EC in particles is an indicator of emission sources from diesel exhaust. Diesel exhaust can alter endothelial function (Mills, 2005) and increase systemic inflammation makers (e.g., vascular endothelial growth factor, tumor necrosis factor-α) (Fang et al., 2012). OC may increase airway and systemic inflammation in elderly people (Delfino et al., 2010).

NO_3^- derives from gas to particle conversion processes of NOx products from vehicle exhaust (Almeida et al., 2006). NO_3^- is acidic in nature. It may lower the pH in the airways and trigger adverse reactions, although no convincing toxicological evidence of NO_3^- has been found for ambient NO_3^- pollution (Reiss et al., 2007). Human studies support the association between nitrate and oxidative stress (Chen et al., 2015; Wu et al., 2012; Wu et al., 2016). For example, Wu et al. (2016) conducted a panel study using 40 healthy college students in Beijing, China and reported the strongest association of nitrate, among all PM_{10} chemical constituents, with activity changes in two enzymes: extracellular superoxide dismutase (EC-SOD) and glutathione peroxidase 1 (GPX1), the two enzymes that play central roles in the body's antioxidant system (Pandey and Rizvi, 2010). It suggested that nitrate in PM_{10} might have a stronger potential to induce oxidative stress than other components in PM_{10}.

The major source of Ni in PM is from residual oils used by marine vessels (Pun et al., 2015). It was linked to diabetes hospitalizations, although the association lost statistical significant in the two-pollutant models. Animal experiments demonstrated that acute and subchronic exposure to Ni could induce hyperglycemia by increasing hepatic glycogenolysis and pancreatic release of glucagon, and decreasing peripheral utilization of glucose and gluconeogenesis (Tikare et al., 2008). One human epidemiological study also reported that Ni was associated with T2DM even after the adjustment for traditional risk factors including lifestyle, body mass index, family history of diabetes, and inflammatory biomarkers (Liu et al., 2015).

Exposure to long-term PM could instigate or accelerate chronic cardiovascular diseases, while short-term exposure to PM could exacerbate existing cardiovascular disease and trigger acute cardiovascular events (Brook et al., 2010). Hypothesized biological mechanisms to explain the association between PM and cardiovascular diseases are also shared with those linking PM to diabetes (Rajagopalan and Brook, 2012). EC, OC, NO_3^-, and Ni were all associated with cardiovascular morbidity (e.g., emergency hospitalizations) and mortality in the epidemiological studies (Kelly and Fussell, 2012), thus it is likely that these components may contribute to diabetes exacerbation.

Our findings should be interpreted with caution for several reasons. First, although we used six monitoring stations in one single city to measure PM_{10} chemical components, spatial variability of PM_{10} chemical components cannot be fully captured. Ito et al. (2005) found that concentrations of EC, OC, and Ni (local combustion sources) tended to have low monitor-to-monitor temporal correlations. Thus, components from local combustion sources might be subject to more measurement error given their higher spatial heterogeneity. Second, components with very low ambient concentrations might be subject to more instrument or laboratory errors. These measurement errors may be one of the reasons for the non-significant associations of arsenic and cadmium with T2DM hospitalizations. Finally, all emergency hospitalizations due to the principal diagnosis of T2DM were included in the current study, emergency visits due to hypoglycemia were not excluded. Hypoglycemia emergency hospitalizations are often associated with strict glycemic control (Leese et al., 2003), but not with air pollution.

5. Conclusions

Our findings add new evidence regarding the differential toxicity of PM_{10} constituents on type 2 diabetes mellitus and suggest PM_{10} constituents from combustion-related particles (EC, OC, NO_3^- and Ni) may cause acute exacerbations of symptoms or complications for type 2 diabetes mellitus. Air pollution control policies may target local gasoline and diesel vehicle exhausts, residual oils from marine vessels, and regional industrial and agricultural combustion.

Conflict of interest

The authors declare no actual or potential conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at doi:10.1016/j.envint.2016.10.022.

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