Environment International 61 (2013) 88–97

Contents lists available at ScienceDirect

Environment International

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

Biomonitoring of the general population living near a modern solid waste incinerator: A pilot study in Modena, Italy

Andrea Ranzi [a], Silvia Fustinoni [b,*], Laura Erspamer [a], Laura Campo [b], Maria Giulia Gatti [c], Petra Bechtold [c], Stefano Bonassi [d], Tommaso Trenti [e], Carlo Alberto Goldoni [c], Pier Alberto Bertazzi [b], Paolo Lauriola [a]

[a] Environmental Health Reference Centre, Regional Agency for Environmental Prevention of Emilia-Romagna, Modena, Italy
[b] Department of Clinical Sciences and Community Health, University of Milan and Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[c] Department of Public Health, Local Health Unit, Modena, Italy
[d] Unit of Clinical and Molecular Epidemiology, IRCCS San Raffaele Pisana, Rome, Italy
[e] Clinical Pathology Department, Local Health Authority, Modena, Italy

ARTICLE INFO

Article history:
Received 26 July 2013
Accepted 16 September 2013
Available online xxxx

Keywords:
Human biomonitoring
Solid waste incinerator
Exposure
Polycyclic aromatic hydrocarbons
Heavy metals

ABSTRACT

Background and goals: As part of the authorization process for the solid waste incinerator (SWI) in Modena, Italy, a human biomonitoring cross-sectional pilot study was conducted to investigate the degree to which people living and working in the proximity of the plant were exposed to SWI emissions.
Methods: Between May and June 2010, 65 subjects living and working within 4 km of the incinerator (exposed) and 103 subjects living and working outside this area (unexposed) were enrolled in the study. Blood, serum and urinary metals (Pb, Cd, Cu, Zn, Hg, Mn, Ni), urinary benzene, toluene, xylene (BTEX), S-phenylmercapturic acid (SPMA), and urinary polycyclic aromatic hydrocarbons (PAHs) were analysed. Information about lifestyle, anthropometric characteristics, residence, and health status was collected by a self-administered questionnaire. Exposure to particulate matter (PM) emitted from the SWI was estimated using fall-out maps from a *quasi*-Gaussian dispersion model. A multiple linear regression analysis investigated the relationship between biomarkers and the distance of a subject's place of residence from the SWI plant or the exposure to PM.
Results: Urinary BTEX and SPMA and blood, serum and urinary metals showed no differences between exposed and unexposed subjects. PAHs were higher in exposed than in unexposed subjects for phenanthrene, anthracene, and pyrene (median levels: 9.5 vs. 7.2 ng/L, 0.8 vs. <0.5 ng/L and 1.6 vs. 1.3 ng/L, respectively, $p < 0.05$). Multiple linear regression analysis showed that blood Cd and Hg and urinary Mn, fluorene, phenanthrene, anthracene and pyrene were inversely correlated to the distance of a subject's residence from the SWI. Urinary Mn, fluorene and phenanthrene were directly correlated to PM exposure.
Conclusions: This study, although not representative of the general population, suggests that specific biomarkers may provide information about the degree of exposure the subjects working and living in the proximity of the SWI plant may have to emissions from that facility.

1. Introduction

Solid waste incinerators (SWIs) can be significant sources of environmental pollution, potentially exposing nearby populations to hazardous chemicals at toxic levels. Both inorganic and organic chemicals have been identified in SWI emissions, including carbon monoxide (CO), carbon dioxide (CO_2), sulphur oxides (SO_X), nitrogen oxides (NO_X), dioxins and furans, volatile organic compounds (VOC), polycyclic aromatic hydrocarbons (PAHs), metals and particle matter (PM) (WHO, 2007). Some of these chemicals have been classified as known (group 1) or probable (group 2A) carcinogens for humans according to the International Agency for Research on Cancer (IARC, 1987, 1997, 2010, 2012).

Directive 2000/76/EC of the European Parliament and the Council on the Incineration of Waste enforces preventive measures to prevent or reduce negative effects to the environment, particularly emissions into air, soil and surface water, as well as to human health which might arise from incineration and co-incineration of waste. In particular, this directive states that incineration facilities shall be subject to a permit to operate, which sets stringent operating conditions, technical requirements and emission limits (European Commission, 2000). A review of European legislation on industrial emissions was launched in November 2005 by the European Commission, leading to a new Directive (2010/75/UE) that will be fully implemented by 7 January 2014 (European Commission, 2010).

In order to meet the enforceable requirements of these regulations, SWI technology has evolved over time, particularly in terms of emission

* Corresponding author at: Department of Clinical Sciences and Community Health, University of Milan and Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Via S. Barnaba, 8, 20122 Milan, Italy. Tel.: +39 02 503 20158; fax: +39 02 503 20111.
E-mail address: silvia.fustinoni@unimi.it (S. Fustinoni).

0160-4120/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.envint.2013.09.008

control in order to guarantee that they are within the limits specified by the European Directive (WHO, 2007).

A daunting array of documents and reports dealing with exposures and risks associated with solid waste treatment, and the possible health effects caused by incinerators, landfills and other waste disposal facilities, have been produced over the last two decades (reviewed in Franchini et al., 2004; Porta et al., 2009). Some studies have suggested associations between incinerator emissions and health effects, particularly adverse impacts on reproduction and cancer (Franchini et al., 2004; Rushton, 2003; Vinceti et al., 2008; WHO, 2007). However, these studies have several deficiencies that must be considered, such as the lack of exposure information, the use of surrogate measurements (e.g., the distance from the source) and the difficulty in controlling for potential confounding factors. These uncertainties, therefore, diminish the impacts of the report findings and the overall interpretation of results. Regardless, concern over the sustainability of the process of solid waste management by incineration, and putative health effects, has not diminished but has grown more acute, especially for the general populations living in proximity to these plants.

Because of these issues that were identified in earlier studies, more recent investigations have been designed and implemented with the goal of establishing a better definition of exposure and/or effects arising from SWI. Some studies have been focused on dispersion models and socio-demographic data (Floret et al., 2006; Hodgson et al., 2007; Ranzi et al., 2011), while others were based of human biomonitoring (HBM) of exposure (Agramunt et al., 2005; Bocio et al., 2005; Domingo et al., 2001; Fierens et al., 2007; Reis et al., 2007; Zubero et al., 2010) and early biological effects (Oh et al., 2005; Sul et al., 2003; Toide et al., 2003), either in workers or in the general population residing close to the SWI.

Eight municipal SWIs operate in the Emilia-Romagna region of Italy. One of these, in the municipality of Modena, has been operating since 1980. Technological upgrades have recently been made to this plant to increase the waste disposal activity up to a total of 180,000 tons/y. Currently, the plant has three emission lines and an 80 m chimney stack. In 2010, as a part of the integrated environmental authorization process issued by the authorization body (Provincia di Modena) to authorise the increase of waste disposal activity, a HBM cross-sectional pilot study was conducted to investigate possible biomarkers of exposure related to incinerator emissions.

Biological monitoring of human exposure to pollutants presents several challenges because of the low concentrations of substances to be measured in complex biological matrices, the difficulty in interpreting results due to the many exposure sources (e.g., air pollution, diet, and personal habits), and several genetic and environmental factors affecting the response of any given individual. In this study the selection of biomarkers to be investigated was based on several considerations: information on the types of pollutants emitted by SWIs and their toxicological relevance, findings of previous studies (see references given above), availability of sensitive and specific biomarkers to be assayed in easily accessible specimens, and costs. The process led to a focus on the determination of the following biomarkers: blood lead (B-Pb), blood cadmium (B-Cd) and blood mercury (B-Hg); serum copper (S-Cu) and serum zinc (S-Zn); urinary lead (U-Pb), urinary cadmium (U-Cd), urinary copper (U-Cu), urinary zinc (U-Zn), urinary manganese (U-Mn) and urinary nickel (U-Ni); urinary polycyclic aromatic hydrocarbons (PAHs); biomarkers of benzene (urinary S-phenylmercapturic acid, SPMA; and benzene, BEN); and other monoaromatic hydrocarbons (urinary toluene, TOL; ethylbenzene, EtBEN; xylenes, Xyl, all together BTEX). Tobacco smoking was assessed by measuring urinary cotinine (COT) (Table 1).

