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Urinary lead in relation to combustion-derived air pollution in urban environments. A longitudinal study of an international panel

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ABSTRACT

Background: Urinary lead (Pb) is generally considered to have limited use in biomonitoring environmental exposure to lead. Carbon load in airway macrophages (AM BC) is an internal marker to assess long-term exposure to combustion-derived aerosol particles. In urban environments, atmospheric Pb and black carbon may have common sources. We aimed to study the temporal change of urinary Pb (U-Pb) when exposure to outdoor air pollution changes, and the relationship between U-Pb and AM BC.

Methods: A panel of 50 young healthy adults [mean (SD) 26.7 (5.2) years], including 17 long-term (> 1 year) residents in Leuven, Belgium (BE), 15 and 18 newcomers (arrived < 3 weeks) from low- and middle-income countries (LMIC) and high-income countries (HIC), respectively, underwent 8 repeated measurements at 6 weeks intervals. In urine spot samples obtained at 5 time points (T1, T2, T4, T6, T8), 24 trace elements were quantified by inductively coupled plasma-mass spectrometry. At each time point, AM BC was quantified as the median surface of black inclusions (in μm^2) by means of image analysis of 25 macrophages obtained by induced sputum. Changes in urinary metal concentrations (with and without creatinine correction) and the relationship between U-Pb and AM BC were estimated using linear mixed models adjusted for covariates and potential confounders.

Results: Only U-Pb differed between groups and exhibited significant time trends. Participants from the LMIC group had significantly higher initial U-Pb (1.18 µg/g creat) than the HIC group (0.44 µg/g creat) and BE group (0.45 µg/g creat). In the LMIC group, U-Pb decreased significantly with time by 0.061 µg/g creatinine per 30 days [95% confidence interval (CI): 0.034, 0.088]. U-Pb remained unchanged in the other two groups. An increase in AM BC of 1 μm^2 was associated with an increase in U-Pb of 0.369 µg/g creat (95% CI: 0.145, 0.593).

Conclusion: This panel study demonstrates that U-Pb may be a valid alternative to blood Pb for biomonitoring changes in exposure to lead, at least at group level. In addition, we identified a positive association between U-Pb and AM BC, a biomarker of exposure to traffic-related air pollution, suggesting the existence of common sources of Pb and black carbon in urban environments.

1. Introduction

Inhalation of atmospheric dust particles is one of the major pathways of exposure to lead (Pb) in the general population (Järup, 2003; Maret, 2017; Skerfving and Bergdahl, 2015). The elimination of lead additives from gasoline and the banning of lead-based paints have led to progressive decreases in atmospheric lead levels around the world, thus resulting in decreased blood Pb levels (B-Pb) in both adults and children, first in industrially developed countries, and then in some developing countries (Skerfving and Bergdahl, 2015). Nevertheless, marked geographical variations in lead exposure still exist on a global scale. Besides a more recent implementation of the phase-out of leaded gasoline in developing countries, such variation can be attributed to multiple other anthropogenic activities, such as metal mining and smelting, waste incineration, battery recycling, wood and coal burning, that may still represent substantial sources of lead pollution in the developing world (Nriagu and Pacyna, 1988; Skerfving and Bergdahl, 2015; UNEP, 2010).

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In urban environments, lead is mainly present in fine particles (Dean et al., 2017; Lyu et al., 2017), thus allowing deposition of lead in the lower respiratory tract (Avino et al., 2016; Geiser and Kreyling, 2010; Möller et al., 2008; Salma et al., 2015), followed by its absorption and distribution through the circulation (Klotz and Göen, 2017). Combustion-derived fine and ultrafine particles are also deposited in the lower respiratory tract where they are phagocytosed by macrophages (Geiser, 2002; Geiser and Kreyling, 2010). This results in the presence of inclusions containing carbonaceous aggregates in the cytoplasm of macrophages (Alexis et al., 2006; Geiser, 2010). These inclusions of black carbon (BC) in airway macrophages (AM) are visible under light microscopy and their amount can be quantified as a surface, thus providing a biomarker of a person's internal exposure to combustion-derived particulate matter (PM) (Bai et al., 2015). AM BC has been used in several studies to estimate personal exposure to traffic-related PM (Belli et al., 2016; Jacobs et al., 2010).

