

Partnership for the Assessment of Risks from Chemicals

Deliverable D4.3

First progress report on the General Survey (PARC Aligned Studies)

WP 4 – T4.1



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Document history

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1	xx/xx/xxxx	The person(s) who prepared/review the version	
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version 2	14/03/2025	Liese Gilles	Updated version (submitted for review by ext. Reviewers)
Version 3	07/05/2025	Liese Gilles	Final version (addressing the reviewers comments)
Version 4	13/06/2025	Liese Gilles WP4 co-leaders	Replacement of links to PARC internal documents with references to their publication in zenodo and validation of the deliverables by WP4 co-leaders for submission

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Abstract

The PARC Aligned Studies are a collection of HBM studies from 25 different European countries and Israel that are coordinated under the framework of the PARC (Partnership for the Assessment of Chemical risks). This means that the studies follow guidelines to make sure they are aligned. Specific age groups were selected for investigation, and for each age group, a specific selection of environmental pollutants and their relevant exposure biomarkers was chosen for measurement. A harmonized questionnaire was developed, and samples will be collected according to best practice guidelines. The aim of the PARC Aligned Studies is to measure concentrations of environmental pollutants in the European population and to have comparable biomarker data across different EU countries. The specific objectives are to obtain HBM data for priority substances which are comparable between EU countries/regions; to calculate European exposure values allowing comparison with international HBM programmes or with previous EU projects; to identify exposure determinants, sources and/or routes; to characterize exposure mixtures and to compare HBM data with available health based HBM guidance values.

These PARC Aligned Studies also provide a framework to build upon for additional research. For example, to investigate exposure effect associations, effect biomarkers will be measured in a subset of the studies. And to further deep-dive into the routes/sources of exposure personal environmental samples will be collected from a subset of the HBM participants to explore associations between the concentrations found in the environmental samples vs. the concentrations observed in the human samples.

Overall, the resulting HBM data is useful for evaluating policies and assessing the impact of regulatory measures to reduce pollution. It is also a tool for highlighting emerging issues and identifying priorities.

In this deliverable the progress of the PARC Aligned Studies is described.

Key Words

Human Biomonitoring (HBM), HBM surveys, aligned studies, internal exposure, environmental chemicals, children, teenagers, adults.

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Authors and Acknowledgements

All partner institutions who are involved in this task and who have been approached for input are listed below: EAA, VITO, PIH, ISSeP, MOH-CY / SGL, SZU-CZ (NIPH), RegionH, UTARTU, SpFrance, UBA, AUTH, NCPHP, UI, UCD, MOH-IL, ISS, RSU, LSMU, LNS, NIPH, RIVM, NIOM, WULS, INSA, SZU-SK, JSI, NIJZ, ISCIII, EASP, EHU/UPV, ULUND, KI, UmU, UKHSA.

Acronyms

HBM: Human Biomonitoring

HBM4EU: European Human Biomonitoring Initiative

MDTA: Material and associated Data Transfer Agreement

NTS: Non-Targeted Screening

SS: Suspect Screening

MOA: Mode of Action

AOPs: Adverse Outcome Pathways

1. Introduction

As a follow-up to the Aligned Studies that have been organized under HBM4EU¹⁻³, PARC will also organize a human biomonitoring (HBM) survey with EU wide coverage by aligning and harmonizing national and/or regional HBM studies across Europe.

The objectives of the PARC Aligned Studies are:

- to obtain HBM data for priority substances which are comparable between EU countries/regions;
- to calculate European exposure values allowing comparison with international HBM programmes or with previous EU projects;
- to identify exposure determinants, sources and/or routes;
- to characterize exposure mixtures;
- to study exposure-effect associations;
- to compare HBM data with available health based HBM guidance values.

The PARC Aligned Studies address the general population and focusses on 3 age groups: children between 6-11 years of age, teenagers between 12-17 years of age and adults between 18-39 years of age.

During the first 1.5 years of PARC, the general criteria for the PARC Aligned Studies (also referred to as PARC General Survey) have been defined (MS10: PARC general survey design)⁴. HBM studies eligible to contribute to the PARC Aligned Studies have been identified and included in the project (L1-landmark)⁵.

Supporting materials have been developed including:

1. best practice guidelines for sampling (blood, urine and hair)
2. questionnaires for each age group
3. a guidance document on sampling strategies (PARC_protocol_sampling strategy⁶)
4. a material and associated data transfer template (MDTA)

Workshops and project meetings (hybrid, with both in-person and virtual participation) were organized by the study coordinators. One in Brussels on 10-11 May 2023, one in Paris on 12 October 2023 (back-to-back with the WP4 meeting), one in Berlin on 7 and 10 October 2024 (back-to-back with the WP4 meeting) and an extra online meeting on 18 June 2024. In Brussels the objectives and harmonization criteria for the PARC Aligned Studies were introduced and the participants presented the HBM studies from their country/region that will contribute to the PARC Aligned Studies. In Paris, REDCap (a secure web application for building and managing online surveys and databases) was introduced as a possible tool to collect questionnaire information and a draft proposal for the implementation of effect biomarkers was presented and discussed. In Berlin all partners shared an update about the progress of their HBM study. All these meetings provided a platform for partners to exchange their experiences related to setting up and performing an HBM campaign.

2. Overview of all countries and partners contributing to the PARC Aligned Studies

In total 26 countries are contributing to the PARC Aligned Studies. The PARC Aligned Studies target 3 age groups: children, teenagers, and adults. 15 countries will contribute with HBM data on children, 12 countries will contribute with HBM data on teenagers and 21 countries will contribute with HBM data on adults.

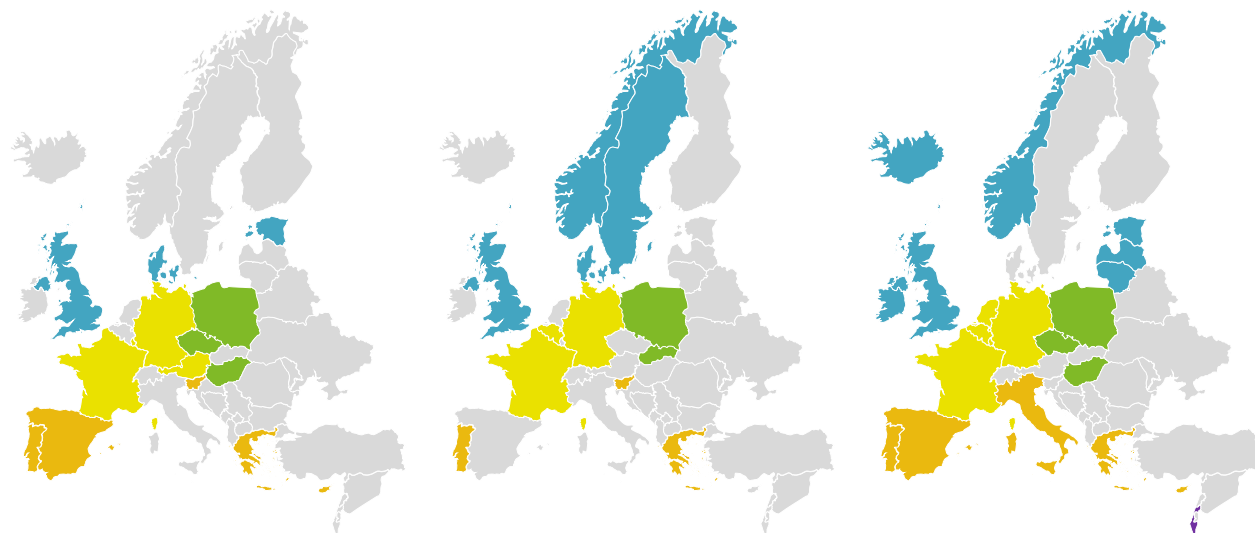


Figure 1: Map of countries contributing with HBM to the PARC Aligned Studies. From left to right, studies targeting children -> teenagers -> adults.

The following changes occurred during the project: Latvia (RSU) initially planned to conduct HBM in all 3 age groups, however due to unforeseen circumstances they will only proceed with the implementation of HBM in adults (for more information see Table 5, Latvia). Ireland has joined the PARC consortium as of (01/10/2024) and will join the project with a HBM study in adults.

Table 1: Overview of countries and institutes contributing with HBM under the PARC Aligned Studies

EU region	Countries	Institute	Children	Teenagers	Adults
W	Austria	EAA	√		
W	Belgium	VITO; PIH; ISSeP		√	√
S	Cyprus	MOH-CY / SGL	√		√
E	Czech Republic	SZU-CZ (NIPH)	√		√
N	Denmark	RegionH	√	√	
N	Estonia	UTARTU	√		√
W	France	SpFrance	√	√	√
W	Germany	UBA	√	√	√
S	Greece	AUTH	√	√	√
E	Hungary	NCPHP	√		√
N	Iceland	UI			√
N	Ireland	UCD			√
-	Israel	MOH-IL			√
S	Italy	ISS			√
N	Latvia	RSU			√
N	Lithuania	LSMU			√

W	Luxembourg	LNS	√		√
N	Norway	NIPH		√	√
W	Netherlands ¹	RIVM			√
E	Poland	NIOM; WULS	√	√	√
S	Portugal	INSA	√	√	√
E	Slovakia	SZU-SK		√	
S	Slovenia	JSI; NIJZ	√	√	
S	Spain	ISCIH; EASP; EHU/UPV	√		√
N	Sweden	ULUND; KI; UmU		√	
N	UK ²	UKHSA	√	√	√
	26		15	12	21

¹ The HBM study in the Netherlands addressing adults will not be fully aligned with the PARC Aligned Studies requirements. PARC questionnaires and SOPs could not be applied, and only PFAS will be analysed, However, overlapping information and data will be integrated into the final EU dataset to include information about the Netherlands.

² UK is a Associated country, participating with their own financial contribution to PARC.

3. Exposure biomarkers selected for the PARC Aligned Studies

The process followed for the selection of the biomarkers for the PARC Aligned Studies, including the criteria applied and the rationale behind the decisions taken, as well as the design of the QA/QC programme is described in the document “PARC Aligned Studies: Selected Exposure Biomarkers”⁷. In this process the 3rd prioritisation exercise carried out in HBM4EU (Deliverable-4.8-Third-list-of-HBM4EU-priority-substances available [here](#)) as well as the scientific results obtained were the basis for further discussions among experts in WP4, consultations with the EU agencies and the national interests of the study owners. Figure 1 below summarises the workflow.

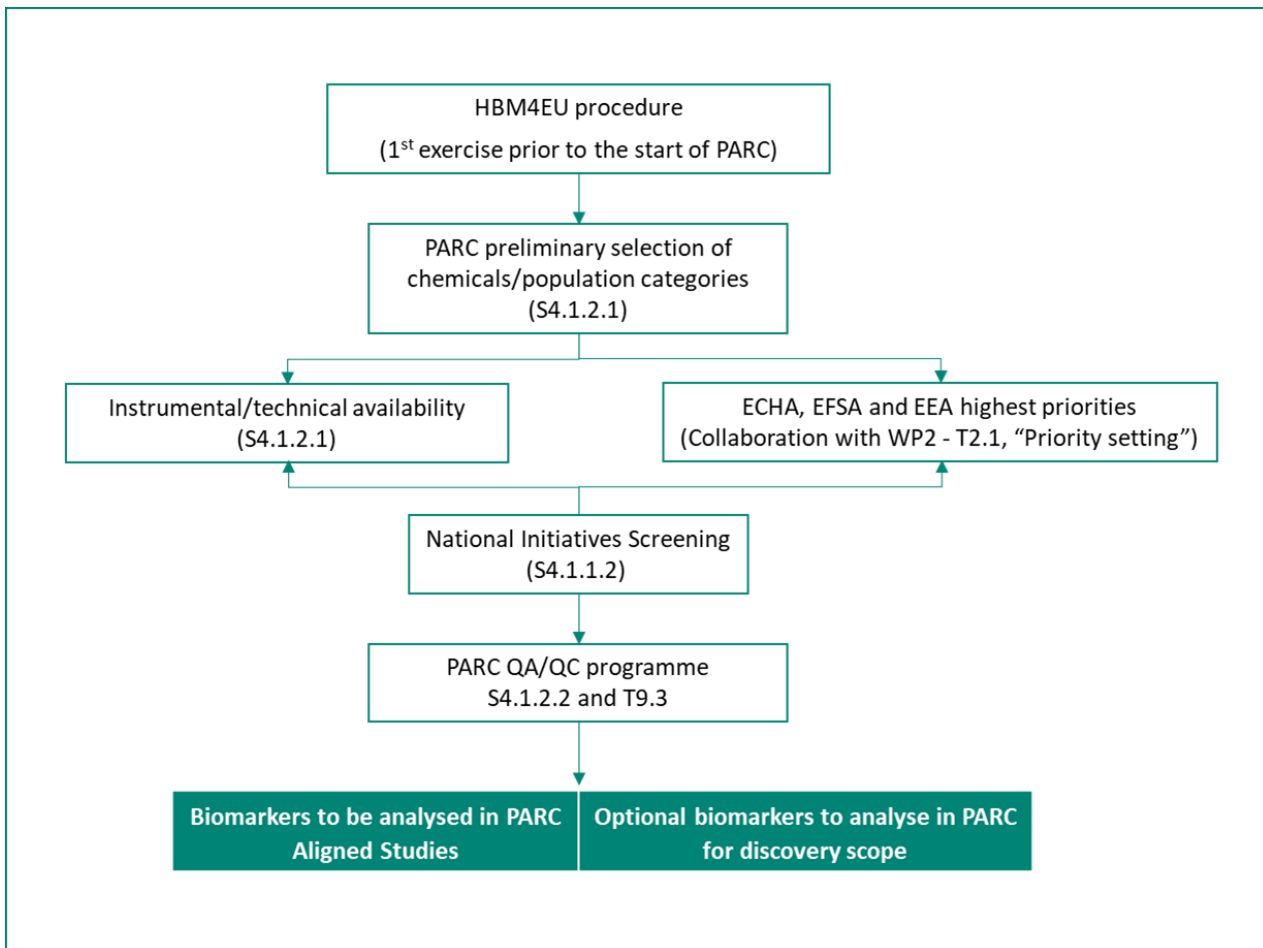


Figure 1. Process for the selection of exposure biomarkers and QA/QC programme for the PARC General Survey / Aligned Studies.

The document presenting the final selection of exposure biomarkers to be measured in the PARC Aligned Studies can be found online⁸. Two levels have been defined, the PARC Aligned Studies scope and the PARC Discovery scope illustrated in Figure Figure 1. All the markers in the PARC Aligned Studies scope and discovery scope are listed in Table 2. Analysis of exposure biomarkers can start after successful participation in 2 rounds of the PARC QA/QC programme.

Following the future needs exercise performed to identify future needs for the remaining years of PARC it will be evaluated if it is feasible to add extra exposure biomarkers to the current selection. In addition, creatinine and specific gravity will be analysed to correct for urinary dilution and cotinine as a confounder.

**For the Complete set:**

-> Known or expected high detection frequency (>60%) in target population at the LOQ requirement set for the PARC Aligned Study

For the minimum compulsory set:

-> Known or expected high detection frequency (>60%) in target population at the LOQ requirement set for the PARC Aligned Study

-> A high percentage (at least 60%) of the surveyed laboratories with experience in a given substance group should be capable of analysing the biomarker.

