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Associations between Long-Term Particulate Matter Exposure and Adult Renal Function in the Taipei Metropolis

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Running title: Long-term air pollution and renal function

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Competing financial interests: The authors declare that they have no actual or potential competing financial interests.
Abstract

**Background:** This study aimed to investigate the associations between particulate matter (PM) exposures and renal function among adults.

**Methods:** We recruited 21,656 adults as subjects from 2007-2009. The Taiwanese Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was used to derive the estimated glomerular filtration rate (eGFR). Subjects with an eGFR lower than 60 mL/min/1.73 m$^2$ were defined as having chronic kidney disease (CKD). Land use regression (LUR) models were used to estimate individual exposures to PM with an aerodynamic diameter <10 µm (PM$\text{}_{10}$), coarse particles (PM$\text{Coarse}$), fine particles (PM$\text{2.5}$) and PM$\text{2.5Absorbance}$. Generalized linear and logistic regression models were used to estimate the associations between PM exposure and renal function.

**Results:** An IQR increase in PM$\text{10}$ (5.83µg/m$^3$) was negatively associated with eGFR by –0.69 (95% CI: –0.89, –0.48) ml/min/1.73 m$^2$ and positively associated with the prevalence of CKD with adjusted OR = 1.15 (1.07, 1.23). An IQR increase in PM$\text{Coarse}$ (6.59µg/m$^3$) was significantly associated with lower eGFR by –1.07 (–1.32, –0.81) ml/min/1.73 m$^2$ and CKD with OR = 1.26 (1.15, 1.38). In contrast, neither outcome was significantly associated with PM$\text{2.5}$ or PM$\text{2.5Absorbance}$. Stratified analyses indicated that associations of CKD with both PM$\text{10}$ and PM$\text{Coarse}$ were limited to participants < 65 years of age, and were stronger (for PM$\text{10}$) or limited to (PM$\text{Coarse}$) women. Associations also appeared to be stronger in those without (vs. with) hypertension, and in normal vs. overweight participants.

**Conclusions:** Exposure during the previous year to PM$\text{10}$ and PM$\text{Coarse}$, but not PM$\text{2.5}$ or PM$\text{2.5Absorbance}$, was associated with reduced renal function among Taiwanese adults.
Introduction

A large body of evidence supports adverse effects of ambient air pollution on vital organs, including the heart, lungs, and central nervous system (Kampa and Castanas 2008). Recent studies suggest that particulate matter (PM) exerts detrimental effects on cardiovascular outcomes through the induction of oxidative injury and proinflammatory pathways and the resultant development and progression of atherosclerosis (Brook et al. 2010; Mills et al. 2009). The presence of cardiovascular disease (CVD) is known to predict a faster progression of chronic kidney disease (CKD) toward end-stage renal disease (ESRD) (Levin 2003), while patients with CKD have a high risk of developing cardiovascular events and of all-cause mortality (Go et al. 2004; Weiner et al. 2004). Because CKD is regarded as a coronary heart disease risk factor (Briasoulis and Bakris 2013; Tonelli et al. 2012), it is tempting to speculate that ambient air pollution or PM may affect kidney function through direct or indirect mechanisms similar to those proposed for cardiovascular effects of these exposures. In Taiwan, ambient air pollutants and PM have been associated with hospital admissions for CVD (Chang et al. 2005; Chen et al. 2015; Hsieh et al. 2010; Yang 2008). In contrast, we are aware of only three observational studies that have explored the potential effects of air pollutants on renal function, with conflicting results (Lue et al. 2013; Mehta et al. 2016; O’Neill et al. 2008). A recent experimental study reported that 16 weeks of exposure to concentrated ambient particles (average 13.3 μg/m3) versus filtered air was positively associated with glomerulosclerosis in a rat model of type 1 diabetes (Yan et al. 2014). A recent longitudinal analysis of participants in the VA Normative Aging Study indicated a negative association between PM$_{2.5}$ exposure during
the previous year and renal function in older men (Mehta et al. 2016). In 2013, Taiwan was ranked as the country with the highest incidence of ESRD among dozens of countries surveyed (United States Renal Data System 2015). Therefore, we conducted a cross-sectional population-based study to investigate associations between particulate matter exposure during the previous year (estimated using a land use regression (LUR) model) and renal function and CKD prevalence in metropolitan adults residing in New Taipei City, Taiwan.
Materials and Methods

