



Human biomonitoring as a tool for exposure assessment in industrially contaminated sites (ICSs). Lessons learned within the ICS and Health European Network

Ann Colles,¹ Elena-Roxana Ardeleanu,² Carla Candeias,^{3,4} Andrea Ranzi,⁵ Zoltan Demeter,⁶ Adam Hofer,⁶ Malgorzata Kowalska,⁷ Konstantinos C. Makris,⁸ Juan Pedro Arrebola,^{9,10,11} Greet Schoeters,¹ Rupert Hough,¹² Francisco Miguel Pérez-Carrascosa,⁹ Ivano Iavarone,^{13,14} Piedad Martin-Olmedo,^{11,15} Olga-Ioanna Kalantzi,¹⁶ Carla Ancona,¹⁷ Roberto Pasetto,^{12,13} Tony Fletcher,¹⁸ Gerard Hoek,¹⁹ Kees de Hoogh^{20,21}

¹ VITO, Mol (Belgium)

² “Vasile Alecsandri” University of Bacau (Romania)

³ EpiUnit, Public Health Institute, University of Porto (Portugal)

⁴ GeoBioTec, Geosciences Department, University of Aveiro, Santiago Campus, Aveiro (Portugal)

⁵ Center for Environmental Health and Prevention, Regional Agency for Prevention, Environment and Energy of Emilia-Romagna, Modena (Italy)

⁶ National Public Health Institute (Hungary)

⁷ Department of Epidemiology, School of Medicine, Medical University of Silesia, Katowice (Poland)

⁸ Water and Health Laboratory, Cyprus International Institute for Environmental and Public Health, Cyprus University of Technology, Limassol (Cyprus)

⁹ Department of Preventive Medicine and Public Health, University of Granada, Granada (Spain)

¹⁰ CIBER de Epidemiología y Salud Pública (CIBERESP) (Spain)

¹¹ Instituto de Investigación Biosanitaria de Granada (Ibs.GRANADA), Granada (Spain)

¹² James Hutton Institute, Craigiebuckler, Aberdeen (UK)

¹³ Department of Environment and Health, Italian National Health Institute (ISS), Rome (Italy)

¹⁴ WHO Collaborating Centre for environmental health in contaminated sites, Rome (Italy)

¹⁵ Escuela Andaluza de Salud Pública, Granada (Spain)

¹⁶ Department of Environment, University of the Aegean, Mytilene (Greece)

¹⁷ Epidemiology Department Lazio Regional Health Authority, Rome (Italy)

¹⁸ Public Health England, London (UK)

¹⁹ Institute for Risk Assessment Sciences, Utrecht University, Utrecht (The Netherlands)

²⁰ Swiss Tropical and Public Health Institute, Basel (Switzerland)

²¹ University of Basel, Basel (Switzerland)

Corresponding author: Ann Colles; ann.colles@vito.be

Supplementary materials

Description of the case studies

1. Case study for Belgium

Genk-Zuid is an industrial area of approximately 16 km², located in the Eastern part of Flanders (Belgium) with a diversity of industrial activities (more than 200 companies), such as a stainless steel plant, a car assembly plant (closed in 2014) and its suppliers, a glue production plant, a chipboard plant, and a coal- and biomass-powered electricity facility, combined with heavy traffic. Some residential areas are located at a short distance (100 meters) from the border of the industrial area. The residential areas are densely populated (approximately 2,000 inhabitants per km²) and some of them concentrate a high proportion of ethnic minorities, a high degree of poverty, high unemployment rates, and social housing.¹

Since 1980, Genk was identified as a region with elevated levels of heavy metals (nickel (Ni), chromium (Cr), molybdenum (Mo), and vanadium (V)) in ambient air. From 1990s, contamination of groundwater with BTEX (benzene, toluene, ethylene, and xylene) and heavy metals was detected at the industrial site. In 2004, an increase in concentrations of Ni and Cr in ambient air was documented, with concentrations of Ni (86 ng/m³) exceeding the annual mean threshold value of 20 ng/m³.

2. Case study for Cyprus

In July 2009, in the community of Mammari (Cyprus), measured concentrations of arsenic in the groundwater with potable use exceeded the legal limit by almost 2 times (18-19 µg As/L compared with 10 µg As/L).² The water supply was discontinued and clean drinking water was distributed to the resident in the area. This historical pollution was spread over an area of 25 km², inhabiting approximately 3,000 people.

