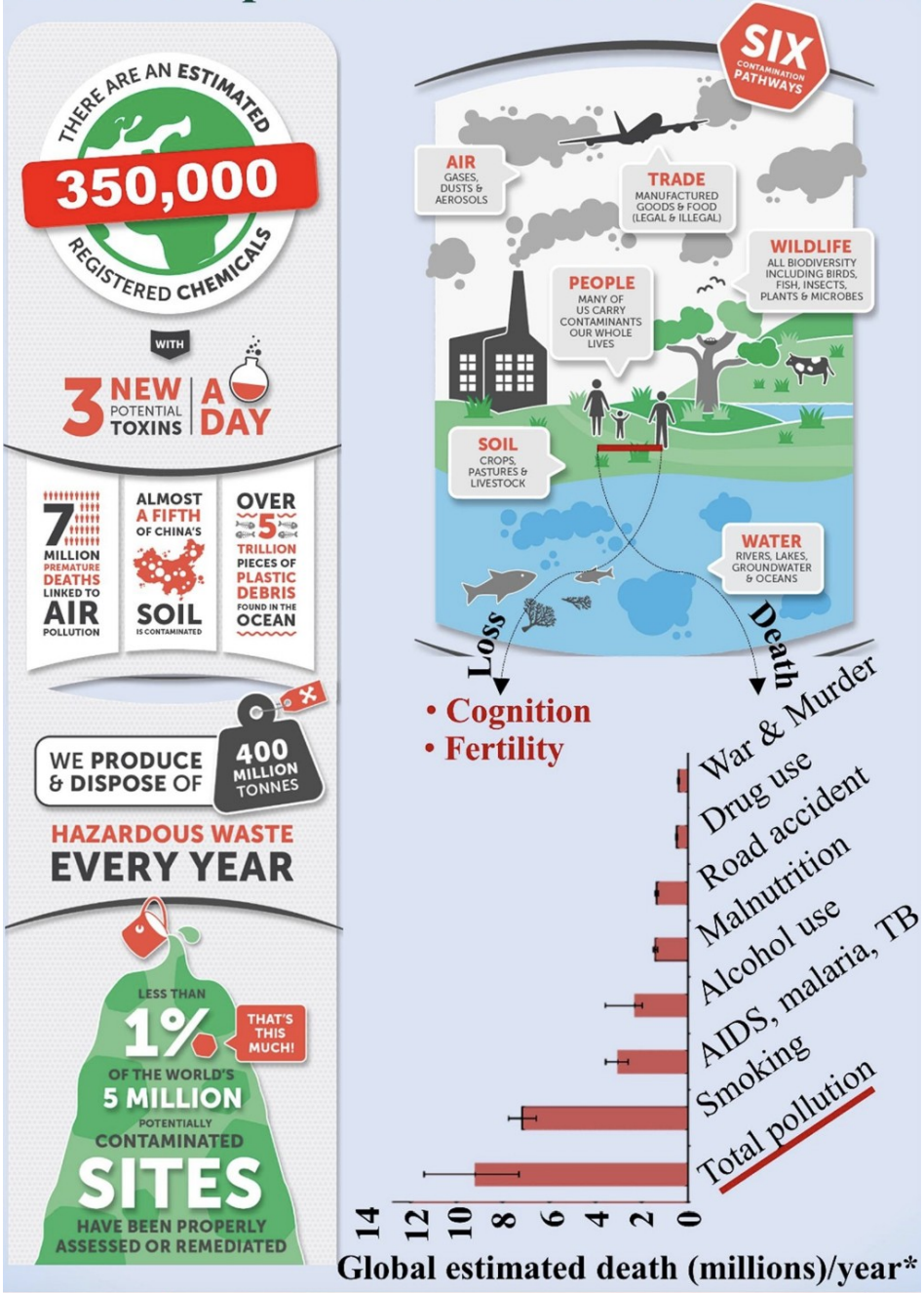# Human biomonitoring for the protection of health

E3040: Public Health Protection

November 2, 2023

Kasia Kordas, PhD

Chemical pollutant: Global PICTURE

THERE ARE AN ESTIMATED **350,000** REGISTERED CHEMICALS

WITH **3 NEW** POTENTIAL TOXINS | **A DAY**

7 MILLION PREMATURE DEATHS LINKED TO **AIR** POLLUTION

ALMOST **A FIFTH** OF CHINA'S **SOIL** IS CONTAMINATED

OVER **5 TRILLION** PIECES OF PLASTIC DEBRIS FOUND IN THE OCEAN

WE PRODUCE & DISPOSE OF **400 MILLION TONNES** HAZARDOUS WASTE EVERY YEAR

LESS THAN **1%** THAT'S THIS MUCH! OF THE WORLD'S **5 MILLION** POTENTIALLY CONTAMINATED **SITES** HAVE BEEN PROPERLY ASSESSED OR REMEDIATED

SIX CONTAMINATION PATHWAYS

AIR GASES, DUSTS & AEROSOLS

TRADE MANUFACTURED GOODS & FOOD (LEGAL & ILLEGAL)

WILDLIFE ALL BIODIVERSITY INCLUDING BIRDS, FISH, INSECTS, PLANTS & MICROBES

PEOPLE MANY OF US CARRY CONTAMINANTS OUR WHOLE LIVES

SOIL CROPS, PASTURES & LIVESTOCK

WATER RIVERS, LAKES, GROUNDWATER & OCEANS

Loss
• Cognition
• Fertility

Death

War & Murder
Drug use
Road accident
Malnutrition
Alcohol use
AIDS, malaria, TB
Smoking
Total pollution
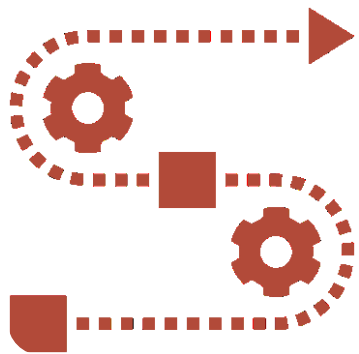
Global estimated death (millions)/year*
14 12 10 8 6 4 2 0

+ Exposure assessment plays a crucial role in understanding the potential harm to human health from environmental chemicals.

+ Individual studies by academic researchers, advocacy groups

Small-scale

Not systematic

Focused on specific/vulnerable population groups

+ Human biomonitoring.

Naidu R et al. Chemical pollution: A growing peril and potential catastrophic risk to humanity. *Environment International* 2021; 156:106616.
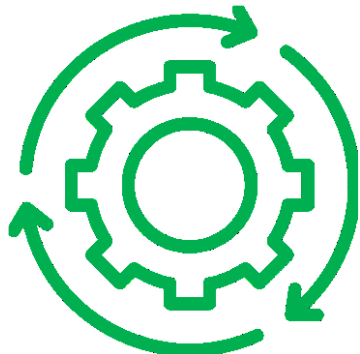
What is human biomonitoring (HBM)?

+ "systematic and continuous or repetitive activity for collection of biological samples for analysis of concentrations of pollutants and its metabolites, with the objective to assess exposure, changes after specific interventions and standardized protocols that allow to compare the data observed over time and with reference levels and—if necessary— leading to corrective actions".

Angerer J, Ewers U, Wilhelm M. Human biomonitoring: state of the art. *Int J Hyg Environ Health*. May 2007; 210(3–4): 201–28

Systematic
- Organized
- Methodology
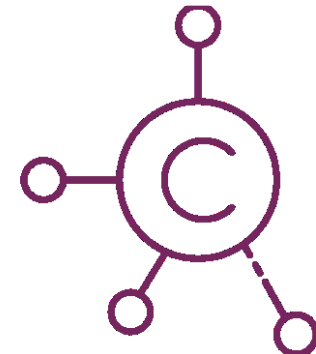- Rigorous implementation