To date, only few studies have assessed how Pb levels evolve in people who moved recently from an area of high air pollution to an area of lower air pollution. We took advantage of a one-year panel study involving participants who had recently arrived in Leuven from various countries (Bai et al., 2018). In that study we had also collected urine, which enabled us to verify if urinary concentrations of metals would also be indicative of past exposure to urban pollution. The present article shows that urinary levels of Pb (U-Pb) reflect past exposure to urban pollution, and that these decline progressively upon moving to an area with lower air pollution.

2. Materials and methods

2.1. Study design and study population

The study was conducted in Leuven, Belgium, between 2013 and 2016. The study area included the city centre of Leuven and its nearby surrounding areas (Fig. 1). As previously described (Bai et al., 2018), we advertised our study on university bulletin boards, social media, and word of mouth to enroll potential participants from 2013 to 2015. The participants had to fulfill the following inclusion criteria: 1) never-smoker or ex-smoker (quit > 1 year), 2) having resided in Belgium for more than one year or having newly arrived in Belgium (< 3 weeks), 3) having lived in the same place in the previous 3 months, and 4) going to be living in Belgium for the following 10 months. The participants were excluded if they had 1) unclear or variable exposure before the relocation to Belgium, and 2) any severe respiratory disease, a history of cardiovascular disease, diabetes, or other conditions that could interfere with the health measurements (Bai et al., 2018). Seventy three nonsmoking young adults (students or researchers) met the inclusion criteria and 61 attended the first health measurement (T1). Over nearly one year follow-up, 8 repeated measurements at intervals of approximately 6 weeks were carried out at the University Hospital Leuven, Belgium (Fig. 1). Fifty participants completed at least the first four measurements (T1–T4) and were included in the present study. Among these 50 participants, 44 had data for all of the 5 chosen time points (T1, T2, T4, T6, and T8), 3 participants had data for 4 time points (T1, T2, T4, and T6), and 3 participants had data for 3 time points (T1, T2, and T4). The demographic variables did not show differences between included (n = 50) and non-included (n = 23) subjects (data not shown). The participants were either long-term residents in Leuven, Belgium (BE group), or people who had recently arrived in Leuven from various countries. The latter subjects were grouped into participants having come from low- and middle-income countries, i.e. mainly China and India (LMIC group), or from high-income countries, mainly Europe (HIC group) [details provided in Bai et al., 2018]. Their background exposure to urban air pollution before inclusion was estimated by the annual average PM_{10} reported for their city of origin in the World Health Organization's database (WHO, 2016). At each time point (T1 to T8), participants replied to a standard questionnaire, and they gave a sputum sample (obtained by sputum induction), a venous blood sample, and a spot sample of urine. The study protocol was approved by the Ethical Committee of KU Leuven (S55729). All participants were given detailed oral and written information on the study and gave their written informed consent.

2.2. Carbon load in airway macrophages

Cytospin slides of sputum plugs were prepared according to standard guidelines (Miller et al., 2005; Seys et al., 2013). AMs were

Fig. 1. Map of Belgium (left panel) indicating the location of Leuven, where participants resided during the study period. Right panel shows the location of the participants' residences (blue pins) and the location of the University Hospital (red pin), where measurements were performed; orange straps represent major roads. Most participants lived within the circular road around the city centre. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 1
Baseline characteristics of included participants (N = 50).[a]