Figure 1: Illustration of the different levels in the exposure biomarker selection

Table 2: Overview of exposure biomarkers selected for analysis in the biological samples collected by the PARC Aligned Studies.

Exposure biomarkers (name/abbreviation)		Child.	Teen.	Adults	PARC selection
Bisphenols					
Bisphenol A total	BPA total	√	√	√	Min. compulsory set
Bisphenol S total	BPS total	√	√	√	Min. compulsory set
Bisphenol F total	BPF total	√	√	√	Min. compulsory set
Bisphenol E total	BPE total	√	√	√	Discovery scope
Bisphenol AP total	BPAP total	√	√	√	Discovery scope
Bisphenol AF total	BPAF total	√	√	√	Discovery scope
Bisphenol Z total	BPZ total	√	√	√	Discovery scope
Bisphenol B total	BPB total	√	√	√	Discovery scope
Bisphenol P total	BPP total	√	√	√	Discovery scope
Phthalates					
Mono-benzyl phthalate	MBzP	√	√	√	Min. compulsory set
Mono-isobutyl phthalate	MiBP	√	√	√	Min. compulsory set
Mono-n-butyl phthalate	MnBP	√	√	√	Min. compulsory set
Mono(2-ethylhexyl) phthalate	MEHP	√	√	√	Min. compulsory set
Mono(2-ethyl-5-hydroxy-hexyl) phthalate	5OH-MEHP	√	√	√	Min. compulsory set
Mono(2-ethyl-5-oxo-hexyl) phthalate	5oxo-MEHP	√	√	√	Min. compulsory set
Mono(2-ethyl-5-carboxy- pentyl) phthalate	5cx-MEPP	√	√	√	Min. compulsory set
7-Carboxy-(mono-methyl- heptyl) phthalate - isomers!	cx-MiNP - isomers!	√	√	√	Min. compulsory set
Mono-ethyl phthalate	MEP	√	√	√	Min. compulsory set
7-OH-(Mono-methyl-octyl) phthalate - isomers!	OH-MiNP - isomers!	√	√	√	Complete set
Mono-n-pentyl phthalate	MnPeP	√	√	√	Discovery scope
Mono-n-octyl phthalate	MnOP, MOP	√	√	√	Discovery scope
Mono-cyclo-hexyl phthalate	MCHP	√	√	√	Discovery scope
6-OH-Mono-propyl-heptyl phthalate - isomers!	OH-MiDP - isomers!	√	√	√	Discovery scope
Mono-carboxy-isodecyl phthalate - isomers!	cx-MiDP - isomers!	√	√	√	Discovery scope
DINCH and alternative Phthalate substitutes					
Cyclohexane-1,2-dicarboxylate-mono-(7-hydroxy-4-methyl)octyl ester	OH-MINCH - isomers!	√	√	√	Min. compulsory set
Cyclohexane-1,2-dicarboxylate-mono-(7-carboxylate-4-methyl)heptyl ester	cx-MINCH - isomers!	√	√	√	Min. compulsory set

Cyclohexane-1,2-dicarboxylate-mono-(7-oxo-4-methyl)octyl ester	oxo-MINCH - isomers!	√	√	√	Min. compulsory set	
Mono(2-ethyl-5-carboxypentyl) terephthalate	5-cx-MEPTP	√	√	√	Complete set	
Mono(2-ethyl-5-hydroxyhexyl) terephthalate	5OH-MEHTP	√	√	√	Complete set	
Mono-2-ethyl-5-hydroxyhexyl adipate	5OH-MEHA	√	√	√	Discovery scope	
Mono-5-carboxy-2-ethylpentyl adipate	5cx-MEPA	√	√	√	Discovery scope	
PFAS						
Perfluorononanoic acid	PFNA		√	√	Min. compulsory set	
Perfluorodecanoic acid	PFDA		√	√	Min. compulsory set	
Perfluorobutane sulfonic acid	PFBS		√	√	Min. compulsory set	
Perfluorohexane sulfonic acid	PFHxS		√	√	Min. compulsory set	
Perfluoroheptane sulfonic acid	PFHpS		√	√	Min. compulsory set	
Perfluorooctanoic acid	PFOA		√	√	Min. compulsory set	
Perfluorooctane sulfonic acid	PFOS		√	√	Min. compulsory set	
4:2 Fluorotelomer sulfonic acid	4:2 FTSA		√	√	Discovery scope	
6:2 Fluorotelomer sulfonic acid	6:2 FTSA		√	√	Discovery scope	
8:2 Fluorotelomer sulfonic acid	8:2 FTSA		√	√	Discovery scope	
9CL-PF3ONS	9CL-PF3ONS		√	√	Discovery scope	
Perfluorohexanoic acid	PFHxA		√	√	Discovery scope	
Perfluoroheptanoic acid	PFHpA		√	√	Discovery scope	
Perfluorododecanoic acid	PFDoDA		√	√	Discovery scope	
Perfluoroundecanoic acid	PFUnDA		√	√	Discovery scope	
Perfluoropentanoic acid	PFPeA		√	√	Discovery scope	
Perfluorobutanoic acid	PFBA		√	√	Discovery scope	
Perfluorononanesulfonic acid	PFNS		√	√	Discovery scope	
N-ethyl-perfluorooctane sulfonamidoacetate	EtFOSAA		√	√	Discovery scope	
N-methyl-perfluorooctane sulfonamidoacetate	MeFOSAA		√	√	Discovery scope	
Ammonium 4,8-dioxa-3H-perfluorononanoate	Adona		√	√	Discovery scope	
GenX	GenX		√	√	Discovery scope	
Pesticides - organophosphates						
3,5,6-Trichloro-2-pyridinol	TCPy		√	√	√	Min. compulsory set
Pesticides - Pyrethroids						
Cis-(2,2-dibromovinyl)-2,2-dimethylcyclopropanecarboxylic acid	cis-DBCA (mix cis-isomers)		√	√	√	Min. compulsory set

Cis-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane-1-carboxylic acid	cis-DCCA (mix cis-isomers)	✓	✓	✓	Min. compulsory set
Trans-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane-1-carboxylic acid	trans-DCCA (mix trans-isomers)	✓	✓	✓	Min. compulsory set
3-Phenoxybenzoic acid	3-PBA	✓	✓	✓	Min. compulsory set
4-Fluoro-3-phenoxybenzoic acid	4-F-3-PBA	✓	✓	✓	Min. compulsory set
Cis-3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylic acid	ClF3CA	✓	✓	✓	Complete set
Pesticides - Neonicotinoids					
Acetamiprid-N-desmethyl		✓		✓	Min. compulsory set
Acetamiprid		✓		✓	Min. compulsory set
Imidacloprid		✓		✓	Min. compulsory set
Imidacloprid olefin		✓		✓	Discovery scope
5-hydroxyimidacloprid		✓		✓	Discovery scope
Pesticides - Glyphosate/AMPA					
Glyphosate	Glyphosate			✓	Min. compulsory set
Aminomethylyphosphonic acid	AMPA			✓	Min. compulsory set
Metals in blood					
Mercury (total)	Hg			✓	Min. compulsory set
Lead	Pb			✓	Min. compulsory set
Cadmium	Cd			✓	Min. compulsory set
Chromium (total)	Cr			✓	Complete set
Manganese	Mn			✓	Complete set
Cobalt	Co			✓	Complete set
Selenium ¹	Se			✓	Complete set
Metals in urine					
Cadmium	Cd	✓		✓	Min. compulsory set
Mercury (total)	Hg	✓		✓	Complete set
Lead	Pb	✓		✓	Complete set
Chromium (total)	Cr	✓		✓	Complete set
Nickel	Ni	✓		✓	Complete set
Aluminum	Al	✓		✓	Complete set
Lithium	Li	✓		✓	Complete set
Manganese	Mn	✓		✓	Complete set
Cobalt	Co	✓		✓	Complete set

D4.3

P-A-R-C HORIZON-HLTH-2021-ENVLTH-03 CONTRACT N. 101057014

Platinum	Pt	√	√	Complete set
Copper	Cu	√	√	Complete set
Strontium	Sr	√	√	Complete set
Zinc	Zn	√	√	Complete set
Molybdenum	Mo	√	√	Complete set

4. Add-ons

Several additional research topics are integrated into the framework of the PARC Aligned Studies. These topics, referred to as “add-ons,” are optional, meaning that not all studies will contribute to them. The following three add-ons are further developed:

- Implementation of effect biomarkers,
- Collection of personal environmental samples,
- Application of NTS/SS on human samples.

The status of each add-on is detailed below.

4.1 Implementation of effect biomarkers

This add-on focuses on the assessment of adverse health effects in human biomonitoring studies through measurement of (molecular) biomarkers of (early/pre-clinical) effects and through standardized assessment of health outcomes. Integrating the analysis of effect biomarkers into human biomonitoring studies enhances our ability to assess early biological responses to chemical exposures, bridging the gap between exposure assessment and potential health outcomes. These biomarkers provide crucial insights into mechanisms of toxicity, individual susceptibility, and early indicators of disease, improving risk assessment accuracy. The biomarkers of effect selected for measurement in the PARC Aligned Studies can be found in Table 3. The selection was performed by P4.1.3.3.a_Y1_RoadmapLinkingHBMhealth in collaboration with P4.1.1.2.a_Y1_GenHBMSurvey partners.

The selection process in short:

Health outcomes to assess in the PARC Aligned Studies were prioritized based on planned chemical exposure measurements for each age group. This resulted in a scoping document listing health measurement for the human biomonitoring surveys including standardized procedures and materials for collecting health, dietary and occupational data. The following health outcomes were prioritized: reproductive, cardio-metabolic-obesity, neurological, and asthma and allergy (focused on respiratory sensitization) outcomes. In parallel, effect biomarkers were identified for implementation in the PARC Aligned Studies. The selection was mainly based on the study owner’s interest, available biological samples to allow measurement of the markers, and scientific interest in gaining mechanistic knowledge in the link between exposure and health outcome. First, a panel of effect biomarkers suitable to increase the causal inference between the exposure to chemical pollutants and the different adverse health effects was identified and classified according to qualitative and quantitative criteria explained in the previous report (RoadmapLinkingHBMhealth2_EFBM implementation plan_M12)⁹. Apart from links to MOA (Mode of Action) and AOPs (Adverse Outcome Pathways), scoring criteria included relevance of measurement in typical HBM matrices (urine/hair/blood/...), previous implementation in epidemiological studies, and general feasibility, based on cost, efficacy, specificity, sensitivity and reliability of the biomarker. Effect biomarkers showing a good quality were grouped according to the health outcome of interest for the study owners from which a preliminary panel of effect biomarkers to be implemented in PARC was obtained. While considering the sample size that would be achieved based on study owner’s interest, the following groups of biomarkers of effect were selected:

- renal markers in urine (children);
- thyroid hormones in serum (teenagers and adults);
- blood lipids in serum (teenagers and adults);
- immune markers in serum (adults);
- oxidative stress markers in urine (children and teenagers),
- neurodevelopmental markers in serum (teenagers and adults).

Furthermore, harmonized health outcome assessment tools which have been prepared and made available to the partners:

Asthma, allergic rhinitis, eczema outcome: an extra questionnaire module was prepared per age group based on ISAAC/ The Global Asthma Network Phase I Manual. See annex 4.1, 4.2 and 4.3.

Neurological outcome extra questionnaire modules to be used are:

For children: CBCL (Child Behavior Checklist)³.

For teenagers: SDQ (Strengths and Difficulties Questionnaire, self-rated SDQ for 11-17 year olds⁴) or CBCL (Child Behavior Checklist)³.

SOP's for anthropometric measurements:

- height, weight, blood pressure, waist and hip circumference in children and teenagers⁵
- height, weight, blood pressure, waist and hip circumference in adults⁶

By including the selected prioritized health outcomes with the proposed effect biomarkers, the PARC Aligned Studies will provide knowledge in chemical exposure –effect biomarker – and health outcome pathways for cardio-metabolic-obesity, neurological, and asthma and allergy outcomes. Additionally, we will gain new insights into exposure –effect biomarker relations for renal health and thyroid function. Combining these data with the information obtained with the PARC general questionnaire, relevant covariates and confounders will be taken into account.

Partners who have committed to analyse effect biomarkers are:

In children: WULS, AUTH, ISCH, LNS, UBA, JSI/NIJZ, NCPHP, MOH-CY/SGL.

In teenagers: AUTH, SPF, NIOM, VITO/PIH, UBA, JSI/NIJZ, NIPH.

In adults: RSU, AUTH, ISSEp, SPF, NCPHP, SZU-CZ, NIPH, NIOM, LNS, MOH-CY/SGL, LSMU

Note that not all partners mentioned above will analyse the full set of effect biomarkers listed in Table 3. For details on which effect biomarkers will be measured per study see Annex 3.

Table 3: Overview of effect biomarkers selected for analysis in the biological samples collected by the PARC Aligned Studies.

Effect Biomarkers	Children	Teenagers	Adults
Markers of renal function	√		
NAG (N-acetyl-β-D glucosaminidase)	√		
A1MG (α1-microglobulin)	√		
albumin to creatinine ratio	√		
Kim-1 (kidney injury molecule-1)	√		
RBP4 (Retinol-binding protein 4)	√		
Markers of oxidative stress			
8-OHdG (8-hydroxy-2'-deoxyguanosine)	√		√
Thyroid hormones			
fT3 (free triiodothyronine)		√	√
fT4 (free Thyroxine)		√	√
TSH (Thyroid stimulating hormone)		√	√
T3 (Triiodothyronine)		√	√
T4 (Thyroxine)		√	√
Metabolic markers			
TG (Triglycerides)		√	√
Chol (total cholesterol)		√	√
HDL (high-density lipoprotein)		√	√

³ | ASEBA Europe

⁴ [sdqinfo.org/py/sdqinfo/b3.py?language=Englishqz\(UK\)](https://sdqinfo.org/py/sdqinfo/b3.py?language=Englishqz(UK))

⁵ SOPs_health_measurements_HBM4EU.pdf part D, section 3 and section 4; EHES Manual section 5.1.4 and 5.2.1

⁶ EHES Manual section 5.1.1-5.1.4; EHES Manual section 5.2.1

LDL (low-density lipoprotein)		✓	✓
Kisspeptin (kisspeptine 54)		✓	✓
Marker of neurodevelopment			
BDNF (Brain Derived Neurotrophic factor)		✓	✓
Markers of immune function			
IgG			✓
IgM			✓
IgE			✓
Interleukins 1			✓
Interleukins 1B			✓
Interleukins 6			✓
Interleukins 8			✓
LTB4 (Leukotriene B4)			✓
TNF α (Tumor necrosis factor alfa)			✓
IFN- γ (Interferon gamma)			✓

4.2 Collection of personal environmental samples

In collaboration with project P4.2.c_Y3_HumanExposure personal environmental samples will be collected from HBM participants. Collecting personal environmental samples—such as tap water, house dust, indoor air or soil — from the home environment of human biomonitoring (HBM) participants is essential for understanding individual exposure pathways. These samples provide valuable context for interpreting HBM concentrations by linking measured chemical levels in the body to specific environmental sources. This approach helps identify key exposure contributors, improves exposure assessment accuracy, and supports more targeted risk management strategies. By integrating environmental sampling with biomonitoring data, researchers can better assess real-life exposure scenarios and inform policies aimed at reducing harmful environmental exposures.

