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Benefit – a neglected aspect of health research ethics

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ABSTRACT

In research ethics, provision of potential benefits to study participants is linked to the principles of beneficence and distributive justice. However, in most research ethical codes the notion of benefit is only superficially elaborated which is extended in vague and general benefit assessments in research proposals and in Research Ethical Committee's (REC) recommendations. The issue gains additional importance in collaborative projects where researchers, study populations and donors from both developing and developed countries are involved. We introduce a checklist for planning and assessment of benefits as part of research ethics and suggest as a first step in unfolding the concept of *benefits* that research project and RECs as a minimum should address *who* (the target groups), *when* (the period of time during which the services are planned to be rendered) and *what* (the nature of the benefits).

It is a common view that research ethics rest on the key principles of respect, beneficence and justice [1]. *Respect* for persons encompasses respect for autonomy as well as "protection of persons with impaired or diminished autonomy". "*Beneficence* refers to the ethical obligation to maximize benefits and to minimize harms" whereas *justice* "refers primarily to *distributive justice*, which requires the equitable distribution of both the burdens and the benefits of participation in research" [1]. Sometimes *non-maleficence* ("a norm of avoiding the causing of harm") is mentioned as a fourth principle [1, 2]. Schüklenk [3] as well as Beauchamp & Childress [2] point out that there are alternative conceptual ethical frameworks at hand such as utilitarianism, deontological bioethics, liberal individualism and communitarianism.

Within the discourse of medical research ethics, the discussion of benefits concentrates to a large extent on the so-called standard of care issue. Thus, the Helsinki Declaration [4] demands that the services rendered should be of the best global standard. This has been widely debated and others [5, 6] take the stand that provision only according to local standards is justified. Some scholars advocate for a broader definition of standard of care (including sustainability and scaling up) [7] and a partnership approach to "provide positive benefits to society" [8].

As a large number of studies today are implemented for commercial rather than health promotion (e.g. trials to prolong patent protection of drugs with minimal medical benefit), there is an increased need to address the concept of benefit and quantify it as an outcome (e.g. number of gained quality adjusted life years). However, aspects of benefit are generally less elaborated in research proposals and in assessments conducted by Research Ethics Committees (REC) than other research ethical issues such as informed consent and avoidance of harm. The aim of the present article is to initiate a discussion on standards for benefit assessments by suggesting a checklist that will allow a more systematic and explicit description of potential benefits in research proposals and subsequent reviews. Clarification of benefits is a prerequisite for an assessment of beneficence in which the balance between potential harms and benefits is gauged. The focus here is on health projects where developed countries sponsor and implement research in developing countries with researchers from both sides to participate making issues of potential benefits more conspicuous.

HOW THE ISSUE OF BENEFITS IS ADDRESSED IN INTERNATIONAL RESEARCH ETHICAL CODES

Among the numerous international ethical codes (laws, directives, conventions, declarations and guidelines) descriptions of the benefit complexity are scarcely met. Here six prominent examples of central codes are addressed.

The seventh version of the Declaration of Helsinki with notes of clarification [4] mentions in point 6 that "understanding of the aetiology and pathogenesis of disease" is "the primary purpose of medical research involving human subjects". In point 19 it is explicitly stated that "Medical research is only justified if there is a reasonable likelihood that the population in which the research is carried out stand to benefit from the results of the research". The obligation to publish "negative as well as positive results" is also mentioned. In point 30 the declaration states that "every patient entered into the study should be assured of access to the best-proven prophylactic, diagnostic and therapeutic methods identified by the study" – and this point is further emphasized in the clarifying note of 2004.

The Council for International Organisations of Medical Sciences (CIOMS) speaks in its International Ethical Guidelines for Biomedical Research Involving Human Subjects [1] in guideline 5, points 10 and 11, of "the direct benefits" for participating subjects and "expected benefits" to the community or to society at large. Further in point 21 it is stated that if "commercial products may be developed from biological specimens it ought to be considered whether the participant will receive monetary or other benefits". The guidelines also speak in point 23 on "the investigator's responsibility to provide medical services to the participant". An overall statement of direct and indirect benefits is found in guideline 8. Guideline 20 describes the need to provide research and ethical capacity building as part of externally sponsored collaborative projects, and guideline 21 draws the attention to the ethical obligation of external sponsors to provide healthcare services. As a whole the CIOMS guidelines deal more with risks and protection than with benefit for participants.

The Council of Europe's Convention on Human Rights and Biomedicine [9] deals primarily with the protection perspective of participants, and also uses the general term *benefit*. The Explanatory Report [10] does not add any specification of this general term. The same is true for the Additional Protocol to the Convention on Human Rights and Biomedicine on Biomedical Research [11].

In its summary of the Commission's six publications, the U.S. National Bioethics Commission [12] uses the terms *risks* and *potential benefits*, and their absolute and relative influence on overall research ethics decisions. The primary target group of the guidelines is the project participants (Recommendation 4.1) whereas the society is only mentioned as an overall term.

The UNESCO Universal Declaration on Bioethics and Human Rights [13] has a broad international perspective. *Benefit* is defined as "direct and indirect benefits to patients, research participants and other affected participants" (Article 4). "Cultural diversity and pluralism have to be given due regard", but not "to be invoked to infringe upon human dignity, human rights and fundamental freedoms" (Article 12), and the perspective of "solidarity among human beings and international cooperation towards that end are to be encouraged" (Article 13). Both statements are relevant for benefit and harm when biomedical research takes place in developing countries. These global perspectives of benefit are even more precisely stated in Article 15, "Sharing of benefits", and in Article 21, "Transnational practices", Sections c-e.

