Environmental Research 164 (2018) 24–31

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Personal exposure to fine particles ($PM_{2.5}$) and respiratory inflammation of common residents in Hong Kong

Zhanlan Fan[a], Vivian C. Pun[b], Xiao-Cui Chen[a,c], Qiu Hong[d], Linwei Tian[d], Steven Sai-Hang Ho[e], Shun-Cheng Lee[f], Lap Ah Tse[a], Kin-Fai Ho[a,c,*]

[a] The Jockey Club School of Public Healthh and Primary Care, The Chinese University of Hong Kong, Hong Kong, China
[b] Saw Swee Hock School of Public Health, National University of Singapore, Singapore
[c] Institute of Environment, energy and Sustainability, The Chinese University of Hong Kong, Hong Kong, China
[d] School of Public Health, The University of Hong Kong, Hong Kong, China
[e] Key Laboratory of Aerosol Chemistry and Physics, SKLLQG, Institute of Earth Environment, Chinese Academy of Sciences, Xi'an 710075, China
[f] Department of Civil and Environmental Engineering, The Hong Kong Polytechnic University, Hong Kong, China

ARTICLE INFO

Keywords:
Fine particles
Personal exposure
Respiratory inflammation
Carbonaceous materials
Polycyclic aromatic hydrocarbons

ABSTRACT

Background: Given the lack of research on the personal exposure to fine particles ($PM_{2.5}$) in Hong Kong, we examined the association between short-term personal exposure to $PM_{2.5}$ and their constituents and inflammation in exhaled breath in a sample of healthy adult residents.

Method: Forty-six participants underwent personal $PM_{2.5}$ monitoring for averagely 6 days to obtain 276 samples. Fractional exhaled nitric oxide (FeNO), a biomarker of inflammation in exhaled breath, was measured at the end of each 24-h personal monitoring. $PM_{2.5}$ chemical constituents, including organic carbon, elemental carbon, 16 polycyclic aromatic hydrocarbons (PAHs), and 6 phthalate esters, were speciated from the personal samples collected. A mixed-effects model was used to estimate the association of $PM_{2.5}$ and their constituents with FeNO. The comparison was also made with parallel analyses using ambient concentrations.

Results: Personal exposures to $PM_{2.5}$ (28.1 ± 23.3 μg/m^3) were higher than the ambient levels (13.3 ± 6.4 μg/m^3) monitored by stations. The composition profile and personal-to-ambient concentration ratio varied among subjects with different occupations. An interquartile range (IQR) change in personal exposure to $PM_{2.5}$ was positively associated with 12.8% increase in FeNO (95% confidence interval, CI: 5.5–20.7%), while nil association was found for ambient $PM_{2.5}$. Among the constituents measured, only the carcinogenic PAHs were significantly associated with 12% increase in FeNO responses (95% CI, 0.0–25.6%).

Conclusion: In conclusion, our study provides the first understanding about personal exposure to $PM_{2.5}$ and possible sources in Hong Kong. The results also showed that personal exposure to $PM_{2.5}$ and c-PAHs were linked to increased FeNO levels among healthy adults.

1. Introduction

Numerous epidemiologic studies have documented that fine particulate matter ($PM_{2.5}$) is associated with inflammation-related diseases such as asthma and chronic bronchitis (Kunzli et al., 2009; Pope and Dockery, 2006). $PM_{2.5}$ is a complex mixture of various organic and inorganic chemical substances and its toxicity changes with its composition (Osornio-Vargas et al., 2003). Therefore, the identification of hazardous components to health is crucial for the implementation of efficient air pollution control strategies. Elemental carbon (EC) and organic carbon (OC), which is frequently measured in epidemiologic studies, are important PM compositions (Jansen et al., 2005; Lin et al., 2011). Polycyclic aromatic hydrocarbons (PAHs) are known for their carcinogenicity; both experimental and epidemiological evidence of PAHs indicated proinflammatory effects on airways (Delfino et al., 2010). Phthalates are common industrial chemicals used in cosmetics, personal care products, plastics, and building materials. Their occurrence in $PM_{2.5}$ have been proved by previous papers (Rakkestad et al., 2007; Tran and Kannan, 2015). Serial investigations done by the US National Health and Nutrition Examination Survey (NHANES) have provided effective evidence for the relationships between total PAEs exposure and airway inflammation, deteriorated lung functions and

Abbreviations: $PM_{2.5}$, Fine particle; FeNO, Fractional exhaled nitric oxide; PAHs, Polycyclic aromatic hydrocarbons; IQR, Interquartile range; CI, Confidence interval; c-PAHs, Carcinogenic PAHs

* Corresponding author at: The Jockey Club School of Public Health and Primary Care, The Chinese University of Hong Kong, Hong Kong, China.
E-mail address: kfho@cuhk.edu.hk (K.-F. Ho).

https://doi.org/10.1016/j.envres.2018.02.009
Received 11 October 2017; Received in revised form 15 January 2018; Accepted 8 February 2018
Available online 22 February 2018
0013-9351/

allergic symptoms (Ferguson et al., 2011; Hoppin et al., 2004). However, there is still lack of reports on the contribution and potential effect of phthalates exposure through inhalation. Most studies have used ambient measure of $PM_{2.5}$ in the assessment of the association between particulate air pollution and health. However, such ambient measurement tends to reflect the urban background of $PM_{2.5}$, rather than the actual personal exposure, which can be significantly affected by different individual activities and the time spent in various microenvironments (Lee et al., 2010; Lim et al., 2012). Currently, a limited number of studies have examined the adverse effect of personal exposure to PM (Auger et al., 2006; Commodore et al., 2013; Huang et al., 2012; Meier et al., 2014), especially in the general healthy population. Means of measuring inflammatory biomarkers made it possible to assess adverse health effects of $PM_{2.5}$ on the general population. Fractional exhaled nitric oxide (FeNO) is a sensitive noninvasive biomarker of airway inflammation that has been used in many epidemiologic studies of the impact of air pollutants on healthy and asthmatic subjects (Jansen et al., 2005; Koenig et al., 2003). The American Thoracic Society (ATS) and the European Respiratory Society (ERS) now recommended FeNO to be a clinical surrogate marker of eosinophilic airway inflammation (Reddel et al., 2009).

In recent years, few researchers have focused on the association between personal exposure to $PM_{2.5}$ and FeNO levels in healthy adults, and the findings are inconsistent (Adar et al., 2007; Boogaard et al., 2013a; Kubesch et al., 2015; Strak et al., 2010). One panel study conducted in USA 2002 estimated personal exposure to $PM_{2.5}$ among healthy non-smokers based on the concentrations measured in microenvironments and found significant effects on FeNO levels (Adar et al., 2007). A cross-sectional study reported a null association between ambient $PM_{2.5}$ and FeNO levels among its 661 adult residents in Netherlands (Boogaard et al., 2013b). In Hong Kong, while numerous epidemiological studies have linked PM measured from central monitors with adverse respiratory outcomes, hospital admission, and mortality, no study has examined levels of personal exposure to $PM_{2.5}$ and its health association among common Hong Kong residents. Thus, this study aimed to fill the data gap and evaluate the association between exposure to $PM_{2.5}$ (and their constituents) and respiratory inflammation in healthy adults in Hong Kong.