Characteristic	All	LMIC	HIC	BE
N	50	15	18	17
Age, yr	26.7 (5.2)	25.7 (3.3)	25.7 (4.7)	28.9 (6.5)
Sex, female †	23 (46.0)	9 (60.0)	6 (33.3)	8 (47.1)
BMI, kg/m^2	22.6 (3.9)	21.2 (3.5)	22.8 (2.7)	23.7 (5.0)
Never/ex-smoker †	46/4 (92/8)	15/0 (100/0)	15/3 (83/17)	16/1 (94/6)
Estimated annual average PM_{10} before inclusion, μg/m^3		97.7 (32.4)**	25.2 (8.1)	22.9 (0.2)
Latency between arrival and inclusion ‡		9 days (1–19)**	10 days (2 – 23)**	1.9 years (1–5.4)[b]

LMIC: participants having recently arrived from low- and middle-income countries, HIC: participants having recently arrived from high-income countries, BE: participants having resided in Belgium for at least one year. Comparison among groups by one-way ANOVA or χ^2 test.

[a] This table is similar to a previously published table (Bai et al., 2018), except for a slightly different number of participants due to different inclusion criteria. Data are described as mean (SD) except for † n (%) and ‡ median (range).

[b] Only for 9 foreign-born residents.

** $p < 0.001$ compared to BE.

visualized under a light microscope at ×100 magnification, and the median area (μm^2) of black inclusions was calculated by ImageJ (National Institutes of Health, USA) of 25 randomly captured AMs, as previously described (Bai et al., 2018; Jary et al., 2015).

2.3. Urinary trace elements

A spot urine sample was collected in a sterile polystyrene container (100 mL) at every health measurement and kept frozen at −20 °C. Urine samples collected at 5 of the 8 time points (T1, T2, T4, T6, and T8) were analyzed (in December 2016) for 24 trace metals/metalloids by means of inductively coupled plasma - mass spectrometry (ICP-MS), according to previously published methods (Hoet et al., 2013) and without knowledge of their exact provenance (blinded analysis), at the Louvain Centre for Toxicology and Applied Pharmacology (LTAP, Université catholique de Louvain, Belgium). The LTAP laboratory is ISO15189-certified for ICP-MS analyses of metals in both urine and blood, and it is a reference laboratory for the German External Quality Assessment Scheme (G_EQUAS) (Göen et al., 2012). Briefly, urine specimens (500 μL) were diluted quantitatively (1 + 9) with acid solution (HNO_3 1% and HCl 0.5%) containing Sc, Ge, Rh and Ir as internal standards, and then analyzed using an Agilent 7500ce instrument, in the no-gas mode for Al, Ba, Be, Bi, Cd, In, Li, Mo, Pb, Pt, Sn, Sb, Te, Tl and U, and in the helium mode for As, Co, Cr, Cu, Mn, Ni, V, Zn and Se. Limits of detection (LOD) were determined as three times the standard deviations of concurrently analyzed blanks. No values of U-Pb were below LOD (0.025 μg/L). Creatinine was determined by a modified Jaffé reaction using a C502 module on a Cobas 8000 analyser (Roche diagnostics, Rotkreuz, Switzerland). In accordance with recommendations (Poulson et al., 1997), highly concentrated (creatinine > 3.0 g/L) and highly diluted (creatinine < 0.3 g/L) urine samples were excluded.

2.4. Statistical analysis

For statistical analysis, we used data from participants with completed health measurements on at least the first four time points (T1 to T4), some subjects having dropped out after T4 (see above). Statistical analysis was performed with SAS software, version 9.4 (SAS Institute Inc., Cary, NC, USA).

We calculated the mean and standard deviation or median and interquartile range (IQR), as appropriate. The baseline characteristics of the different groups were compared using Pearson's chi-square tests for categorical variables and with analysis of variance (ANOVA) for continuous variables. When over 50% of the samples were below the LOD, only the percentile distribution was supplied. The urinary concentrations of metals were expressed in μg/L and, to make allowance for urinary dilution, also in μg/g of creatinine (μg/g creat).