Continuous or repeated
- Regular

Biological samples
- Blood
- Urine

Pollutants or their metabolites
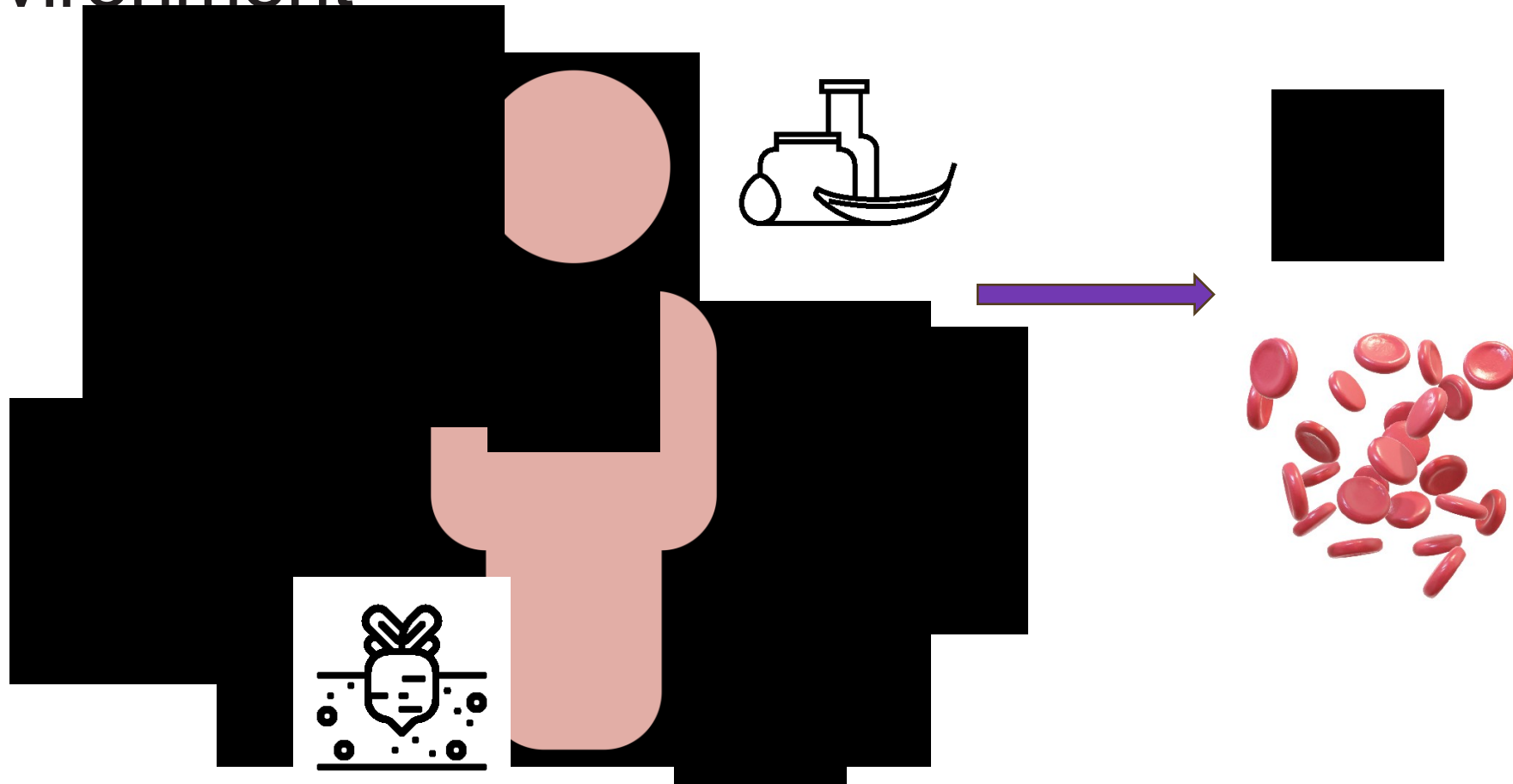- Inorganic
- Organic

Long-term monitoring → Study of trends → Comparison to reference values → Take corrective actions
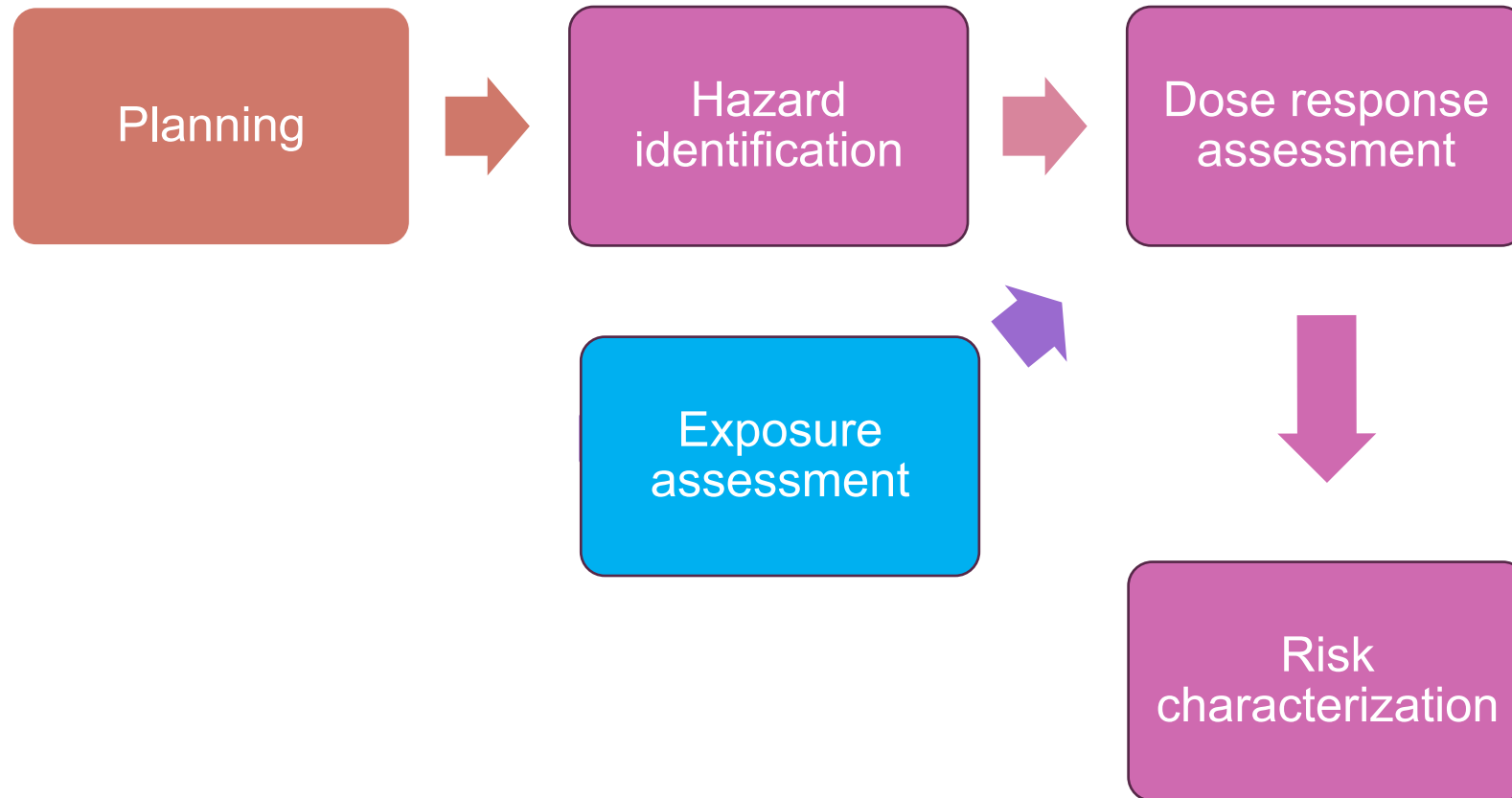
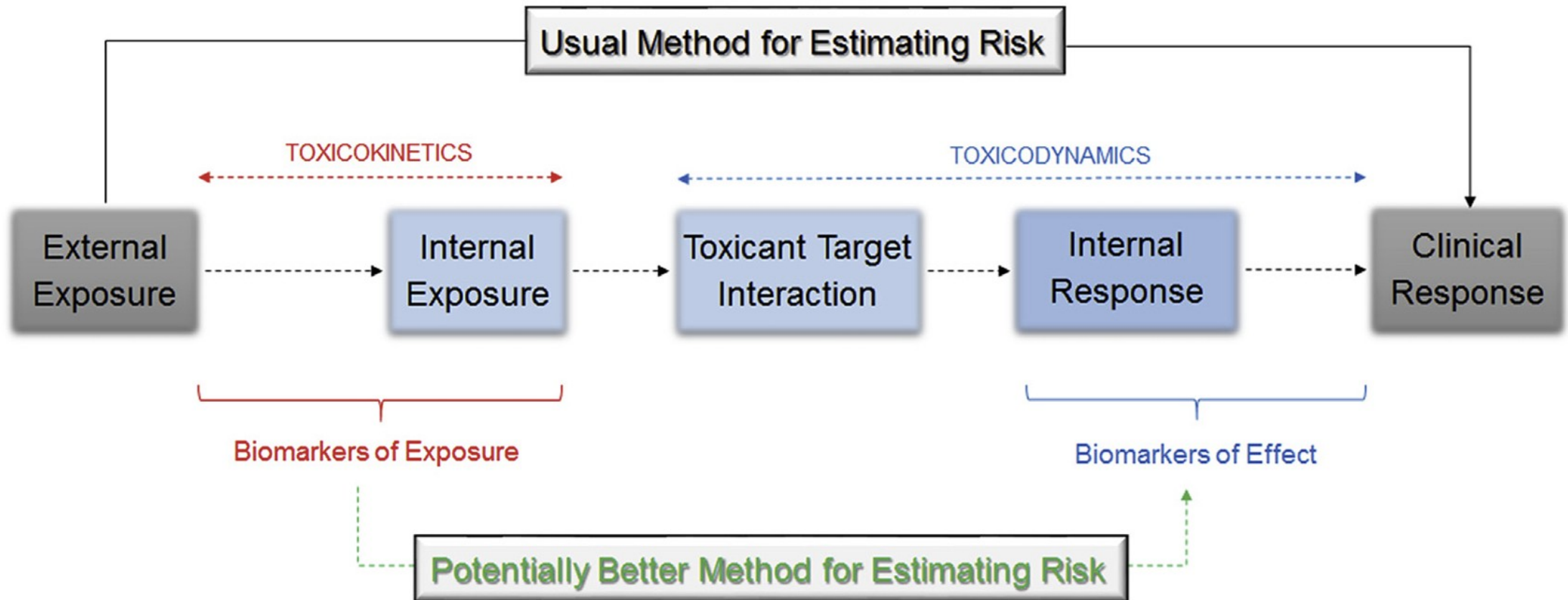HBM reflects the internal dose of chemicals taken up from any or all sources in the environment

Ambient monitoring is complementary but different

+ Measurement of chemicals in environmental samples, including air, water, soil and food.

