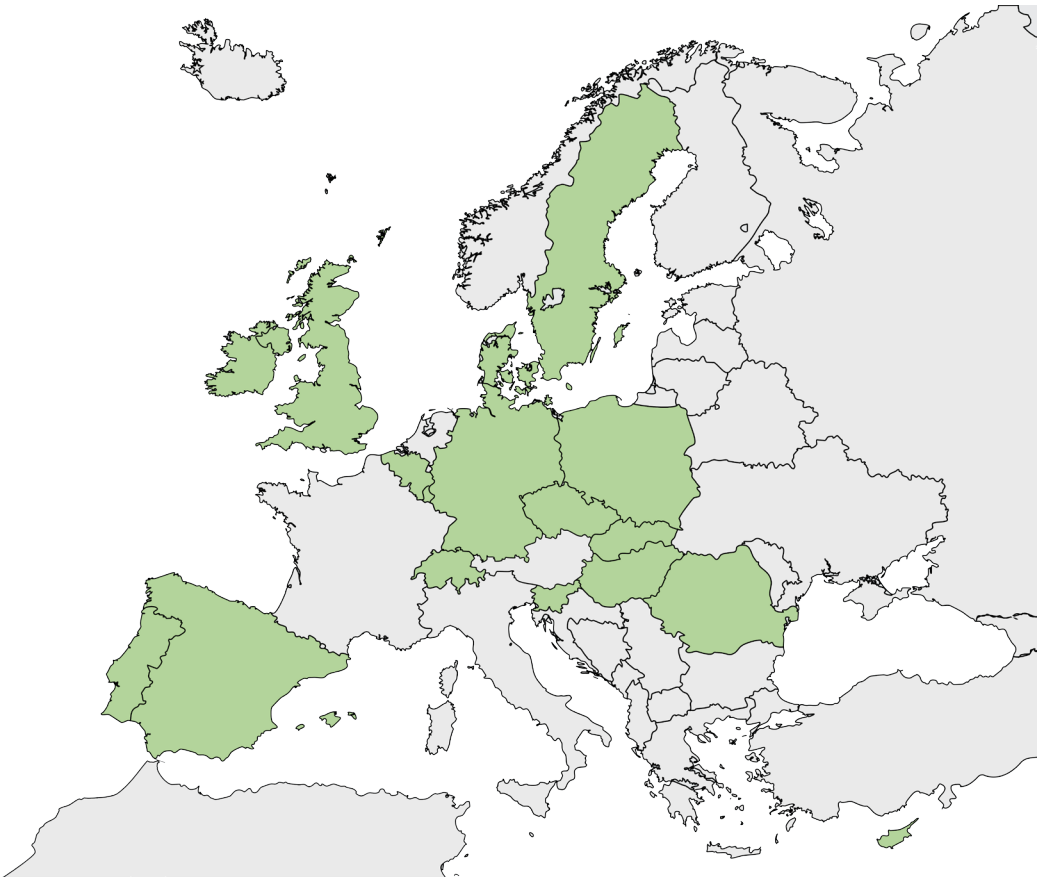
© Fotolia.fr

DEMOCOPHES

Human biomonitoring on a European scale

DEMOCOPHES
Demonstration of a study to coordinate and perform human biomonitoring on a European scale

Project realised with LIFE+ co-financing
LIFE09 ENV/BE/000410



Acknowledgements

We would like to thank the European Commission for their co-funding, the COPHES consortium for their scientific support, the teams in the 17 countries for having implemented the project, as well as the mothers and children for volunteering to participate in this European human biomonitoring pilot study.

DEMOCOPHES (LIFE09 ENV/BE/000410) was jointly financed by the European Commission LIFE+ programme (50%) and partners from 21 countries. Information on the national co-funding institutions is accessible via the 'Partners' page of the DEMOCOPHES website: http://www.eu-hbm.info/DEMOCOPHES/project-partners.

Contents

DEMOCOPHES in brief

DEMOCOPHES (DEMOnstration of a study to COordinate and Perform Human biomonitoring on a European Scale) ran from September 2010 to November 2012, demonstrating the feasibility of a harmonised approach to human biomonitoring surveys to obtain comparable results in Europe.

Teams in Belgium, Cyprus, Czech Republic, Denmark, Germany, Hungary, Ireland, Luxembourg, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland and the United Kingdom studied exposure to mercury, cadmium, tobacco smoke and some phthalates and possible relations to lifestyle, using biomarkers and questionnaire data. Bisphenol A was added as an additional substance for a group of 6 countries.

The national teams translated the European common protocol, which describes in detail how to implement the study. Without compromising the comparability of the results, small adaptations were allowed to suit cultural differences and sometimes specific national needs. Before starting the study, ethics authorities in each country approved the necessary documents.

In DEMOCOPHES, 17 European countries tested a common approach for human biomonitoring surveys which was developed by COPHES. They produced data on the distribution of specific biomarkers and related lifestyle data among defined study populations which, for the first time, are comparable on a European scale. These comparable data are a step towards European reference values[1]. Now that the feasibility of an EU-harmonised approach has been demonstrated, policy-makers can start to envisage a European survey programme using the lessons learned. To ensure a sustainable way forward, Europe needs a structure that will enable suitable coordination and decision-taking.

Participants in this study were children aged 6-11 years and their mothers aged 45 years and under. Fieldworkers in the participating countries collected hair and urine samples from a total of 3688 volunteers, half from urban areas and half from rural areas. Mothers provided details on their living environment, nutrition, smoking behaviour, and other information that could help to explain the levels of the biomarkers measured in hair and urine.

The laboratories analysing the samples were selected through a strict quality assurance process, comprising Interlaboratory Comparison Investigations (ICI) and External Quality Assessment Schemes (EQUAS).

Statistical analysis and interpretation of the results was performed in each country as well as at EU level. The 17 partners transferred the cleaned national databases to a European central database.

The countries' teams translated and adapted centrally provided communication material. This material comprised templates for invitation letters, information leaflets, consent forms, questionnaires, etc.

