

1 **Chemical components of respirable particulate matter associated with emergency**

2 **hospital admissions for Type II diabetes mellitus in Hong Kong**

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15 **Abstract**

16 **Background:** Epidemiological studies have shown that short-term exposure to particulate  
17 matter (PM) mass was associated with diabetes morbidity and mortality, although  
18 inconsistencies still exist. Variation of chemical components in PM may have contributed to  
19 these inconsistencies. We hypothesize that certain components of respirable particulate matter  
20 (PM<sub>10</sub>), not simply PM<sub>10</sub> mass, can exacerbate symptoms or cause acute complications for  
21 type II diabetes mellitus (T2DM).

22

23 **Methods:** We used a Poisson time-series model to examine the association between 17  
24 chemical components of PM<sub>10</sub> and daily emergency hospital admissions for T2DM among  
25 residents aged 65 years or above from January 1998 to December 2007 in Hong Kong. We  
26 estimated excess risk (ER%) for T2DM hospitalizations per interquartile range (IQR)  
27 increment in chemical component concentrations of days at lag<sub>0</sub> through lag<sub>3</sub>, and the moving  
28 average of the same-day and previous-day (lag<sub>0-1</sub>) in single-pollutant models. To further  
29 evaluate the independent effects of chemical components on T2DM, we controlled for PM<sub>10</sub>  
30 mass and major PM<sub>10</sub> chemical components and gaseous pollutants in two-pollutant models.

31

32 **Results:** In the single-pollutant models, PM<sub>10</sub> components associated with T2DM admissions  
33 include: elemental carbon, organic carbon, nitrate, and nickel. The ER% estimates per IQR  
34 increment at lag<sub>0-1</sub> for these four components were 3.79% (1.63, 5.95), 3.74 (0.83, 6.64), 4.58  
35 (2.17, 6.99), and 1.91(0.43, 3.38), respectively. Risk estimates for nitrate and elemental  
36 carbon were robust to adjustment for co-pollutant concentrations.

37

38 **Conclusions:** Short-term exposure to some PM<sub>10</sub> chemical components such as nitrate and  
39 elemental carbon increases the risk of acute complications or exacerbation of symptoms for  
40 the T2DM patients. These findings may have potential biological and policy implications.

41

42 **Keywords:** Particulate matter; Chemical component; Air pollution; Diabetes; Time-series  
43 analysis

44 **List of abbreviations and their full forms**

45 **Abbreviations Full form**

PM <sub>10</sub>	Particulate matter with aerodynamic diameter less than or equal to 10µm
T2DM	Type II diabetes mellitus
NO <sub>2</sub>	Nitrogen dioxide
SO <sub>2</sub>	Sulfur dioxide
O <sub>3</sub>	Ozone
ICD-9	Ninth revision of the international classification of diseases
OC	Organic carbon
EC	Elemental carbon
NO <sub>3</sub> <sup>-</sup>	Nitrate
SO <sub>4</sub> <sup>2-</sup>	Sulfate
NH <sub>4</sub> <sup>+</sup>	Ammonium
Ni	Nickel
Na <sup>+</sup>	Sodium ion
K <sup>+</sup>	Potassium ion
Cl <sup>-</sup>	Chloride ion
Al	Aluminum
As	Arsenic
Ca	Calcium
Cd	Cadmium
Fe	Iron
Mg	Magnesium
Mn	Manganese
Pb	Lead

46 **1. Introduction**

47 The global diabetes epidemic is becoming a serious threat to public health. The first WHO  
48 Global Report on Diabetes showed that the number of people living with diabetes almost  
49 quadrupled to 422 million in 2014 from 108 million in 1980 (World Health Organization,  
50 2016). This number is projected to be 592 million in 2038 (International Diabetes Federation,  
51 2013). Type II diabetes mellitus (T2DM) is a metabolic disorder characterized by high  
52 glucose levels in the blood caused by insulin resistance and relative insulin deficiency,  
53 accounting for more than 90% of all diabetes cases (American Diabetes Association, 2006).

54  
55 The increase in diabetes prevalence in recent years may be primarily attributable to modern  
56 lifestyles including obesity, physical inactivity, and the growing aging population (Van  
57 Dieren et al., 2010). Both long-term (Anderson et al., 2012; Brook et al., 2013; Chen et al.,  
58 2016; Eze et al., 2014; Liu et al., 2016) and short-term exposure to (Goldberg et al., 2013;  
59 Kan et al., 2004) particulate matter (PM) have been linked to diabetes, although there are still  
60 a lot of inconsistencies among studies. For example, a  $10 \mu\text{g}/\text{m}^3$  increment in long-term fine  
61 particulate matter ( $\text{PM}_{2.5}$ ) exposure was associated with 1.49 fold higher risk (95% CI, 1.37,  
62 1.62) for diabetes-related mortality in the 1991 Canadian follow-up study (Brook et al., 2013),  
63 while the findings were negative in the American Cancer Society Cancer Prevention II study  
64 (Pope et al., 2004). Positive associations were reported for short-term  $\text{PM}_{10}$  exposure in  
65 Shanghai, China (Kan et al., 2004), but not in the ten metropolitan areas in the European  
66 Mediterranean region (Samoli et al., 2014).