2. Materials and methods

2.1. Subjects

The target study population was designed to be non-smoking healthy adults aged 18–45 years old, with no known allergies and other chronic diseases, and with regular living lifestyles. On-site and online advertisements were produced for three months; seventy-nine residents responded to the advertisements with informed consent and subsequently completed a self-administrated questionnaire about demographics, health status, smoking and symptoms related to asthma, rhinitis, and eczema. Among them, 46 met the inclusion criteria and agreed to participate.

This longitudinal study spanned across two sampling sessions: June 23, 2014 - September 7, 2014 and June 23, 2015. Each participant was required to complete one sampling session, with daily active personal monitoring (24 h) to measure personal exposure to air pollutants for six consecutive days in each session. FeNO, the biomarker of respiratory inflammation, was measured at the end of each sampling day (5–7 pm) and at least two hours after meal. Every subject was instructed to avoid taking anti-inflammatory medication and vitamin supplementation during the sampling period, and sampling would be stopped and rescheduled if participants developed acute infectious illnesses. Daily activities and respiratory symptoms of the participants were recorded hourly on a self-administered diary and checked by our research assistants. The time duration each participant spent at different locations (indoor, outdoor or on transportation) was estimated according to the diary and used for analysis. Meteorological parameters, including temperature and relative humidity (RH), were obtained from the website of Hong Kong Observatory (Zhu et al., 2010). In this study, the impact of confounding by between-subject characteristics was limited, as each subject acted as his/her control over time in this kind of longitudinal study with repeated measurements.

2.2. Personal exposure to $PM_{2.5}$

Personal $PM_{2.5}$ were collected with a sampler operated by battery-powered Leland Legacy pump (SKC Inc., PA) at a flow rate of 10 liter per minute (L/min). Each participant was equipped with a suitcase containing the pump connected to an impactor loaded with a 37-mm quartz filter (Whatman Ltd, Maidstone, UK). They were asked to carry, or keep the personal suitcases near them and attach sampler inlets near the breathing zone as they underwent their daily activities. Five participants in a batch were evaluated in parallel with the other five samplers stored for replacement and temporary use. After sampling, the exposed quartz filters were collected by our research assistants and stored in a refrigerator at about − 20 °C until chemical analysis. All the filters were cut into two sections for chemical analysis. The first section was analyzed for OC and EC using thermal optical reflectance (TOR) and the second section was analyzed for PAHs and PAEs by thermal desorption-gas chromatography/mass spectrometer (TD/GC/MS) method. 16 PAHs, including acenaphthylene (ACN), acenaphthene (ACE), fluorene (FLU), phenanthrene (PHE), anthracene (ANT), fluoranthene (FLUT), pyrene (PY), benzo[a]anthracene (BaA), chrysene (CHR), benzo[b]fluoranthene (BbF), benzo[k]fluoranthene (BkF), benzo[*a*]pyrene (BaP), indeno[1,2,3-cd]pyrene (IND), dibenzo[a,h]anthracene (DBA), benzo[ghi]perylene (BP), and six PAEs, including dimethyl phthalate (DMP), diethyl phthalate (DEP), di-n-butyl phthalate (DnBP), butyl benzyl phthalate (BBP), bis(2-ethylhexyl)phthalate (DEHP), di-n-octyl phthalate (DnOP) were selected as the targeted constituents. The detailed analytical procedures and performance characterization were described in previous papers (Cao et al., 2005; Ho and Yu, 2004; Ho et al., 2008).

The ambient concentrations of $PM_{2.5}$ and other pollutants, i.e., SO_2, NO_2, O_3 and PM_{10}, from seven general air quality monitoring stations (i.e., Central Western, Eastern, Kwun Tong, Sha Tin, Tai Po, Tap Mun and Yuen Long) were downloaded from the website of Hong Kong Environmental Protection Department (HKEPD) (Zhao et al., 2006). Fig. S1 displays the locations of the seven stations on map. The ambient data points were matched with personal exposure data points according to the location information provided by each subject's daily activity diary. Ambient concentrations of coarse particles (PMc) were calculated as the difference between ambient PM_{10} and $PM_{2.5}$. In our previous studies, PMc were found to be associated with hospital admissions of cardiovascular and respiratory diseases in Hong Kong (Qiu et al., 2014). Therefore, ambient PMc were included in this study as a potential confounder. Data from different stations was used for analysis according to the sampling date and living district of various subjects.

2.3. FeNO data

FeNO was measured at the end of each sampling day with a handheld FeNO device (NIOX MINO Airway Inflammation Monitor; Aerocrine AB, Solna, Sweden) in accordance with the ATS guidelines (2005). Subjects were instructed to exhale and then inhale to total lung capacity through the device, which provides nitric oxide–scrubbed air. Scrubbed air is used for the zero-reference comparison performed in the instrument during every measurement cycle. Subsequent exhalation at a steady rate for 10 s at a flow of 50 ± 5 mL/s was aided by a built-in flow control unit of the device, consisting of a mechanical pressure-flow regulator establishing a constant flow when applying an exhalation pressure of 10–20 cm H_2O. The lowest detection limit is 5 ppb. The accuracy range of NIOX MINO is ± 5 ppb for measured values less than

50 ppb and ± 10% for 50 ppb or greater. Data were stored electronically in the device and written down by our research assistants on the record form of each subject for the whole study period.

2.4. Quality assurance and quality control (QA/QC)

Appropriate quality assurance and quality control were implemented in handling of filters, personal sampling, and chemical analysis. During the sampling campaign, the pump flow rate was measured and adjusted to 10 L per minute (± 5%) before sampling and measured again at the end of each sampling session with a DryCal Lite flow meter (Bios Int., USA). The pre- and post-sampling flow rates were averaged to calculate the $PM_{2.5}$ air concentrations. Two field blanks were collected per sampling batch for correction. These PEMs were placed in a sealed plastic bag and carried to corresponding workplaces to imitate the transportation process of real monitors.

Other QA/QC procedures used in the chemical analysis were as the same as those have been previously presented by Ho et al. (2006, 2011). In brief, the analyzer was calibrated with known quantities of CH_4 every day. Twenty blank filters collected were also analyzed, and the sample results were corrected by the average of the blank concentrations, which were 1.0 μg/m^3, 0.1 μg/m^3, 3.1 ng/m^3 and 10.5 ng/m^3 for OC, EC, total PAHs and total PAEs, respectively. The targeted $PM_{2.5}$ constituents and their detection limits are listed in Table S1.