All study volunteers received their personal results unless they chose to do otherwise. The national webpages give information on national results communicated through symposia, press releases, etc. During the DEMOCOPHES-COPHES Cyprus Presidency Conference, as well as in scientific and policy-makers' meetings, partners of both projects presented the European aggregated results and conclusions.

1 Indicate the uppermargin of the current background exposure of the general population to a given environmental toxin at a given time.

Human biomonitoring involves collecting samples from human volunteers and measuring in those indicators of chemical uptake and effect, known as biomarkers

Human biomonitoring

Human biomonitoring (HBM) involves collecting samples from human volunteers – urine, blood, hair, saliva, nails or other human tissue – and measuring in those indicators of chemical uptake and effect, known as biomarkers. For a given chemical, HBM surveys can highlight spatial trends of exposure, help uncover contributing lifestyle factors, and indicate at-risk groups. When integrated with other data, the biomarker data can be translated into intervention strategies or early-warning tools aimed at reducing exposure to environmental pollutants. Repeated surveys can reveal changes in chemical exposure levels over time, providing an additional focus for policy initiatives. More than measurements in air, water or soil, HBM makes pollution 'personal'. It not only provides valuable information on total exposure through all possible routes but also on possible relations with lifestyle and habits, helping raising awareness with possible implications for prevention.

Project history and objectives

Project history

In 2004, the Commission launched the Environment and Health Action Plan 2004-2010[2] which recognises the value of HBM and the relevance and importance of coordinating HBM programmes in Europe.

In some countries, HBM is already used extensively at national and regional level, but the results cannot be easily compared across projects and programmes. Improved comparability would allow for a clearer understanding of exposure of the population to pollutants across Europe and would help identify potential high-exposure populations and relations to possible sources, thus supporting the development of better regulations and preventive actions.

In December 2009, the COPHES project[3] started to set up the scientific framework for a European project implementing action 3 of the Action Plan, which entails the development of a coherent approach to HBM in Europe.

In September 2010, 21 countries launched the two-year DEMOCOPHES project to demonstrate that a European common approach to HBM is feasible, and to generate, for the first time, comparable European HBM data.

2 http://europa.eu/legislation_summaries/public_health/health_determinants_environment/l28145_en.htm

3 Consortium to Perform Human Biomonitoring on a European Scale funded under the EU Seventh Research Framework Programme – Grant Agreement 244237.

Participants were children aged 6-11 and their mothers aged up to 45 years

© Arialdo Rescigno - Fotolia.fr

Cotinine is formed from nicotine after it enters the human body. It is an excellent biomarker of exposure to tobacco smoke and is detectable for several days after inhalation

Choosing the study population

The 2004 EU Action Plan focuses on children, as they are particularly vulnerable to exposure to chemicals in their environment and food. The age group for children in DEMOCOPHES was defined as pre-pubescent: 6-11 years. The selection of this specific age group also facilitates comparison with results from other studies, in particular the US National Health and Nutrition Examination Survey (NHANES)[4].

Participating children's mothers were included for a number of reasons:

1. Mothers serve as indicators of foetal and infant exposure and represent a target group for prevention;
2. Data for mothers living in the same household as the children being studied could lead to more insights into exposure sources and pathways;
3. Widening the survey provides an opportunity to collect more information on the whole population and to stimulate wider public interest.

In DEMOCOPHES, each participating country had to recruit 120 mother and child pairs, with the exception of two small countries, Cyprus and Luxembourg, which recruited 60 pairs. In total, 3688 volunteers were recruited: half of them were from urban areas and the other half from rural areas.
To guarantee protection of the rights and dignity of every volunteer, all study activities followed the legal and ethical framework established by several international directives, conventions, and guidelines.

Choosing the biomarkers to be investigated

All participating countries analysed 4 human biomarkers: mercury in hair, cadmium, cotinine and some metabolites[5] of phthalates in urine. The substances measured are of public concern due to their widely recognised health effects.

At the start of the DEMOCOPHES project, Bisphenol-A was added as an additional optional biomarker. This was seen as a test of the feasibility of adding 'new' biomarkers quickly to the EU-harmonised HBM programme, i.e. with some uncertainties at the scientific level.

To facilitate recruitment and sampling, blood samples were not taken during this project.

4 The National Health and Nutrition Examination Survey (NHANES) is a programme of studies designed to assess the health and nutritional status of adults and children in the United States. http://www.cdc.gov/nchs/nhanes.htm

5 Most of the phthalates are rapidly broken down in the body into simple compounds called metabolites.

Mercury

Mercury is a naturally occurring element in the earth's crust. It is also released into the environment through man-made sources such as the burning of fossil fuels, waste incineration, forest fires and waste-water discharge from plastic production plants. The mercury released into the air and water is washed into seas and oceans, ending up in fish. Large fish at the top of the food chain are particularly affected by this pollution. Chronic exposure to mercury can cause damage to the central nervous system, kidneys and stomach. It also affects the immune system, blood pressure and may cause behavioural problems. During pregnancy, methylmercury compounds cross the placenta and can affect the development of the foetus, causing neurodevelopmental abnormalities and loss of Intelligence Quotient (IQ).

Cadmium

Cadmium is a metal present in small quantities in air, water and soil. It is a by-product of the extraction of zinc, lead and copper and is used in batteries and paint. Exposure to cadmium is primarily through active and passive smoking but it is also present in some food types such as vegetables, shellfish and liver. High levels of cadmium can cause cancer in humans. Long-term exposure to low levels of cadmium through air, water and soil can affect the kidneys, bone density and the cardiovascular system.

Cotinine

Cotinine is formed from nicotine after it enters the human body. It is an excellent biomarker of exposure to tobacco smoke and is detectable for several days after inhalation. Smoking may cause lung cancer, heart disease and respiratory diseases. Non-smoking adults and children exposed to second-hand smoke face the same dangers as smokers themselves. Children exposed to tobacco smoke have an increased risk of sudden infant death, chest infections and asthma. Exposure to tobacco smoke during pregnancy can result in low birth weights in newborns and pre-term deliveries.

