HBM4EU science and policy for a healthy future

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Annex 2.2.1 to D7.3

SOP 1:

Selection of Participants and Recruitment

WP 7

Task 7.2

D 7.3

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1 Introduction

This guideline is intended to be used in the framework of HBM4EU. HBM4EU aims at establishing a European human biomonitoring platform and filling knowledge gaps in representative exposure data. HBM4EU supports the countries with several documents heading for a harmonisation of study conduct to facilitate generating European reference values. This SOP, together with other documents, is part of the Deliverable 7.3 on study design focussing on recruitment, fieldwork and sampling. Deliverables focussing on other parts of study conduct like ethics, analytics and data management provided by other work packages complement D7.3 for a proper study conduct in the frame of HBM4EU.

Presented here is a guideline or template for a SOP on Selection of Participants and recruitment which will have to be elaborated in each country describing the actual situation and planning in the country.

This template has been created with the premise in mind that every participating country is obliged to try best as possible to follow the HBM4EU documents to achieve comparable data in a (as much as possible) harmonised way. Deliverable 7.3 and its Study Protocol provide additional input on the selected items described below.

2 Study design and participants

This part provides an overview of the general study design and the plans for the participants to be involved. It serves to introduce and explain what is planned to be done in short, precise paragraphs. Below, the topics necessary to be addressed and to be filled with content are listed in bullet point form.

Depending on target population and sampling frame, the methods best suited for obtaining a representative sample can vary.

Describe here:

- The target population (age, gender): The sampling domains for which at least specified reliability is desired in Europe are gender and age groups. The seven age groups that are targeted within the HBM4EU surveys are: 0-2y, 3-5y, 6-11y, 12-19y, 20-39y, 40-59y, 60-79y.
- The sampling frame derived from the target population according to the Concept for a Study Protocol (Deliverable 7.3 Annex 1): The way of recruiting the participants (via schools, work, registries) is not prescribed within HBM4EU. However, a good sampling frame model for selection of individuals is the stratified clustered multi-stage design. Using this design, geographical areas (stratification) are selected within a country. Within each of the geographical areas, primary sampling units (PSU: schools, work registries, general practitioners) are selected randomly, however that can be done in a way that there is an increased selection chance proportional to the number of individuals in these PSU. Furthermore, individuals are selected randomly within the PSU.
- The number of participants required for a (representative) sample size. Keep in mind to refer to the selection of sampling locations here (see Chapter 4): In each participating country, and for each of the selected age groups, 150 male and 150 female participants recruited from the general population (i.e. non-hospitalized individuals) are included. The sample size was chosen to ensure also inclusion of participants from different socio-economic strata and from different community sizes (urban, suburban, rural). To include different socio-economic classes, education level can be used as a proxy (International Standard Classification of Education (ISCED), which includes 9 levels of education (ISCED 2011, see task 7.2 report). The sample size is indicative and may need further adjustment for the specific chemical group because of expected population variability of the biomarker.
- What measures are taken to deal with unknown response rates (e.g. assumption of response rate and calculation of extra samples to be taken to make up for this): One must anticipate a response rate of around 30%, meaning that the sample frame must have a size which is at least 3 times as large as the targeted sample size needed.
- Consider a backup solution in case your primary sampling frame is not applicable in a country (e.g. switch from register to school approach)

3 Selection of sampling locations

Description of number and kind (densely, intermediate and thinly populated areas) of sampling locations being selected for the study.

In case one wants to obtain a representative sample in each country, different approaches could be followed depending on the size of the country and the previous experience in national HBM studies. Within a country, sampling could be done in national geographical entities (e.g. provinces, communities, municipalities) with selection probability of these entities proportional to population size. Another approach could be random selection from population registers. Within HBM4EU no prescriptions are set.

After selection of the participants, they will be categorized into three degrees of urbanisation (DEGURBA) http://ec.europa.eu/regional_policy/sources/docgener/work/2014_01_new_urban.pdf). Within this classification system, three types of areas have been identified: densely, intermediate and thinly populated areas. They are defined using a criterion of geographical contiguity in combination with a minimum population threshold based on population grid square cells of 1 km^2. Based on these grid cells, three urbanization types are defined:

Densely populated area (**cities)**: at least 50% living in high-density clusters (alternative name: urban centre);

Intermediate density area (**towns and suburbs**): less than 50% of the population living in rural grid cells, and less than 50 % living in a high-density cluster;

Thinly populated area (**rural area**): more than 50% of the population living in rural grid cells.

With: rural grid cells = grid cells outside urban clusters; urban clusters = clusters of contiguous grid cells of 1 km^2 with a density of at least 300 inhabitants per km^2 and a minimum population of 5000; high-density cluster = contiguous grid cells of 1 km^2 with a density of at least 1500 inhabitants per km^2 and a minimum population of 50000.

