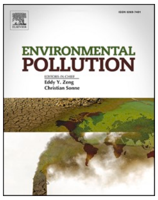
Environmental Pollution 312 (2022) 120028

Contents lists available at ScienceDirect

Environmental Pollution

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



Human biomonitoring survey (Pb, Cd, As, Cu, Zn, Mo) for urban gardeners exposed to metal contaminated soils[☆]

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ARTICLE INFO

Keywords:
Soil contamination
Urban food production
Health risk assessment
Metal exposure
Urinary arsenic speciation
Urinary and blood exposure biomarkers

ABSTRACT

Eighty eight adult gardeners and their relatives volunteered to provide urine and blood samples for a human biomonitoring survey among users of one of the biggest allotment garden from Wallonia, showing high trace metal(oid) concentrations in soils. The purpose was to determine if environmental levels of lead (Pb), cadmium (Cd) and arsenic (As) led to concentrations of potential health concern in the study population. Blood and urine biomarkers were compared to reference and intervention cut-off values selected from the literature. The study population exhibited (i) moderately high blood lead levels with median value of 23.1 μg/L, (ii) high urinary concentrations of speciated As (inorganic arsenic and its metabolites) with a median value of 7.17 μg/g.cr., i.e. twice the median values usually observed in general populations, and (iii) very high Cd levels in urine with a median value of 1.23 μg/L, in the range of 95th-97.5th percentiles measured in general adult populations. Biomarker levels in the study population were also mostly above those measured in adults from local populations living on contaminated soils, as reported in the current literature. All biomarkers of Pb, Cd and As showed weak to strong statistically significant correlations, pointing towards a joint environmental source to these three contaminants as being at least partially responsible for the high exposure levels observed. Urine and blood biomarkers show statistically significant associations with variables related to individual characteristics (age, smoking status, …) and Pb domestic sources (Pb pipes, cosmetics, …) but involves also behavioral and consuming habits related to gardening activities on the contaminated allotment garden. At such levels, owing to co-exposure and additive effects of Cd, As and Pb regarding renal toxicity known from literature, the study strongly suggests that this population of gardeners is at risk with respect to chronic kidney diseases.

1. Introduction

Urban food production and gardening are increasingly promoted for their positive outcomes on the urban environment, on human health and on household purchasing power. However, urban soils may not always meet quality standards for health and food production, since edible parts of plants may accumulate toxic metals and potentially cause adverse toxicological effects (e.g. Beccaloni et al., 2013). In pan-European countries, Pb and Zn smelting activities have been going on for many years near or within urban areas, leading to long lasting contaminations of soils with toxic trace metal(oid)s such as Cd, Pb and As. Even after several decades of decline and regulations, chronic exposure to these contaminants is still probably widespread in urban areas with past metallurgical industries.

In this context, urban gardeners are considered as a sub-population at higher risk, being more intensively exposed via unintentional ingestion of soil/dust particles and consumption of (contaminated) vegetables grown on these soils. In this respect, higher Pb, Cd and As biomarker concentrations in populations exposed to local soil contaminations have been evidenced several times and were sometimes positively correlated

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[☆] This paper has been recommended for acceptance by Prof. Wen-Xiong Wang.

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https://doi.org/10.1016/j.envpol.2022.120028
Received 12 March 2022; Received in revised form 16 August 2022; Accepted 19 August 2022

to the presence/frequentation of vegetable gardens or the consumption of homegrown food (e.g., Durand et al., 2008; Fillol et al., 2010). However, very few studies have strictly focused on a population of gardeners (Bramwell et al., 2021) and none has reported an extended set of biomarker values.

High chronic exposure conditions were suspected for gardeners from one of the biggest (about 6 ha) allotment garden in Wallonia (CTB, “Coin de Terre de Bressoux”, in the Bressoux area of Liege city). The CTB is made of 200 allotments rented for several decades (probably back to 1940’s) by a population with rather low income, pursuing social and economic benefits. After first tiered investigations, an extensive sampling campaign of soils (Table 1; supplementary material) and vegetables (Table 2; supplementary material) was carried out in summer 2017. All soil samples from CTB were above legal residential soils standards from the Walloon soil decree (Région Wallonne, 2018) for Pb and Cd (mean of 500 mg/kg and 4.7 mg/kg, up to 1000 mg/kg and 6.2 mg/kg for Pb and Cd, respectively). In comparison, As soil contaminations were moderate (mean concentrations of 32 mg/kg, up to 50 mg/kg, with only 13% of samples above the residential soil standard). Trace metal concentrations in CTB soils were also in the range of 90th percentile concentrations of overall Walloon soils as determined in Pereira et al. (2015).

Vegetables and fruits grown at CTB showed systematically higher Cd and Pb concentrations than commercial ones (as evaluated by the EAT2 study from ANSES (2011). Compared to the maximum limits in commercial food products (European regulation EC 2006/1881), non-compliance frequencies were very high for several categories (e.g up to 83% for Pb in root vegetables and 77% for Cd in leaf vegetables). As a whole, 30% of the vegetables from CTB were above EU norms, therefore contributing to a higher exposure compared to a diet relying on market vegetables only.

Health risk assessments based on (i) slope factor by Health Canada (2004) for As carcinogenicity (lifetime exposure); and (ii) BMDL values (Lower Confidence Interval of the Benchmark Dose) by EFSA (2010) for renal effects (adults), gave rise to unacceptable health risks for both adults and children gardening and/or eating vegetables grown on the site. Exposure assessment for Cd also showed that high consumers such as CTB gardeners experience two to three time the total dietary exposure of people from the general population feeding on market stores only. Other soil contaminants such as Cu, Zn, and Mo exhibited high to very high concentrations in soils (mean of 214 mg/kg, 1410 mg/kg and 2.8 mg/kg; and up to 390 mg/kg; 2200 mg/kg and 6.0 mg/kg, respectively), also above legal soil standards but not causing potential health risk at these concentrations.

Based on these results, the Officials from the Walloon administration settled on not closing the site. Instead, they provided a panel of recommendations to gardeners aiming at reducing their exposure and decided to plan a human biomonitoring survey. Lead, Cd and As exposure biomarker concentrations were measured in blood and urine samples provided by the adult gardeners to verify if these contaminated soils resulted in anomalously high internal exposure, that could potentially cause adverse health effects in the study population. In addition, Mo, Cu and Zn exposure biomarkers were also monitored due to the higher concentrations than usual measured soils. Besides addressing potential health risks at the individual and the community scales, the purpose was to rely on new data to improve the management of the site and further confirm precautionary measures.

