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Short-term effects of ambient PM_1, $PM_{2.5}$, and PM_{10} on internal metal/metalloid profiles in older adults: A distributed lag analysis in China

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ABSTRACT

There is limited evidence linking exposure to ambient particulate matter (PM) with internal doses of metals and metalloids (metal(loid)s). This study aimed to evaluate the effects of short-term exposure to ambient PM on urine metal(loid)s among Chinese older adults. Biological monitoring data of 15 urine metal(loid)s collected in 3, 970 community-dwelling older adults in Fuyang city, Anhui Province, China, from July to September 2018, were utilized. PMs with an aerodynamic diameter $\leq$ 1 μm (PM_1), $\leq$ 2.5 μm ($PM_{2.5}$), and $\leq$ 10 μm (PM_{10}) up to eight days before urine collection were estimated by space–time extremely randomized trees (STET) model. Residential greenness was reflected by Normalized Difference Vegetation Index (NDVI). We used generalized additive model (GAM) combined with distributed lag linear/non-linear models (DLMs/DLNMs) to estimate the associations between short-term PM exposure and urine metal(loid)s. The results suggested that the cumulative exposures to PM_1, $PM_{2.5}$, or PM_{10} over two days (lag0-1 days) before urine collection were associated with elevated urine metal(loid)s in DLMs, while exhibited linear or "inverted U-shaped" relationships with seven urine metal(loid)s in DLNMs, including Gallium (Ga), Arsenic (As), Aluminum (Al), Magnesium (Mg), Calcium (Ca), Uranium (U), and Barium (Ba). Aforementioned results indicated robust rather than spurious associations between PMs and these seven metal(loid)s. After standardizations for three PMs, PM_1 was the greatest contributor to U, $PM_{2.5}$ made the greatest contributions to Ga, As, Al, and Ba, and PM_{10} contributed the most to Mg and Ca. Furthermore, the effects of three PMs on urine Ga, As, Al, Mg, Ca, and Ba were reduced when exposed to higher levels of NDVI. Overall, short-term exposures to ambient PMs contribute to elevated urinary metal(loid) levels in older adults, and three PMs exhibit various contributions to different urine metal(loid)s. Moreover, residential greenness may attenuate the effects of PMs on urine metal(loid)s.

1. Introduction

Ambient particulate matter (PM) is a complex mixture comprised of liquid droplets and solid particles in the air, and often divided into PM_{10} (an aerodynamic diameters $\leq$ 10 μm), $PM_{2.5}$ ($\leq$2.5 μm), and PM_1 ($\leq$1μm) based on its aerodynamic diameters (EPA 2016). According to the Global Burden of Diseases, Injuries, and Risk Factors Study (Yin et al., 2020; Zhou et al., 2019), PM is the fourth leading risk factor for death in China, accounting for over 1 million deaths in 2017. In recent years, great efforts have been taken at reducing air pollution in China,

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with annual average concentrations of $PM_{2.5}$ being steadily reduced from 46 μg/m^3 in 2016 to 30 μg/m^3 in 2021 (Bulletin 2016; 2021), achieving the annual $PM_{2.5}$ grade 2 standard (35 μg/m^3) of the Chinese Ambient Air Quality Standards (CAAQS, GB 3095–2012) (MEP. 2012), but still higher than $PM_{2.5}$ grade 1 standard (15 μg/m^3) of CAAQS and the WHO air quality guidelines levels (5 μg/m^3) (WHO, 2021). Therefore, continued efforts to reduce air pollution are still needed.

The health effects caused by exposure to PM depend on multiple factors, including but not limited to its concentrations, sizes, and chemical compositions, and population susceptibility (Buczynska et al., 2014; Daellenbach et al., 2020). Among the most common chemical compositions, metals and metalloids (metal(loid)s), including essential and non-essential metal(loid)s, have been widely detected in PM samples, although their concentrations varied across areas and seasons (Li et al., 2016; Ronkko et al., 2018; Song et al., 2022). Metal(loid)s in PMs have been linked with multiple adverse health outcomes, such as cardiovascular diseases, respiratory diseases, and abnormal fasting blood glucose, etc (Bell et al., 2014; Liu et al., 2021; Schraufnagel, 2020; Tian et al., 2022). Metal(loid) compounds on PM's surface could be moved into the lung and circulatory system, in turn causing direct negative health effects by encroaching on multiple organs and/or indirect effects by setting off a cascade of inflammation events (Valavanidis et al., 2008). Thus, internal (such as blood and urine) metal(loid)s could be used as biomarkers of metal(loid) compounds in PM and mediators between PM and negative health effects (Lan et al., 2021).

However, the directed evidence linking PM exposure with internal metal(loid) levels is still limited, with only some preliminary evidence by a few ecological studies. For example, the studies conducted in Belgium (Bai et al., 2019), Mexico (Castro-Larragoitia et al., 2021), and China (Zeng et al., 2016) found that urine Arsenic (As), Aluminium (Al), Thallium (Tl), Cobalt (Co), Cadmium (Cd), Molybdenum (Mo), Selenium (Se), and Lead (Pb) (Bai et al., 2019), blood Antimony (Sb) and Cd (Castro-Larragoitia et al., 2021), and blood Cd and Pb (Zeng et al., 2016) were higher in the people residing in air polluted areas than in those residing in non-polluted areas. A study consisting of 304 American adults from 6 urban communities showed that elevated annual mean concentrations of $PM_{2.5}$ were associated with higher urinary concentrations of Uranium (U) and Tungsten (W) (Pang et al., 2016). Also, recent cross-sectional and longitudinal panel studies further provided supporting evidence on the effects of short-term exposure to PM on internal metal(loid) levels in human body. In a study comprising 13, 626 children under 14 years old in Beijing, China, blood Cd levels were positively associated with average $PM_{2.5}$ in the two days prior to the survey date (Wu et al., 2021). A panel study in Korea (n = 88) found that a 10 μg/m^3 increment in PM_{10} in the previous day was associated with a 2.8 % increase in blood Cd and a 1.5 % increase in blood Pb (Lee et al., 2021). Another longitudinal panel study (n = 35) observed that $PM_{2.5}$ concentrations in the 1st, 3rd, and 7th days prior to visit were positively related to serum As, while $PM_{2.5}$ in the 7th, 30th, and 60th days prior to visit exhibited positive associations with serum Manganese (Mn) (Lan et al., 2021). A recent study conducted in Israel found that an interquartile range (IQR) increment in monthly mean concentrations of PM_{10} was associated with a 16.6 % increase in blood Pb (Hassan et al., 2023). These studies preliminarily provided the direct evidence on the contributions of PMs to internal metal(loid) doses in human body. Several knowledge gaps, however, remained unaddressed. First, the interests of aforementioned studies were limited to a few toxic metal(loid)s such as As, Cd, Pb, and Hg, etc, which limits our knowledge on the toxicokinetics of other metal(loids) widely detected in PMs. Second, single-day (e.g., the 1st or 2nd day prior to visit) PM exposure (Lee et al., 2021; Wu et al., 2021) was selected to examine its associations with internal metal(loid) doses, ignoring possible cumulative lag effect of continuous multiple days of PM exposure. Third, no study has examined the associations between PM_1 and internal metal(loid) doses so far although toxicological studies suggested that PM_1 could be more likely to carry metal(loid)s on its surface into the deep lung and circulatory system than $PM_{2.5}$ and PM_{10} (Valavanidis et al., 2008). Fourth, whether the associations between PMs and internal metal(loid) doses are modified by other factors (e.g., physical activity and residential greenness) remains unknown.

To address these knowledge gaps, this study used the biological monitoring data of 15 urine metal(loid)s collected in community-dwelling older adults in Fuyang city, Anhui Province, China, from July to September 2018, and applied distributed lag linear/non-linear models (DLMs/DLNMs) to examine single-day and cumulative lag effects of exposures to ambient PM_1, $PM_{2.5}$, and PM_{10} on urinary metal (loid) profiles, with the objectives of (1) which urine metal(loid)s are associated with short-term exposure to PMs? (2) what are the relative contributions of PM_1, $PM_{2.5}$, and PM_{10} to urine metal(loid)s? (3) dose physical activity (PA) and/or residential greenness reduce the effects of PMs on urine metal(loid)s?

2. Materials and methods

2.1. Study design and population

Study data were derived from the baseline survey of a cohort study: *Older Adults Health and Modifiable Factors*, which was conducted in Fuyang city, Anhui Province, China, from July to September 2018. Fuyang city is located in the northwest of Anhui Province, with a geographic area of 10, 118.17 square kilometers (Statistics 2020). Detailed recruitment procedures of older adults have been described elsewhere (Cheng et al., 2022; Zhou et al., 2021). Local residents aged 60 years or over who have been living in the same community on their own for at least 6 months (i.e., community-dwelling older adults) were eligible for inclusion in this study, and those who have been living in institutional settings such as nursing homes or assisted living facilities were excluded. A total of 6, 000 older adults from 451 villages/towns (Fig. 1) were selected using the probability proportional sampling method, and 5, 186 accepted this survey. Each participant was invited to participate in a face-to-face interview with a structured questionnaire conducted in his (her) house in the afternoon one day in advance, and then was asked to collect the first fasting urine sample in the next morning. After the exclusion of older adults without available urine samples (n = 1, 216), we included 3, 970 older adults in the final analysis. This research was approved by the biomedical ethical committee of Anhui Medical University (No. 20190288). All participants signed a written consent form.