The overall objective of this pilot study was to scrutinise the capability of exposure biomarkers to highlight, at a detectable level, the exposure to selected pollutants in the population living in areas exposed to SWI emissions. In addition, information collected during the study was used to evaluate the feasibility of this type of study, such as the compliance of the target population, the technical and logistical constraints and the suitability of operative procedures.

2. Methods

2.1. Study population

The field study was conducted between May and June 2010 in Modena, Italy, a medium-sized town (180,000 residents) located in the middle of the Emilia-Romagna region, in the Po Valley. The SWI is located in the industrial/rural area of Modena, northwest of the town centre.

A circular area (radius of 4 km), centred on the incinerator, was defined as the exposure area. This was based on the previous knowledge of incinerator PM fall-out maps and air monitoring campaigns (Ranzi et al., 2011). Approximately 38% of the whole municipal population lives in this area. The area outside, but within 15 km, of the incinerator was defined as the non-exposure area. Inhabitants working and residing within the circular exposure area were defined as exposed subjects, while those working and residing outside the exposure area were considered unexposed subjects (controls).

The exposed group was recruited at the department of public health, local health unit (USL) of Modena, the main building of which is located less than 2 km away from the plant itself. The control group was recruited at the teaching hospital of Modena (Policlinico), which is located outside the exposure area, about 6 km from the incinerator. Among all workers, eligible subjects were identified based on the location of their residence (geo-referenced) using the street number database provided by the cartographic service of the Emilia-Romagna region. Another recruitment criterion was working and residing at the present location for at least three years. All eligible subjects were invited to join the study by e-mail and/or by phone call. A total of 168 participants were recruited, of which 65 fell into the exposed group and 103 into the unexposed group (Table 2).

Each participant completed an ad hoc questionnaire to evaluate personal and professional characteristics, personal habits and lifestyle with particular attention to smoking and diet. Traffic near the home was evaluated using a subjective judgement of the presence and amount of soot on the windowsill.

The study was approved by the ethical committee of the Local Health Authority of Modena. All subjects were informed about the goal and protocol of the study and signed an informed consent.

2.2. Environmental exposure

In addition to the binary classification of exposure based on the recruitment criteria, two other exposure variables were evaluated: the distance of each subject's residence from the incinerator and the average exposure to incinerator PM.

The distance (km) was calculated as the linear distance from each individual geo-referenced location of residences to the solid waste incinerator. Subjects were than categorised into four groups based on their distance, each group with roughly the same number of individuals (Table 2).

The average exposure to incinerator PM (ng/m^3) was calculated using simulation modelling of the PM emitted from the incinerator for a period of 30 d prior to the sampling date, taking into account the concentration values of the monthly fall-out pollution maps. This time lag was chosen as representative of an average exposure, irrespective of atmospheric conditions and plant work load. The pollution maps were provided by the Environmental Regional Agency (ARPA Emilia Romagna Provincial Department of Modena). The software used for the simulations was the quasi-Gaussian model Atmospheric Dispersion Modelling System (ADMS) Urban 2.2 (Cambridge Environmental Research Consultants, Cambridge, UK). The maps account for a 7 × 8 km

Table 1
Summary of the investigated biomarkers, biological matrices (B blood, S serum, U urine), limit of quantification (LOQ), analytical techniques, and reference values (RV).

Analytes	Abbreviation	Biological matrix	Unit	LOQ	Analytical technique	RV all subjects	RV non-smokers	RV smokers
Lead	B-Pb	B	μg/L	10	GF-AAS	11–30		
Cadmium	B-Cd	B	μg/L	0.2	GF-AAS	<1.5		
Copper	S-Cu	S	μg/L	150	GF-AAS	600–1600		
Zinc	S-Zn	S	μg/L	100	F-AAS	800–1600		
Mercury	B-Hg	B	μg/L	0.1	ICP/MS	1.0–4.5		
Lead	U-Pb	U	μg/L	0.05	ICP/MS	0.01–2.0		
Cadmium	U-Cd	U	μg/L	0.02	ICP/MS		0.1–1.0	0.1–1.5
Copper	U-Cu	U	μg/L	5	GF-AAS	4–15		
Zinc	U-Zn	U	μg/L	70	F-AAS	250–650		
Manganese	U-Mn	U	μg/L	0.1	ICP/MS	0.2–4.0		
Nickel	U-Ni	U	μg/L	0.1	ICP/MS	0.1–5.0		
Creatinine	crt	U	g/L	0.1	UV	0.3–3.0		
Cotinine	COT	U	μg/L	0.1	LC–MS/MS		≤30[a]	>30[a]
S-phenylmercapturic acid	SPMA	U	μg/L	0.10	LC–MS/MS		<0.25[b]	≤6[b]
Benzene	BEN	U	ng/L	15	GC/MS		≤200[b]	≤2700[b]
Toluene	TOL	U	ng/L	15	GC/MS		≤500[c]	≤700[c]
Ethylbenzene	EtBen	U	ng/L	15	GC/MS	≤130[b]		
m + *p*-xylene	m + p-Xyl	U	ng/L	15	GC/MS		≤165[c]	≤215[c]
o-Xylene	o-Xyl	U	ng/L	15	GC/MS		≤60[c]	≤80[c]
Naphthalene	Nap	U	ng/L	5.4	GC/MS	na		
Acenaphthylene	Acy	U	ng/L	1.7	GC/MS	na		
Acenaphthene	Ace	U	ng/L	1.7	GC/MS	na		
Fluorene	Flu	U	ng/L	1.1	GC/MS	na		
Phenanthrene	Phe	U	ng/L	0.5	GC/MS	na		
Anthracene	Ant	U	ng/L	0.5	GC/MS	na		
Pyrene	Pyr	U	ng/L	0.5	GC/MS	na		
Fluoranthene	Flt	U	ng/L	1.1	GC/MS	na		
Benz[a]anthracene	BaA	U	ng/L	1.5	GC/MS	na		
Chrysene	Chr	U	ng/L	0.6	GC/MS	na		

na = not available.
[a] Fustinoni et al. (2013).
[b] Fustinoni et al. (2011).
[c] Fustinoni et al. (2010b).

area around the incinerator, and include all the residents within the municipality of Modena. PM was calculated by taking the weighted average concentrations of the monthly fall-out pollution maps from the incinerator estimated at the place of residence ($PM_{residence}$) and work (PM_{work}). Assumed exposure durations were 16 h/d for the residential exposure and 8 h/d for working exposure:

$$PM = 8/24\ PM_{work} + 16/24\ PM_{residence}$$

The subjects were categorised into five groups of roughly the same size based on their average exposure to PM (Table 2).

2.3. Sample collection and biological monitoring

Specimen collection was performed in the morning and subjects were asked to refrain from having breakfast. For determination of blood and serum metals, samples were collected using a standardised

Table 2
Summary of study subject characteristics divided according to different exposure categories.

	Categories of exposure based on recruitment criteria		Categories of exposure based on distance of residence from the SWI (km)				Categories of PM exposure based on fall-out maps (ng/m^3)					Total
	Exposed	Unexposed	<3.0	3.0–<4.5	4.5–5.5	>5.5	<0.65	0.65–<0.725	0.725–<0.85	0.85–1.00	>1.00	
Enrolled, n	65	103	29	49	50	40	41	29	30	35	33	168
Male, n, (%)	29 (44.6)	46 (44.7)	16 (55.2)	20 (40.1)	24 (48.0)	15 (37.5)	15 (36.6)	11 (37.9)	17 (56.7)	14 (40.0)	18 (54.5)	75 (44.6)
Age, year (mean ± SD)	48.2 ± 6.2	48.1 ± 6.8	49.1 ± 5.9	48.0 ± 7.6	48.1 ± 6.0	47.7 ± 5.7	49.6 ± 5.3	47.9 ± 6.2	46.9 ± 6.4	48.3 ± 6.5	47.4 ± 7.4	48.1 ± 6.4
BMI, kg/cm^2 (mean ± SD)	24.5 ± 4.1	25.6 ± 4.6	24.3 ± 3.6	24.9 ± 4.4	26.0 ± 5.0	25.2 ± 4.3	24.7 ± 4.8	25.6 ± 4.8	26.4 ± 5.1	249. ± 4.0	24.6 ± 3.2	25.2 ± 4.4
Education, n (%)												
Secondary school	6 (9.5)	18 (17.5)	5	3	8	8	4	6	5	5	4	24 (14.5)
High school	28 (44.4)	56 (54.4)	16	19	26	23	22	16	11	19	16	84 (50.6)
Degree	29 (46.0)	29 (28.2)	7	26	16	9	15	6	14	10	13	58 (34.9)
Missing	2		1	1	–	–	–	1	–	1	–	
Smoking (questionnaire), n (%)												
Smokers	15 (23.8)	20 (19.6)	1	18	12	4	8	5	4	12	6	35 (21.2)
Ex-smokers	21 (33.3)	32 (31.4)	8	18	15	12	14	11	8	8	12	53 (32.1)
Non-smokers	27 (42.9)	50 (49.0)	19	12	23	23	19	11	18	15	14	77 (46.7)
Missing	2	1	1	1	–	1	–	2	–	–	1	3
Smoking (based on cotinine), n (%)												
Smokers	15 (23.1)	23 (22.3)	1	17	14	6	11	6	5	11	5	38 (22.6)
Non-smokers	50 (76.9)	80 (77.7)	28	32	36	34	30	23	25	24	28	130 (77.4)