2. Materials and methods

2.1. Study population and recruitment

The only inclusion criteria upon recruitment, based on volunteering, was the consumption of products cultivated at CTB or CTB attendance. This cross sectional study took place in summer 2018 (beginning of July to the end of September) when vegetable harvest and consumption were the most favorable. This study was approved by the Ethic Committee of the University Hospital of Liege. All participants signed an informed consent, provided urine and blood samples collected respectively in a polypropylene vessels and clot activator tube (without gel), and answered a questionnaire during a face-to-face meeting to collect information’s on demographic characteristics (age, sex), CTB attendance and dietary habits related to fruits and vegetables grown on site, smoking status, presence of lead water pipe at home, consumption of fish/seafood, and meat offal the week before sampling. All data were anonymized and analyzed according to the rules of the General Regulation on Data Protection.

2.2. Selection of exposure biomarkers

2.2.1. Trace metal(oid)s

Blood Pb (PbB), urinary Cd (CdU) and speciated urinary arsenic (AsU = DMA + MMA + As(III) + As(V)) were measured as being the most relevant exposure biomarkers for these environmental contaminants, allowing to evaluate the body burden against toxicity and against ‘normal’ population values. In addition, urine Pb (PbU) and blood Cd (CdB) were also measured, as well as essential elements molybdenum (MoU), zinc (ZnU) and copper (CuU), because of their high concentrations compared to moderately contaminated soils.

2.2.2. Cotinine and creatinine determination

Cotinine was measured in urine to identify smokers and non-smokers, because smoking is a known and significant source of Cd, but also of As and Pb. Creatinine was measured to allow normalization of trace metal(oid) concentrations in urine.

2.3. Analytical methodology

2.3.1. Chemicals

Ultra-pure water for HPLC-ICP-MS analysis was generated by purifying home produced double distilled water with a Milli-Q Gradient A10 system combined to an Elix 3 pre-system (Millipore S.A. Billerica, USA). Stock solutions of the individual As species and ICP-MS tuning solution were purchased and prepared according to the information provided by Cheyns et al. (2017).

2.3.2. Total trace metal(oid) analysis in urine and blood

Trace metal(oid)s in blood and urine samples were measured at the Laboratory of Clinical, Forensic and Environmental Toxicology of CHU of Liege using ICP-MS (Agilent 7700×) equipped with an ORS collision cell and an Integrated Sample Introduction System (ISIS). Samples were 10× diluted in a solution of nitric acid 0.5% for urine, and a solution of nitric acid 0.5% containing 0.2% of n-butanol and 0.1% of Triton for blood samples. Calibration was performed with the standard addition method to build curves ranging from 0.2 to 100 μg/L for CdB, from 1 to 500 for PbB, from 5 to 2000 μg/L for MoU, CuU and ZnU, and from 0.2 to 100 μg/L for CdU and PbU. Non-spectral matrix effects and instrumental drift were corrected with internal standards (Sc, Ge, Rh, Ir). Analytical methods for blood and urine were validated separately according to the rigorous total error approach already previously described (Dubois et al., 2012; Hubert et al., 2007) using E-noval software V4.0 (Arlenda, Liege, Belgium). For this purpose, real matrices (blood or urine) were fortified with analytes at 10 to 14 different levels within the dosing range (depending on the analyte and the matrix) analyzed in triplicate in a single day, and these triplicates were measured again on two distinct days. Then, the linearity, inter and intra assay precisions (repeatability and reproducibility) and trueness were evaluated on these measurements. The quantification limits (LOQ) were determined as the smallest concentrations measured in urine or blood samples with a total error not exceeding 30%. This very rigorous validation process ensures that the method produces accurate results even on very low levels, as long as above the LOQ values. The following LOQs were obtained: 0.1 μg/L for

CdB, 0.5 μg/L for PbB, 0.12 μg/L for CdU, 0.38 μg/L for PbU, 1.65 μg/L for CuU, 5.00 μg/L for MoU, and 15.0 μg/L for ZnU. The lab is accredited for many years for these measurements under the ISO 15189 norm. Moreover, to ensure high quality results, the lab regularly participates to several external quality assurance programs for element analyses in urine and blood: the QMEQAS organized 3 times a year by the Institut national de santé publique du Québec (Centre de toxicologie du Québec, Canada); and the Trace Elements External Quality Assessment Scheme organized monthly by Sciensano (Belgium).

Certified reference materials were included in each sequence of 30 unknown samples: Trace Element Whole Blood level I and II (Seronorm) for blood analyses, Lyphocheck Urine Metals Control (BIORAD) and Trace Element Urine level II (Seronorm) for urine analyses. Because urinary Mo was not present in the certified materials used, a former QMEQAS was also run as additional QC. The target concentrations, the certified or acceptable ranges (if materials are not certified), and the range measured during the different sequences are gathered in Table 3 (supplementary material).

2.3.3. *Arsenic speciation analysis in urine*

Because As toxicity is dependent on its chemical forms, urinary As speciation analysis was performed focusing on the sum di- and tri-valent inorganic arsenic and their metabolites. Speciated urinary As was determined as AsU = As(III) + As(V) + DMA + MMA with DMA = dimethyl arsenate, MMA = monomethyl arsonate, As(III) = trivalent inorganic arsenic; As(V) = pentavalent inorganic arsenic. Arsenic speciation analyses (DMA, MMA and inorganic arsenic-(=As(III) + As (V))), were performed at the Trace Element unit of Sciensano by HPLC-ICP-MS with a Varian 820 ICP-MS coupled to a Prostar solvent delivery module (Varian, Mulgrave, Australia) and using a Hamilton PRP-X-100 column (Reno, Nevada, USA). Samples were 10× diluted with MilliQ water and centrifuged for 5 min at 1500 g (Sorvall Legend XT, Thermo Fisher Scientific, Waltham, USA) prior to injection. The As signal was monitored on mass ^{75}As and H_2 was used as a reaction gas to remove ^{40}Ar^{35}Cl interference. For each individual As species, an external calibration of the linear type was performed using the following concentrations: 0–0.2–0.5–1.0–2.0–5.0 μg/L. These daily calibration standards were prepared from the multispecies stock solution of 250 μg/L. The limit of quantification (LOQ) for each As species was calculated as ten times the standard deviation of the background signal of the chromatogram. The following LOQs were achieved: 0.8 μg/L for As(III) and DMA and 0.5 μg/L for As(V) and MMA. Within day standard deviation (sr) and between day variation (sd) were calculated as described by Neven et al. (2020) based on duplicate analysis of the German External Quality Assessment Scheme programs (G-EQUAS) 62 8A sample (Institute and Outpatient Clinic for Occupational, Social and Environmental Medicine of the University of Erlangen-Nuremberg, Germany) on 3 different days and resulted in the following values: for DMA: sr = 0.3% and sd = 3.4%, for MMA: sr = 2.0% and sd = 4.3%, for As(III): sr = 11% and sd = 19%, for As(V): sr = 3.0% and sd = 19%.