2.2. Exposure assessment

The daily data of PM_1, $PM_{2.5}$, and PM_{10} at a 1 km spatial resolution and of carbon monoxide (CO), nitrogen dioxide (NO_2), ozone (O_3), and sulfur dioxide (SO_2) at a 10 km spatial resolution were obtained from ChinaHighAirPollutants database (CHAP, available at https://weijing-rs.github.io/product.html). These data were estimated by the space–time extremely randomized trees (STET) model combined with various data including ground measurements data, satellite remote sensing products, pollution emissions, meteorological data, land cover, topographic data, traffic data, and the population data to complete the model simulation (Wei et al., 2019; Wei et al. 2022; Wei et al. 2021a; Wei et al., 2023; Wei et al. 2021b). The STET model has good stability, with cross-validation coefficients of 0.83, 0.92, 0.90, 0.80, 0.84, 0.87, and 0.84 for PM_1, $PM_{2.5}$, PM_{10}, CO, NO_2, O_3, and SO_2, respectively. Based on the corresponding geocoded location (longitude and latitude) of each participant's home address, we assigned daily average exposure data of seven air pollutants up to eight days before urine collection for each participant.

We obtained the data of air temperature and relative humidity at 2 m above the earth's surface from the ERA5 reanalysis data with a resolution of 0.1° × 0.1° (Hersbach et al., 2020), and then extracted daily average temperatures and relative humidity up to three days before

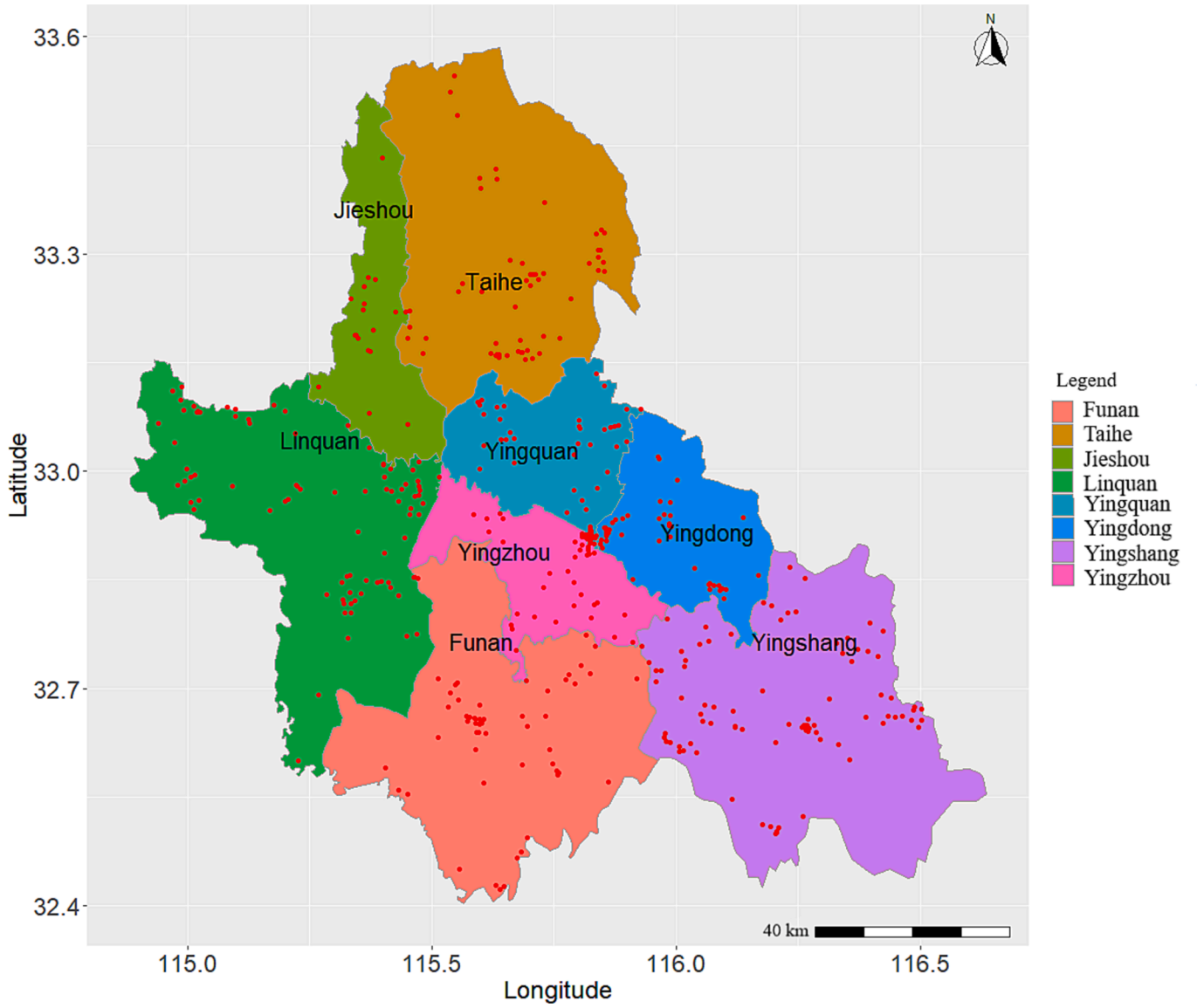

Fig. 1. Spatial distribution of residence addresses of the study subjects in Fuyang city, Anhui province, China. Red dots represent the residence addresses (n = 451) of the study subjects; the eight districts/counties in Fuyang city, Anhui province, China, are Yingzhou, Yingquan, Yingdong, Linquan, Taihe, Yingshang, Funan, and Jieshou, respectively. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

urine collection. Based on the corresponding geocoded location (longitude and latitude) of each participant's home address, we used the inverse distance weighting method to calculate the daily average temperature and relative humidity for each participant.

2.3. Collection of urine samples and assessment of 15 urine metal(loid)s

The first morning urine sample was collected from each participant. Methods of collection and analysis of biological samples have been previously described (Cheng et al., 2022; Zhou et al., 2021). Briefly, one urine sample (at least 30 mL) was collected from each participant using 100 mL polypropylene (PP) tube, then poured into 10 mL PP tubes, centrifuged for 10 min at 2000 rpm, and finally stored at − 80 °C until analysis.

Inductively coupled plasma-Mass spectrometry (ICP-MS) (Nexion350X, PerkinElmer, USA) was used to detect 15 urine metal(loid)s, including Gallium (Ga), As, Al, Magnesium (Mg), Calcium (Ca), U, Barium (Ba), Vanadium (V), Tl, Co, Strontium (Sr), Cesium (Cs), Cd, Mo, and Se. In short, all urine samples were placed in a refrigerator at 4 °C to be thawed before analyses. Then they were diluted 1:10 with diluent (0.05 %TritonX-100 + 1 %HNO3, Sigma, USA) thoroughly.

Quality control was conducted to assess the method's accuracy and instrument stability using human urine standard reference materials (Seronorm TM Trace Elements Urine L-1, SERO, Norway). The recovery percentages of the standard reference materials of 15 metal(loid)s ranged from 86 % to 126 %, and the coefficients of variation (CVs) for the intra-day and inter-day assays were all below 9.81 %. The limits of detection (LODs) for Ga, As, Al, Mg, Ca, U, Ba, V, Tl, Co, Sr, Cs, Cd, Mo, and Se were 0.0099 μg/L, 0.0212 μg/L, 0.4139 μg/L, 0.0022 mg/L, 0.0127 mg/L, 0.0002 μg/L, 0.0132 μg/L, 0.0048 μg/L, 0.0004 μg/L, 0.0009 μg/L, 0.0150 μg/L, 0.0005 μg/L, 0.0016 μg/L, 0.0024 μg/L, and 0.2744 μg/L, respectively. The urinary creatinine concentrations were measured using an automated clinical biochemistry analyzer (BS200, Mindray Bio-medical Electronics co. LTD, Shenzhen, China). Urinary metal(loid) concentrations were corrected for urine dilution using urinary creatinine levels and expressed as mg/g for Mg and Ca, and as μg/g for remaining metal(loid)s.

2.4. Covariates

Potential covariates included individual- and neighborhood-level characteristics. Individual-level characteristics included sex (*male or female*), age (*60–64, 65–69, 70–74, or 75–97 years old*), residential location (*rural or urban areas*), educational level (*illiteracy, primary, junior, or senior school or above*), occupation (*technical labor-related occupation, manual labor-related occupations, no regular job, or loss job*), married status (*with or without a spouse*), living arrangement (*living alone or living with others*), economic condition (*poor, average or wealthy*), smoking status (*non-smoker, former smoker, or current smoker*), secondhand smoking (*no or yes*), PA (*no PA, moderate PAs, or severe PAs*), body mass index (BMI) (*underweight, normal weight, overweight, or obesity*), hypertension (*no or yes*), diabetes (*no or yes*), residential greenness (*normalized differential vegetation index, $NDVI_{500m}$*). Neighborhood-level characteristics included per capita disposable income, population density, and proportion of minimum living guarantee population.

Of these factors, the economic condition was assessed by the following question: "how was economic condition of your family when compared to neighbors *(poor, average or wealthy)*?". Normalized differential vegetation index at a spatial resolution of 500 m ($NDVI_{500m}$) was used to assess residential greenness, which was calculated via the Moderate Resolution Imaging Spectroradiometer (MODIS) data. The values of the $NDVI_{500m}$ range from − 1.0 to 1.0, with higher values indicating greater greenness coverage. MODIS has a temporal resolution of 16 days. For our analysis, we extracted $NDVI_{500m}$ values based on the investigation date of older adults. If the time interval between the two dates for our extracted $NDVI_{500m}$ and the investigation date were equal, NDVI values from the earlier date were included. For example, if a participant was investigated on July 20, 2018, the length between the investigation date and July 12 or July 28, 2018 (dates for our extracted $NDVI_{500m}$), would be the same, so we would use their $NDVI_{500m}$ values assessed on July 12, 2018. Rural and urban data on per capita disposable income, population density, and proportion of minimum living guarantee population for eight districts/counties were extracted from the Fuyang Statistical Yearbook (Statistics, 2019). Details of other covariates have been previously described (Cheng et al., 2022; Zhou et al., 2021).