Phthalates

Phthalates are a group of compounds widely used in the manufacture of plastics, to make them soft and flexible, and in personal care products. They are widespread, found in common products such as soaps, suntan lotion, soft plastic toys, plastic bottles, raincoats, shoes and food packaging. Continuous and repeated exposure to high levels is associated with changes in the hormonal system, causing a decrease in fertility, premature births and genital defects, among other consequences. More research is needed to assess the exact health effects of long-term exposure to low levels of phthalates.

Bisphenol-A

Bisphenol-A (BPA) is used in coatings on the inside of cans, in plastics, in paints, varnishes and glues, and in the thermal paper used, for example, in supermarkets' cash tickets. In animal experiments, elevated levels of BPA are linked to fertility and developmental problems, cardiovascular disorders and diabetes, among other conditions. More research is needed to assess the exact health effects of long-term exposure to low levels of BPA.

Project objectives

DEMOCOPHES aims at testing *"the hypothesis that HBM can be performed in a coherent and harmonised manner throughout Europe, by means of commonly developed protocols, strategies and scientific tools, ensuring reliable and comparable data, whilst also leading to a more effective use of resources"*.

More specifically, the DEMOCOPHES project in the participating countries wants to:

1. Test the COPHES developed guidelines, protocols and technical procedures for communication, fieldwork, chemical analyses, data handling and processing;
2. Gain practical knowledge of accessing study populations, recruitment procedures and response rates;
3. Improve the overall performance of national teams and laboratories involved;
4. Obtain comparable data on the distribution of specific biomarkers among the defined population in relation to cultural and lifestyle factors through statistical analysis and interpretation;
5. Develop practices and guidelines for effective communication and awareness-raising towards participants, stakeholders, wider public and policy-makers.

Project implementation

The countries applied the same European protocol, which describes in detail how to implement the study, and followed the same guidelines for the 5 main tasks, comprising:

1. Developing the national framework, protocol and materials;
2. Finding suitable volunteers and taking the samples;
3. Analysing the chosen biomarkers;
4. Performing statistical analysis and data interpretation;
5. Communicating properly throughout the study.

Fieldworkers in the participating countries collected hair samples from a total of 3 688 volunteers

Developing the national framework, protocol and materials

A number of key steps have to be taken before launching a wide-ranging survey. During the first months of the project, each participating country had to translate and adapt the COPHES study protocol to fit its own circumstances and to prepare for implementation. This included:

Developing a national protocol: each country had to delineate criteria defining both rural and urban areas, decide whether to recruit through schools or population registers, and test the feasibility and added value of the proposed Computer Assisted Personal Interview system (CAPI) to collect information on lifestyle and habits.

Setting up a national team to implement the protocol, gathering necessary expertise from own organisations and/or hiring or subcontracting: coordinators from each national team were trained at the COPHES 'train the trainer' session in June-July 2011 in Berlin. Back in their own countries, they then trained their fieldwork teams accordingly.

Making additions to the protocol, e.g. to shed light on other topics of interest: for example, one country decided to extend its study population, analysing mother-child pairs but also fathers, while another country decided to take blood samples and investigate additional substances.

Translating and adapting communication and background material such as questionnaires provided by COPHES, while maintaining comparability: each team translated the documents provided and proposed changes, detailing some specific national considerations for approval at the EU coordination level. Partners got together to exchange experiences and solutions in February 2011 in Brussels and April 2011 in Budapest.

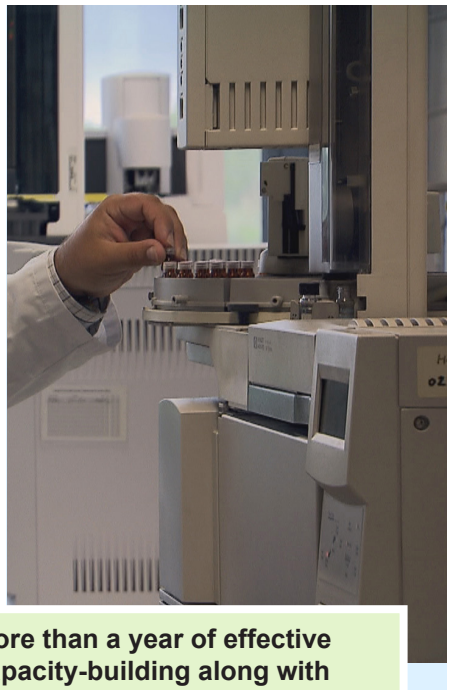
Finding suitable volunteers and taking the samples

From September 2011 until February 2012, possible volunteers were contacted and samples were taken. Different approaches were tested for finding volunteers: 3 countries recruited via the national population registries and 14 in schools, involving local communities and school directors. Most countries had difficulties finding suitable volunteers, although small educational gifts for children and/or mothers were provided. The start of the project was given press coverage in several countries.

Analysing the chosen biomarkers

The levels of the biomarkers measured in the general population are usually relatively low, in contrast to worker exposure to a specific known agent in a factory. Laboratory-introduced variations and detection limits must therefore be considered carefully. For the laboratories analysing the DEMOCOPHES samples, more than a year of effective capacity-building along with a strict quality assurance and control process made it possible to obtain comparable biomarker measurements. This was achieved through the Interlaboratory Comparison Investigations (ICI) and External Quality Assessment Scheme (EQUAS) organised by COPHES.

Scientists collected information on the participant's lifestyle, eating and smoking habits and socio-economic status



More than a year of effective capacity-building along with a strict quality assurance and control process made it possible to obtain comparable biomarker measurements

The ICI were seen as a first test for newcomers to HBM, to improve laboratory skills in measuring relatively low levels. Experienced labs could receive confirmation of their measuring skills. Labs received two control samples per round with different concentrations of the target biomarkers and prepared from native biological samples. During the different rounds the range of expected concentrations was covered. A consensus value among participating labs was calculated. The aim was to obtain comparability across the labs.
In the EQUAS, the control samples were analysed again in experienced reference laboratories. Their results were used to define an assigned value and tolerance ranges for each of the concentrations of biomarker in the samples. The aim was to attain accuracy, i.e. the 'true' assigned values.