2.5. Statistical analysis

We analyzed the association between repeated measures (within-subject) of FeNO and personal exposures to air pollutants using linear mixed effects models with random subject effects. A compound symmetry structure was preferable for the covariance matrix to model the correlation between repeated measures for each subject based on the Akaike's Information Criterion (Zhao et al., 2013). Since FeNO was right skewed, it was log-transformed to fulfill the assumption of residual normality for linear mixed models. Since the samples with concentrations below the detection limit (5 ppb) only accounted for 8% (22 out of 276) of the total observation points (Lubin et al., 2004), and these values were substituted by half of the detection limit (2.5 ppb) for statistical analysis. Personal exposures to $PM_{2.5}$ were characterized by calculating the individual 24-h average concentration immediately preceding the FeNO monitoring. Personal exposures to $PM_{2.5}$ constituents were later characterized by chemical analysis.

Time-dependent variables including day of the week and relative humidity (RH) were controlled in the crude model as covariates. Additional time-independent variables, including age, gender, BMI, education level, occupation, and household income, were also added in the adjusted model to examine their confounding effects. Furthermore, two-pollutant models were conducted to examine whether the association between $PM_{2.5}$ and FeNO was consistent while controlling for ambient gas phase pollutants (SO_2, NO_2, and O_3) or ambient PMc. The relationship between $PM_{2.5}$ constituents and FeNO was also adjusted for personal $PM_{2.5}$ to examine the possible confounding effects. β was the estimated coefficient of a pollutant from the mixed-model. In order to allow hazards risk for different pollutants to be compared by limiting differences due to units of measurement or concentration range, magnitudes of association are also expressed at pollutant interquartile ranges (IQR; 25th–75th percentile) following calculation: $(\exp^{\beta \times IQR} - 1) \times 100\%$ (Wu et al., 2010).

Residual analyses were performed to examine deviations from standard linear mixed model assumptions and the presence of influential observations. Sensitivity analysis was conducted to explore the model robustness (1) by using a more parsimonious model and an extended one (covariates and ambient gaseous pollutants included), (2) by removing FeNO levels lower than the detection limit and (3) by removing FeNO levels higher than 50 ppb since it is the cut point for high FeNO level in adults suggested by ATS (Dweik et al., 2011). All the data analyses were implemented in the R software version 3.1.3 with package '*nlme*'.

2.6. Ethics statement

This study was carried out after obtaining approval from Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee (Ref. No. CRE-2014.154). All the data and sample collections were conducted after informed consent was obtained. The consent form included a general description of the study. It assured the subject of the confidentiality of information and his/her right to opt out of the study with no consequence. All questions regarding the study were answered prior to the interview.

3. Results

A total of 276 observations were obtained for the 46 subjects recruited. Five subjects participated for more or less than six days due to unforeseen conditions or logistical reasons. The detailed participating schedule is listed in Table S2. Of the 276 exposure observations, three (from different subjects) had no corresponding FeNO concentration because of emergencies of subjects or unexpected mistakes during field sampling, yielding only 273 FeNO values. As shown in Table 1, FeNO levels were averagely higher in males (Mean: 20.6 ± 19.4 ppb) than in females (Mean: 7.7 ± 3.7 ppb). The age of 46 healthy adults participated in this study ranged from 18 to 30 years of age, and the average BMI was 21.4 ± 3.1 kg/m^2. According to the classification of World Health Organization (WHO) (Zhang et al., 2014), most subjects had normal weight, four subjects were underweight (BMI < 18.5 kg/m^2) and one subject was obese (BMI ≥ 30 kg/m^2). The subjects' occupations include teacher, student, office worker and unemployment. As displayed in Fig. 1, subjects in this study spent 14.9 ± 17.3% of their time outdoors, 4.3 ± 6.0% of their time on transportation and 80.7 ± 18.0% of their time indoors. Among all the subjects with different occupations, unemployed subjects averagely spent the longest time indoors (84.2 ± 11.4%), while the average time spent by office workers indoors is shortest (76.5 ± 26.5%).

Table 1
Descriptive statistics of meteorological information and characteristics of subjects.

Total number of observations: 276	Total number of subjects: 46
BMI [kg/m^2 (mean ± SD)]	21.4 ± 3.1
Age [years (mean ± SD)]	25 ± 3
Gender [n (%)]	
Male	27/46 (58.7)
Female	19/46 (41.3)
Day of week [n (%)]	
Weekday	196/276 (71.0)
Weekend	80/276 (29.0)
Relative humidity [% (mean ± SD)]	81.2 ± 5.5
Temperature [°C (mean ± SD)]	29.2 ± 1.2
Household income[a] *[n (%)]*	
< HKD 8500	12/46 (26.1)
HKD 8500–20,000	27/46 (58.7)
> HKD 20,000	8/46 (17.4)
Education [n (%)]	
Vocational/technical school	9/46 (19.6)
College and above	37/46 (80.4)
Occupation [n (%)]	
Unemployed	5/46 (10.9)
Office worker	6/46 (13.0)
Student	18/46 (39.1)
Teacher	17/46 (37.0)
Median FeNO [ppb (mean ± SD)]	
Male	20.6 (20.6 ± 19.4)
Female	7.7 (7.7 ± 3.7)
All Subjects	15.4 (15.4 ± 16.4)

[a] Income per capital per month.

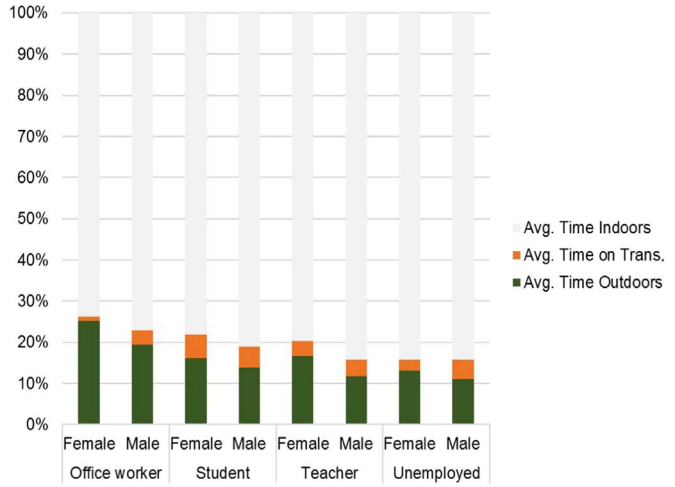

Fig. 1. Percentages of the time subjects spent indoors, outdoors and on transportation. *The circles denote observed points outside (75th percentile + 1.5 IQR) or (25th percentile – 1.5 IQR).

