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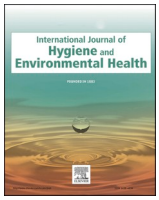

Health information for human biomonitoring studies

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Numerous studies have shown that human exposures to contaminants present in our environment are associated with adverse health outcomes (Tolonen et al., 2021; Pruss-Ustun et al., 2019; Fuller et al., 2018) and therefore, contribute to the overall burden of non-communicable diseases (Pruss-Ustun et al., 2011). It has been estimated that environmental factors globally, can be attributed to 5.2% of disability-adjusted life years (DALYs) (Global Burden of Disease Risk Factors Collaborators Forouzanfar et al., 2015).

Furthermore, it has been estimated that almost 2% of the total annual health care costs in high-income countries and 7% in middle-income countries are caused by pollution-related diseases (Landrigan et al., 2018). The associated worldwide health costs of human exposure to environmental chemicals have been estimated to possibly exceed 10% of the global domestic product (Grandjean and Bellanger, 2017). Theoretically, this disease burden and the associated costs are avoidable through preventive initiatives such as legal restrictions related to production and use of such substances, and guidelines on how to minimize the exposure to harmful substances. It is, however, necessary to obtain information on chemical exposure burden as well as health of the population to support evidence-informed policy making.

People are part of their living environment which includes their personal characteristics such as age, sex and other constitutional factors, e.g. genetic markup, individual lifestyle factors, social and community networks, and living and working conditions (Dahlgren and Whitehead, 2007). Human biomonitoring (HBM) provides information on individual level exposure to environmental chemicals by measuring the substance itself, or its metabolites, in biological matrices such as urine or blood. To be able to evaluate the impact of environmental exposures on health, extensive data on socio-demographic characteristics, lifestyles, and health itself is also needed. Thus, a holistic approach when evaluating the impact of environmental exposures on health is warranted.

In the framework of the HBM4EU project (HBM4EU, 2021; Ganzleben et al., 2017), possible ways to add more extensive health information to HBM studies were evaluated. Two main sources of health information were identified: health examination surveys and linkage to administrative health registers.

1. Different study settings provide different possibilities

Data comprising both chemical exposure information as well as health outcomes, can be used in many ways to provide evidence to support policy decision making. Depending on the level of granularity of available data, either analysis using aggregated data or individual level data can be utilised (Coggon et al., 2003).

Ecological analysis allows investigation of geographical correlation of exposure level and disease incidence, prevalence, or mortality. For ecological analysis where the level of observation is country, region or other similar entity, required health information can usually be obtained

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from official, national level statistics, such as mortality statistics, without any additional data collection. Ecological analysis can however become biased if exposure or disease outcomes are not uniformly distributed across the unit/area of interest e.g. country, region. Further, both exposures as well as diseases may have time dependent variations, i.e. some diseases may be more prevalent during the hot or cold seasons. For time trend analysis, it is important also to consider factors such as improvement of diagnoses and health care services, differences in disease registration and procedures over time, changes in population structure in different geographical areas due to aging, migration, etc.

Etiological studies, on the other hand, allow examination into associations between exposures and health outcomes on an individual level. Cross-sectional studies provide a snapshot of the situation at a given time point within a defined target population. Because information on exposure and outcomes are collected at the same time point, it does not allow estimation of causal relationships between exposures and health outcomes, only observed associations. To determine a causal relationship, either a longitudinal approach following a cohort or case-control studies would be required although these study designs also have their limitations.

Longitudinal studies, refer to studies characterised by repeated measurements of exposure and/or health outcomes. However, re-examinations of study participants is time consuming and expensive and is often challenged by attrition bias (Nunan et al., 2018). For many health outcomes such as cardiovascular diseases (CVD), cancer or diabetes, large cohorts are needed, and they must be followed up for a long time before any results can be seen as these diseases take a long time to develop. If we, however, have the possibility to link previously collected cohorts/surveys to administrative registers such as electronic health records and mortality registers, we could facilitate retrospective information as well. This would allow us to study if those exposed at baseline in comparison to those non-exposed at baseline differ in relation to the incidence or prevalence of disease of interest during the follow-up.

2. Health data obtained through a health examination module

Combining a HBM study with a health examination survey (HES) where information is collected through questionnaires, objective health measurements and by analysing biological samples, is one approach to add more extensive health information to the exposure data. This can be done either by adding a HES module to an ongoing HBM study, adding an HBM module to an ongoing HES or planning a new combined study. A combined HBM and HES approach allows collection of both chemical exposure information as well as health information on the same individuals.

In HBM and health surveys, self-administered questionnaires or interviews are often used to collect information on lifestyle factors such as smoking dietary habits and physical activity, but also on diagnosed diseases and use of medications. Self-reported questionnaire data may suffer from social desirability, recall or awareness bias (Althubaiti, 2016). When an activity, for example smoking among adolescents or pregnant women, is considered an undesirable behaviour, there will be a risk of experiencing social desirability bias in the survey resulting in an underestimation of the true situation. For recall bias, participants may for example have trouble remembering which medications they are using, or they are not sure of their consumption of specific foods within the asked time frame. Awareness bias may occur when we for example ask if a person has a specific disease which may be asymptomatic for a long time before actual diagnoses. A good example of this is hypertension.