Only those laboratories that successfully passed the quality assurance process, according to the criteria defined under COPHES/DEMOCOPHES, were allowed to analyse the DEMOCOPHES samples. Thus, in early 2012, 16 labs carried out the mercury analysis in hair, 14 labs did cadmium, 9 did cotinine, 7 did phthalate metabolites (countries agreed to analyse at least 5 phthalate metabolites from a list of 20, taking into account their policy relevance), 5 did Bisphenol-A and 14 did creatinine (creatinine levels in urine need to be measured to adjust urinary concentration of the biomarkers).

Performing statistical analysis and data interpretation

A statistical working group considered a number of issues with respect to data analysis and interpretation. These were discussed at two training sessions: December 2011 in Brussels and March 2012 in Copenhagen.

To enable the compiling of a single European database, all national DEMOCOPHES databases had to be set up in the same way. Detailed instructions were provided in a centrally developed codebook and in guidelines for quality control. A process was set up to check the quality of the national databases and to merge them into one European database.

A plan for statistical analysis was applied to the biomarker and questionnaire data and guidelines were given on interpretation of the results, including:

1. Calculation of response rate and non-responder analysis obtained on the basis of the inventory made during recruitment;
2. Description of the general characteristics of the study population, i.e. age, gender, anthropometry, social class, etc.;
3. Statistical analysis of the five biomarkers.

At European level, the statistical analysis was performed in a similar way as in the individual countries.

Communicating properly throughout the study

Communication was a key task throughout the project, from the recruitment phase until the publication of the results. National team coordinators were trained during 2 workshops: December 2011 in Brussels and March 2012 in Copenhagen.

Communication at recruitment

Children aged 6-11 years and their mothers received an information leaflet and a letter inviting them to participate in the pilot study, along with a reply card and consent form. Volunteers who met the inclusion criteria then received a confirmation letter, along with urine containers and an instruction leaflet for urine sampling. The start of the project and of the recruitment period was covered by several newspapers in participating countries and at European level. Project websites, both at European and at national level, provided key information and documents throughout the project.

Communication of individual results

Communication of individual results to study participants took place as early as possible, unless the participant chose not to be informed. Each participating mother received a letter with her and her child's results, explaining that:

- For some substances, this study gives only a snapshot of their exposure. Elevated levels of chemicals that are excreted quickly can occur due to temporary exposure and give no indication of a person's overall exposure.
- Heavy metals like mercury accumulate in the body and the levels measured give an indication of the accumulated lifetime exposure.
- If available, current health-based guidance values explained the potential health significance of measured levels. For some chemicals measured, it was only possible to indicate what the levels were and how they compared with the aggregated results, but not what the health implications might be.

Contacts details of a national team member were given for further clarification if needed. If the values measured indicated possible health risks, the mother was contacted to explain what could be done to reduce exposure.

Each participating mother received a letter with her and her child's results

Meetings were organised to explain the project to the participants

Communication of aggregated results

Dissemination to the general public: The results and conclusions of COPHES and DEMOCOPHES were presented at the Cyprus Presidency Conference, 'Human Biomonitoring: Linking Environment to Health and Supporting Policy', held in Larnaca on 23 and 24 October 2012. A press release on this Conference can be found on the Cyprus Presidency website[6]. As a result, several European journals showed interest and press articles were published.

Between July 2012 and January 2013, each country organised a national symposium to report on the aggregated results to the general public and to their policy-makers.

A 50-minute documentary on DEMOCOPHES is available for further use.

Dissemination to the policy-makers: Topics of particular interest include using HBM results for policies, feasibility of an EU-harmonised programme, and the next steps required in line with both the European Environment and Health Action Plan 2004-2010[2] and the WHO Parma Conference on Environment and Health[7].

Dissemination to the scientific community: The results of COPHES and DEMOCOPHES were presented at the 22nd Annual Meeting of the International Society of Exposure Science in Seattle. DEMOCOPHES results on mercury were used for an economic calculation of the cost of the actual exposure of Europeans to this widespread heavy metal[8]. More results will be published in peer-review journals and communicated at other scientific meetings.

The results and conclusions of COPHES and DEMOCOPHES were presented at the Cyprus Presidency Conference

6 http://www.cy2012.eu/index.php/en/news-categories/areas/employment-social-policy/press-release-european-projects-measure-chemicals-in-people-across-europe-for-the-first-time

7 http://www.euro.who.int/en/what-we-do/event/fifth-ministerial-conference-on-environment-and-health

8 Economic benefits of methylmercury exposure control in Europe: Monetary value of neurotoxicity prevention, Environmental Health 2013, 12:3 http://www.ehjournal.net/content/12/1/3/abstract

Project results

A common approach for HBM was tested in 17 European countries; data on the distribution of specific biomarkers among the defined study population and relations to possible sources were produced and, for the first time, are comparable on an EU scale, which is a step towards European reference values.

Findings on the chemicals under investigation

Data from 1844 mother-and-child pairs were collected for the 4 basic chemicals and from 621 pairs for Bisphenol-A. Although not yet representative of the European population, this is the first time information made available on the distribution of chemicals in 17 European countries can be compared across the countries' borders and with international data from NHANES, Health Canada and European national studies.