Human health risk assessment process

Planning

Hazard identification

Dose response assessment

Exposure assessment

Risk characterization

How HBM fits with risk assessment process

Luoro H et al. Human biomonitoring in health risk assessment in Europe: Current practices and recommendations for the future. International Journal of Hygiene and Environmental Health 2019: 222: 727-37.

Why is HBM for risk assessment conducted?

Bar chart showing responses for why HBM for risk assessment is conducted, comparing General population (blue) and Occupational health (grey):

- Do not know: General population 4%, Occupational health 4%
- Biomonitoring is not usually performed in my country: General population 16%, Occupational health 7%
- To confirm data from environmental monitoring/modelling campaigns: General population 24%, Occupational health 4%
- To support risk management measures: General population 24%, Occupational health 26%
- Health Surveillance: General population 32%, Occupational health 67%
- To support risk assessment and define priorities for intervention: General population 50%, Occupational health 22%
- Assess the magnitude of internal exposure to a substance: General population 52%, Occupational health 52%
- Confirm exposure to a specific substance: General population 54%, Occupational health 48%
- Regulations: Occupational health 67%

Legend: ■ General population ■ Occupational health

Luoro H et al. Human biomonitoring in health risk assessment in Europe: Current practices and recommendations for the future. International Journal of Hygiene and Environmental Health 2019: 222: 727-37.

HBM is not universally implemented

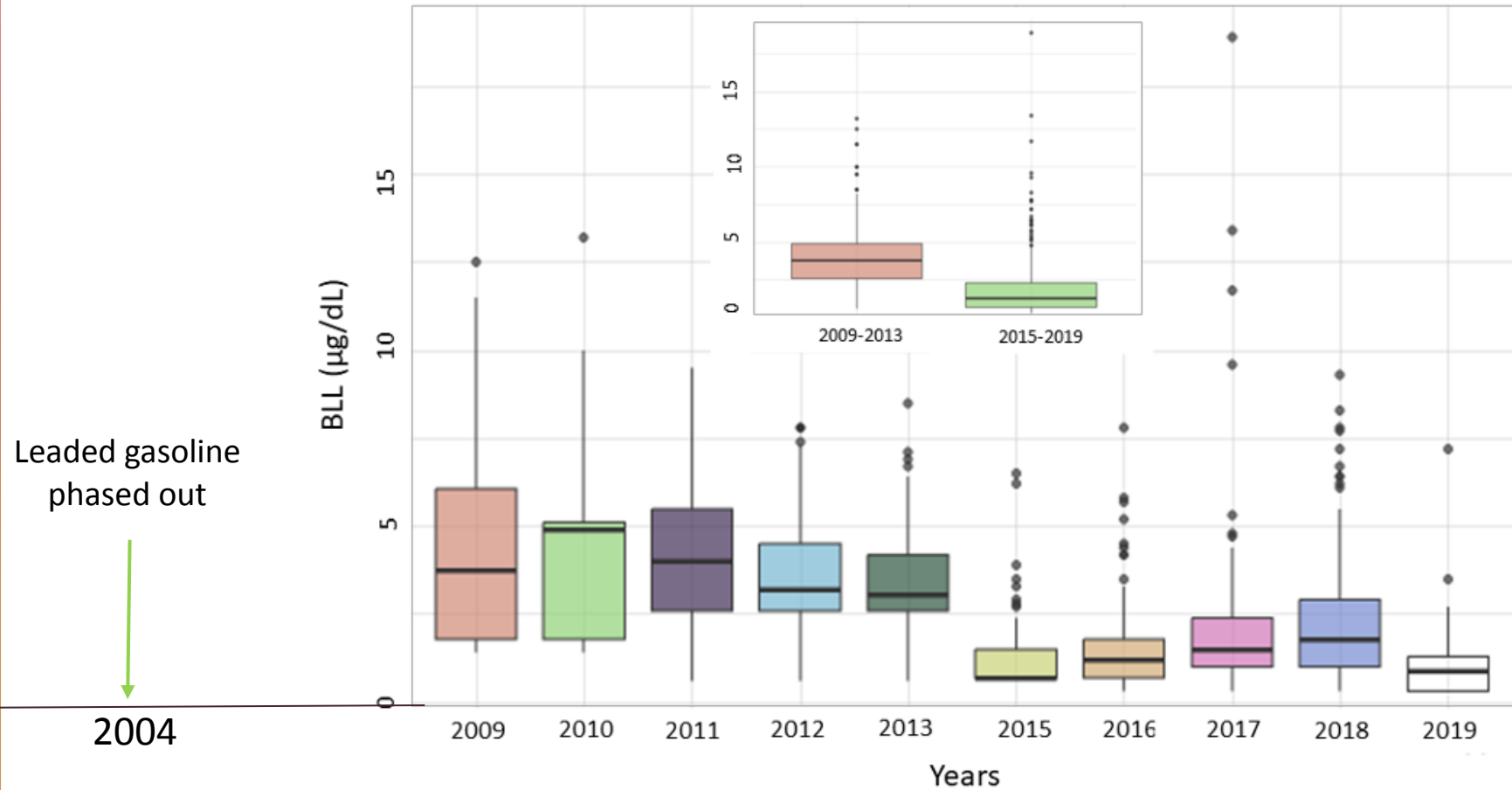+ HBM is very costly – mostly rich countries or regions do it

  USA, Canada

  EU

  (China)

+ Not in Latin America & Caribbean

A Call for Biomonitoring Systems in Latin America and the Caribbean: Considerations for Potentially Toxic Metals/ Metalloids

Tamayo-Ortiz M et al. *Annals of Global Health*. 2022; 88(1): 80, 1–11.

Secular trends in blood Pb, 2009-19, n=759

Leaded gasoline phased out

2004

Queirolo, Kordas, Martínez, Barg, Mañay. Secular trends in blood lead concentrations of school-age children in Montevideo, Uruguay from 2009 to 2019 (under review).

Enormous effort to develop & implement HBM

1. Government needs to recognize that HBM is important for population health.
2. Funding is essential – start-up costs & sustained investment.
3. Human resources with appropriate expertise and adequate level of training.
4. Laboratory set-up capable of handling samples
   1. Standard operating procedures
   2. Method validation
   3. Implementation of QC/QA

Tamayo-Ortiz M et al. *Annals of Global Health*. 2022; 88(1): 80, 1–11.
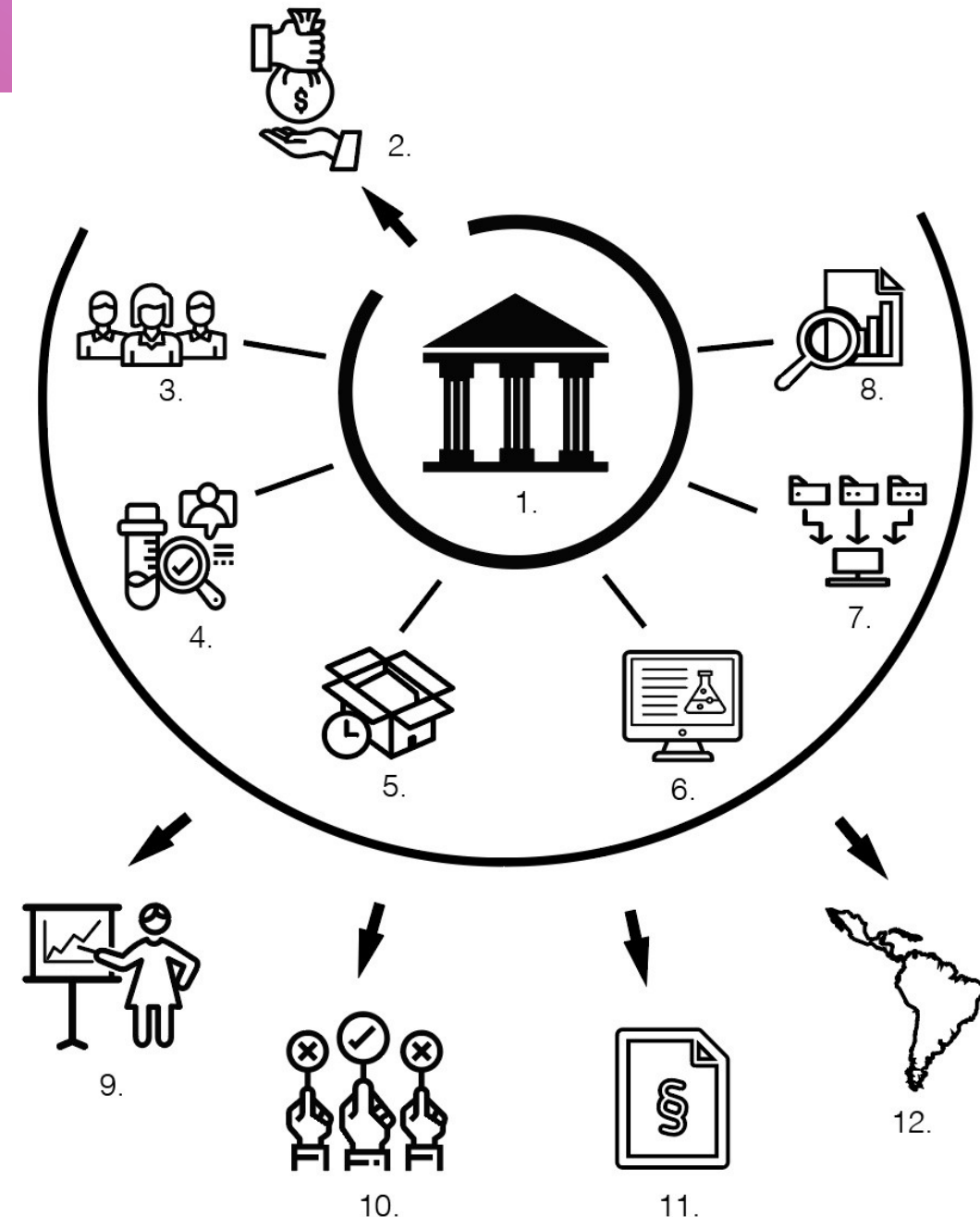
Enormous effort to develop & implement HBM

