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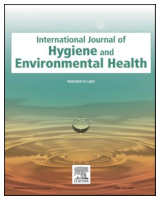

What is required to combine human biomonitoring and health surveys?

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ABSTRACT

Obtaining holistic information about health and health determinants at the population level should also include data on environmental risk factors of health. So far, only a few countries have combined, at the national level, health and human biomonitoring (HBM) surveys to collect extensive information on health, lifestyles, biological health determinants and environmental exposures. This paper will provide guidelines on how to combine health and HBM surveys and what is the added value of doing so. Health and HBM surveys utilize similar infrastructure and data collection methods including questionnaires, collection and analysis of biological samples, and objective health measurements. There are many overlapping or comparable steps in these two survey types. At the European level, detailed protocols for conducting a health examination survey or HBM study exists separately but there is no protocol for a combined survey available by now. Our recommendations for combined health and HBM surveys focus on a cross-sectional survey on general population aged 6–79 years. To avoid unnecessary participant burden, for the selection of included measurements basic principle would be to ensure that results of the measurements have a public health relevance and clear interpretation. Combining health and HBM surveys into one survey would produce an extensive database for research to support policy decisions in many fields such as public health and chemical regulations. Combined surveys are cost-effective as only one infrastructure is needed to collect information and recruit participants.

1. Introduction

Epidemiological studies are a well-established scientific tool to obtain information about health and health determinants of a population and population sub-groups. Randomized control trials (RCTs), cohort and case-control studies, and systematic reviews, are the most appropriate study designs for aetiological research in clinical medicine, public health including environmental health, and health policy. However, other study designs can be also considered. Cross-sectional studies provide a snapshot of the situation of the target population at a given time. Although, they do not allow causal inference to be drawn between environmental exposure and health effects, they can provide indications of possible associations (Levin, 2006). Population-based surveys are a type of observational studies that provide descriptive information about the population (Kumar Yadav et al., 2019) and can be used for evidence-informed decision making.

Cross-sectional studies can be transferred to cohort or longitudinal studies, if study participants are followed-up either through linkage to administrative registers such as hospitalizations and mortality or repeated survey measurements or questionnaires are conducted. This

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would allow for more in dept analysis of associations between observed risk factors and lifestyles and their health effects. For causal inference, the gold standard has been RCTs. From observational studies such as cross-sectional surveys with follow-up and longitudinal studies, a quasi-experimental research design based on observational data can be set up to draw causal inference (Nichols, 2007; Shadish et al., 2002). The choice between different study designs depends on feasibility aspects related to time, and technical and financial resources which are context specific.

Dahlgren and Whitehead (2007) have outlined a holistic perspective for the social determinants of health. These determinants include individual level lifestyle factors, social and community networks, and socio-economic, cultural, and environmental conditions (e.g., traffic related air pollution, occupational or residential chemical exposures, living near an industrially contaminated site). Within this perspective, health surveys are often used to collect information about individual level lifestyle factors and socio-economic status as well as about health status and biological risk factors such as obesity, hypertension, and diabetes. However, due to the focus on health-related aspects, health surveys might not automatically be feasible to reveal all the diverse and complex details of human exposure. In connection with the increased environmental awareness over the past decade, in parallel to existing health surveys, human biomonitoring (HBM) studies have been established as an important tool for investigating human exposure to chemicals and for quantifying body burden (internal dose). Compared to health surveys, HBM studies are specifically designed to investigate all relevant aspects of human exposure and hence more specific data on exposure relevant aspects are recorded to uncover exposure routes and adverse outcome pathways (Human biomonitoring: facts and figures, 2015; Sexton et al., 2004).

For the collection of information, questionnaires are commonly used in survey research. At first inspection, these questionnaires may differ between health surveys and HBM studies. Health surveys, often also called health interview surveys (HIS), use questionnaires to collect information on lifestyles including smoking habits and diet, diagnosed diseases, and use of medications and health care services. At the European Union (EU) level, the European Health Interview Survey (EHIS) is mandatory health interview survey for the EU Member States defining data collection periods, sample size and questionnaire items (European Commission, 2018). More extensive health surveys called health examination surveys (HES), also include health measurements such as anthropometric measurements (e.g. heigh and weight) and blood pressure, and collection of biological samples to obtain more objective information about health and its determinants (European Health Examination Survey, 2021).

HBM studies, on the other side, use questionnaires to obtain more detailed information about exposure-related behaviours such as living conditions and area, food consumption, occupational exposure, and lifestyles. In addition, HBM studies collect biological samples (e.g. whole blood, plasma and urine) for the analysis of health and/or environment-related chemicals and/or their metabolites.