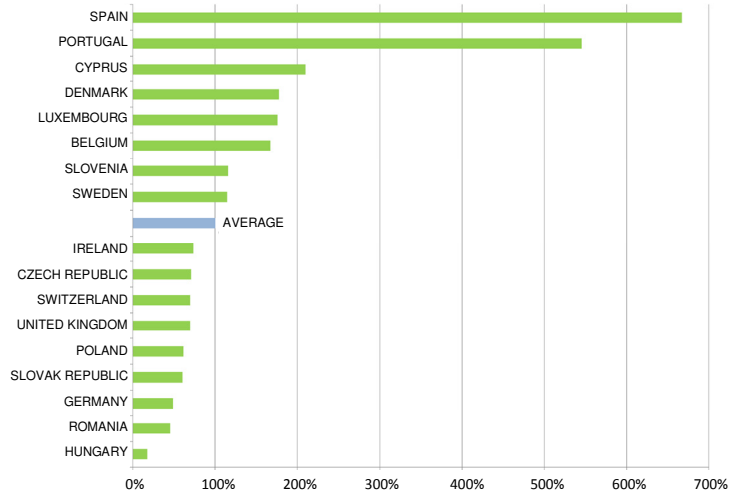
Table 1: Values at European level in mothers and children: mean, P90 and used health guidance values for the investigated biomarkers

		Children			Mothers		
Biomarker	**Unit**	**Mean**	**P90**[1]	**Guidance value**	**Mean**	**P90**	**Guidance value**
Mercury	µg/g	0.14	0.82	2.3 (FAO/WHO)[2]	0.22	1.3	2.3
Cotinine	µg/l	0.80	5.1	Not defined (Nd)	2.7	1237.0	Nd
Cadmium	µg/l	0.07	0.22	0.5 (HBMI)- 2 (HBMII)[3]	0.22	0.62	1 (HBMI)- 4 (HBMII)
Phthalates metabolites							
DEHP metabolites	µg/l	47.6	141.0	500 (HBMI)	29.2	93.0	300 (HBMI)
MnBP	µg/l	34.8	98.0	Nd	23.9	68.0	Nd
MBzP	µg/l	7.1	27.8	Nd	4.5	18.0	Nd
MEP	µg/l	34.4	160.0	Nd	48.2	259.1	Nd
MiBP	µg/l	45.4	135.0	Nd	30.1	89.0	Nd
Bisphenol A	µg/l	2.0	7. 4	2500 (HBMI)	1.8	6.7	2500 (HBMI)

1 90% of the studied population presented values below P90.
2 Guidance value defined by JECFA (Joint FAO/WHO Expert Committee on Food Additives) at their 67th meeting in 2006.
3 HBM values are defined according to the knowledge and judgement of the German Commission on Human Biomonitoring, HBMI values correspond to the concentration of a substance in human biological material below which adverse health effects are not expected. HBMII values correspond to the concentration of a substance in human biological material above which there is an increased risk of adverse health effects in susceptible individuals in the general population.

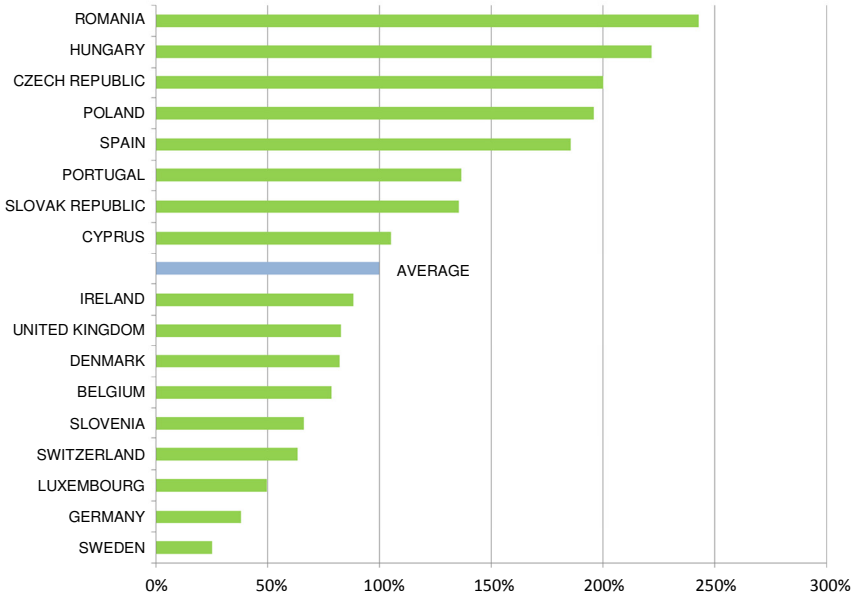
In general, DEMOCOPHES results show that younger children (6-8 years) have higher exposure levels compared to older children (9-11 years). This emphasises the importance of paying specific attention to the younger age group. Biomarker levels vary widely, both within and between countries. The information reported by participants on their environment and lifestyle enables the identification of influencing factors and hence possible intervention strategies. Overall, exposure levels are well below the health-based guidance values used. Few participants have values above these. Biomarker levels in children are highly correlated with levels in their mothers, which may indicate common exposure to environmental stressors. Social class, determined by the educational level of the mother, has a significant influence on each of the biomarker levels. This factor may hide underlying and undiscovered determinants of exposure.

Figure 1: Mercury in hair of mothers, % of the DEMOCOPHES countries average, adjusted for age[9]



Mercury accumulates in the body throughout life and the higher values found in mothers compared to children are due to this accumulation. Eating sea fish has the greatest influence on mercury levels found in both mothers and children. In a European context, the Spanish and Portuguese mercury levels are relatively high. The average Spanish mother has more than six times the DEMOCOPHES countries average in her body and the average Portuguese mother more than five times. Cyprus, Denmark, Luxembourg and Belgium have averages that are just above the DEMOCOPHES countries average. The other countries in the project, mainly from Central and Eastern Europe, score on or below this average. In the south of Europe, people eat large quantities of fish. In countries like Cyprus, Denmark, Luxembourg and Belgium people eat quite a lot of fish too, but they are not used to eat big predator fish. In this study, 1.4% of the children and 3.4% of the mothers have mercury levels above the FAO/ WHO health-based guidance value of 2.3 µg/g (see table 1).