Table 2
Description of the air pollutants measured by personal samplers and ambient stations.

Pollutant	Mean	SD[b]	Min	Median	Max
Personal $PM_{2.5}$ ($\mu g/m^3$)	28.1	23.3	5.8	21.2	208.9
Ambient $PM_{2.5}$ ($\mu g/m^3$)	13.3	6.4	4.5	11.8	38.1
Personal OC ($\mu g/m^3$)	10.1	14.7	2.3	6.4	126.7
Personal EC ($\mu g/m^3$)	2.4	2.1	0.1	1.9	15.4
PAHs (ng/m^3)					
ACN	0.021	0.015	0.002	0.017	0.071
ACE	0.011	0.013	0.000	0.006	0.078
FLU	0.018	0.011	0.004	0.016	0.079
PHE	0.061	0.043	0.013	0.051	0.358
ANT	0.092	0.068	0.010	0.071	0.410
FLUT	0.099	0.052	0.022	0.088	0.314
PY	0.048	0.024	0.008	0.043	0.124
BaA	0.016	0.011	0.001	0.014	0.060
CHR[a]	0.087	0.054	0.012	0.070	0.300
BbF[a]	0.064	0.050	0.004	0.050	0.325
BkF[a]	0.051	0.040	0.003	0.042	0.254
BaP[a]	0.017	0.014	0.001	0.013	0.076
PER	0.011	0.011	0.000	0.008	0.054
IND[a]	0.031	0.022	0.002	0.026	0.102
DBA[a]	0.006	0.004	0.001	0.005	0.018
BP[a]	0.047	0.039	0.003	0.035	0.231
c-PAHs	0.303	0.208	0.022	0.246	1.306
All PAHs	0.665	0.330	0.127	0.592	1.804
PAEs (ng/m^3)					
DMP	0.079	0.074	0.003	0.056	0.593
DEP	1.6	1.6	0.007	1.1	10
DnBP	14	13	0.02	11	58
BBP	64	94	0.02	7	546
DEHP	400	483	0.1	218	3123
DnOP	25	48	0.03	5	268
All PAEs	471	603	0.1	232	3800

[a] Carcinogen (belonging to c-PAHs).
[b] Standard deviation.

The 24-h average concentrations of ambient $PM_{2.5}$, personal $PM_{2.5}$ and their constituents are listed in Table 2. Corresponding concentration information of PMc and ambient gaseous pollutants (NO_2, SO_2, O_3) are shown in Table S3. About 7% of the personal exposure data were missing due to filter damages during sampling. The average concentrations of ambient $PM_{2.5}$ ($13.3 \pm 6.4\ \mu g/m^3$) was significantly lower ($p < 0.001$) than that of personal exposures ($28.1 \pm 23.3\ \mu g/m^3$). The Spearman's correlation coefficient was 0.236 ($p < 0.001$), indicating a relatively weak correlation between personal and ambient $PM_{2.5}$ concentrations. Personal to ambient $PM_{2.5}$ ratio is a good indicator of the exposure differences caused by individual-level factors

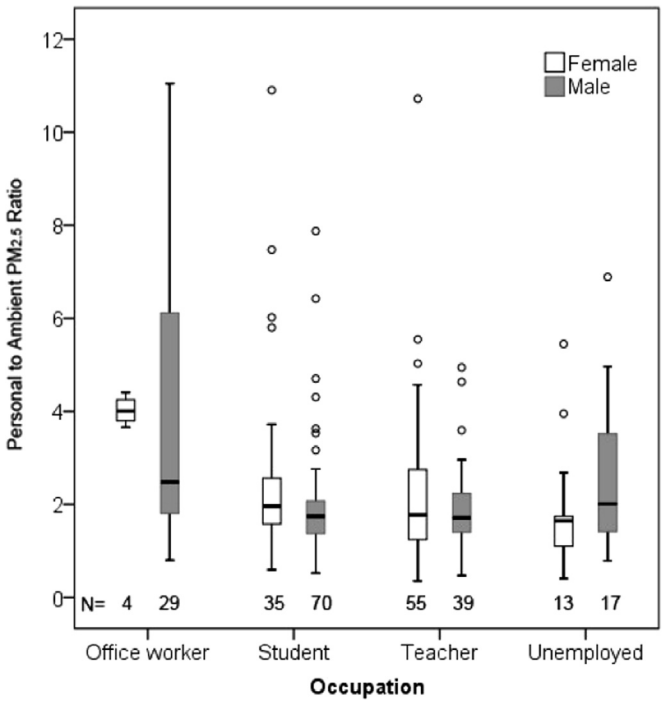

Fig. 2. $PM_{2.5}$ concentration ratios of personal exposure to ambient levels for males and females with different occupations.

rather than the ambient concentrations. It can be seen from the Fig. 2 that personal/ambient ratios for subjects with different occupation and different gender varied. The average ratios for office workers (3.9 ± 2.7) were higher than those for students (2.2 ± 1.5), teachers (2.1 ± 1.4) and unemployed subjects (2.3 ± 1.5) with *p-value* < 0.01. Comparable average ratios were found for males (2.4 ± 1.8) and females (2.3 ± 1.8).

The mean concentrations of OC, EC, sum of eight c-PAHs, sum of six PAEs, and sum of 16 PAHs were $10.1 \pm 14.7\ \mu g/m^3$, $2.4 \pm 2.1\ \mu g/m^3$, $0.3 \pm 0.2\ ng/m^3$, $0.7 \pm 0.3\ ng/m^3$, and $471 \pm 603\ ng/m^3$, respectively. The composition profiles of personal samples are shown in Fig. 3. On average, OC, EC, sum of six PAEs and sum of 16 PAHs accounted for 35.9%, 8.5%, 1.7% and 0.0023% of personal $PM_{2.5}$, respectively. Whereas, the composition profiles of personal $PM_{2.5}$ varied among subjects since different constituents have different sources including biomass combustion, vehicle diesel, cleaning products, etc. and the contribution percentages of different sources were influenced by personal activities, living, and working environments and ambient levels simultaneously. It can be seen from Fig. 3 that the average concentration percentage of total OC was highest for the subject group of unemployment ($47.2 \pm 17.3\%$), while the percentages were $42.0 \pm 17.4\%$, $34.3 \pm 12.6\%$ and $24.1 \pm 10.2\%$ for office workers, students, and teachers, respectively. The obvious difference between the composition profiles of PAHs/PAEs for different occupation groups was not found. On average, c-PAHs accounted for $46.8 \pm 13.4\%$ of the 16 PAHs monitored in this study and DEHP was the predominant PAE ($79.3 \pm 16.3\%$). The concentrations of personal $PM_{2.5}$ were highly correlated with OC ($r = 0.56$, $p < 0.05$) and EC ($r = 0.54$, $p < 0.05$), moderately correlated with PAHs ($r = 0.35$, $p < 0.05$) and weakly correlated with PAEs ($r = 0.17$, $p < 0.05$) (Table 3). We observed significant correlations between personal $PM_{2.5}$ and all the other variables in Table 3. Ambient $PM_{2.5}$ levels were significantly associated all the other pollutants except for PAEs. Ambient RH has a negative relationship with all the air pollutants listed. Concentrations of total PAHs and c-PAHs were highly correlated ($r = 0.90$, $p < 0.05$).