needle and stored in suitable trace element free tubes for the analysis of the various markers. In particular, three 6 mL aliquots were collected for the analysis of S-Zn and S-Cu, B-Pb and B-Cd, and B-Hg, respectively. For urinary biomarkers, urine spot samples (about 40 mL) were collected at the first morning void in disposable polyurethane bottles. For urinary BTEX and PAHs, two aliquots (6 mL each) were poured immediately into pre-evacuated and thermally-cleaned 8 mL glass vials, capped with a rubber lid with a PTFE lining and crimped with an aluminium seal to prevent the loss of volatile chemicals. For the analysis of SPMA, metals, cotinine and creatinine, 2 mL urine aliquots were stored in polyethylene tubes. Once in the laboratory, samples were stored at −20 °C and analysed within 60 d, according to the analyte stability protocol.

B-Pb, B-Cd, S-Cu and U-Cu were measured by graphite furnace atomic absorption spectrometry (GF-AAS, Thermo Scientific), while S-Zn and U-Zn were determined using flame atomic absorption spectrometry (F-AAS). B-Hg, U-Pb, U-Cd, U-Mn and U-Ni were measured by inductively coupled plasma mass spectrometry (ICP-MS, Thermo Scientific) combined with a collision cell to reduce interferences, in the presence of gallium, rhodium and iridium as internal standards. For each analyte, accuracy and precision were assessed by internal quality controls using certified reference materials (Seronorm, Sero, Norway) and by the participation in external quality control assessments.

Urinary BEN, TOL, EtBen, *m* + *p*-xylene (m + p-Xyl) and *o*-xylene (o-Xyl) were measured by headspace solid-phase microextraction (HS-SPME) followed by gas chromatography/mass spectrometry analysis (CG/MS). Prior to analysis, samples were spiked with deuterated internal standards (benzene-d6, toluene-d8 and p-xylene-d10) (Fustinoni et al., 1999, 2010a).

Urinary SPMA was measured using a liquid chromatography/triple quadruple mass detector (LC-MS/MS) with a heated electron spray ionisation source, after acid hydrolysis of urine samples and solid phase extraction, in the presence of SPMA-d2 as an internal standard (Fustinoni et al., 2010a).

Urinary PAHs (naphthalene, Nap; acenaphthylene, Acy; acenaphthene, Ace; fluorene, Flu; phenanthrene, Phe; anthracene, Ant; fluoranthene, Flt; pyrene, Pyr; benz[a]anthracene, BaA; chrysene, Chr) were measured by solid-phase microextraction (SPME) followed by GC/MS. Prior to analysis, samples were spiked with a mixture containing seven deuterated PAHs as internal standards (Campo et al., 2011).

Urinary COT, a surrogate metric for tobacco smoking, was determined using LC-MS/MS, in the presence of cotinine-d3 as an internal standard (Fustinoni et al., 2013).

Urinary creatinine was determined using Jaffe's colorimetric method (Kroll et al., 1986).

A summary of biomarkers, biological matrices, limits of quantification (LOQ), analytical techniques, and reference values (RV) for each biomarker is provided in Table 1. RV refer either to those suggested in 2011 by the Italian Society for Reference Values (SIVR, 2011) or to the specific experience of the laboratory where the analyses were performed (Fustinoni et al., 2010b, 2011, 2013).

2.4. Statistical analysis

For statistical analyses, any analytical value less than the limit of quantification (LOQ) was replaced with one half the LOQ (LOQ/2) (ISS, 2004). In exposed and unexposed subjects the distribution of each analyte was described by the percentage of sample above the LOQ, arithmetic mean, median, and 5th and 95th percentiles.

Comparison between groups and the multiple regression analysis were performed only for analytes with at least 50% of the data above the LOQ. The comparison was performed using the ratio of medians, and both a non-parametric test (Wilcoxon rank-sum/Mann–Whitney, MW) and a parametric test (Student's *t* test, tS) were employed on log-transformed data to obtain the normal distribution. As U-Ni was abnormally elevated, its levels were not further considered for statistical analysis.

For analytes with more than 50% of the data below the LOQ, the comparison between groups was performed using the one-tail (left) analysis and the chi-square test. The differences between groups were considered statistically significant at $p < 0.05$. To evaluate the associations between the study biomarkers and exposure to SWI emissions, according to the exposure categories based on recruitment criteria (exposed subjects = 1 and unexposed subjects = 0), distance of subjects' residence from the SWI, and exposure to PM based on fall-out maps, a multivariate linear regression analysis was performed. An initial "a priori" model was applied to all biomarkers, using age, gender, BMI, education level, urinary creatinine and smoking habit as covariates. A second "a posteriori" model was applied to account for the confounding factors (diet items, traffic, dental amalgams) found to have a significant effect in a preliminary regression analysis of our data, or known to affect biomarkers based on previous reports (IARC, 2010; Nordberg et al., 2007). These factors are reported in the Supplementary table.

Statistical analysis was performed using the Stata 12 package (StataCorp LP, College Station, TX, USA).

3. Results

3.1. Study population

The characteristics of the study subjects, divided according to different exposure categories, are shown in Table 2. Although there were more unexposed than exposed subjects in the study, a balance was achieved for gender (55% women and 45% men) and age (mean of 48 y). The median of the body mass index (BMI) was slightly higher in the unexposed subjects, but subjects in both groups were in the "normal weight" range. Level of education was different between the two groups, with a higher percentage of exposed subjects having graduated. With regard to tobacco smoking, data are reported using results from the questionnaire responses and measurement of urinary cotinine, dividing subjects into active smokers (urinary cotinine > 30 μg/L) and non-smokers (urinary cotinine ≤ 30 μg/L). Regarding location and configuration of the subject residences, there was a higher percentage of exposed subjects who reported having windows that overlooked busy streets, with sills that were dirty with soot, compared to the unexposed subjects. Conversely, a higher percentage of unexposed subjects reported having busy junctions/intersections and/or heavier bus and truck traffic in the vicinity of the house. There were no substantial differences in eating/food habits between the two groups, although the diet of unexposed subjects appeared healthier and more balanced, with a greater consumption of vegetables and fish, and lower consumption of animal fats, as well as lower alcohol (wine, beer and liquor) consumption (data not shown).

3.2. Environmental exposure

Study subjects lived a mean distance of 4.5 ± 1.6 km (range 0.7–8.9 km) from the SWI; 2.9 ± 0.8 km for exposed subjects and 5.5 ± 1.1 km for unexposed subjects. Based on this distance, subjects were categorised into four groups: <3 km, 3–<4.5 km, 4.5–5.5 km and >5.5 km. The characteristics of subjects included in each group are reported in Table 2.

The fall-out maps for the three months prior to biological sample collection are reported in Fig. 1. Mean personal exposure to incinerator PM estimated using the fall-out maps was 0.87 ± 0.37 ng/m^3; exposed and unexposed subjects had a mean PM exposure level of 1.02 ± 0.53 and 0.77 ± 0.14 ng/m^3, respectively. Based on these PM data, exposure subjects were categorised into five groups: <0.65 ng/m^3, 0.65–<0.725 ng/m^3, 0.725–<0.85 ng/m^3, 0.85–1 ng/m^3 and >1 ng/m^3. The characteristics of the subjects included in each group are reported in Table 2.

The relationships between the exposure categories based on recruitment criteria, distance of residence from the SWI, and exposure to PM based on fall-out maps are shown in Fig. 2.