Study Population. Subjects for the present study were selected from participants in the New Taipei City Health Screening Program, an annual health screening program supervised by the Department of Health of the New Taipei City Government (http://www.health.ntpc.gov.tw/english/index.aspx). All citizens > 30 years of age who resided in New Taipei City were invited to participate in the program every three years. The present study included those who participated during 2007–2009 and were residents of the metropolitan area (population density > 20,000/km² in 2009) and 30–97 years of age. After excluding 2,630 participants with incomplete information, the final population for the present study included 21,656 subjects living in six districts. The Department of Health of the New Taipei City Government approved our use of de-identified screening program data (with names and IDs unlinked from medical records to ensure confidentiality), and the study was approved by the Joint Institutional Review Boards of National Health Research Institutes.

Health Data. The health screening program conducted by the Department of Health of the New Taipei City Government included a clinician interview, self-reported questionnaire, and collection of a venous blood sample. The clinician interview and questionnaire gathered information that included each subject’s home address, age, sex, height, weight, body mass index (BMI), smoking status, alcohol consumption, and betel-nut-chewing status. Measurements of blood pressure were taken once with the subject seated in an upright position during the morning with an electronic sphygmomanometer (Model HEM-770A; Omron Health Care) by trained medical personnel. One of three cuff-sizes, including adult standard, large, and thigh-sized, were
used depending on the circumference of the participant’s left arm. Serum creatinine was analyzed by isotope dilution mass spectrometry (IDMS)-traceable enzymatic method (Chen et al. 2014). Hypertension was defined as a systolic blood pressure ≥ 140 mm Hg or a diastolic blood pressure ≥ 90 mm Hg; overweight was defined as having a BMI ≥ 24 (kg/m²); diabetes mellitus was defined as having a fasting glucose ≥ 126 mg/dL; and hyperlipidemia was defined as having cholesterol ≥ 200 mg/dL. All of these classifications were classified based only on measurements taken at the time of the screening examination, without regard for prior history or treatment.

**Renal Function.** We used the CKD-EPI-Taiwan equation to estimate eGFR:

\[
eGFR = 1.262 \times \left\{ 141 \times \min(\frac{\text{Scr}}{\kappa}, 1) \times \max(\frac{\text{Scr}}{\kappa}, 1) \right\}^{1.209} \times 0.993^{\text{Age}} \times 1.018 \times [\text{if female}] \times 1.159 \times [\text{if black}]^{0.914},
\]

where Scr is the serum creatinine, \(\kappa\) is 0.7 for females and 0.9 for males, \(\alpha\) is -0.329 for females and -0.411 for males, min indicates the minimum of \(\text{Scr}/\kappa\) or 1, and max indicates the maximum of \(\text{Scr}/\kappa\) or 1 (Chen et al. 2014). The CKD-EPI-Taiwan equation performed better (when compared with inulin clearance) than the Modification of Diet in Renal Disease (MDRD) equation (Levey et al. 1999) or the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (Levey et al. 2009) in a validation study of Taiwanese adults. We classified CKD based on eGFR < 60 mL/min/1.73 m², which represents a ≥ 50% reduction in normal kidney function (Levey et al. 2003).