The regression results for the association between FeNO and air pollutants are listed in Table 3. FeNO showed increases of 11.1% (95%

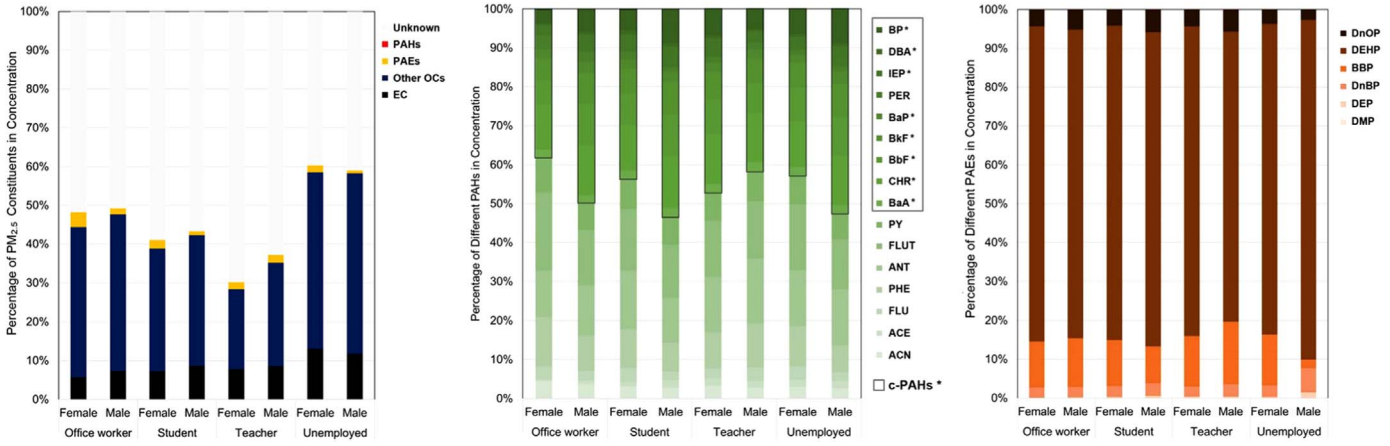

Fig. 3. Composition profiles of personal $PM_{2.5}$ samples for males and females with different occupations.

CI: 3.9–18.8%) in the crude model and 12.8% (95% CI: 5.5–20.7%) in the multivariable-adjusted model per 16.4 μg/m^3 increment of personal $PM_{2.5}$. The IQRs were 3.2 μg/m^3, 1.5 μg/m^3, 0.43 ng/m^3, 0.277 ng/m^3 and 597 ng/m^3 for OC, EC, PAHs, c-PAHs and PAEs, respectively. As displayed in Table 4, the highest estimated effect was observed for c-PAHs (12.0%, 95% CI: 0.0–25.6%), followed by total PAHs (8.5%, 95% CI: − 3.2, 21.7%), EC (4.5%, 95% CI: − 3.3, 12.8%), OC (1.8%, 95% CI: − 0.7, 4.4%) and PAEs (1.5%, 95% CI: − 6.1, 9.6%) according to adjusted models. The regression results for the associations between FeNO and different PAHs are shown in Fig. 4 and Table S4. Effect estimates of the 16 monitored PAHs varies from − 5.6–12.6% in the crude model and from − 4.8–12.8% in the adjusted model. Significant associations were observed for BbF and BkF according to both crude and adjusted models. The effect estimates for other c-PAHs (BaA, CHR, BaP, INP, DBA and BP) are in the range of 0.9–9.5% according to adjusted models. In comparison with personal $PM_{2.5}$, ambient $PM_{2.5}$ concentrations were weakly and insignificantly associated FeNO in both crude and adjusted models (0.8%, 95% CI: − 7.5, 9.9% for the adjusted model). Adjusting for confounders led to increases in the effect estimates, and the significance of the association between exposures and FeNO in this study.

Sensitivity analyses were performed to test the robustness of the associations. Table S5 lists the association between personal $PM_{2.5}$ and FeNO from the adjusted model based on all data points, a dataset with FeNO > 50 ppb removed and dataset with FeNO < 5 ppb removed. Neither of removing FeNO values higher than 50 ppb and removing FeNO values lower than 5 ppb showed significant influence on the association between personal $PM_{2.5}$ and FeNO. Removing values less than 5 ppb slightly increased the effect estimate and significance of the association. Table S6 displays all the associations between ambient or personal $PM_{2.5}$ (and their constituents) and FeNO determined by the crude model, adjusted model and two-pollutant models. A significant association between ambient PMc/NO_2/SO_2/O_3 and FeNO was not found in any of the models used in this study. The inclusion of ambient PMc, gaseous pollutant or covariates into the crude model led to small changes (< 20% of the effect estimate) in the associations between FeNO and personal exposures to $PM_{2.5}$, OC, EC, PAHs, and c-PAHs, respectively. The only exception was that the effect of EC on FeNO decreased from 3.8% to 0.8% after being adjusted for ambient PMc. Since all the constituents were significantly correlated with personal $PM_{2.5}$ in concentration (Table 3), their associations with FeNO were also adjusted for personal $PM_{2.5}$ in Two-Pollutant models. As displayed in Table S4 and S6, The inclusion of personal $PM_{2.5}$ into the adjusted model generally led to obvious decreases in the effect estimates of different constituents, while the significance of the association between personal $PM_{2.5}$ and FeNO was barely influenced.

4. Discussion

This is the first study to examine the association between personal exposure to $PM_{2.5}$, their constituents, and respiratory inflammation among healthy adults in Hong Kong. One of the hypotheses of underlying biologic mechanisms responsible for the association is that inhaled particles can rapidly react with extracelluar macromolecules or cell constituents in the airway epithelium to generate reactive oxygen species and lipid peroxidation products (Auger et al., 2006). These products further induce local and systemic oxidative or nitrosative stress and subsequent inflammation. NO in human body is generated from the oxidation of L-arginine to L-citrulline by nitric oxide synthase (NOS), which is released by many cells in the lung and up-regulated by cytokines (Redington et al., 2001). In this study, statistically significant and positive association between FeNO and personal $PM_{2.5}$ was found in all the models adjusted for potential confounders. Previous studies using FeNO as an outcome in healthy adults are quite limited. Two

Table 3
Pollutant data (daily averages): Spearman rank correlation coefficients for the study period.