5. Logistics related to sample collection, transport, storage and processing.
6. Development and updating of data collection forms & data entry systems. Regular data checks.
7. Design and maintenance of (centralized) database system for long-term data storage and sharing.
8. Staff with appropriate data management skills needed.

Tamayo-Ortiz M et al. *Annals of Global Health*. 2022; 88(1): 80, 1–11.
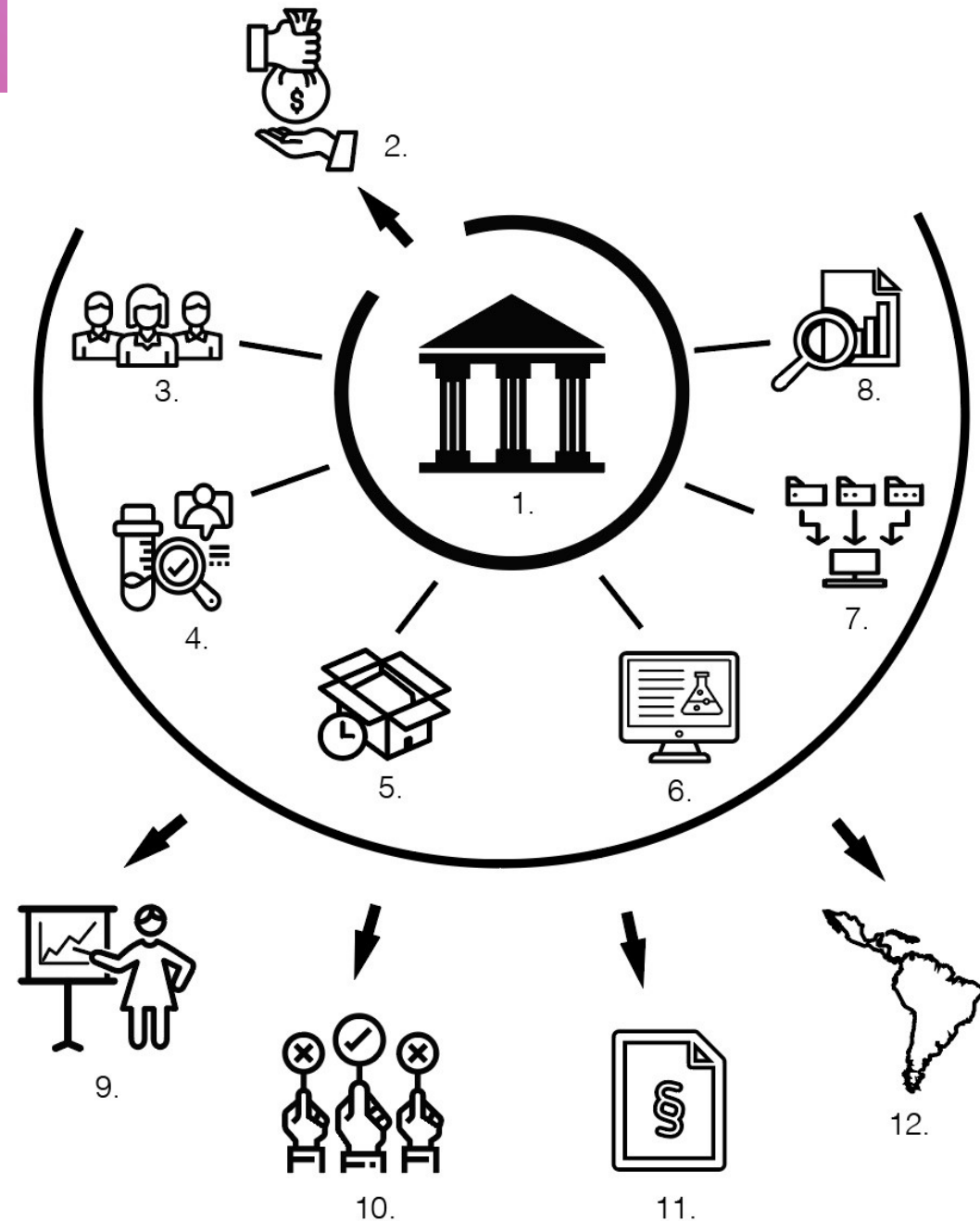
Additional considerations

9. Regular data sharing with scientific community.
10. Institutional accountability is required to ensure appropriate/efficient use of resources and data release to inform policy.
11. Regular measurement of pollutants should result in policies and regulations.
12. Regional cooperation may reduce costs, and harmonize protocols, data sharing, and cross-country comparisons.

Tamayo-Ortiz M et al. *Annals of Global Health*. 2022; 88(1): 80, 1–11.
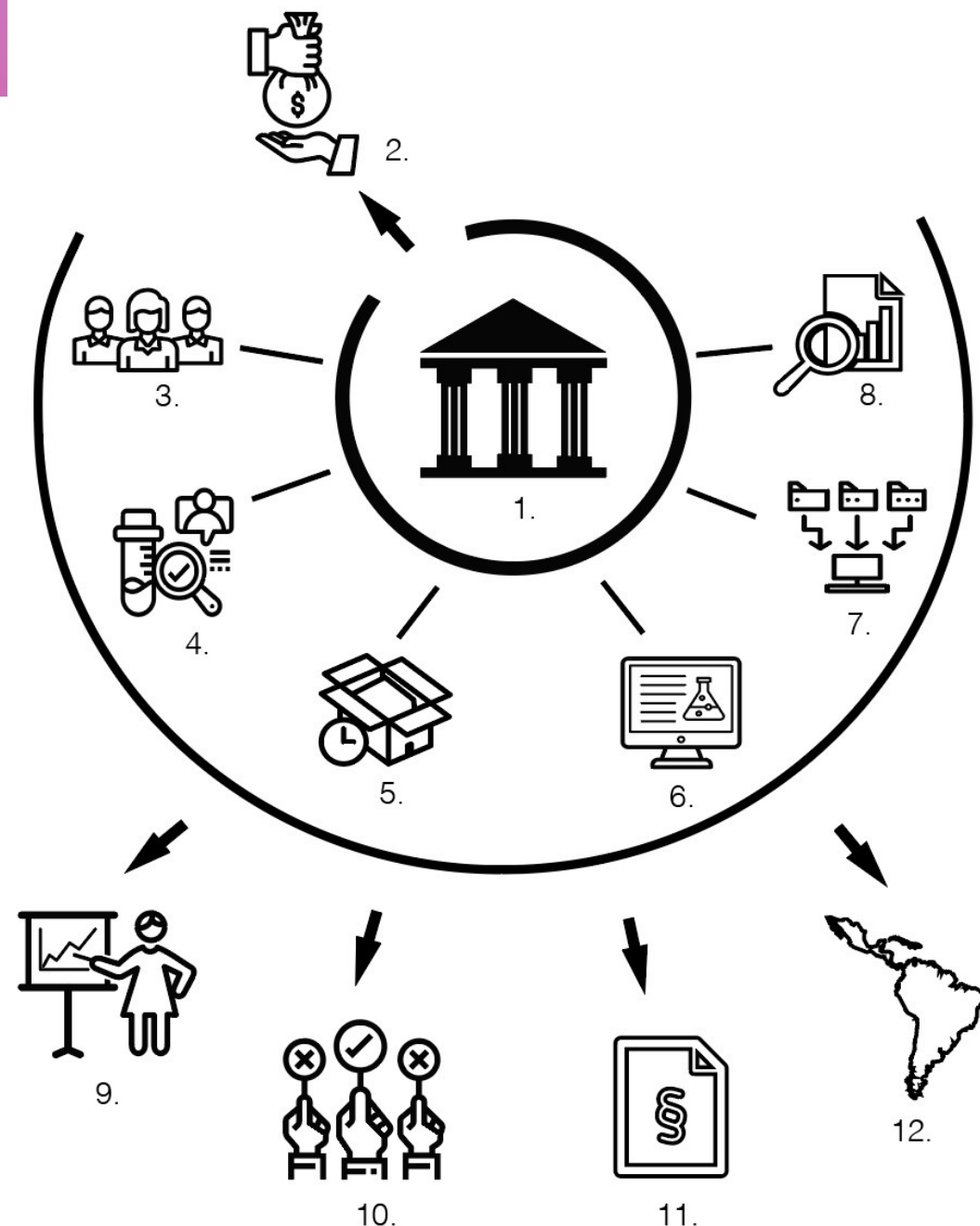
European programs, 1

+ **Human biomonitoring for Europe（HBM4EU）**

Joint initiative of 28 countries – the 24 EU member states plus Norway, Switzerland, Iceland and Israel – and the European Environment Agency.