3. Case study for Hungary

On October 4th, 2010, the dam of a red mud reservoir ruptured caused a large ecological disaster. The red mud contained a residue from aluminum production (a sodium hydroxide solution known as lye) and the processed mud was stored in open reservoirs using wet disposal techniques. The dam, constructed from soot and sludge, was not designed for wet disposal and collapsed under the pressure. About 1.5 million m³ of strongly alkaline red sludge flooded the areas of Kolontárand Devecser (2 and 5 km downstream of the dam) and reached five other villages, as well as the Torna and Marcal rivers. A total area of about 1,000 hectares was flooded. Quick actions were taken in the affected area to neutralize the high pH of the red sludge to curtail the corrosive effects in order to protect human health and to prevent contamination of the River Danube.³

4. Case study for Italy

The ICS is located in Modena, Italy, a medium-sized town (180,000 residents) located in the middle of Emilia-Romagna region, in the Po Valley. The site is characterized by a flat topography and meteorological conditions that favour accumulation of atmospheric pollutants and their associated deposition. In the Emilia-Romagna region, eight municipal solid waste incinerators (MSWIs) are operative. The MSWI in Modena has been operating since 1980. MSWIs can be significant sources of environmental pollution, potentially exposing nearby populations to hazardous chemicals at toxic levels. Approximately 38% of the whole municipal population lives within the exposure area, defined as a circular area with radius of 4 km, centred on the incinerator.^{4,5}

5. Case study for Poland

The Silesian voivodeship (South Poland) was a heavily industrialised region, characterised by elevated environmental concentrations of heavy metals. About a quarter of the Piekary Śląskie area consists of a large landfill containing lead, cadmium, and zinc, making this area one of the most polluted cities of this region.⁶ The city covers 40 km², with a population density of 1,472 people/km². In Piekary Śląskie, 8,141 children are registered, with 2,196 children in pre-school age. Most of the children attend kindergartens (1,752; 79.7%), including 3-year-olds: 332 (54.1% of the population), 4 years: 442 (79%), 5 years: 509 (96.9%), 6 years old: 467 (93.8%) (data of the education department in the city, 20.02.2012).

6. Case for Portugal

The Panasqueira mine is an active mine located in Central Portugal, Castelo Branco district. The activity of the mine started in the last decade of the 19th century and covers an area of 2,000 ha.⁷ During this time, concentrated ore residues were deposited in the Rio and Barroca Grande tailings and mud dams. The total volume of the concentrated ore residues, which contains metals, is over 9,200,000 m³ and this value is growing. If due to slippage zones, the Rio tailings collapses, mining waste will be deposited in the Zêzere river, the main water supply of Lisbon. Since the 1990s, the mining activities are carried out in Barroca-Grande, and the rejected materials are deposited in Barroca-Grande tailing and mud dam, which are exposed to weather events and longer-term climatic conditions.

In the surroundings of the mining area, there are villages of which the inhabitants are strongly dependent on the mine (mostly men), private agriculture (mostly women), and groundwater, both for irrigation and for drinking. The impacted study area (not including considered background areas) covers about 32 km² and includes S. Francisco de Assis, Barroca Grande, Dornelas do Zêzere, Barroca, and S. Martinho villages. In 2011, the total residents in these villages was estimated to be 2,268. The site is characterized by deep valleys and hills.

RESULTS

The results of the inventarisation of available data in the six case studies using a four-stages HBM framework from our own experiences are presented in the following tables (tables S1-S4).

Table S1. Summary of the available pre-phase information for each of the six case studies.

| Data available on environmental pollution and health conditions residents | | | | | |
|--|---|---|--|--|--|
| Belgium | Cyprus | Hungary | Italy | Poland | Portugal |
| Published | | | | | |
| Toxicity profile of particulate matter: increased mutagenic and estrogenic activity, a higher inflammatory potential and a higher oxidative capacity ⁸ Ambient air concentrations of heavy metals ⁹ | In drinking water a concentration level of arsenic which exceeded the legal limit by almost 2 times (18-19 µgAs/L compared with 10 µgAs/L) ² | Concentrations of toxic pollutants in soil (e.g. arsenic, cadmium, cobalt, lead, titanium, strontium, etc.). Concentrations of PM ₁₀ , PM _{2.5} and heavy metals in ambient air. Toxicity profiles of PM. Ten people died in the catastrophe. Most of the injured suffered chemical burns from the lye, post-traumatic stress, sleeping problems and respiratory diseases. ³ | At address level, calculated PM ₁₀ concentrations were available using fallout maps of PM ₁₀ emitted by the plant. The presence of other environmental exposure sources at the residence was assessed with respect to: zone classification, traffic and residential heating ^{4,5} | In the gardens of Piekary Śląskie soil levels for lead and cadmium reached mean values of 569.7 (201-2,159) mg/kg for lead and 16.9 (5.52-58.6) mg/kg for cadmium, raising health concerns. Blood tests for children conducted between 1991 and 2009 showed decreasing, but still high levels of heavy metals ⁶ | Presence of potentially toxic elements (silver (Ag), As, bismuth (Bi), copper (Cu), Cd, antimony (Sb), tin (Sn), tungsten (W), and Zn) in soils, road dust, plants for human consumption, groundwater, stream waters and sediments, on the surroundings of the mine ¹⁰⁻¹² |