**Particulate Matter Exposures.** We estimated annual average concentrations of PM_{2.5}, PM_{2.5} Absorbance, PM_{10}, and PM_{Coarse} (defined as PM_{10} – PM_{2.5}) at each subject’s residence address using a land use regression (LUR) model developed for the ESCAPE project (http://www.escapeproject.eu/manuals) (Eeftens et al. 2012; Wang et al. 2013). To derive the
model, we measured PM concentrations at 20 sampling sites (most of which were located in metropolitan Taipei) during three 14-day periods representing the intermediate (October to December 2009), cold (January to March 2010), and warm (June to August 2010) seasons. We used Harvard impactors (Air Diagnostics and Engineering Inc.) to collect the particles, and a Smoke Stain Reflectometer (Model 43, Diffusion Systems Ltd.) to determine the PM$_{2.5}^{\text{Absorbance}}$ for the collected filters. We used ArcGIS (ESRI) to obtain Geographic Information System (GIS) information for land use and population data (buffers with radii of 100, 300, 500, 1,000, and 5,000 m), traffic data (buffers of 25, 50, 100, 300, 500, and 1,000 m), and major roads (national highway, provincial highway, expressway, and city street) and elevated highways (roads established above ground level or highway ramp), and used supervised forward stepwise multiple regression to derive the final LUR models. Cross-validated $R^2$ values were 0.74, 0.52, 0.91, and 0.92 for PM$_{10}$, PM$_{\text{Coarse}}$, PM$_{2.5}$, and PM$_{2.5}^{\text{Absorbance}}$, respectively (Lee et al. 2015).

**Statistical analyses.** We use adjusted generalized linear regression models to estimate associations between interquartile range (IQR) increases in annual average PM exposures and eGFR, and used adjusted logistic regression models to estimate associations with prevalent CKD. Model covariates were age, fasting blood glucose, cholesterol, BMI, and distance to a major road (all modeled as continuous variables); gender; hypertension (yes if SBP $\geq$ 140 mmHg or DBP $\geq$ 90 mmHg, otherwise no); smoking (never, former, or current); alcohol consumption (never, former, seldom, or current); and education (uneducated, elementary or junior high, high school, college or graduate school). We used stratified analyses to examine whether associations with CKD differed according to gender, hypertension (yes or no), overweight (BMI $\geq$ 24 kg/m$^2$ vs. $<$ 24 kg/m$^2$), diabetes mellitus (yes or no), smoking status (never, former, or current), distance to a
major road (distance < 667.96 vs. ≥ 667.96 m), hyperlipidemia (cholesterol ≥ 200 mg/dL vs. < 200 mg/dL), age (age < 65 vs. ≥ 65), alcohol use (never, former, seldom, or current), or education (uneducated, elementary or junior high, high school, college or graduate school). Hierarchical models were used to control the confounding effect of the district. All of the analyses were performed using SAS software (Version 9.3; SAS Institute).
Results

Our study population consisted of adults with a mean age of 53.65 years, and the female to male ratio was approximately 2:1 (Table 1). Furthermore, 50.4% of the subjects had a BMI higher than 24 kg/m\(^2\), and 33.2% were defined as hypertensive subjects. Regarding health behaviors, 18.4% of patients had smoked, 36.6% had consumed alcohol, and 3.5% had chewed betel nut. The mean eGFR was 77.05 ± 13.18 mL/min/1.73 m\(^2\), and 10.3% (n = 2,226) were classified as having CKD based on eGFR < 60 mL/min/1.73 m\(^2\). The annual average concentration of PM\(_{2.5}\) was 26.64 µg/m\(^3\), which exceeded the guidelines of the WHO in 2005 (10 µg/m\(^3\)), the National Ambient Air Quality Standard (NAAQS) in 2005 (12 µg/m\(^3\)) and the standard of Taiwan in 2012 (15 µg/m\(^3\)). The annual average concentrations of PM\(_{2.5Absorbance}\), PM\(_{10}\), and PM\(_{Coarse}\) were 1.94 \(10^{-5}\) m\(^{-1}\), 49.48 µg/m\(^3\) and 23.13 µg/m\(^3\), respectively. The concentration of PM\(_{10}\) exceeded the annual mean value from the WHO guidelines in 2005 (20 µg/m\(^3\)).