€74 million in funding under Horizon 2020 (European Commission).

Jointly implemented by 120 partners.

Aimed to measure **Europeans' exposure to chemicals** and their health effects and develop human biomonitoring (HBM) as an exposure assessment method.

Program ended in June 2022.

European programs, 2

**+** **PARC** – Partnership for the Assessment of Risks from Chemicals

Launched in May 2022, with €400 million in funding (50% from EC & 50% from member states).

200 partner institutions, 3 EU authorities

European Chemical Agency (ECHA), European Food Safety Authority (EFSA), European Environment Agency (EEA)

Program aims to develop next-generation chemical risk assessment to protect human health and the environment.

Results are intended to help launch European and member state strategies to reduce health risks from hazardous chemicals.
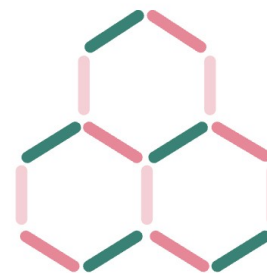
https://www.eu-parc.eu/
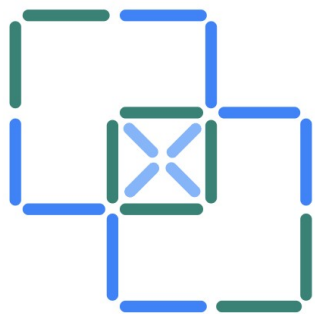
Risk assessment

Monitoring   +

Hazard assessment   +

Innovation   +

Tools & resources

Innovative tools and methods   +

Safe and sustainable by design   +

Building capacities

Laboratory networks   +

Online catalogue on environmental monitoring networks   +
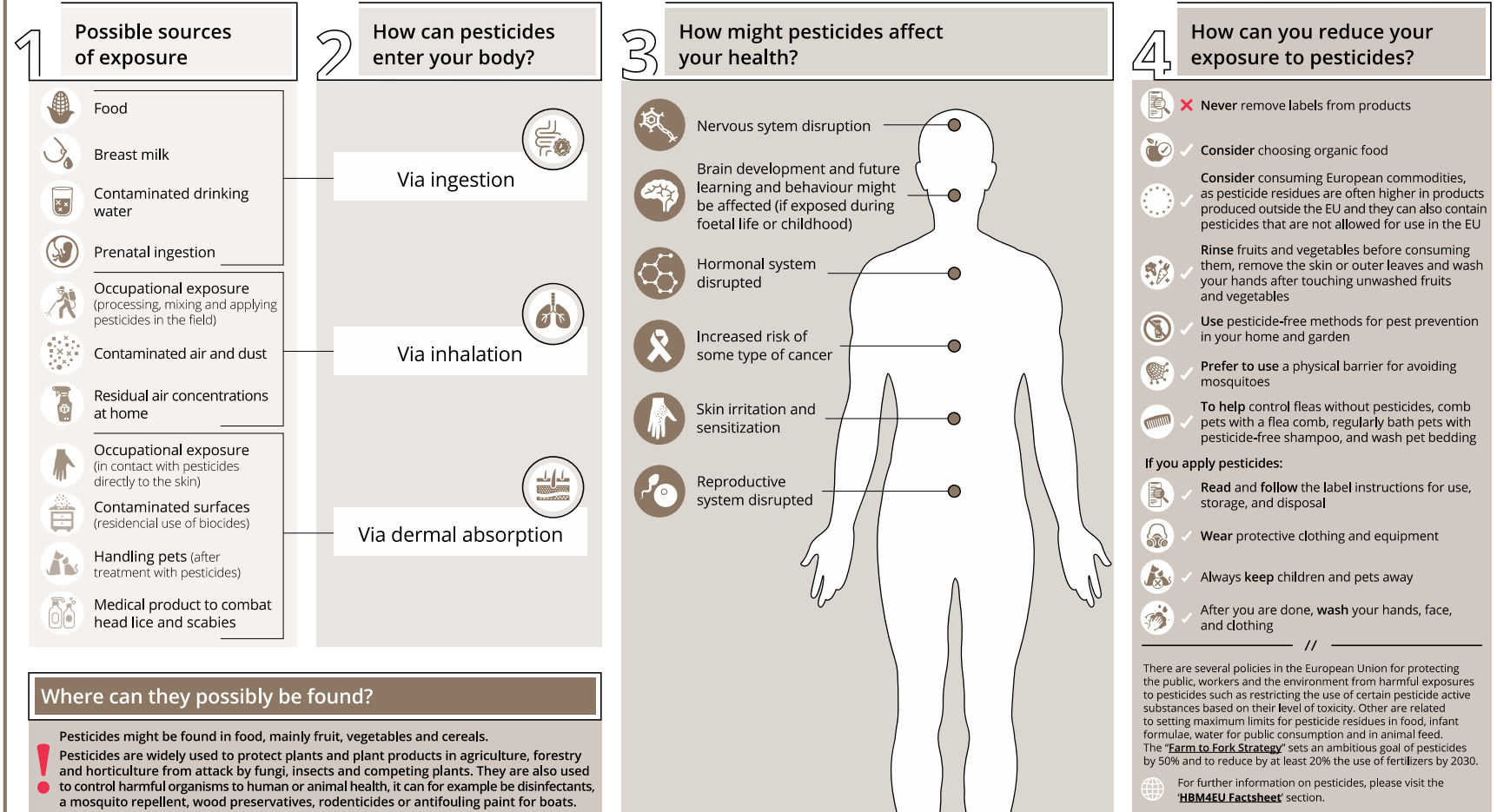
Trainings   +

Science to policy

Science to policy dialogue network   +

PARCopedia   +

PARCroute   +

Policy uptake and regulatory achievements   +

https://www.eu-parc.eu/
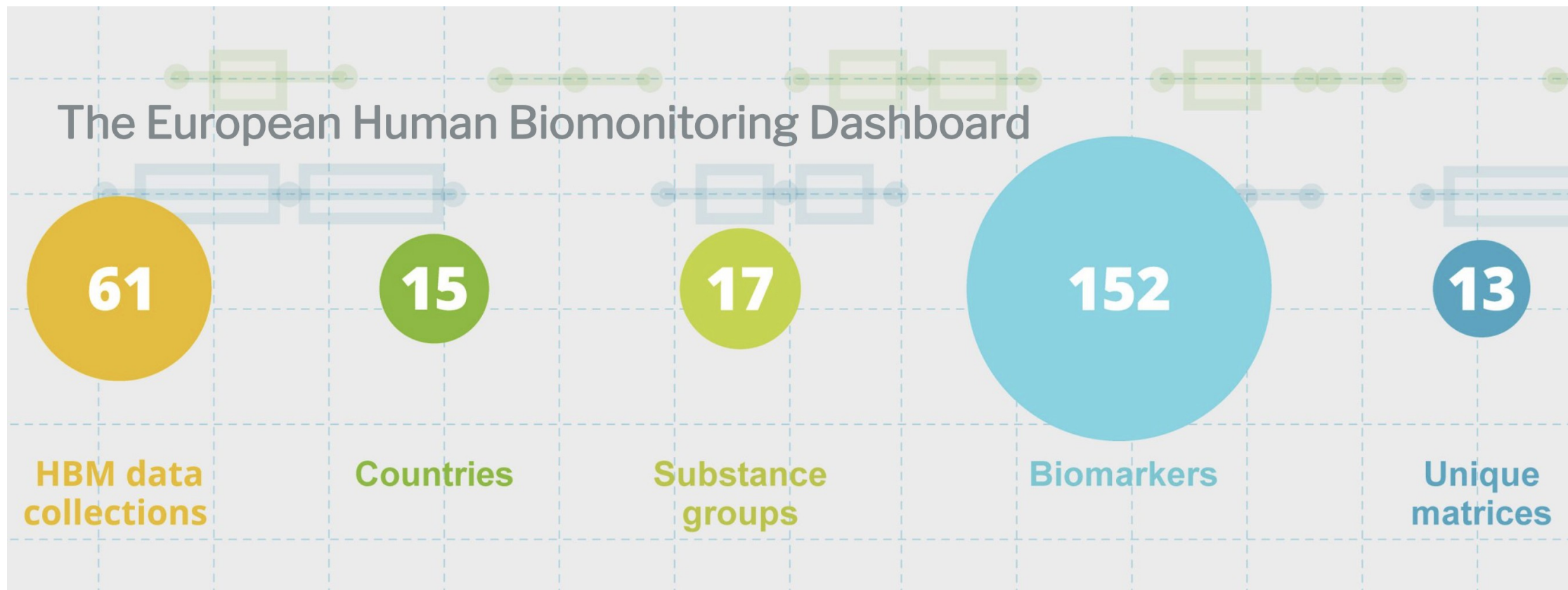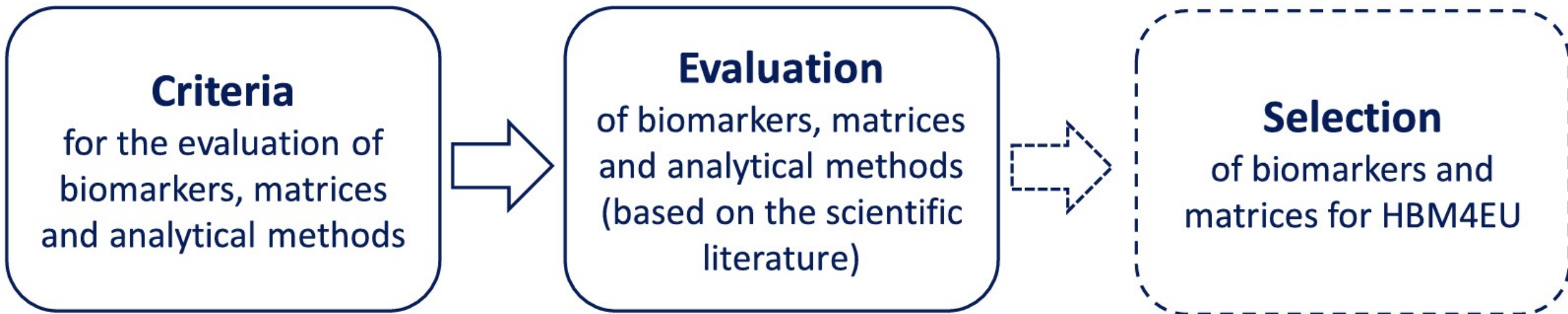
Overview of HBM4EU & PARC