Linear mixed models (LMM) with random intercept and slope in time for each subject, to account for the repeated measures design of the study, were used to analyze the temporal change between the dates of signing up and sampling urinary metals throughout the study period. Both linear and non-linear (quadratic) evolutions were considered. Adjustments were made for the geographical origin of participants (three groups), as well as for previously determined possible confounders [age, sex (reference: female), sampling season (reference: December–February), sampling time (reference: am vs pm), and creatinine (only for concentrations of urinary metals expressed as μg/L) (Hoet et al., 2013)]; interactions between time and these variables were not considered. Moreover, we conducted stratified analyses by geographical origin (three groups). We additionally studied the association between AM BC and U-Pb concentrations. LMM were used for this analysis with U-Pb concentrations as response variable and AM BC as predictor variable. A random intercept and slope in time were modelled to deal with the longitudinal nature of the data. Correction was performed for group and time, and, in a separate model, additionally for age, sex, sampling time (am vs pm) and season. The results of temporal changes of U-Pb and the association between U-Pb and AM BC are presented for creatinine-corrected U-Pb. The crude values of U-Pb were also used for these analyses and served as a sensitivity analysis. All tests are two-sided, and a 5% significance level is assumed for all tests.

3. Results

3.1. Participant characteristics and baseline data

Participant characteristics are presented in Table 1, according to their geographic origin before the study. There were no significant differences in baseline characteristics among groups (Table 1) except, by design, for estimated prior background exposure to PM. Thus, participants in the LMIC group had a significantly higher previous exposure to PM_{10} (estimated annual average close to 100 μg/m^3) than participants in the other groups (estimated annual average around 25 μg/m^3). Participants of the LMIC and HIC groups underwent their first measurement within a median of 9 days and 10 days after arrival, respectively.

3.2. Urinary creatinine and trace elements

Based on urinary creatinine concentrations, we excluded 29 too diluted samples (creatinine < 0.3 g/L) and 9 too concentrated samples (creatinine > 3 g/L), thus leaving 194 urine samples for analyses. Creatinine concentrations did not differ between groups or between study time points (Supplementary Table S1).

Supplementary Table S2 contains the detailed results for all the trace elements in urine, except for five elements (Be, In, Pt, Bi and U) for which > 85% of the values were below LOD, thus leaving 19

elements for analyses. For all elements, except Pb (see further), the linear slopes with time did not differ significantly from zero, whether or not interactions of time with geographical origin were considered (Table S2). No significant trends emerged when non-linear evolutions were tested, except for urinary Mn and Cd (without creatinine correction), thus explaining why the changes between 0 and 6 months and between 6 and 12 months are presented for these variables (Table S3).

Fig. 1 depicts the individual and average levels of U-Pb at different time points for the three groups separately. In Group HIC and BE, U-Pb values fluctuated from one time point to another in individual subjects [average (range) intra-individual coefficient of variation: Group BE, 59% (34–90%) for crude values and 40% (5–111%) for creatinine-corrected values; Group HIC, 43% (10–75%) for crude values and 25% (12–39%) for creatinine-corrected values]. However, in both groups the average concentrations of U-Pb remained stable around 0.5 μg/g creat with minor fluctuations (Fig. 1). In contrast, Group LMIC had higher U-Pb levels than the other two groups at T1 (1.18 μg/g creat) and underwent a sustained decrease in U-Pb throughout the study period to a similar level as the two other groups at T8 (Fig. 1).

The quantitative changes over time in U-Pb are shown in more detail in Table 2. Overall, U-Pb decreased significantly by 0.017 μg/g creat per month (30 days) for the whole group; these decreases were somewhat attenuated after adjustments for age, sex, sampling time and sampling season (Table 2). The interaction between group and time was highly significant and stratification by group demonstrated that U-Pb decreased over time only in Group LMIC (by 0.061 μg/g creat per month), whereas no significant change occurred over time in Group HIC and Group BE. Using the crude values (μg/L) to study the temporal change of U-Pb did not modify the effect. Testing quadratic time trends did not provide better fits to the data than the linear models.