eGFR was significantly lower in association with IQR increases in annual average PM\(_{10}\) (\(\beta = -0.69\); 95% CI: -0.89, -0.48 for 5.83 µg/m\(^3\)) and PM\(_{Coarse}\) (\(\beta = -1.06\); 95% CI: -1.32, -0.81 for 6.59 µg/m\(^3\)) based on a fully adjusted linear regression model (Table 2). The prevalence of CKD also was significantly higher in association with IQR increases in PM\(_{10}\) (OR = 1.15; 95% CI: 1.07, 1.23) and PM\(_{Coarse}\) (OR = 1.26; 95% CI: 1.15, 1.38) based on a fully adjusted logistic regression model (Table 2). In contrast, neither eGFR nor CKD was significantly associated with IQR increases in PM\(_{2.5}\) or PM\(_{2.5Absorbance}\).
Overall, model estimates for associations of the PM exposures with eGFR and CKD were consistent with results from the main models when we adjusted for age only, and when we used hierarchical models to adjust for district of residence in addition to the other covariates included in the main model (Supplemental Material, Tables S1 and S2).

Stratified analyses indicated that associations between CKD and PM$_{10}$ were positive for those < 65 years of age, but null for older participants (Figure 2). In addition, positive associations between CKD and PM$_{10}$ were stronger in females than males, in those without versus with hypertension, and in those who were normal weight versus overweight. PM$_{10}$ also was more strongly associated with CKD among those who lived > 667.96 m from a major road compared with those who lived closer to a major road. Associations varied according to smoking status and alcohol use, but stratum-specific estimates were imprecise due to small numbers of cases within some of the groups. There was little variation in associations according to education or other factors evaluated. Patterns of associations between PM$_{Coarse}$ and CKD according to population subgroups were similar to those for PM$_{10}$, though the association appeared to be limited to females, as the association was null in males. Stratum-specific associations between CKD and PM$_{2.5}$ and PM$_{2.5Absorbance}$ were generally close to the null, without clear evidence of subgroup-specific effects (Figure 1). The same stratification analysis on eGFR showed the similar results (Supplemental figure 1 and 2).
Discussion

We successfully used LUR models to estimate within-city variation in PM exposures among 21,656 adult residents of New Taipei City, and used the CKD-EPI-Taiwan equation, a modified version of the CKD-EPI equation (Chen et al. 2014), to estimate eGFR as a measure of renal function. We found that eGFR was inversely associated with average PM\textsubscript{10} and PM\textsubscript{Coarse} concentrations during the previous year. In addition, both exposures were associated with a higher prevalence of CKD, which was identified in 10% of our study population, consistent with the prevalence reported for Taiwan as a whole in 2003 (Kuo et al. 2007). Our findings are generally consistent with a recent longitudinal study that reported a negative association between long-term PM\textsubscript{2.5} exposure and eGFR in 669 older American men (Mehta et al. 2016), though associations were specific to coarser fractions of PM in our study population. Living closer to a major road, an indicator of traffic related air pollution exposure, also was associated with lower eGFR in a study of 1,103 patients hospitalized for ischemic stroke (Lue et al. 20013). However, the urinary albumin/creatinine ratio, another indicator of renal function, was not associated with average 20-year exposure to PM\textsubscript{10} or PM\textsubscript{2.5} in 3,901 participants in the MESA cohort study (O’Neill et al. 2008).

Our findings also suggest that associations of CKD with PM exposures were stronger in females than males for PM\textsubscript{10}, and limited to females for PM\textsubscript{Coarse}. Previous studies have reported inconsistent findings for the effect of gender on the progression of CKD. A meta-analysis found that male patients with CKD displayed a faster rate of eGFR decline than their female counterparts (Neugarten et al. 2000). Conversely, another meta-analysis found that the adjusted
hazard ratio for all-cause mortality was significantly higher in females than in males among those who had lower eGFR (Nitsch et al. 2013). An epidemiological study of CKD in Taiwan also showed that females had a higher incidence rate and risk of CKD compared with males (Kuo et al. 2007).

Due to lack the information on socioeconomic or income data, we used the variable of education level as an indicator of socioeconomic level instead. A previous study found that a lower socioeconomic status might be related to greater risk of CKD among white men (Merkin et al. 2005) and African Americans (Bruce et al. 2010). Although we adjusted for education as a proxy measure of socioeconomic status, we cannot rule out residual confounding by socioeconomic status in our study (Forastiere et al. 2007).