67

68 The inconsistencies among previous studies might relate to numerous factors such as the  
69 population susceptibilities, diabetes prevalence, sample size, exposure assessment, and  
70 statistical methods in controlling for confounders. Another key factor is that PM composition  
71 may vary from location to location because PM is a mixture of different components  
72 associated with particular local and regional sources of air pollution.

73

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

81

## 82 **2. Materials and Methods**

### 83 *2.1 Air pollution and meteorological data*

84 The Hong Kong Environmental Protection Department (HKEPD) established the PM<sub>10</sub>  
85 chemical speciation network to measure twenty-six PM<sub>10</sub> chemical components, in addition  
86 to PM<sub>10</sub> mass. PM<sub>10</sub> samples were collected with quartz filters using High Volume PM<sub>10</sub>  
87 samplers. The filters were analyzed for gravimetric mass, elements (e.g., nickel, aluminum)  
88 by inductively coupled plasma atomic emission spectroscopy (ICP-AES), ions (e.g., sulfate,  
89 nitrate) by ion chromatography (IC), and elemental carbon/organic carbon by a

90 thermal/optical transmittance method (Yuan et al., 2013). During the study period, 24-hour  
91 PM<sub>10</sub> sampling was carried out at six air quality monitoring stations, these six monitoring  
92 stations interspersed in different districts of Hong Kong, which include Yuen Long, Tsuen  
93 Wan, Sham Shui Po, Tung Chung, Central Western, and Kwun Tong, and were reported to  
94 well represent the general population exposure on a regular basis (**Fig. S1**) (Pun et al., 2014b).  
95 After excluding those chemical components that had a contamination issue or that had more  
96 than 25% of samples below the analytical detection limit or that had more than 25% of  
97 missing values, in the end a total of 17 chemical components were retained for data analysis.  
98 They were elemental carbon (EC), organic carbon (OC), nitrate (NO<sub>3</sub><sup>-</sup>), sulfate (SO<sub>4</sub><sup>2-</sup>),  
99 ammonium ion (NH<sub>4</sub><sup>+</sup>), chloride ion (Cl<sup>-</sup>), sodium ion (Na<sup>+</sup>), potassium ion (K<sup>+</sup>), aluminum  
100 (Al), arsenic (As), calcium (Ca), cadmium (Cd), iron (Fe), magnesium (Mg), manganese  
101 (Mn), nickel (Ni), and lead (Pb). Nitrogen dioxide (NO<sub>2</sub>), sulfur dioxide (SO<sub>2</sub>), and ozone (O<sub>3</sub>)  
102 were also monitored at the same day and the same monitoring stations with PM<sub>10</sub> chemical  
103 components. Air pollutant concentrations generally had moderate-to-very high monitor-to-  
104 monitor correlations (**Table S1**). We also obtained daily mean temperature and relative  
105 humidity data from the Hong Kong Observatory for the same study period.

106

## 107 *2.2. Type II diabetes mellitus hospitalizations*

108 We computed daily counts of emergency hospital admissions for the elderly aged 65 years or  
109 older with the principal diagnosis of T2DM [International Classification of Diseases, 9<sup>th</sup>  
110 revision (ICD-9): 250.X0 and 250.X2, X=0-9] recorded in the Hospital Authority Corporate  
111 Data Warehouse, which covered all publicly funded hospitals that provide 24-hour accident

112 and emergency services and cover 90% of hospital beds for Hong Kong residents (Tian et al.,  
113 2016). The Accident and Emergency (A&E) Departments in all publicly funded hospitals of  
114 Hong Kong adopted a triage system to ensure that patients with more serious conditions were  
115 accorded higher priority in medical treatment (Ho, 2013). Patients who did not require  
116 emergency attendance would not be treated in A&E Department but rather transferred to  
117 public or private clinics. The diabetes patients included in the current study were those with  
118 acute complications or with acute symptoms related to chronic conditions.

119

### 120 2.3. *Statistical analysis*

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

131

132 This was a time-series study, and we used generalized additive models to estimate  
133 associations between PM<sub>10</sub> chemical components and emergency hospital admissions for

134 T2DM. The same-day mean temperature ( $Tmean_0$ ) was used to control for the immediate  
 135 effect of temperature, while the moving average of lag 1-3 days ( $Tmean_{1-3}$ ) was used to  
 136 control for the delayed effects of temperature. Natural cubic splines with 8 degrees of  
 137 freedom ( $df$ ) per year were used to control for time trend and seasonality. We used natural  
 138 cubic splines with 3  $df$  for both  $Tmean_0$  and  $Tmean_{1-3}$  to account for the nonlinearity of  
 139 temperature effect, and included them simultaneously in the model (Tian et al., 2014). We  
 140 used natural cubic spline with three  $df$  to control for the same-day mean relative humidity  
 141 ( $rh$ ). We also adjusted for day of the week ( $DOW$ ), public holidays ( $Holiday$ ), and influenza  
 142 epidemics ( $influenza$ ) as dummy variables. Our model is shown as follows:

$$\begin{aligned}
 143 & \\
 144 & \log[E(Y)] = \mu + \beta_1 COMP + ns(time, df = 8/year \times no. of year) + ns(Tmean_0, df = 3) + \\
 145 & \quad ns(Tmean_{1-3}, df = 3) + ns(rh, df = 3) + \beta_2 DOW + \beta_3 influenza + \beta_4 Holiday \\
 146 & \hspace{20em} \text{----- (1)}
 \end{aligned}$$

147 where  $COMP$  represents  $PM_{10}$  chemical components,  $ns(.)$  denotes natural cubic splines, and  
 148  $\beta_i$  indicates regression coefficients.