Furthermore, religious belief, dietary pattern, alcohol consumption, and kidney function were also investigated. These four factors have been linked with some urine metal(loid)s in previous studies (Barbosa et al., 2023; Hwang et al., 2014; Jin et al., 2018; Lozano et al., 2022), whereas their associations with PM still lack available evidence. Thus, we did not adjust these four variables in main analyses and adjusted them in sensitivity analyses.

Religious belief was obtained by self-report and classified into two groups: (1) no, (2) yes. Dietary intake was assessed using the Food Frequency Questionnaire (FFQ) (Ruan et al., 2018) including 15 foods (pork, beef and mutton, poultry, fish, vegetables, fruits, sugar, coarse cereals, soya, mushrooms, egg, nut, milk, animal oils, and animal viscera). Participants were asked to recall intake frequencies of these foods during the year prior to the investigation. The frequencies in each food included five categories (*"never", "less than once/month", "less than once/week", "less than once/day", and "one or more times a day"*). Five dietary patterns were then extracted using principal component analysis (PCA): (1) the first factor (*including pork, beef and mutton, poultry, and fish*), (2) the second factor (*including coarse cereals, soya, and mushrooms*), (3) the third factor (*including vegetables, eggs, and fruits*), (4) the fourth factor (*including sugar, nut, and milk*), and (5) the fifth factor (*including animal oils and viscera*). Details were provided in Table S1. Alcohol consumption was obtained by self-report and classified into three groups: (1) never, (2) < once a day, (3) ≥ once a day. According to the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, we calculated the estimated glomerular filtration rate (eGFR) (Matsushita et al., 2012). The eGFR was classified into three categories to evaluate kidney function: (1) normal (GFR ≥ 90 mL/min/1.73 m2), (2) slightly damaged (GFR 60–89 mL/min/1.73 m2), (3) obviously impaired (GFR < 60 mL/min/1.73 m2) (National Kidney, 2002).

2.5. Statistical analysis

Participant characteristics were expressed as means (±standard deviation (SD)) for continuous variables and as the number (percentages (%)) for categorical variables. Urinary metal(loid) concentrations below the LODs were assigned as their LODs divided by $\sqrt{2}$. Urine metal(loid)s were natural logarithmic transformed (ln-transformed) to satisfy model assumptions of normality of residuals. Two lag structures were created to examine the delayed effects of PMs on urine metal(loid)s. Single-day lag was presented as lag0, lag1, … lag7. Cumulative lag was presented as lag0-1, lag0-2, … lag0-7. For example, Lag0 and Lag1 reflect the single-day lag effects of exposures to PMs in the 1st and 2nd days before urine collection on urine metal(loid)s, respectively. Lag0-1 reflects the cumulative lag effects of exposures to PMs over the 1st to 2nd days before urine collection on urine metal(loid)s. Bivariate correlations among the 3-day moving average concentrations for PM_1, $PM_{2.5}$, and PM_{10}, and 15 urinary metal(loid) concentrations were assessed using Spearman's rank correlation coefficients.

We used generalized additive model (GAM) combined with DLMs to estimate the effects of short-term exposures to ambient PM_1, $PM_{2.5}$, PM_{10} on 15 urine metal(loid)s. The following GAM with DLMs was used:

$$\text{Log E(Yt)} = \alpha + \text{Cb.PM} + \text{ns (Temperature, df} = 6) + \text{ns (Relative humidity, df} = 3) + \text{ns (Time trend, df} = 3) + \text{factor (Dow)} + \text{covariates}$$

where t is the day of investigation; E(Yt) is the urinary metal(loid) concentrations on day t; Log E(Yt) follows a normal distribution, and GAM with a Gaussian link was used (Zheng et al., 2021); α is the intercept; Cb.PM is a cross-basis matrix, in which the exposure–response function is assumed to be linear and the lag-response function was modeled using a natural cubic spline function with 3 degrees of freedom; ns represents the natural cubic spline function; the 3-day moving average temperature and relative humidity were used to control for their potential confounding effects (Gu et al., 2020); Dow is an indicator variable for day of the week; covariates in main analyses included sex, age, residential location, educational level, occupation, married status, living arrangement, economic condition, smoking status, secondhand smoking, PA, BMI, hypertension, diabetes, residential greenness, per capita disposable income, population density, and proportion of minimum living guarantee population. Based on previous research (Goldberg et al., 2013), we reported single-day lag effects (lag0-lag7), thereby justifying the use of eight days in the DLMs.

The percentage change of each urine metal(loid) per 10 μg/m^3 increment in PM_1, $PM_{2.5}$, or PM_{10} was calculated as follows: $100 \times [\exp^{(10\times\beta)} - 1]$. A two-tailed $P < 0.05$ was considered statistically significant. In addition, to examine the relative importance of PM_1, $PM_{2.5}$, and PM_{10} for urine metal(loid)s, the concentrations of PM_1, $PM_{2.5}$, and PM_{10} were standardized (Daily PM concentration subtracted its median and was divided by its IQR). We estimated single-day (lag0-lag7) and cumulative lag effects (lag0–1, lag0–2, and so on).

To explore possible nonlinear exposure–response associations of PM_1, $PM_{2.5}$, and PM_{10} with 15 urine metal(loid)s, GAM combined with DLNMs was performed. Briefly, the exposure–response function was fitted using a natural cubic spline with 2 internal spline knots at equally spaced points and the lag-response function was modeled using a natural cubic spline with 3 degrees of freedom (Gu et al., 2020). If a non-linear exposure–response relationship existed, the percent changes of urinary metal(loid) concentrations were further calculated by comparing the 50th, 75th and 95th percentiles of PM_1, $PM_{2.5}$, PM_{10} with their corresponding 25th percentiles using DLNMs, respectively (Duan et al., 2018).

We conducted stratified analyses to examine potential effect modifications by: (1) age (*< 70 and ≥ 70 years old*), (2) sex (*male and female*), (3) residential location (*rural and urban areas*), (4) PA (*no PA, moderate*

PAs, and *severe PAs*), and (5) residential greenness (*low and high NDVI$_{500m}$*). The NDVI$_{500m}$ was categorized into low and high NDVI$_{500m}$ groups based on its median (0.68). The heterogeneity between subgroups was assessed using the following equation: $z = (\beta 1 - \beta 2)/\sqrt{SE_1^2 + SE_2^2}$, where β1 and β2 are effect estimates for two subgroups; SE_1 and SE_2 are the corresponding standard errors (Payton et al., 2003; Schenker and Gentleman, 2001). Then, *P* value was obtained from standard normal distribution based on the z value. Bonferroni correction was conducted for multi-group comparisons.

Sensitivity analyses were conducted to assess the robustness of the estimates. (1) We used two-pollutant models adjusted by CO, NO_2, O_3, or SO_2. (2) Considering that impaired kidney function could decrease urinary metal elimination, we refitted the models by excluding the participants with obviously impaired kidney function. (3) Given that religious belief, dietary pattern, alcohol consumption, and kidney function have been reported to be associated with urine metal(loid)s, we selected these four factors as covariates based on the recommendation by VanderWeele TJ (VanderWeele, 2019) and ran the model by further adjusting for them.

The data were analyzed in R software (version 4.1.3; R Foundation for Statistical Computing) using the "dlnm" package.

3. Results

3.1. Characteristics of participants and environmental data

Demographic characteristics of older adults are provided in Table 1. Of 3970 older adults, the average age was 71.01 ± 5.46 years old, 51.11 % were female, and 83.65 % lived in rural areas.

Detection rates and urinary concentrations of 15 metal(loid)s are summarized in Table 2. Except for Ga (Detection rate: 99.72 %), U (99.90 %), Ba (99.97 %), Tl (99.97 %), and Se (99.69 %), remaining metal(loid)s were detected in all urine samples. The median concentrations of 15 metal(loid)s in a decreasing order were as follows: 83.40 mg/L for Ca, 72.51 mg/L for Mg, 134.29 μg/L for Sr, 72.00 μg/L for Mo, 48.73 μg/L for Al, 15.76 μg/L for As, 13.44 μg/L for Se, 4.26 μg/L for Cs, 3.77 μg/L for Ba, 1.45 μg/L for V, 0.84 μg/L for Cd, 0.40 μg/L for Ga, 0.27 μg/L for Co, 0.11 μg/L for Tl, and 0.05 μg/L for U.

Table 3 shows the distributions of air pollutants and meteorological variables. The eight-day moving average concentrations of ambient PM_1, $PM_{2.5}$, PM_{10}, CO, NO_2, O_3, and SO_2 were 14.43 μg/m^3, 24.04 μg/m^3, 47.95 μg/m^3, 0.52 mg/m^3, 18.21 μg/m^3, 123.93 μg/m^3, and 9.42 μg/m^3, respectively. Spearman's rank correlation coefficients between three PMs (3-day moving average of the lag0, lag1, and lag2 days) and urine metal(loid)s are shown in Fig. 2 and Table S2. Urine metal(loid)s were positively correlated with each other (r = 0.106–0.872, all $P < 0.05$) and three PMs (r = 0.004–0.305, most of $P < 0.05$) with an exception of Co and PM_{10} (r = -0.010, $P > 0.05$).