Following environmental matrices are prioritized:

- Tap water,
- Indoor (house) dust,
- Indoor air,
- Soil.

Substances to be analysed in the environmental samples are still to be decided as part of P4.2.c_Y3_HumanExposure but will be aligned with the exposure biomarkers measured in the human samples.

Following partners are involved in this add-on:

In children: AUTH*, MOH-CY/SGL*, LNS*, ISCIII

In teenagers: AUTH*, VITO/PIH

In adults: AUTH*, MOH-CY/SGL*, LNS*, ISSeP, ISS, RSU

*Participants in the different age groups are recruited within families therefore multiple participants (parent-child) can be linked to the same indoor environment measurement.

Table 4 illustrates the environmental samples that are planned to be collected by the involved partners and the number of households from which the samples are planned to be collected. Not all partners will collect all the different types of environmental samples listed above.

Table 4: environmental matrices collected by HBM studies

	AUTH	MOH-CY/SGL	LNS	ISCIII	VITO/PIH	ISSeP	ISS	RSU
Tap water	150	<150	150-300	20-50	50	40	50-150	50

Indoor (house) dust	150	<50	150-300	20-50	50	100		50
Indoor air	150	<50	150-300	20-50				50 t.b.c
Soil	150	<50			50	40		50 t.b.c

4.3 Application of Suspect Screening, Non Target Screening

In collaboration with project P4.3.2.c_H03, samples from the PARC Aligned Studies can be analysed using suspect screening (SS) and non-targeted screening (NTS) approaches, to screen for exposure biomarkers. Selected human samples from the PARC Aligned Studies will be exchanged with the T4.3 project (P4.3.2.c_H03) as an add-on. This exchange enables the conventional targeted analyses planned within T4.1 to be complemented by exploratory SS analyses, broadening the scope of the assessed chemical exposome.

The selection of samples and participating partners is currently ongoing in coordination with the P4.3.2.c_H03 project leads. Final partner involvement will be determined based on the research question and the selected samples. The screening efforts on the P4.3.2.c_H03 side will focus on human exposure biomarkers and aim to maximise compound coverage through the use of complementary extraction and analytical techniques. At the same time, strict and harmonised QA/QC procedures will be applied throughout all stages of sample preparation, acquisition, and data processing to ensure robust and comparable results across participating laboratories.

5. Status of the studies

In

Table 5, a full list of the contributing studies is provided together with a short description of the status of each study as of February 2025. Following information is reported for each study:

- Study name and Study Acronym;
- Responsible Institute;
- Country;
- Age range (original study) and Age range in PARC (if different);
- Complete study sample size and Sample size contribution under PARC (if different);
- Study implementation level;
- Type of study;
- Sampling method;
- Effect biomarkers included (yes/no);
- Short status description;
- Difficulties encountered during study planning/implementation.

A Summary of the difficulties encountered:

Difficulties in Recruiting Participants:

Many studies reported challenges in recruiting participants, particularly: low response rates, difficulty in engaging specific subpopulations (e.g. participants with low socio-economic backgrounds) or when recruiting children or teenagers via schools limited interest from schools is also reported as hurdle. Also, participant reluctance to complete the long questionnaires is reported.

Ethical and Administrative Delays:

Many studies faced delays due to ethical approval processes.

Budget Constraints:

Many studies struggled with funding shortages for sampling, logistics, and personnel since the resources allocated within PARC are only 45% EU financed and insufficient to cover the complete planning and conduct of the study.

Challenges in Harmonizing Study Protocols:

Some studies struggled to integrate PARC requirements into their existing frameworks. Aligning national studies with PARC's standardized questionnaires and procedures was time-consuming.

Annex 1 presents an overview of when following milestones are achieved per study.

- ✓ Ethical dossier submitted
- ✓ Ethical dossier approved
- ✓ Recruitment started
- ✓ Sample collection & interviews started
- ✓ Sample collection & interviews concluded
- ✓ Chemical analysis started
- ✓ Chemical analysis completed

To date, 37/49 studies have submitted their ethical dossier to the competent national bioethics board, 30/49 studies have obtained approval, 17/49 studies have started the recruitment of participants, 17/49 have started sample collection and interviews, 4/49 have finalized the sample collection and interviews, 3/49 have started chemical analysis.

Annex 2 presents an overview of the participants enrolled in the studies. To date (31/12/2024), 1499 participants have been enrolled (583 children, 310 teenagers, 606 adults).

Table 5: Basic information and status of the studies

Austria
<p>Study name: PARC Children's Survey Austria Study Acronym: PARC-CSA Responsible Institute: EAA Country: Austria Age range (original study): children 6-11 years Age range in PARC (if different): children 6-11 years Complete study sample size: 200 Sample size contribution under PARC (if different): 200 Study implementation level: national level Type of study: cross-sectional Sampling method: convenience sampling. Children from randomly selected regions in urban and rural areas are included. For logistical reasons, several participants from one location are preferred. Effect biomarkers included: no Short status description: Sampling has started in June 2024. So far, samples from 66 children were collected from 3 Austrian federal states including Vienna, Lower Austria and Styria. Next samplings are planned in the Federal States Vorarlberg and Upper Austria. Difficulties encountered during study planning/implementation: difficulties in recruitment of participants, schools are only supportive in rare cases, low response rates.</p>
Belgium
<p>Study name: Flemish Environment and Health Survey-5 Study Acronym: FLEHS-5 Responsible Institute: VITO / PIH Country: Belgium (Flanders) Age range (original study): teenagers 14-16 years. Age range in PARC (if different): the same, teenagers 14-16 years. Complete study sample size: 300 Sample size contribution under PARC (if different): 300 (on condition of consent) Study implementation level: Regional (Flanders) Type of study: Cross-sectional Sampling method: Stratified clustered two-stage sampling design</p>

<p>Effect biomarkers included: yes</p> <p>Short status description: Recruitment and field work ongoing</p> <p>Difficulties encountered during study planning/implementation: A delay in the start of recruitment and field work was experienced, as schools (primary sampling units) were difficult to reach at the end of the past school year (06/2024) and beginning of current school year (09/2024).</p>
<p>Study name: BioMonitoring Humain Wallon – PARC</p> <p>Study Acronym: BMH-Wal-PARC</p> <p>Responsible Institute: ISSeP</p> <p>Country: Belgium (Wallonia)</p> <p>Age range (original study): adults 18 –39 years</p> <p>Age range in PARC (if different): same, adults 18 –39 years</p> <p>Complete study sample size: 300</p> <p>Sample size contribution under PARC (if different): 300</p> <p>Study implementation level: Regional (Wallonia)</p> <p>Type of study: Cross-sectional</p> <p>Sampling method: Stratified and convenience sampling</p> <p>Effect biomarkers included: Yes (thyroid hormones and blood lipids)</p> <p>Short status description: Recruitment since December 2024, samplings and field work will start April 2025.</p> <p>Difficulties encountered during study planning/implementation: Difficulties in recruiting participants, especially those from lower socio-economic backgrounds; issues with the timing of the QA/QC program; and a tight budget, limiting the available resources for the study.</p>
Cyprus
<p>Study name: EnVironmental hEalth foR policY suppOrt aNd disease prEvention in Cyprus</p> <p>Study Acronym: everyone_CY</p> <p>Responsible Institute: MOH-CY / SGL</p> <p>Country: Cyprus</p> <p>Age range (original study): children & adults (parents)</p> <p>Age range in PARC (if different): As in PARC, children 6-11y and adults 18-39y.</p> <p>Because the aim of study design is to recruit families (i.e. a child with his/her parents), it is anticipated that some parents may be older than 39y (i.e. in the 40-70y age group). It is therefore expected that some adults-only of the 18-39y (i.e. no child) will be recruited, to complete the PARC target sample size for this age group.</p> <p>Complete study sample size: 150 children and ≥150 adults.</p> <p>(It was agreed that small countries can aim to recruit half as many participants as the large countries, in accordance to what was implemented in the DEMOCOPHES pilot study).</p> <p>Sample size contribution under PARC (if different): We may exceed the 150 adults (see above)</p> <p>Study implementation level: national</p> <p>Type of study: Cross-sectional</p> <p>Sampling method: We are currently in discussions with the National Health Insurance Organization, to facilitate recruitment via the National HealthCare System to achieve the desired stratification and selection according to the study criteria.</p> <p>Effect biomarkers included: Yes, planned</p> <p>Short status description: Under preparation. Samplings are intended to start in May 2025.</p> <p>Difficulties encountered during study planning/implementation: Cyprus aims to collected environmental samples in the homes of participants, in the frame of T4.2 (Human Exposure Project). The prioritization of substances/matrices and preparation of SOPs is still ongoing. This may create added difficulties and delays, which for Cyprus and of greater impact, due to the complications associated with ordering and receiving lab consumables in the frame of being a small island state at the outskirts of the European Union.</p>
Czech Republic
<p>Study name: Czech National HBM programme / Children’s exposure</p> <p>Study Acronym: CZ-HBM/CE</p> <p>Responsible Institute: SZU-CZ (NIPH)</p> <p>Country: Czech Republic</p> <p>Age range (original study): 6 – 11 years</p> <p>Age range in PARC (if different): children 6-11 years</p> <p>Complete study sample size: 200</p> <p>Sample size contribution under PARC (if different): 200</p> <p>Study implementation level: national</p>

<p>Type of study: cross-sectional</p> <p>Sampling method: convenience sampling; the participants were recruited to study at schools willing to cooperate</p> <p>Effect biomarkers included: no</p> <p>Short status description: the sampling was finished in 2024.</p> <p>Difficulties encountered during study planning/implementation: difficulties occurred in recruiting participants with lower socio-economic status, some legal representatives of child participants did not give consent with biobanking, low response rate, QA/QC rules for labs were formulated vague at the beginning of the general study planning and get stricter and burdensome over time.</p>
<p>Study name: Czech National HBM programme / Adult exposure</p> <p>Study Acronym: CZ-HBM/AE</p> <p>Responsible Institute: SZU-CZ (NIPH)</p> <p>Country: Czech Republic</p> <p>Age range (original study): adults</p> <p>Age range in PARC (if different): adults 18 – 39 years</p> <p>Complete study sample size: 200</p> <p>Sample size contribution under PARC (if different): 200</p> <p>Study implementation level: national</p> <p>Type of study: cross-sectional</p> <p>Sampling method: purposive sampling</p> <p>Effect biomarkers included: yes</p> <p>Short status description: the ethical permission obtained, questionnaires etc. prepared, contracts with clinical laboratories concluded, start of the study in spring 2025</p> <p>Difficulties encountered during study planning/implementation: In Czechia there is not possible to enter any resident's or electoral registries for random sampling within research/monitoring. Therefore, purposive sampling method was chosen.</p>
Denmark
<p>Study name: Copenhagen Puberty Study</p> <p>Study Acronym: COPUS</p> <p>Responsible Institute: RegionH</p> <p>Country: Denmark</p> <p>Age range (original study): children and adolescents aged 5-20 years of age</p> <p>Age range in PARC (if different): 6- 11 years (children) and 12-17 years (teenagers)</p> <p>Complete study sample size: ~3000 individuals</p> <p>Sample size contribution under PARC (if different): 2 x 150 individuals</p> <p>Study implementation level: regional with the possibility of sampling on a national level</p> <p>Type of study: Add-on to an ongoing cross-sectional study (Copenhagen Puberty Study 'COPUS')</p> <p>Sampling method: Convenience sampling; Children and adolescents from randomly selected schools in urban and rural areas will be included. For logistical reasons, schools have to be located close to hospitals (laboratories).</p> <p>Effect biomarkers included: No</p> <p>Short status description: Ethical permission for the use of the PARC questionnaire as well as the collection of additional biological samples has been obtained. Currently, we are working on recruiting new schools to the study, and we expect that PARC participants will be enrolled during spring 2025 and onwards.</p> <p>Difficulties encountered during study planning/implementation: Alignment of PARC questionnaire with the ongoing study setup to avoid overlap between questions. We expect difficulties regarding participation rates because in the ongoing COPUS data collection, this seems to be a challenge.</p>
Estonia
<p>Study name: Conducting biomonitoring among the population exposed to the oil shale sector (workers and residents), second stage - biomonitoring</p> <p>Study Acronym: SOHOS</p> <p>Responsible Institute: University Tartu</p> <p>Country: Estonia</p> <p>Age range (original study): tbc</p> <p>Age range in PARC (if different): 6 – 11 years</p> <p>Complete study sample size: 500</p>

<p>Sample size contribution under PARC (if different): 150 Study implementation level: national level Type of study: cross-sectional, but will become cohort in the future Sampling method: Participants will be recruited by family physicians and occupational physicians. Effect biomarkers included: Only metabolic markers Short status description: Ethical permission for the use of the PARC questionnaire as well as the collection of biological samples has been obtained. Currently, we are working on approval from Data Protection Inspectorate that is need for such a study based on national legislations. Difficulties encountered during study planning/implementation: Getting approval from Data Protection Inspectorate have taken more time than expected.</p> <p>Study name: Conducting biomonitoring among the population exposed to the oil shale sector (workers and residents), second stage - biomonitoring Study Acronym: SOHOS Responsible Institute: University Tartu Country: Estonia Age range (original study): adults Age range in PARC (if different): tbc Complete study sample size: 500 Sample size contribution under PARC (if different): 150</p> <p>Study implementation level: national level Type of study: cross-sectional, but will become cohort in the future Sampling method: Participants will be recruited by family physicians and occupational physicians. Effect biomarkers included: Only metabolic markers Short status description: Ethical permission for the use of the PARC questionnaire as well as the collection of biological samples has been obtained. Currently, we are working on approval from Data Protection Inspectorate that is need for such a study based on national legislations. Difficulties encountered during study planning/implementation: Getting approval from Data Protection Inspectorate have taken more time than expected.</p>
<p>France</p> <p>Study name: National survey on Health, Biomonitoring, Food, Nutrition and Environment Study Acronym: ALBANE Responsible Institute: SpFrance Country: France Age range (original study): children (3-11 years), teenagers (12-17 years), adults (18-79 years) Age range in PARC (if different): children (6-11 years), teenagers (12-17 years), adults (18-39 years) Complete study sample size: 1000 Children + Teenagers, 1000 Adults Sample size contribution under PARC (if different): 300 children, 300 teenagers, 300 adults Study implementation level: National level Type of study: Cross-sectional (repeated in time) Sampling method: Random sampling Effect biomarkers included: yes, Thyroid hormones, Blood lipids, IgE Short status description: The pilot survey has ended in December 2024. Preparation for the fieldwork of the national survey is ongoing. Questionnaires are now under programming and laboratories for health examination and biological sampling are being selected. Ethical permission and reglementary authorization (GDPR) have been obtained. The study protocol is also under evaluation by national experts to obtain a national labelling for “statistical survey of public interest”. The launching is expected on the 2nd of June, 2025. Difficulties encountered during study planning/implementation: The integration of a complete set of PARC obligatory questions has been a real challenge. Albane questionnaires are already very long and this might be the highest difficulties to keep participants involved in the survey. “Optional” and “nice to have” questions have not been implemented in Albane. As the sampling starts in June 2025, Albane will not provide any data for participants sampled in May if the ending date at PARC level is maintained to April 2026.</p>
<p>Germany</p> <p>Study name: Aligned Study for Environmental Health Study Acronym: ALISE Responsible Institute: UBA</p>