149  
 150 We first used single-pollutant models to examine the association of emergency  
 151 hospitalizations for T2DM with each  $PM_{10}$  component on the same day ( $lag_0$ ) and the  
 152 previous 1-3 days ( $lag_1$  to  $lag_3$ ), and the moving average of same-day and previous-day ( $lag_{0-1}$ )  
 153 while adjusting for time-varying confounders. For chemical components demonstrating  
 154 statistically significant associations at  $lag_{0-1}$  in single-pollutant models, we further constructed  
 155 two-pollutant models. We adjusted one at a time for  $PM_{10}$  mass, the major  $PM_{10}$  components  
 156 (those contributing  $\geq 4\%$  to  $PM_{10}$  mass:  $EC$ ,  $OC$ ,  $SO_4^{2-}$ ,  $NO_3^-$ , and  $NH_4^+$ ) and gaseous



157 pollutants (SO<sub>2</sub>, NO<sub>2</sub>, and O<sub>3</sub>). Risk estimates were treated with caution when correlation  
158 between the two pollutants was  $\geq 0.6$  (Bell et al., 2014; Mostofsky et al., 2012; Tian et al.,  
159 2013). Besides that, we also included Ni which was significantly associated with diabetes  
160 hospitalizations in the single-pollutant models. For sensitivity analysis, we reanalyzed the  
161 time-series data using linear interpolation to fill in missing data for the days without data  
162 from any stations via the *na.approx* function in the R *zoo* package (Pun et al., 2015; Pun et al.,  
163 2014b).

164

165 The results were reported in terms of the percentage excess risk (ER%) increase in daily  
166 T2DM emergency hospitalizations for an interquartile range (IQR) increment of PM<sub>10</sub>  
167 chemical components, and respective 95% confidence intervals (CI). All statistical  
168 significance tests were two-sided, and values of  $p < 0.05$  were considered statistically  
169 significant. The data were analyzed using the statistical software R (version 3.1.2), and the  
170 “mgcv” (version 1.8-12) package.

171

### 172 **3. Results**

173 During the 10-year study period of 3,652 days, we identified 40,150 T2DM emergency  
174 admissions ( $11.0 \pm 3.8$  admissions per day), with a mean age of 76 (range: 65-104) and  
175 female percentage 57.4%. Among these 3,652 days, 2,520 (~69%) days had non-missing  
176 values for PM<sub>10</sub> chemical component concentrations. **Table 1** shows summary statistics of  
177 emergency hospital admissions for T2DM, meteorological conditions, and concentrations of  
178 PM<sub>10</sub> mass and its chemical components. The daily mean temperature and relative humidity

179 were 23.6 °C and 78.0 %, respectively. Gaseous pollutants concentrations were 59.9, 20.2,  
180 and 30.1  $\mu\text{g}/\text{m}^3$  for  $\text{NO}_2$ ,  $\text{SO}_2$ , and  $\text{O}_3$ , respectively. The daily mean concentrations of  $\text{PM}_{10}$   
181 was 55.7  $\mu\text{g}/\text{m}^3$ , with EC, OC,  $\text{NO}_3^-$ ,  $\text{SO}_4^{2-}$ ,  $\text{NH}_4^+$ , and Ni accounting for 7.18%, 15.62%,  
182 6.28%, 19.39%, 5.39%, and 0.01% of the  $\text{PM}_{10}$  mass, respectively.

183

184 **Fig. 1** shows the ER (%) of T2DM emergency hospitalizations per IQR increment in the  
185 concentrations of  $\text{PM}_{10}$  chemical components using single-pollutant models.  $\text{PM}_{10}$  mass was  
186 associated with emergency hospital admissions for T2DM at lag<sub>2</sub> with ER (%) of 2.42 (95%  
187 confidence interval (CI), 0.30, 4.53) per IQR (41.5  $\mu\text{g}/\text{m}^3$ ). EC, OC,  $\text{NO}_3^-$ , Ni, and  $\text{K}^+$  were  
188 all significantly associated with T2DM hospitalizations at certain lags from lag<sub>0</sub> to lag<sub>3</sub>.  
189 Based on previous studies in Hong Kong (Wong et al., 2008), we used lag<sub>0-1</sub> as a *priori* lag  
190 structure and found EC, OC,  $\text{NO}_3^-$ , and Ni were all associated with emergency hospital  
191 admissions for T2DM (**Fig. 1**). With one IQR increment in pollution level at lag<sub>0-1</sub>, the ER (%)  
192 of T2DM emergency admissions for EC, OC,  $\text{NO}_3^-$ , and Ni were 3.79 (1.63, 5.95), 3.74 (0.83,  
193 6.64), 4.58 (2.17, 6.99), and 1.91 (0.43, 3.38), respectively.