3.3. Biological monitoring

Measurable concentrations of metals were found in the majority of biological fluid samples (Table 3). No significant differences between exposed and unexposed subjects were observed for blood, serum or urinary metals, but a significant difference was found for U-Cu, with higher values in unexposed subjects. The comparison with RV (Table 1) showed that B-Cd, S-Cu, S-Zn, U-Pb, U-Cd and U-Mn were within the range of values normally detected in the Italian general population, while the other metals were up to 2.6-fold higher than the upper reference values. Abnormal values were found for U-Ni, for which concentrations up to 4-fold higher than expected values were observed both in exposed and in unexposed subjects.

Urinary BTEX were above the LOQ in all samples, with no differences between exposed and unexposed subjects, although there was a tendency to values >1 for the ratio of the medians. SPMA, a specific metabolite of benzene, was above the LOQ in 80% of the exposed subjects but only 29% of the unexposed subjects.

Five PAH analytes, Nap, Flu, Phe, Ant and Pyr were detected in more than 50% of the samples. Phe, Ant and Pyr were significantly higher among exposed subjects. The one-tailed analysis conducted on analytes for which the number of values <LOQ was greater than 50% showed significant differences between exposed and unexposed subjects for Ace, Ant, BaA and Chr.

The data suggest that certain lifestyle factors, specifically traffic exposure, diet and dental amalgams, had a significant effect on some of the investigated biomarkers, as reported in the Supplementary table.

3.4. Multivariate linear regression analysis to evaluate the effect of SWI exposure

Serum, blood and urinary metals and urinary PAHs were used as dependent variables and the different exposure indices were included as independent variables in the multiple linear regression analyses (Table 4). The sign of the β vector ("slope") of the linear regression varied depending on the indices of exposure, and is expected to be positive for exposed vs. unexposed subjects and for exposure to PM, but negative for the distance between subjects' residence and the SWI plant.

Considering the first exposure variable (exposed vs. unexposed), a positive and significant correlation was found for U-Zn and Ant both in the "a priori" and in the "a posteriori" models. An additional positive, though less significant, correlation was found for S-Cu in the "a priori" model, but not in the "a posteriori" model. An unexpected negative correlation was found for U-Cu and Nap.

Several significant correlations were found for the variable distance of residence from the SWI; these correlations corresponded to the expected sign for B-Cd, U-Mn, Phe, Ant and Pyr in both the "a priori" and the "a posteriori" models. The concentrations of S-Cu, B-Hg and Flu were inversely correlated with the distance from the SWI, but only in the "a priori" model or the "a posteriori" model, but not both.

Considering exposure to PM, a positive correlation was identified with the levels of U-Mn, Flu and Phe in both the "a priori" and the "a posteriori" models. The correlation was negative with the levels of B-Pb and S-Zn.

The multivariate linear regression analysis performed on urinary BTEX and SPMA did not show any significant relationships (results not shown).

Fig. 3 shows, for selected biomarkers, forest plots with correlation coefficients (and confidence interval) for the different categories of distance of residence from the SWI, considering the highest exposure category (<3 km) as the reference. Similarly, Fig. 4 shows the correlation coefficients (and confidence interval) for the different categories of exposure to PM, considering the lowest exposure category (<0.65 ng/m^3) as the reference.

4. Discussion

In this study a human biomonitoring protocol was applied to assess the exposure to SWI emissions in a group of the general population living and working in the proximity of the plant. The spatial criteria for the recruitment of the study population were based on the definition of a circular area with a 4 km radius around the SWI plant, from which the exposed subjects were selected (Ranzi et al., 2009, 2011). This area includes the highest concentration of the relapse fumes, as shown in the fall-out maps (Fig. 1), but it doesn't represent homogeneous exposure throughout, neither does it take into account atmospheric conditions such as the direction of dominant winds (NW–SE). Realistically, there is an exposure gradient associated with the distance from the source. Due to this limit, two additional a-posteriori exposure variables were defined. The first was the distance of the dwelling from the plant, which incorporates the concept of continuous exposure gradient, but does not take into account the occupational location (where the subject works), nor does it consider the actual shape of relapse emissions. The second variable was calculated based on the fall-out dispersion maps, according to the months of recruitment of the study population. This allowed for the derivation of the personal exposure to PM, and is expected to be a more accurate exposure variable, in accordance with previous information (Floret et al., 2006; Forastiere et al., 2011). Both models were previously used to assess exposure to incinerator emissions

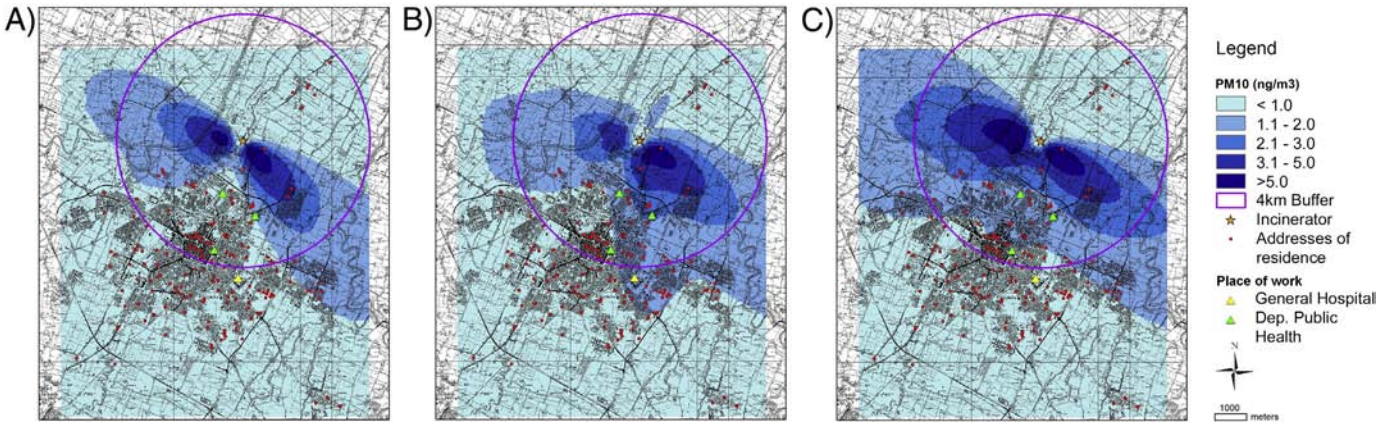

Fig. 1. Fall-out maps of SWI particulate matter (PM) emission in the three months (April, May and June 2010) prior to the collection of biological samples.

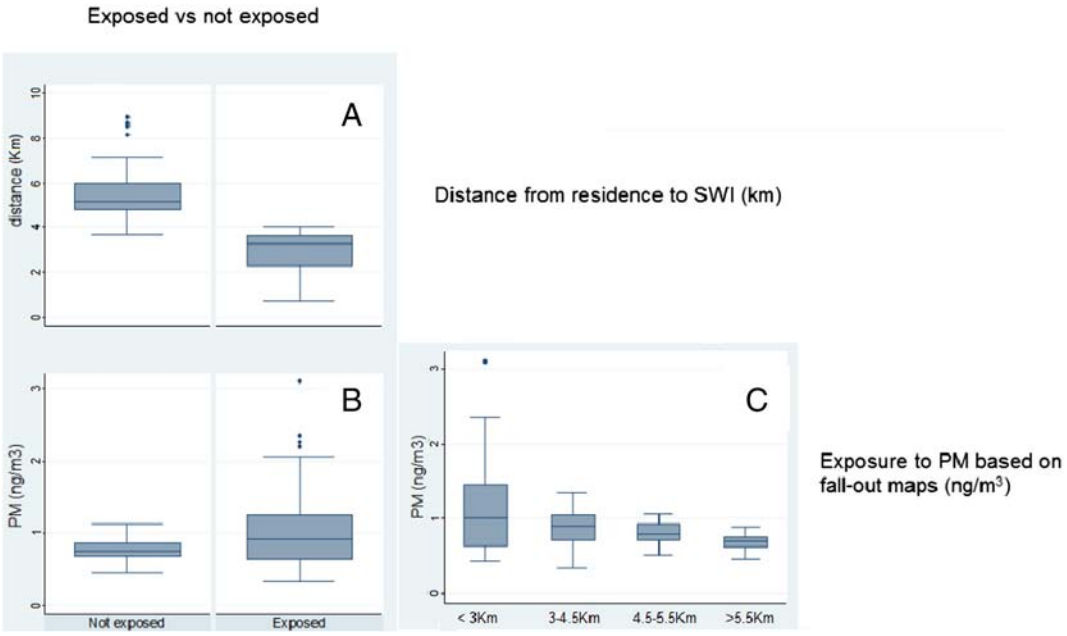

Fig. 2. Relationship between the categories of exposure based on recruitment criteria (exposed and unexposed subjects), A) distance of residence from the SWI, B) PM exposure concentration for exposed or unexposed subjects and C) PM exposure concentration depending on a distance from SWI based on fall-out maps.