We also found stronger associations of PM$_{10}$ and PM$_{Coarse}$ with CKD among subjects who were normal weight vs. overweight, non-hypertensive vs. hypertensive, and in those who lived > 667.96 m from a major road compared with those who lived closer to a major road. Previous studies have rarely addressed the population susceptibility of renal function to air pollution, but a few studies have observed an association between long-term PM exposure and impaired renal function among subjects with comorbid diseases. In contrast with our findings, Mehta et al. reported that the negative association between PM$_{2.5}$ and eGFR was stronger in non-diabetic than diabetic subjects (interaction p-value 0.09), and stronger in those with high blood pressure versus normal blood pressure, and in obese vs. non-obese participants (interaction p-values of 0.17 and 0.20, respectively) (Mehta et al. 2016). The protective effects of medication may be attributed to our findings of stronger PM-CKD associations among subjects with healthy statuses or behaviors.
Urinary 8-hydroxy-2’-deoxyguanosine (8-OHdG), a biomarker of reactive oxygen species (ROS)-induced DNA damage, was inversely associated with recent exposure to PM$_{2.5}$ in 12 subjects with hypertension, but positively associated with PM$_{2.5}$ in 9 normotensive subjects (Christiani 2009). Although hypertensive subjects were significantly older, and were more likely to be smokers and to have diabetes or inflammatory lung disease than normotensive subjects, 11 of 12 were taking antihypertensive medication that the authors suggested might have reduced DNA damage in response to PM$_{2.5}$ through antioxidant effects (Christiani 2009). We did not have information on medication use in our study population, so were not able to determine whether medication use among participants with hypertension might have reduced their susceptibility to effects of PM on renal function.

Information from the National Health Interview Survey (https://olap.hpa.gov.tw/index.aspx) about the general population of New Taipei City > 30 years of age in 2009 suggests that our study population was more likely than the general population to be overweight (50% compared with 47%) and to have hypertension (33% compared with 22%), but were less likely to be current smokers (11% vs. 20%), alcohol consumers (37% vs. 55%), and betel nut chewers (3.5% vs. 8.3%).

There is limited research on the renal toxicity of inhaled ambient PM; however, it may partially share the pathway of PM-related cardiovascular toxicity. According to the American Heart Association’s scientific statement in 2010, airborne PM might lead to systematic oxidative stress, inflammation, thrombosis, vascular dysfunction, and atherosclerosis, which result in both macro- and micro-vascular damage (Brook et al. 2010). Because the kidney is highly
vascularized and susceptible to atherosclerotic disease, PM might induce ischemic insults to the micro-vascular system of the kidney and might facilitate the progression toward chronic tubular damage (Tran et al. 2011). Previous studies also found that the risk of cardiovascular disease increased with a decline in eGFR (Go et al. 2004), and the risk of CKD was associated with inflammation (Muntner et al. 2004). An experimental study using a rat model of type 1 diabetes reported increased carotid intima thickness media and advanced glomerulosclerosis and tubular damage after 16 weeks of exposure to PM (average 13.30 μg/m³) compared with fresh air (Yan et al. 2014). The nephrotoxicity of smoking may also support our findings. Smoking has been recognized as an independent risk factor for CKD, and smoking might result in intraglomerular hypertension, vascular damage, or glomerulosclerosis via multiple complex interactions of nonhemodynamic (angiotensin II, transforming growth factor-β1, endothelin-1) and hemodynamic factors (Orth and Hallan 2008). Environmental (Galażyn-Sidorczuk et al. 2008) and occupational (El-Safty et al. 2004) exposures to cadmium and lead may affect the magnitude of kidney damage conferred by smoking. Pinto-Sietsma et al. found that subjects who smoked more than 20 cigarettes/day might have a higher degree of eGFR decrease than others (Pinto-Sietsma et al. 2000).