Outputs

PESTICIDES | WHAT YOU NEED TO KNOW

1 Possible sources of exposure

- Food
- Breast milk
- Contaminated drinking water
- Prenatal ingestion
- Occupational exposure (processing, mixing and applying pesticides in the field)
- Contaminated air and dust
- Residual air concentrations at home
- Occupational exposure (in contact with pesticides directly to the skin)
- Contaminated surfaces (residencial use of biocides)
- Handling pets (after treatment with pesticides)
- Medical product to combat head lice and scabies

Where can they possibly be found?

Pesticides might be found in food, mainly fruit, vegetables and cereals.

Pesticides are widely used to protect plants and plant products in agriculture, forestry and horticulture from attack by fungi, insects and competing plants. They are also used to control harmful organisms to human or animal health, it can for example be disinfectants, a mosquito repellent, wood preservatives, rodenticides or antifouling paint for boats.

2 How can pesticides enter your body?

- Via ingestion
- Via inhalation
- Via dermal absorption

3 How might pesticides affect your health?

- Nervous sytem disruption
- Brain development and future learning and behaviour might be affected (if exposed during foetal life or childhood)
- Hormonal system disrupted
- Increased risk of some type of cancer
- Skin irritation and sensitization
- Reproductive system disrupted

4 How can you reduce your exposure to pesticides?

- ✗ **Never** remove labels from products
- ✓ **Consider** choosing organic food
- ✓ **Consider** consuming European commodities, as pesticide residues are often higher in products produced outside the EU and they can also contain pesticides that are not allowed for use in the EU
- ✓ **Rinse** fruits and vegetables before consuming them, remove the skin or outer leaves and wash your hands after touching unwashed fruits and vegetables
- ✓ **Use** pesticide-free methods for pest prevention in your home and garden
- ✓ **Prefer to use** a physical barrier for avoiding mosquitoes
- ✓ **To help** control fleas without pesticides, comb pets with a flea comb, regularly bath pets with pesticide-free shampoo, and wash pet bedding

If you apply pesticides:
- ✓ **Read** and **follow** the label instructions for use, storage, and disposal
- ✓ **Wear** protective clothing and equipment
- ✓ **Always keep** children and pets away
- ✓ After you are done, **wash** your hands, face, and clothing

There are several policies in the European Union for protecting the public, workers and the environment from harmful exposures to pesticides such as restricting the use of certain pesticide active substances based on their level of toxicity. Other are related to setting maximum limits for pesticide residues in food, infant formulae, water for public consumption and in animal feed. The "Farm to Fork Strategy" sets an ambitious goal of pesticides by 50% and to reduce by at least 20% the use of fertilizers by 2030.

For further information on pesticides, please visit the '**HBM4EU Factsheet**' section.

HBM4EU
science and policy for a healthy future

www.hbm4eu.eu

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 733032

HBM4EU coordinator:
German Environment Agency hbm4eu@uba.de

Knowledge Hub coordinator:
European Environment Agency hbm4eu@eea.europa.eu

What's being monitored?

The European Human Biomonitoring Dashboard

61 HBM data collections

15 Countries

17 Substance groups

152 Biomarkers

13 Unique matrices

Lengthy process for compound & biomarker selection

Vorekamp K et al. Biomarkers, matrices and analytical methods targeting human exposure to chemicals selected for a European human biomonitoring initiative. *Environment International* 2021: 146: 106082.

Summary of substances prioritized for HBM

Compound (group)	Main commercial use	(Suspected) Toxicity	References
Phthalates and 1,2-cyclohexane dicarboxylic acid diisononyl ester (DINCH)	Plasticizers	Endocrine disruption, leading to reproduction toxicity and neurodevelopmental effects	CHAP (2014), EU (2006)
Bisphenols	Manufacture of polycarbonate, epoxy resins and other polymers	Endocrine disruption, associated with diabetes and cardiovascular diseases	EFSA (2015), Lang et al. (2008), vom Saal and Hughes (2005)
Per- and polyfluoroalkyl substances (PFASs)	Surfactants, stain repellents, dispersants	Hyperchlesterolemia, reproduction toxicity, immunosuppression; some substances are classified as persistent organic pollutants (POPs)	EFSA (2018), UNEP (2006a, 2016)
Halogenated flame retardants (HFRs)	Flame retardants in polymers	Thyroid homeostasis disruption, neurodevelopmental effects; some substances are classified as POPs	Lyche et al. (2015), UNEP (2006b, 2010)
Organophosphorous flame retardants (OPFRs)	Flame retardants and plasticizers in polymers	Cancer (chlorinated OPFRs), neurotoxicity	Reemtsma et al. (2008)
Polycyclic aromatic hydrocarbons (PAHs)	By-product of combustion processes, manufacture of pigments, dyes, pesticides, pharmaceuticals etc.	Cancer, mutagenicity, immunosuppression, endocrine disruption	Andersson and Achten (2015), EU (2013)
Arylamines	Manufacture of polymers, rubbers, adhesives, dyes, pharmaceuticals etc.	Methemoglobinemia; cancer	Neumann (2005), IARC (2010), Skipper et al. (2010)
Cadmium	Pigment production, solar panels	Cancer, effects on liver and kidney, bone mineralisation	EFSA (2009), IARC (2012)
Chromium	Stainless steel production, electroplating, paint additive, tanning agent	Cr (VI): Cancer, effects on liver and kidney, contact allergen	EFSA (2014), IARC (2012)

Vorekamp K et al. Biomarkers, matrices and analytical methods targeting human exposure to chemicals selected for a European human biomonitoring initiative. *Environment International* 2021: 146: 106082.

Biomonitoring in the US in conjunction with the National Health and Nutrition Examination Survey (NHANES)

+ Conducted by the Centers for Disease Control and Prevention through National Center for Environmental Health

+ Monitors >400 chemicals and >80 nutritional biomarkers in human blood and urine

+ Periodically publishes the *National Report on Human Exposure to Environmental Chemicals & Updated Tables*

+ Data publicly available on NHANES website

Blood Lead (2011 - 2018)

CAS Number 7439-92-1

Geometric mean and selected percentiles of blood concentrations (in µg/dL) for the U.S. population from the National Health and Nutrition Examination Survey.