Health surveys and HBM studies both use a survey methodology including questionnaires and collection of biological samples on general population or population sub-groups and the required infrastructure to operate are similar. Since both study types are also investigating the determinants of health, one would expect that combining health surveys and HBM studies would have added value for health and exposure monitoring, research, and policymaking.

Until now, only few countries such as Germany (Kolossa-Gehring et al., 2007), France (Balicco et al., 2017), Israel (Berman et al., 2017), the USA (Centers for Disease Control and Prevention (CDC), 2021), and Canada (St-Amand et al., 2014) have successfully combined their national health survey and HBM study. All three European examples (Germany, France and Israel) have been focused on the general population, but age groups covered by them have varied as well as included health measurements and analysed environmental biomarkers. This makes the comparison of the results between these studies possible for only a limited number of common outcomes and age groups (Tolonen et al., 2018). In many European countries, only a small-scale, research driven studies combining health measurements and HBM analysis have been conducted or samples collected in health surveys have been used to investigate selected environmental biomarkers (Tolonen et al., 2021). Comparability of these small-scale studies is difficult due to differences in used study protocols. Especially when biobanked samples from health surveys are used for analysis of environmental biomarkers, we may be lacking relevant supporting information on exposures, living and working conditions, and lifestyles.

The most common reasons why in Europe health surveys and HBM studies are rarely combined were investigated within the European Human Biomonitoring Initiative (HBM4EU) (HBM4EU, 2021; Ganzleben et al., 2017). It turned out that in addition to the lack of or difficulty to secure funding, there is a lack of knowledge and capacities for sample handling and analysis, difficulties in managing large and diverse data from combined studies which possibly include several study visits, and a lack of flexibility between health and HBM part of the combined survey (Tolonen et al., 2018).

To tackle the reported lack of knowledge on conducting a combined health and HBM survey, this paper aims to provide a general guideline on how to proceed. An overview of the different phases of the organization of a cross-sectional survey will be provided with a special focus on steps where needs and/or approaches between health and HBM surveys may differ. Until now, at the European level guidelines and recommendations for health and HBM surveys exist separately, and guidelines for combined studies are not available so far. For international comparison, protocols from the National Health and Nutrition Examination Survey (NHANES) from the USA (National Center for Health StaticsNHANES, 2019–2020) and Canadian Health Measures Survey (NHMS) (Statistics Canada, 2019, 2020), which have a well-established biomonitoring module included to the national health examination survey, are available. These may not be directly applicable for European situation due to cultural and societal differences.

2. Material and methods

This overview and guidelines were prepared in the framework of the HBM4EU. HBM4EU is a joint effort of 30 countries, the European Environment Agency, and the European Commission, co-funded under Horizon 2020. HBM4EU generates evidence of the actual exposure of citizens to chemicals and the possible health effects to support policy-making (HBM4EU, 2021; Ganzleben et al., 2017).

The guidelines for combining cross-sectional health surveys and HBM studies presented here are based on existing European level recommendations and standardized operating procedures (SOPs) for both health surveys and HBM studies.

Standardized procedures for health examination surveys with the main focus being on cardiovascular disease epidemiology, have been available at the international level since 1968 (Rose and Blackburn, 1968) and have been updated several times over the years (Luepker et al., 1066; Rose et al., 1982). The World Health Organization (WHO) has also set up the 'STEPwise Approach to non-communicable disease (NCD) Risk Factor Surveillance (STEPS)', which provides detailed guidelines for conducting a health survey (World Health Organization, 2021). For health surveys, we have used both EHIS methodological guidelines (European Health Interview Survey (EHIS wave 3), 2018) and European Health Examination Survey (EHES) guidelines (Tolonen, 2013, 2016). EHES guidelines are in line with WHO STEPS guidelines.

For HBM studies, we have used guidelines and SOPs prepared under the HBM4EU initiative (Fiddicke et al., 2021; Esteban Lopez et al., 2021; Vorkamp et al., 2021; Santonen et al., 2019). The HBM4EU online library (HBM4EU Online library. 2021) includes SOPs for study design, recruitment of participants, collection and handling of biological samples, and chemical analysis and quality assurance. Also, guidelines

developed in COPHES and DEMOCOPHES projects (Becker et al., 2014; Fiddicke et al., 2015; Schindler et al., 2014; Exley et al., 2015) have been reviewed for these recommendations.