| Other | | | | | |
|---|---|---|-------|--|----------|
| Ambient air concentrations of dioxins, polychlorinated biphenyls (PCBs) and polycyclic aromatic hydrocarbons (PAHs). heavy metals in soil, vegetables of local gardens and indoor dust higher cancer risk for both Ni and Cr exposure, lower scores for perceived health status and a higher indication of respiratory symptoms | | | | | |
| Public concern | | | | | |
| Belgium | Cyprus | Hungary | Italy | Poland | Portugal |
| Published | | | | | |
| Other | | | | | |
| Growing concern among the citizens, who were anxious about how much pollution was entering the human body and what effect this might have on their health. | High concern of the citizens when the pollution incidence was discovered back in 2008, but interest is still strong even in 2019 as the residents want to be informed if they are still exposed to Arsenic. | The extent of the catastrophe, the number of injured people and casualties and the partial evacuation caused major concern. The dust from the dried red sludge caused significant respiratory symptoms that further increased the concern of the population | | Persistent concern of parents about the health of their children and their future quality of life. | |

| Involvement of stakeholders and local actors | | | | | |
|---|--|---|-------|--------|----------|
| Belgium | Cyprus | Hungary | Italy | Poland | Portugal |
| Published | | | | | |
| | A mixed community-local government collaboration was established to identify the causes of environmental pollution and also to evaluate possible health effects associated with these exposures ² | | | | |
| Other | | | | | |
| When the HBM study was about to start, changing economic conditions lead to reduced activities in one of the largest companies at the industrial site. The relevance of organizing a HBM study under these conditions was discussed with the Community Advisory Board | | The Crisis Center of the Office of the Chief Medical Officer was in continuous contact with the health service providers, the local organizations of the National Public Health and Medical Officer Service, the experts of the background scientific institutions, the emergency response authorities, and the armed services and also informed the WHO. The Chief Medical Officer established an assessment committee consisting of experts of different fields. The Committee performed hazard and risk analyses and ordered an environmental health surveillance as well as human biomonitoring | | | |

| Decision point to start HBM | | | | | |
|---|--|--|---|--|---|
| Belgium | Cyprus | Hungary | Italy | Poland | Portugal |
| Published | | | | | |
| | Various exposure sources for arsenic ² | To strengthen the exposure estimates, based on model analysis ³ | As part of the authorization process for the solid waste incinerator in Modena, Italy, the degree to which people living and working in the proximity of the plant were exposed to SWI emissions was studied using HBM ⁵ | Because of the still high lead and cadmium blood levels in children and taking into account the stability of lead and cadmium in soil and insufficient remediating actions, it was decided in 2013 to perform a study on correlations between the level of heavy metals in blood and determinants of exposure ⁶ | To evaluate whether environmental and occupational contamination related to the Panasqueira mine activities is associated with the internal dose of several pollutants (As, Cd, Cr, Hg, Mn, Nobellium (No), Ni, Pb and Selenium (Se)) measured in blood, urine, hair and nails ⁷ |
| Other | | | | | |
| Despite the closing of one of the factories, the elevated environmental measurements caused growing concern of citizens about the body burden and health risks due to this chemical exposure. | To prevent adverse health effects, the authorities started a medical investigation immediately to establish the degree of exposure of the residents to arsenic and the potential health effects. | | | | |

| Funding | | | | | |
|---|--|--|--|---|--|
| Belgium | Cyprus | Hungary | Italy | Poland | Portugal |
| Published | | | | | |
| The HBM study was funded by the Environment Department, the Health Department and the Department of Scientific Innovation of the Flemish government ¹³ | The HBM study was funded by the Ministry of Health ¹⁴ | | | Project was co-financed by the National Fund for Environmental Protection and Water Management, City Hall of Piekary Śląskie and Institute for Ecology of Industrial Areas ⁶ | The study was funded by the Foundation for Science and Technology (FCT Portugal) with research grants SFRH/BD/63349/2009, SFRH/BD/47781/2008 and SFRH/BPD/26689/2006, and project PTDC/SAU-ESA/102367/2008 ¹⁵ |
| Other | | | | | |
| | | The costs of the laboratory tests were financed from government sources, from the fund created specifically for the expenses in relation to this event | The study was funded by the Province of Modena in the frame of the authorization for an upgrade of the local SWI | | |

Table S2. Summary of the study design and fieldwork of the six case studies.

| Study design | | | | | |
|--|---|---|---|--|--|
| Belgium | Cyprus | Hungary | Italy | Poland | Portugal |
| Published | | | | | |
| <p>Results from adolescents with residence in the study area were compared with the results of a Flemish reference group of the same age¹³</p> <p>Community-based participatory approach: At the start of the study a Community Advisory Board was established, consisting of societal gatekeepers as well as representatives of local government and industry¹⁶</p> | <p>Investigate a group from the Mammari population (exposed population) and an unexposed population from the rest of Cyprus²</p> | <p>Biomarker levels in children from the exposed settlements were compared with those of a control group</p> <p>To observe changes in concentrations over time</p> <p>To compare the measured concentrations to the values published in the international literature¹⁷</p> | <p>Biomarker levels in residents of the exposed area were compared with those of a control group⁴</p> <p>Cross-sectional study of residents near the ICS⁵</p> | <p>Cross-sectional study⁶</p> <p>During the project implementation scientists were closely cooperated with the self-government authorities of the Piekary Śląskie Municipal Council, the kindergarten managements, the Silesian Children's Association "Bratek" and the Medical Center EKO-PROF-MED in Miasteczko Śląskie and also with the Children's Foundation "Miasteczko Śląskie"¹⁸</p> | <p>Biomarker levels of residents near the mine area were compared with levels of subjects living in a control area⁷</p> |
| Other | | | | | |
| <p>The Community Advisory Committee discussed and co-constructed the study design, the recruitment strategy, definition of the study area and selection of the biomarker. Community members also actively engaged in study promotion and door-to-door visits to help recruit participants.</p> | | | | | |