3.3. Relationship between urinary lead and carbon load in airway macrophages

With adjustment for geographical origin and follow-up time, each 1 μm^2 increment in AM BC was associated with an increase in U-Pb of 0.289 μg/g creat (95% CI: 0.075, 0.503; p = 0.009). This association was strengthened [0.369 (95% CI: 0.145, 0.593), p = 0.002] after additional adjustment for other covariates, including age, sex, sampling season, and sampling time.

4. Discussion

In this one-year panel study of young healthy nonsmokers, we found that urinary lead concentrations declined progressively in those who moved from an area with high PM_{10} pollution to Leuven, an area of moderate urban pollution. In participants whose background exposure to PM_{10} remained stable, urinary lead concentrations remained unchanged. The main novelty of the present study is the significantly positive association found between urinary lead and black carbon in airway macrophages, a novel biomarker of chronic exposure to combustion-related air pollution (Bai et al., 2015, 2018).

A possible criticism of our study is that we measured lead concentrations in urine and not in blood. Blood-lead (B-Pb) is indeed regarded as the most appropriate parameter for biomonitoring lead exposure in clinical practice, in occupational surveillance and in population studies (Barbosa Jr et al., 2006; Sakai, 2000; Skerfving and Bergdahl, 2015). Although our research protocol also involved repeated venous blood sampling, the blood samples were processed for other laboratory analyses in serum or leukocytes (unpublished) and, therefore, whole blood was no longer available for measuring trace metals. However, measuring urinary lead (U-Pb) can also be used for assessing exposure since lead is mainly excreted in the urine (Bergdahl and Skerfving, 2008). The utility of U-Pb for lead exposure biomonitoring is supported by the association between B-Pb and U-Pb, although this relation is not perfect and has high variance and uncertainty (Barbosa et al., 2005; Skerfving and Bergdahl, 2015). Nevertheless, even though, in theory, urinary lead may have been less suitable than blood lead for our purpose, the present observations do indicate that measuring lead in urine was capable not only of differentiating groups of subjects with presumably different past exposures to lead, but also to demonstrate time-related changes in the body burden of lead.

Another relative weakness of our study is that we do not have data on the exact sources of exposure to lead in our participants. This could have been partly addressed by measuring the isotopic composition of lead (Gulson et al., 2006), but this was beyond the scope of our study. Conceivably, the progressive decline in lead observed in the participants from the LMIC, could be due to decreases in lead intake via food or drink, but we do not think this to be likely. Indeed, although lead exposure may result from contamination of the water supply [e.g. the Flint episode (Hanna-Attisha et al., 2016)], from occupational exposures (Koh et al., 2014), from the use of traditional cosmetics or remedies (Parnia et al., 2018), or from pollution by nearby mining or smelting operations (Zheng et al., 2013), none of these circumstances were likely to apply to our participants. Moreover, it is accepted that ambient air and dust nowadays substantially contribute to environmental exposure to lead in the general population, especially in urban areas (IARC, 2006; Järup, 2003; UNEP, 2010). The association found here between urinary lead and black carbon in airway macrophages appears to corroborate this.

4.1. Changes in urinary lead over time

In the group of participants having lived in Leuven for more than one year before enrollment (Group BE), average concentrations of U-Pb remained stable (Fig. 2). The values found in the present study are lower than those measured, by the same laboratory, in 1022 Belgian adults without occupational exposure to metals recruited in 2010–2011 (Hoet et al., 2013) (Table 3). The authors of the latter publication noted that Belgium completed the phase-out of leaded gasoline later than the USA and Canada, thus explaining the higher Pb levels in that Belgian population than in American and Canadian populations during the

Table 2
Changes (Δ) in urinary lead concentration (U-Pb) over time.