It should be noted that we found a stronger association with PM_{10} and PM_{Coarse} than with PM_{2.5}, which may be related to differences in the constituents of the particles that may influence their toxicity. An in vitro study found that the level of coarse particles was related to the endotoxin levels, which act as a pro-inflammatory indicator (Stehnof et al. 2011). Macrophages in the human lung were more easily stimulated by coarse particles than fine particles (Becker et
al. 2002). The level of tumor necrosis factor-α was also more correlated with coarse particles than fine particles according to one study performed in Taipei (Huang et al. 2002). Cadmium, metallic mercury and lead exposures were reported to be related to kidney damage (Järup 2003). Cadmium exposure was reported to increase with the size of PM in Taipei (Wu et al. 2010). The size and composition of particulate matter also appeared to have different effects on renal function, which warrants further study for confirmation.

There are several limitations of this investigation. First, we only estimated exposures to PM air pollution, and associations with gaseous pollutants and specific PM components should be evaluated in future studies. Second, although we have considered and controlled for individual characteristics and comorbid diseases, we did not have information on dietary habits or medication use, which may have confounded or modified exposure-outcome associations. Third, We did not adjust for proteinuria, which, along with low eGFR, is one of the most important risk factors for the progression of CKD (Astor et al. 2011; Tangri et al. 2011; Tonelli et al. 2011). Fourth, the fact that the stratum-specific OR for non-diabetics is significantly different from the null, while the stratum-specific OR for diabetics is not, is largely a consequence of the difference in the sample sizes. Additionally, eGFR was estimated based on a single serum creatinine measurement, which might have been influenced by recent diet, nutrition status, or inflammatory status. (Branten et al. 2005; Quan et al. 1997). Finally, our findings, which were based on a population-based sample of adults ≥30 years of age, may not apply to specific population subgroups such as the elderly or those with specific comorbid conditions that might increase their susceptibility renal disease as a consequence of PM exposure.
In conclusion, exposures to PM$_{10}$ and PM$_{Coarse}$ during the previous year were associated with lower eGFR and an increase in the prevalence of CKD among adult residents of Taipei City. Subgroup analyses suggested that these associations may be stronger in females than males and in younger vs. older adults, in those who are normal weight vs. overweight and non-hypertensive vs. hypertensive, and in those who live > 667.96 m from a major road. Longitudinal cohort studies are needed to confirm our findings.
References


Eeftens M, Beelen R, de Hoogh K, Bellander T, Cesaroni G, Cirach M, et al. 2012. Development of land use regression models for pm(2.5), pm(10) and pm(coarse) in 20 european study areas; results of the escape project. Environmental science & technology 46:11195-11205.


### Tables

Table 1. Characteristics of the 21,656 subjects in New Taipei City.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD or N (%)</th>
<th>Missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>53.65 ± 10.37</td>
<td>0</td>
</tr>
<tr>
<td>Age &lt; 65</td>
<td>18,355 (84.8)</td>
<td></td>
</tr>
<tr>
<td>65 ≤ Age</td>
<td>3,301 (15.2)</td>
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</tr>
<tr>
<td>Female Gender</td>
<td>14,477 (66.9)</td>
<td>0</td>
</tr>
<tr>
<td>Body Mass Index (BMI) (kg/m²)</td>
<td>24.35 ± 3.51</td>
<td>44</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>79.21 ± 9.97</td>
<td>486</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>128.8 ± 20.16</td>
<td>46</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>81.8 ± 12.15</td>
<td>48</td>
</tr>
<tr>
<td>Fasting Glucose (mg/dL)</td>
<td>100.61 ± 25.75</td>
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</tr>
<tr>
<td>Cholesterol (mg/dL)</td>
<td>204.42 ± 36.54</td>
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</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>118.73 ± 81.49</td>
<td>1</td>
</tr>
<tr>
<td>HDL (mg/dL)</td>
<td>68.96 ± 36.52</td>
<td>100</td>
</tr>
<tr>
<td>LDL (mg/dL)</td>
<td>113.06 ± 41.52</td>
<td>192</td>
</tr>
<tr>
<td>BUN (mg/dL)</td>
<td>13.48 ± 4.36</td>
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</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>0.84 ± 0.31</td>
<td>0</td>
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<tr>
<td>Hypertension, Yes&lt;sup&gt;a&lt;/sup&gt;</td>
<td>7,164 (33.2)</td>
<td>46</td>
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<tr>
<td>Overweight, Yes&lt;sup&gt;b&lt;/sup&gt;</td>
<td>10,902 (50.4)</td>
<td>44</td>
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<tr>
<td>Diabetes Mellitus (DM), Yes&lt;sup&gt;c&lt;/sup&gt;</td>
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<tr>
<td>Hyperlipidemia, Yes&lt;sup&gt;d&lt;/sup&gt;</td>
<td>11,405 (52.7)</td>
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<tr>
<td>Distance to Major Road (meter)</td>
<td>667.96 ± 453.78</td>
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</tr>
<tr>
<td>Away from Major Road&lt;sup&gt;e&lt;/sup&gt;</td>
<td>9,729 (44.9)</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td>13</td>
</tr>
<tr>
<td>Never</td>
<td>17,664 (81.6)</td>
<td></td>
</tr>
<tr>
<td>Former</td>
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<tr>
<td>Current Smoker</td>
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<tr>
<td>Alcohol Consumption</td>
<td>9</td>
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<tr>
<td>Never</td>
<td>13,716 (63.4)</td>
<td></td>
</tr>
<tr>
<td>Former</td>
<td>406 (1.9)</td>
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</tr>
<tr>
<td>Seldom&lt;sup&gt;f&lt;/sup&gt;</td>
<td>6,430 (29.7)</td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>1,095 (5.1)</td>
<td></td>
</tr>
<tr>
<td>Ever Chew Betel Nut</td>
<td>763 (3.5)</td>
<td>22</td>
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### Education level

