Requirements for research involving vulnerable or deceased persons – Summary of Final Report

Background and objective

The Federal Act on Research involving Human Beings (HRA), together with the associated Ordinances, has been in force since 1 January 2014. This legislation includes specific requirements for research involving persons considered to be particularly vulnerable (e.g. children/adolescents or adults lacking capacity). Also specifically regulated is research involving deceased persons. BSS Economic Consultants was requested by the Federal Office of Public Health (FOPH) to investigate the effectiveness and appropriateness of these specific requirements.
As regards methodology, an analysis of the data on approved research projects was first carried out. This was followed by a comparison with the regulations existing in the EU/Germany and in the UK, as well as international guidelines. Finally, the provisions were discussed in 28 qualitative interviews with representatives from the research sector and ethics committees.

Subject of study

Research involving persons, deceased persons, embryos and foetuses, biological material and health-related personal data is regulated by the HRA. As well as general requirements, the HRA specifies additional requirements for research involving particularly vulnerable persons. These include children, adolescents, adults lacking capacity, pregnant women, embryos and foetuses *in vivo*, prisoners, and persons in emergency situations.

Research involving particularly vulnerable persons

Each year, approx. 200–270 projects involving vulnerable groups are carried out. This represents around 20–30% of the total number of approved research projects (not including projects which are exclusively further use projects). Most frequently, these projects involve children and adolescents.

Definition of vulnerable groups

The identification of vulnerable groups in the HRA is based on the definitions given in international declarations and guidelines. For the purposes of the HRA, persons are considered to be particularly vulnerable if “they cannot understand or fully appreciate the purpose, benefits and risks of a study and are therefore not capable of making a well-informed and considered decision”.[1] The concrete application of this principle in the HRA largely corresponds to the regulations adopted in the comparator countries considered.
The stakeholders interviewed regard the definition of vulnerable groups in the HRA, for the most part, as appropriate, while also emphasising the importance of the specific situation and context. Thus, persons in a group designated as vulnerable are considered not always to require special protection (e.g. pregnant women completing a questionnaire). At the same time, according to interviewees, there may be situations in which persons are particularly vulnerable even if they do not generally belong to a group legally defined as vulnerable.

[1] Dispatch concerning the Federal Act on Research involving Human Beings, 21 October 2009

Conditions and requirements

Conditions: For research involving human beings and especially research involving particularly vulnerable persons to be permissible under the HRA, various conditions must be met:

- ***Subsidiarity:*** Under the HRA, the subsidiarity principle is generally applicable for research involving human beings. Thus, "a research project involving persons may only be carried out if equivalent findings cannot be obtained by other means." In relation to vulnerable groups, this means that research is only permissible if comparable findings cannot be obtained with the aid of persons not considered to be particularly vulnerable.

- ***Risk-benefit ratio:*** As a prerequisite for research involving human beings, the HRA calls for an assessment of the risks and benefits of participation in a research project. Thus, more restrictive conditions are applicable for a research project where no direct benefit is expected. In relation to vulnerable groups, for example, research with no direct benefit is only permissible if it entails only minimal risks and burdens.

The subsidiarity principle and the assessment of risks and benefits are similarly applicable in the comparator countries considered.

Requirements: For research projects, the HRA specifies requirements that are applicable in cases where the conditions for research are met, i.e. when it is in principle permissible. Here, the central aspect is informed consent, with the following points applying: children, adolescents and adults lacking capacity are to be involved as far as possible in the consent procedure. Thus, for example, they must not visibly express opposition to the research intervention either verbally or by their behaviour; previous decisions are to be taken into account; and post hoc consent is to be obtained in cases of temporary lack of capacity. In addition, the interests of the persons concerned are to be protected on a proxy basis by legal representatives or other persons (trusted person, relatives, independent physicians in emergency situations).

Challenges from the stakeholders' perspective

In practice, according to interviewees, challenges arise in the case of research in the emergency field or in intensive care medicine: obtaining proxy consent from relatives was said to be difficult given the exceptional nature of the situation in which they find themselves. Obtaining post hoc consent was also said to involve considerable effort (since the persons concerned often still lacked capacity when transferred to a different department or institution). The requirements were judged to be disproportionate particularly in those cases where the research involved a standard procedure. The researchers cited as a consequence a decrease in research projects and a reduction in Switzerland's competitiveness in this area.

Research involving deceased persons

Each year, approx. 15–35 projects involving deceased persons are carried out. This represents around 1–3% of the total number of approved research projects (not including projects which are exclusively further use projects).

Requirements for research

Deceased persons must have given their consent before their death. If such consent is not available, relatives or a trusted person may consent on their behalf. These requirements are not applicable in cases where death occurred more than 70 years previously (Art. 36 HRA) or where small quantities of bodily substances are removed in the course of an autopsy or transplantation (Art. 38 HRA).

The HRA also specifies stricter requirements for cases where a deceased person is undergoing artificial respiration: here, a research project may only be carried out if equivalent findings cannot be obtained with deceased persons not undergoing artificial respiration, and the person carrying out the research must not have been involved in the determination of death.

Challenges from the stakeholders' perspective

Obtaining consent from relatives was cited as the main challenge. In some cases, in connection with further use, Art. 34 is applied (provisions for exceptional cases where informed consent is lacking), although according to the FOPH this is not permissible in the case of deceased persons. There is also uncertainty as to the definition of what counts as a "small quantity" in accordance with Art. 38 HRA.

Conclusions

Results

The legal requirements specified in the HRA for research involving particularly vulnerable or deceased persons are regarded by the experts interviewed as generally reasonable and appropriate. They are also based on internationally established ethical principles. The regulations thus duly recognise the particular need for protection of vulnerable groups and deceased persons. At the same time, the study shows that the application of certain provisions in practice involves considerable administrative and organisational efforts – especially in intensive care medicine and in research involving deceased persons. The consequence is a decrease in research involving these groups.

Recommendations

Vulnerable persons:

- ***Definition of vulnerable groups:*** From our perspective, it would be worth considering whether vulnerability should be defined in the Act in a more general way, taking into account dependence on the context and situation. This would also reflect the current practice of ethics committees, which take context dependence into account when reviewing research applications. At the same time, it should be noted that the effects in practice would probably be limited (given the ethics committees' existing practice).
- ***Physician-patient dependence:*** In our view, the physician-patient relationship is intrinsically a constellation in which dependence may arise and, accordingly, a context in which persons may be particularly vulnerable. Against this background, we would recommend consideration of the suggestion made by one interviewee that the roles of treating physician and researcher should be largely separated.
- ***Risk-adapted and simplified consent procedures:*** In our view, especially in the case of persons temporarily lacking capacity in intensive care medicine, consideration should be given to procedures distinguishing between low-risk standard treatments and higher-risk interventions. For example, prior proxy consent could be dispensed with for standard treatments. It could also be examined whether consent procedures can be simplified with the aid of digital tools.

Deceased persons:

- ***Further use (existing data and samples):*** At present, no HRA regulations exist in this area. In some cases, Art. 34 HRA is applied, even though this is not permissible according to the FOPH. In our view, its (non-)applicability should therefore be clearly communicated. At the same time, we would recommend the establishment of similar regulations in this area.

- ***Collection of new data and samples:*** In contrast, the collection of new data/samples is regulated by the HRA, but the requirements give rise to difficulties in practice. In our view, they should be critically discussed and possibly simplified (e.g. extension of Art. 38 HRA to cover data, possibly an opt-out solution). In addition, the term “small quantities” in Art. 38 HRA should be clarified, so as to permit more consistent/easier application in practice.