Each analytical batch included internal quality control measures including (i) two procedure blanks and a reagent blank as a monitor for possible cross-contamination, (ii) a QC standard check every 20 samples to allow verification of potential instrument drift, and (iii) a former G-EQUAS PT sample to verify trueness. A series of acceptance criteria were applied to each batch, including calibration blank value below LOQ/2, procedure blank below the LOQ and drift below 10%. The measured value of the former G-EQUAS sample were, for DMA: 25.7 μg/L, for MMA: 2.8 μg/L, for As(III): 1.0 μg/L, for As(V): 3.3 μg/L. They were evaluated against the certified range (for DMA: 18.2–30.8 μg/L, for MMA: 1.7–4.1 μg/L, for As(III): 1.0–2.2 μg/L, for As(V): 1.9–4.3 μg/L).

2.3.4. *Creatinine*

Creatinine was measured at CHU based on enzymatic chain reactions using the automate ARCHITECT ci 4100 (ABBOTT, Illinois, USA) according to the manufacturer's instructions, and using Abbott reagent and calibration kits.

2.3.5. *Cotinine*

Cotinine was measured by liquid-liquid extraction using a diethylether/dichloromethane/hexane/pentan-1-ol mixture on basified urine (with sodium carbonate) prior to injection on UHPL-HR-TOF-MS with a TripleTOF4600 (Sciex) at CHU, providing a LOQ of 22 μg/L.

2.4. *Statistics*

Statistical analyses were completed using Excel 2010 (Microsoft Office) and SPSS (IBM SPSS Statistics 25). Over-diluted or over-concentrated urine samples, showing urinary creatinine concentrations <0.3 or >3.0 g/L, respectively, were excluded from the statistical analysis, in accordance with the recommendations from Bader et al. (2016) and WHO (1996). No metal outlier values needed to be excluded. Concentrations below LOQ were assigned a value of LOQ/2 for statistical calculations (Hornung and Reed, 1990).

For each biomarker, the distribution was characterized by the arithmetic mean (AM), geometric mean (GM) as well as 10th, 25th, 50th, 75th, 90th and the 95th percentiles.

Univariate statistic (Table 4, supplementary material) were performed after verification of normality for data distribution using the quantile-quantile plot and the Shapiro-Wilk test. As Gaussian distribution was not confirmed, the non-parametric Mann-Withney *U* test was used for categorical variables with 2 modalities (k = 2). The Kruskal-Wallis test was used for categorical variables with more than 2 modalities (k > 2), using the Bonferroni correction. Correlations between continuous variables were performed using Spearman's correlation coefficient, used for variables that do not follow a normal distribution (Table 5; supplementary material). In the case of 2 × 2 tables, Fisher's Exact Test was used to determine the p-value, with 95% confidence level.

2.5. *Methodological approach*

Exposure biomarker levels in the study population were evaluated with two complementary approaches:

1. A comparison of individual data against commonly accepted cut-off values, selected from relevant national biomonitoring surveys (Becker et al., 2003; Hoet et al., 2013; Hutse et al., 2005; Apel et al., 2017; Bismuth et al., 2000; CDC (Center for Disease Control and Prevention), 2019; Fréry et al., 2011). As recommended in HBM4EU methodology (Buekers et al., 2018; Louro et al., 2019; Schwedler et al., 2017), two types of cut-off values were used to report and evaluate Pb, Cd and As biomarker results: (a) reference cut-off values (RC), typical of upperbound values considered as acceptable in the general population or below which there is no potential health risk and (b) intervention cut-off values (IC) that could be upper percentile values (p95 or p97.5) and/or values above which there are potential adverse effects requiring intervention such as a medical follow-up. The 'increased alert' situation was defined for biomarker values between RC et IC. For CuU, MoU and ZnU, an alert situation was deemed unnecessary because these are essential trace elements and few cases of intoxication have been identified in the literature.
2. Comparison of descriptive statistics determined for the CTB population with those retrieved from recent surveys, either related to the general population or to populations exposed to local soil contaminations in trace metals and arsenic.

In addition, variables from survey questionnaire were used to determine statistically significant associations with exposure biomarker levels.

3. Results and discussion

3.1. Characteristics of the study population

Eighty-eight adult volunteers from over 50 different allotments at the CTB were recruited from the beginning of July until the end of September 2018. They provided 88 urine samples, 81 blood samples and 86 filled questionnaires. Of the 88 adults, 41 were men (47%) with a mean age of 61.7 and 47 were women (53%) with a mean age of 57.2 years old. Eighty-three percent of the population consisted in non-smokers and 59% reported eating fish or seafood within the week before providing urine samples.

The study population consisted mostly of Belgian natives (40%) with relatively high proportions of Italian (19%) and Moroccan (20%) natives. About 40% of the study population completed elementary school as their highest scholarly achievement. These population characteristics are potentially affecting exposure biomarker levels with potentially higher exposure levels for individuals from lower income countries and lower education achievement. Other information on the study population, as well as gardening and consuming habits from survey questionnaires are available in Table 4 (supplementary material).

Trace metals concentrations in soils were homogenous on the study site. About 85% of participants also lived in the Bressoux neighborhood (within a 1.5 km radius from the allotment garden), showing similar levels of soil contaminations, without spatial trend.

3.2. Blood and urine descriptive results

General statistics on biomarker concentrations are reported in Table 6 (supplementary material). Eight urine samples were excluded on the basis of creatinine (urinary creatinine $<$0.3 g/L or $>$3.0 g/L). In addition of being reported for the whole population, descriptive statistics were also adjusted according to the smoking status (excluding smokers based on measurable cotinine) for PbB, PbU, CdB and CdU; and to exclude volunteers reporting fish or seafood consumption within the week prior sampling, for speciated AsU.