The following recommendations and guidelines for combined health survey and HBM study are focused on a general population survey. With some modifications, these recommendations and guidelines can also be used for targeted studies, where the focus will be on a specific population group, chemical or health outcome. For targeted studies, the definition of target group, and included chemical analysis and health measurements needs to be adjusted based on the study aims.

3. Results

The survey process can be divided into different phases (Fig. 1): 1) Design; 2) Planning and preparation; 3) Pre-testing and piloting; 4) Final survey design, planning and preparation; 5) Fieldwork and data collection; and 6) Data file construction, analysis and reporting. Quality control measures go across all the phases. In surveys from the domains of health and HBM, later referred to as health module and HBM module, many of these phases are identical or similar and only in some phases, domain specific features need to be considered. These guidelines will focus only on the phases where requirements for health and HBM module may deviate and decisions between them need to be made.

Since both survey types follow a general epidemiological approach, for combined health and HBM survey, several general requirements are applicable. However, differences in needs between the two modules also exist. Therefore, during the design phase, and planning and preparation of the fieldwork, analysis of specific requirement of the different needs with respective decisions should be made. The key differences in existing standardized protocols and guidelines for health and HBM surveys, that require decisions when two modules are combined, are described below.

3.1. Scope, objectives, and design of the study

The first task in the elaboration of any survey protocol is to define its specific scope and objectives. Pertaining to a combined health and HBM survey to provide a coherent scope and clear objectives covering the needs of both modules, is very important for subsequent implementation steps.

For decision-making on the study design of a combined health and HBM survey, the following questions should be considered:

- Is there an existing health survey into which an HBM module can be included or vice versa? Or is there any other type of cross-sectional study such as a nutritional survey into which both HES and HBM can be added? Or are you planning a completely new combined health and HBM survey?

As part of the study design, it is required to decide if all the survey components should be conducted during one study visit or will participation in the survey require several visits. For example, health module components may be conducted at first and as an add-on to this, participants are asked to attend the second examination visit/home visit for the HBM module within the coming weeks.

3.2. Population sample selection and sample size

To combine two study types, target population and selected sample should serve the needs for both health and HBM modules. The main questions are: What is the target population? What is the required sample size (i.e. number of invited persons)? What sampling frame (i.e. a list of all individuals from the target population) should be used? How should the sample be drawn? What is the minimum required participation rate?

At the European level, recommendations for health examination surveys focus on the adult population. Children and adolescents are equally important but their inclusion in health surveys would require some additional considerations, e.g. legal and ethical issues, use of specific equipment for measurement of children and age group specific health measurements. Therefore, the EHES recommendations, are focused on adults only. From a health survey perspective, also the elderly without an upper age limit would be of interest to be able to capture the impact of functional limitations and morbidity for disease burden and health care needs of the population. In contrast, the inclusion of children and adolescents is of great interest for HBM research since many chemicals might interfere with developing organisms. For this reason, it is recommended to focus on age group 0–70 years, but if