3.2. Associations of urine metal(loid)s with PM_1, $PM_{2.5}$, and PM_{10} exposures

Fig. 3 and Table S3 show single-day and cumulative lag effects of short-term exposures to PMs on urine metal(loid)s estimated by DLMs. Except for Cd, Mo, and Se, the percentage changes of remaining urine metal(loid)s exhibited a "L-shaped" trend from the lag0 to lag7 day: the percentage changes attributed to three PMs were all the largest at the lag0 day, rapidly attenuated at the lag1 day, and dropped around 0 at the lag2 day. Thus, the cumulative lag effects (lag0-1 days) of exposures to PM_1, $PM_{2.5}$, and PM_{10} on urine metal(loid)s were examined and further plotted in a decreasing order, shown in Fig. 4A. Of 15 urine metal (loid)s, urine Ga (PM_1: 15.62 %; $PM_{2.5}$: 13.31 %; PM_{10}: 4.74 %), As (PM_1: 8.86 %; $PM_{2.5}$: 10.03 %; PM_{10}: 2.65 %), Al (PM_1: 8.22 %; $PM_{2.5}$: 9.50 %; PM_{10}: 3.01 %), Mg (PM_1: 8.34 %; $PM_{2.5}$: 8.60 %; PM_{10}: 4.18 %), Ca (PM_1: 5.55 %; $PM_{2.5}$: 8.35 %; PM_{10}: 5.43 %), U (PM_1: 12.29 %; $PM_{2.5}$: 8.23 %; PM_{10}: 2.17 %), and V (PM_1: 5.50 %; $PM_{2.5}$: 6.06 %; PM_{10}: 1.97 %) were significantly associated with PM_1, $PM_{2.5}$, and PM_{10} exposures. In addition, urine Ba (PM_1: 8.94 %; $PM_{2.5}$: 6.83 %) and Tl (PM_1: 3.60 %; $PM_{2.5}$: 4.87 %) were significantly associated with PM_1 and $PM_{2.5}$ exposures, while Co ($PM_{2.5}$: 4.75 %), Sr ($PM_{2.5}$: 3.17 %), and Cs ($PM_{2.5}$: 1.80 %) were exclusively associated with $PM_{2.5}$ exposure.

Table 1
Basic characteristics of older adults from Older Adults Health and Modifiable Factors (n = 3970).

Characteristic		n(%)
Sex	Male	1941(48.89)
	Female	2029(51.11)
Age (years old)	60–64	316(7.96)
	65–69	1444(36.37)
	70–74	1275(32.12)
	75–97	935(23.55)
Residential location	Rural areas	3321(83.65)
	Urban areas	649(16.35)
Educational level	Illiteracy	2134(53.75)
	Primary school	636(16.02)
	Junior school	551(13.88)
	Senior school or above	649(16.35)
Occupation	Technical labor-related occupations	186(4.69)
	Manual labor-related occupations	1760(44.33)
	No regular job	1629(41.03)
	Loss job	395(9.95)
Married status	With a spouse	3660(92.19)
	Without a spouse	310(7.81)
Living arrangement	Living alone	169(4.26)
	Living with others	3801(95.74)
Religious belief	No	3422(86.20)
	Yes	548(13.80)
Economic condition[a]	Poor	802(20.83)
	Average	2967(77.06)
	Wealthy	81(2.10)
Smoking status[a]	Non-smoker	2701(68.57)
	Former smoker	779(19.78)
	Current smoker	459(11.65)
Second hand smoking[a]	No	2612(66.31)
	Yes	1327(33.69)
Alcohol consumption[a]	Never	2745(75.29)
	<Once a day	390(10.70)
	≥Once a day	511(14.02)
PA[a]	No PA	1404(35.57)
	Moderate PAs	1190(30.15)
	Severe PAs	1353(34.28)
BMI[a]	Low weight	150(3.90)
	Normal weight	1662(43.16)
	Overweight	1413(36.69)
	Obesity	626(16.26)
Kidney function[a]	Normal	913(28.58)
	Slightly damaged	1775(55.57)
	Obviously impaired	506(15.84)
Hypertension	No	1565(39.42)
	Yes	2405(60.58)
Diabetes[a]	No	3275(82.83)
	Yes	679(17.17)
NDVI$_{500m}$, Mean (SD)		0.64(0.15)
Per capita disposable income (¥), Mean (SD)		15007(7076.60)
Population density (people/square kilometers)[b], Mean (SD)		1187(626.93)
Proportion of minimum living guarantee population[c], Mean (SD)		0.03(0.01)

Abbreviations: PA: physical activity BMI: body mass Index; NDVI: Normalized Difference Vegetation Index; SD: standard deviation.
a Due to missing covariate data, subgroup totals may not sum to the total sample population.
b Population density refers to the number of people living in an average unit of land area. It is generally expressed as the number of people living per square kilometer. The population of a region (country) divided by the land area of the region (country). The calculation formula is: Population density = total population of a region/area of the region (people/square kilometers). This definition is from Fuyang Bureau of Statistics.
c The proportion of minimum living guarantee population is equal to the minimum living guarantee population of a region/ total population of a region. This definition is from Fuyang Bureau of Statistics.

Table 2
Detection rates and urinary concentrations of 15 metal(loid)s in older adults (n = 3970).

Metal(loid)s	LOD	DR(%)	Unadjusted (Creatinine adjusted)[a]					
			GM	5th	25th	50th	75th	95th
Ga	0.0099	99.72	0.40(0.48)	0.09(0.09)	0.23(0.24)	0.40(0.46)	0.68(0.93)	1.94(3.29)
As	0.0212	100	15.75(19.24)	4.07(6.73)	9.23(12.03)	15.76(18.09)	26.38(28.88)	59.28(64.98)
Al	0.4139	100	48.58(59.34)	13.27(12.52)	29.19(31.65)	48.73(56.37)	80.53(108.94)	174.82(308.69)
Mg	0.0022	100	65.22(79.67)	14.29(22.56)	42.51(56.11)	72.51(86.76)	117.77(130.27)	230.88(239.35)
Ca	0.0127	100	76.34(93.25)	14.24(18.52)	43.31(55.30)	83.40(100.95)	145.46(168.77)	309.84(337.85)
U	0.0002	99.90	0.05(0.06)	0.01(0.01)	0.02(0.03)	0.05(0.05)	0.10(0.11)	0.31(0.36)
Ba	0.0132	99.97	3.85(4.70)	0.85(0.84)	2.22(2.34)	3.77(4.53)	6.73(9.05)	18.54(30.02)
V	0.0048	100	1.38(1.68)	0.47(0.50)	0.95(1.04)	1.45(1.69)	2.11(2.72)	3.24(5.42)
Tl	0.0004	99.97	0.10(0.12)	0.03(0.04)	0.06(0.08)	0.11(0.12)	0.16(0.18)	0.31(0.35)
Co	0.0009	100	0.27(0.33)	0.08(0.12)	0.17(0.21)	0.27(0.31)	0.42(0.49)	0.93(1.18)
Sr	0.0150	100	128.76(157.28)	34.19(43.13)	76.60(101.37)	134.29(164.25)	224.17(252.29)	439.33(464.36)
Cs	0.0005	100	4.09(5.00)	1.49(2.24)	2.77(3.78)	4.26(4.99)	6.14(6.62)	9.89(10.49)
Cd	0.0016	100	0.82(1.00)	0.24(0.39)	0.49(0.69)	0.84(1.00)	1.38(1.42)	2.69(2.54)
Mo	0.0024	100	69.32(84.68)	14.88(24.74)	37.98(51.54)	72.00(84.48)	127.74(136.44)	292.73(286.69)
Se	0.2744	99.69	12.16(14.86)	2.90(4.77)	8.15(10.63)	13.44(15.67)	20.76(22.05)	35.83(38.1)

Abbreviations: LOD, limit of detection (Mg & Ca (mg/L),other metal(loid)s (μg/L)); DR, detection rate; GM, Geometric mean; Ga, Gallium; As, Arsenic; Al, Aluminium; Mg, Magnesium; Ca, Calcium; U, Uranium; Ba, Barium; V, Vanadium; Tl, Thallium; Co, Cobalt; Sr, Strontium; Cs, Cesium;Cd, Cadmium Mo, Molybdenum; Se, Selenium.
a Unadjusted: volume-based urinary metal concentrations (Mg & Ca (mg/L), other metal(loid)s (μg/L)); Creatinine adjusted: urinary metal concentrations were corrected for urine dilution by urinary creatinine levels (Mg & Ca mg/g creatinine, other metal(loid)s (μg/g creatinine)).

Table 3
Distribution characteristics of estimated air pollutants at lag0-lag7 days and meteorological variables before morning urine samples collection.

Variable		mean	SD	Minimum	25th	50th	75th	Maximum
PM_1 (μg/m^3)	Lag0	15.28	3.52	10.00	13.08	14.63	16.32	30.39
	Lag1	14.34	2.53	9.80	12.40	14.11	15.69	21.55
	Lag2	14.50	2.54	9.57	12.55	14.19	16.07	22.49
	Lag3	14.22	2.27	8.66	12.63	14.09	15.53	21.16
	Lag4	14.24	2.24	7.57	12.35	14.48	15.76	21.11
	Lag5	14.49	2.63	8.57	12.43	14.76	16.62	19.82
	Lag6	14.19	2.79	6.70	12.01	13.64	16.80	21.28
	Lag7	14.20	3.28	6.03	12.12	13.19	17.24	23.09
	Lag0-7	14.43	1.12	11.68	13.54	14.58	15.29	17.85
$PM_{2.5}$ (μg/m^3)	Lag0	25.39	5.76	14.89	22.34	24.35	27.34	46.78
	Lag1	23.65	4.06	14.89	20.69	23.17	26.13	33.87
	Lag2	24.06	3.84	15.11	21.34	23.16	26.40	35.23
	Lag3	23.56	3.38	14.63	21.30	23.34	25.84	31.99
	Lag4	23.78	3.87	12.31	20.59	24.31	26.15	34.49
	Lag5	24.21	4.13	14.78	21.16	23.84	27.79	33.69
	Lag6	23.82	4.04	11.66	21.21	23.06	27.39	35.82
	Lag7	23.83	4.55	10.83	21.48	22.82	28.08	33.71
	Lag0-7	24.04	1.68	19.39	22.65	24.33	25.34	28.03
PM_{10} (μg/m^3)	Lag0	49.40	8.15	29.01	43.64	49.35	54.79	71.73
	Lag1	47.31	8.22	29.01	42.36	46.13	54.95	65.05
	Lag2	48.22	7.70	30.38	42.46	46.31	55.13	65.36
	Lag3	47.00	6.24	28.70	43.22	46.15	51.54	62.41
	Lag4	47.48	8.04	25.62	42.04	47.78	52.78	74.04
	Lag5	48.32	7.87	24.46	43.15	47.96	54.48	74.11
	Lag6	48.33	7.68	31.05	43.18	46.75	52.79	75.48
	Lag7	47.52	8.08	24.60	43.99	46.28	52.04	76.89
	Lag0-7	47.95	3.48	41.18	44.93	47.66	51.26	56.03
CO (mg/m3)	Lag0-7	0.52	0.05	0.37	0.49	0.51	0.55	0.64
NO_2(μg/m^3)	Lag0-7	18.21	1.39	15.23	17.51	18.01	18.83	23.27
O_3 (μg/m^3)	Lag0-7	123.93	15.84	74.73	116.6	125.65	137.21	149.37
SO_2 (μg/m^3)	Lag0-7	9.42	1.59	4.52	9.14	9.64	9.96	12.78
Temperature (℃)	Lag0-2	30.47	1.38	27.48	28.97	31.04	31.50	32.10
Humidity (%)	Lag0-2	72.26	5.24	63.82	68.67	70.42	78.82	82.42