All Pb, Cd and speciated As measurements in urine or blood were above quantification limits, while only a few measurements, from 1.1 to 4.3%, were below LOQ for MoU, CuU and ZnU.

3.3. Comparison with reference and intervention cut-off values

The relative (and absolute) amount of individuals exceeding selected reference (RC) and intervention (IC) cut-off values are presented in Table 7 (supplementary material).

Eighty-four percent of the CTB sample population exceeds the RC values for CdB. In addition, respectively 55%, 50% and 28% of people at CTB show results above RC values for CdU, PbU and AsU, but much less for PbB (10%). As a whole, 90% of individuals exceed at least 1 out of 5 RC values, while 73%, 36% and 10% simultaneously exceed 2, 3 and 4 out of the 5 RC values, respectively (Fig. 1A). When excluding people with smoking habits, as well as those having reported eating fish/seafood prior sampling, these relative proportions show a slight decrease with 85%, 60%, 40%, 15% and 5% above 1, 2, 3, 4 and 5 RC values, respectively.

The relative amount of individuals from the CTB exceeding selected IC values is rather high for PbU (15%), CdB (15%) and AsU (13%). Forty-one percent of the study population exceeds 1 out of 8 intervention cut-off values while, 9% and 1% only simultaneously exceeds 2 and 3 out of the 8 IC values, respectively (Fig. 1B). Excluding smokers, as well as participants reporting recent fish/seafood consumption, small changes in the relative amount of individuals exceeding IC values for CdB and AsU are observed (see Table 7) while % of participants above 1 IC values drops to 30%, but still remains high.

3.4. Comparison with biomonitoring data from general population

Descriptive statistical parameters for PbB, PbU, CdB, CdU and AsU in our study population are compared to similar values (GM, p50 and p95) retrieved from biomonitoring surveys in general adult populations (Table 8; supplementary material).

Comparison to general population data could be limited by some peculiar socio-demographic features of the CTB gardeners, showing proportionally a lower level of scholarly achievement, more diverse birth origins and more aged individuals. However, univariate statistics show that level of education is not significantly associated with higher biological exposure in Pb, Cd and As, also likely ruling out potential occupational exposures involving “blue collar” workers in the CTB population ($0.13 < p\text{-value} < 0.91$, depending on the biomarker). In addition, country of birth was not associated with significant differences in PbB, PbU, CdU and AsU biomarker levels ($0.22 < p\text{-value} < 0.72$,

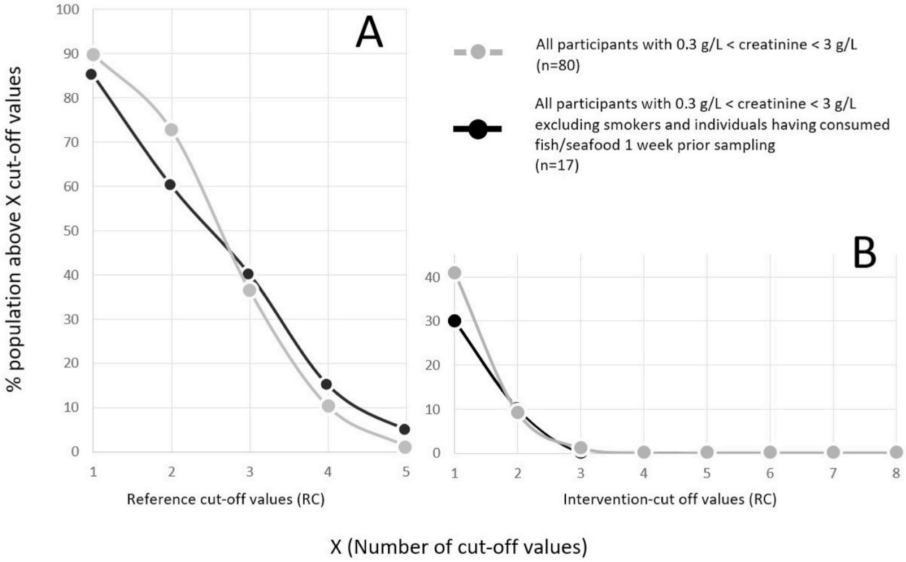

Fig. 1. Cumulative % of the CTB population above X cut-off values for (A) reference cut-offs and (B) intervention cut-offs for all participants (grey) and participants excluding smokers or having reported eating fish or seafood within the week before sampling (black).

depending on the biomarker). The statistically significant (p-value = 0.033) difference between CdB levels in Belgian and Italian natives compared to Moroccan natives, is not consistent with the conjecture of higher exposure for newcomers from lower income countries. In fact, higher CdB levels are observed for Belgians compared to Italians, to Moroccans and to natives from other countries.

These first observations provide some elements allowing to rule out some confounding factors, thereby showing that the CTB population is more comparable to a general adult population than initially expected.

3.4.1. *Lead*

Blood lead levels have been observed to decrease over time due to several policies implemented these last decades (i.e. ban on leaded gazoline, replacement of lead pipes, European regulation on food contaminants, etc.) (Becker et al., 2013; Nisse et al., 2017). However, PbB geometric mean, p50 and p95 measured at the CTB in 2018 are higher than corresponding statistics from the three most recent studies relevant to general populations sampled in 2008, 2013 and 2014 (Nisse et al., 2017, Haines et al., 2017; Oleko et al., 2020), and close to or slightly lower than values from the two other studies performed 12–13 years before the CTB survey, despite the general decreasing trend in PbB over time (Hutse et al., 2005; Fréry et al., 2011).

This offset can be due to the relatively more aged population of gardeners from CTB compared to general adult population surveys. Blood Pb concentrations are typically correlated with age (e.g. Fréry et al., 2011; Oleko et al., 2020), as seen also for the CTB population (r = 0.456, p-value = 0.000) showing statistically significant lower PbB levels in younger (30–50 years old) compared to older age categories (p-value = 0.000). Age, as a cofounding factor, can be evaluated by comparing PbB data from CTB with french general biomonitoring surveys (Fréry et al., 2011; Nisse et al., 2017; Oleko et al., 2020) according to similar age classes (Fig. 2A). Once similar age classes are compared, the CTB population still exhibit higher PbB levels than the most recent general survey (Oleko et al., 2020). Although this observation is certainly hampered by the small sample size of the CTB study, it is consistent with a higher exposure to environmental sources of Pb for the CTB population compared to the actual general population, once age is taken into account. Fig. 2A also show similar PbB levels for the CTB gardeners compared to PbB levels reported for the population living in Northern France (Nisse et al., 2017), in similar environmental conditions (large scale historical soil contamination in Pb due to past metal processing industries), but sampled 10 years before the CTB survey. Due to PbB decreasing trend with time, this observation actually suggests that Pb exposure for the gardeners from CTB could be higher than for residents from Nisse et al. (2017), probably more passively exposed to soils, or not including gardeners for the most part.