4 Selection of participants and their recruitment

Inclusion and exclusion criteria need to be elaborated and translated into a practical approach. Exclusion criteria, for example, can be related to age, sex, duration of living at the sampling location (e.g. less than 5 years), being in hospital, being homeless, suffering from special diseases, etc.

In brief for HBM4EU: inhabitants from ‘densely’, ‘intermediate’ and ‘thinly populated’ areas are accepted (see Chapter 4). Hot spot areas, with known historical/actual environmental contamination need to be excluded. No further inclusion and exclusion criteria are set. However, following minimal information needs to be collected (in the questionnaire), to have an indication of the population included:

- Life style: information on smoking and alcohol/drugs use, diet, housing conditions, hobbies and occupational exposure
- Socio-economic status needs to be documented (using ISCED education levels)
- Residential history: number of years living in the country
- Geographical coverage: densely, intermediate and thinly populated areas
- Sampling time period needs to be reported (no seasonal restrictions are set).

Correct selection of participants with regard to their age is essential. Depending on sampling frame, a selection using age on a key date is not feasible or too difficult (e.g. in schools). It is therefore recommended to use the year of birth as selection criterion.

Just for an overview some popular methods to select participants of different age groups are presented in the following as options depending on the target population. Table 1 provides an overview on the sampling frames feasible for a specific target population, the partner to contact and the recruitment methods to use.

Table 1: Overview on sampling frames, specific target population, contact partner and recruitment methods

Target population (results will be extrapolated for…)	**Sampling frame** (to select from the list of...)	**Contact partner for participant recruitment** (providers of participant addresses)	**Recruitment methods** (individuals are contacted through…)
General population (or separated according to gender/age)	Population register (country, regional)	Registration offices	1. letter 2. letter, email, text message, telephone, internet, personal visit
	Telephone directory (if a valuable source)	Telephone lists (Internet, organisations)	1. telephone 2. See above
Vulnerable population (pregnant, newborns, seniors etc.)	Patient files	GP, Paediatrician, Gynaecologist, Midwife, Hospital/Clinic, Health Centre, Maternity hospital	1. letter, email, telephone, personal visit, information event, 2. See general pop.
Children, adolescents (different age groups)	Kindergartens, kindergarten groups /day care centres, day care centre groups	Kindergarten / daycare centre	1. letter to principal, letter to parents, personal visit, information event for parents 2. See general pop.
	Schools, school classes/Vocational schools, vocational school classes	School/ Vocational school	
Specific occupational population	Employment records, branch organisations	workplace	1. letter to employer, letter to employee, information event 2. See general pop-

The first contact is mainly to the organisation providing the address of the participant. For this purpose, a written document is recommended. The second contact is directed to the participant itself, which is preferable also done by letter but telephone or direct face-to-face information are sometimes possible, too.

The country specific SOP should describe here in detail how the participants will be selected.

Examples for some commonly used sampling frames are given in the following.

4.1 Population register

When choosing e.g. regions or towns as sampling locations, a population register, be it regional or country-wide, can be immensely helpful to allow for a random sampling at the location(s). Population registers usually can provide addresses of individuals, separated by age and/or gender. Therefore, population registers as a method to select participants can be used for adults and mostly for children as well.

They can usually be accessed through registration offices contacted by an official letter. In this letter, the population register is asked to select a set amount of individuals (including a surplus to deal with a minimum assumed response rate of 30%) according to strict procedures elaborated to them.

The letter also includes inclusion and exclusion criteria and an information leaflet on the study.

The random selection of subjects via population registries, stratified by age group and sex is shown in Table 2.

Table 2: Procedure for random selection of 35 subjects via population registries

	Procedure	Note
1	Definition of age groups	Exact definition of age groups according to year of birth (year x - x)
2	List for each age group	Creation of a random list of all subjects of the age group and placement of an at least 8-digit random number to each child
3	Sorting each list	Sort the numbers in ascending order according to the digit number
4	Selection of subjects	Selection of the first 35 subjects in the list per age group
5	List of subjects selected	First name/s Last name Street Street number Postal code Date of birth Sex Nationality Random number Legal representative

If the described procedure is not possible to conduct for the specific registration office or fees taken by the register are unreasonable high, the population registry contact person should be asked to send the list of addresses of all people included in the age group to the study office. The study office will then take care of the randomization according to the procedure described in Table 2.

In case the number of participants in the target group is not sufficient, another population registry of a similar neighbour district has to be contacted, the lists of target groups have to be combined and the procedure described above has to be conducted with that list.