194

195 We observed relatively high correlations ( $r > 0.8$ ) of  $\text{PM}_{10}$  mass with OC and Mn. We  
196 observed high correlations ( $r > 0.8$ ) of Fe with Al, Ca, and Mn, of Pb with  $\text{K}^+$ , and of  $\text{NH}_4^+$   
197 with  $\text{SO}_4^{2-}$  (**Table 2**).

198

199 In the two-pollutant models, we further controlled for co-pollutants to examine the  
200 independent effects of chemical components for EC, OC,  $\text{NO}_3^-$ , and Ni. However, cautions

201 should be taken when interpreting the results due to the high correlations between pairs of  
202 certain components. For example, it is possible that the non-statistically significant risk  
203 estimate of OC after adjustment for PM<sub>10</sub> mass, NO<sub>3</sub><sup>-</sup>, or NO<sub>2</sub> may relate to over-adjustment.  
204 In general, the associations of EC and NO<sub>3</sub><sup>-</sup> with T2DM hospitalizations were robust to co-  
205 pollutant adjustment, while the risk estimates for Ni and OC lost statistical significance in the  
206 two-pollutant models (**Fig. 2**). When linear interpolation was used to fill in missing values for  
207 the concentrations of chemical components, the risk estimates for the chemical components  
208 did not change substantially (**Fig. S3**).

209

## 210 **4. Discussion**

211 We examined the effects of PM<sub>10</sub> chemical components on the emergency hospital  
212 admissions for T2DM among residents aged 65 years or above in Hong Kong from 1998 to  
213 2007. This was one of the few studies in the literature to explore the association between  
214 chemical components and emergency T2DM hospitalizations. EC, OC, NO<sub>3</sub><sup>-</sup>, and Ni in PM<sub>10</sub>  
215 were linked to increased risks of T2DM emergency admissions. The associations of EC and  
216 NO<sub>3</sub><sup>-</sup> with T2DM hospitalizations were robust to co-pollutant adjustment.

217

### 218 *4.1. Association between PM mass and diabetes mellitus*

219 We identified 8 studies examining the associations between short-term PM mass and diabetes  
220 mellitus mortality or hospital admission (**Table S2**). Most of the studies found positive  
221 association of PM mass with diabetes mellitus mortality or hospital admissions. But the  
222 current study found no positive associations, in line with the multicity study conducted in the

223 European Mediterranean region (Samoli et al., 2014).

224

#### 225 *4.2. Association between PM components and diabetes mellitus*

226 We identified only one earlier study on the associations between PM<sub>10</sub> chemical components  
227 and emergency hospital admissions for diabetes (Zanobetti et al., 2009). The study conducted  
228 in the 26 U.S. communities reported that PM<sub>2.5</sub> higher in EC and OC were associated with  
229 lower rates of diabetes admissions whereas the PM<sub>2.5</sub> higher in SO<sub>4</sub><sup>2-</sup> and As were associated  
230 with higher rates of diabetes. In our current study, the number of daily emergency hospital  
231 admissions for T2DM was positively associated with NO<sub>3</sub><sup>-</sup> and EC, but not with SO<sub>4</sub><sup>2-</sup> or As.  
232 Disparities in findings might be attributable to differences in sample size (e.g., daily average  
233 counts of emergency hospital admissions for diabetes, and the number of years of the time-  
234 series), study population (e.g., population susceptibility), and air pollution characteristics  
235 (e.g., air pollutant concentrations and PM composition). The multicity study in America  
236 (Zanobetti et al., 2009) used the proportion of chemical components to PM<sub>2.5</sub> mass to  
237 investigate the modification of the PM<sub>2.5</sub> mass association by PM<sub>2.5</sub> composition, so the effect  
238 estimates could not be quantitatively compared with ours, which explored directly the  
239 component effect on Type II diabetes mellitus.

240

#### 241 *4.3. Biological mechanisms*

242 There is evidence that exposure to short-term PM can alter endothelial function (Schneider et  
243 al., 2008), increase fasting glucose (Chen et al., 2016), and trigger systemic inflammation  
244 (Gurgueira et al., 2002; Sun et al., 2013), and therefore may increase insulin resistance (Sun

245 et al., 2009). Thus, it is biologically plausible that the number of hospitalizations for diabetes  
246 could be elevated on days with higher PM pollution.

247  
248 EC and OC are mainly from combustion-related source, such as local gasoline and diesel  
249 vehicle exhausts, and regional industrial and agricultural combustion (Pun et al., 2015).  
250 Exposure to EC and OC has a potential to increase oxidative stress, which is considered to be  
251 a major risk factor for both the onset and progress of T2DM (Rains and Jain, 2011) and its  
252 associated complications, such as endothelial dysfunction, systemic inflammation, and  
253 dyslipidemia (Rajagopalan and Brook, 2012). One in vitro experimental study found that  
254 lipid peroxidation in BEAS-2B cells was associated with EC and OC when human bronchial  
255 epithelial BEAS-2B cells were exposed to particle extracts at 100 µg/ml for 8 hours (Huang  
256 et al., 2002). Epidemiological studies generally support pro-inflammatory effects of EC and  
257 OC. EC in particles is an indicator of emission sources from diesel exhaust. Diesel exhaust  
258 can alter endothelial function (Mills, 2005) and increase systemic inflammation makers (e.g.,  
259 vascular endothelial growth factor, tumor necrosis factor- $\alpha$ ) (Fang et al., 2012). OC may  
260 increase airway and systemic inflammation in elderly subjects (Delfino et al., 2010).