Gender difference in PbB level is expected from literature, with higher exposure for men, (e.g. Fréry et al., 2011; Nisse et al., 2017). It is observed for the CTB gardeners but is not statistically significant (p-value = 0.34). Similarly, smoking status is associated with higher PbB for smokers, but not significantly (p-value = 0.27).

It appears obvious that other important factors such as dietary habits and/or lifestyle would result in these higher PbB levels. Gardeners who report having lead pipes at home show statistically significant higher PbB concentrations (p-value = 0.029). Consistently, higher PbB levels is also associated with preferential consumption of tapwater rather than bottled water (p-value = 0.035).

Urinary Pb concentrations for the CTB population show geometric mean and p95 values about twice those of general population statistics listed in Table 8 (Hoet et al., 2013; Nisse et al., 2017). Urinary Pb concentrations shows a statistically significant and strong correlation with PbB (μg/g.cr, r = 0.531, p-value = 0.000), as evidenced in other studies (e.g. Moreira and Neves, 2008). As for PbB, younger individuals from the CTB (30–50 years old) show statistically significant lower PbU concentrations compared to older gardeners (p-value = 0.02). There no statistically significant differences in PbU levels according to gender or smoking status but reporting lead pipes at home and the use of traditional cosmetics such as khôl is associated with higher PbU concentrations (p-value = 0.035 and p-value = 0.029, respectively).

3.4.2. *Cadmium*

Urinary Cd levels for the CTB population are systematically higher than typical values attributed to some general populations listed in Table 8. For instance, median CdU at CTB (1.23 μg/L) is higher than the 95th percentile from general population in Belgium (1.06 μg/L; Hoet et al., 2013), France (0.95 μg/L; Fréry et al., 2011) and Germany (0.96 μg/L; Wilhelm et al., 2004).

Due to the cumulative behavior of Cd in kidney during lifetime, age difference in CdU levels is typically observed in the general population (e.g. Fréry et al., 2011; Oleko et al., 2021). Age of CTB gardeners is not associated with statistically significant differences in CdU concentrations (p-value = 0.44), however, the difference in age distribution at CTB compared to general adult population survey could contribute to higher CdU levels. Again, the effect of age, as a confounding factor, can be evaluated by comparing CdU (μg/g.cr.) from CTB gardeners with data from the general biomonitoring survey by Fréry et al. (2011), Nisse et al.

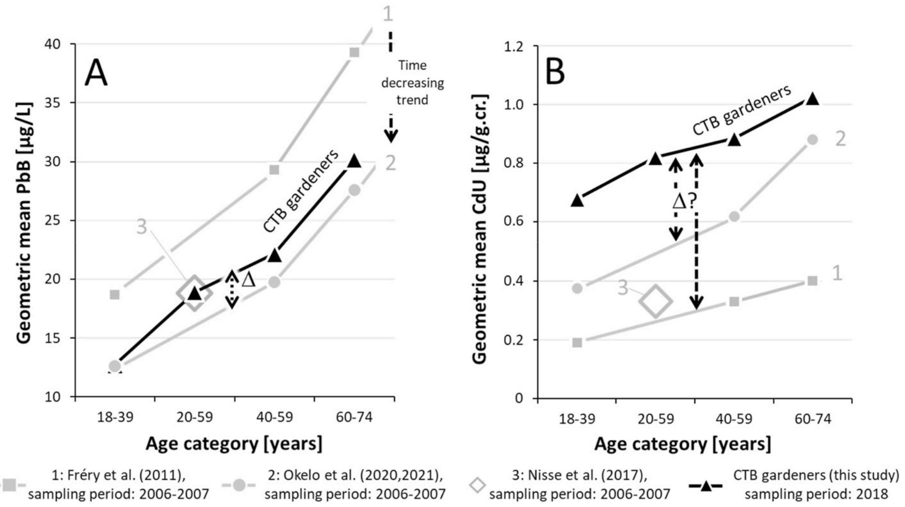

Fig. 2. Comparison of CTB data with general population surveys according to similar age categories for (A) PbB (μg/L) and (B) CdU (μg/g.cr.) geometric mean concentrations. "Δ" symbol depicts qualitative exposure differences in PbB and CdU between the CTB population and general population survey data, that are not likely related to age.

(2017) and Oleko et al. (2021) for identical age categories (Fig. 2B). The effect of age on CdU values for gardeners from CTB is not sufficient in explaining high CdU levels compared to the above references. In fact, Fig. 2B shows an average CdU concentration for CTB gardeners that is 1.5 (compared to Oleko et al., 2021) to 3 times (compared to Fréry et al., 2011) higher than those measured in the general adult population, for similar age categories.

Urinary Cd concentrations typically shows gender differences in the general population when data are expressed on a volumetric (i.e. μg/L) basis, with men having slightly higher CdU concentrations (e.g. Fréry et al., 2011). This is observed for the CTB gardeners at much higher CdU concentration levels with a statistically significant difference (p-value = 0.028). However, when CdU is creatinine normalized, gender difference in CdU levels for the CTB gardeners cancels and becomes statistically insignificant (p-value = 0.24), ruling out a significant gender effect on Cd exposure levels for the CTB population. This can be related to higher urinary creatinine levels in men compared to women, as known from literature (e.g. Cocker et al., 2011).

Smoking status is responsible for statistically significant differences in CdU levels in general adult population surveys, with higher CdU concentrations for individuals with smoking habits (e.g. Fréry et al., 2011; Nisse et al., 2017; Oleko et al., 2021). However, this is not observed for the CTB gardeners. In fact, individuals with measurable urinary cotinine (defining the smoking status in our study) have lower CdU levels, not statistically different than those of non-smoker (p-value = 0.099). In contrast, a statistically significant association (p-value = 0.012) between smoking status and CdB levels (sensitive to more recent exposure compared to CdU), with higher values for smokers, is evidenced in the study.

