HBM4EU science and policy for a healthy future

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HBM4EU

POLICY BRIEF

JUNE 2022

European Human Biomonitoring Initiative

Cadmium

This policy brief summarises the adverse human health effects of cadmium, its main exposure pathways for humans, and how human biomonitoring could be of value in the development of EU policy.

KEY MESSAGES

- New HBM4EU data from human biomonitoring studies carried out across Europe supports the recommendation by EFSA to reduce Cd exposure since the estimated mean dietary exposure of adults in the EU is close or slightly exceeding the tolerable weekly intake (TWI) (EFSA, 2009; EFSA, 2012).
- Based on HBM4EU findings from the aligned studies (2014–2021), the risk of adverse health effects on the kidney cannot be excluded. In the majority of the sampling sites, 5% of the study participants (non-smoking) overlap with (and possibly exceed) age-dependent alert values for adverse effects on kidney functioning.
- Findings from HBM4EU suggest geographical variations in human internal cadmium levels, with higher levels observed in Western and Eastern Europe, but differences between the regions were not statistically significant. Median values varied up to a factor of 3 between the EU-sampling sites.
- Long-term formal EU-wide human biomonitoring activities are required to provide reliable assessment of the risks posed by pollutants such as cadmium to our health.
- In terms of health effects, cadmium particularly affects the kidneys, but HBM4EU data also identifies that Cd exposure contributes to the risk of osteoporosis. In women above 55 years old, 23% of the cases were attributable to Cd exposure. Cd is also classified as a human carcinogen.

BACKGROUND: HBM4EU

The European Human Biomonitoring Initiative, HBM4EU, running from 2017 to June 2022, is a joint effort of 28 countries, the European Environment Agency and the European Commission, and co-funded under Horizon 2020. The main aim of the initiative is to coordinate and advance human biomonitoring in Europe. HBM4EU has provided a wealth of improved evidence of the actual exposure of citizens to chemicals and their possible health effects. Human biomonitoring allows us to measure our exposure to chemicals by measuring either the substances themselves, their metabolites or markers of subsequent health effects in body fluids or tissues. Information on human exposure can be linked to data on sources and epidemiological surveys to inform research, prevention, and policy with the objective of addressing knowledge gaps and promoting innovative approaches. If you would like to read more about the project itself, please visit the HBM4EU website.

HBM4EU RESULTS

In order to further support current and future HBM studies, HBM4EU has produced a variety of publicly available groundwork materials for a harmonised approach to study HBM planning and conduct in Europe.

Based on the EFSA guidance value for tolerated daily intake of 1 µg/g creatinine for kidney effects in adults (> 50 years) and based on physiologically based pharmacokinetic (PBPK) modelling, HBM4EU derived age dependent alert values to prevent exceeding the guidance value of 1 µg/g creatinine at later age (> 50 years). These were set to 0.1 µg/g creatinine (crt) for children of 10 years of age or younger, 0.2 µg/g crt for 11-20 years, 0.3 µg/g crt for 21-30 years, 0.5 µg/g crt for 31-40 years, 0.8 µg/g crt for 41-50 years.

HBM4EU analysed cadmium levels in urine samples of 20-39 years-old adults, sampled all over Europe (DK, IS, PL, CZ, HR, PT, DE, FR, LU) between 2014 and 2021. Median values varied by a factor of 3-4 between the EU locations.

The HBM4EU data (2014–2020) for the European adult population aged 20-39 years, shows that at most sampling sites 5% of the study participants exceeded recommended alert values for urinary cadmium levels. Exceedances in the different studies and locations range from 1.42% up to 41.98%. The studies with most adults exceeding the guidance value were from Western and Eastern Europe.

The current cadmium levels are broadly similar to the previous DEMOCOPHES study that sampled children and their mothers between 2010 and 2012 in DK, SE, CZ, HU, PL, SK, ES, SI, BE, LU, DE). This indicates that current cadmium regulations and measures are not protective enough and that further reduction of Cd exposure in the general population is needed.

The implementation of the neurological effect marker (BDNF) linking cadmium to health effects in HBM4EU-related studies has shown promising results constituting an added value for human studies.

HBM4EU also laid the foundations for a European HBM Network to monitor human exposure to priority chemicals, including cadmium.