	Δ U-Pb (95% CI) for 1 month (μg/g creat)	p-Value	p-Value for interaction between group and follow-up time
All subjects[a]	−0.017 (−0.034, −0.001)	0.044	
All subjects[b]	−0.013 (−0.030, 0.004)	0.125	0.0002
LMIC group[c]	−0.061 (−0.088, −0.034)	< 0.0001	
HIC group[c]	0.015 (−0.011, 0.040)	0.265	
BE group[c]	−0.004 (−0.027, 0.020)	0.763	

LMIC, low and middle-income countries; HIC, high-income countries; BE, Belgium. One month is 30 days.
Data were analyzed by linear mixed models. Interaction between geographical origin (group) and follow-up time [group × time (month)].
[a] Adjusted for group.
[b] Adjusted for group and for age, sex, sampling time (am vs pm), sampling season.
[c] Adjusted for age, sex, sampling season, sampling time (am vs pm).

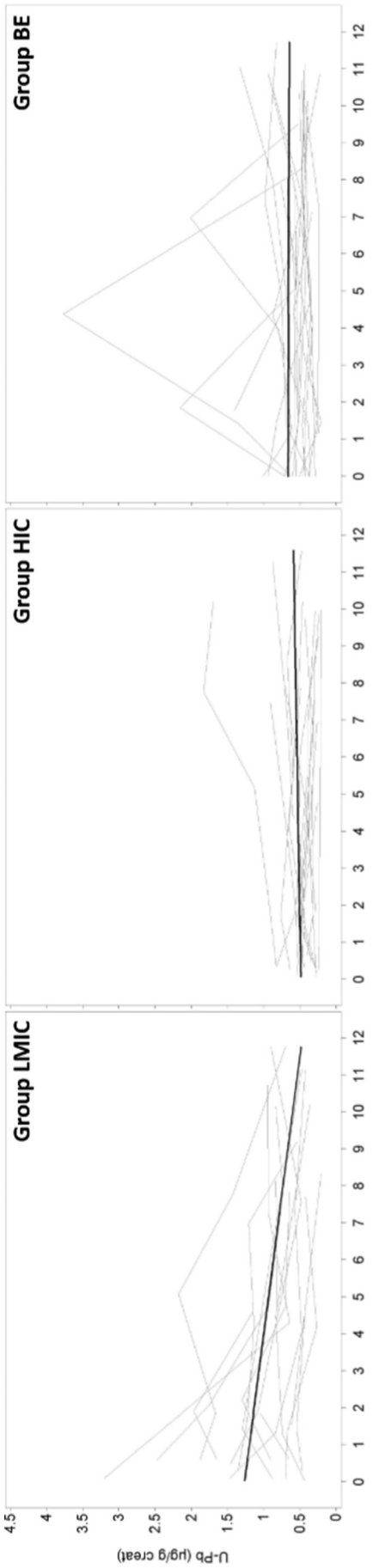

Fig. 2. Urinary lead concentrations expressed as µg/g creatinine during almost 1-year follow-up in healthy volunteers having arrived in Belgium from low- and middle-income countries (LMIC, n = 15) or high-income countries (HIC, n = 18) and long-term residents in Leuven (BE, n = 17). Grey lines represent the observed change for individual subjects. Black bold lines represent average change for group estimated by linear statistical model.

same monitoring period. However, in the past years the environmental lead levels in airborne dust and surface water have decreased further (Flemish Environment Agency, 2013) and this has been paralleled with decreasing blood Pb levels in newborns and adolescents from the Flemish community of Belgium (Schoeters et al., 2017). This probably explains why our current findings in Belgian residents are close to the American and Canadian reference values obtained approximately 5 years earlier.