Blood cadmium concentrations for the CTB population are nearly twice as high compared to statistics from the general populations listed in Table 8, with a median value of 0.75 μg/L, in the range of 75th to 90th percentiles from Nisse et al. (2017) or Haines et al. (2017). As for CdU, age and gender are not associated with statistically significant differences in CdB. Blood Cd concentrations are not correlated to CdU concentrations (p-value = 0.92), they show instead a rather weak but statistically significant correlation with PbB (r = 0.327, p-value = 0.003). In contrast CdU concentrations are moderately to strongly correlated with PbU when expressed in μg/g.cr (r = 0.541, p-value = 0.000) or in μg/L (r = 0.624, p-value = 0.000). Albeit loosely, these correlations point also towards a joint environmental Cd and Pb contamination source such as CTB soils, as being responsible for the observed biological exposure levels in the CTB population.

As a whole, CdU levels for the CTB population are not fully explained by smoking status, age and gender, nor by scholarly achievement (as representing roughly socio-economic status) or birth country, as seen earlier. The lack of statistically significant differences in CdU values for the CTB gardeners according to some typical master variables found to explain CdU variations may be due to the higher exposure level experienced for CTB gardeners, concealing known explanatory factors expected for a general adult population.

3.4.3. *Speciated arsenic*

Speciated AsU (inorganic As + MMA + DMA) descriptive statistics for the CTB population are more than twice those of the French reference population, with a median value for the CTB study population of 7.17 μg/g.cr., very close to the 95th percentile (8.90 μg/g.cr.) reported by Fréry et al. (2011). They are also above AsU concentrations reported for the general American population in 2015–2016 (NHANES) (CDC, 2019).

The CTB population shows a statistically significant gender difference (p-value = 0.04) with higher AsU concentrations for women, as observed in the general population survey by Fréry et al. (2011), but at much lower exposure levels. Age and smoking status are not associated with statistically significant differences in AsU. Typically, higher AsU levels is observed for individuals reporting fish/seafood consumption the week prior sampling (p-value = 0.04). Eventually, the use of traditional food containers such as non-EU ceramic vessels is associated with higher AsU levels (p-value = 0.016) as well. These two environmental factors cannot, however be solely responsible for the high As exposure observed in the CTB population.

3.4.4. *Other biomarkers*

The study population from CTB shows median CuU, MoU and ZnU comparable to median values reported in Nisse et al. (2017); Haines et al. (2017) and Hoet et al. (2013), the only three European studies having examined the distribution of these biomarkers in the general population. The population at CTB does not show significantly higher levels of exposure with respect to these micronutrient trace metals.

3.5. *Comparison with studies on populations exposed local soil contaminations*

3.5.1. *Lead*

In contrast to studies on children, PbB data for adults exposed to local soil contaminations are very scarce. However, a rather similar study by Bramwell et al. (2021) on gardeners exposed to Pb contaminated soils in allotments from Newcastle (UK) showed lower PbB levels (p50 = 16 μg/L and p90 = 27 μg/L) compared to those from CTB (p50 = 23.1 μg/L and p90 = 52 μg/L), despite the similar age distributions between both studies. Pb concentrations in the allotment soils in the CTB (500 mg/kg, in average) were higher than those from Newcastle (300 mg/kg, in average) and could thus contribute to the higher blood lead levels observed in our study. Blood Pb concentrations of Newcastle gardeners were also close to those reported at the same time period in a general population living in the north of France (Nisse et al., 2017).

Higher PbB levels compared to the general population could not be fully attributed or related to the age distribution for the CTB population (see Fig. 2A), although being likely influenced by domestic sources such as Pb pipes (see section 3.4.1). On the other hand, Pb concentrations in soils from CTB and neighboring private gardens are very high (see Table 1), as are Pb concentrations in local vegetables and fruits, showing a 10 to 40-fold increase compared to market vegetables (see Table 2). High non-compliance frequencies for vegetable and fruits at CTB thereby contributes to a higher dietary exposure compared to the general population.

Not surprisingly, variables related to exposure to CTB soils such as attendance of CTB allotments, as well as gardening practices and homegrown consumption habits are also significantly associated with higher PbB (and PbU) levels. Gardeners spending more than 4 days per month on site during the cultural season (p-value = 0.011), who cultivate several allotments (p-value = 0.034), and who ate homegrown within the week prior sampling (p-value = 0.001) showed higher PbB levels. Similarly, gardeners whose favourite food category are fruit vegetables (one of the least contaminated category, with the lowest non-compliance frequency to EU norms) show lower PbU levels (p-value = 0.02).

3.5.2. *Cadmium*

With respect to CdU, only four case studies relevant to adults exposed to Cd contaminated soils were available for comparison with CTB data (Durand et al., 2008; ORS PACA, 2001; OVAM, 2008; Fierens et al., 2016). Descriptive statistics show a CdU distribution strongly shifted toward higher values for the CTB population compared to other outstanding case studies such as the CASSIOPEE study (Durand et al., 2008), even when excluding smokers from descriptive statistics (Fig. 3). The percentages of the population with CdU above 1 μg/g.cr. and 2 μg/g.cr. (cut-off values considered in the CASSIOPEE study) are also much higher at the CTB, despite Cd concentrations in soils lower by a factor 5 compared to other case studies.

Gender, age and smoking status fail at explaining high CdU and CdB level in the gardeners from CTB, while no statistically significant differences in CdB and CdU with scholarly achievement makes the effect of