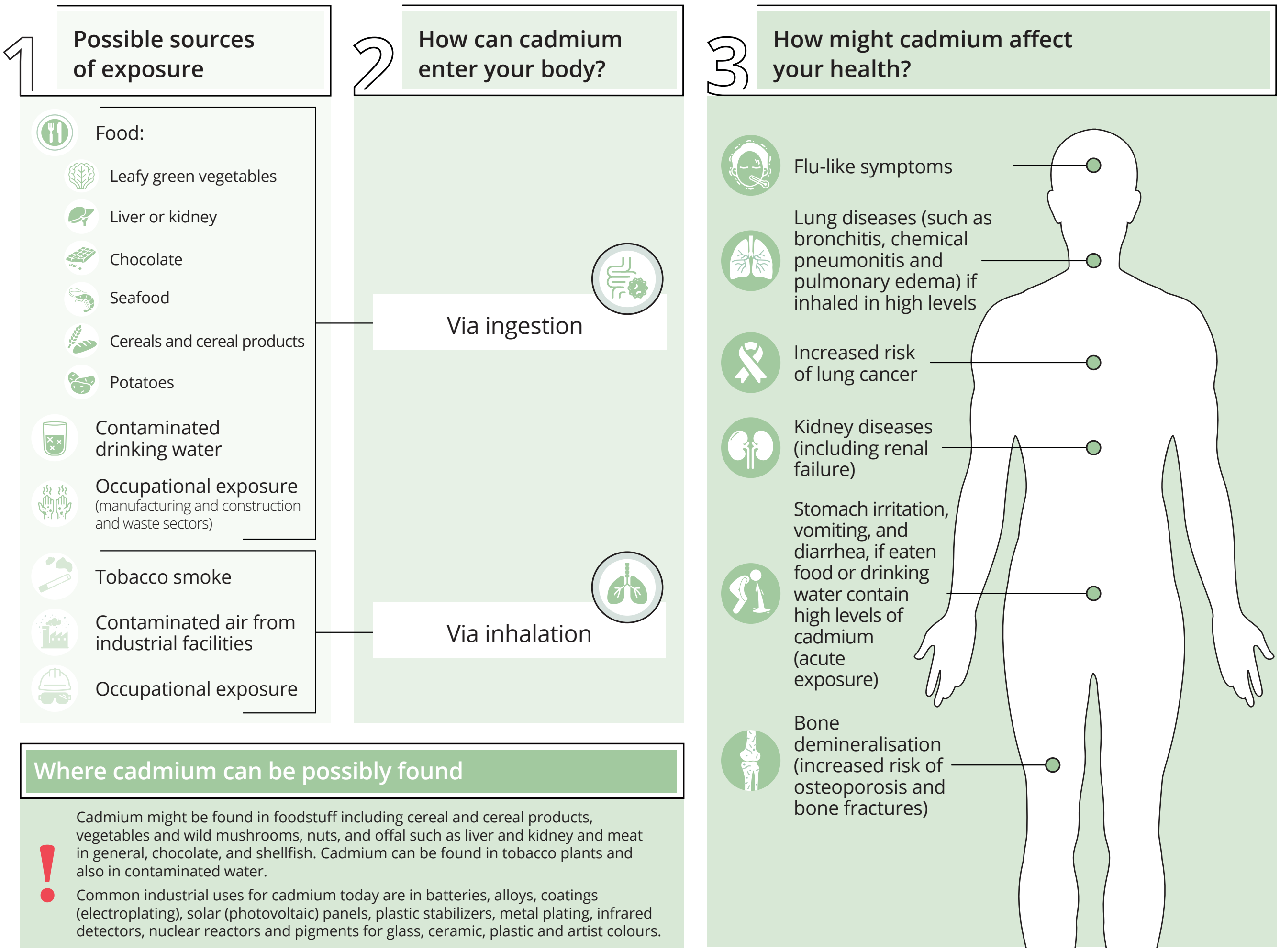
EXPOSURE AND HEALTH EFFECTS

Cadmium particularly affects the kidneys and can cause renal failure. In addition, cadmium is classified as a human carcinogen and a suspected mutagen and reproductive toxin. HBM4EU data also identified that cadmium exposure contributes to the risk of osteoporosis, with 23% of cases of osteoporosis in women over 55 years being attributable to cadmium exposure (Ougier *et al.*2021).

The primary exposure route for the general population is food. Smoking is also a source of cadmium exposure. Occupational exposure is a potentially significant source of exposure for those working in relevant industries such as manufacturing/use of pigments and the metal industry.

Available information on the typical intake of cadmium from food indicates that the intake of the average population is slightly below the tolerable weekly intake. However, the average dietary intake for certain groups (e.g. toddlers) is higher.

Figure 1. Overview of exposure sources, pathways and health effects associated with cadmium



INPUT TO POLICY PROCESSES AND RELEVANT POLICY MEASURES

HBM4EU results have contributed to consultations for the Chemicals' Strategy for Sustainability, the Zero-Pollution Action Plan, as well as ECHA. These are available in the HBM4EU Science to Policy section.

Policy measures have been taken to reduce the risks posed by cadmium and to reduce environmental pollution, including:

- Limits have recently been set for maximum Cd levels in specific foodstuffs including fruits, vegetables, mushrooms, chocolate, seafood, meat and baby food. These foodstuffs can potentially have elevated cadmium levels and present a risk to vulnerable groups.
- Use of cadmium in certain applications (such as in a range of plastics) is also restricted under the EU REACH regulation.
- Existing regulations ban cadmium use in cosmetics and limit Cd in toys and in electrical and electronic equipment.
- Occupational exposure limits are set for cadmium under the Carcinogens and Mutagens Directive for the protection of workers.
- Maximum allowable limits for cadmium in water are specified, and it is defined as a priority hazardous substance under the Water Framework Directive.