Biomarkers of exposure and selection criteria

| Belgium | Cyprus | Hungary | Italy | Poland | Portugal |
|---|---|---|---|---|---|
| <p>Markers for heavy metals, POPs, PAH, benzene¹ selected based on available emission data from the industrial plants and the environmental measurements⁹</p> | <p>Arsenic in nails, based on elevated levels in drinking water²</p> | <p>Published Metals (such as Cadmium, Nickel, Vanadium, Chromium, Cobalt and Arsenic) in the urine samples. Selection of the metals studied was based on the metal concentrations observed in the particulate matter and on their risk to human health¹⁷</p> | <p>Ten metabolized polycyclic aromatic hydrocarbons (PAHs), from naphthalene to chrysene, 1-hydroxypyrene and twelve metals (Cd, Cr, Cu, mercury (Hg), Ni, Pb, Zn, V, thallium (Tl), As, Sn) were measured in spot urine, selected based on literature data, monitoring data of the emissions of the incinerator and results of the pilot study⁵</p> | <p>Based on soil measurements and previous measurements in blood of children, lead and cadmium blood levels were measured⁶</p> | <p>Metal(loids) (As, Cr, Cu, Hg, Mg, Mn, Mo, Ni, Pb, S, Se, Si and Zn) in blood, first morning urine, hair and nails (toe finger) samples. selection was based on results from previous studies on samples of soil, road dust, plants for human consumption, superficial and groundwater and stream sediments⁷</p> |
| Other | | | | | |
| | | | | | |

Biomarkers of effect and selection criteria

| Belgium | Cyprus | Hungary | Italy | Poland | Portugal |
|--|--|---|-------|--------|--|
| Published | | | | | |
| For health effects related to these exposure biomarkers in literature, appropriate biomarkers of effect were selected, such as markers for DNA damage, renal function, inflammation, endocrine system, cardiovascular disorders, neurotoxicity, allergy and asthma ¹³ | Possible dermatitis and dermal lesions in exposed population ¹⁴ | Respiratory diseases, asthma, post-traumatic stress, sleeping problems ³ | | | Biomarkers for immunotoxic and genotoxic effects, based on the health effects associated with the metals reported in literature ^{19,20} |
| Other | | | | | |

Information on determinants of exposure

| Belgium | Cyprus | Hungary | Italy | Poland | Portugal |
|--|--|---------|---|---|--|
| Published | | | | | |
| All participants signed an informed consent and completed an extensive questionnaire to provide information about socioeconomic factors, home environment, habits, diet and life style factors. Multiple regression models were used to study the effect of residence in the ICS on biomarker levels, after correcting for other modifying factors ^{1,9,21} | Questionnaire regarding socioeconomic, demographic factors and smoking habits ² | | Influencing factors, such as diet, smoking, traffic, occupation and personal characteristics were assessed by questionnaires and objective measurements, and included into multivariate linear regression models ⁵ | Questionnaire about determinants of exposure, such as sources of pollution with heavy metals in the home environment and socioeconomic factors. Statistical analysis consisted of ANOVA Kruskal-Wallis or Mann Whitney U test and Stepwise regression models ⁶ | Questionnaires provided information about the individual health conditions, medical history, medication, diagnostic tests (X-rays, etc.) and lifestyle factors. Multiple regression models to estimate the effect of the exposure, adjusted for influencing factors ⁷ |
| Other | | | | | |

Selection of the study population

| Belgium | Cyprus | Hungary | Italy | Poland | Portugal |
|---|--|--|--|---|--|
| 200 adolescents (14-15 years old), The number of participants needed was assessed by statistical power calculations. Adolescents were selected as study population since they are not subjected to occupational exposure and their physical and mental development makes them a susceptible population ^{1,9,13,21} | Exposed group (No. 56) and control group (No. 48). The selection of the two groups was made taking into account the results of a questionnaire regarding socioeconomic, demographic factors and smoking habits to maximize the representability and comparability ² | Published Children: because their exposure to environmental compounds is higher compared to the adult population, their developing bodies makes them more vulnerable to health effects and exposure through active smoking could be eliminated. The study group was composed of 351 children, aged 6-14 years, 50% from the flooded area, 50% from the control area ¹⁷ | 65 subjects living and working within 4 km of the incinerator and 103 subjects living and working outside this area ⁴ 500 people, aged 18-69 years, living within 4 km from the incinerator ⁵ | Preschool children (No. 678) were selected as study group since they spend a lot of time playing outdoor and they are not occupationally exposed ⁶ | 122 subjects (41 environmentally exposed, 41 occupationally exposed (miners) and 40 in the control group) ⁷ |
| Other | | | | | |