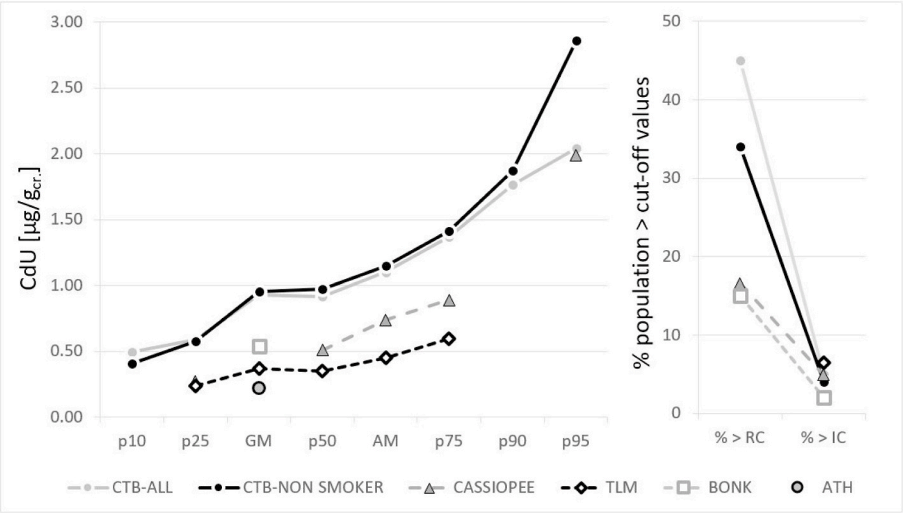

Fig. 3. Comparison of (A) CdU descriptive statistics and (B) % population above cut off values for all participants ("CTB-ALL") and participants excluding smokers ("CTB-NON SMOKER") with other populations exposed to local soil contaminations from studies reporting data in µg/g$_{cr.}$. "CASSIOPEE", "TLM", "BONK" and "ATH" refer to studies by Durand et al. (2008); ORS PACA (2001); OVAM (2008) and Fierens et al. (2016), respectively. RC (1 µg/g$_{cr.}$) and IC (2 µg/g$_{cr.}$) values were chosen from Durand et al. (2008).

occupational exposure rather unlikely at the scale of the study group (see section 3.4.2).

Compared to the above case studies, which included residents (more passive exposure to soil contaminants) for the most part, the CTB population is exclusively made of gardeners, hence more exposed to non-intentional ingestion of soil particles and intentional consumption of Cd contaminated local food products. This can result in higher CdU levels, even more when accounting for age in this more aged population from the CTB.

Cd is prone to bioaccumulation in vegetables. In fact, Cd concentrations in vegetable grown at CTB show a 2 to 9-fold increase compared to those from market stores sampled by ANSES (2011) (see Table 2), who also evaluated vegetables consumption as having a strong contribution of 22% on the total background dietary exposure for adults in the general population. Obviously, the substitution of market vegetables by vegetable grown on CTB soils will contribute to a higher exposure, especially for high consumers. In fact, external dose exposure assessment showed that high consumers feeding on contaminated Cd soils experiences two times the total dietary exposure compared to people of similar age from the general population feeding on market stores only (0.34 µg$_{Cd}$/kg$_{BW}$/d, against 0.16 µg$_{Cd}$/kg$_{BW}$/d as determined by ANSES, 2011). This is also consistent with the exposure assessment by Franz et al. (2008) on Kempen soils with similar Cd concentrations (high vegetable consumer's scenario). A lifetime integrated exposition to twice the dietary exposure dose attributed to the general adult population may therefore result in CdU levels within the range of 1.5–3 times those measured in general adult population surveys (see section 3.4.2 and Fig. 2B).

Compared to PbB, fewer variables from survey questionnaires show statistically significant associations with high CdU levels in the CTB population. This can be tentatively attributed to generally high CdU levels, making the contribution from the kidney burden (integrating Cd exposure over lifetime), more prominent compared to more recent intake (especially in aged individuals) and dietary habits seized by the questionnaire (gardening practice and consumption habits may also change from year to year and over decades). Gardeners who report owning an additional vegetable garden at home showed higher CdU levels ($p\text{-value} = 0.04$), while those reporting (i) the use of raised bed with clean soil ($p\text{-value} = 0.048$) and (ii) the preferential consumption of fruits ($p\text{-value} = 0.023$) showed lower CdU levels, accordingly. The latter association is consistent with the fact that fruits are among the least Cd contaminated food categories at CTB (see Table 2).

3.5.3. Arsenic

Nine human biomonitoring studies related to populations exposed to potentially harmful As levels in soils from France (Durand et al., 2008; OVAM, 2008; Fréry & Ohayon, 1998; Fillol et al., 2010), Europe (Kavanagh et al., 1998; Ranft et al., 2003) or elsewhere in the World (Do et al., 2011; Tsuji et al., 2005; Hinwood et al., 2004), have reported data on AsU (Asi + MMA + DMA) in adults. These data are plotted with CTB data in Fig. 4. Speciated AsU distributions are strongly shifted towards higher values for people from CTB (all participants or those excluding recent fish/seafood consumers) compared to other local populations, as are the proportions of people above selected RC and IC values. However, arsenic concentrations in soils from CTB are lower by at least an order of magnitude compared to those measured in other local HBM studies.

The survey questionnaire fails at providing meaningful associations between variables related to soil exposure and AsU levels in the CTB population. Other variables involving statistically significant differences according to gender, fish/seafood consumption and the use of traditional food containers, cannot explain the observed AsU levels. However, AsU levels in the CTB population are significantly but moderately correlated to PbU ($r = 0.417$, $p\text{-value} = 0.000$) and weakly correlated to CdU ($r = 0.356$, $p\text{-value} = 0.01$), when expressed in µg/L. Albeit loosely, this points towards a joint environmental source common to the three environmental contaminants, represented by CTB and neighboring soils. The apparent contradiction between high AsU levels and low to moderate soil concentrations is tentatively explained by a more intense exposure to As by unintentional ingestion of soil particles due to gardening and consumption of local vegetables, contributing to a higher exposure for this population made solely of gardeners. Speciation of trace elements in solid matrices readily affects their environmental reactivity (Petit et al., 2009) and exposure to humans. Potentially higher As bioavailability due to authigenic precipitation of Pb phosphate (Cui et al., 2010), as observed by Scanning Electron Microprobe in CTB soils may also contribute the high AsU levels observed. In fact, soil As concentrations at CTB combined to a high bioaccessibility is in the range of values giving rise to a measurable increase in AsU levels at the population scale (Petit et al., 2021).