<p>Country: Germany Age range (original study): children (6-11) years Age range in PARC (if different): children (6-11) years Complete study sample size: 300 Sample size contribution under PARC (if different): 300 Study implementation level: national level Type of study: cross-sectional Sampling method: Random sampling Effect biomarkers included: yes Short status description: ethics dossier accepted, recruitment will be done via resident's registries, questionnaire implementation ongoing, field work in preparation, sampling starting April 2025 Difficulties encountered during study planning/implementation: very high costs of field work, not enough PMs for planning and implementation of the whole study available, no PARC materials available for reporting to participants, no well-designed PARC layouts available for materials for participant recruitment.</p>
<p>Study name: Aligned Study for Environmental Health Study Acronym: ALISE Responsible Institute: UBA Country: Germany Age range (original study): teenagers 12-17 years Age range in PARC (if different): teenagers 12-17 years Complete study sample size: 300 Sample size contribution under PARC (if different): 300 Study implementation level: national level Type of study: cross-sectional Sampling method: Random sampling Effect biomarkers included: yes Short status description: ethics dossier accepted, recruitment will be done via resident's registries, questionnaire implementation ongoing, field work in preparation, sampling starting April 2025 Difficulties encountered during study planning/implementation: very high costs of field work, not enough PMs for planning and implementation of the whole study available, no PARC materials available for reporting to participants, no well-designed PARC layouts available for materials for participant recruitment</p>
<p>Study name: German Environmental Survey VI Study Acronym: GerES VI Responsible Institute: UBA Country: Germany Age range (original study): adults 18-79 years Age range in PARC (if different): adults 18-39 years Complete study sample size: 1500 Sample size contribution under PARC (if different): 300 Study implementation level: national level Type of study: cross-sectional Sampling method: Random sampling Effect biomarkers included: no Short status description: field work finished, chemical analysis still ongoing Difficulties encountered during study planning/implementation: low response rate, no supporting materials from PARC available at start of study so no harmonisation of questionnaires possible, QA/QC rules of PARC not available at start of study, biomarker prioritization list not available during planning phase of study.</p>
<p>Greece</p> <p>Study name: Exposome and Health Survey in PARC Study Acronym: HERACLES Responsible Institute: AUTH Country: Greece Age range (original study): Children (6-11) Age range in PARC (if different): Children 6-11 Complete study sample size: We are expecting to have a total number of 300 children Sample size contribution under PARC (if different): 300 children Study implementation level: national</p>

<p>Type of study: Cross-sectional</p> <p>Sampling method: Convenience Sampling and Cluster Sampling. Both convenience sampling and cluster sampling will be applied in this study. Children and teenagers will be selected from schools that are willing to participate. Additionally, further members of their families, including adult siblings and parents, will be invited to participate in the study.</p> <p>Effect biomarkers included: Yes</p> <p>Short status description: Ethical approval has been obtained, and all necessary study materials, including questionnaires, flyers, posters, and school materials, have been prepared. Contracts with clinical laboratories have been finalized, ensuring all logistical and analytical aspects are in place. Additionally, a comprehensive portfolio outlining the study has been submitted to the Ministry of Education, and we are currently awaiting their official response. With everything ready for implementation, the study is set to commence on February 1, 2025, marking the official start date for the first sample collection.</p> <p>Difficulties encountered during study planning/implementation: The planning and implementation of HERACLES presented several challenges due to the complexity of the study and the need for everything to function seamlessly. Ensuring that all aspects were properly set up and executed with precision required significant coordination and effort. One of the main challenges is navigating the Ministry of Education's approval process. Even if we successfully obtained permission to enter schools and integrate the study as an educational program—introducing children to key concepts of environmental health—this approval is granted for the current academic year. To continue the study in the next educational year, we must reactivate and renew the program's authorization. This presents an ongoing administrative challenge, requiring continuous engagement with the Ministry to ensure the study's sustainability and long-term impact. Furthermore, the financial demands of conducting such a complex study extend beyond standard research expenses, encompassing specialized laboratory analyses, advanced equipment, personnel training, and logistical coordination. As a result, securing sufficient funding and resource allocation remains a critical challenge for the study's successful execution and long-term sustainability.</p>
<p>Study name: Exposome and Health Survey in PARC</p> <p>Study Acronym: HERACLES</p> <p>Responsible Institute: AUTH</p> <p>Country: Greece</p> <p>Age range (original study): Teenagers (12-17)</p> <p>Age range in PARC (if different): Teenagers (12-17)</p> <p>Complete study sample size: We are expecting to have a total number of 300 teenagers</p> <p>Sample size contribution under PARC (if different): 300 teenagers</p> <p>Study implementation level: national</p> <p>Type of study: Cross-sectional</p> <p>Sampling method: Convenience Sampling and Cluster Sampling. Both convenience sampling and cluster sampling will be applied in this study. Children and teenagers will be selected from schools that are willing to participate. Additionally, further members of their families, including adult siblings and parents, will be invited to participate in the study.</p> <p>Effect biomarkers included: Yes</p> <p>Short status description: Ethical approval has been obtained, and all necessary study materials, including questionnaires, flyers, posters, and school materials, have been prepared. Contracts with clinical laboratories have been finalized, ensuring all logistical and analytical aspects are in place. Additionally, a comprehensive portfolio outlining the study has been submitted to the Ministry of Education, and we are currently awaiting their official response. With everything ready for implementation, the study is set to commence on February 1, 2025, marking the official start date for the first sample collection.</p> <p>Difficulties encountered during study planning/implementation: The planning and implementation of HERACLES presented several challenges due to the complexity of the study and the need for everything to function seamlessly. Ensuring that all aspects were properly set up and executed with precision required significant coordination and effort. One of the main challenges is navigating the Ministry of Education's approval process. Even if we successfully obtained permission to enter schools and integrate the study as an educational program—introducing children to key concepts of environmental health—this approval is granted for the current academic year. To continue the study in the next educational year, we must reactivate and renew the program's authorization. This presents an ongoing administrative challenge, requiring continuous engagement with the Ministry to ensure the study's sustainability and long-term impact. Furthermore, the financial demands of conducting such a complex study extend beyond standard research expenses, encompassing specialized laboratory analyses, advanced equipment, personnel training, and</p>

logistical coordination. As a result, securing sufficient funding and resource allocation remains a critical challenge for the study's successful execution and long-term sustainability.

Study name: Exposome and Health Survey in PARC

Study Acronym: HERACLES

Responsible Institute: AUTH

Country: Greece

Age range (original study): Adults (18-70)

Age range in PARC (if different): Adults 18-39. We are going also to recruit adults 40-70 as we are recruiting families (parents and kids).

Complete study sample size: We are expecting to have a total number of ~500 participants in the end.

Sample size contribution under PARC (if different): 300 Adults (18-39)

Study implementation level: national

Type of study: Cross-sectional

Sampling method: Convenience Sampling and Cluster Sampling. Both convenience sampling and cluster sampling will be applied in this study. Children and teenagers will be selected from schools that are willing to participate. Additionally, further members of their families, including adult siblings and parents, will be invited to participate in the study.

Effect biomarkers included: Yes

Short status description: Ethical approval has been obtained, and all necessary study materials, including questionnaires, flyers, posters, and school materials, have been prepared. Contracts with clinical laboratories have been finalized, ensuring all logistical and analytical aspects are in place.

Additionally, a comprehensive portfolio outlining the study has been submitted to the Ministry of Education, and we are currently awaiting their official response.

With everything ready for implementation, the study is set to commence on February 1, 2025, marking the official start date for the first sample collection.

Difficulties encountered during study planning/implementation: The planning and implementation of HERACLES presented several challenges due to the complexity of the study and the need for everything to function seamlessly. Ensuring that all aspects were properly set up and executed with precision required significant coordination and effort. The financial demands of conducting such a complex study extend beyond standard research expenses, encompassing specialized laboratory analyses, advanced equipment, personnel training, and logistical coordination. As a result, securing sufficient funding and resource allocation remains a critical challenge for the study's successful execution and long-term sustainability.

Hungary

Study name: Human Biomonitoring Programme for Hungary I.

Study Acronym: HBM-HU I.

Responsible Institute: NCPHP

Country: Hungary

Age range (original study): children (6-11 years)

Age range in PARC (if different): -

Complete study sample size: 300

Sample size contribution under PARC (if different): -

Study implementation level: national

Type of study: cross-sectional

Sampling method: quota sampling

Effect biomarkers included: yes

Short status description: The field campaign started in May 2024, and we expect to conclude it in June 2025. Our laboratory has been participating in the QA/QC program, and we plan to perform all analyses in-house. The questionnaires were completed on a paper basis, and we are waiting for the RedCap files to create a database.

Difficulties encountered during study planning/implementation: We aimed to recruit volunteers from across the entire country; therefore, we asked school managers to forward our invitations through the digital educational platform used in Hungarian schools for administrative and communication purposes. Unfortunately, the response rate has been very low; therefore, we also involved local governmental offices in the recruitment process. We had more success in the HBM4EU project, where we reached fewer schools but maintained direct contact with parents. In parallel with the HBM study, we are investigating air quality in the homes of more than 150 children. We found that interest in indoor air quality measurements is higher than in the HBM component.

Study name: Human Biomonitoring Programme for Hungary I.
Study Acronym: HBM-HU I.
Responsible Institute: NCPHP
Country: Hungary
Age range (original study): adults (18-39 years)
Age range in PARC (if different): -
Complete study sample size: 150
Sample size contribution under PARC (if different): -
Study implementation level: national
Type of study: cross-sectional
Sampling method: quota sampling / convenient sampling
Effect biomarkers included: yes
Short status description: We are currently preparing the ethical dossier. We expect to submit the documents for ethical approval in April.
Difficulties encountered during study planning/implementation: We do not have experience in blood collection; therefore, we are still working on the most efficient method for sample collection.

Iceland

Study name: HBM2-IS
Study Acronym: HBM2-IS
Responsible Institute: UI
Country: Iceland
Age range (original study): 18- to 39-year-old
Age range in PARC (if different): 18- to 39-year-old
Complete study sample size: n=200
Sample size contribution under PARC (if different): n=200
Study implementation level: Metropolitan area of Iceland, where 2/3 of the population live.
Type of study: Cross-sectional
Sampling method: We have a list of 800 persons, we will continue until we have 200 participants
Effect biomarkers included: No
Short status description: Ethical permission has been obtained. Translation of PARC questionnaire and adaptation for Icelandic reality (different types of fish and living conditions) and omitting irrelevant questions to shorten the questionnaire in interest of better participation. Putting the questions into RedCap, was a challenge, but is done. An agreement with a private laboratory to collect samples is also at hand. A list of randomly selected participants from the national registry, but limited to the metropolitan area, is also at hand. Recruitment is eminent. We plan to make first contact by surface mail followed by a phone call.
Difficulties encountered during study planning/implementation: We anticipate difficulties due to previous experience in HBM4EU but have made changes to hopefully help with participation. Even with a shorter version of the questionnaire, it will still take about 40 min to answer. This age group does not respond well to phone calls from an unknown source, so we will first let them know what to expect.

Ireland

Study name: /
Study Acronym: HBM4IE
Responsible Institute: UCD
Country: Ireland
Short status description:
 Ireland has only recently joined PARC (date) and they are in the phase of planning a HBM study in adults Aligned to the PARC Aligned Studies.

Israel

Study name: Israel Biomonitoring Study Cycle II
Study Acronym: IBS II
Responsible Institute: MOH-IL
Country: Israel
Age range (original study): 20-59 years
Age range in PARC (if different): 20-39 years
Complete study sample size: 150

Sample size contribution under PARC (if different): 150

Study implementation level: National

Type of study: Cross-sectional

Sampling method: Quota sampling

Effect biomarkers included: No

Short status description: Ethical committee approval has been obtained, adult obligatory questionnaire translated and adopted to Israeli culture (for example dietary restrictions in part of the population). The questionnaire is set up online so that each participant can fill it out on their own devices. Laboratory has ordered supplies for sample collection and analysis and is set for receiving blood and urine samples.

Difficulties encountered during study planning/implementation: Preparing the online version questionnaire was a challenge since we made a few adaptations to fit the Israeli cultural nuances (for example dietary restrictions in part of the population). We will not be able to include certain populations in the study (specifically North and South of the country) that have been evacuated from their homes, these areas are not included in the study population.

Italy

Study name: ITalian National Exposure to environmental contaminants and REference values

Study Acronym: ITINERE

Responsible Institute: ISS

Country: Italy

Age range (original study): adults 18 –39 years

Age range in PARC (if different): 18 –39 years

Complete study sample size: 300

Sample size contribution under PARC (if different): 300

Study implementation level: National

Type of study: cross-sectional

Sampling method: convenience sampling

Effect biomarkers included: no

Short status description: Ethical permission has been obtained. Currently, we are working on translation of PARC questionnaire in Italian and implementation in RedCap.

Difficulties encountered during study planning/implementation:

We expect difficulties regarding participation rates because of the difficulty of the participants in completing a very long questionnaire.

Latvia

Study name: General Human Biomonitoring Survey in Latvia

Study Acronym: Gen_HBM_Survey_LV

Responsible Institute: RSU

Country: Latvia

Age range (original study): adults (18-39)

Age range in PARC (if different): -

Complete study sample size: adults (300).

Sample size contribution under PARC (if different): -

Study implementation level: National level

Type of study: Cross-sectional

Sampling method: Convenience sampling

Effect biomarkers included: Yes

Short status description: Ethical permission has been obtained, the questionnaire is already translated and programmed in RedCap, further testing in progress. Participants identified, we expect to start recruiting shortly.

Difficulties encountered during study planning/implementation:

We have failed to receive ethical permission for sampling urine from minors in our study (children and teenagers). The procurement procedure and drawing a list of exact materials (vacutainers, tubes, labels) have been challenging due to many details that have to be taken into account but are not described in SOPs. The long questionnaire will probably affect participation rates.