Abbreviations:PM_1: particle matter with an aero-dynamic diameter $\leq$ 1 μm; $PM_{2.5}$: particle matter with an aero-dynamic diameter $\leq$ 2.5 μm; PM_{10}: particle matter with an aero-dynamic diameter $\leq$ 10 μm; CO: carbon monoxide; NO_2: nitrogen dioxide; O_3: ozone; SO_2: sulfur dioxide; lag 0 to lag 7: Lag-specific effects from day to day; Lag 0–2: 3-day moving average;Lag 0–7: 8-day moving average; SD: standard deviation.

We further used DLNMs to model the exposure–response function over lag0-1 days, shown in Fig. 5. PM_1 and $PM_{2.5}$ shared similar relationships to urine metal(loid)s, with the linear relationships to Ga, As, Al, Mg, Ca, U, and Ba, while with the "U-shaped" relationships to V, Tl, Co, Sr, Cs, Cd, Mo, and Se. Slightly different from PM_1 and $PM_{2.5}$, PM_{10} exhibited linear relationships to Ga, As, Mg, Ca, U, Tl, Sr, Cs, Cd, Mo, and Se, "inverted U-shaped" relationships to Al and Ba, and "U-shaped" relationships to V and Co. For the non-linear relationships between PMs and urine metal(loid)s, we further estimated the effects of PM_1, $PM_{2.5}$, and PM_{10} on urine metal(loid)s by comparing the 50th, 75th, and 95th percentiles of their concentrations with the responding 25th percentiles, shown in Fig. S2 and Table S4. Combining the results from DLMs and DLNMs, the associations of three PMs with urine Ga, As, Al, Mg, Ca, U, and Ba were robust, while the associations of three PMs with remaining

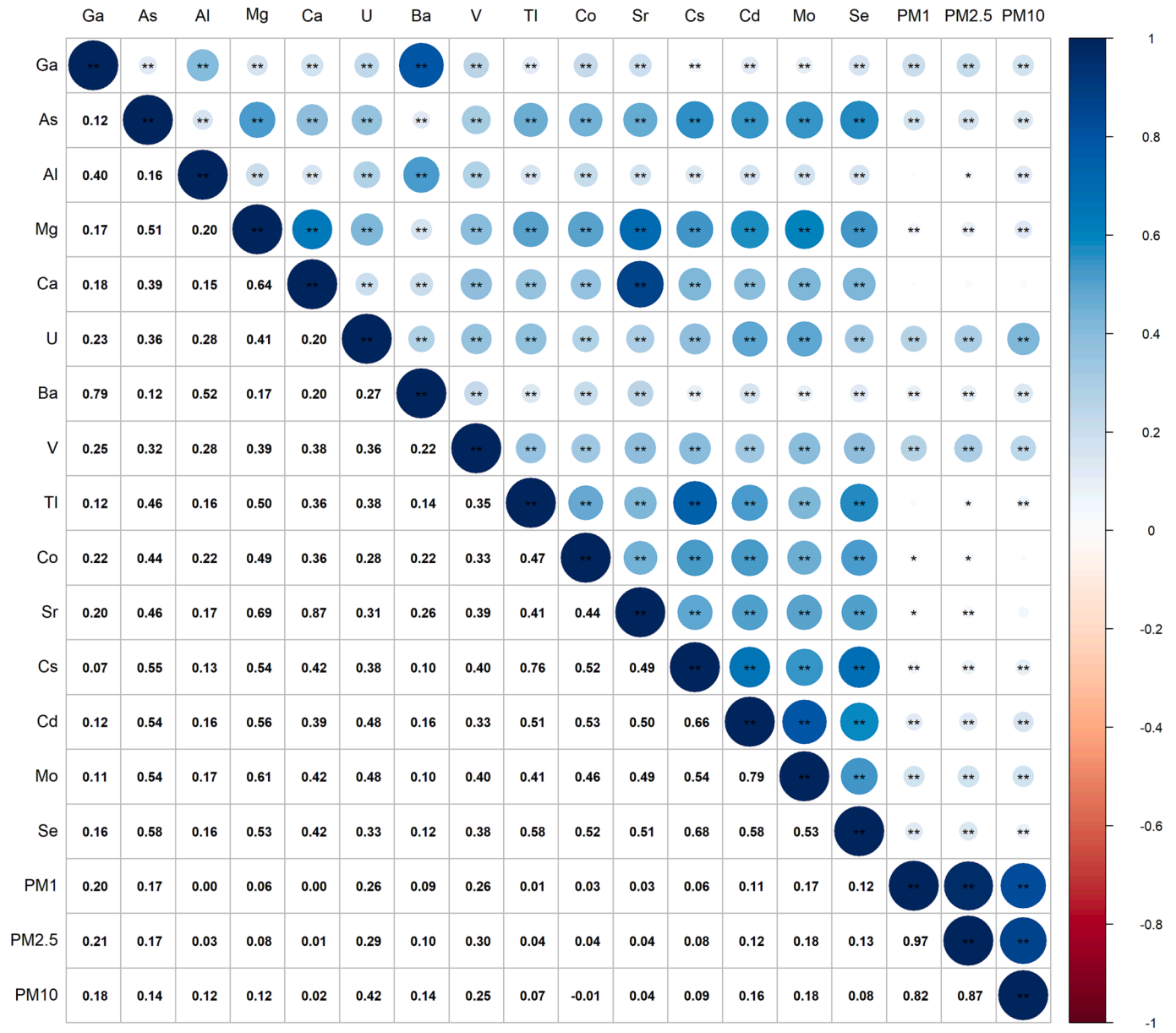

Fig. 2. Spearman correlation coefficients between PM_1, $PM_{2.5}$, PM_{10}, and urine metal(loid)s. Ga, Gallium; As, Arsenic; Al, Aluminium; Mg, Magnesium; Ca, Calcium; U, Uranium; Ba, Barium; V, Vanadium; Tl, Thallium; Co, Cobalt; Sr, Strontium; Cs, Cesium; Cd, Cadmium; Mo, Molybdenum; Se, Selenium; PM_1: particle matter with an aero-dynamic diameter $\leq$ 1 μm; $PM_{2.5}$: particle matter with an aero-dynamic diameter $\leq$ 2.5 μm; PM_{10}: particle matter with an aero-dynamic diameter $\leq$ 10 μm. The sizes of dots indicate the intensities of Spearman correlation coefficients. The colors of dots indicate the intensities and directions of Spearman correlation coefficients. * $P < 0.05$. * * $P < 0.01$.

metal(loid)s may be spurious, and need be explained with caution.

3.3. Relative contributions of PM_1, $PM_{2.5}$, and PM_{10} to urine metal(loid)s

To compare relative contributions of PM_1, $PM_{2.5}$, and PM_{10} to urine metal(loid)s, we standardized the concentrations of PM_1, $PM_{2.5}$, and PM_{10}, and re-estimated their single-day and cumulative lag effects on urine metal(loid)s, shown in Fig. 4B, Fig. S1, and Table S3. Cumulative lag (lag0-1) effects shown in Fig. 4B indicated that PM_1 was the greatest contributor to U (PM_1: 3.38 %; $PM_{2.5}$: 3.09 %; PM_{10}: 1.98 %), $PM_{2.5}$ exhibited the greatest contributions to Ga ($PM_{2.5}$: 5.35 %; PM_{10}: 5.00 %; PM_1: 4.38 %), As ($PM_{2.5}$: 5.04 %; PM_{10}: 3.16 %; PM_1: 2.80 %), Al ($PM_{2.5}$: 4.06 %: PM_{10}: 3.23 %; PM_1: 2.43 %), and Ba ($PM_{2.5}$: 2.59 %; PM_1: 2.54 %; PM_{10}: −0.22 %), and PM_{10} showed the greatest contributions to Mg (PM_{10}: 4.70 %; $PM_{2.5}$: 3.69 %; PM_1: 2.31 %) and Ca (PM_{10}: 6.10 %; $PM_{2.5}$: 3.46 %; PM_1: 1.45 %).