(Floret et al., 2006; Ranzi et al., 2011). A specific validation study demonstrated the models' reliability where topography was relatively simple, such as in the current study area (Floret et al., 2006). The relationships between the exposure variables were generally good (Fig. 2). The results of the study suggest that these a-posteriori exposure variables better define the influence of the incinerator on the study population exposure.

Controlling the sources of variability is one of the critical issues associated with the application of biomonitoring in the study of

Table 3
Summary statistics for biomarkers of exposure to metals, tobacco smoke (cotinine), BTEX and PAHs in exposed and unexposed subjects.

Biomarkers	Unit	Exposed (n = 65)				Unexposed (n = 103)				Ratio exposed/unexposed	*p*MW	*p*tS
		% > LOQ	Mean	Median	5th–95th percentiles	% > LOQ	Mean	Median	5th–95th percentiles			
B-Pb	μg/L	80.0	27	26	<10–55	86.4	24	21	<10–52	1.22	0.31	>0.50
B-Cd	μg/L	83.1	0.5	0.3	<0.2–1.3	77.7	0.5	0.3	<0.2–1.4	1.02	>0.50	>0.50
S-Cu	μg/L	100.0	992	939	616–1564	100.0	924	866	637–1378	1.09	0.1	0.11
S-Zn	μg/L	100.0	1261	1240	1020–1559	100.0	1291	1290	1065–1550	0.96	0.32	0.18
B-Hg	μg/L	100.0	4.2	3.1	1.0–11.9	100.0	4.5	3.5	0.9–11.0	0.9	>0.50	>0.50
U-Pb	μg/L	100.0	0.52	0.33	0.1–1.5	100.0	0.40	0.26	0.1–1.2	1.23	0.22	0.29
U-Cd	μg/L	100.0	0.22	0.19	0.05–0.46	100.0	0.19	0.16	0.07–0.35	1.00	>0.50	>0.50
U-Cu	μg/L	95.3	13	11	5–23	100.0	14	13	6–26	0.92	0.03	0.01
U-Zn	μg/L	92.3	411	352	<70–1250	85.5	395	339	<70–1144	0.97	0.44	0.11
U-Mn	μg/L	98.5	0.69	0.18	<0.1–2.7	100.0	0.59	0.18	0.1–2.7	1.00	>0.50	>0.50
U-Ni	μg/L	100.0	8.68	6.98	2.7–19.7	100.0	7.88	7.58	1.7–17.5	0.87	>0.50	>0.50
COT	μg/L	100.0	197.8	0.7	0.3–1172.0	100.0	202.9	0.8	0.2–1578.0	0.87	>0.50	>0.50
SPMA	μg/L	80.0	0.43	<0.10	<0.10–2.37	29.1	0.54	<0.10	<0.10–3.83	0.75	0.34	0.39
BEN	ng/L	100.0	505	128	41–960	100.0	347	117	41–2406	0.81	0.12	0.12
TOL	ng/L	100.0	203	185	121–293	100.0	233	185	108–425	0.92	>0.50	0.22
EtBen	ng/L	100.0	55	50	26–98	100.0	61	37	21–104	1.36	0.09	0.40
m + p-Xyl	ng/L	100.0	131	115	72–199	100.0	126	100	63–205	1.11	0.37	>0.50
o-Xyl	ng/L	100.0	39	33	22–60	100.0	40	32	19–65	1.09	>0.50	>0.50
Nap	ng/L	100.0	50.8	48.1	23.9–83.5	100.0	54.5	45.7	24.6–122.3	1.02	>0.50	>0.50
Acy	ng/L	9.2	2.4	<1.7	<1.7–3.7	4.9	1.0	<1.7	<1.7–<1.7	na	na	na
Ace	ng/L	53.9	3.0	1.9	<1.7–9.8	17.5	2.3	<1.7	<1.7–11.1	na	na	na
Flu	ng/L	87.7	3.2	1.9	<1.1–10.4	92.2	2.6	1.9	<1.1–4.6	0.87	>0.50	>0.50
Phe	ng/L	100.0	10.5	9.5	5.0–20.8	100.0	8.5	7.2	3.5–16.9	1.15	0.05	0.10
Ant	ng/L	73.9	0.9	0.8	<0.5–2.3	44.7	0.6	<0.5	<0.5–1.9	1.81	<0.01	<0.01
Pyr	ng/L	98.5	1.7	1.6	0.7–2.8	97.1	1.5	1.3	<0.5–2.8	1.27	0.02	0.13
Flt	ng/L	32.3	<1.1	<1.1	<1.1–2.0	27.2	<1.1	<1.1	<1.1–2.2	na	na	na
BaA	ng/L	20.0	<1.5	<1.5	<1.5–2.3	1.9	<1.5	<1.5	<1.5–<1.5	na	na	na
Chr	ng/L	23.1	<0.6	<0.6	<0.6–1.1	6.8	<0.6	<0.6	<0.6–0.6	na	na	na

% > LOQ: percentage of samples above LOQ.
Ratio E/NE = ratio between the median level of biomarker in exposed and unexposed subjects.
*p*MW = *p* for Mann Whitney comparison between exposed and unexposed subjects.
*p*tS = p for t-Student comparison between exposed and unexposed subjects.
na = not applicable for the low number of samples above LOQ.

Table 4
Beta coefficients and significances of multiple linear regression analysis performed using serum, blood, and urinary metals and urinary PAHs as dependent variables and different exposure indices as independent variables in the "a priori" model (age, gender, BMI, education level, urinary creatinine and smoking habit), and in the "a posteriori" model ("a priori" and other variables specifically introduced for each biomarker).

	Exposed vs. unexposed		Distance of residence from the SWI (km)		Exposure to PM based on fall-out maps (ng/m^3)	
	β "a priori" model	β "a posteriori" model	β "a priori" model	β "a posteriori" model	β "a priori" model	B "a posteriori" model
B-Pb	ns	ns	ns	ns	−0.10**	−0.10**
B-Cd	ns	ns	−0.13*	−0.20*	ns	ns
S-Cu	0.07*	ns	−0.04**	ns	ns	ns
S-Zn	ns	ns	ns	ns	−0.02**	−0.02*
B-Hg	ns	ns	ns	−0.21**	ns	ns
U-Pb	ns	ns	ns	ns	ns	ns
U-Cd	ns	ns	ns	ns	ns	ns
U-Cu	−0.21**	−0.22**	0.06*	ns	ns	ns
U-Zn	0.33*	0.38**	ns	ns	ns	ns
U-Mn	ns	ns	−0.20*	−0.27**	0.16**	0.14*
U-Ni	na	na	na	na	na	na
Nap	ns	−0.16*	ns	ns	ns	ns
Flu	ns	ns	ns	−0.24**	0.11**	0.11**
Phe	ns	ns	−0.12**	−0.13**	0.05*	0.04*
Ant	0.39**	0.38**	−0.19**	−0.18*	ns	ns
Pyr	ns	ns	−0.10**	−0.12**	ns	ns

ns = not significant; na = the statistical analysis was not performed due to the abnormal values found for U-Ni.
** $p < 0.05$.
* $p < 0.1$.

environmental exposure. To account for this variability, a detailed questionnaire was employed to collect information about potential confounding variables. This exercise was specifically focused on 1) items in the diet that are known to be potential sources of selected chemicals (Nordberg et al., 2007) and 2) habits and actions that elicit exposure to traffic exhaust (a selection of these variables is reported in the Supplementary table). In addition, dental amalgams were considered a source of mercury in this study. Special attention was devoted to tobacco smoking, since it is a potential source of a myriad of harmful chemicals that may impact biomonitoring results. For this reason, in addition to the questionnaire information, quantitative data on urinary cotinine (a nicotine metabolite) was obtained. The results of this assessment were sufficient to allow us to propose 30 μg/L as a cotinine threshold above which active tobacco smoke exposure could be discerned. Based on this value it was possible to correctly classify 6.5% of the study subjects who 1) had not provided smoking information (1.5%) and 2) had incorrectly self-classified themselves (5%) (Table 2) (see also Fustinoni et al., 2013).