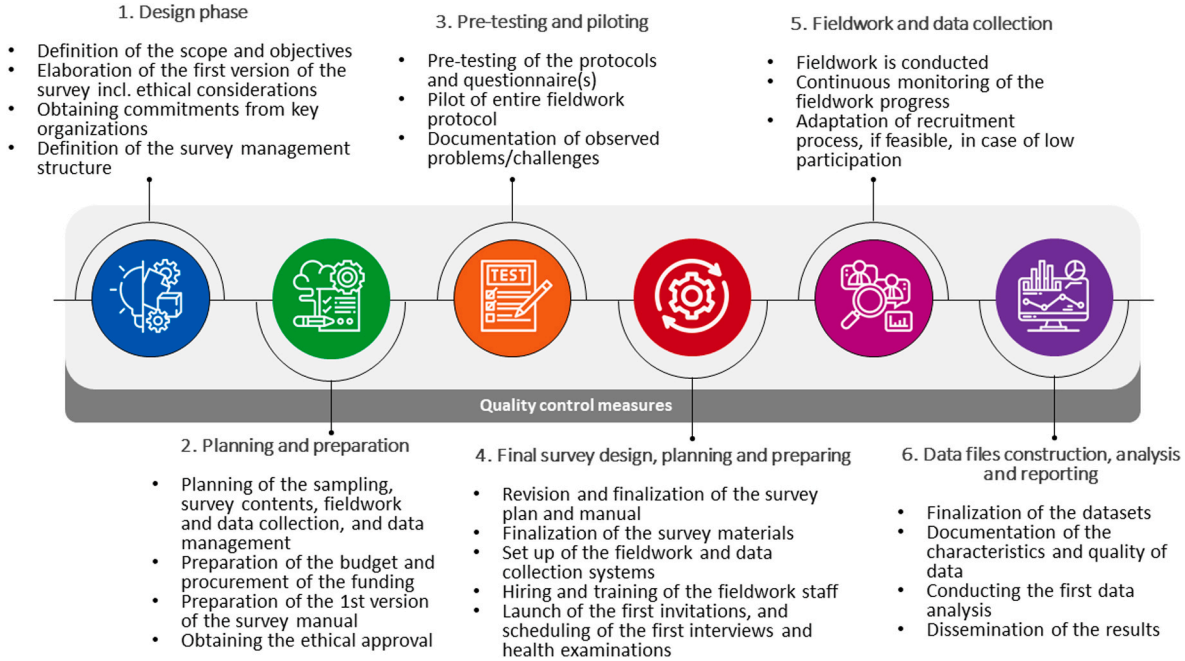

Fig. 1. Different phases of the survey process.

including small children is difficult, at least ages 6–79 years should be covered with a combined health and HBM survey.

All population groups, including institutionalized persons, are of interest and none of them should be excluded even though they would be difficult to recruit/examine. For more targeted studies of specific population sub-groups, people with specific profiles may need to be excluded.

National health surveys require a large sample size (number of persons invited). For example, based on a power calculation done within EHES, when the target group is the population aged 25–64 years and the interest is to estimate outcomes by 10-year age group, sex and educational level, the required sample size is 4000 persons, 500 persons per 10-year age group-sex domain. If results are to be presented also regionally, sample size needs to be increased to allow large enough sample for each region to ensure representativeness of the results. A survey statistician should always be consulted to ensure a large enough sample size based on power calculations and expected participation rate. (Tolonen, 2013). It may not always be feasible to conduct a HBM module on an entire sample of 4000 persons. However, since a smaller sample could be sufficient for HBM research questions, the HBM module could be conducted in a sub-sample. This sub-sample should include at least 500 randomly selected persons (expecting that at least 300 participate) in the age group(s) relevant for the substances of interest to ensure required representativeness. In this case, the sub-sample for the HBM module should be selected from the full sample of 4000 persons selected for the health module, not only among participants, to avoid double selection bias for the results.

The best available sampling frame, ideally a population register, should be used to ensure good coverage of the target population. In case a population register is not available or cannot be used for survey sampling, other available sampling frames which are frequently updated and include sufficient contact information for individuals can be used.

Two-stage sampling supports the logistics and fieldwork organization and ensures that both rural and urban areas will be coved with selected sample by large enough samples to allow inference by area.

Each study should aim for as high a participation rate as possible, ideally at least 60%, although participation rates this high are not common in Europe any longer (Tolonen, 2013; Mindell et al., 2015). For representativeness, it is better to target available resources to the recruitment activities rather than increasing sample size, as survey participation is often selective for socio-demographic factors as well as for health status and lifestyles (Karvanen et al., 2016; Christensen et al., 2015; Knapstad et al., 2016; Tolonen et al., 2010).

3.3. Survey content

Combined health and HBM surveys have three main data collection tools: questionnaire(s), collection and analysis of biological samples, and objective health measurements. Questionnaires and collection of biological samples are used for both health and HBM modules, while objective health measurements are more relevant for the health module.

3.3.1. Questionnaires

While questionnaire items in both health surveys and HBM studies overlap in many aspects, there are still certain differences, and some topics may be asked from a different perspective. HBM module requires specific questions related to the exposure to the substance(s) of interest as well as from occupational activities, household environment, and domestic exposures which are usually not included in health surveys. On the other hand, the health module usually requires more detailed information about health, health determinants including lifestyle and health behaviour information, and use of medication and access to health care services.

When preparing a questionnaire for the combined health and HBM survey, a balance between the needs of both domains should be found, keeping at least the key questions for both domains. The main questionnaire, which is provided for all participants, should include at least socio-demographic and socio-economic background questions on sex, age, marital status, labour status and occupation, household composition and income unless these can be obtained from the sampling frame or through record linkage to other data sources. From health status, at least general health, medical history and use of health care services should be asked. Lifestyle questions should cover smoking, alcohol consumption, physical activity, sedentary behaviours, and diet, and information on height and weight should be asked even though they may also be measured later during the health examination. Additional to this, more detailed questionnaires may be provided for example for a sub-sample to obtain better characterization of different sub-groups, to reduce participant burden, and to keep the main questionnaire within reasonable limits to promote a high participation rate.