Figure 2: Cotinine in urine of children, % of the DEMOCOPHES countries average,adjusted for urinary creatinine, age and gender[9]

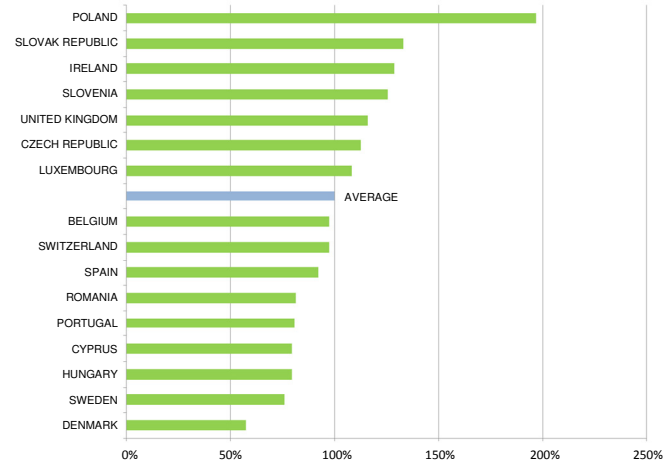


Cotinine levels in the children clearly reflect the smoking habits of adults in the household. Children who were exposed daily to

9 Based on the COPHES WP4 report "Human biomonitoring in children and mothers - European analysis", elaborated by VITO in close collaboration with DEMOCOPHES

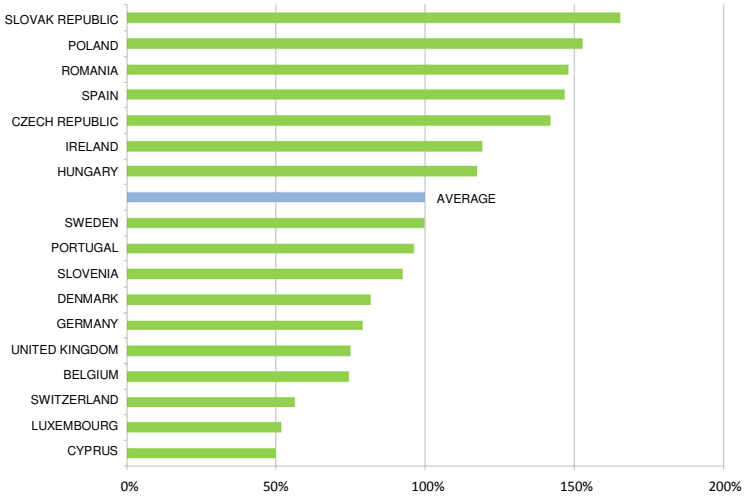
tobacco smoke in the environment had values five times higher than children who were never exposed. Mothers who smoke daily have mean cotinine values 30 times higher than the values in occasional smokers and 700 times higher than former or non-smokers. The cotinine level found in the urine of Romanian mothers is more than 5 times the DEMOCOPHES countries mean. Exposure to tobacco smoke is relatively high in other Eastern European countries and in Spain and Portugal as well. In the rest of Northern and Western Europe the cotinine concentrations are considerably lower. Cotinine levels in children follow the same trend, although the levels are much lower. As expected, we see that children in Europe are exposed to environmental tobacco smoke.

Figure 3: Cadmium in urine of mothers, % of the DEMOCOPHES countries average, adjusted for urinary creatinine, age and smoking[9]



Cadmium accumulates in the body with age. Mothers have much higher values than children. Not one mother in this study had a cadmium level in her urine which indicates an adverse health effect on the kidneys. In Poland, the values measured are relatively high. The main reason for this might be that farmers are still using fertilisers with a high cadmium content. This cadmium is ingested through food and inhalation of dust.

Figure 4: Sum of DEHP metabolites in urine of children, % of the DEMOCOPHES countries average, adjusted for urinary creatinine, age and gender[9]



Phthalate metabolites generally showed higher levels in children compared to mothers, with the exception of MEP which is not regulated and is mainly used in cosmetics. A possible explanation is children's relatively higher intake: they are more exposed to dust, playing nearer the ground, and have more frequent hand-to-

mouth contact; and they eat more than adults in relation to their weight. Consumption of convenience food, use of personal care products and indoor exposure to vinyl floors and wallpaper have all been linked to higher phthalate levels in urine.

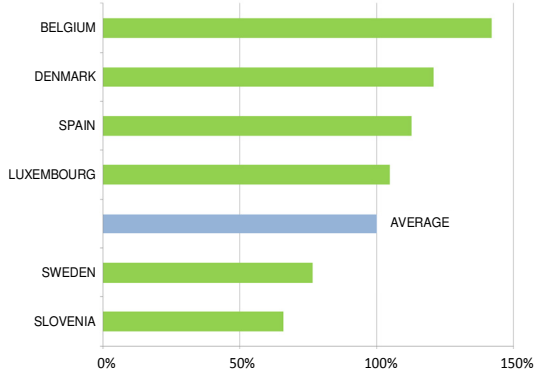


Figure 5: Bisphenol A in urine of mothers, % of the DEMOCOPHES countries average, adjusted for urinary creatinine and age[9]

Bisphenol-A levels in urine are of the same order of magnitude in mothers and children and are well in line with previously reported values in European populations. The measured values are very close to each other around the DEMOCOPHES countries average of 1.78 µg/L urine, which is still far below the health guidance value of 2500 µg/L urine.

The development of capacities in Europe

A European common approach was tested in 17 European countries. The following conclusions can be drawn at this stage:

- Sufficient harmonisation can be achieved to successfully conduct HBM surveys on an EU scale.
- It is possible to adapt fieldwork procedures to a certain extent to suit national needs without influencing the comparability of the results.
- Only strict quality assurance and control can guarantee comparable and reliable results. Although capacity-building was one of the major aims of the study, this process should not compromise the strict criteria needed to achieve comparability.
- Targeted communication is key from the very start and must include social science strategies.
- Training, helpdesk and telephone conferences were essential additional tools to guide and maintain the harmonised approach.

A European common approach for human biomonitoring was tested in 17 European countries

Assessment of the benefit/impact and cost-benefit discussion on the project results

Well-designed HBM programmes are scientific tools that can provide the evidence base to drive policy-relevant evaluations and recommendations.

The chemicals investigated in the project were chosen for their relevance with respect to policy actions. The Bisphenol-A biomarker was also analysed by 6 DEMOCOPHES countries following a request by their policy-makers.

During the course of the project, the European Chemicals Agency (ECHA) called for data on certain phthalates and the European Food Safety Authority (EFSA) for data on Bisphenol-A in order to re-evaluate their recommendations in the light of new scientific information. The results will be available on request for European agencies and related scientific committees in the framework of their reporting or risk-assessment activities.