3.4. Subgroup analysis

Considering that both DLMs and DLNMs suggested the robust associations of three PMs with urine Ga, As, Al, Mg, Ca, U, and Ba, we chose aforementioned metal(loid)s to examine their associations with three PMs in the subgroup analyses by five variables, including age, sex, residential location, PA, and residential greenness. We did not find significant differences in single-day (lag0, lag1) and cumulative (lag0-1) lag effects of PM_1, $PM_{2.5}$, and PM_{10} on urinary metal(loid) concentrations across age (Figs. S3-S5 and Table S5), and sex (Figs. S6-S8 and Table S6) subgroups. In addition, for the associations of three PMs with urine As, Al, Mg, Ca, and U, a "L-shaped" curve trend from the lag0 day to lag7 day was found in rural participants, whereas an "inverted U-shaped" curve trend was found in urban groups, but the differences in most of the lag effects between rural and urban participants were not significant (Figs. S9-S11 and Table S7). As for PA, the percent change of urine As

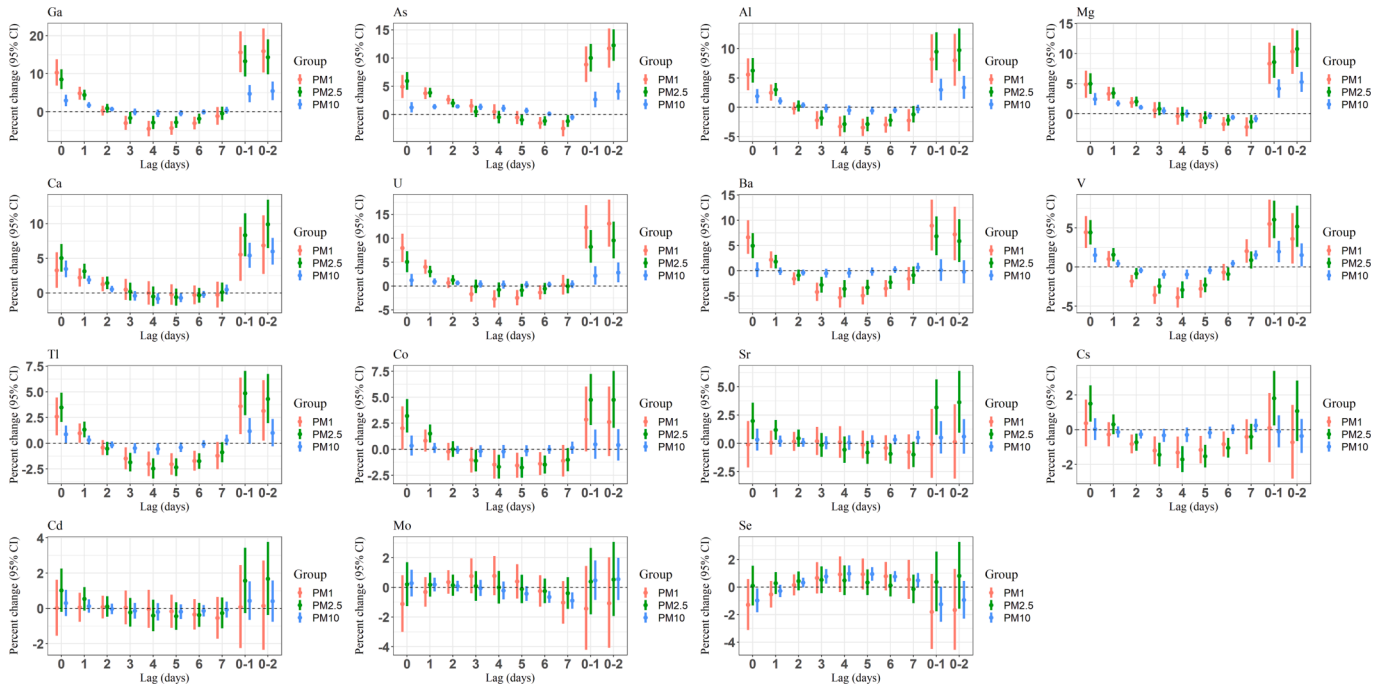

Fig. 3. Percent change (95 % CI) in urinary metal(loid) concentrations per 10 μg/m^3 increase in PM_1, $PM_{2.5}$, and PM_{10} at different single and cumulative lag days. Ga, Gallium; As, Arsenic; Al, Aluminium; Mg, Magnesium; Ca, Calcium; U, Uranium; Ba, Barium; V, Vanadium; Tl, Thallium; Co, Cobalt; Sr, Strontium; Cs, Cesium; Cd, Cadmium; Mo, Molybdenum; Se, Selenium; PM_1: particle matter with an aero-dynamic diameter $\leq$ 1 μm; $PM_{2.5}$: particle matter with an aero-dynamic diameter $\leq$ 2.5 μm; PM_{10}: particle matter with an aero-dynamic diameter $\leq$ 10 μm.

per 10 μg/m^3 increment in PM_{10} significantly increased in participants with severe PAs and the percent change of urine Ca per 10 μg/m^3 increment in PM_{10} significantly decreased in participants with severe PAs at the lag0, lag1, and lag0-1 days (Figs. S12-S14 and Table S8). Impressively, single-day (lag0, lag1) and cumulative (lag0-1) lag effects of PM_1, $PM_{2.5}$, and PM_{10} on urine Ga, As, Al, Mg, Ca, and Ba were significantly reduced when exposed to high $NDVI_{500m}$ (Figs. S15-S17 and Table S9).

3.5. Sensitivity analyses

A series of sensitivity analyses were conducted, including two-pollutant models adjusted for CO (Fig. S18 and Table S10), NO_2 (Fig. S19 and Table S11), O_3 (Fig. S20 and Table S12), or SO_2 (Fig. S21 and Table S13), the model excluding the participants with obviously impaired kidney function (Fig. S22 and Table S14), and the model further adjustment for religious belief, dietary pattern, alcoholic consumption, and kidney function (Fig. S23 and Table S15). No significant difference was identified in sensitivity analyses.

4. Discussion

In this study, we used both DLMs and DLNMs to comprehensively examine the single-day and cumulative lag effects of short-term exposures to PM_1, $PM_{2.5}$, and PM_{10} on urinary metal(loid) profiles. First, combining the results from DLMs and DLNMs, exposures to PM_1, $PM_{2.5}$, and PM_{10} at the lag0 and lag1 days were associated with elevated urinary concentrations of Ga, As, Al, Mg, Ca, U, and Ba. The cumulative lag (lag0-1 days) percentage changes of urinary concentrations of these seven metal(loid)s per 10 μg/m^3 increment in three PMs ranged from 0.13 % to 15.62 %, with most of them around 10 %. Second, within these three standardized PMs, PM_1 was the greatest contributor to U, followed by $PM_{2.5}$ and PM_{10}; PM_{10} contributed the most to Mg and Ca, followed by $PM_{2.5}$ and PM_1; and $PM_{2.5}$ contributed the most to Ga, As, and Al, followed by PM_{10} and PM_1, while $PM_{2.5}$ also contributed the greatest to Ba, followed by PM_1. Third, the cumulative lag (lag0-1 days) effects of PM_1, $PM_{2.5}$, and PM_{10} on Ga, As, Al, Mg, Ca, and Ba were significantly reduced when exposed to high $NDVI_{500m}$.

4.1. Assessment of PMs exposure and 15 urine metal(loid)s

The eight-day moving average concentrations of ambient PM_1, $PM_{2.5}$, and PM_{10} were 14.43 μg/m^3, 24.04 μg/m^3, and 47.95 μg/m^3, respectively, with lower ratios of PM_1/ $PM_{2.5}$ (0.60) and $PM_{2.5}$/ PM_{10} (0.50) than measurements across 24 China Atmosphere Watch Network (CAWNET) stations during 2006–2014 (Wang et al., 2015). It has been known that PM_1 mainly originates from direct emissions of motor vehicles during combustion process in cities (Talbi et al., 2018). By contrast, PM_{10} is mostly generated by mechanical processes, such as wind resuspension of loose soil or construction activities (Talbi et al., 2018). $PM_{2.5}$ can be determined by either of these sources (Talbi et al., 2018). As a result, the ratios of these particles vary across regions and seasons (Wang et al., 2015). The lower ratios of PM_1/ $PM_{2.5}$ and $PM_{2.5}$/ PM_{10} in this study may be explained from two perspectives. On the one hand, approximately 84 % of participants in this study were from rural areas, where natural and agricultural activities may contribute more to PM_{10} than to PM_1 and $PM_{2.5}$. On the other hand, this study was conducted from July to September, during which the ratios of PM_1/ $PM_{2.5}$ and $PM_{2.5}$/ PM_{10} have been reported to be the lowest within a year (Wang et al., 2015).

Of the 15 urine metal(loid)s in this study, the median concentrations of Ga, As, Mg, Ca, V, Tl, Sr, Cd, Mo, and Se were comparable with previous reports, while the concentrations of urine Al, U, Ba, Co, and Cs were near the upper (Al, U, and Ba) or lower (Co and Cs) ranges of reports in previous studies (Chen et al., 2022; Li et al., 2022; Liu et al., 2014; Lu et al., 2016; Wu et al., 2018; Xiao et al., 2016; Zhang et al., 2016).