3.6. Potential health implications for the CTB gardeners

A large number of CTB gardeners exceed simultaneously several reference and intervention cut-off values for toxic environmental contaminants such as Pb, Cd and As (see section 3.3 and Table 7). They also show higher PbB, AsU and CdU biomarker levels compared to surveys for general adult populations across Europe (see section 3.4) and to

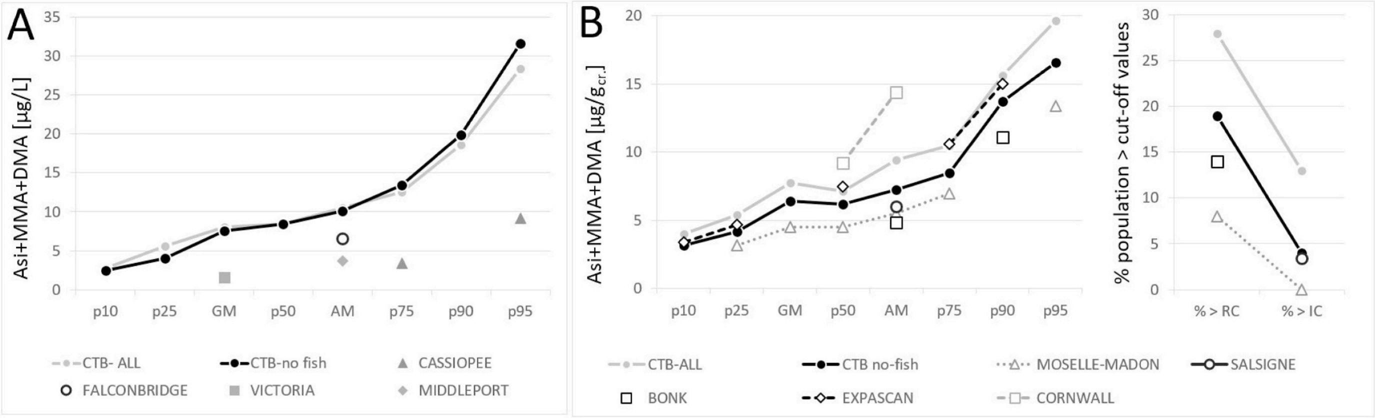

Fig. 4. Comparison of AsU descriptive statistics and % population above RC and IC cut off values, with studies on population exposed to local soil contamination reporting data in (A) [µg/L] or (B) [$\mu g/g_{cr.}$]. "CTB-ALL": all participants from CTB; "CTB-NO FISH": CTB participants excluding recent fish/seafood consumers. "CASSIOPEE", "FALCONBRIDGE", "VICTORIA", "MIDDLEPORT" "MOSELLE-MADON", "SALSIGNE", "BONK", "EXPASCAN", "CORNWALL" refer to studies by Durand et al. (2008); Do et al. (2011); Hinwood et al. (2004); Tsuji et al. (2005); Fillol et al. (2010); Fréry & Ohayon (1998); OVAM (2008); Ranft et al. (2003); Kavanagh et al. (1998).

other populations exposed to local soil contaminations (see section 3.5). As known from literature, chronic toxicity effects of these three elements are diverse: dysfunction of the renal system leading to chronic renal disease for Cd (Buchet et al., 1990; Järup and Åkesson, 2009); skin lesions, cardiovascular diseases and metabolic disorders as well as bladder, skin and lung cancer for As (Ratnaike, 2003; Saha et al., 1999); and renal and cardiovascular toxicity for adults exposed to Pb (Harari et al., 2018; Navas-Acien et al., 2007). There are also evidence for additional and cumulative effects due to co-exposure to Cd, As and Pb. For instance, several studies have reported additive/multiplicative nephrotoxic effects related to Cd and As chronic co-exposure (Buchet et al., 2003; Hong et al., 2004; Nordberg et al., 2005, Nordberg, 2010), while Lim et al. (2016) highlighted interaction on renal tubular impairment following a co-exposure of Pb and Cd.

Consequently, current literature suggests that gardeners from CTB may experience a higher prevalence of chronic disease related to Pb, Cd and As. Effect biomarkers of renal dysfunction were not measured in our study. However, a higher incidence of chronic kidney disease can be suspected when CdU levels are compared to those from the CASSIOPEE study (Durand et al., 2008). In this study, out of the 23% individuals who showed CdU >1 µg/g.cr., 16% had measureable tubular and/or glomerular renal function impairments. Proportionally, for the CTB population, in which 55% of participants show CdU levels above 1 µg/g.cr., tubular and/or glomerular renal function impairments could potentially affect about 30% of the study population.

4. Conclusion

Gardeners from a contaminated allotment garden in Liege (Belgium) show moderately high blood Pb, high urinary speciated As, and very high urinary Cd biomarker levels, sometimes above high percentiles values from current general adult population surveys in Europe. Biomarker levels of Cd and As are also more elevated compared to other populations locally exposed to soil contaminations, despite lower As and Cd concentrations, in the low to medium range of common values for contaminated soils.

Some peculiar characteristics of the study population (country of birth, level of scholarly achievement) show no significant and meaningful association with differences in biomarker levels. Other individual characteristics such as gender, smoking status and age, as well as some household sources (lead pipes, traditional cosmetics and food containers), provide statistically significant differences in biomarker levels but cannot fully explain high values observed in the gardener population. Statistically significant differences in biomarker levels with several variables relevant soil exposure (attendance frequency, gardening practices and consuming habits) as well as weak to strong correlation coefficients between various biomarkers of Pb, Cd and As point toward the soil contamination as the joint additional source partially responsible for higher biomarker concentrations in urine and blood.

Compared to general and local population surveys, higher biomarker levels of potential health concern are best attributed to a combination of (i) a rather aged population, (ii) solely made of actively exposed gardeners (ii) and high consumers of contaminated vegetables and fruits grown on these local soils.

CRediT author statement

Jérôme C.J. Petit: writing, conceptualisation, investigation, formal analysis. **Patrick Maggi**: investigation, conceptualisation, methodology, formal analysis. **Catherine Pirard**: methodology, investigation. **Corinne Charlier**: supervision. **Ann Ruttens**: methodology, investigation. **Gilles Colinet and Amandine Liénard**: sampling, investigation, formal analysis (vegetable and soils) **Suzanne Remy**: supervision, funding acquisition, project administration.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Jerome, Jerome Petit reports financial support was provided by Public Service of Wallonia.

Data availability

Data will be made available on request.

Acknowledgement

The authors sincerely acknowledge all volunteers at CTB for providing blood and urine samples, as well as the "Ligue du Coin de Terre de Bressoux" for their support. Thanks should also go to Dr Benoit Pereira (UCLouvain –Earth and Life Institute), Delphine Fontenoy (Espace-Environnement), Maud Lebel and Marie Jaillier (SPAQuE), for their contribution on the study as partners from the SANISOL project. This work was supported by the grant agreement SANISOL, provided by Dr Esther Goidts and Dr Pol Gosselin (Service Public de Wallonie).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envpol.2022.120028.

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