261  
262  $\text{NO}_3^-$  derives from gas to particle conversion processes of  $\text{NO}_x$  products from vehicle exhaust  
263 (Almeida et al., 2006).  $\text{NO}_3^-$  is acidic in nature. It may lower the pH in the airways and  
264 trigger adverse reactions, although no convincing toxicological evidence of  $\text{NO}_3^-$  has been  
265 found for ambient  $\text{NO}_3^-$  pollution (Reiss et al., 2007). Human studies support the association  
266 between nitrate and oxidative stress (Chen et al., 2015; Wu et al., 2012; Wu et al., 2016). For

267 example, Wu et al. (2016) conducted a panel study using 40 healthy college students in  
268 Beijing, China and reported the strongest association of nitrate, among all PM<sub>10</sub> chemical  
269 constituents, with activity changes in two enzymes: extracellular superoxide dismutase (EC-  
270 SOD) and glutathione peroxidase 1 (GPX1), the two enzymes that play central roles in the  
271 body's antioxidant system (Pandey and Rizvi, 2010). It suggested that nitrate in PM<sub>10</sub> may  
272 have a stronger potential to induce oxidative stress than other components in PM<sub>10</sub>.

273

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

283

284 Exposure to long-term PM could instigate or accelerate chronic cardiovascular diseases,  
285 while short-term exposure to PM could exacerbate existing cardiovascular disease and trigger  
286 acute cardiovascular events (Brook et al., 2010). Hypothesized biological mechanisms to  
287 explain the association between PM and cardiovascular diseases are also shared with those  
288 linking PM to diabetes (Rajagopalan and Brook, 2012). EC, OC, NO<sub>3</sub><sup>-</sup>, and Ni were all

289 associated with cardiovascular morbidity (e.g., emergency hospitalizations) and mortality in  
290 the epidemiological studies (Kelly and Fussell, 2012), thus it is likely that these components  
291 may contribute to diabetes exacerbation.

292  
293 Our findings should be interpreted with caution for several reasons. First, although we used  
294 six monitoring stations in one single city to measure PM<sub>10</sub> chemical components, spatial  
295 variability of PM<sub>10</sub> chemical components cannot be fully captured. Ito et al. (2005) found that  
296 concentrations of EC, OC, and Ni (local combustion sources) tend to have low monitor-to-  
297 monitor temporal correlations. Thus, components from local combustion sources might be  
298 subject to more measurement error given their higher spatial heterogeneity. Second,  
299 components with very low ambient concentrations might be subject to more instrument or  
300 laboratory errors. These measurement errors may be one of the reasons for the non-significant  
301 associations of arsenic and cadmium with T2DM hospitalizations. Finally, all emergency  
302 hospitalizations due to the principal diagnosis of T2DM were included in the current study,  
303 but emergency visits due to hypoglycemia were not excluded. Hypoglycemia emergency  
304 hospitalizations are often associated with strict glycaemic control (Leese et al., 2003), but not  
305 with air pollution.

306

## 307 **5. Conclusions**

308 Our findings add new evidence regarding the differential toxicity of PM<sub>10</sub> constituents on  
309 Type II Diabetes mellitus and suggest PM<sub>10</sub> constituents from combustion-related particles  
310 (EC, OC, NO<sub>3</sub><sup>-</sup> and Ni) may cause acute exacerbations of symptoms or complications for type

311 II diabetes mellitus. Air pollution control policies may target local gasoline and diesel vehicle  
312 exhausts, residual oils from marine vessels, and regional industrial and agricultural  
313 combustion.

314

#### 315 **Conflict of interest**

316 The authors declare no actual or potential conflicts of interest.

317

#### 318 **Acknowledgements**

319 This study was supported by the Health and Medical Research Fund [grant number 11120311]

320 and the Natural Science Foundation of China [grant number 41272180]. We thank the

321 Hospital Authority for providing hospital admissions data, the Hong Kong Environmental

322 Protection Department for providing the air pollution monitoring data, and the Hong Kong

323 Observatory for providing the temperature and relative humidity data.



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479 **Table 1.** Summary statistics of emergency hospital admissions, meteorological conditions,  
 480 and concentrations of PM<sub>10</sub> and its chemical components in Hong Kong, China, 1998-2007.