	Ambient $PM_{2.5}$	Ambient PMc	Ambient NO_2	Ambient O_3	Ambient SO_2	Personal OC	Personal EC	Personal PAHs	Personal c-PAHs	Personal PAEs
Personal $PM_{2.5}$	0.52*	0.41*	0.09*	0.42*	0.15*	0.56*	0.54*	0.35*	0.32*	0.17*
Ambient $PM_{2.5}$		0.74*	0.22*	0.57*	0.33*	0.28*	0.47*	0.15*	0.14*	−0.04
Ambient PMc			0.26*	0.43*	0.38*	0.11	0.14*	−0.23	−0.05	−0.10
Ambient NO_2				−0.36*	0.35*	0.07	0.31*	−0.07	−0.08	−0.17*
Ambient O_3					0.02	0.09	0.02	0.14	0.11	0.17*
Ambient SO_2						0.06	0.17*	0.01	0.01	−0.06
Personal OC							0.63*	0.19*	0.14*	0.04
Personal EC								0.38*	0.30*	0.09
Personal PAHs									0.90*	0.17*
Personal c-PAHs										0.01

* Correlation is significant at the 0.05 level (2-tailed).

Table 4
Estimated effects of an IQR change in concentration of ambient or personal $PM_{2.5}$ and its constituents on FeNO.

Pollutant	N	IQR	Crude		Adjusted[a]	
			Effect estimate (%)[b] (95% CI)	p-value	Effect estimate (%) (95% CI)	p-value
Ambient $PM_{2.5}$	273	6.9 μg/m^3	0.1 (−8.3, 9.2)	0.98	0.8 (−7.5, 9.9)	0.85
Personal $PM_{2.5}$	259	16.4 μg/m^3	11.1 (3.9, 18.8)	0.002**	12.8 (5.5, 20.7)	< 0.001**
OC	222	3.2 μg/m^3	1.7 (−0.8, 4.3)	0.19	1.8 (−0.7, 4.4)	0.16
EC	222	1.5 μg/m^3	3.7 (−4.0, 12)	0.36	4.5 (−3.3, 12.8)	0.26
PAHs	242	0.4 ng/m^3	7.8 (−4.0, 20.9)	0.20	8.5 (−3.2, 21.7)	0.16
c-PAHs	242	0.3 ng/m^3	12.2 (0.1, 25.9)	0.04*	12.0 (0.0, 25.6)	0.05*
PAEs	242	597 ng/m^3	0.8 (−6.7, 8.8)	0.84	1.5 (−6.1, 9.6)	0.71

[a] Adjusted for age, gender, BMI, education level, occupation, and household income.
[b] Percent changes per IQR of corresponding pollutant.
* Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.01 level (2-tailed).

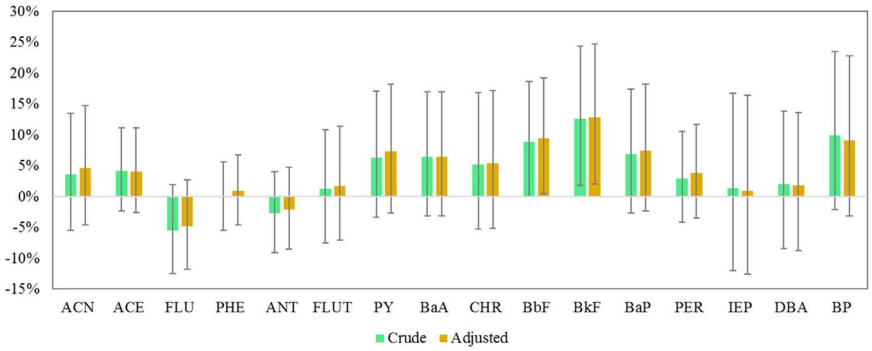

Fig. 4. Estimated effects of an IQR change in concentration of different PAHs on FeNO based on crude and adjusted models.

previous panel studies with similar sample sizes reported significant associations, and higher effect estimates on FeNO (29% in non-smoking seniors in the USA; 40.7% in non-smoking adults in China (Adar et al., 2007; Zhang et al., 2013)). Since FeNO levels may be influenced by a lot of time-dependent factors, several earlier studies using cross-sectional study design found insignificant results. Other possible explanations for the discrepancy include but not limited to data scarcity, population susceptibility and different chemical profiles (Boogaard et al., 2013b; Kubesch et al., 2015; Meier et al., 2014).

In comparison with ambient concentrations, personal exposures to $PM_{2.5}$ yielded much more significant and robust association with inflammatory biomarker in this study, suggesting that ambient $PM_{2.5}$ concentrations from monitoring stations may not be an appropriate proxy for actual $PM_{2.5}$ exposures. On the other hand, the higher effect estimates associated with personal $PM_{2.5}$ exposure could also be attributed to the different sources and composition profile of personal $PM_{2.5}$ compared with ambient $PM_{2.5}$. Indoor sources of $PM_{2.5}$ can increase the percentage of OC, EC, and the toxicity of exposure. According to the results of this study, unemployed subjects and office workers were exposed to relatively higher average percentages of OC and EC, which suggests the existence of indoor sources. Cooking, smoking and incense burnings are typical indoor sources related to Chinese culture and living styles (Lung et al., 2007). Previous studies also reported that printing could significantly increase the concentration of $PM_{2.5}$ in the offices at Guangzhou, China (Zhang et al., 2017). On the other hand, poor ventilation is another factor contributing to the moderate correlation coefficient between personal exposures and ambient levels. It is suspected that poor ventilation of the subjects' offices or potential indoor sources (e.g. office printer, secondhand smoke) led to the significantly higher personal-to-ambient $PM_{2.5}$ concentration ration for office workers in this study. Therefore, the correlations between personal exposure and ambient levels on weekdays and weekends for all the subjects were compared (Fig. 5). It was found that personal and ambient $PM_{2.5}$ levels were better correlated on weekends ($r = 0.52$, $p < 0.001$) than on weekdays ($r = 0.37$, $p < 0.001$) and that the correlation on weekdays for office workers was especially weak ($r = 0.18$, $p = 0.23$) compared with that for students, teachers, and unemployed subjects ($r = 0.623$, $p < 0.001$ when treated as one group). This result supports our speculation and the health risks caused by poor ventilation or potential indoor sources from office should not be neglected.