<table>
<thead>
<tr>
<th>Level</th>
<th>Count (Percentage)</th>
</tr>
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<tbody>
<tr>
<td>Uneducated</td>
<td>1,523 (7.1)</td>
</tr>
<tr>
<td>Elementary or junior high school</td>
<td>9,179 (42.7)</td>
</tr>
<tr>
<td>High school</td>
<td>6,417 (29.9)</td>
</tr>
<tr>
<td>College or graduate school</td>
<td>4,371 (20.3)</td>
</tr>
</tbody>
</table>

### Estimated Glomerular Filtration Rate (eGFR)

77.05 ± 13.18

### Chronic Kidney Disease (CKD)

2,226 (10.3)

### One-year Exposure

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± SD (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PM$_{2.5}$ (µg/m$^3$)</td>
<td>26.64 ± 5.01</td>
</tr>
<tr>
<td></td>
<td>(IQR$^i$ = 5.67)</td>
</tr>
<tr>
<td>PM$_{2.5}$ Absorbance (10$^{-5}$m$^{-1}$)</td>
<td>1.94 ± 0.39</td>
</tr>
<tr>
<td></td>
<td>(IQR = 0.48)</td>
</tr>
<tr>
<td>PM$_{10}$ (µg/m$^3$)</td>
<td>49.48 ± 4.13</td>
</tr>
<tr>
<td></td>
<td>(IQR = 5.83)</td>
</tr>
<tr>
<td>PM$_{coarse}$ (µg/m$^3$)</td>
<td>23.13 ± 3.68</td>
</tr>
<tr>
<td></td>
<td>(IQR = 6.59)</td>
</tr>
</tbody>
</table>

---

a. Hypertension defined as SBP$\geq$140 mmHg or DBP$\geq$90 mmHg.
b. Overweight defined as BMI$\geq$24(kg/m$^2$).
c. Diabetes mellitus (DM) defines as fasting glucose$\geq$126 mg/dL.
d. Hyperlipidemia defined as cholesterol$\geq$200 mg/dL.
e. Away from major road indicated as distance from major road greater than 667.96 m.
f. Seldom indicated drink in special occasions, eg. wedding or business entertainment
g. eGFR estimated by equation of CKD-EPI-Taiwan.
h. CKD defined as eGFR$\leq$60 mL/min per 1.73 m$^2$.
i. IQR: interquartile range.
Table 2. Estimated associations of IQR increases in annual average PM exposures and eGFR or CKD (New Taipei City, n = 21,656)\textsuperscript{a}