| Selection of the study area | | | | | |
|---|---|---|--|--|--|
| Belgium | Cyprus | Hungary | Italy | Poland | Portugal |
| Published | | | | | |
| Based on location of industrial activities, environmental data, health survey data, population density ⁹ | Based on the coverage of the population exposed to the contaminated drinking water source ¹⁴ | Two flooded areas, Kolontár and Devecser, and a control area close to the dam but not flooded, Ajka ¹⁷ | 4 km from the incinerator. The study area was defined by exposure to particulate matter (PM) emitted from the SWI estimated using fall-out maps from a quasi-Gaussian dispersion model, also taking into account the results of the pilot study ⁵ | Based on location of industrial sources of hazard, environmental data and number of preschool children. In the vicinity of the non-ferrous metal smelters concentration of lead and cadmium in soil exceed the limit values for residential buildings and areas of cultivated soil ^{6,22} | Villages near the Panasqueira mine and a control area ⁷ |
| Other | | | | | |
| Air quality dispersion models were used to define the possible contaminated area and the study area. | | | | | |

| Exposure assessment | | | | | |
|--|--|---|---|---|--|
| Belgium | Cyprus | Hungary | Italy | Poland | Portugal |
| Published | | | | | |
| Substances of concern identified: compared to the Flemish reference group ICS-study participants had higher blood levels of Cr (+32%), Cu (+5%) and Tl (+11%), higher urine levels of Cd (+18%), Cu (+11%), toxic arsenic components (+32%) ⁹ | arsenic concentration of about 2.84 times higher for Mammari's population as compared to the control population ² | No statistically significant difference in the urinary levels of any metals between the exposes area and the control area. Measured concentrations in the range of the published data measured in other countries. No increasing tendency in the urinary level of the measured components during the 7 months of the study, except for chromium during the non-heating period in both areas ¹⁷ | Compared to Italian reference limits, urinary metal concentrations in the study area were comparable or higher. Identified substances of concern: Cr, V, naphthalene and phenanthrene. ⁴ Metal levels showed no clear association with calculated PM exposure categories of the solid waste incinerator (SWI). For some PAHs (naphthalene, fluorene, fluoranthene and pyrene) positive associations with SWI exposure were observed. In particular fluorene levels were significantly higher in samples from participants with residence in exposure zone 3 and 4 ⁵ | preschool children living in Piekary Śląskie are exposed to lead and cadmium ⁶ | Substances of concern identified: both exposed groups higher values for As, Cr, Mg, Mn, Mo, Ni, Pb, S, Se and Zn, occupationally exposed group higher levels of Cu, Mn and Pb in hair and Se in blood. Environmentally exposed group: pronounced past and recent exposure to As, moderate exposure to Mg, Mn and Zn, recent exposure to Mo and past exposure Cr, Ni and S. Occupational exposed group: continuous exposure to Zn, recent exposure to Se and long term exposure to As, Mn and Pb ⁷ |

Other

Substances of concern identified:
compared to the Flemish
reference group ICS-study
participants had higher urinary
levels of a polycyclic aromatic
hydrocarbons (PAHs) marker
(+33%).



| Health assessment | | | | | |
|--|---|--|-------|---|---|
| Belgium | Cyprus | Hungary | Italy | Poland | Portugal |
| Published | | | | | |
| <p>HBM guidance values for internal exposure exceeded in: 19.6% of the participants for urinary Cd, in 64.5% of the participants for toxic relevant arsenic, in 0.5% of the participant for blood Cd.⁹ higher levels of biomarkers reflecting DNA-damage associated with higher urinary levels of the PAH marker and the benzene marker, higher urinary concentrations of cadmium, chromium and nickel, higher blood levels of arsenic, DDT and HCB and higher levels of methylmercury in hair²³</p> | <p>the study did not show a health risk for the population, based on the assessment of dermatitis or skin lesions²</p> | <p>Increase in respiratory diseases, post-traumatic stress and sleep problems.</p> <p>Increase in PM₁₀ levels associated with increase in respiratory diseases^{3,17}</p> | | <p>When compared to HBM guidance values for lead in blood 32% (No. 218) of the children exceeded the value of 2 µg/dl, 8.5% (No. 58) exceeded the value of 5 µg/dl and 0.9% (No. 6) exceeded the value of 10 µg/dl. The reference value for cadmium of 5 µg/dl was exceeded in 0.8% of the children⁶</p> | <p>Environmentally exposed group: lower levels of T cytotoxic lymphocytes(CD8+) and higher CD4+/CD8+ ratios. Occupational exposed group: decrease in T lymphocytes (CD3+) and T helper lymphocytes (CD4+) and increase in natural killer cells(CD16+56+).²⁰ All measured biomarkers of genotoxicity increased in the exposed groups generally higher levels in the environmentally exposed compared to the occupational exposed participants.¹⁹ Higher blood levels of Mn associated with decrease of T cytotoxic lymphocytes (CD8+) and B lymphocytes (CD19+) and increase in the CD4+/CD8+ ratio.²⁰ Higher Mn and As levels in toenails associated with increased genotoxicity markers.¹⁹ Higher concentrations of lead in toenails associated with increasing levels of immunotoxicity biomarkers,²⁰ as well as with higher genotoxicity markers¹⁹</p> |