The associations between FeNO and several $PM_{2.5}$ constituents were also examined in this study. Although c-PAHs only accounted for less than 0.01% of the personal $PM_{2.5}$ mass and 42.6% of all the PAHs measured, they showed significant association with FeNO levels. According to adjusted models, the effect estimate of total c-PAHs was comparable with that of personal $PM_{2.5}$ and higher than those of other constituents. Among c-PAHs, BbF and BkF had the highest effect estimates, while FLU had the lowest effect estimate. Significant association between EC and FeNO was reported in an earlier study, but it was not found in this one, possibly attributed to our low statistical power for constituents. Total exposure to PAEs had been linked with pulmonary function (Hoppin et al., 2004). However, for PAEs in $PM_{2.5}$, the effect estimate observed in this study was close to null.

Various other kinds of possible confounders were considered and controlled for in the study design procedures or by using mixed-effects models. In a multivariate linear regression analysis, FeNO levels were positively associated with male gender ($p = 0.01$) after adjusting for age, BMI, RH, occupation, income, weekday and $PM_{2.5}$. The difference between the FeNO levels in healthy males and females was also observed by previous studies and should be paid attention in the future (Bayram et al., 2014; Kim et al., 2010). Confounding by other covariates (age, BMI, education level, occupation, household income, ambient gaseous pollutants and ambient PMc) on the association between personal $PM_{2.5}$ and FeNO was minimal, suggesting the robustness of our model, and that changes in biomarker levels were unlikely driven by other time-dependent factors. However, residual confounding remains in this study, which could be attributed to the fact that ambient levels of

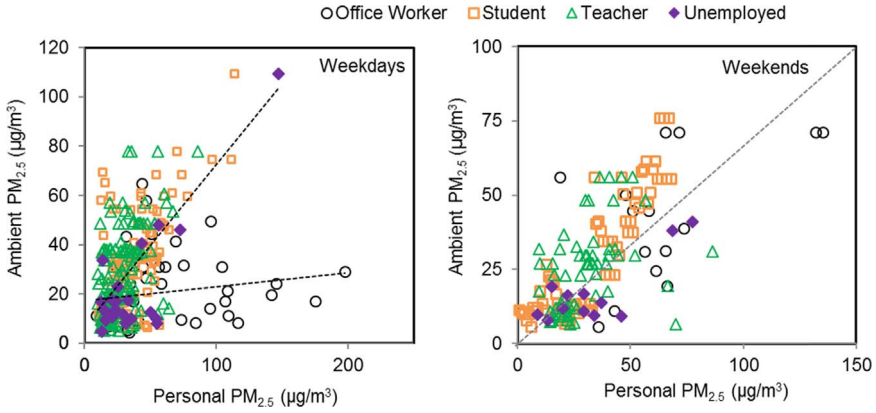

Fig. 5. General linear regression on the associations between personal and ambient $PM_{2.5}$ on weekdays and weekends.

PMc and gaseous pollutants cannot reflect the actual personal exposures to these pollutants. If enough resources are accessible, pollutants in gas-phase (such as PAHs and formaldehyde) should be measured at individual level and included in the regression model.

Several strengths make this study unique and meaningful. 1) The two methods of exposure assessments were used and compared in examining their associations with FeNO levels in residents in Hong Kong. 2) Several kinds of constituents in personal $PM_{2.5}$ were considered simultaneously for comparison. 3) Repeated measures based on a robust number of samples decreased the chance of confounding by time-independent variables as each subject served as his or her control. 4) Comprehensive confounder adjustment was also made by including meteorological variables, demographic and socioeconomic covariates, and gaseous pollutants. 5) Estimates for personal exposures to all the pollutants except PAEs were robust to different combinations of covariates and when extreme FeNO values were removed.

Limitations of our study include that certain daily activities may have been suppressed by carrying a $PM_{2.5}$ sampler, which may lead to bias in exposure measurement. Nonetheless, all participants were encouraged to conduct their regular study or working activities during the sampling periods. Colinearity is a major issue when studying the effects of different $PM_{2.5}$ constituents. In this study, the correlations between constituents were examined and the results of Two-Pollutant models indicate that the effect of personal $PM_{2.5}$ mass is more robust than that of the constituents monitored. The small number of observation points for constituents measured limited the statistical power to detect meaningful findings, as well as the generalizability of the study results. FeNO is the only biomarker measured in the study, so we cannot directly assess the association between targeted air pollutants and respiratory inflammation. Also, since $PM_{2.5}$ constituents are collinear variables, which might be confounded by each other, the effect estimates could be meaningful for comparison but must be interpreted with caution.

In summary, this study offered valuable new information about personal exposure to $PM_{2.5}$ and their constituents as well as their short-term effects on FeNO levels in healthy adults of Hong Kong, in comparison with ambient concentrations. Considering the inconsistent associations found both in our study, and when compared to other published studies, it is important to validate our findings with future research to reach meaningful conclusions.

Acknowledgements

This work was supported by the Research Grants Council-General Research Fund of the Hong Kong Special Administrative Region of China [grant number 4054074].

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

ZF conceived the study and was involved in the statistical analyses and preparation of the manuscript. VCP was involved in the statistical analyses and revised the manuscript. XCC was involved in the exposure assessment and chemical analysis. QH and LT assisted in the interpretation of the results. SCL and SSH helped to perform the chemical analysis. SLT and KH conceived the study, participated in its design and revise the manuscript. All authors have read and approved the final manuscript.

Additional file available

Tables are addressing target species of PAHs and PAEs, subjects' participating schedule, correlations between meteorological variables and air pollutants and sensitivity analysis.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.envres.2018.02.009.

References

ATS/ERS recommendations for standardized procedures for the online and offline measurement of exhaled lower respiratory nitric oxide and nasal nitric oxide, 2005. Am. J. Respir. Crit. Care Med. 171, pp. 912-930.

Adar, S.D., et al., 2007. Ambient and microenvironmental particles and exhaled nitric oxide before and after a group bus trip. Environ. Health Perspect. 115, 507–512.

Auger, F., et al., 2006. Responses of well-differentiated nasal epithelial cells exposed to particles: role of the epithelium in airway inflammation. Toxicol. Appl. Pharmacol. 215, 285–294.

Bayram, M., et al., 2014. The difference of FENO levels according to gender in healty subjects never smoked. Eur. Respir. J. 44, P1006.

Boogaard, H., et al., 2013a. Respiratory effects of a reduction in outdoor air pollution concentrations. Epidemiology 24, 753–761.

Boogaard, H., et al., 2013b. Respiratory effects of a reduction in outdoor air pollution concentrations. Epidemiology 24, 753–761.

Cao, J.J., et al., 2005. Characterization and source apportionment of atmospheric organic and elemental carbon during fall and winter of 2003 in Xi'an, China. Atmos. Chem. Phys. 5, 3127–3137.

Commodore, A.A., et al., 2013. Concentrations of urinary 8-hydroxy-2 '-deoxyguanosine and 8-isoprostane in women exposed to woodsmoke in a cookstove intervention study in San Marcos, Peru. Environ. Int. 60, 112–122.