<table>
<thead>
<tr>
<th>Exposure</th>
<th>IQR</th>
<th>eGFR β (95% CI)</th>
<th>CKD\textsuperscript{b} OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PM\textsubscript{2.5}</td>
<td>5.67 µg/m\textsuperscript{3}</td>
<td>-0.09 (-0.25, 0.07)</td>
<td>1.03 (0.97, 1.09)</td>
</tr>
<tr>
<td>PM\textsubscript{2.5 Absorbance}</td>
<td>0.48 × 10\textsuperscript{-5}/m</td>
<td>0.02 (-0.16, 0.19)</td>
<td>1.03 (0.96, 1.09)</td>
</tr>
<tr>
<td>PM\textsubscript{10}</td>
<td>5.83 µg/m\textsuperscript{3}</td>
<td>-0.69 (-0.89, -0.48)</td>
<td>1.15 (1.07, 1.23)</td>
</tr>
<tr>
<td>PM\textsubscript{Coarse}</td>
<td>6.59 µg/m\textsuperscript{3}</td>
<td>-1.06 (-1.32, -0.81)</td>
<td>1.26 (1.15, 1.38)</td>
</tr>
</tbody>
</table>

\textsuperscript{a}All models adjusted for age (years), gender, fasting glucose (mg/dL), cholesterol (mg/dL), hypertension (yes/no), BMI (kg/m\textsuperscript{2}), distance to major road (m), smoking (never, former, current), alcohol consumption (never, former, seldom, current), and education (uneducated, elementary or junior high school, high school, college or graduate school).

\textsuperscript{b}CKD defined as eGFR ≤ 60 mL/min per 1.73 m\textsuperscript{2}
Figure 1. The odds of CKD for PM$_{2.5}$ and PM$_{2.5,\text{Absorbance}}$ exposures stratified by age, gender, diabetes mellitus, hyperlipidemia, hypertension, overweight, distance to major road, smoking status, alcohol consumption, and education level among the 21,656 subjects of New Taipei City.

Figure 2. The odds of CKD for PM$_{10}$ and PM$_{\text{Coarse}}$ exposures stratified by age, gender, diabetes mellitus, hyperlipidemia, hypertension, overweight, distance to major road, smoking status, alcohol consumption, and education level among the 21,656 subjects of New Taipei City.
Figure 1.
Figure 2.

A

PM$_{10}$ (per IQR)

Below 65 yrs (N=18,355)
Above 65 yrs (N=3,301)
Female (N=14,477)
Male (N=7,179)
Without Diabetes Mellitus (N=20,106)
With Diabetes Mellitus (N=1,550)
Without Hyperlipidemia (N=10,249)
With Hyperlipidemia (N=11,405)
Without Hypertension (N=14,446)
With Hypertension (N=7,164)
Without Overweight (N=10,710)
With Overweight (N=10,902)
Near Major Road (N=11,927)
Away from Major Road (N=9,729)
Never Smoke (N=17,664)
Former Smoker (N=1,502)
Current Smoker (N=2,477)
Never Drink (N=13,716)
Former Drinker (N=406)
Seldom Drink (N=6,430)
Current Drinker (N=1,055)
Uneducated (N=1,523)
Elementary or junior high school (N=9,179)
High school (N=6,417)
College or graduate school (N=4,371)

B

PM$_{Coarse}$ (per IQR)

Below 65 yrs (N=18,355)
Above 65 yrs (N=3,301)
Female (N=14,477)
Male (N=7,179)
Without Diabetes Mellitus (N=20,106)
With Diabetes Mellitus (N=1,550)
Without Hyperlipidemia (N=10,249)
With Hyperlipidemia (N=11,405)
Without Hypertension (N=14,446)
With Hypertension (N=7,164)
Without Overweight (N=10,710)
With Overweight (N=10,902)
Near Major Road (N=11,927)
Away from Major Road (N=9,729)
Never Smoke (N=17,664)
Former Smoker (N=1,502)
Current Smoker (N=2,477)
Never Drink (N=13,716)
Former Drinker (N=406)
Seldom Drink (N=6,430)
Current Drinker (N=1,055)
Uneducated (N=1,523)
Elementary or junior high school (N=9,179)
High school (N=6,417)
College or graduate school (N=4,371)