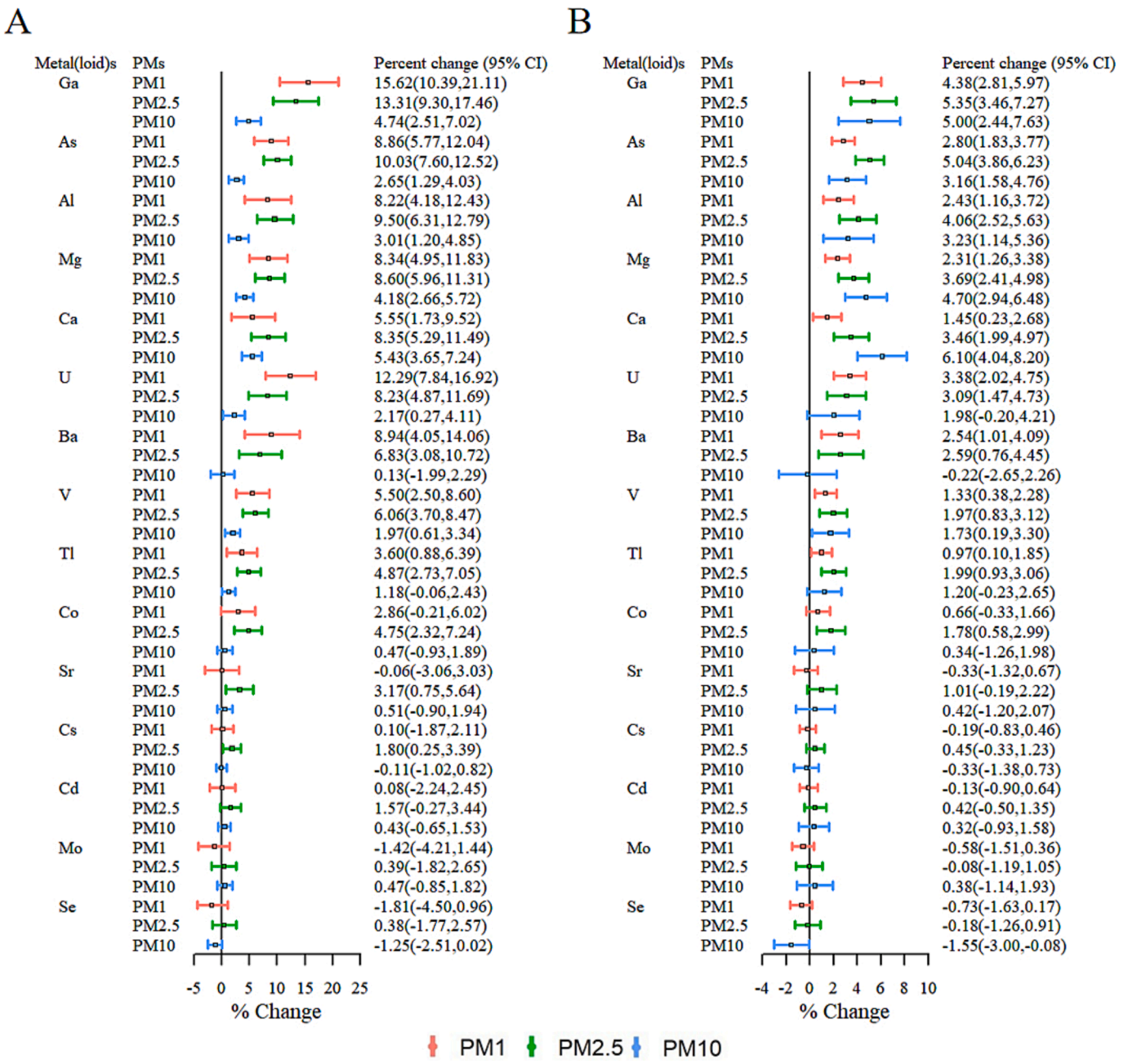

Fig. 4. Percent change (95 % CI) of urinary metal(loid) concentrations per 10 μg/m^3 or standardization unit increment in PM_1, $PM_{2.5}$, and PM_{10} over the cumulative lag days (0 to 1 days). (A) per 10 μg/m^3 increment; (B) standardization unit increment. Ga, Gallium; As, Arsenic; Al, Aluminium; Mg, Magnesium; Ca, Calcium; U, Uranium; Ba, Barium; V, Vanadium; Tl, Thallium; Co, Cobalt; Sr, Strontium; Cs, Cesium; Cd, Cadmium; Mo, Molybdenum; Se, Selenium; PM_1: particle matter with an aero-dynamic diameter $\leq$ 1 μm; $PM_{2.5}$: particle matter with an aero-dynamic diameter $\leq$ 2.5 μm; PM_{10}: particle matter with an aero-dynamic diameter $\leq$ 10 μm.

4.2. Associations of urine metal(loid)s with PM_1, $PM_{2.5}$, and PM_{10}

Although inhalation has been considered as one of the routes for metal(loid)s for human beings, direct evidence linking PMs with internal metal(loid)s was limited to a few toxic metal(loid)s (e.g., As, Cd, Pb, and Hg, etc.), and did not yield consistent results (Hassan et al., 2023; Lan et al., 2021; Lee et al., 2021; Pang et al., 2016; Wu et al., 2021). We used biological monitoring data of 15 urine metal(loid)s in older adults to examine the effects of short-term exposures to PMs on urinary metal (loid) profiles. Consistent with our expectations, DLMs showed that exposures to PM_1, $PM_{2.5}$, and PM_{10} over 1–2 days prior to urine collection were positively associated with all metal(loid)s but Cd, Mo, and Se. This study confirmed and extended previous findings, further indicating the links between short-term exposure to PM and internal doses of many metal(loid)s in human body, some of which are first reported.

DLNMs were further used to examine possible non-linear exposure–response associations between PMs and urine metal(loid)s. Exposures to PMs over lag0-1 days exhibited a linear or an "inverted U-shaped" association with Ga, As, Al, Mg, Ca, U, and Ba, whereas a "U-shaped" association with V, Tl, Co, Sr, Cs, Cd, Mo, and Se, indicating that the former associations may be robust, while the later associations need be explained with caution. In fact, whether or not and the extent to which there exist associations between PMs and internal metal(loid)s mainly depend on the concentrations of metal(loid) compositions in PMs, which are determined by natural (e.g., crustal minerals, volcanic eruption, soil

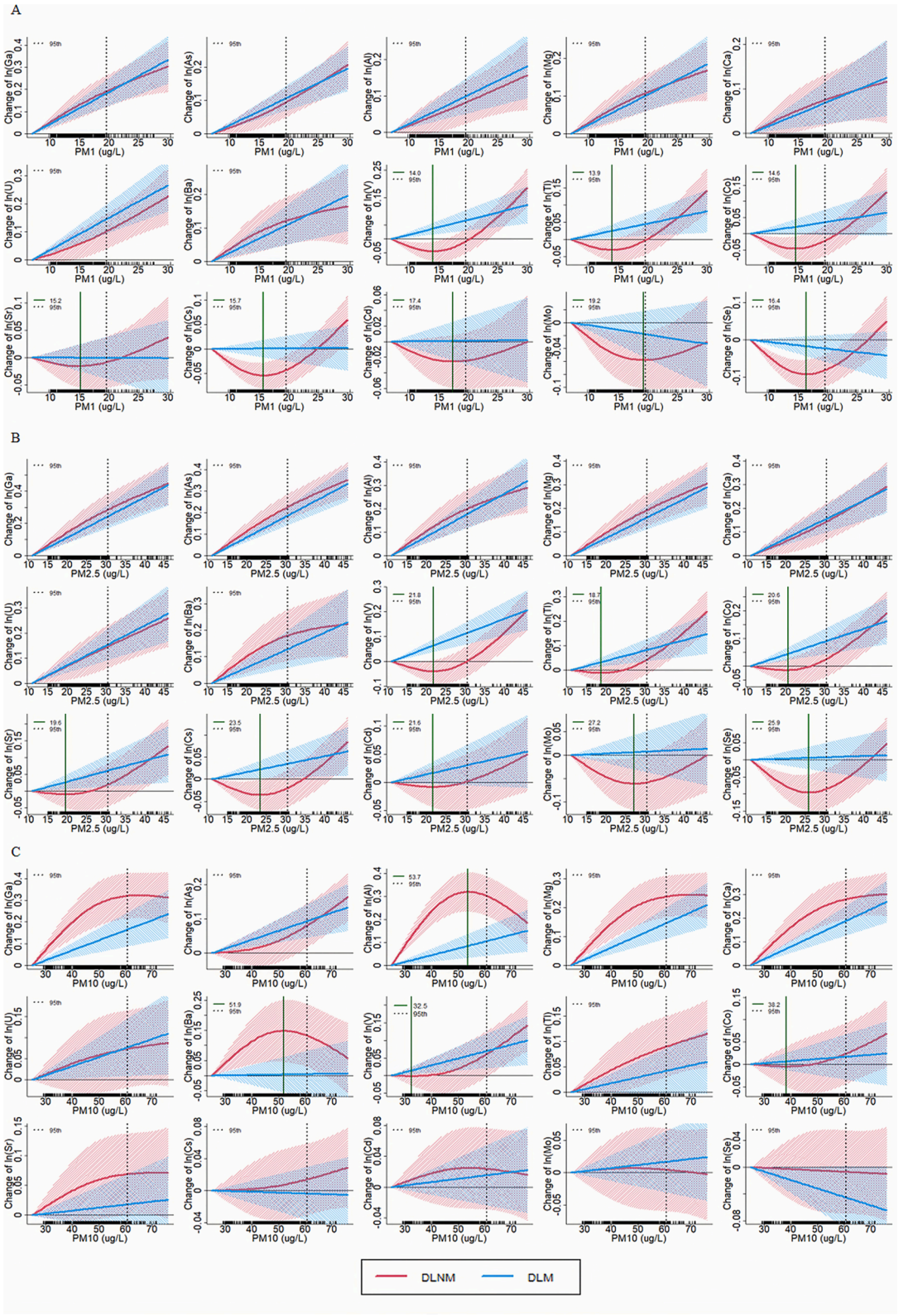

Fig. 5. The exposure–response curves of PM_1, $PM_{2.5}$, and PM_{10} with urinary metal(loid) concentrations over the cumulative lag days (0 to 1 days). (A) PM_1 effects; (B) $PM_{2.5}$ effects; (C) PM_{10} effects. Ga, Gallium; As, Arsenic; Al, Aluminium; Mg, Magnesium; Ca, Calcium; U, Uranium; Ba, Barium; V, Vanadium; Tl, Thallium; Co, Cobalt; Sr, Strontium; Cs, Cesium; Cd, Cadmium; Mo, Molybdenum; Se, Selenium; PM_1: particle matter with an aero-dynamic diameter $\leq$ 1 μm; $PM_{2.5}$: particle matter with an aero-dynamic diameter $\leq$ 2.5 μm; PM_{10}: particle matter with an aero-dynamic diameter $\leq$ 10 μm; the blue and red lines with shadings in the corresponding colors represent the cumulative (lag0-1) estimates of exposure–response curves and their 95 % confidence intervals (CI) from DLMs and DLNMs, respectively; the black dashed lines represent the 95th percentile of PMs concentrations; the green solid lines represent PMs concentrations where the inflection point of the exposure–response curves occur. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

erosion, oceans, and forest fires) and/or anthropogenic (e.g., traffic, industrial, and agricultural activities) sources. The participants in this study were mainly from rural areas, where metal(loid) compositions in PMs may be predominantly determined by natural and/or agricultural activities (Pan et al., 2013; Song et al., 2017). Al, Mg, Ca and Ba are among the most abundant crustal elements, ranking the 3rd, 4th, 5th and 14th in the Earth's crust, respectively (Hawkesworth and Kemp, 2006). Natural weathering processes and agricultural activities help to make them abundant in the dust (ATSDR 2019; Hawkesworth and Kemp, 2006). Previous studies have detected high concentrations of Al, Mg, Ca, and Ba in $PM_{2.5}$ and PM_{10} (Pan et al., 2013; Yang et al., 2022). Despite this, no study has assessed the associations of three PMs with Al, Mg, Ca, and Ba to date, and this study firstly provides the direct evidence on these associations internationally.