Delfino, R.J., et al., 2010. Association of biomarkers of systemic inflammation with organic components and source tracers in quasi-ultrafine particles. Environ. Health Perspect. 118, 756–762.

Dweik, R.A., et al., 2011. An official ATS clinical practice guideline: interpretation of exhaled nitric oxide levels (FeNO) for clinical applications. Am. J. Respir. Crit. Care Med. 184, 602–615.

Ferguson, K.K., et al., 2011. Urinary phthalate metabolites in relation to biomarkers of

inflammation and oxidative stress: NHANES 1999–2006. Environ. Res. 111, 718–726.
Ho, K.F., et al., 2006. Variability of organic and elemental carbon, water soluble organic carbon, and isotopes in Hong Kong. Atmos. Chem. Phys. 6, 4569–4576.
Ho, S.S.H., et al., 2011. Precautions for in-injection port thermal desorption-gas chromatography/mass spectrometry (TD-GC/MS) as applied to aerosol filter samples. Atmos. Environ. 45, 1491–1496.
Ho, S.S.H., Yu, J.Z., 2004. In-injection port thermal desorption and subsequent gas chromatography-mass spectrometric analysis of polycyclic aromatic hydrocarbons and n-alkanes in atmospheric aerosol samples. J. Chromatogr. A 1059, 121–129.
Ho, S.S.H., et al., 2008. Evaluation of an in-injection port thermal desorption-gas chromatography/mass spectrometry method for analysis of non-polar organic compounds in ambient aerosol samples. J. Chromatogr. A 1200, 217–227.
Hoppin, J.A., et al., 2004. Phthalate exposure and pulmonary function. Environ. Health Perspect. 112, 571–574.
Huang, W., et al., 2012. Inflammatory and oxidative stress responses of healthy young adults to changes in air quality during the Beijing olympics. Am. J. Respir. Crit. Care Med. 186, 1150–1159.
Jansen, K.L., et al., 2005. Associations between health effects and particulate matter and black carbon in subjects with respiratory disease. Environ. Health Perspect. 113, 1741–1746.
Kim, S.-H., et al., 2010. Reference values and determinants of exhaled nitric oxide in healthy korean adults. J. Asthma 47, 563–567.
Koenig, J.Q., et al., 2003. Measurement of offline exhaled nitric oxide in a study of community exposure to air pollution. Environ. Health Perspect. 111, 1625–1629.
Kubesch, N.J., et al., 2015. Respiratory and inflammatory responses to short-term exposure to traffic-related air pollution with and without moderate physical activity. Occup. Environ. Med. 72, 284–293.
Kunzli, N., et al., 2009. Traffic-related air pollution correlates with adult-onset asthma among never-smokers. Thorax 64, 664–670.
Lee, K., et al., 2010. In-vehicle exposures to particulate matter and black carbon. J. Air Waste Manag. Assoc. 60, 130–136.
Lim, S., et al., 2012. Personal exposures to PM2.5 and their relationships with micro-environmental concentrations. Atmos. Environ. 47, 407–412.
Lin, W.W., et al., 2011. Acute respiratory inflammation in children and black carbon in ambient air before and during the 2008 Beijing olympics. Environ. Health Perspect. 119, 1507–1512.
Lubin, J.H., et al., 2004. Epidemiologic evaluation of measurement data in the presence of detection limits. Environ. Health Perspect. 112, 1691–1696.
Lung, S.C.C., et al., 2007. Residents' particle exposures in six different communities in Taiwan. Sci. Total Environ. 377, 81–92.
Meier, R., et al., 2014. Associations of short-term particle and noise exposures with markers of cardiovascular and respiratory health among highway maintenance workers. Environ. Health Perspect. 122, 726–732.
Osornio-Vargas, A.R., et al., 2003. Proinflammatory and cytotoxic effects of Mexico City air pollution particulate matter in vitro are dependent on particle size and composition. Environ. Health Perspect. 111, 1289–1293.
Pope, C.A., Dockery, D.W., 2006. Health effects of fine particulate air pollution: lines that connect. J. Air Waste Manag. Assoc. 56, 709–742.
Qiu, H., et al., 2014. Coarse particulate matter associated with increased risk of emergency hospital admissions for pneumonia in Hong Kong. Thorax 69, 1027–1033.
Rakkestad, K.E., et al., 2007. Phthalate levels in Norwegian indoor air related to particle size fraction. J. Environ. Monit. 9, 1419–1425.
Reddel, H.K., et al., 2009. An official american thoracic society/european respiratory society statement: asthma control and exacerbations standardising endpoints for clinical asthma trials and clinical practice. Am. J. Respir. Crit. Care Med. 180, 59–99.
Redington, A.E., et al., 2001. Increased expression of inducible nitric oxide synthase and cyclooxygenase-2 in the airway epithelium of asthmatic subjects and regulation by corticosteroid treatment. Thorax 56, 351–357.
Strak, M., et al., 2010. Respiratory health effects of ultrafine and fine particle exposure in cyclists. Occup. Environ. Med. 67, 118–124.
Tran, T.M., Kannan, K., 2015. Occurrence of phthalate diesters in particulate and vapor phases in indoor air and implications for human exposure in Albany, New York, USA. Arch. Environ. Contam. Toxicol. 68, 489–499.
Wu, S.W., et al., 2010. Association of heart rate variability in taxi drivers with marked changes in particulate air pollution in Beijing in 2008. Environ. Health Perspect. 118, 87–91.
Zhang, J., et al., 2013. Cardiorespiratory biomarker responses in healthy young adults to drastic air quality changes surrounding the 2008 Beijing Olympics. Res. Rep. Health Eff. Inst. 5–174.
Zhang, M., et al., 2017. Indoor airborne particle sources and outdoor haze days effect in urban office areas in Guangzhou. Environ. Res. 154, 60–65.
Zhang, N., et al., 2014. Characterization, health risk of heavy metals, and source apportionment of atmospheric PM < inf > 2.5 < /inf > to children in summer and winter: an exposure panel study in Tianjin, China. Air Qual. Atmos. Health 8, 347–357.
Zhao, J., et al., 2013. The biological effects of individual-level PM(2.5) exposure on systemic immunity and inflammatory response in traffic policemen. Occup. Environ. Med. 70, 426–431.
Zhao, W., et al., 2006. Source apportionment and analysis on ambient and personal exposure samples with a combined receptor model and an adaptive blank estimation strategy. Atmos. Environ. 40, 3788–3801.
Zhu, X., et al., 2010. Evaluation and comparison of measurement methods for personal exposure to fine particles in Beijing, China. Bull. Environ. Contam. Toxicol. 84, 29–33.