Variable	No. of days	Mean (SD)	Percent of PM <sub>10</sub> mass	Percentile			IQR
				25th	50th	75th	
Emergency hospital admissions (counts)							
T2DM	3,652	11.0 (3.8)	-	9	11	13	5
Meteorological conditions							
Temperature, °C	3,652	23.6 (4.9)	-	19.7	24.8	27.8	8.1
Relative humidity, %	3,652	78.0 (10.0)	-	73.5	79.1	84.7	11.2
Pollutant concentration, µg/m <sup>3</sup>							
Nitrogen dioxide	2,497	59.9 (24.7)	-	42.6	59.0	75.0	32.4
Sulfur dioxide	2,499	20.2 (16.1)	-	9.8	16.0	25.2	15.5
Ozone	2,497	30.1 (20.3)	-	15.0	25.4	40.0	25.0
PM <sub>10</sub>	2,520	55.7 (30.8)	100.00	31.9	50.1	73.4	41.5
SO <sub>4</sub> <sup>2-</sup>	2,520	10.8 (7.0)	19.39	5.4	9.6	14.3	8.9
OC	2,511	8.7 (5.6)	15.62	4.5	7.4	11.5	7.0
EC	2,511	4.0 (1.8)	7.18	2.9	3.8	4.9	2.0
NO <sub>3</sub> <sup>-</sup>	2,520	3.5 (3.1)	6.28	1.5	2.5	4.8	3.3
NH <sub>4</sub> <sup>+</sup>	2,520	3.0 (2.6)	5.39	1.0	2.5	4.4	3.3
Na <sup>+</sup>	2,520	1.5 (1.0)	2.69	0.8	1.3	2.0	1.2
Cl <sup>-</sup>	2,520	0.9 (1.1)	1.62	0.3	0.6	1.2	0.9
Ca	2,520	0.8 (0.6)	1.44	0.4	0.6	1.0	0.6
K <sup>+</sup>	2,520	0.6 (0.6)	1.08	0.2	0.4	0.9	0.7
Fe	2,520	0.5 (0.4)	0.90	0.3	0.4	0.7	0.4
Al	2,520	0.3 (0.3)	0.54	0.1	0.2	0.3	0.2
Mg	2,520	0.3 (0.2)	0.54	0.2	0.2	0.3	0.2
Pb	2,520	0.07 (0.07)	0.13	0.02	0.04	0.10	0.08
Mn	2,520	0.02 (0.02)	0.04	0.01	0.02	0.03	0.02
As	2,520	0.005 (0.006)	0.01	0.001	0.003	0.007	0.006
Ni	2,520	0.006 (0.006)	0.01	0.002	0.004	0.007	0.005
Cd	2,520	0.002 (0.003)	0.00	0.0	0.001	0.003	0.002

481 Abbreviations: IQR, interquartile range; SD, standard deviation; T2DM, type II diabetes  
 482 mellitus; EC, elemental carbon; OC, organic carbon; NO<sub>3</sub><sup>-</sup>, nitrate; SO<sub>4</sub><sup>2-</sup>, sulfate; NH<sub>4</sub><sup>+</sup>,  
 483 ammonium; Na<sup>+</sup>, sodium ion; K<sup>+</sup>, potassium ion; Cl<sup>-</sup>, chloride ion; Al, aluminum; As, arsenic,  
 484 Ca, calcium; Cd, cadmium; Fe, iron; Mg, magnesium; Mn, manganese; Ni, nickel

485

486

**Table 2.** Pearson correlation of air pollutants.

	EC	OC	NO <sub>3</sub> <sup>-</sup>	Ni	SO <sub>4</sub> <sup>2-</sup>	NH <sub>4</sub> <sup>+</sup>	Na <sup>+</sup>	K <sup>+</sup>	Cl <sup>-</sup>	Al	As	Ca	Cd	Fe	Mg	Mn	Pb	PM <sub>10</sub>	NO <sub>2</sub>	SO <sub>2</sub>	O <sub>3</sub>	
EC	1.00																					
OC	0.39	1.00																				
NO <sub>3</sub> <sup>-</sup>	0.30	0.69	1.00																			
Ni	0.31	0.40	0.37	1.00																		
SO <sub>4</sub> <sup>2-</sup>	0.22	0.64	0.53	0.43	1.00																	
NH <sub>4</sub> <sup>+</sup>	0.25	0.72	0.67	0.48	0.93	1.00																
Na <sup>+</sup>	-0.12	-0.17	0.22	-0.05	0.09	-0.03	1.00															
K <sup>+</sup>	0.31	0.82	0.61	0.28	0.67	0.69	-0.12	1.00														
Cl <sup>-</sup>	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 <sub>10</sub>	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 <sub>2</sub>	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 <sub>2</sub>	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 <sub>3</sub>	-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	

487 Abbreviations: EC, elemental carbon; OC, organic carbon; NO<sub>3</sub><sup>-</sup>, nitrate; SO<sub>4</sub><sup>2-</sup>, sulfate; NH<sub>4</sub><sup>+</sup>, ammonium; Na<sup>+</sup>, sodium ion; K<sup>+</sup>, potassium ion;488 Cl<sup>-</sup>, chloride ion; Al, aluminum; As, arsenic, Ca, calcium; Cd, cadmium; Fe, iron; Mg, magnesium; Mn, manganese; Ni, nickel; Pb, lead.