Note:

Initially RSU aimed at setting up a HBM study in all 3 age groups (children, teenagers and adults). Due to encountered difficulties RSU will not be continuing with the HBM survey for teenagers and children. Due to

<p>the ongoing challenges with obtaining ethical approvals and the delayed establishment of the Central Medical Ethics Committee, we are unable to proceed with this part of the project.</p>
<p>Lithuania</p> <p>Study name: National health and lifestyle examination survey Study Acronym: NHALES-LT Responsible Institute: LSMU Country: Lithuania Age range (original study): adults Age range in PARC (if different): adults 18-39 years Complete study sample size: 750-900 Sample size contribution under PARC (if different): 300 Study implementation level: National level Type of study: cross-sectional Sampling method: random sampling Effect biomarkers included: yes Short status description: ethical permission has been obtained; the questionnaires have been translated into Lithuanian and formatted; a pilot study to validate the general questionnaire has been conducted; the documents for the Lithuanian Population Register and material for training of the interviewers is being prepared. Difficulties encountered during study planning/implementation: a very long questionnaire and a low response rate may be the greatest challenges during the data collection that is planned to start in May 2025.</p>
<p>Luxembourg</p> <p>Study name: General BM Survey in Luxembourg Study Acronym: LëtzhBM Responsible Institute: LNS Country: Luxembourg Age range (original study): children (6-11 years), adults (parents) (18-39 years) Age range in PARC (if different): As in PARC, children 6-11y and adults 18-39y. Because we will recruit one child and one parent per each household, it is anticipated that some parents may be older than 39y (i.e. in the 40-70y age group). We will use other recruitment methods to reach the expected PARC target sample size for this age group. Complete study sample size: 300 children and 300 adults Sample size contribution under PARC (if different): 150 children, 150 adults Study implementation level: National level Type of study: Cross-sectional Sampling method: Cluster sampling and quota sampling. Children and their parents will be invited to participate in collaboration with national school medical services located in each electoral district across the country. Those who are willing to participate will be included based on our eligibility criteria and the need for representativeness. Effect biomarkers included: Yes Short status description: Ethical permission has been obtained; the questionnaires have been translated into German and French; the information leaflets and consent forms have been also translated and adapted for communication purposes; logistics for conducting the survey are being implemented; a pilot home visit has been conducted; the laboratory has been participating in the QA/QC program for the exposure biomarkers analysis. The recruitment is planned to start on 1st March 2025. Difficulties encountered during study planning/implementation: Obtaining the ethical approval is a long process in Luxembourg. A very long questionnaire for adults and children may be a challenge. There is limited support for questions regarding digitalisation of questionnaires (RedCap), training and QA sessions should be implemented. Delay in the harmonisation process for the environmental samples (P 4.2.1c.Y3_Human Exposure), SOPs and chemical prioritisation are still not finalised.</p>
<p>Norway</p> <p>Study name: Norwegian Environmental Biobank III Study Acronym: NEB III Responsible Institute: NIPH Country: Norway Age range (original study): teenagers, adults Age range in PARC (if different): 14-17 years and 18-22 years Complete study sample size: 600 triads of mothers, fathers and their children which are 14-22y.</p>

<p>Sample size contribution under PARC (if different): 200 teenagers, 200 adults Study implementation level: national Type of study: cross sectional and partly also longitudinal Sampling method: Purposive sampling, approximately 20% (n= approx. 21500) of the second generation in the nation-wide Norwegian mother, father and child cohort study has been invited to participate in NEB III, either as adults (<18 years) or teenagers (<18 years). Participants or their legal guardians (if participant was <16 years) have consented electronically. Sample equipment has been sent to the participants by mail. Urine samples are collected by the participants themselves, while blood samples are collected by their GPs or similar. Samples are sent by mail to the biobank at NIPH. Questionnaires are completed by the participants electronically (main questionnaire) and on paper (questions on recent exposure). Effect biomarkers included: yes Short status description: Recruitment started in February 2024 and sampling campaign is planned to be finished by March 2025. Difficulties encountered during study planning/implementation: In general, very low participation rate. Further, only approx. 40% of consented participants has provided samples and completed the questionnaires, while costs for sampling equipment etc is the same for the remaining 60%. Feedback from participants that the questionnaire is too demanding to complete. Very high direct costs compared to budget from PARC.</p>
<p>The Netherlands</p> <p>Study name: PFAS exposure in the Netherlands Study Acronym: - Responsible Institute: RIVM Country: The Netherlands Age range (original study): adults 18-65 years. Age range in PARC (if different): 18-39 years Complete study sample size: still unknown. 1500 is targeted for adults 18-65 Sample size contribution under PARC (if different): 300 Study implementation level: national Type of study: cross-sectional Sampling method: Leftover serum of blood from blood donors that is used for testing on infections by the Blood Bank of the Netherlands will be used. All donors on certain days are asked to participate. Sampling will not cover all 4 seasons. Effect biomarkers included: no Short status description: Awaiting ethical approval Difficulties encountered during study planning/implementation: Sampling method and questionnaire will differ from PARC SOPs. A much smaller questionnaire will be used. Side note: The HBM contribution from the Netherlands is not in full alignment with the PARC criteria. The study will only deliver data on PFAS.</p>
<p>Poland</p> <p>Study name: Biomonitoring in Poland on Children Study Acronym: BIOPOL-CH Responsible Institute: WULS Country: Poland Age range (original study): children (6 – 11 y) Age range in PARC (if different): The same as in PARC Complete study sample size: 300 children Sample size contribution under PARC (if different): The same as in PARC (300 children) Study implementation level: national Type of study: cross sectional Sampling method: random sampling Effect biomarkers included: yes Short status description: Recruitment started in December 2024 and sampling campaign is planned to be finished by December 2025 Difficulties encountered during study planning/implementation: High cost of trips to the examined persons, very long questionnaire - parents' reluctance to fill it out, difficulties in obtaining a morning urine sample, collecting hair samples from small boys is almost impossible</p> <p>Study name: Polish Aligned Environmental Study Study Acronym: POLAES_PARC</p>

Responsible Institute: NIOM
Country: Poland
Age range (original study): teenagers (12-17y), adults (18-39y)
Age range in PARC (if different): The same as in PARC: teenagers (12-17y), adults (18-39y)
Complete study sample size: 300 teenagers, 300 adults
Sample size contribution under PARC (if different): The same as in PARC
Study implementation level: national
Type of study: cross-sectional
Sampling method:
Effect biomarkers included: yes
Short status description: ethics dossier accepted, questionnaire implementation ongoing, field work in preparation, sampling starting February 2025
Difficulties encountered during study planning/implementation: High cost of survey preparation and implementation, extensive questionnaires used to discourage survey participation.

Portugal

Study name: Exposure of the Portuguese Population to Environmental Chemicals
Study Acronym: ExpoQuim-Kids
Responsible Institute: INSA
Country: Portugal
Age range (original study): children (6-11 years old)
Age range in PARC (if different):
Complete study sample size: 300 participants
Sample size contribution under PARC (if different):
Study implementation level: national
Type of study: cross-sectional
Sampling method: Stratified and convenience sampling. Schools were randomly selected (including from urban and rural areas) and children from the selected schools will be invited to participate.
Effect biomarkers included: no
Short status description: awaiting ethical approval
Difficulties encountered during study planning/implementation: difficulties to contact and involve schools.

Study name: Exposure of the Portuguese Population to Environmental Chemicals
Study Acronym: ExpoQuim-Teen
Responsible Institute: INSA
Country: Portugal
Age range (original study): teenagers (12-17 years old)
Age range in PARC (if different):
Complete study sample size: 300 participants
Sample size contribution under PARC (if different):
Study implementation level: national
Type of study: cross-sectional
Sampling method: Stratified and convenience sampling. Schools were randomly selected (including from urban and rural areas) and teenagers from the selected schools will be invited to participate.
Effect biomarkers included: no
Short status description: awaiting ethical approval
Difficulties encountered during study planning/implementation: difficulties to contact and involve schools.

Study name: Exposure of the Portuguese Population to Environmental Chemicals
Study Acronym: ExpoQuim2
Responsible Institute: INSA
Country: Portugal
Age range (original study): adults (18-39 years old)
Age range in PARC (if different):
Complete study sample size: 300 participants
Sample size contribution under PARC (if different):
Study implementation level: national

Type of study: cross-sectional
Sampling method: two-stage random sampling
Effect biomarkers included: no
Short status description: awaiting ethical approval
Difficulties encountered during study planning/implementation: difficulties to contact health centers and to obtain the list of users from the National Health System for the selected areas.

Slovakia

Study name: Harmonized human biomonitoring study in Slovak teenagers
Study Acronym: SK-PARC Teens
Responsible Institute: SZU-SK
Country: Slovakia
Age range (original study): teenagers (12-17 years)
Age range in PARC (if different): -
Complete study sample size: 160
Sample size contribution under PARC (if different): 160
Study implementation level: national
Type of study: cross-sectional
Sampling method: convenience sampling
Effect biomarkers included: no
Short status description: Waiting for ethical approval, preparation of fieldwork
Difficulties encountered during study planning/implementation: Securing sufficient funding and resource allocation remains a critical challenge for the study's successful execution and long-term sustainability.

Slovenia

Study name: National HBM II campaign
Study Acronym: SLO HBM II
Responsible Institute: JSI / NIJZ
Country: Slovenia
Age range (original study): children (6-9 years), teenagers (12-15 years)
Age range in PARC (if different): the same as in original study
Complete study sample size: 300 children, 300 teenagers
Sample size contribution under PARC (if different): 150 children, 150 teenagers
Study implementation level: national, but only three distinct regions part of PARC Aligned Studies
Type of study: cross-sectional
Sampling method: convenience sampling
Effect biomarkers included: yes
Short status description: sampling completed
Difficulties encountered during study planning/implementation: low response rate, not equal distribution across different socio-economic classes; Since the national HBM study was already underway, adjustments were made to the existing questionnaire to better align it with the PARC project. Due to considerable length of the PARC questionnaire, only mandatory questions were included. Participants also expressed concerns about the questionnaire's length. Additionally, recoding the adapted HBM questionnaire to match the PARC codebook will require extra time and effort.

Spain

Study name: Exposición a Sustancias Químicas en Población Infantil
Study Acronym: ESQUIPI
Responsible Institute: ISCIII
Country: Spain
Age range (original study): children (6-11)
Age range in PARC (if different): children (6-11)
Complete study sample size: 300-500
Sample size contribution under PARC (if different): 300
Study implementation level: national (>6 NUTS3)
Type of study: cross-sectional
Sampling method: convenience sampling

<p>Effect biomarkers included: Yes</p> <p>Short status description: PARC documents for Aligned Studies translated and adapted, submission of ethical dossier pending as we need details on the environmental sampling in project 4.2.c_Y3.</p> <p>Difficulties encountered during study planning/implementation: The alignment with project 4.2.c_Y3 has led to a delay from the original planning.</p>
<p>Study name: Implementing a HBM module into VIII Basque Health Survey (PARC Euskadi) *</p> <p>Study Acronym: PARC Euskadi</p> <p>Responsible Institute: UPV/EHU</p> <p>Country: Spain</p> <p>Age range (original study): Adults (18-39 years old)</p> <p>Age range in PARC (if different):</p> <p>Complete study sample size: 150</p> <p>Sample size contribution under PARC (if different):</p> <p>Study implementation level: national</p> <p>Type of study: cross-sectional</p> <p>Sampling method: random sampling and purposive sampling for underrepresented ISCED level.</p> <p>Effect biomarkers included: no</p> <p>Short status description: Ethical dossier approved, questionnaires translated and implemented. Almost all necessary study materials (questionnaires and participant's documentation, recruitment letters, flyers, posters, participant's information leaflets, and other materials have been prepared and printed. Logistics with the Basque health system have been arranged, ensuring a smooth –albeit intense- workflow for the collection of blood and urine samples. Field work started in autumn 2024 and is ongoing for winter season as of Feb 2025; all fieldwork is planned to be completed in October 2025.</p> <p>Difficulties encountered during study planning/implementation: Lack of participants with ISCED levels 0-2 corresponding to basic education in the Basque Health survey database to make up to 33% of the sampled population. We have complemented the random sampling with purposive sampling approach to ensure that at least 10% of our sample is from that education level.</p> <p>We have encountered very low response rates among male participants, and lower education levels. Also, co-funding constraints have made impossible to implement effect biomarkers.</p>
<p>Study name: Human Biomonitoring in Andalusia</p> <p>Study Acronym: PARC-Andalusia</p> <p>Responsible Institute: EASP</p> <p>Country: Spain</p> <p>Age range (original study): adults</p> <p>Age range in PARC (if different):</p> <p>Complete study sample size: 150</p> <p>Sample size contribution under PARC (if different): -</p> <p>Study implementation level: national</p> <p>Type of study: cross-sectional</p> <p>Sampling method: random sampling</p> <p>Effect biomarkers included: no</p> <p>Short status description: ethical dossier approved, PARC questionnaires for adults translated, availability of the population database for selection of participants, planning of fieldwork tasks, including staff training. Start date of recruitment and fieldwork: March,2025.</p> <p>Difficulties encountered during study planning/implementation: delay of 6 months to have access to the population database of users of the Andalusian Health System (needed for a random sampling). Difficulties in getting access to healthcare facilities where collecting and processing biological samples, which limits the obtention of first-morning urine samples and fasting blood samples. Long distances to access rural areas, which leads increased study costs.</p>
<p>Sweden</p> <p>Study name: Swedish Adolescent Study</p> <p>Study Acronym: SAS</p> <p>Responsible Institute: ULUND; KI; UmU</p> <p>Country: Sweden</p> <p>Age range (original study): teenagers 15-19</p> <p>Age range in PARC (if different): 15-17 years</p> <p>Complete study sample size 300</p>

Sample size contribution under PARC (if different): 150

Study implementation level: national (3 NUTS)

Type of study: cross-sectional

Sampling method: convenience sampling

Effect biomarkers included: no

Short status description: PARC documents for Aligned Studies in progress, submission of ethical dossier during spring 25. Sampling is planned during august 2025 until May 2026.

Difficulties encountered during study planning/implementation: Adjustments are ongoing for existing questionnaire to better align it with the PARC project. But we are worried with the considerable length of the PARC questionnaire.

UK

Study name: Implementing a HBM module into Health Survey for England

Study Acronym: HBM in HSfE

Responsible Institute: UKHSA

Country: UK

Age range (original study): children (6-11 years), teenagers (12-17 years), adults (18-49 years)

Age range in PARC (if different): 6-11 years, 12-17 years, 18-39 years

Complete study sample size: 450

Sample size contribution under PARC (if different): 300

Study implementation level: national

Type of study: cross-sectional

Sampling method: Stratified randomised

Effect biomarkers included: No

Short status description: This HBM module in been implemented into the Health Survey for England which is a national health examination survey. The study should have commenced on January 2025 but unfortunately due to some restructuring with the national examination work programme we were informed that no HBM work would take place this year. We are still awaiting a decision from the programme owner whether the 2026 work programme will go ahead and if this will include our HBM work.

Difficulties encountered during study planning/implementation: The dependency on a national study has been a problem given that we do not have the necessary framework in place to do a standalone HBM programme.

6. Next steps

6.1 Data management and data analysis

The supporting data management procedures and statistical analysis plan are under development to ensure a robust and standardized approach to data processing and evaluation. They build further on the data management approaches and statistical analysis plan developed under HBM4EU.

Codebook development

First a questionnaire codebook has been developed specifying how the questionnaire responses should be formatted into a dataset. This codebook is to support the studies in their primary data collection and processing. Next, a data sharing codebook is developed. This codebook builds further on the Questionnaire codebook and defines the final format/coding for the data to be shared and pooled at EU level. The data sharing codebook is directly linked to the data template for providing the data itself.

Compared to the questionnaire codebook, the data sharing codebook in addition contains:

- analytical variables (exposure and effect biomarker results)
- sample related variables
- field work variables
- flagging of direct identifiable information and excluding them from the data template
- health outcome modules (asthma/allergy, neurological)

The data sharing codebook is in the final stages of development (lead by VITO, support PIH).

Statistical analysis plan development

The Statistical analysis plan is under development (lead by VITO) to prepare the statistical approaches that should be followed when evaluating the data. It describes the following sections:

General statistical principles including (how to treat values below LOD/LOQ, transformations, adjustments for urinary dilution or blood lipid content, calculation of sum parameters, handling outliers and missing data etc.) Furthermore, specific statistical methods are described per research topic/question:

European exposure values, geographical comparisons, comparison to health-based guidance values, time patterns, identification of exposure determinants, sources and routes, exposure-effect associations, pathway analysis and mixture analysis.