In the participants who had moved from high-income countries (mostly within western Europe), the values of U-Pb at inclusion and over the further course of the study were similar to those of the BE group, which is compatible with the absence of substantial differences in current blood lead levels among high-income countries (Nisse et al., 2017). In contrast, the participants from low- and middle-income countries had markedly higher initial U-Pb levels than the other participants (Fig. 2), indicating that they had experienced higher exposure to environmental lead before moving to Belgium. This is not surprising in view of the existing global variations in lead exposure, much of which has been attributed to differences in phasing out leaded gasoline (Skerfving and Bergdahl, 2015). Since ten out of the fifteen subjects of the LMIC group came from China, we compared our results with those of a multi-regional study in China (Ding et al., 2014). U-Pb levels in our participants having recently arrived from China were similar to those in the same age group in the Chinese study (Table 3). However, by the end of the observation period of almost one year, U-Pb of the LMIC group was only slightly higher than that of the HIC and BE groups. The decline from T1 (1.37 µg/L) to T8 (0.55 µg/L) appeared linear with a relatively slow rate (−0.067 µg/L per month), compared to what would be expected based on half-lives of 1 to 2 months reported for blood and soft tissue lead (Centers for Disease Control and Prevention, 2016; Furtado Rahde, 1994; National Research Council, 1993). To our knowledge, few studies have investigated the time course of early changes in Pb levels upon moving from an area of high air pollution to an area of lower air pollution. For instance, Gulson et al. (1996) reported a 20–69% decrease in B-Pb in six persons from two families 8 months after relocating from a high lead exposure area (Broken Hill mining community) to less lead-polluted rural areas in Australia. The same group measured B-Pb monthly in eleven female immigrants from Eastern Europe up to 300 days after their arrival in Australia, and derived half-lives for B-Pb of 25 to 175 days (in the six most exposed women) (Gulson et al., 1995). However, tissue lead stores continued to contribute to blood Pb well beyond 300 days. More recently, B-Pb levels in South and East Asian women having lived in Canada for 1 to 5 years were shown to decrease slightly with length of residence in Canada (Dix-Cooper and Kosatsky, 2018; Parnia et al., 2018). These findings show that B-Pb levels change in response to alterations in lead exposure brought about by changes in geographical locations. Our findings using urinary lead corroborate these observations.

4.2. Association between urinary lead and carbon in airway macrophages

Although other studies have described declining Pb levels after moving from one country to another (Gulson et al., 1995; Dix-Cooper and Kosatsky, 2018; Parnia et al., 2018), our study, for the first time, demonstrates a positive association between U-Pb, a biomarker of lead exposure, and AM BC, a novel biomarker of inhaled combustion-related particles. Finding such association was only possible thanks to the unique study design that provided sufficient spatial and temporal variation in both U-Pb and AM BC. The simplest explanation for the association observed between both biomarkers is that they reflect past exposure to a common source of pollution, most likely ambient particulates. Admittedly, U-Pb reflects the renal excretion of Pb absorbed by inhalation and ingestion, but even after the phase-out of leaded gasoline, road traffic is still a major source for lead exposure in urban environments, mainly because of the resuspension of previously contaminated dust (Gemeiner et al., 2017; Novák et al., 2003). Moreover,

Table 3
Comparison of U-Pb in the present study with data from other national surveys.

	Present study						Belgium (Hoet et al., 2013)[a]	France (Nisse et al., 2017)[b]	Canada (Health Canada, 2013)[c]	USA (Centers for Disease Control and Prevention (CDC), 2017)[d]	China (Ding et al., 2014)[e]
	LMIC		HIC		BE						
	T1	T8	T1	T8	T1	T8					
GM (95% CI), μg/L	1.37 (0.98, 1.75)	0.55 (0.26, 0.83)	0.46 (0.35, 0.62)	0.46 (0.33, 0.58)	0.50 (0.33, 0.74)	0.41 (0.21, 0.60)	0.74 (0.69, 0.78)	0.82 (0.75, 0.90)	0.45 (0.41, 0.49)	0.38 (0.35, 0.42)	0.95 (0.89, 1.02)
GM (95% CI), μg/g creat	1.18 (0.76, 1.59)	0.62 (0.48, 0.75)	0.44 (0.35, 0.55)	0.45 (0.23, 0.67)	0.53 (0.43, 0.66)	0.54 (0.37, 0.71)	0.73 (0.70, 0.77)	0.61 (0.56, 0.66)	0.37 (0.34, 0.40)	0.43 (0.40, 0.47)	N/A