Ongoing human biomonitoring can help inform the effectiveness of these policy measures and the need for additional measures to further reduce risks.

POLICY QUESTIONS

The answers below are summarised. For more details, please consult the substance report available on the dedicated substance page of the HBM4EU website.

1 What is the current exposure of the European population to Cd?

The European HBM dashboard has 41 datasets with Cd exposure data integrated and metadata for 74 datasets for Cd are available in IPCHEM. New data for cadmium from the HBM4EU Aligned Studies is based on 2510 individuals. P50 and P95 of urinary cadmium concentrations are in the range of 0.10-0.37 µg/g crt and 0.26-1.71 µg/g crt across studies in adults. For the subpopulation of non-smokers, P50 and P95 of urinary cadmium concentrations are in the range of 0.09-0.36 µg/g crt and 0.23-1.56 µg/g crt across studies in adults.

2 Does the exposure to Cd differ significantly between countries and population groups? What are the main reasons for differences in exposure?

No distinct geographical patterns were observed, although the HBM4EU Aligned Studies revealed differences in internal exposure up to a factor of 3 between the specific EU study sites.

When comparing the four regions, higher levels were observed in West and East than in North and South, but after accounting for the main influencing factors (age, sex, smoking and sampling year), the differences between the regions were not statistically significant.

3 Is there a link between high soil contamination with Cd and human exposure via dietary sources?

Linking HBM and environmental data revealed that there is a significant contribution of Cd exposure in humans from phosphorous fertilizers.

Meta-analysis of existing data in HBM4EU, representing the period 2007-2018, showed inconsistent associations between levels determined by HBM and soil cadmium concentrations across different countries, population groups or different types of biomarkers. However, there were strong positive associations observed for some groups in certain areas, suggesting a potential association between Cd in soil and exposure through consumption of local food in these areas and/or population groups. This was also confirmed by the positive associations between HBM data and the percentage of agricultural and/or cropland, and consumption of phosphorous fertilizer. The latter was observed in 3 out of 4 datasets for which fertilizer data was available and also in the HBM4EU Aligned Studies. This finding suggests that phosphorous fertilizers present a significant contribution to cadmium exposure in humans. Furthermore, the HBM4EU Aligned Studies data revealed that vegetarian diet contributes to 35% higher cadmium levels in urine as opposed to non-vegetarian diet.

4 Which population groups are most at risk?

HBM data for both children (2010 data from DEMOCOPHES) and adults (HBM4EU Aligned Studies 2014-2021) show exceedances of guidance values. Cadmium accumulates over time; it is therefore important to keep exposure low at all ages. HBM studies showed that 23% of osteoporosis cases in women above 55 years are attributable to cadmium exposure.

A cross-sectional study has explored the relationship between Cd levels and a potential biomarker of effect, the brain-derived neurotrophic factor (BDNF). It found that higher urinary Cd concentrations were associated with lower BDNF protein levels and more behavioral problems in Spanish adolescent males (Rodríguez-Carrillo et al. 2022).

5 Are the overall exposure levels (in different population groups) above any health-relevant assessment levels (HBM guidance values, TDI)?

Based on internal exposure data of European children (2010-2012), urinary Cd exposure of some children in the EU exceeds recommended alert values. For studies that have exceedances, the extent of exceedance (= P95/alert value) in the different studies and locations range from 1.03 up to 3.40 for 0.1 µg/g crt and 1.19 up to 1.7 for 0.2 µg/g crt. The studies with largest extent of exceedance were from Luxembourg, Poland and Hungary.

Based on internal exposure data from the European adult population (20-39 yrs) (2014-2020), the urinary Cd exposure of some adults in the EU exceeds recommended alert values. The studies with the largest extent of exceedance were ESTEBAN (France) and POLAES (Poland). Exceedances in the different studies and locations range from 1.42% up to 41.98%. The studies with most adults exceeding the guidance value were from Western and Eastern Europe.

The studies support the recommendation by EFSA to reduce Cd exposure since the estimated mean dietary exposure of adults in the EU is close or exceed slightly the tolerable weekly intake.

It is noteworthy that HBM4EU investigations show exceedances of HBM-GVs for Cd exposure, indicating that so far regulations are not protecting the population sufficiently.

6 Are environmental quality standards for Cd in water sufficiently restrictive to protect human health from exposure to cadmium via the environment and via dietary sources?

Based on the available HBM data, mean daily intake of Cd is in the range of 0.1 to 0.7 µg/kg bw/day, with the highest levels observed in Poland, indicating that the highly exposed individuals might be close to the EFSA tolerable weekly intake of 2.5 µg/kg bw/week.

This shows that the current cadmium regulations and measures are not protective enough and that further reduction of Cd exposure in the general population is needed.

KNOWLEDGE GAPS

The HBM4EU project has identified that further assessment is required to increase the understanding of the variations in Cd exposure between different countries and different population groups (for example in areas where cadmium levels in soil are higher). In addition, there is also insufficient data on temporal trends in Cd exposure, which would help assess the impacts of policy measures.

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