Epidemiological analyses of data from populations exposed to mixtures of chemical and non-chemical agents can be used to address a number of different research questions (Gibson et al., 2019; Joubert et al., 2022):

1. Mixture identification, i.e., which exposures tend to occur in combination? An obvious limitation here is that this evaluation is limited to the a priori selection of chemical exposures that will be covered by targeted analysis in PARC. However, the results of SS/NTS analysis can deliver additional insights into real-life exposure mixtures.
2. What is the overall effect of the mixture?
3. Which of the mixture components are important and what effects do they have?

6.2 Other next steps and timeline

In 2025, the chemical analysis phase will commence as soon as the results from the first two G-EQUAS rounds become available. A communication plan is currently in development to establish clear agreements on the external dissemination of EU-level results from the PARC Aligned Studies (P4.1.1.2.a_Y1_GenHBMSurvey_VITO). A physical workshop/meeting is scheduled for May 2025 to facilitate discussions and progress updates.

The anticipated project timeline (under condition) is presented in Figure 3.

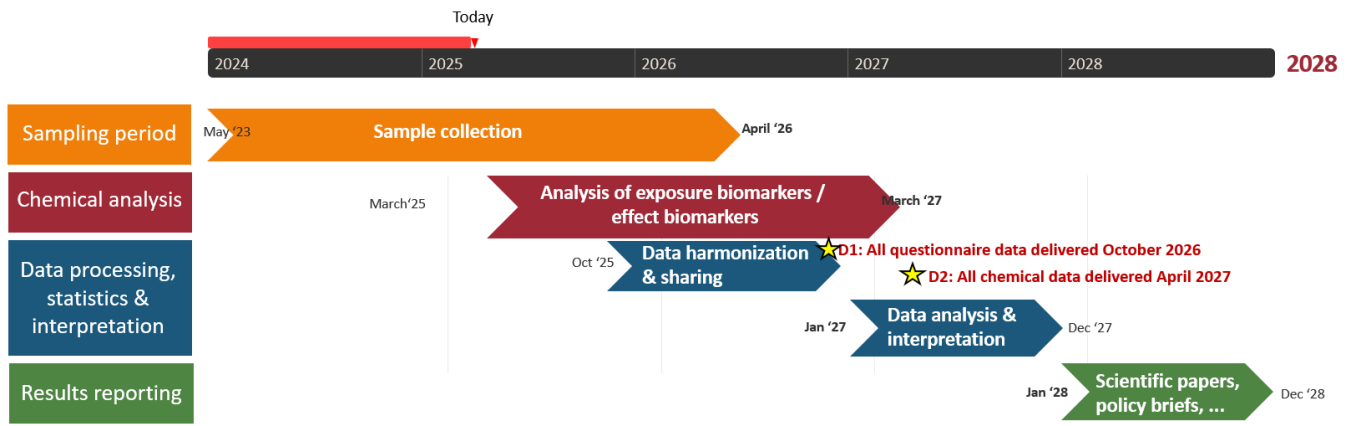


Figure 3: timeline of the PARC Aligned Studies

Sampling period: Samples can be collected between **May 2023 – April 2026**. *Chemical analysis:* Can start after 2 successful rounds of QA/QC (**expected timing March 2025**). *Data preparation:* All supporting processes will be ready **October 2025**, so data owners can start harmonization/preparation of the dataset that should be shared within PARC. *Data sharing: October 2026: D1 = deadline to deliver all questionnaire data + already available chemical data. April 2027: D2 = deadline to deliver all questionnaire data + all chemical data.* *Data analysis & interpretation:* First (incomplete) data extracts will be shared to initiate data analysis and interpretation within PARC **January 2027**. *Results reporting:* Scientific publications and other results communication **expected in 2028**.

Annex 1: Progress of studies per milestone

Country	Partner(s)	Study acronym	Ethical dossier submitted	Ethical dossier approved	Recruitment started	Sample collection & interviews started	Sample collection & interviews concluded	Chemical analysis started	Chemical analysis concluded	Data delivered in Chemical harmonized format to PEH
						interviews started	interviews concluded	started	concluded	
CHILDREN										
UK	PHE	HBM in HSFE	-	-	-	-	-	-	-	-
Denmark	RegionH	COPUS	07/10/2024	27/12/2024	-	-	-	-	-	-
Estonia	UTARTU	SOHOS	23/08/2024	7/10/2024	-	-	-	-	-	-
Poland	WULS	BIOPOL-CH	16/08/2023	12/09/2023	27/05/2024	10/12/2024	-	-	-	-
Czech Republic	SZU-CZ (NIPH)	CZ-HBM/CE	13/09/2023	01/11/2023	15/12/2023	10/01/2024	30/11/2024			
Hungary	NPHC	HBM-HU I.	12/02/2024	07/03/2024	16/04/2024	09/05/2024	-	-	-	-
Spain	ISCI3	ESQUIPI	18/03/2025	-	-	-	-	-	-	-
Portugal	INSA	ExpoQuim- Kids	15/04/2025	-	-	-	-	-	-	-
Greece	AUTH	HERACLES	04/07/2024	16/07/2024	01/02/2025	01/02/2025	-	-	-	-
Slovenia	JSI / NIJZ	SLO HBM II	29/03/2019; 30/11/2022	23/05/2019*	07/09/2023	16/01/2024	27/11/2024	DD/07/2024 ⁷		
Cyprus	MOH-CY / SGL	everyone_CY	-	-	-	-	-	-	-	-
Germany	UBA	ALISE	09-10/2024	DD/12/24	-	-	-	-	-	-
France	SpFrance	ALBANE	24/08/2023	18/09/2023	-	-	-	-	-	-
Austria	EAA	PARC-CSA	12/12/2023	10/05/2024	21/05/2024	06/06/2024	-	-	-	-
Luxembourg	LNS	LëtzhBM	18/01/2024	-	-	-	-	-	-	-

⁷ JSI/NIJZ are obliged to report the results to the national funding body (Ministry of Health) and could not postpone the analysis for this reason, as an exception their participation in G-EQUAS RV72 + RV 73 will be evaluated.

Country	Partner(s)	Study acronym	Ethical dossier submitted	Ethical dossier approved	Recruitment started	Sample collection & interviews started	Sample collection & interviews concluded	Chemical analysis started	Chemical analysis concluded	Data delivered in harmonized format to PEH
TEENAGERS										
UK	PHE	HBM in HSfE	-	-	-	-	-	-	-	-
Denmark	RegionH	COPUS	07/10/2024	27/12/2024	-	-	-	-	-	-
Norway	NIPH	NEB III	24/10/2023	15/11/2023	05/02/2024	21/02/2024				
Sweden	ULUND/KI/UmU	SAS	-	-	-	-	-	-	-	-
Poland	NIOM	POLAES_PARC	08/02/2024	15/02/2024	01/08/2024	17/02/2025	-	-	-	-
Slovakia	SZU	SK-PARC Teens	07/02/2025	-	-	-	-	-	-	-
Slovenia	JSI / NIJZ	SLO HBM II	29/03/2019 30/11/2022	23/05/2019*	07/09/2023	16/01/2024	27/11/2024	DD/07/2024 ⁸	-	-
Greece	AUTH	HERACLES	04/07/2024	16/07/2024	01/02/2025	01/02/2025	-	-	-	-
Portugal	INSA	ExpoQuim- Teens	15/04/2025	-	-	-	-	-	-	-
Belgium	VITO / PIH	FLEHS 5	26/03/2024	15/04/2024	07/01/2025	07/01/2025	-	-	-	-
Germany	UBA	ALISE	09-10/2024	DD/12/24	-	-	-	-	-	-
France	SpFrance	ALBANE	24/08/2023	18/09/2023	-	-	-	-		

⁸ JSI/NIJZ are obliged to report the results to the national funding body (Ministry of Health) and could not postpone the analysis for this reason, as an exception their participation in G-EQUAS RV72 + RV 73 will be evaluated.

Country	Partner(s)	Study acronym	Ethical dossier submitted	Ethical dossier approved	Recruitment started	Sample collection & interviews started	Sample collection & interviews concluded	Chemical analysis started	Chemical analysis concluded	Data delivered in harmonized format to PEH
ADULTS										
UK	PHE	HBM in HSFE	-	-	-	-	-	-	-	-
Norway	NIPH	NEB III	24/10/2023	15/11/2023	05/02/2024	21/02/2024	-	-	-	-
Lithuania	LSMU	NHALES-LT	23/09/2024	23/02/2025	-	-	-	-	-	-
Latvia	RSU	Gen_HBM_Survey_LV	27/11/2024	03/02/2025	-	-	-	-	-	-
Estonia	UTARTU	SOHOS	23/08/2024	7/10/2024	-	-	-	-	-	-
Iceland	UI	HBM2-IS	29/01/2025; 26/03/2025 ⁹	12/02/2025; 09/04/2025	01/03/2025;09/04/2025	-	-	-	-	-
Ireland	UCD	HBM4IE	-	-	-	-	-	-	-	-
Czech Republic	SZU-CZ (NIPH)	CZ-HBM/AE	20/09/2024	-	-	-	-	-	-	-
Hungary	NPHC	HBM-HU	-	-	-	-	-	-	-	-
Poland	NIOM	POLAES_PARC	08/02/2024	15/02/2024	01/06/2024	01/03/2025				
Portugal	INSA	ExpoQuim2	15/04/2025	-	-	-	-	-	-	-
Spain	EHU/UPV	PARC Euskadi	05/09/2023	02/02/2024	09/02/2024	10/11/2024	-	-	-	-
	EASP	HBM in AHS VI	12/06/2024	25/06/2024	-	-	-	-	-	-
Cyprus	MOH-CY / SGL	everyone_CY	-	-	-	-	-	-	-	-
Italy	ISS	ITINERE	23/04/2024	13/05/2024	-	-	-	-	-	-
Greece	AUTH	HERACLES	04/07/2024	16/07/2024	01/02/2025	01/02/2025	-	-	-	-
Belgium	ISSeP	BMH-Wal-PARC	13/06/2024	05/11/2024	01/12/2024	01/05/2025	-	-	-	-
Germany	UBA	GerES VI	28/02/2023	23/03/2023	22/05/2023	29/05/2023	13/07/2024	24/07/2023	-	-
France	SpFrance	ALBANE	24/08/2023	18/09/2023	-	-	-	-	-	-
Luxembourg	LNS	LëtzhBM	18/01/2024	-	-	-	-	-	-	-

⁹ Due to difficulties in recruitment to research plan was adapted and renewed ethical approval was obtained.

The Netherlands	RIVM	-	-	-	-	-	-	-	-	-
Israel	MOH-IL	IBS II	12/12/2023	30/06/2024	-	-	-	-	-	-

Annex 2: Participants enrolled in the studies by 31/12/2024

Country	Partner(s)	Study acronym	N of participants enrolled to date	N of participants enrolled to date	N of participants enrolled to date
			31/12/2023	31/05/2024	31/12/2024
CHILDREN					
UK	UKHSA	HBM in HSfE	0	0	0
Denmark	RegionH	COPUS	0	0	0
Estonia	UTARTU	SOHOS	0	0	0
Poland	WULS	BIOPOL-CH	0	0	10
Czech Republic	SZU-CZ (NIPH)	CZ-HBM/CE	0	100	200
Hungary	NPHC	HBM-HU I	0	7	158
Spain	ISCIH	ESQUIPI	0	0	0
Portugal	INSA	ExpoQuim-Kids	0	0	0
Greece	AUTH	HERACLES	0	0	0
Slovenia	JSI / NIJZ	SLO HBM II	0	95	150
Cyprus	MOH-CY / SGL	everyone_CY	0	0	0
Germany	UBA	ALISE	0	0	0
France	SpFrance	ALBANE	0	0	0
Austria	EAA	PARC-CSA	0	0	65
Luxembourg	LNS	LëtzhBM	0	0	0
			0	202	583

Country	Partner(s)	Study acronym	N of participants enrolled to	N of participants enrolled to	N of participants enrolled to
			date	date	date
			31/12/2023	31/05/2024	31/12/2024
TEENAGERS					
UK	UKHSA	HBM in HSFE	0	0	0
Denmark	RegionH	COPUS	0	0	0
Norway	NIPH	NEB III	0	73	144
Sweden	ULUND/KI/UmU	SAS	0	0	0
Poland	NIOM	POLAES-PARC	0	0	0
Slovakia	SZU	SK-PARC Teens	/	/	0
Slovenia	JSI / NIJZ	SLO HBM II	0	97	150
Greece	AUTH	HERACLES	0	0	0
Portugal	INSA	ExpoQuim-Teens	0	0	0
Belgium	VITO / PIH	FLEHS-5	0	0	16
Germany	UBA	ALISE	0	0	0
France	SpFrance	ALBANE	0	0	0
			0	170	310

Country	Partner(s)	Study acronym	N of participants enrolled to date	N of participants enrolled to date	N of participants enrolled to date
			31/12/2023	31/05/2024	31/12/2024
ADULTS					
UK	UKHSA	HBM in HSfE	0	0	0
Norway	NIPH	NEB III	0	73	144
Lithuania	LSMU	NHALES-LT	0	0	0
Latvia	RSU	Gen_HBM_Survey_LV	0	0	0
Estonia	University Tartu / Health board	SOHOS	0	0	0
Iceland	UI	HBM2-IS	0	0	0
Ireland	UCD	HBM4IE	/	/	/
Czech Republic	SZU-CZ (NIPH)	CZ-HBM/AE	0	0	0
Hungary	NPHC	HBM-HU I	0	0	0
Poland	NIOM	POLAES-PARC	0	0	0
Portugal	INSA	ExpoQuim2	0	0	0
Spain	EHU/UPV	PARC-Euskadi	0	48	102
	EASP	HBM in AHS VI	0	0	0
Cyprus	MOH-CY / SGL	everyone_CY	0	0	0
Italy	ISS	ITINERE	0	0	0
Greece	AUTH	HERACLES	0	0	0
Belgium	ISSeP	BMH-Wal-PARC	0	0	60
Germany	UBA	GerES VI	150	300	300
France	SpFrance	ALBANE	0	0	0
Luxembourg	LNS	LëtzhBM	0	0	0
The Netherlands	RIVM	?	0	0	0
Israel	MOH-IL	IBS II	0	0	0
			150	421	606

Annex 3: Detailed overview of implementation of effect biomarkers per study

Children					
Country	Institute	Matrix	Sample size	Outcome	Biomarkers
Poland	WULS	UM	300	Renal function	NAG, A1MG, Creatinine, Albumin (albumin to creatinine ratio), Kim-1, RBP4
				Respiratory sensitization	8-OHdG
Greece	AUTH	UM	300	Respiratory sensitization	8-OHdG
Spain	ISCIII	UM	300	Renal function	NAG, A1MG, Creatinine, Albumin (albumin to creatinine ratio), Kim-1, RBP4
				Respiratory sensitization	8-OHdG
Luxembourg	LNS	UM	150	Renal function	NAG, A1MG, Creatinine, Albumin (albumin to creatinine ratio), Kim-1, RBP4
				Respiratory sensitization	8-OHdG
Germany	UBA	UM	300	Renal function	NAG, A1MG, Creatinine, Albumin (albumin to creatinine ratio), Kim-1, RBP4
Slovenia	JSI / NIJZ	UM	150	Renal function	NAG, A1MG, Creatinine, Albumin (albumin to creatinine ratio), Kim-1, RBP4
				Respiratory sensitization	8-OHdG
Hungary	NCPHP	UM	300	Respiratory sensitization	8-OHdG
Cyprus	MOH-CY/SGL	UM	150	Renal function	NAG, A1MG, Creatinine, Albumin (albumin to creatinine ratio), Kim-1, RBP4
				Respiratory sensitization	8-OHdG