Human exposure data have a strong impact on action at both collective and personal level. The national symposia organised in each country provided the opportunity to inform policy-makers and the public and to discuss the relevance of and interest in actions at national level. The broad press attention and the documentary raised the awareness of the general public and provided recommendations on eating habits and consumption patterns.

DEMOCOPHES mercury results were used in a publication[8] issued in January 2013. The benefits of controlling mercury pollution were calculated to more than 600 000 IQ points per year and consequently monetary benefits were of €8 to 9 billion per year for the entire EU. Exposure abatement requires global-scale co-operation on policies and source reductions, which are currently addressed by the United Nations Environment Programme[10]. WHO Europe has also decided to use this mercury biomarker as one of the indicators, following the Parma Commitments.

The major costs of a survey are linked to the recruitment and sampling of the targeted population. Moreover, biological samples are precious and should be used extensively for the common good. That is why the storage of DEMOCOPHES samples has been arranged for at least 10 years. DEMOCOPHES aimed to develop capacities and test the feasibility of the European harmonised approach with a very limited set of biomarkers. By storing the samples, there will be further possibilities for investing more biomarkers in these.

DEMOCOPHES has opened the way for future developments. Thanks to this pilot study, the costs of upcoming HBM surveys on a European scale, with a larger set of agreed biomarkers, could be reduced while the benefits could be higher. In the COPHES project, an overall cost of between €3.7 million to €13.7 million per year has been estimated as the minimum and maximum scenario, respectively, for implementing an HBM programme for the 27 EU Member States.

The storage of DEMOCOPHES samples has been arranged for at least 10 years

10 http://www.unep.org/hazardoussubstances/Mercury/Negotiations/tabid/3320/Default.aspx

© violetkaipa - Fotolia.fr

HBM data can now be compared in Europe

Feasibility of the EU-harmonised approach and transferability of project results

DEMOCOPHES has demonstrated that it is feasible to produce data that can be compared across borders if harmonised and standardised protocols are used and if internal and external quality assurance is guaranteed.

On the basis of the description of work – including comments and suggestions – reported in the DEMOCOPHES deliverables, the European study protocol can be updated. The following recommendations have been made for future European harmonised studies:

- Define inclusion and exclusion criteria that can be met in all countries;
- Measure one substance in one lab thus avoiding uncertainties regarding comparability of measurements of small doses between different laboratories;
- Provide user-friendly programmes for statistical analysis, to reduce the resources needed to perform them;
- Involve national social scientists from the start of the study, to help understand and take into account cultural differences;
- Develop communication materials that are well adapted to the target groups allowing adaptations to national situations.

HBM can be used to assess and track trends, both temporally and spatially, in the exposure level of the population to environmental pollutants, and can be used to inform and monitor policy measures. From a policy point of view, further progress is necessary in the development of reliable biomarkers and analytical methods and structures for a long-term European programme to increase the use of HBM for preventive policies[11].

Now that the feasibility of the EU harmonised approach has been demonstrated, policy-makers could think about developing a more global EU-wide programme, guided by the lessons learned in DEMOCOPHES. Close collaboration is already envisaged, with the network having implemented the European Health Examination Survey project (EHES) and with the network implementing the mandatory Health Information Survey (HIS). This would provide considerable cost savings and create unforeseen opportunities for research and policy assessment.

However, to pave the way forward, Europe needs a structure that will allow for suitable coordination and organisation. This structure could receive a specific mandate and adopt a transparent decision-making strategy with respect to choices to be made for the future implementation of HBM in Europe.

11 The REACH Regulation, the new biocide Regulation, the POP's Regulation (2004/850/EC of 29 April 2004 modified), Directive 2009/128/EC of 21 October 2009 establishing a framework for Community action to achieve the sustainable use of pesticides, Regulations on cosmetics, drugs and food, and Directive 98/24/EC.

Glossary

BPA:	Bisphenol-A
CAPI:	Computer Assisted Personal Interview
COPHES:	Consortium to Perform Human Biomonitoring on a European Scale
DEHP:	di(2-ethlyhexyl) phthalate
DEMOCOPHES:	DEMOnstration of a study to COordinate and Perform Human biomonitoring on a European Scale
ECHA:	European Chemicals Agency
EFSA:	European Food Safety Authority
EQUAS:	External Quality Assessment Schemes
HBM:	Human BioMonitoring
ICI:	Interlaboratory Comparison Investigation
IQ:	Intelligence Quotient
MEP:	mono-ethyl phthalate
Nd:	Not defined
NHANES:	US National Health and Nutrition Examination Survey
µg/g:	Microgram/gram
µg/l:	Microgram/liter

DEMOCOPHES partners

Meeting Budapest
April 2011

The following partners have implemented the project:

Belgium:
FPS Health, Food chain safety and environment (FPS)
Dominique Aerts and Pierre Biot

Cyprus:
Ministry of Health represented by State General Laboratory (SGL)
Andromachi Katsonouri and Adamos Hadjipanayis

Czech Republic:
National Institute of Public Health (NIPH)
Milena Cerna and Andrea Krskova

Denmark:
University of Copenhagen (UCPH)
Lisbeth E. Knudsen and Jeanette KS Nielsen

Germany:
Umweltbundesamt (UBA)
Marike Kolossa-Gehring and Kerstin Becker

Hungary:
National Institute of Environmental Health (NIEH)
Peter Rudnai and Szilvia Középesy

Ireland:
Health Service Executive (HSE)
Maurice Mulcahy and Damien Burns

Luxembourg:
Centre de Recherche Public - Gabriel Lippmann (CRP-GL)
Arno Gutleb and Marc Fischer (LNS)

Poland:
Nofer Institute of Occupational Medicine (NIOM)
Danuta Ligocka and Marek Jakubowski

Portugal:
Institute of Preventive Medicine, Lisbon Faculty of Medicine (IMP/FML)
Fatima Reis and Sónia Namorado

Romania:
Environmental Health Centre (EHC)
Eugen S. Gurzau and Ioana-Rodica Lupsa