The fact that some metal concentrations were higher than expected with respect to reference values may have been due to differences in analytical technique (Tables 2 and 3). AAS and ICP-MS may lead to different results due to differences in the manner in which the two methods handle matrix interferences. As the U-Ni values were abnormally high, our working hypothesis is that a contamination has occurred in the sample collection/storage/analysis procedure; this hypothesis will be tested in the ongoing study on a larger population sample. No differences were found between exposed and unexposed samples (Table 3). This result is in accordance with those reported in other recent studies investigating exposure to heavy metals in populations living near incinerators of municipal solid waste (Nadal et al., 2005; Gonzalez et al., 2000; Fierens et al., 2007; Reis et al., 2007; Ferré-Huguet et al., 2009). Indeed, out of several studies, only two reported higher urinary Cd or Pb in subjects living near a SWI (Schroijen et al., 2008; Zubero et al., 2010). Considering the contribution of confounders, we found that urinary metals were influenced by factors such as cigarette smoking (Cu, Cd), ingestion of specific food and road traffic (Cd). The multiple linear regression analysis showed significant relationships between selected metal biomarkers and the exposure variables. In particular, U-Mn was inversely related to the distance of each subject's residence from the incinerator and directly associated with exposure to PM, while B-Cd was inversely correlated to the distance of residence from the SWI (Table 4, Figs. 3 and 4). These results are in agreement with recent evidence indicating that Mn was present at the highest level among the so-called heavy metals in fine and coarse fractions of PM collected downwind of an incinerator plant in Italy (Buonanno et al., 2010), and was elevated in soil and air near a SWI in Spain (Rovira et al., 2010).

The comparative evaluation of benzene and other BTEX biomarkers showed no significant differences between exposed and unexposed subjects. The analysis of confounders confirmed the influence of smoking habits on these biomarkers, especially for benzene, and the effect of variables associated with vehicular traffic; there were some significant associations related to some dietary items (see the Supplementary table). After grouping subjects according to active smoking, all values were within the laboratory reference ranges (Table 1). Moreover, the levels of BTEX biomarkers were comparable to those previously measured in adults and children residing in urban and rural areas (Fustinoni et al., 2005, 2010b, 2012; Lovreglio et al., 2011; Protano et al., 2012). Since the multiple linear regression analysis showed no effect of SWI exposure variables on the levels of BTEX biomarkers, we concluded that a SWI was not a significant source of BTEX exposure in the study subjects. Similar results were obtained in Spain, where no exposure difference to airborne VOCs, including BTEX, was found when sites near a SWI were compared to reference sites (Vilavert et al., 2009).

Recent studies suggest that simultaneous measurements of multiple PAH analytes are a preferable alternative to the measurement of single markers (typically urinary 1-hydroxypyrene) (Campo et al., 2010; Li et al., 2006; Sobus et al., 2009), as the former approach allows for the acquisition of a multi-chemical profile, inclusive of suspected carcinogens, such as Nap, found in all of our study subjects, and BaA and Chr, measured in 9% and 13% of subjects, respectively. Median urinary PAHs were in the low ng/L range; however, a comparison to reference values was not possible since reliable data on general population urinary PAH levels were not available. However, urinary PAH concentrations in our study were always lower than levels previously reported for occupationally-exposed individuals. For PAH analytes that were measured at significantly higher concentrations in the exposed group (Phe, Ant and Pyr), those concentrations were up to one order of magnitude lower than those observed in Italian workers exposed to bitumen fumes or diesel exhausts (Campo et al., 2007). The analysis of confounders confirms the influence of tobacco smoking on some PAHs (Phe, Ant and Pyr), and the effect of other variables associated with vehicular traffic (Phe, Ant). Some dietary items showed a significant influence, as indicated in the Supplementary table. The comparison

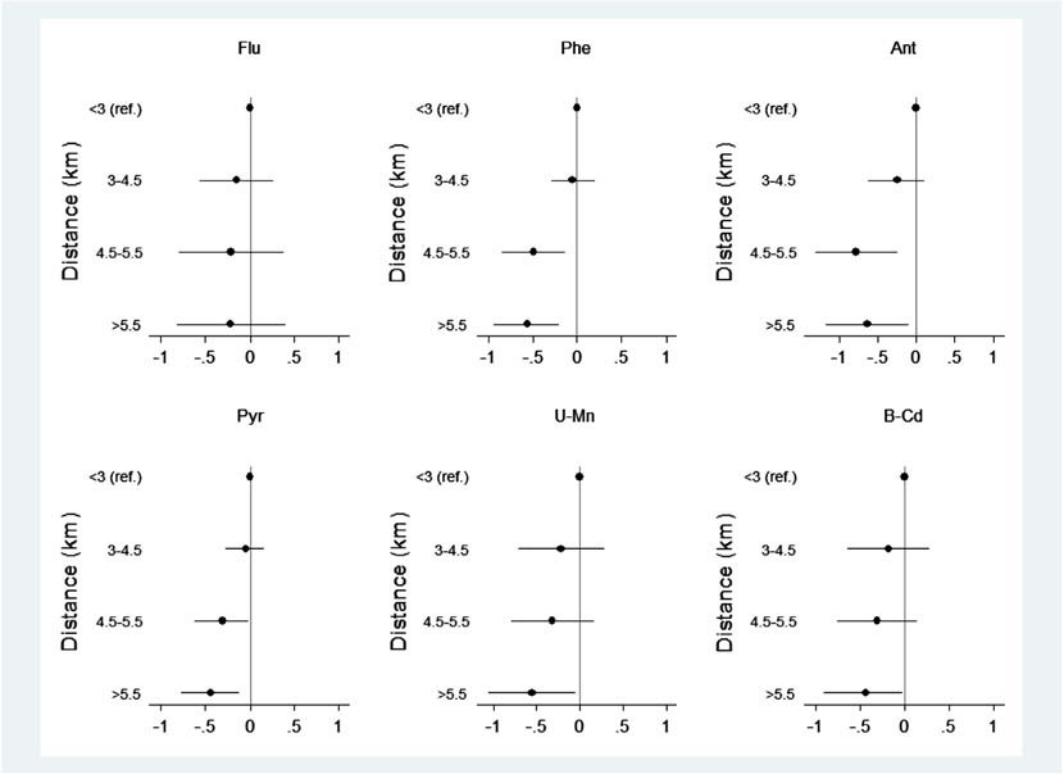

Fig. 3. Forest plots for selected biomarkers: the plots report the correlation coefficients (CI) for different categories of distance of residence from the SWI. The highest exposure category (<3 km) was considered the reference.

between groups showed significant differences for selected PAHs, i.e., Phe, Ant and Pyr were higher; Ace, Ant, BaA and Chr were at measureable levels in a higher percentage of exposed, than in unexposed, subjects (Table 3). This first result was further supported by multiple linear regression analysis that showed several significant relationships with all the investigated exposure variables, strongly suggesting that a