| Other | | | | | |
|--|--|---------|---|--|---|
| DNA damage was the main health effect of concern. Higher levels of biomarkers reflecting DNA-damage (+26% and +69%) the adolescents residing the ICS compared to the Flemish reference group, after correction for confounders and covariates. | | | | | |
| Identified determinants of exposure or health effects | | | | | |
| Belgium | Cyprus | Hungary | Italy | Poland | Portugal |
| Published | | | | | |
| Age, gender, smoking habits, season, fish consumption, urine density, proximity to ICS, immission data ⁹ | This high level of the concentration was probably linked to the consumption arsenic contaminated drinking water for an unknown period of time ² | | Tobacco smoking was associated with higher levels of almost all PAHs, as well as Cd and Pb. Traffic exposure was associated with higher urinary levels of Acy, Phe and Ant. Females had higher levels of Cu, Pb, Cd, Ni and As. Increasing age was associated with higher urinary levels of Pb, Cd, As and V ⁵ | Higher blood levels of lead in younger children and associated with a higher attained level of education of the father, exposure to cigarettes smoke at home and living in the vicinity of any environmental hazard. Higher cadmium levels in blood associated with an older age and not living near environmental hazard ⁶ | Females: higher levels of As, Cr, Mg, Mn and Se in urine, fingernails and toenails, and Hg in hair, males: higher levels of Fe, Hg, Mg, Pb, S and Zn in blood and hair samples. Older age associated with higher levels in blood and urine of As, Cu, Mg and Zn, younger age associated with higher concentrations of As, Cr, Fe, Mg, Mn and Se in nails and hair. Almost all biomarkers were significantly higher in smokers compared to non-smokers, with exception for Hg in hair which was higher in non-smokers ⁷ |
| Other | | | | | |

| Identified vulnerable populations | | | | | |
|---|--------|---------|--|---|---|
| Belgium | Cyprus | Hungary | Italy | Poland | Portugal |
| Published | | | | | |
| Identified socioeconomic groups as vulnerable subpopulations for exposure to environmental compounds. adolescents with low socio-economic status (SES) had higher internal exposure of Cd, Cu, lead and PAHs compared to adolescents with higher SES ¹ | | | Social inequalities in exposure were reported: higher internal doses of Cu, Pb and V were associated with lower education levels, while higher urinary Hg levels were associated with higher education levels. Foreign citizenship was associated with higher urinary levels of Sn, Tl and all PAHs, except acenaphthene and anthracene ⁵ | The highest risk was documented in children living in the vicinity of metallurgical slag heaps located in Brzeziny district, this region also had the highest concentration of both pollutants in the soil ⁶ | Populations living nearby and working in the mine are exposed to several metal(loid)s originated by mining activities, ⁷ particularly to As ⁷ |
| Other | | | | | |
| Communication of the results, audiences | | | | | |
| Belgium | Cyprus | Hungary | Italy | Poland | Portugal |
| Published | | | | | |

Other

| | | | | | |
|--|--|--|--|---|--|
| <p>Flemish and local authorities implemented a communication strategy to inform citizens about the study results. All participants first received the collective results of the study as well as their personal results, if requested, followed by informing the local authorities about the collective results, and finally, the press and the general public. All participants were given the opportunity to consult a physician, to discuss their personal results.</p> | | <p>The study results were included in reports on the health consequences of the red sludge catastrophe, which are available to the general public. The results were also mentioned in policy briefs. No press communication was organized.</p> | <p>Personal results were reported back to participants who indicated to be willing to receive their results.</p> | <p>The research was accompanied by informational and educational activities addressed to parents, carers, educators of kindergartens and other members of the Piekary Śląskie community. Printed educational materials were prepared, as well as an electronic information and educational package "How to protect children against lead and cadmium?" posted on the websites of each kindergarten. Information meetings were organized with the municipality's self-government and the kindergartens' directorates as well as two educational and information campaigns during local public events. Information on the implementation of the project was included in local and regional media.</p> | <p>The study results were not communicated to the participants or to the general public.</p> |
|--|--|--|--|---|--|

Table S4. Summary of the available information on impact of the six case studies.

| Short term impact | | | | | |
|--|---|---|-------|--|----------|
| Belgium | Cyprus | Hungary | Italy | Poland | Portugal |
| Published | | | | | |
| Improved communication between authorities, industry and citizens and in shared responsibilities, elaboration and adjustment of the environmental monitoring ¹⁶ | Contaminated water source (groundwater) was not used and residents connected to source of water free from arsenic (measured data) | | | Improved communication between authorities and citizens (parents and preschool teachers), and in shared responsibilities about health status of children | |
| Other | | | | | |
| Awareness raising about the health impact of environmental pollution. More than 100 individuals asked for a personal consult with the study physician, because they needed more information. | To give residents more accurate information about the magnitude of risk to which they had been exposed | Remediation (cleanup of the red mud) was completed before the end of biomonitoring of metals in urine of school children. | | The study identified 160 participants for which potential sources in their environment should be assessed 6 participants for which medical care should be implemented. There is no information on the implementation of these recommendations. | |