In order to minimize quality-neutral drop outs (e.g. potential participants move away or are hospitalized) the selection should take place close to the start of the actual fieldwork.

The result of this selection process should be to have a list of a set amount (including a surplus to deal with unknown response rates) of potential participants in the chosen age group, stratified by sex.

4.2 Schools (or kindergartens)

If school children have been chosen as the target population, schools are a viable option for participant recruitment. In case population registers are not feasible, schools or the respective school authority can be contacted to request recruitment of pupils. Areas for schools that fit into the sampling location scheme (e.g. ‘densely’ or ‘intermediate’) should be selected. It is essential that this selection does not favour specific socio-economic (SES) backgrounds (e.g. different school types like private and governmental schools) as this could lead to social bias which should be avoided. The population should ideally be mixed with regard to socio-economic structure in the chosen areas.

A first step is to settle which institutions are required to give permission before pupils can be contacted. Such institutions could be a ministry or agency, a superintendent of the district or others.

Once the responsible authority is contacted, they can be asked to help create a list of all schools in the selected areas.

Sufficient schools (depending on the number of intended participants) are selected at random. Preferable are those schools that are attended by pupils with different socio-economic background.

When a school has been selected according to these criteria, the principal has to be asked for his or her permission and to support the study and the selection of the classes.

As the principal is in direct contact with the teachers who in turn are in direct contact with potential participants, it is of the essence from here on out to explain the survey and garner interest in it with the involved persons. After consultation of the principal, it is therefore helpful to hold a meeting with the teachers of the eligible classes and representatives of the survey office.

The survey should be introduced to the teachers and the tasks of pupils (and their parents) addressed in detail. Information leaflets shall be handed out for distribution.

Following this meeting, the teachers will soon after explain the survey in class and hand out the information material to the pupils. The teacher has to be instructed if all pupils of the class shall get an invitation or only those born in a selected year. The information material can already include reply cards to be returned within the next two to three days, or an information evening for the parents can be arranged to hand over the reply cards. For motivation, the teachers should be informed that, regardless of their participation, every pupil who brings back the reply card is foreseen to receive a small incentive (e.g. pen, keychain, etc.) from the teacher who collects all reply cards (hidden in envelopes).

The filled out reply cards are then either sent collectively to the survey office by the teacher, or the field staff will pick them up (e.g. directly at the information evening).

An alternative route to select participants from schools requires specific prerequisites in the country. If it is possible to obtain from the school secretariat the list of addresses of the pupils in the selected school(s), the information material and reply cards can be sent directly to the parents of the eligible children. This avoids relying on the support of the school principal and teachers for study participation.

In any way, the result of the selection should be a plethora of positive reply cards collected in the school(s). The next step is then to contact the families to fix an appointment for the involvement in the study with e.g. a home visit and answering questionnaires and providing samples.

4.3 Maternity hospitals

If vulnerable group(s) such as pregnant women or women with a newborn child are to be selected, it is possible to do so via maternity care clinics. Maternity care clinics are generally selected from the list available in a country. As a starting point, the responsible of the selected maternity hospital is contacted via phone. More information on the study is sent after via a letter addressed to the maternity authority, the gynaecologists and the head of the midwives. The maternity authorities will need to discuss participation in their board meeting, and an additional local ethical approval may be needed. Sometimes maternities ask the HBM fieldwork coordinator to introduce the study in front of the maternity board or local maternity ethical committee.

At least, the HBM fieldwork coordinator will visit the maternity care clinic to practically explain the study sampling protocol, sampling materials, and informed consent for study participation to the maternity care clinic personal in charge of the sample collection and recruitment. Within the maternity, the tasks on recruitment are divided, as it suits them best. As principal practical local contact point functions mostly the head midwife or a selected responsible midwife of the hospital.

They need to be very well informed about all sampling details, sample storage conditions, and the study informed consent, so that they are able to further instruct the other midwifes. It is of importance that all midwifes are familiar with the protocols and sampling procedures, as deliveries happen during different work shifts. Alternatively, for practical reasons, the clinic may organize themselves, so that, only some part of the days (i.e. by part of the midwives), samples are collected.

The women will be asked for participation the day of delivery, upon arrival in the clinic, by the midwife on duty at that moment. She/he collects the signed informed consents and (e.g. cord blood) samples. The samples may be potentially immediately further processed by the midwife or sent internally to the internal maternity clinical lab. In the latter case, the field workers need to give clear instructions, possibly training, and written protocols to the lab personnel.

Within the first days after delivery, further contact with the mothers (that have given their written informed consent) is taken up by the fieldworkers of the study. They visit the mothers within the maternity, or alternatively (in case the mother has returned home), the fieldworker will contact her via phone or email, to collect the filled out questionnaire, and provide any further information needed.