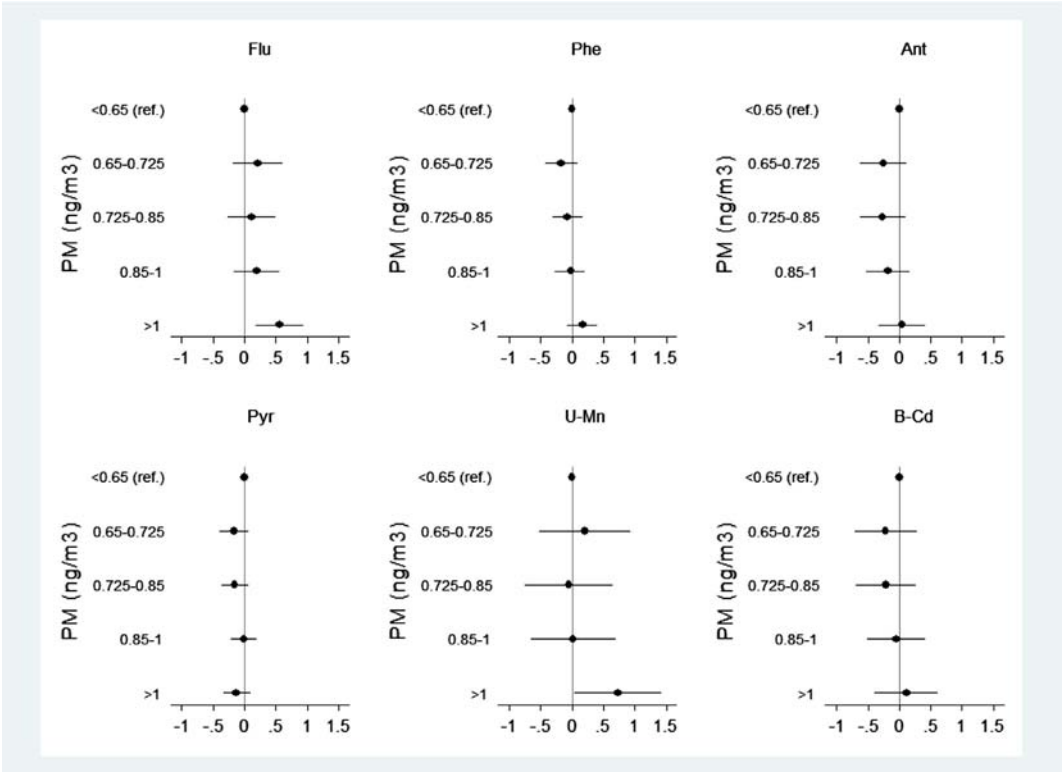

Fig. 4. Forest plots for selected biomarkers: the plots report the correlation coefficients (CI) for different categories of exposure to PM. The lowest exposure category (<0.65 ng/m^3) is considered the reference.

SWI is a significant source of PAHs to the study population (Table 4, Figs. 3 and 4). Similar reported results have not been identified in the extant literature, possibly due to the paucity of studies investigating PAH exposure from SWIs, and to the use of the only 1-hydroxypyrene as a biomarker of exposure (Maitre et al., 2003; Schroijen et al., 2008).

Overall, the implementation of this pilot study demonstrated the feasibility of a human biomonitoring investigation among the population living in the proximity of the SWI of Modena. The study provided substantive information regarding technical–logistical constraints as well as the suitability of operative procedures. An important consideration of this, and other investigations that incorporate data collection from a resident populace, is that the compliance of the target population could not be completely assessed since the recruited individuals were not representative of the entire population living and working in the proximity of the SWI. In fact, due to convenience criteria, recruitment was performed among the employees of two health facilities who were regarded as more available and motivated than others to volunteer for the study and provide accurate information. Moreover, it was not possible to assess bias associated with the individuals who refused to participate (which was around 23%). This is true even if there was no reason to believe that the "refusal" population was significantly different from the studied population by some determinant that could otherwise influence the concentration/levels of the measured biomarkers.

Another open issue is the proper use of short-term biomarkers, as those applied in the present study, to evaluate the average exposure arising from SWI in the previous 30 days. It may be useful to underline that the behaviour over time of these biomarkers is well known in a frame of occupational exposure, but in general population subjects it has been investigated poorly. Based on studies on repeated measurements (Lin et al., 2005) it has been shown that biomarkers have smaller variance than air measurements, particularly in environmental scenarios, and they provide a better surrogate of exposure than air measurement. Therefore we expect the applied biomarkers to give a picture of a steady-state status that takes into account several sources of exposure (i.e. diet, air pollution, personal habits), and include the equilibrium between different body compartments (e.g. accumulation sites/blood), rather than a short-term exposure.

The results of this pilot study suggest that the exposure to BTEX cannot be attributed to the presence of a SWI. If a SWI is contributing to BTEX exposure, the contribution is minimal and likely insignificant when compared to the primary sources such as active tobacco smoking and traffic emissions. In contrast, PAH exposure appears to be affected by the presence of the incinerator, and therefore the measurements of urinary PAHs seem to be relevant to detecting exposure to these persistent organic pollutants. Regarding metals, results suggest that some of them, especially Mn and Cd, may be associated with SWI emissions. These results strongly indicate that human biomonitoring can be an important component of epidemiological studies. To support the results obtained in the present pilot study, human biomonitoring will be included in a future study on a larger representative group of subjects living in the proximity of the investigated SWI.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.envint.2013.09.008.

References

Agramunt MC, Schuhmacher M, Hernandez JM, Domingo JL. Levels of dioxins and furans in plasma of nonoccupationally exposed subjects living near a hazardous waste incinerator. J Expo Anal Environ Epidemiol 2005;15:29–34.

Bocio A, Nadal M, Garcia F, Domingo JL. Monitoring metals in the population living in the vicinity of a hazardous waste incinerator: concentrations in autopsy tissues. Biol Trace Elem Res 2005;106:41–50.

Buonanno G, Stabile L, Avino P, Vanoli R. Dimensional and chemical characterization of particles at a downwind receptor site of a waste-to-energy plant. Waste Manag 2010:1325–33.

Campo L, Fustinoni S, Buratti M, Cirla PE, Martinotti I, Foà V. Unmetabolized hydrocarbons in urine as biomarkers of low exposure in asphalt workers. J Occup Environ Hyg 2007;4(S1):100–10.

Campo L, Rossella F, Pavanello S, Mielzynska D, Siwinska E, Kapka L, et al. Urinary profiles to assess polycyclic aromatic hydrocarbons exposure in coke-oven workers. Toxicol Lett 2010;192:72–8.

Campo L, Fustinoni S, Bertazzi PA. Quantification of carcinogenic 4- to 6-ring polycyclic aromatic hydrocarbons in human urine by solid-phase microextraction gas chromatography-isotope dilution mass spectrometry. Anal Bioanal Chem 2011;401:625–34.

Domingo JL, Schuhmacher M, Agramunt MC, Muller L, Neugebauer F. Levels of metals and organic substances in blood and urine of workers at a new hazardous waste incinerator. Int Arch Occup Environ Health 2001;74:263–9.

European Commission. Directive 2000/76/EC of the European Parliament and of the Council of 4 December 2000 on the incineration of waste. Brussels, Belgium: European Commission; 2000.

European Commission. Directive 2010/75/EU of the European Parliament and of the Council of 24 November 2010 on industrial emissions (integrated pollution prevention and control). Brussels, Belgium: European Commission; 2010.

Ferré-Huguet N, Nadal M, Schuhmacher M, Domingo JL. Monitoring metals in blood and hair of the population living near a hazardous waste incinerator: temporal trend. Biol Trace Elem Res 2009;128:191–9.

Fierens S, Mairesse H, Heilier JF, Focant JF, Eppe G, De PE, et al. Impact of iron and steel industry and waste incinerators on human exposure to dioxins, PCBs, and heavy metals: results of a cross-sectional study in Belgium. J Toxicol Environ Health A 2007;70:222–6.

Floret N, Viel JF, Lucot E, Dudermel PM, Cahn JY, Badot PM, et al. Dispersion modeling as a dioxin exposure indicator in the vicinity of a municipal solid waste incinerator: a validation study. Environ Sci Technol 2006;40:2149–55.

Forastiere F, Badaloni C, de Hoogh K, von Kraus MK, Martuzzi M, Mitis F, et al. Health impact assessment of waste management facilities in three European countries. Environ Health 2011;10:53.

Franchini M, Rial M, Buiatti E, Bianchi F. Health effects of exposure to waste incinerator emissions: a review of epidemiological studies. Ann Ist Super Sanita 2004;40:101–15.

Fustinoni S, Giampiccolo R, Pulvirenti S, Buratti M, Colombi A. Headspace solid-phase microextraction for the determination of benzene, toluene, ethylbenzene and xylenes in urine. J Chromatogr B Biomed Sci Appl 1999;723:105–15.

Fustinoni S, Consonni D, Campo L, Buratti M, Colombi A, Pesatori AC, et al. Monitoring low benzene exposure: comparative evaluation of urinary biomarkers, influence of cigarette smoking, and genetic polymorphisms. Cancer Epidemiol Biomarkers Prev 2005;14:2237–44.

Fustinoni S, Campo L, Mercadante R, Manini P. Methodological issues in the biological monitoring of urinary benzene and S-phenylmercapturic acid at low exposure levels. J Chromatogr B Biomed Sci Appl 2010a;878:2534–40.

Fustinoni S, Rossella F, Campo L, Mercadante R, Bertazzi PA. Urinary BTEX, MTBE and naphthalene as biomarkers to gain environmental exposure profiles of the general population. Sci Total Environ 2010b;408:2840–9.