For HBM studies, HBM4EU has prepared a set of standardized questionnaires (HBM4EU Online library. 2021) which are recommended to be used in future HBM studies conducted in Europe. For health surveys, a set of standardized questions is available through European Health Interview Survey (EHIS) regulations (European Commission, 2018) as well as through European Health Examination Survey (EHES) guidelines (Tolonen, 2016).

Both surveys can use a variety of questionnaire administration modes; self-reported either by paper-and-pen or online through a web questionnaire, and interviews conducted either face-to-face, by telephone or through a virtual format (video interview), or a mixture of these. The selection of used questionnaire administration mode(s) depends on national practices, setting of the fieldwork (availability of staff and premises), and by literacy level and coverage of internet access within the respective country.

3.3.2. Collection of biological samples and analysis of biomarkers

Biological samples are needed for both health and HBM modules. For health surveys, EHES recommends collecting at least blood samples to analyse lipids and glucose but also a collection of urine samples, especially 24h urine, is highly recommended to analyse sodium intake. For HBM studies, the required biological matrix depends on the compounds to be measured. The most frequently used sample types are either blood or blood compartments (serum, plasma) and/or urine.

For combined health and HBM survey, prioritization of biomarkers and/or compounds of interest needs to be done during the design phase of the survey since only a limited amount of blood can be drawn from an individual. For urine, the available quantity is not as critical. Some biomarkers and/or compounds can also be measured from other, non-invasive samples such as hair, saliva, nails, or breast milk or cord blood for women, and therefore, it should also be considered if reliable and validated methods exist to analyse some of the biomarkers and/or compounds of interest from other matrices than blood (Esteban and Castano, 2009).

For some health biomarkers such as glucose or insulin, or lipoprotein factions, fasting blood samples are required. However, fasting can be problematic for some of the compounds measured in the HBM module, especially for short-term exposure of non-persistent chemicals for which the diet is the major exposure route (Fromme et al., 2007; Koch et al., 2013; Preau et al., 2010). One solution to overcome the impact of fasting is to collect fasting blood samples on a sub-sample. This may also help survey logistics since fasting samples are often collected in the morning after overnight (8–12 h) fasting. Limiting the collection of fasting samples to a sub-sample of those who come to the examination in the morning also allows the use of afternoon and evening times for appointments. If this type of arrangement is made, it should be ensured that those assigned for the fasting samples, and who therefore are assigned for morning appointments, are a random sample from the total sample and represent the target population.

For blood samples in combined health and HBM survey, serum, plasma, and whole blood should be collected if feasible. For plasma samples, both citrate and EDTA as anticoagulants are recommended for

many health-related biomarkers while sodium-heparin is recommended for some other biomarkers and e.g. for metals. At least cotinine, total and HDL cholesterol, and glucose and/or glycated haemoglobin (HbA_{1c}) should be analysed in the combined HBM and health survey additional to selected environmental substances.

Basic blood sample collection and handling procedure do not differ for samples used for health and HBM modules. It is recommended to collect as much blood (serum, plasma and/or whole blood) as possible to facilitate analysis of a wide range of biomarkers and/or compounds but also supporting storage of some aliquots for future use. When samples are stored for a long time, i.e. in a biobank, they should be stored at the lowest possible temperature to minimize any recrystallization that might negatively impact the sample integrity.

For urine, 24h pool would be preferred for the analysis of many biomarkers but often this is difficult to collect in a survey setting. Therefore, collection of the first-morning void, whenever logistically feasible, or at least a random spot urine is recommended as many of the biomarkers and environmental substances can also be measured from them. From urine samples, at least total urine volume (especially relevant for 24-h urine samples), and urinary creatinine and specific gravity, which is also used to normalize the concentrations of HBM parameters should be analysed (Lermen et al., 2019).

Pertaining to sample collection for HBM purposes, special attention must be paid to the sample collection materials, both for blood and urine samples, to avoid potential cross contamination. It is recommended to clean all sample collection and storage materials according to standardized procedures to minimize possible inorganic and/or organic contamination through the manufacturing process (Lermen et al., 2015). Also, the collection of field blank samples can be used to document the background concentrations (Centers for Disease Control and Prevention (CDC), 2018).