489 **Figure legends:**

490

491 **Fig. 1.** Percentage excess risk (ER %) of emergency hospital admission for type II diabetes  
492 mellitus per interquartile range (IQR) increment in the concentrations of respirable particulate  
493 matter (PM<sub>10</sub>) and its chemical components on single-days (the lag<sub>0</sub> through lag<sub>3</sub>, and moving  
494 average of lag<sub>0-1</sub>) in the single-pollutant models adjusted for meteorological factors, time  
495 trends, public holiday, day of the week, and influenza epidemic, Hong Kong, China, 1998-  
496 2007. Filled circle indicates that the risk estimate is not statistically significant while hollow  
497 circle indicates it is statistically significant. EC, elemental carbon; OC, organic carbon; NO<sub>3</sub><sup>-</sup>,  
498 nitrate; SO<sub>4</sub><sup>2-</sup>, sulfate; NH<sub>4</sub><sup>+</sup>, ammonium; Na<sup>+</sup>, sodium ion; K<sup>+</sup>, potassium ion; Cl<sup>-</sup>, chloride  
499 ion; Al, aluminum; As, arsenic, Ca, calcium; Cd, cadmium; Fe, iron; Mg, magnesium; Mn,  
500 manganese; Ni, nickel; Pb, lead.

501

502 **Fig. 2.** Percentage excess risk (ER %) of emergency hospital admission for type II diabetes  
503 mellitus per interquartile range (IQR) increment in the concentrations of 2-day moving  
504 average (current day and previous day, lag<sub>0-1</sub>) of daily respirable particulate matter (PM<sub>10</sub>)  
505 and its chemical components with additional adjustment for co-pollutant in the two-pollutant  
506 models. Circle indicates that correlation between the second pollutant and the first is <0.6 in  
507 the two-pollutant model while square denotes the correlation is ≥ 0.6. Filled circle or square  
508 represents the risk estimate is not statistically significant while hollow circle or square  
509 indicates it is statistically significant. The vertical dash line denotes the point estimate of the  
510 chemical components in the single-pollutant models. EC, elemental carbon; OC, organic  
511 carbon; NO<sub>3</sub><sup>-</sup>, nitrate; SO<sub>4</sub><sup>2-</sup>, sulfate; NH<sub>4</sub><sup>+</sup>, ammonium; Na<sup>+</sup>, sodium ion; K<sup>+</sup>, potassium ion;  
512 Cl<sup>-</sup>, chloride ion; Al, aluminum; As, arsenic, Ca, calcium; Cd, cadmium; Fe, iron; Mg,  
513 magnesium; Mn, manganese; Ni, nickel; Pb, lead.