| Long term impact | | | | | |
|--|--|---------|-------|---|----------|
| Belgium | Cyprus | Hungary | Italy | Poland | Portugal |
| Published | | | | | |
| Additional research projects concerning locally grown food, sources of environmental pollution and exposure routes, a follow-up program on public health in the ICS region, additional research on local sources of PAHs and facilitating communication between local stakeholders ¹⁶ | | | | | |
| Other | | | | | |
| <p>Building trust in the study results and in the local and Flemish authorities</p> <p>Actions reducing emissions (such as an inventory of emission sources, creating green buffer zones, optimizing spatial planning and traffic circulation) and measures stimulating a healthy life-style (such as informative sessions, awareness rising, brochures, website and health monitoring).</p> | Two years after the discontinuation of exposure a follow-up study was initiated including nail arsenic measurements. | | | The study emphasizes that improvements of environment quality in Piekary Śląskie are necessary to assure expected quality of health in children and local efforts achieve the desired goals are to be continued. To continue informing parents and nurseries about environmental hazards of heavy metals and how behavior and life style can interact with exposure is important. | |

Levels: scientific, societal, policy making

| Belgium | Cyprus | Hungary | Italy | Poland | Portugal |
|--|--------|---------|-------|--------|----------|
| Published | | | | | |
| <p>Policy uptake: use of an analytic-deliberative and iterative process, involving experts, policy makers and stakeholders.¹⁶ This resulted in an improved communication between authorities, industry and citizens and in shared responsibilities. Actions on elaboration and adjustment of the environmental monitoring, additional research projects concerning locally grown food, sources of environmental pollution and exposure routes, a follow-up program on public health in the ICS region, additional research on local sources of PAHs and facilitating communication between local stakeholders.</p> | | | | | |

Other

Societal level:

Contribution to awareness raising about the health impact of environmental pollution. Information on determinants of exposure can offer solutions for reducing exposure to environmental chemicals. Using an open and transparent communication strategy throughout the study helped building trust in the study results and in the local and Flemish authorities. However, the subject is very complex and often difficult to understand for a lay audience. More than 100 individuals asked for a personal consult with the study physician, because they needed more information. Also, scientists and policy makers received a lot of questions during the communication events.

Societal level:

Helped to give residents more accurate information about the magnitude of risk to which they had been exposed

The results were mentioned in policy briefs.

Obtained results helped community to understand how important is environmental hazard and individual prophylaxis to health status of preschool children. The research was accompanied by informational and educational activities addressed to parents, carers, educators of kindergartens and other members of the Piekary Śląskie community. Printed educational materials were prepared, as well as an electronic information and educational package "How to protect children against lead and cadmium?" posted on the websites of each kindergarten. Information meetings were organized with the municipality's self-government and the kindergartens' directorates as well as two educational and information campaigns during local public events. Information on the implementation of the project was included in local and regional media.

Policy: Well-informed and socially robust policy actions of the Flemish government were complemented with a separate policy plan initiated by the local authorities of the ICS. Actions on reducing emissions (such as an inventory of emission sources, creating green buffer zones, optimizing spatial planning and traffic circulation) and measures stimulating a healthy lifestyle (such as informative sessions, awareness rising, brochures, website and health monitoring).

Policy: Specific recommendations on further monitoring and remediating actions

| Involvement of stakeholders and local actors | | | | | |
|--|--------|--|-------|--|----------|
| Belgium | Cyprus | Hungary | Italy | Poland | Portugal |
| Published | | | | | |
| | | The established Committee ensured that technical guidelines, general information materials on the potential health risks and their prevention, and answers for frequently asked questions were readily available ¹⁷ | | All interested were informed about the final results: - city authorities and kindergartens received a full report - parents received educational materials - parents of children with elevated heavy metal concentrations have been informed on necessity of contact with medical doctor ⁶ | |
| Other | | | | | |
| The human biomonitoring study used a community-based participatory approach: community members, practitioners, researchers and local authorities were involved in all aspects of the research process. | | | | | |