If feasible with available samples and other resources (e.g., financial resources), additional biomarkers of interest, which are relevant for both survey types, e.g., biomarkers of effect for different health outcomes, should be included. Biomarkers of effect could for example include reproductive hormones, thyroid hormones, liver enzymes, biomarker of renal function, and nutritional biomarkers such as vitamin D.

3.3.3. Health examinations

Health measurements are an integral part of health surveys but are also included in many of the HBM studies on a smaller scale. The number of health measurements depends on the extent of health information needed. For combined health and HBM survey, at least anthropometric measurements of height, weight and waist circumference, and blood pressure should be included. Other possible health measurements could, for example, be spirometry, body composition using a bioimpedance device, cognitive function tests, and physical activity/fitness tests.

All additional measurements which can be included in the combined survey will provide valuable information about the health and health determinants of the target group. The number and type of additional measurements should be considered carefully in each survey to avoid unnecessary burden for participants. For the selection of additional measurements, criteria presented in Table 1 could be used, all points applying.

Table 1
Criteria for the selection of health measurements for a survey.

Criteria
1. Measurement result has a public health relevance
2. Measurement has a clear interpretation of the results
3. There are international standards for the measurement protocol
4. Measurement is practical and easy to administer in the survey setting
5. Information cannot or is difficult to obtain from any other data source, i.e. survey is the primary source of information
6. Cost of the measurement is feasible within the survey budget
7. Measurement is ethically acceptable in the survey setting
8. Measurement is well accepted by the participants

3.4. Ethics and data protection

For both HBM studies and health surveys, approval from the ethics committee and in some countries, a separate approval from the data protection authorities is required. Even though ethics are the code of conduct, not legislation, there are several ethical documents which guide the preparation and organization of health surveys including the Declaration of Helsinki (World Medical Association, 2018), which is considered as the pillar for ethical standards in medical research. Also, the Belmont Report on "Ethical Principles and Guidelines for the Protection of Human Subjects of Research" (The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979), the Recommendation of the Committee of ministers No. R(90) 3 concerning medical research on human beings (Council of Europe and Committee of Ministers, 1990), the Oviedo Convention on Human Rights and Biomedicine (Oviedo, 1997), the Council of Europe protocol to the convention on Human Rights and Biomedicine (Council of Europe, 2005), and the International Ethical Guidelines for Biomedical Research Involving Human Subjects by the Council of International Organizations of Medical Sciences and WHO (Council for International Organizations of Medical Sciences (CIOMS) and World Health Organization (WHO), 2016) are important documents to be considered when planning and implementing a survey.

Approval by the ethics committee must be obtained before any of the fieldwork can start. For the process of obtaining ethical approval, required documents may vary by country and/or ethics committee but in general, the following documents are required:

- detailed study protocol including a detailed description of recruitment protocol, eventual justification for including children and other vulnerable population groups as well as procedures to be used for the collection of biological samples and the objective health measurements,
- information material about the study to be provided for the invitees,
- informed consent form,
- questionnaire(s),
- respective data protection notification stating that data are stored in pseudonymised in which case the identification code is kept only by survey coordination, or in fully anonymised in which case the identification code is deleted, and
- eventual use of incentives.

From each survey participant, and in the case of children their parents/legal guardian, a written informed consent is needed before any biological samples can be collected or objective health measurements conducted (Tolonen, 2013; Lermen et al., 2015). Combined health and HBM surveys provide valuable information for later follow-up studies. Therefore, participants must be informed about eventual further handling of their data and samples together with information of the storage of data and samples in pseudonymised format. Procedures for approvals for future studies must be described.

The format of the informed consent may vary from traditional consent which is asked from the participants each time their data or stored biological samples are used for a new project, to a broad consent allowing future use by new investigators (secondary use) and/or exchange of data. A newer concept of dynamic consent fosters continuous contact with the study participants feeding back results and invitations to participate in new studies in collected data and/or samples (Teare et al., 2021).

From the legal side, several EU and national regulations/legislations need to be considered when preparing a survey protocol. These include the EU General Data Protection Regulation (Regulation (EU), 2016), national data protection regulation, national medical research

legislation, act of the rights of the patients, biobank act and archives act.

3.5. Training of the personnel

Training of the survey personnel both at the central office and those conducting the fieldwork is essential for all surveys. A training seminar or workshop at the beginning of the study is recommended for all staff members to make the procedures standardized across the teams but also for cross-country and over time comparability purposes. Entire survey personnel should be given training on the main components of the study process including.