By the contrast, the crustal abundances of Ga, As, and U are relatively low (Hawkesworth and Kemp, 2006). However, they have been widely used in industry and agricultural products (ATSDR, 1999; 2007; Nordberg 2014b). For example, Ga is increasingly used in integrated circuits, LEDs, solar cells, and medication (Nordberg 2014a); As has been widely added into pesticides, herbicides, and insecticides (ATSDR 2007); and U can also be applied in fertilizer and medication (ATSDR, 1999). As a result, these metal(loid) elements are easily released into the environments, including air. Several studies have detected Ga, As, and U in PM samples (Ali et al., 2017; Li et al., 2018; Pan et al., 2013; Xiong et al., 2016; Zhang et al., 2022). In previous studies, serum As and urine U have been reported to be associated with exposure to PMs (Lan et al., 2021; Pang et al., 2016). Our findings further supported the links between short-term exposures to PMs and internal doses of As and U. To date, no epidemiological study explored the links between three PMs and Ga. This is the first report on the significant correlations between three PMs and urine Ga.

Our findings did not support the positive associations of short-term exposure to PMs with urine V, Tl, Co, Sr, Cs, Cd, Mo, and Se. In previous studies, internal does of Cd and Se have been reported to be associated with exposure to PMs. For example, a panel study showed that a 10 $\mu g/m^3$ increment in PM_{10} in the previous day was associated with a 2.8 % increase in blood Cd (Lee et al., 2021). Another study found that an IQR increment in $PM_{2.5}$ in the previous day was significantly associated with a 4.12 % increase in serum Se (Lan et al., 2021). Cd in the air possibly originates from the application of phosphate fertilizers, fossil fuel combustion, and waste incineration and disposal (ATSDR, 2012), while Se in the air is mainly from the combustion of fossil fuels (ATSDR, 2003). This study was conducted from July to September, during which aforementioned anthropogenic activities rarely occurred in rural areas, which may explain no significant association of short-term exposures to PMs with Cd and Se in our study.

So far, no epidemiological study explored the associations of exposures to PMs with internal does of V, Tl, Co, Sr, Cs, and Mo, although they have been detected in PM samples (Leclercq et al., 2017; Li et al., 2016; Pan et al., 2013). This study found no significant association of three PMs with V, Tl, Co, Sr, Cs, and Mo. Given no available data on the compositions and sources of PMs in this study, future studies are needed to examine metal(loid) compositions in PMs and their associations with internal doses of these metal(loid)s.

Moreover, most of the cumulative lag (lag0-1 days) effects of three PMs (per 10 $\mu g/m^3$ increment) on urine Ga, As, Al, Mg, Ca, U, and Ba were around 10 %. These findings were obtained after wide adjustment for confounding factors and were not altered in sensitivity analyses, which strongly support that exposure to PM is one of main sources for internal doses of metal(loid)s in human body.

4.3. The relative contributions of PM_1, $PM_{2.5}$, and PM_{10} to urine metal (loid)s

We found that PM_1 (per 10 $\mu g/m^3$ increment) exhibited the largest cumulative (lag0-1) effects on Ga, U, and Ba, while $PM_{2.5}$ showed the largest effects on As, Al, Mg, and Ca. However, a 10 $\mu g/m^3$ increment in PM_{10} is not comparable with that in PM_1 or $PM_{2.5}$, because PM_{10} includes all PM particles size 10 μm and under (PM_1 and $PM_{2.5}$). Therefore, we standardized the concentrations of PM_1, $PM_{2.5}$, and PM_{10} to compare their relative importance for urine metal(loid)s. After standardizations (per IQR increment) for three PMs, we observed that PM_1 was the largest contributor to U, $PM_{2.5}$ contributed the most to Ga, As, Al, and Ba, and PM_{10} contributed the greatest to Mg and Ca. These standardized results may better reflect distribution differences of aforementioned metal(loid)s in three PMs than unstandardized results. For instance, U, Ga, and Ba were mainly detected in fine (<2.1 μm) and coarse particles (2.1–9 μm) (Dordevic et al., 2014; Pan et al., 2013), while Al can be detected in both coarse particles (2.1–9 μm) and large particles (Pan et al., 2013; Yang et al., 2022). As had a bimodal distribution, with the first peak at fine mode (<2.1 μm) and the second minor peak at coarse mode (2.1–9 μm) (Zhi et al., 2021). Mg and Ca concentrations were higher in $PM_{2.5\text{-}10}$ than in $PM_{2.5\text{-}1}$ or $PM_{1\text{-}0.2}$ (Yang et al., 2022). In this study, although the data on the distributions of metal(loid)s in various sized fractions of PMs were not collected, our findings on dominating contributions of PM_1 to U, $PM_{2.5}$ to Ga, As, Al, and Ba, and PM_{10} to Mg and Cd were consistent with previous reports on their dominating distributions in PM_1, $PM_{2.5}$, and PM_{10} (Dordevic et al., 2014; Pan et al., 2013; Yang et al., 2022; Zhi et al., 2021).

4.4. The modification effects of residential greenness

We found that the lag0, lag1 and lag0-1 effects of exposures to PM_1, $PM_{2.5}$, and PM_{10} on Ga, As, Al, Mg, Ca, and Ba were significantly reduced when exposed to high $NDVI_{500m}$. Green spaces can affect PMs through deposition, dispersion, and modification (Diener and Mudu, 2021), thereby mitigating the effects of PMs on internal levels of metal(loid)s in human body.

4.5. Limitations and strengths

This study had several strengths. First, to our knowledge, this is the first research with a large sample size to examine the short-term effects of ambient PMs on internal metal(loid) profiles in older adults. Second, DLMs/DLNMs enabled us to flexibly examine single-day and cumulative lag effects of short-term exposures to PMs on urine metal(loid)s. Third, the results stratified by residential greenness further confirmed the effects of short-term exposures to PMs on internal metal(loid) profiles. Nevertheless, limitations should be noted. First, PM concentrations were obtained from a data fusion model instead of personal exposure measurement. PM concentrations used in this study may not be accurate estimates for individual exposure levels. Second, this study was conducted from July to September, during which there are relatively lower concentrations of PM_1, $PM_{2.5}$, and PM_{10}, as well as the lowest ratios of PM_1/ $PM_{2.5}$ and $PM_{2.5}$/ PM_{10} within a year, which may underestimate the effects of exposures to three PMs on urine metal(loid)s. Whether the generalizability of our findings to other seasons needs further investigations. Third, despite the inclusions of important covariates in our models, residual confounding by unmeasured variables cannot be ruled out. For example, indoor PMs were not measured and controlled in this study. Fourth, our study only used spot urine sample instead of urine samples taken over several consecutive days, which may bias our assessments of urinary metal(loid) concentrations. We tried to reduce this error by using the first-morning urine sample and adjusting urinary metal(loid) concentrations by creatinine content.

5. Conclusions

In summary, short-term exposures to ambient PMs are associated with elevated internal-exposure levels of Ga, As, Al, Mg, Ca, U, and Ba in older adults, in which PM_1 exerts the greatest contribution to U, $PM_{2.5}$ contributes the most to Ga, As, Al, and Ba, and PM_{10} contributes the

greatest to Mg and Ca. Moreover, the effects of ambient PMs on internal metal(loid)s may be reduced by residential greenness. Our study provides direct evidence that exposure to PM is one of main routes for internal metal(loid)s, and indicates that the increase of residential greenness can mitigate the effects of PMs on internal metal(loid)s in human body. Further studies are needed to examine metal(loid) compositions in PMs and their associations with internal metal/metalloid profiles.

CRediT authorship contribution statement

Yuan Wang: Writing – original draft, Formal analysis, Validation. **Qiang Liu:** Writing – original draft, Formal analysis, Validation. **Ziwei Tian:** Writing – original draft, Formal analysis, Validation. **Beijing Cheng:** Investigation, Data curation, Validation. **Xianwei Guo:** Investigation, Data curation, Validation. **Hongli Wang:** Investigation, Data curation, Validation. **Bo Zhang:** Investigation, Data curation. **Yan Xu:** Investigation, Data curation. **Liang Sun:** Investigation, Validation. **Bing Hu:** Investigation, Validation. **Guimei Chen:** Methodology, Investigation, Validation. **Jie Sheng:** Methodology, Investigation, Validation. **Chunmei Liang:** Methodology, Investigation, Validation. **Fangbiao Tao:** Methodology, Investigation, Validation. **Jing Wei:** Investigation, Data curation, Methodology, Writing – review & editing, Validation. **Linsheng Yang:** Investigation, Data curation, Methodology, Writing – review & editing, Validation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The authors do not have permission to share data.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2023.108341.

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