Demographic Categories	Survey (Years)	Geometric Mean (95% CI)	50th Percentile (95% CI)	75th Percentile (95% CI)	90th Percentile (95% CI)	95th Percentile (95% CI)	Sample Size
Total population	11-12	.973 (.916-1.04)	.930 (.880-.980)	1.52 (1.41-1.61)	2.38 (2.17-2.61)	3.16 (2.77-3.68)	7920
Total population	13-14	.858 (.813-.906)	.830 (.780-.870)	1.32 (1.24-1.42)	2.10 (1.96-2.30)	2.81 (2.49-3.14)	5215
Total population	15-16	.820 (.772-.872)	.780 (.740-.840)	1.32 (1.21-1.42)	2.14 (2.02-2.24)	2.75 (2.50-2.98)	4988
Total population	17-18	.753 (.723-.784)	.730 (.690-.770)	1.22 (1.17-1.27)	1.86 (1.75-1.95)	2.41 (2.24-2.67)	7513
Age 1-5 years	11-12	.970 (.877-1.07)	.950 (.870-1.04)	1.34 (1.20-1.65)	2.26 (1.88-2.65)	2.91 (2.41-3.83)	713
Age 1-5 years	13-14	.782 (.705-.869)	.740 (.680-.800)	1.08 (.940-1.24)	1.58 (1.33-1.90)	2.24 (1.68-2.64)	818
Age 1-5 years	15-16	.758 (.675-.850)	.690 (.610-.790)	1.10 (.950-1.32)	1.86 (1.50-2.65)	2.76 (1.94-3.81)	790
Age 1-5 years	17-18	.670 (.600-.748)	.620 (.540-.740)	.980 (.810-1.18)	1.49 (1.28-1.72)	2.02 (1.67-2.44)	629
Age 6-11 years	11-12	.681 (.623-.744)	.640 (.600-.700)	.930 (.820-1.05)	1.34 (1.14-1.60)	1.89 (1.36-2.94)	1048
Age 6-11 years	13-14	.567 (.529-.607)	.530 (.500-.570)	.760 (.700-.820)	1.13 (1.01-1.23)	1.42 (1.21-1.83)	1075
Age 6-11 years	15-16	.571 (.523-.623)	.550 (.510-.600)	.780 (.720-.830)	1.18 (.970-1.44)	1.59 (1.24-2.24)	1023
Age 6-11 years	17-18	.475 (.456-.494)	.460 (.430-.490)	.650 (.610-.690)	.930 (.840-1.04)	1.19 (1.04-1.40)	833
Age 12-19 years	11-12	.554 (.511-.601)	.530 (.490-.570)	.740 (.660-.830)	1.09 (.960-1.19)	1.31 (1.16-1.65)	1129
Age 12-19 years	13-14	.506 (.464-.551)	.460 (.420-.500)	.670 (.600-.750)	1.13 (.870-1.53)	1.69 (1.27-2.06)	627
Age 12-19 years	15-16	.467 (.433-.504)	.450 (.410-.490)	.680 (.610-.730)	.930 (.820-1.03)	1.17 (.990-1.36)	565
Age 12-19 years	17-18	.411 (.387-.436)	.390 (.370-.410)	.530 (.490-.600)	.830 (.730-.940)	1.09 (.930-1.45)	1030
Age 20+ years	11-12	1.09 (1.03-1.16)	1.05 (1.00-1.12)	1.67 (1.56-1.79)	2.56 (2.33-2.77)	3.36 (2.98-3.93)	5030
Age 20+ years	13-14	.967 (.921-1.02)	.940 (.900-.980)	1.45 (1.37-1.55)	2.26 (2.09-2.49)	3.03 (2.65-3.55)	2695
Age 20+ years	15-16	.920 (.862-.982)	.880 (.810-.960)	1.46 (1.35-1.59)	2.30 (2.15-2.44)	2.89 (2.65-3.07)	2610

How are chemicals selected for analysis & inclusion in National Exposure Report?

- Scientific data that suggested exposure in the U.S. population

- Seriousness of health effects known, or thought to result from some levels of exposure

- Need to assess the efficacy of public health actions to reduce exposure to a chemical

- Availability of an analytical method that is accurate, precise, sensitive, specific, and rapid

- Availability of adequate blood or urine samples from the National Health and Nutrition Examination Survey (NHANES) survey

- Analytical cost to perform the analysis

A little about NHANES
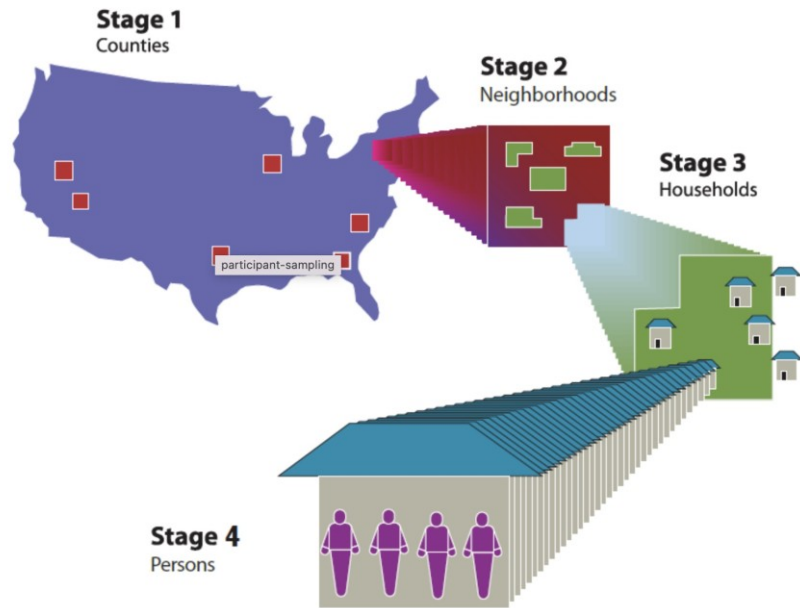
Nationally representative survey

+ **Operating since 1959**

  Periodic at first

  Continuous since 1999 – 2-year cycles

+ **Complex – survey design**

All the counties in the United States are divided into 15 groups based on their characteristics. One is selected from each group and together they form the 15 counties in the NHANES survey for the year.

Within each of the 15 NHANES counties, smaller groups (such as neighborhoods) are formed, and between 20 and 24 of these small groups are selected.

All the houses or apartments within those selected small groups are identified, and a sample of about 30 households are chosen within each group.

NHANES will contact the selected household and ask a short set of questions (age, race, and gender) about everyone in the household.

A computer process randomly selects some, all, or none of the household members.

Survey components

+ ## Telephone interview @ home

Head of household & some targeted participants (>16 y)

Survey questions

  Sleep

  Diet

  Mood, behavior, etc.

+ ## Mobile Examination Center

Height, weight, waist circumference

Blood pressure

Body composition scan

Balance test

Liver function scan

Blood draw

Participants get some results back

+ Glucose test

+ Cholesterol

+ Nutritional status

+ Kidney function tests

+ Infectious diseases

+ Exposure to environmental chemicals

Data are publicly available

Data, Documentation, Codebooks

- Demographics Data
- Dietary Data
- Examination Data
- Laboratory Data
- Questionnaire Data
- Limited Access Data

Survey Methods
Plan & Operations, Sample Design, Estimation & Weighting Procedures, Analytic Guidelines, etc.

Search Variables
Simple keyword search for Continuous NHANES (1999 and on) variables

Continuous NHANES

NHANES 08/2021-08/2023	NHANES 2017-March 2020 Pre-Pandemic Data	NHANES 2019-2020
NHANES 2017-2018	NHANES 2015-2016	NHANES 2013-2014	NHANES 2011-2012
NHANES 2009-2010	NHANES 2007-2008	NHANES 2005-2006	NHANES 2003-2004
NHANES 2001-2002	NHANES 1999-2000		

Contents in Detail

- Questionnaire Instruments
- Laboratory Methods
- Procedure Manuals
- Brochures and Consent Documents

Feeds into scientific publications

Low-level exposure to lead, mercury, arsenic, and cadmium, and blood pressure among 8-17-year-old participants of the 2009–2016 National Health and Nutrition Examination Survey

Gauri Desai [a],[*], Zhongzheng Niu [a],[1], Wei Luo [b], Seth Frndak [a], Amy L. Shaver [a], Katarzyna Kordas [a]

[a] Department of Epidemiology and Environmental Health, University at Buffalo, The State University of New York, USA
[b] Department of Sociology, University at Buffalo, The State University of New York, USA

Associations of total urinary arsenic with total cholesterol and high-density lipoprotein among 12-17-year-old participants from the 2009–2016 NHANES cycles: A cross-sectional study

Yihua Yue [*], Nisha Nair, Sarah Quinones, Katarzyna Kordas, Gauri Desai

Department of Epidemiology and Environmental Health, University at Buffalo, SUNY, Buffalo, NY, USA

Targeted HBM—biomonitoring for specific purpose

+ The Stockholm Convention on Persistent Organic Pollutants was adopted on 22 May 2001 and entered into force on 17 May 2004

+ Persistent Organic Pollutants (POPs)

- remain intact for long periods of time (many years);

- become widely distributed throughout the environment through natural processes involving soil, water and, most notably, air;

- accumulate in living organisms including humans, and are found at higher concentrations at higher levels in the food chain;

- are toxic to both humans and wildlife.

Targeted HBM—biomonitoring for specific purpose

+ ## Initial 12

Pesticides: aldrin, chlordane, DDT, dieldrin, endrin, heptachlor, hexachlorobenzene, mirex, toxaphene;

Industrial chemicals: hexachlorobenzene, polychlorinated biphenyls (PCBs);

By-products: hexachlorobenzene; polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans (PCDD/PCDF), and PCBs.