- purpose and aims,
- legal and ethical aspects including privacy issues,
- design of the survey and survey organization,
- recruitment strategy,
- importance and methods of SOPs,
- hygiene and safety issues,
- quality assurance procedures,
- data management system, and
- publicity and communication strategy.

Additionally, fieldwork personnel should receive training in communication skills, interviewing techniques, motivating participants, and giving feedback. It is also important that they know when and how to consult survey physicians and supervisors and be aware of safety issues and protocols. Those conducting measurements and/or collecting biological samples and/or preparing/handling the samples must go through detailed training and certification. If questionnaires are administered through interviews, specific interviewer training should be organized to explain the purpose of each question and provide instructions on how the interviewer can probe the interviewee if needed, to prevent interviewer biases.

3.6. Requirements for fieldwork site

Basic requirements for the fieldwork sites are the same for health surveys and HBM studies, i.e., the fieldwork site should be organized so that it is easily accessible for participants also by public transportation. For persons with functional limitations, easy access by elevators/ramps is needed. Since some measurements have special requirements, these should be considered to ensure that measurements are not compromised due to the setting in which they are taken. Blood pressure measurement requires a quiet room with a comfortable temperature as any sudden loud sounds and too cold temperature may affect the blood pressure levels. Also, if blood pressure is measured using the auscultation method, all noise from the other rooms or corridor may disturb the measurement. For all anthropometric measurements, participants are asked to undress and therefore privacy is required. Body fluids like e.g., blood, plasma, serum, and urine are considered as potentially infectious materials and therefore are assigned biosafety level 2. The fieldwork sites must provide a corresponding biosafety level 2 containment in order to be able to process such samples (World Health Organization (WHO), 2004). In addition, special care must be put on the selected rooms to minimize any potential contamination. Also, for all measurements and discussions between survey personnel and survey participants, privacy and data protection need to be ensured.

3.7. Recruitment of participants

Successful recruitment of participants is of vital importance for any study. There are no one-size-fits-all solutions for a recruitment strategy. It must be adjusted based on the study design, target population, available funds, and previous experience. However, the same basic principles apply to both health surveys and HBM studies.

The recruitment strategy should be well planned, and sufficient resources should be allocated for the planning and recruitment process itself. The strategy should include plans on how to ensure the publicity of the study, what are the format and timing of contact attempts, what kind of supporting materials are needed during the recruitment, and by whom and when they are prepared. The use of incentives (financial or gifts) has been found to increase participation rates in many studies and could be considered if nationally allowed (Rao, 2020; Castiglioni et al., 2008). However, incentives may also introduce selection bias if some specific population groups, such as more deprived people, are more prone to participate due to offered incentives. However, this varies considerably between countries. In some countries, the use of incentives in population health surveys is not allowed by ethics committees/national legislation. Therefore, other formats of promotion should be considered. In this regard, personal study results can also be used as an incentive especially when there is a clear interpretation of the results such as BMI for obesity, blood pressure levels for elevated blood pressure, or in HBM module the interpretation of the analytical results in accordance with available health-based guidance values. Procedures for the feedback of study results to the study participants must be clarified in the protocol. This protocol should also include how to deal with cases on incidental findings, including who to involve in eventual medical follow-up.

It is important to raise people's awareness of the study through publicity. How this is done depends on study design and country. If the study is organized as a random sample of the population, announcements in media such as local newspapers and radio, as well as through social media are often good choices. Also providing posters about the study to public places such as health care centres, libraries, and community houses etc. could be used. Nowadays, the internet and social media are increasingly used for publicity and are valuable, low-cost tools for promotion. The survey should have its own website, and in some countries, communities/cities have their own Facebook/Twitter accounts which could be used to distribute information about the survey.

The first personal contact can be by mail, telephone or as a personal visit depending on the country. It is important that the invitee receives all relevant information to make an informed decision about participation. This usually means that an invitation letter together with an information leaflet is provided for the invitee. There must also be a possibility to ask for further information for example by phone. In some countries, the informed consent form is sent together with the information leaflet allowing invitees to read it at home before attending the survey visit. If a person cannot be reached by the first contact or he/she is reluctant to participate but does not refuse explicitly, re-contacts should be made. The number, format, and timing of the re-contact attempts depend on the survey and available resources. Sometimes also national regulations/legislation or ethics committees may limit the possible number and format of re-contacts.

3.8. Data access and reporting

As combined health and HBM surveys are often conducted in collaboration with several institutes, it will be important to agree on data ownership and use well in advance. Having a clear agreement of data ownership, possible embargo periods after data have been collected, when and how results can be published, and by whom and how data can be accessed for further research is important in order to avoid unnecessary delays in data use after data collection has ended.