UM= first morning urine

Teenagers					
Country	Institute	Matrix	Sample size	Outcome	Biomarkers
Greece	AUTH	SS	300	Cardio-metabolic obesity	FT3, FT4, TSH, T3, T4 TG, Chol, HDL, LDL Kisspeptin
				neuro	BDNF
France	SPF	FS	300	Cardio-metabolic obesity	FT3, FT4, TSH, T3, T4
Poland	NIOM	SS	300	Cardio-metabolic obesity	FT3, FT4, TSH, T3, T4 TG, Chol, HDL, LDL Kisspeptin
				neuro	BDNF
Belgium	VITO/PIH	SS	300	Cardio-metabolic obesity	FT3, FT4, TSH, T3, T4 TG, Chol, HDL, LDL Kisspeptin
				neuro	BDNF
Germany	UBA	SS	300	Cardio-metabolic obesity	FT3, FT4, TSH, T3, T4 TG, Chol, HDL, LDL
Slovenia	JSI / NIJZ	SS	300	Cardio-metabolic obesity	FT3, FT4, TSH, T3, T4 TG, Chol, HDL, LDL Kisspeptin
				neuro	BDNF
Norway	NIPH	SS	200	Cardio-metabolic obesity	FT3, FT4, TSH, T3, T4 TG, Chol, HDL, LDL Kisspeptin

SS = spot serum, FS = fasting serum

Adults					
Country	Institute	Matrix	Sample size	Outcome	Biomarkers
Latvia	RSU	SS	300	Cardio-metabolic obesity	FT3, FT4, TSH, T3, T4 TG, Chol, HDL, LDL Kisspeptin
				neuro	BDNF
		UM		Respiratory sensitization	IgG, IgM, IgE, Interleukins 1, 1B, 6, 8; LTB4, TNF α , IFN- γ 8-OHdG
Greece	AUTH	SS	300	Cardio-metabolic obesity	FT3, FT4, TSH, T3, T4 TG, Chol, HDL, LDL Kisspeptin
				neuro	BDNF
		SS & UM		Respiratory sensitization	IgG, IgM, IgE, Interleukins 6 8-OHdG
Belgium	ISSeP	SS	300	Cardio-metabolic obesity	FT3, FT4, TSH, T3, T4 TG, Chol, HDL, LDL
France	SPF	FS	300	Cardio-metabolic obesity	FT3, FT4, TSH, T3, T4 TG, Chol, HDL, LDL
Hungary	NCPHP	SS	150	Cardio-metabolic obesity	FT3, FT4, TSH, T3, T4
		neuro	BDNF		
Czech Republic	SZU-CZ	SS	200	Cardio-metabolic obesity	FT3, FT4, TSH, T3, T4 TG, Chol, HDL, LDL
Norway	NIPH	SS	200	Cardio-metabolic obesity	FT3, FT4, TSH, T3, T4 TG, Chol, HDL, LDL Kisspeptin
Poland	NIOM	SS	300	Cardio-metabolic obesity	FT3, FT4, TSH, T3, T4 TG, Chol, HDL, LDL
				neuro	BDNF
		SS & UM		Respiratory sensitization	IgG, IgM, IgE, Interleukins 1, 1B, 6, 8; LTB4, TNF α , IFN- γ 8-OHdG
Luxembourg	LNS	SS	150	Cardio-metabolic obesity	FT3, FT4, TSH, T3, T4 TG, Chol, HDL, LDL
				Neuro	BDNF

		SS & UM		Respiratory sensitization	IgG, IgM, IgE, Interleukins 1, 1B, 6, 8; LTB4, TNF α , IFN- γ 8-OHdG
Cyprus	MOH-CY / SGL	SS	150	Cardio-metabolic obesity	FT3, FT4, TSH, T3, T4 TG, Chol, HDL, LDL Kisspeptin
				neuro	BDNF
		SS UM		Respiratory sensitization	IgG, IgM, IgE, Interleukins 1, 1B, 6, 8; LTB4, TNF α , IFN- γ 8-OHdG
Spain (Andalusian HBM)	EASP	SS	150	Cardio-metabolic obesity	FT3, FT4, TSH, T3, T4 TG, Chol, HDL, LDL Kisspeptin
				neuro	BDNF
	SS & UM	Respiratory sensitization		IgG, IgM, IgE, Interleukins 1, 1B, 6, 8; LTB4, TNF α , IFN- γ 8-OHdG	
Lithuania	NHALES-LT	SS	300	Cardio-metabolic obesity	FT3, FT4, TSH TG, Chol, HDL, LDL Kisspeptin
				neuro	BDNF

UM= first morning urine, SS = spot serum, FS = fasting serum; *Interest confirmed but not sure they have the necessary co-fin available.*

Annex 4.1: PARC questionnaire to assess asthma / allergy / eczema in PARC children

This document contains the questions on asthma/rhinitis/allergy to include in the PARC Aligned Studies in **children**. The studies that engage to assess these outcomes, are expected to implement them as similar as possible (and preferably exact) to enable pooling of the children data later on.

It contains the questions to assess asthma/allergy/eczema in the study subjects (based on standardized questionnaire used by the Global Asthma Network Phase I Manual); and important covariates/confounders that will later on be needed for the statistical analyses.

A (draft) codebook accompanies this file, entitled: “Codebook_AsthmaAllergy_Children”.

Questions to assess asthma / allergy / eczema

The questions in this section are obtained from the Global Asthma Network Phase I Manual (http://globalasthmanetwork.org/publications/manual/Global_Asthma_Network_Manual.pdf).

The Global Asthma Network emerged from the success of the International Study of Asthma and Allergies (ISAAC) programme which began in March 1991, whereby pre-existing multinational collaborative projects from Auckland, New Zealand and Bochum, Germany, each investigating variations in childhood asthma at the population level joined to form ISAAC.

The Global Asthma Network (<http://www.globalasthmanetwork.org>) was established in 2012 to identify and address the problem of asthma which is an important Non-Communicable Disease (NCD) globally. The Global Asthma Network evolved from ISAAC and the International Union Against Tuberculosis and Lung Disease (The Union), two organizations dedicated to helping countries identify and address this important NCD for more than two decades, and from the Global Asthma Report 2011.

The questions from the Global Asthma Network Phase I Manual are targeted towards 6/7 year olds.

Notes:

- Please adapt the questions below for your country specifically:

Question 10. After e.g. Please delete the words “puffers (*use local terminology*)” and insert your local terminology for inhalers, prior to printing the questionnaire.

Question 10a. Please insert the name of your local brand of SABAs, LABAs, ICSs and combination ICS and LABA prior to printing the questionnaire.

Question 11. After e.g. Please delete the words “pills (*use local terminology*)” and insert your local terminology for tablets, capsules, liquids or pills, prior to printing the questionnaire

Question 11a. We are only interested in 4 categories of medicines: leukotriene receptor antagonists, β_2 agonist bronchodilator, theophylline and oral corticosteroid. Please delete the words (*Put your local brand name here*) and insert the chemical name, and then in brackets the brand/local name of the tablets, capsules, liquids or other medicines e.g. pills (using your local terminology), prior to printing the questionnaire.

- Some words are **emphasized** (bold and underlined), please take this over in your questionnaire.
- Include the **subheadings**, such as “Questions 1-17 are about this [your] child’s breathing (the child named on this questionnaire)” to make the questionnaire easy to read and to fill out.
- Take over the suggestions to **skip questions** based on the provided answers.
- Take over the **layout** and the **chronological order** of the questions as much as possible.
- The following questions are considered **“optional” for PARC (grey highlight): Question 4, 9, 10a, 10b, 10c, 10d, 11a, 11b, 11c, 11d, 12, 13, 14, 15, 23**. All other questions, including all covariates and confounders, are considered obligatory.

Questions 1-17 are about this [your] child's breathing (the child named on this questionnaire)

1. Has this child ever had wheezing or whistling in the chest **at any time** in the past?

Yes

No

***IF YOU HAVE ANSWERED "NO"
PLEASE SKIP TO QUESTION 7***

2. ***IF YOU ANSWERED "YES"*** – How old was this child when the wheezing or whistling started?

Less than 1 year

1-2

3-4

5-6

More than 6 years

3. Has this child had wheezing or whistling in the chest **in the past 12 months?**

Yes

No

***IF YOU HAVE ANSWERED "NO"
PLEASE SKIP TO QUESTION 7***

4. How many attacks of wheezing has this child had **in the past 12 months?**

None

1 to 3

4 to 12

More than 12

5. **In the past 12 months**, how often, on average, has this child's sleep been disturbed due to wheezing?

Never woken with wheezing

Less than one night per week

One or more nights per week

6. **In the past 12 months**, has wheezing ever been severe enough to limit this child's speech to only one or two words at a time between breaths?

Yes

No

7. Has this child **ever** had asthma?

Yes

No

***IF YOU HAVE ANSWERED "NO"
PLEASE SKIP TO QUESTION 16***

8. Was this child's asthma confirmed by a doctor?

Yes

No

9. Does this child have a written plan which tells you/him/her how to look after his/her asthma?

Yes

No

10. Has this child used any inhaled medicines e.g. puffers (*use local terminology*) to help his/her breathing problems at any time **in the past 12 months?** (when he/she did not have a cold)

Yes

No

***IF YOU HAVE ANSWERED “NO”
PLEASE SKIP TO QUESTION 11***

10a-d. Please indicate how often this child used each of the **inhaled** medicines listed below **in the past 12 months:**

(delete the words below and put your local brand) only when needed / in short courses / every day

Short acting β - agonists (SABA)

Long acting β - agonists (LABA)

Inhaled corticosteroids (ICS)

Combination ICS and LABA

11. Has this child used any tablets, capsules, liquids or other medicines e.g. pills (*use local terminology*) that he/she swallowed to help his/her breathing at any time **in the past 12 months?** (when he/she did not have a cold)

Yes

No

***IF YOU HAVE ANSWERED “NO”
PLEASE SKIP TO QUESTION 12:***

11a-d. Please indicate how often this child used each of the tablets, capsules, liquids or other medicines e.g. pills (*use local terminology*) listed below **in the past 12 months:**

only when needed / in short courses / every day

(Put your local brand name here)

(Put your local brand name here)

(Put your local brand name here)

(Put your local brand name here)

12. **In the past 12 months**, how many times have you **urgently** taken this child to a doctor because of his/her breathing problems?

None 1-3 4-12 more than 12

13. **In the past 12 months**, how many times have you **urgently** taken this child to an Emergency Department, without being admitted to hospital, because of his/her breathing problems?

None 1-3 4-12 more than 12

14. **In the past 12 months** how many times has this child been admitted to hospital because of his/her breathing problems.

None 1 2 more than 2

15. **In the past 12 months**, how many days (or part days) of school has this child missed because of his/her breathing problems?

None 1-3 4-12 more than 12

16. **In the past 12 months**, has this child's chest sounded wheezy during or after exercise?

Yes

No

17. **In the past 12 months**, has this child had a dry cough at night, apart from a cough associated with a cold or chest infection?

Yes

No

Questions 18-25 are about nose problems which occurred when this child did not have a cold or the flu

18. Has this child **ever** had a problem with sneezing, or a runny or blocked nose when he/she DID NOT have a cold or the flu?

Yes

No

***IF YOU HAVE ANSWERED “NO”
PLEASE SKIP TO QUESTION 24***

19. *IF YOU ANSWERED “YES”* - How old was this child when the nose problem started?

Less than 1 year 1-2 3-4 5-6 More than 6 years

20. **In the past 12 months**, has this child had a problem with sneezing, or a runny, or blocked nose when he/she DID NOT have a cold or the flu?

Yes

No

***IF YOU HAVE ANSWERED “NO”
PLEASE SKIP TO QUESTION 24***

21. **In the past 12 months**, has this child’s nose problem been accompanied by an itchy nose?

Yes

No

22. **In the past 12 months**, has this child’s nose problem been accompanied by itchy-watery eyes?

Yes

No

23. **In the past 12 months**, how much did this child's nose problem interfere with his/her daily activities?:

Not at all	<input type="checkbox"/>
A little	<input type="checkbox"/>
A moderate amount	<input type="checkbox"/>
A lot	<input type="checkbox"/>

24. Has this child **ever** had hay fever? (include local names for hay fever such as allergic rhinitis)

Yes	<input type="checkbox"/>
No	<input type="checkbox"/>

***IF YOU HAVE ANSWERED "NO"
PLEASE SKIP TO QUESTION 26***

25. Was this child's hay fever confirmed by a doctor?

Yes	<input type="checkbox"/>
No	<input type="checkbox"/>

Questions 26 – 33 are about this child's skin

26. Has this child **ever** had an itchy rash which was coming and going for at least six months?

Yes	<input type="checkbox"/>
No	<input type="checkbox"/>

***IF YOU HAVE ANSWERED "NO"
PLEASE SKIP TO QUESTION 32***

27. Has this child had this itchy rash at any time **in the past 12 months?**

Yes

No

***IF YOU HAVE ANSWERED “NO”
PLEASE SKIP TO QUESTION 32***

28. Has this child’s itchy rash **at any time** affected any of the following places: the folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears or eyes?

Yes

No

29. At what age did this child’s itchy rash first occur?

Under 2 years

Age 2-4 years

Age 5 or more

30. Has this child’s rash cleared completely at any time **during the past 12 months?**

Yes

No

31. **In the past 12 months**, how often, on average, has this child been kept awake at night by this itchy rash?

Never in the past 12 months

Less than one night per week

One or more nights per week

32. Has this child ever had eczema?

Yes

No

***IF YOU HAVE ANSWERED "NO"
PLEASE SKIP TO QUESTION 34***

33. Was this child's eczema confirmed by a doctor?

Yes

No

Important covariates and confounders

Family history

- Has this child's biological father, mother, or one of this child's biological brothers or sisters ever had asthma?

Yes

No

- Has this child's biological father, mother, or one of this child's biological brothers or sisters ever had allergic rhinitis?

Yes

No

- Has this child's biological father, mother, or one of this child's biological brothers or sisters ever had eczema?

Yes

No

Personal characteristics

Parameters that shall already be collected in the context of the “basic codebook”:

- Age of the data subject in years
- Age of the data subject in months
- ISCED of the household
- Smoking status of the mother during pregnancy (non-smoker during pregnancy / smoker during pregnancy)
- Height + method
- Weight + method

Parameters that shall be collected additionally if not yet in the “basic codebook”:

- Date that the questionnaire was filled (if different from the biological sample collection in which the exposures are assessed)

Annex 4.2: PARC questionnaire to assess asthma / allergy / eczema in PARC teenagers

This document contains the questions on asthma/rhinitis/allergy to include in the PARC Aligned Studies in **teenagers**. The studies that engage to assess these outcomes, are expected to implement them as similar as possible (and preferably exact) to enable pooling of the teenager data later on.