LMIC: low and middle-income countries; HIC: high-income countries; BE: Belgium. GM: geometric mean.
[a] Population aged 40 years on average, data obtained from 2010 to 2011.
[b] Population aged 20 to 29 years, data obtained from 2008 to 2010.
[c] Population aged 20 to 39 years, data obtained from 2009 to 2011.
[d] Population aged above 20 years, data obtained from 2011 to 2012.
[e] Population aged between 21 and 30 years, data obtained from 2009 to 2010.

combustion of other fuels, particularly coal, contributes a considerable portion of atmospheric lead emissions in both developed and developing countries (Junninen et al., 2009; Novák et al., 2003; Pan et al., 2015; Pinto et al., 2015; Querol et al., 2006; Zhou et al., 2013). Although in urban areas airborne Pb shares the same sources as EC in aerosol particles, we found no published evidence for a relationship between Pb and EC in aerosol particles in modern day urban air pollution studies. We attempted to quantify lead (and other elements) in sputum samples at T1, but the levels were mostly below detection, even in the sputum samples from Group LMIC (not shown in the results). Other analytical techniques will be necessary to determine the extent to which Pb and BC are co-localized in airway macrophages.

The good correlation between U-Pb and AM BC, with a qualitatively similar kinetic behavior in Group LMIC, is indicative of a common exposure source. Nevertheless, further studies are necessary to investigate the clearance of the various storage compartments of AM BC (lung macrophages or lung interstitium) and Pb (soft tissue, bone, and kidney).

4.3. Other trace elements

None of the trace elements measured in urine showed the variation by geographical origin or the temporal changes observed with Pb, although the LMIC group tended to have slightly higher urinary concentrations of several elements (notably Cd) than the two other groups. Admittedly, the number of participants in our study was not high (fewer than 20 in each group), which may have prevented us from detecting subtle differences between groups. On the other hand, the high number of repeated measurements in each subject represents a strength in terms of consistency. Consequently, we speculate that the absence, in our study, of significant spatial differences or temporal trends in the urinary concentrations of trace elements other than Pb, indicates that sources of exposure other than air pollution, such as food or drinking water, predominantly influence urine levels of these trace elements. This is notably the case for arsenic (Hoet et al., 2013) and cadmium (Sughis et al., 2014).

5. Conclusion

By making repeated measurements over approximately one year, we successfully demonstrated changes in urinary lead in young healthy adults with differing prior exposure to air pollution. The participants coming from low- and middle-income countries exhibited significantly higher initial U-Pb than those from high-income countries, and they progressively reached a similar level as the host country. Our findings demonstrate that U-Pb may be a valid alternative to B-Pb for biomonitoring changes in exposure to lead, at least at group level. In addition, we identified a positive association between U-Pb and AM BC, a biomarker of exposure to traffic-related air pollution, suggesting the existence of common sources of Pb and BC in urban environments.

Finally, as we demonstrated that decreased exposure to urban air pollution was accompanied by a progressive reduction in internal lead among our participants from LMIC, this suggests that reducing urban air pollution might result in lowering lead exposure in the population. In view of the well-established adverse health effects of even low levels of lead, this would constitute a substantial co-benefit of fighting urban air pollution in emerging economies.

Conflict of interest

The authors declare no conflict of interest.

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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.2019.01.044.

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