4. Discussion

Non-communicable diseases (NCDs) such as cardiovascular disease and cancer cause a major health burden worldwide. In the EU, it has been estimated that about one third of the adult population aged 15 and over live with a NCD (OECD, 2016). Traditionally, NCD risk factors include metabolic syndrome including raised blood pressure,

overweight and obesity, high blood glucose level and high cholesterol levels together with lifestyle risk factors of smoking and heavy alcohol use, and socio-economic and socio-demographic position. These have been monitored through health examination surveys over the past decades. More recently, the scientific understanding of the health impact of environmental risk factors including air pollution, noise and chemicals has increased, and are today considered as plausible and most likely an important contributing factor to the observed increase in a range of NCDs (Pruss-Ustun et al., 2019; Chowdhury et al., 2018).

Obtaining holistic information about health and health determinants of the population should therefore also include data on environmental risk factors of health. In line with this, it is important to be able to monitor the evolution of exposure levels of the general population to support sound chemical regulation and health-related mitigation measures. HBM studies are seen as the "gold standard" for the measurement of environmental exposures of humans (Sexton et al., 2004).

Having extensive information on health, biological risk factors, lifestyles, socio-demographic characteristics, as well as environmental risk factors on the same individuals would generate a more complete database which can foster wide scientific research potentials. Moreover, when a wide range of biomarkers including biomarkers of effects are analysed in combined health and HBM surveys, the assessment of the association between exposure to chemicals and health effects could be more easily conducted. Through research on this extensive database, we could support policymaking in several fields such as public health including allocation of health care resources and setting up public health prevention measures, and chemical regulations. When some of the collected biological samples are stored in biobanks for future use with related informed consents allowing secondary use of these samples, samples could be used to answer many additional medical/clinical and health-related questions.

Examples from Germany (Kolossa-Gehring et al., 2007), France (Balicco et al., 2017), Israel (Berman et al., 2017), the USA (Centers for Disease Control and Prevention (CDC), 2021) and Canada (St-Amand et al., 2014) demonstrate that it is possible to combine health surveys and HBM studies at the national level. Introducing the HBM module as part of general health surveys has been discussed and considered in many European countries (Tolonen et al., 2018, 2021). In health surveys, biological samples are already commonly collected which would, in theory, make it easier to extend them to integrate the HBM module. In Europe, there are also a lot of health surveys (national, regional or targeted/disease specific) which have collected and stored biological samples for future use. Often, in these surveys, ethical approval already allows the measurement of environmental biomarkers/combounds from collected samples (Tolonen et al., 2018).

Even though combining health and HBM modules into one survey requires a lot of work and prioritization of identified needs for both domains, there are several identified advantages in this (Tolonen et al., 2018; Paalanen et al., 2019). The combined survey will provide a wide range of detailed data on several domains as well as the possibility to collect a larger sample. When the HBM module is added to the existing health survey, already existing logistical infrastructure can be used for recruitment of participants, collection of information through questionnaires and health measurements, and collection and handling of biological samples. The combined survey also benefits from joint public health relations for promotion of the survey during the fieldwork. All these contribute to the reduced cost of the surveys.

To ensure that this potential for a growing number of combined health and HBM surveys in Europe is best used for multinational research projects and monitoring purposes, it is essential to support standardization of used survey methods. These guidelines would be the first step towards standardized procedures to ensure comparability of surveys between different countries. The guidelines presented here are prepared in focus for national surveys but can well be implemented in regional or targeted surveys as well with small modifications for the target population, sample size, and possibly for included measurements as well.

5. Conclusions

Due to the similar logistic infrastructure required for both health surveys and HBM studies, combining them is feasible and cost-effective. The combination will provide a wider information base for more holistic analysis of human health and its determinants, including the effects of environmental substances.

Declaration of competing interest

The authors declare no conflict of interest.

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Abbreviations

BMI – Body mass index
EHES – European Health Examination Survey
EHIS – European Health Interview Survey
EU – European Union
HbA_{1c} – Glycated haemoglobin
HBM – Human biomonitoring
HBM4EU – European Human Biomonitoring Initiative
HDL – High density lipoprotein
HES – Health Examination Survey
HIS – Health Interview Survey
NCD – Non-communicable disease
RCT – Randomized Control Trial
SOP – Standardized Operating Procedure
STEPs – STEPwise Approach to NCD Risk Factor Surveillance
WHO – World Health Organization

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