Fustinoni S, Campo L, Mercadante R, Consonni D, Mielzynska D, Bertazzi PA. A quantitative approach to evaluate urinary benzene and S-phenylmercapturic acid as biomarkers of low benzene exposure. Biomarkers 2011;16:334–45.

Fustinoni S, Campo L, Satta G, Campagna M, Ibba A, Tocco MG, et al. Environmental and lifestyle factors affect benzene uptake biomonitoring of residents near a petrochemical plant. Environ Int 2012;39:2–7.

Fustinoni S, Campo L, Polledri E, Mercadante R, Erspamer L, Ranzi A, et al. A validated method for urinary cotinine quantification used to classify active and environmental tobacco smoke exposure. Curr Anal Chem 2013;9:447–56.

Gonzalez CA, Kogevinas M, Gadea E, Huici A, Bosch A, Bleda MJ, et al. Biomonitoring study of people living near or working at a municipal solid-waste incinerator before and after two years of operation. Arch Environ Health 2000;55:259–67.

Hodgson S, Nieuwenhuijsen MJ, Colvile R, Jarup L. Assessment of exposure to mercury from industrial emissions: comparing "distance as a proxy" and dispersion modelling approaches. Occup Environ Med 2007;64:380–8.

International Agency for Research on Cancer (IARC). IARC monographs on evaluation of carcinogenic risk of chemicals to humans. Overall evaluations of carcinogenicity: an updating of IARC monographs, volumes 1 to 42. Suppl. 7. Lyon, France: World Health Organization; 1987.

International Agency for Research on Cancer (IARC). IARC monographs on evaluation of carcinogenic risk of chemicals to humans. Polychlorinated, dibenzo-*para*-dioxins and polychlorinated dibenzofurans, vol 69. Lyon, France: World Health Organization; 1997.

International Agency for Research on Cancer (IARC). IARC monographs on evaluation of carcinogenic risk of chemicals to humans. Air pollution, part I. Some non-heterocyclic aromatic hydrocarbons and some related industrial exposures, vol 92. Lyon, France: World Health Organization; 2010.

International Agency for Research on Cancer (IARC). IARC monographs on evaluation of carcinogenic risk of chemicals to humans. A review of human carcinogens: arsenic, metals, fibres, and dusts, vol 100. Lyon, France: World Health Organization; 2012.

Istituto Superiore di Sanità (ISS). Trattamento dei dati inferiori al limite di rivelabilità nel calcolo dei risultati analitici. In: Menichini E, Viviano G, the Working group Istituto Superiore di Sanità, editors. Treatment of data below the detection limit in the calculation of analytical results. Metodiche per il rilevamento delle emissioni in atmosfera da impianti industriali. Rapporti ISTISAN 04/15Roma, Italy: Istituto Superiore di Sanità; 2004. [in Italian].

Kroll MH, Chesler R, Hagenbruger C, Blank DW, Kestner J, Rawe M. Automated determination of urinary creatinine without sample dilution: theory and practice. Clin Chem 1986;32:446–52.

Li Z, Romanoff LC, Trinidad DA, Hussain N, Jones RS, Porter EN, et al. Measurement of urinary monohydroxy polycyclic aromatic hydrocarbons using automated liquid-liquid extraction and gas chromatography/isotope dilution high-resolution mass spectrometry. Anal Chem 2006;78:5744–51.

Lin YS, Kupper LL, Rappaport SM. Air samples versus biomarkers for epidemiology. Occup Environ Med 2005;62:750–60.
Lovreglio P, D'Errico MN, Fustinoni S, Drago I, Barbieri A, Sabatini L, et al. Biomarkers of internal dose for the assessment of environmental exposure to benzene. J Environ Monit 2011;13:2921–8.
Maître A, Collot-Fertey D, Anzivino L, Marques M, Hours M, Stoklov M. Municipal waste incinerators: air and biological monitoring of workers for exposure to particles, metals, and organic compounds. Occup Environ Med 2003;60:563–9.
Nadal M, Bocio A, Schuhmacher M, Domingo JL. Monitoring metals in the population living in the vicinity of a hazardous waste incinerator: levels in hair of school children. Biol Trace Elem Res 2005;104:203–13.
Nordberg GF, Fowler BA, Nordberg M, Freeberg LT. Handbook on the toxicology of metals 3th ed. MA, USA: Academic Press; 2007.
Oh E, Lee E, Im H, Kang HS, Jung WW, Won NH, et al. Evaluation of immuno- and reproductive toxicities and association between immunotoxicological and genotoxicological parameters in waste incineration workers. Toxicology 2005;210:65–80.
Porta D, Milani S, Lazzarino AI, Perucci CA, Forastiere F. Systematic review of epidemiological studies on health effects associated with management of solid waste. Environ Health 2009;8:60.
Protano C, Andreoli R, Manini P, Guidotti M, Vitali M. A tobacco-related carcinogen: assessing the impact of smoking behaviours of cohabitants on benzene exposure in children. Tob Control 2012;21:325–9.
Ranzi A, Sartini C, Erspamer L, Rossi M, Candela S, Poluzzi V, et al. Exposure assessment of newborn babies near incinerators: a geographical approach. Epidemiology 2009;20:S79–80.
Ranzi A, Fano V, Erspamer L, Lauriola P, Perucci CA, Forastiere F. Mortality and morbidity among people living close to incinerators: a cohort study based on dispersion modelling for exposure assessment. Environ Health 2011;10:22.
Reis MF, Miguel JP, Sampaio C, Aguiar P, Melim JM, Papke O. Determinants of dioxins and furans in blood of non-occupationally exposed populations living near Portuguese solid waste incinerators. Chemosphere 2007;67:S224–30.
Rovira J, Mari M, Nadal M, Schuhmacher M, Domingo JL. Environmental monitoring of metals, PCDD/Fs and PCBs as a complementary tool of biological surveillance to assess human health risks. Chemosphere 2010;80:1183–9.
Rushton L. Health hazards and waste management. Br Med Bull 2003;68:183–97.
Schroijen C, Baeyens W, Schoeters G, Den Hond E, Koppen G, Bruckers L, et al. Internal exposure to pollutants measured in blood and urine of Flemish adolescents in function of area of residence. Chemosphere 2008;71:1317–25.
Sobus JR, McClean MD, Herrick RF, Waidyanatha S, Nylander-French LA, Kupper LL, et al. Comparing urinary biomarkers of airborne and dermal exposure to polycyclic aromatic compounds in asphalt-exposed workers. Ann Occup Hyg 2009;53:561–71.
Società Italiana Valori di Riferimento (SIVR). Terza lista dei valori di riferimento per elementi, composti organici e loro metaboliti (Third list of reference values for elements, organic compounds and their metabolites). Available on line at: www.valoridiriferimento.it; 2011 [Last accessed 3 May 2012].
Sul D, Oh E, Im H, Yang M, Kim CW, Lee E. DNA damage in T- and B-lymphocytes and granulocytes in emission inspection and incineration workers exposed to polycyclic aromatic hydrocarbons. Mutat Res 2003;538:109–19.
Toide K, Yamazaki H, Nagashima R, Itoh K, Iwano S, Takahashi Y, et al. Aryl hydrocarbon hydroxylase represents CYP1B1, and not CYP1A1, in human freshly isolated white cells: trimodal distribution of Japanese population according to induction of CYP1B1 mRNA by environmental dioxins. Cancer Epidemiol Biomarkers Prev 2003;12:219–22.
Vilavert L, Nadal M, Inza I, Figueras MJ, Domingo JL. Baseline levels of bioaerosols and volatile organic compounds around a municipal waste incinerator prior to the construction of a mechanical-biological treatment plant. Waste Manag 2009;29:2454–61.
Vinceti M, Malagoli C, Teggi S, Fabbi S, Goldoni C, De Girolamo G, et al. Adverse pregnancy outcomes in a population exposed to the emissions of a municipal waste incinerator. Sci Total Environ 2008;407:116–21.
World Health Organization (WHO). Population health and waste management: scientific data and policy options. Report of a WHO workshop, Rome, Italy. Copenhagen, Denmark: Regional Office for Europe; 2007.
Zubero MB, Aurrekoetxea JJ, Ibarluzea JM, Arenaza MJ, Rodríguez C, Sáenz JR. Heavy metal levels (Pb, Cd, Cr and Hg) in the adult general population near an urban solid waste incinerator. Sci Total Environ 2010;408:4468–74.