Data warehouse
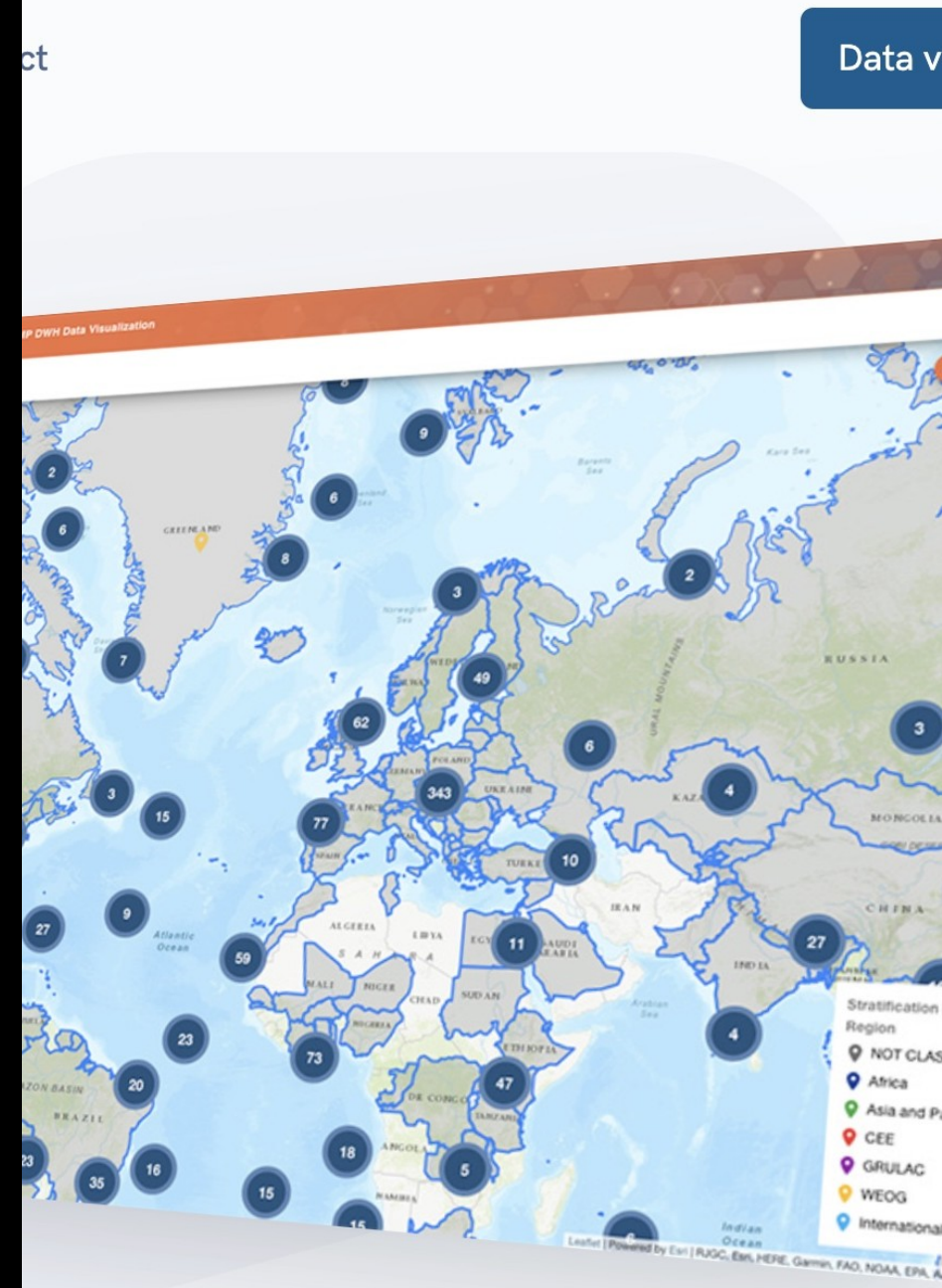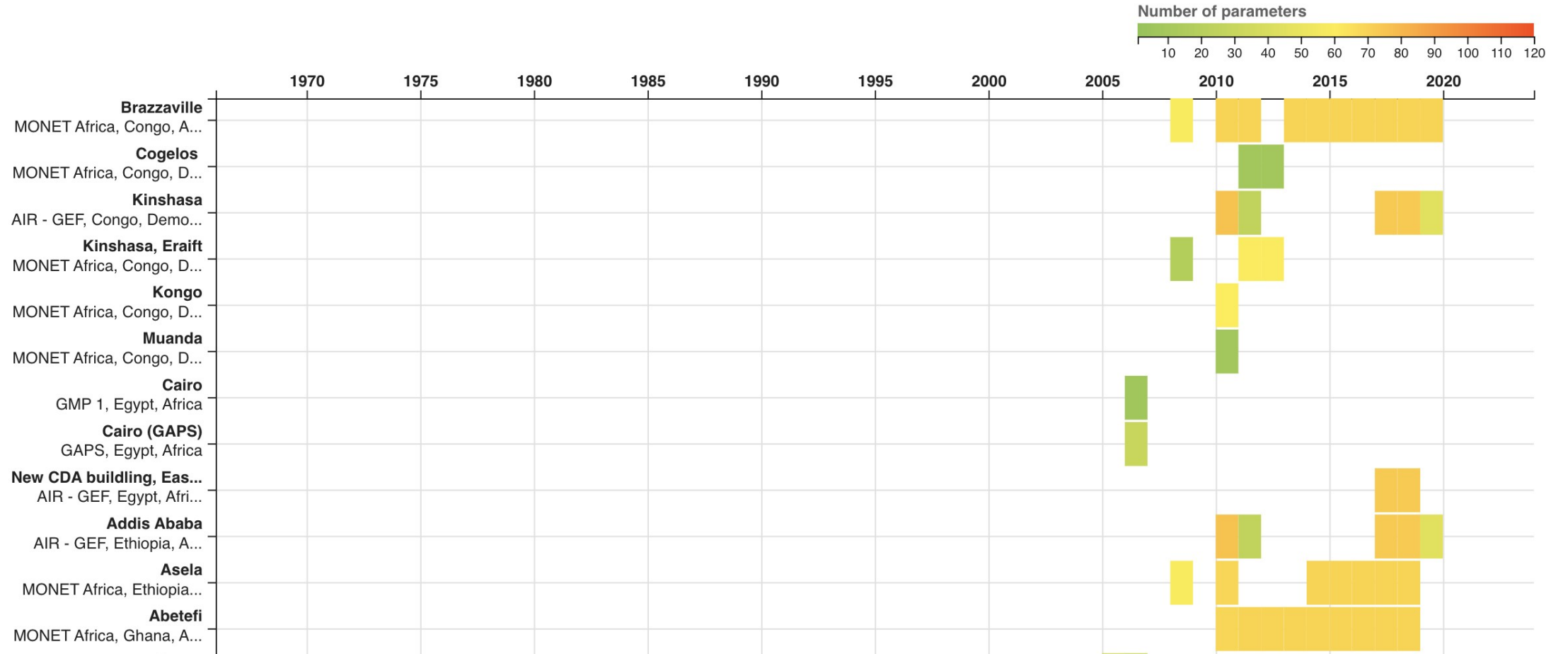
DESIGN PLAN ELEMENTS	HUMAN BIOMONITORING PROGRAM – DESIGN OPTIONS AND CONSIDERATIONS		
	INDIVIDUAL/CENSUS (ALL INDIVIDUALS PARTICIPATE)	SURVEY (INTEGRATED INTO HEALTH EXAMINATION POPULATION SURVEYS)	BIOBANK (BLOOD BANKS, BREASTMILK BANKS, BLOOD DONORS)
	Pro: Comprehensive; can utilize existing health system infrastructures (ex., vaccination campaigns, well-child visits); allows QC in bio-sample collection and storage. Con: Very costly. Challenges for implementation.	Pro: Utilizes existing infrastructure; allows periodic monitoring, allows QC in bio-sample collection & storage. Con: requires knowledge of probabilistic sampling.	Pro: Utilizes existing infrastructure; allows continuous monitoring; ensures sufficient sample volume. Con: Convenience sample; possibly low age, sex- and regional representativeness; lower possibility of QC in bio-sample collection & storage.
Participating Institutions	Involvement of national-level research or regulatory institutions, along with central government funding ensures program success and sustainability for use of data and information.		
Target population	Can include the general, non-institutionalized population, be age-specific (neonates—via umbilical cord blood sampling or assays in neonatal blood spot; children) or focus on particularly vulnerable (ex., pregnant women) populations. Some programs over-sample for ethnic/racial groups or poverty, calculating survey weights to extrapolate information to total populations. Multi-stage sampling strategies are common to achieve nationally representative sample.		

Designing HBM programs

Tamayo-Ortiz M et al. *Annals of Global Health*. 2022; 88(1): 80, 1–11.

Designing HBM programs

Specific national context	Can cover all geographic areas of a country or be area-specific according to national priorities (ex., oversampling in regions of specific concern).
Sampling frequency	Can be continuous/repeated annually or conducted occasionally (ex., every 5 years). We advocate for the former.
Sample criteria and size	Based on variation in the biomarker measures, enough individuals should be randomly recruited to provide reliable area or national estimates, depending on the geographical coverage. ** *does not apply to the Individual/Census*
Matrix selection	Should consider feasibility of collecting biological samples, cold chain maintenance, assurance of appropriate storage conditions, and generation of biomarkers that have established reference values.
Biomarkers of exposure*	Can include a comprehensive suite of toxic metals or a core set of metals representing greatest concern for the population or highest possible health risk. We advocate for the inclusion of Pb, Mn, Hg, Cd, As. At a minimum, Pb should be assessed.

How would you design a biomonitoring program?

+ Design type

    Census

    Survey

    Biobank

+ Target population?

+ Geographic coverage?

+ Frequency

+ Biological amples collected

+ Chemicals