It contains the questions to assess asthma/allergy/eczema in the study subjects (based on standardized questionnaire used by the Global Asthma Network Phase I Manual); and important covariates/confounders that will later on be needed for the statistical analyses.

A (draft) codebook accompanies this file, entitled: “Codebook_AsthmaAllergy_Teenagers”.

Questions to assess asthma / allergy / eczema

The questions in this section are obtained from the Global Asthma Network Phase I Manual (http://globalasthmanetwork.org/publications/manual/Global_Asthma_Network_Manual.pdf).

The Global Asthma Network emerged from the success of the International Study of Asthma and Allergies (ISAAC) programme which began in March 1991, whereby pre-existing multinational collaborative projects from Auckland, New Zealand and Bochum, Germany, each investigating variations in childhood asthma at the population level joined to form ISAAC.

The Global Asthma Network (<http://www.globalasthmanetwork.org>) was established in 2012 to identify and address the problem of asthma which is an important Non-Communicable Disease (NCD) globally. The Global Asthma Network evolved from ISAAC and the International Union Against Tuberculosis and Lung Disease (The Union), two organizations dedicated to helping countries identify and address this important NCD for more than two decades, and from the Global Asthma Report 2011.

The questions from the Global Asthma Network Phase I Manual are targeted towards 13/14 year olds.

Notes:

- **Please adapt the questions below for your country specifically:**

Question 9. After e.g. Please delete the words “puffers (use local terminology)” and insert your local terminology for inhalers, prior to printing the questionnaire.

Question 9a. Please insert the name of your local brand of SABAs, LABAs, ICSs and combination ICS and LABA prior to printing the questionnaire.

Question 10. After e.g. Please delete the words “pills (use local terminology)” and insert your local terminology for tablets, capsules, liquids or pills, prior to printing the questionnaire

Question 10a. We are only interested in 4 categories of medicines: leukotriene receptor antagonists, β_2 agonist bronchodilator, theophylline and oral corticosteroid. Please delete the words (Put your local brand name here) and insert the chemical name, and then in brackets the brand/local name of the tablets, capsules, liquids or other medicines e.g. pills (using your local terminology), prior to printing the questionnaire.

- Some words are **emphasized** (bold and underlined), please take this over in your questionnaire.
- Include the **subheadings**, such as “Questions 1 – 16 are about your breathing” to make the questionnaire easy to read and to fill out.
- Take over the suggestions to **skip questions** based on the provided answers.
- Take over the **layout** and the **chronological order** of the questions as much as possible.
- The following questions are considered **“optional” for PARC (grey highlight): Question 3, 8, 9a, 9b, 9c, 9d, 10a, 10b, 10c, 10d, 11, 12, 13, 14, 21**. All other questions, including all covariates and confounders, are considered obligatory.

Questions 1 – 16 are about your breathing

1. Have you **ever** had wheezing or whistling in the chest at any time in the past?

Yes

No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 6

2. Have you had wheezing or whistling in the chest **in the past 12 months?**

Yes

No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 6

3. How many attacks of wheezing have you had **in the past 12 months?**

None

1 to 3

4 to 12

More than 12

4. **In the past 12 months,** how often, on average, has your sleep been disturbed due to wheezing?

Never woken with wheezing

Less than one night per week

One or more nights per week

5. **In the past 12 months**, has wheezing ever been severe enough to limit your speech to only one or two words at a time between breaths?

Yes

No

6. Have you **ever** had asthma?

Yes

No

*IF YOU HAVE ANSWERED "NO"
PLEASE SKIP TO QUESTION 9*

7. Was asthma confirmed by a doctor?

Yes

No

8. Do you have a written plan which tells you how to look after your asthma?

Yes

No

9. Have you used any inhaled medicines e.g. puffers (*use local terminology*) to help your breathing problems at any time **in the past 12 months**? (when you didn't have a cold)

Yes

No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 10

9a. Please indicate how often you used each of the **inhaled** medicines listed below **in the past 12 months**:

(delete the words below and put your local brand) **only when needed / in short courses / every day**

<i>Short acting β- agonists (SABA)</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Long acting β- agonists (LABA)</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Inhaled corticosteroids (ICS)</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Combination ICS and LABA</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

10. Have you used any tablets, capsules, liquids or other medicines e.g. pills (*use local terminology*) that you swallowed to help your breathing at any time **in the past 12 months**? (when you didn't have a cold)

Yes

No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 11

10a. Please indicate how often you used each of the tablets, capsules, liquids or other medicines e.g. pills (*use local terminology*) listed below **in the past 12 months**:

only when needed / in short courses / every day

<i>(Put your local brand name here)</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>(Put your local brand name here)</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>(Put your local brand name here)</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>(Put your local brand name here)</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

11. **In the past 12 months**, how many times have you **urgently** been to a doctor because of breathing problems?

None	1-3	4-12	more than 12
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

12. **In the past 12 months**, how many times have you **urgently** been to an Emergency Department without being admitted to hospital because of breathing problems?

None 1-3 4-12 more than 12

13. **In the past 12 months** how many times have you been admitted to hospital because of breathing problems?

None 1 2 more than 2

14. **In the past 12 months**, how many days (or part days) of school have you missed because of breathing problems?

None 1-3 4-12 more than 12

15. **In the past 12 months**, has your chest sounded wheezy during or after exercise?

Yes

No

16. **In the past 12 months**, have you had a dry cough at night, apart from a cough associated with a cold or chest infection?

Yes

No

Questions 17-23 are about **nose problems** which occur when you **do not have a cold or the flu**

17. Have you **ever** had a problem with sneezing, or a runny, or blocked nose when you DID NOT have a cold or the flu?

Yes

No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 22

18. **In the past 12 months**, have you had a problem with sneezing, or a runny or blocked nose when you DID NOT have a cold or the flu?

Yes

No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 22

19. **In the past 12 months**, has this nose problem been accompanied by an itchy nose?

Yes

No

20. **In the past 12 months**, has this nose problem been accompanied by itchy-watery eyes?

Yes

No

21. **In the past 12 months**, how much did this nose problem interfere with your daily activities?

Not at all

- A little
- A moderate amount
- A lot

22. Have you **ever** had hay fever? (*include local names for hay fever such as allergic rhinitis*)

- Yes
- No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 24

23. Was your hay fever confirmed by a doctor?

- Yes
- No

Questions 24 – 30 are questions about your skin

24. Have you **ever** had an itchy rash which was coming and going for at least six months?

- Yes
- No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 29

25. Have you had this itchy rash at any time **in the past 12 months?**

- Yes
- No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 29

26. Has this itchy rash **at any time** affected any of the following places: the folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears or eyes?

Yes

No

27. Has this rash cleared completely at any time **during the past 12 months?**

Yes

No

28. **In the past 12 months**, how often, on average, have you been kept awake at night by this itchy rash?

Never in the past 12 months

Less than one night per week

One or more nights per week

29. Have you **ever** had eczema?

Yes

No

30. Was your eczema confirmed by a doctor?

Yes

No

Important covariates and confounders

Family history

- Has your biological father, mother, or one of your biological brothers or sisters ever had asthma?
 Yes
 No
- Has your biological father, mother, or one of your biological brothers or sisters ever had allergic rhinitis?
 Yes
 No
- Has your biological father, mother, or one of your biological brothers or sisters ever had eczema?
 Yes
 No

Personal characteristics

Parameters that shall already be collected in the context of the “basic codebook”:

- Age of the data subject in years
- Age of the data subject in months
- ISCED of the household
- Smoking status of the data subject (past active smoker / current active smoker / never smoker)
- Height + method
- Weight + method

Parameters that shall be collected additionally if not yet in the “basic codebook”:

- Date that the questionnaire was filled (if different from the biological sample collection in which the exposures are assessed)

Annex 4.3: PARC questionnaire to assess asthma / allergy / eczema in PARC adults

This document contains the questions on asthma/rhinitis/allergy to include in the PARC Aligned Studies in **adults**. The studies that engage to assess these outcomes, are expected to implement them as similar as possible (and preferably exact) to enable pooling of the teenager data later on.

It contains the questions to assess asthma/allergy/eczema in the study subjects (based on standardized questionnaire used by the Global Asthma Network Phase I Manual); and important covariates/confounders that will later on be needed for the statistical analyses.

A (draft) codebook accompanies this file, entitled: “Codebook_AsthmaAllergy_Adults”.

Questions to assess asthma / allergy / eczema

The questions in this section are obtained from the Global Asthma Network Phase I Manual (http://globalasthmanetwork.org/publications/manual/Global_Asthma_Network_Manual.pdf).

The Global Asthma Network emerged from the success of the International Study of Asthma and Allergies (ISAAC) programme which began in March 1991, whereby pre-existing multinational collaborative projects from Auckland, New Zealand and Bochum, Germany, each investigating variations in childhood asthma at the population level joined to form ISAAC.

The Global Asthma Network (<http://www.globalasthmanetwork.org>) was established in 2012 to identify and address the problem of asthma which is an important Non-Communicable Disease (NCD) globally. The Global Asthma Network evolved from ISAAC and the International Union Against Tuberculosis and Lung Disease (The Union), two organizations dedicated to helping countries identify and address this important NCD for more than two decades, and from the Global Asthma Report 2011.

The questions from the Global Asthma Network Phase I Manual are targeted towards adults, specific age range is not mentioned.

Notes:

- **Please adapt the questions below for your country specifically:**

Question 14. After e.g. Please delete the words “puffers (*use local terminology*)” and insert your local terminology for inhalers, prior to printing the questionnaire.

Question 14a. Please insert the name of your local brand of SABAs, LABAs, ICSs and combination ICS and LABA prior to printing the questionnaire.

Question 15. After e.g. Please delete the words “pills (*use local terminology*)” and insert your local terminology for tablets, capsules, liquids or pills, prior to printing the questionnaire.

Question 15a. We are only interested in 4 categories of medicines: leukotriene receptor antagonists, β_2 agonist bronchodilator, theophylline and oral corticosteroid. Please delete the words (*Put your local brand name here*) and insert the chemical name, and then in brackets the brand/local name of the tablets, capsules, liquids or other medicines e.g. pills (using your local terminology), prior to printing the questionnaire.

- Some words are **emphasized** (bold and underlined), please take this over in your questionnaire.
- Include the **subheadings**, such as “Questions 1 – 20a are about your breathing” to make the questionnaire easy to read and to fill out.
- Take over the suggestions to **skip questions** based on the provided answers.
- Take over the **layout** and the **chronological order** of the questions as much as possible.
- The following questions are considered **“optional” for PARC (grey highlight): Question 3, 11, 14a, 14b, 14c, 14d, 15a, 15b, 15c, 15d, 16, 17, 18, 19**. All other questions, including all covariates and confounders, are considered obligatory.

Questions 1-20a are about your breathing

1. Do you ever have trouble with your breathing? (Tick one box only)

- never
- only rarely
- repeatedly, but it always gets completely better
- continuously, so that your breathing is never quite right

2. Have you had wheezing or whistling in your chest at any time **in the past 12 months?**

- Yes
- No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 9

3. How many attacks of wheezing have you had **in the past 12 months?**

- None
- 1-3
- 4-12
- more than 12

4. **In the past 12 months,** how often, on average, has your sleep been disturbed due to wheezing?

- Never woken with wheezing
- Less than one night per week
- One or more nights per week

5. Have you ever been breathless when the wheezing noise was present?

Yes

No

6. **In the past 12 months**, how often, on average, has your sleep been disturbed due to shortness of breath?

Never

Less than one night per week

One or more nights per week

7. **In the past 12 months**, how often, on average, has your sleep been disturbed due to coughing?

Never

Less than one night per week

One or more nights per week

8. **In the past 12 months**, has wheezing ever been severe enough to limit your speech to only one or two words at a time between breaths?

Yes

No

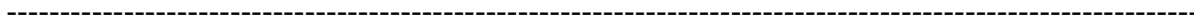


9. Have you ever had asthma?

Yes

No

IF YOU HAVE ANSWERED “NO” PLEASE SKIP TO QUESTION 20



10. Was your asthma confirmed by a doctor?

Yes

No

11. Do you have a written plan which tells you how to look after your asthma?

Yes

No

12. How old were you when you had your first attack of asthma?

Years

13. Have you had an attack of asthma **in the past 12 months?**

Yes

No

14. Have you used any inhaled medicines e.g. puffers (*use local terminology*) to help your breathing at any time **in the past 12 months?** (when you did not have a cold)

Yes

No

IF YOU HAVE ANSWERED “NO” PLEASE SKIP TO QUESTION 15

14a. Please indicate how often you used each of the **inhaled** medicines listed below **in the past 12 months:**

(delete the words below and put your local brand) **only when needed / in short courses / every day**

<i>Short acting β- agonists (SABA)</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Long acting β- agonists (LABA)</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Inhaled corticosteroids (ICS)</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Combination ICS and LABA</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

15. Have you used any tablets, capsules, liquids or other medicines e.g. pills (*use local terminology*) that you swallowed to help your breathing at any time **in the past 12 months**? (when you didn't have a cold)

Yes

No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 16

15a. Please indicate how often you used each of the tablets, capsules, liquids or other medicines e.g. pills (*use local terminology*) listed below **in the past 12 months**:

	only when needed / in short courses / every day		
(Put your local brand name here)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
(Put your local brand name here)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
(Put your local brand name here)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
(Put your local brand name here)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

16. **In the past 12 months**, how many times have you **urgently** been to a doctor because of your breathing problems?

None	1-3	4-12	more than 12
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

17. **In the past 12 months**, how many times have you **urgently** been to an Emergency Department without being admitted to hospital because of breathing problems?

None	1-3	4-12	more than 12
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

18. **In the past 12 months** how many times have you been admitted to hospital because of your breathing problems?

None	1	2	more than 2
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

19. **In the past 12 months**, how many days was your usual activity (at work or in the home) limited because you had breathing problems?

None	1-3	4-12	more than 12
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

20. Have you ever worked in any job that caused wheezing or whistling in your chest?

Yes

No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 21

If yes:

20a. Have you had to leave any of these jobs because they affected your breathing?

No

Yes

Questions 21-22 are about nose problems which occur when you do not have a cold or the flu

21. Have you ever had hay fever?

Yes

No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 23

22. Was your hay fever confirmed by a doctor?

Yes
No

Questions 23-24 are questions about your skin

23. Have you ever had eczema?

Yes
No

***IF YOU HAVE ANSWERED "NO"
PLEASE SKIP TO QUESTION 25***

24. Was your eczema confirmed by a doctor?

Yes
No

Important covariates and confounders

Family history

- Has your biological father, mother, or one of your biological brothers or sisters ever had asthma?
Yes
No
- Has your biological father, mother, or one of your biological brothers or sisters ever had allergic rhinitis?
Yes
No
- Has your biological father, mother, or one of your biological brothers or sisters ever had eczema?
Yes
No

Personal characteristics

Parameters that shall already be collected in the context of the “basic codebook”:

- Age of the data subject in years
- ISCED of the household
- Smoking status of the data subject (past active smoker / current active smoker / never smoker)
- Height + method
- Weight + method

Parameters that shall be collected additionally if not yet in the “basic codebook”:

- Date that the questionnaire was filled (if different from the biological sample collection in which the exposures are assessed)

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