514

Figure-1

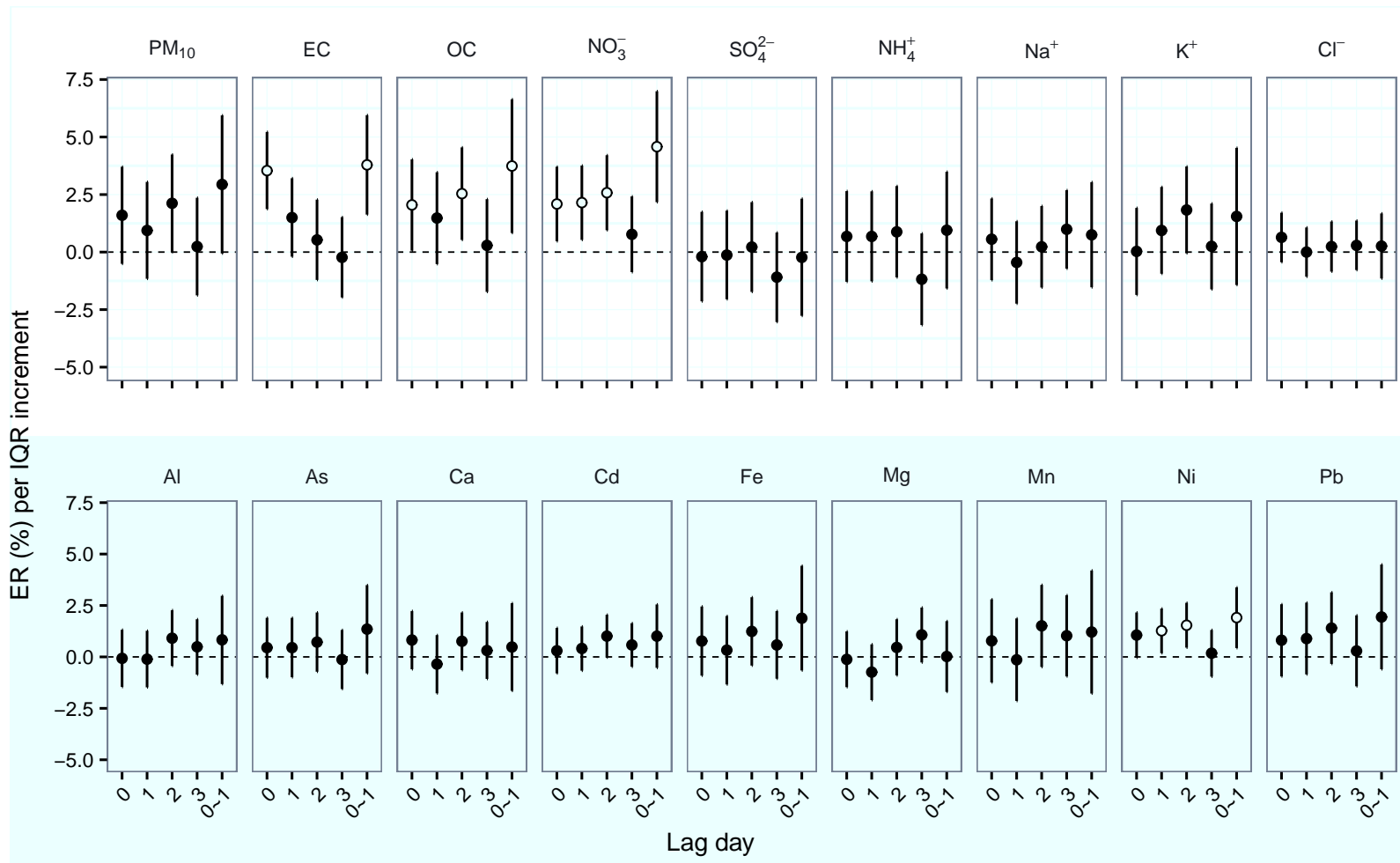
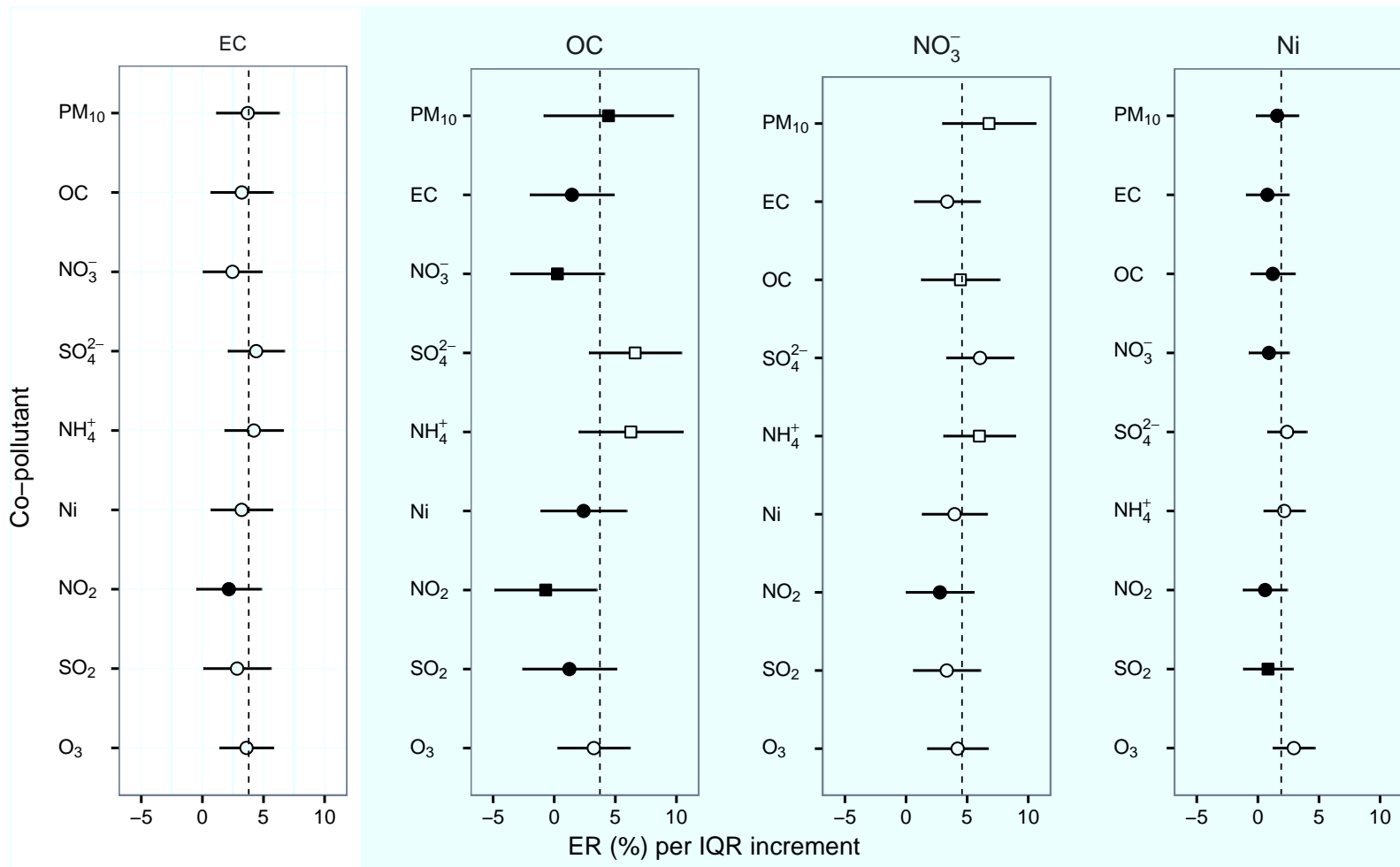




Figure-2



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