Slovakia:
Public Health Authority of the Slovak Republic (UVZ SR)
Katarina Halzlova and Michal Jajcaj

Slovenia:
Jozef Stefan Institute (JSI)
Milena Horvat and Darja Mazej

Spain:
Instituto de Salud Carlos III (ISCIII)
Argelia Castaño and Marta Esteban

Sweden:
Karolinska Institutet (KI-IMM)
Marika Berglund and Kristin Larsson

Switzerland:
Federal Office of Public Health (FOPH)
Pierre Crettaz and Andrea Lehmann

United Kingdom:
Health Protection Agency (HPA)
Ovnair Sepai and Karen Exley

The following partners have contributed to the project:

Austria:
Umweltbundesamt GmbH (UBA)
Philipp Hohenblum

Croatia:
Institute for Medical Research and Occupational Health (IMROH)
Aleksandra Fucic

France:
Institut de Veille Sanitaire (InVS)
Nadine Frery and Georges Salines

Norway:
National Institute of Public Health Norway (NIPH-NO)
Georg Becher

COPHES Consortium[3]

All DEMOCOPHES partners are also partners in the COPHES consortium.

The following additional COPHES partners have given scientific support to the project:

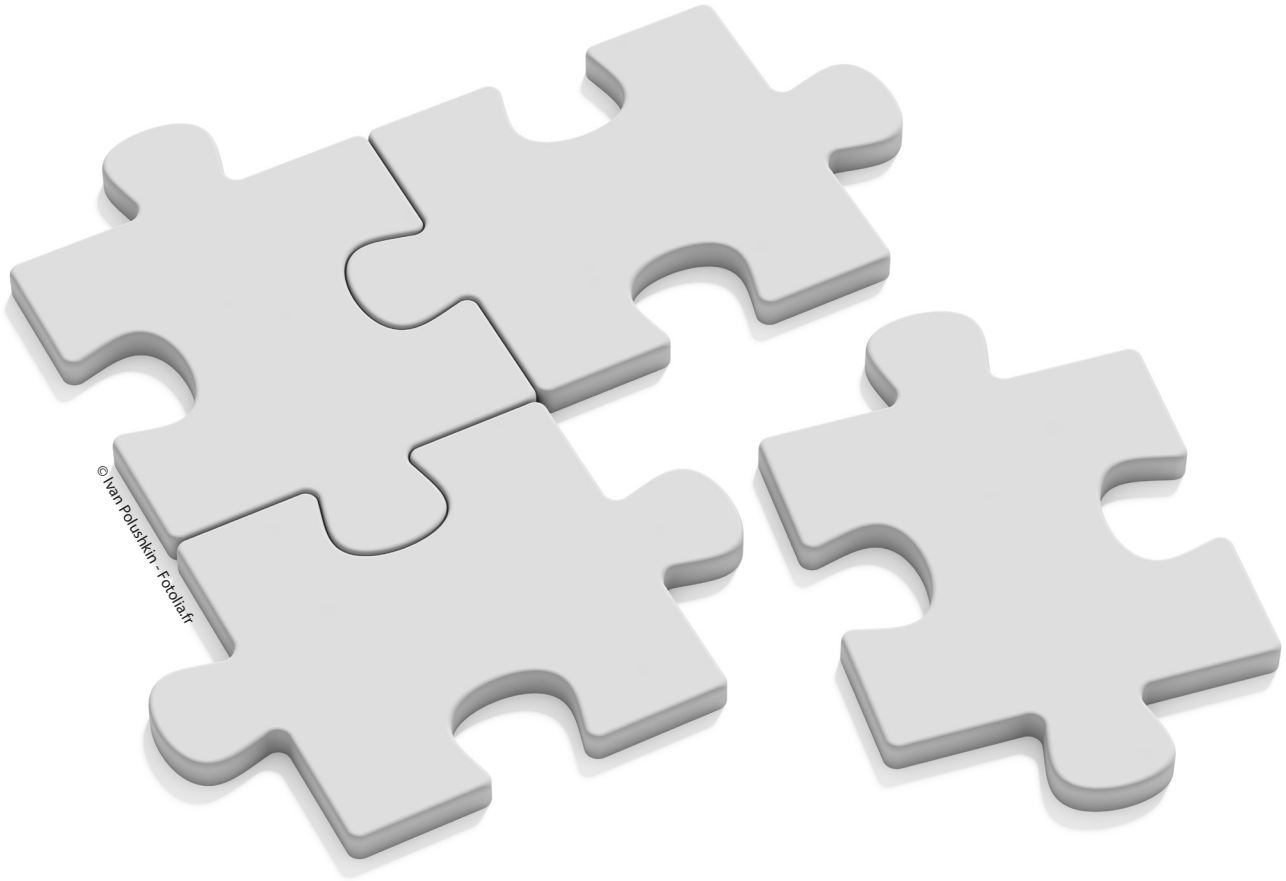
Belgium:
Center for Human Genetics - University of Leuven (KUL)
Ludwine Casteleyn and Birgit Dumez
Flemish Institute for Technological Research (VITO)
Greet Schoeters and Elly Den Hond

Germany:
Institut für Prävention und Arbeitsmedizin der Deutschen Gesetzlichen Unfallversicherung - Institut der Ruhr-Universität-Bochum (IPA)
Jürgen Angerer and Holger Koch
BiPRO Gmbh (BiPRO)
Reinhard and Anke Joas

Netherlands:
Environmental Health Sciences International (EHSI)
Louis Bloemen

Meeting Brussels
November 2011

Training Berlin
June 2011



www.eu-hbm.info

federal public service

HEALTH, FOOD CHAIN SAFETY AND ENVIRONMENT

Directorate General for Environment
Multilateral and Strategic Affairs
Place Victor Horta 40/10
1060 Brussels - Belgium
Tel: +32 (0)2 524 97 97
Mail: democophes@health.fgov.be
www.health.belgium.be

Ed. Resp. : Dr. Dirk Cuypers, Place Victor Horta 40 Bte 10, 1060 - Bruxelles | Conception graphique : Thierry Sauvenière | D/2013/2196/1