Therefore, whenever possible, direct health measures, such as weight and height measurement, blood pressure measurement, spirometry to determine lung function, or analysis of biomarkers from blood, urine or other biological samples, should be used as they provide more reliable information (Maukonen et al., 2018; Prince et al., 2020; Taylor et al., 2010; Paalanen et al., 2019). It should also be noted that, health measurements are prone to bias through device and measurement procedures (Tolonen et al., 2015), and laboratory analysis may also suffer from bias due to pre-analytical procedures (Tolonen et al., 2005), but also during the actual laboratory analysis due to variability between reagents, devices and laboratory procedures (Alfthan et al., 2018). However, with detailed, standardised measurement protocols and adequate training of qualified personnel, many of the sources of bias for objective health measurements and analysis of biomarkers can be minimised. Especially when cross-country comparisons are done, or time trends are analysed, a special attention should be paid for the selection of laboratories to ensure that they have passed accreditation, but also external quality assessment.

2.1. Potential for adding HBM module to ongoing or planned HES in Europe

From the evaluations conducted within the framework of HBM4EU, we know that the vast majority (90%) of the health surveys conducted in Europe collect and store biological samples for future use or have the potential to include collection of such samples in their future surveys. The most frequently collected samples are blood (plasma or serum) (71%) and urine (64%), the latter either as first morning void or spot samples. Obtained ethics approvals for these surveys often (83%) cover the possibility to analyse environmental markers from collected and/or stored samples (Tolonen et al., 2021).

The feasibility of combining HBM studies with health surveys has been demonstrated in several studies around the world (Balicco et al., 2017; Berman et al., 2017; Kolossa-Gehring et al., 2007; St-Amand et al., 2014; Centers for Disease Control and Prevention (CDC), 2021) and currently guidelines for doing this exists (Tolonen et al., 2022). Nevertheless, many study principal investigators still avoid this combination, due to lack of required knowledge and resources. The added value of extended data with both chemical exposure and health outcomes is not always seen to fit the focus of the survey (Tolonen et al., 2021).

3. Health data obtained through record linkage

Since self-reported information on diagnosed diseases may suffer from recall and awareness bias, but also social acceptability may affect the reporting behaviours (Althubaiti, 2016), administrative health records could provide a more reliable and cost-effective way to obtain required health information. Electronic health records, information on medical prescriptions, as well as birth and mortality data can be used to obtain both information on medical history, but also follow-up of morbidity and mortality if linkage to survey data is technically possible, legally allowed and required practices in the country are in place. Usually, these kinds of administrative registers have a good coverage of the population, and they tend to accumulate automatically as a result of health care services and recording of vital statistics. Therefore, there is no additional data collection costs if they also can be used for research.

For linkage of HBM survey data to administrative registers, the key requirement is that national legislation allowing the secondary use of such administrative data sources for research are available. After that, more technical details come to play a role, i.e. different data sources which are to be linked together should have common identifier(s) to allow linkage. Ideally, there is one common identifier, such as a national identification code, which is used systematically across different data sources. Then deterministic data linkage can be done. When a national identification code is not available, but all data sources to be linked have enough common elements, such as age, name, address and data of birth, linkage can be done using probabilistic methods (Harron et al., 2015).

To perform record linkage between HBM survey data and data from administrative registers, in most of the countries, informed consent from the survey participants is required together with approval from the ethics committee and data owners. It should also be noted that administrative registers are primarily generated for other purposes than

research. Even though data is accumulating continuously and tend to cover the entire population of the country/region, the quality of data may vary over time and regions due to differences in recording practices, changes in personnel, etc.

3.1. Possibilities for record linkage in Europe

The availability of different types of health-related administrative registers is good in Europe (Tolonen et al., 2021; Meltzer et al., 2022). All countries have vital statistics on births and deaths as well as either national or regional cancer registers. Availability of in-patient and out-patient hospital records (electronic health records) or medical prescriptions are, on the other hand, not systematically available in all countries. Based on this, at least mortality follow-up should, in theory, be possible in all European countries.

However, findings from the evaluation within the HBM4EU frame showed that only about half of the countries use a national identification code systematically in their administrative registers as well as in survey samples to allow simple deterministic record linkage. A few countries in Europe do not have a national identification code in use. Also, in some countries strict data protection regulations related to sensitive health data are preventing the record linkage (Tolonen et al., 2021; Meltzer et al., 2022).

4. Summary

Many environmental contaminants have been shown to be associated with adverse health effects. Up-to-date and high-quality scientific research results are needed to guide and support evidence-informed policy decision making. Data on both exposures to environmental substances as well as health outcomes in the same individuals are essential. To this end, there is a great potential to combine HBM and health surveys in Europe.

Human biomonitoring studies can be used to obtain information on exposure levels. Information on health outcomes can be obtained through health examination surveys or record linkage to administrative health registers. The availability and feasibility to use different data sources varies by country.

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HT, AMA, SAH and HMM wrote this commentary.

Declaration of competing interest

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