REFERENCES

1. Morrens B, Bruckers L, Loots I et al. Environmental Justice under our skin? Socio-stratifying human biomonitoring results of adolescents living near an industrial hotspot in Flanders, Belgium. In: Druffel K (ed). *Looking within: Finding an environmental justice and global citizenship lens. Critical Issues*. Oxford, United Kingdom: Inter-Disciplinary Press; 2013.
2. Pavlou P, Katsonouri A, Gregoriou I et al (eds). Human biomonitoring and policy relevant investigation of the health effects of drinking water arsenic pollution in the community of Mammari, Cyprus. *Human biomonitoring (HBM) - Linking environment to health and supporting policy*; 2012 October 22nd - 25th, 2012; Larnaca, Cyprus: COPHES and DEMOCOPHES consortia.
3. Dura G, Faludi G, Szabo Z et al. Aspects of health risk assessment related to the red mud disaster in Hungary. *Central European Journal of Occupational and Environmental medicine*. 2016;22(1-2):83-95.
4. Ranzi A, Fustinoni S, Erspamer L et al. Biomonitoring of the general population living near a modern solid waste incinerator: a pilot study in Modena, Italy. *Environ Int* 2013;61:88-97.
5. Gatti MG, Bechtold P, Campo L et al. Human biomonitoring of polycyclic aromatic hydrocarbons and metals in the general population residing near the municipal solid waste incinerator of Modena, Italy. *Chemosphere* 2017;186:546-57.
6. Kowalska M, Kulka E, Jarosz W, Kowalski M. The determinants of lead and cadmium blood levels for preschool children from industrially contaminated sites in Poland. *Int J Occup Med Environ Health* 2018;31(3):351-59.
7. Coelho P, Costa S, Costa C et al. Biomonitoring of several toxic metal(loid)s in different biological matrices from environmentally and occupationally exposed populations from Panasqueira mine area, Portugal. *Environ Geochem Health* 2014;36(2):255-69.
8. Van Den Heuvel R, Witters H, Nawrot T. *Opmaak van een concreet en praktisch toepasbaar draaiboek voor toepassing van effectgerichte metingen in het lopende en toekomstige milieu- en gezondheidsbeleid met inbegrip van validatie door toepassing op de geselecteerde hot spot Genk-Zuid van het 2de generatie Steunpunt Milieu en Gezondheid. Deelrapport 2: werkpakket 2: Hotspot Genk-Zuid*. Mol, Belgium: VITO; 2011.
9. Vrijens J, Leermakers M, Stalpaert M et al. Trace metal concentrations measured in blood and urine of adolescents in Flanders, Belgium: reference population and case studies Genk-Zuid and Menen. *Int J Hyg Environ Health* 2014;217(4-5):515-27.
10. Candeias C, Ferreira da Silva E, Avila PF, Teixeira JP. Identifying sources and assessing potential risk of exposure to heavy metals and hazardous materials in mining areas: the case study of Panasqueira mine (Central Portugal) as an example. *Geosciences* 2014;4:240-68.
11. Candeias C, Melo R, Avila PF, da Silva EF, Salgueiro AR, Teixeira JP. Heavy metal pollution in mine-soil-plant system in S. Francisco de Assis - Panasqueira mine (Portugal). *Appl Geochem* 2014;44:12-26.
12. Candeias C, Avila PF, da Silva EF, Ferreira A, Duraes N, Teixeira JP. *Water-Rock Interaction and Geochemical Processes in Surface Waters Influenced by Tailings Impoundments: Impact and Threats to the Ecosystems and Human Health in Rural Communities (Panasqueira Mine, Central Portugal)*. *Water Air Soil Poll* 2015;226(2):23.



13. Schoeters G, Den Hond E, Colles A et al. Concept of the Flemish human biomonitoring programme. *Int J Hyg Environ Health* 2012;215(2):102-08.
14. Makris KC, Christophi CA, Paisi M, Ettinger AS. A preliminary assessment of low level arsenic exposure and diabetes mellitus in Cyprus. *BMC Public Health* 2012;12:334.
15. Coelho P, Costa S, Silva S et al. Metal(loid) levels in biological matrices from human populations exposed to mining contamination--Panasqueira Mine (Portugal). *J Toxicol Environ Health A* 2012;75(13-15):893-908.
16. Reynders H, Colles A, Morrens B et al. The added value of a surveillance human biomonitoring program: The case of FLEHS in Flanders (Belgium). *Int J Hyg Environ Health* 2017;220(2 Pt A):46-54.
17. Rudnai P, Naray M, Rudnai T, Toth E, Kanizsai J. Concentrations of some toxic metals in the urine samples of children in the red sludge area. *Népegészségügy* 2011;89(3):230-36.
18. Kulka E. Report from the research of children carried out in kindergartens located in Piekary Slaskie, as a part of the project 'We protect children before lead and cadmium' - assessment of the exposure in preschool children in Piekary Slaskie. Katowice; 2014.
19. Coelho P, Garcia-Leston J, Costa S et al. Genotoxic effect of exposure to metal(loid)s. A molecular epidemiology survey of populations living and working in Panasqueira mine area, Portugal. *Environ Int* 2013;60:163-70.
20. Coelho P, Garcia-Leston J, Costa S et al. Immunological alterations in individuals exposed to metal(loid)s in the Panasqueira mining area, Central Portugal. *Sci Total Environ* 2014;475:1-7.
21. Croes K, Den HE, Bruckers L et al. Monitoring chlorinated persistent organic pollutants in adolescents in Flanders (Belgium): concentrations, trends and dose-effect relationships (FLEHS II). *Environ Int* 2014;71:20-28.
22. Strugala-Stawik H, Rutkowski Z, Pastuszek B, Morawiec K. Biomonitoring of lead in blood of children - short assessment of results 1991-2009. *Environ Med* 2010;13(3):11-4.
23. Franken C, Koppen G, Lambrechts N et al. Environmental exposure to human carcinogens in teenagers and the association with DNA damage. *Environ Res* 2017;152:165-74.