The Nuffield Council of Ethics' report [5], provides a detailed analysis of various global perspectives of research ethics including

benefits. The working party behind the publication emphasizes clearly that the researchers in developing countries need to obtain a benefit via "the development of local expertise in the provision of healthcare and in healthcare research", and that such a benefit "should be an integral component of any proposed research".

When a research project is over, the Nuffield report strongly advocates three aspects of benefit: 1) the monitoring of "possible long-term deleterious outcomes arising from the research", 2) "the possibility of providing participants with the intervention shown to be the best", and 3) "the possibility of introducing and maintaining the availability to the wider community of treatment shown to be successful".

The report summarizes the ethical dilemmas related to the control group, which should be offered the benefit of "a universal standard of care for the disease being studied; where it is not appropriate to offer a universal standard of care, the minimum standard of care that should be offered to the control group is the best intervention available for that disease as part of the national public health system". Further the report stresses that "before research begins, agreement should be reached about the standard of care that should be provided to participants in research who already have or who develop diseases other than the diseases being studied". "The minimum standard of care that should be offered" is also here "the best intervention available as part of the national public health system".

Common for all six codes are the brief and general description of required benefits as outcomes of a research project.

BENEFITS AS PART OF RESEARCH ETHICS

If a project is based on an original scientific idea and includes an appropriate methodology, relevant variables and reaches the planned termination, there will always be a potential scientific benefit. But, in addition to the standard questions of research ethics, we suggest that an analysis of the *potential benefits* should be included in a project proposal and should be part of ethical reviews.

We contend that determination of *benefit* in a research project should as a minimum address three dimensions:

- *Who?* The target group (varying from the study participants exposed to the active intervention, over the possible control group, to other members of the study community, the nation or the global community of relevant patients and humankind in general).
- *When?* The period of time during which the services are planned to be rendered (varying from the direct effect of intervention during the trial to long-term provision beyond the duration of the project per se).
- *What?* The nature of benefit provided (varying from the specific intervention on trial, over provision of clinical care for critical medical conditions and basic medical services in general, to provision of even non-medical assistance such as improved water supply or schools in the study community).

These three dimensions can be seen as continua along which benefits may be perceived in terms of the beneficiaries, the duration, and the sort of benefit provided. In order to facilitate the analysis, a checklist of questions is provided below.

A CHECKLIST FOR POTENTIAL BENEFIT IN A HEALTH RESEARCH PROJECT

The list of questions is structured according to the first dimension, the target group, addressing the study participants, community members at large (local, regional, or national community members), and the researchers involved in the study. Table 1 illustrates the questions of relevance for the three target groups.

Study participants

1. Has it been ensured that study participants (both the intervention and the control group of a trial) will get access to the new diagnostic or therapeutic tool if found more efficient than the standard? If yes, for how long?
2. Will the project provide (emergency or general) clinical services to the study participants apart from what is directly related to the procurement of the study variables? If yes, to which extent and for how long?
3. Will the project provide non-medical services (e.g. related to education, monetary or other material benefits) to the study participants? If yes, what, to which extent and for how long?
4. Has the protocol considered giving feedback to the participants about the general research results?
5. Has the protocol considered participants' right to receive feedback about their personal results along with suggestions about clinical consequences for themselves?
6. Does the project include elements of capacity building for the study participants?

Community members (local, regional, national)

Questions 1-4 and 6 apply equally to other community members not participating in the study although a borderline must be drawn depending on the magnitude of the study. However, an expansion could be made to question 4: Has it been considered how the study findings are to be disseminated to relevant public health or medical stakeholders at national and international level in order to achieve utilisation where relevant (e.g. changed policies or procedures)?

Additionally for communities it should be asked: 7. Will the community (local, regional, national) receive a share of any profits derived from industrial processing of their belongings (e.g. material from biobanks), developed during a research project? If yes, to which extent and in which way?

Researchers participating in the project

Questions 6 and 7 should also be asked regarding this group. Options for both scientific and technical elements of capacity building should be explored for team members from developing countries. Additionally for participating researchers, the following question should be asked: 8. Is the collaboration between researchers from the developed and the developing countries involved based on equity (e.g. in terms of intellectual property rights and equal access to co-authorship)?

It is assumed that the altruistic satisfaction of benefiting fellow patients in a general way and making a contribution to increased general knowledge is known to and appreciated by the participants. This pertains to new knowledge about diagnostic or therapeutic

Table 1. A graphic visualisation of questions for planning and assessing benefits in connection with research projects. Grey cells indicate non-relevance.

Benefits	Questions	Study participants	Community members	Researchers
Access to new tools	1			
Provision of clinical services	2			
Provision of other services	3			
Feedback about research findings	4			
Feedback about personal results	5			
Capacity building	6			
Rights to share profits from research	7			
Equity between researchers	8			

tools as well as basic insights into pathogenesis or taxonomy of the diseases studied.

Not all parts of the checklist are relevant for all research protocols involving humans in developing countries. Both the types of studies and the political and economic conditions in the collaborating recipient country necessitate a selective use of the checklist. But during the planning and assessment of such studies it is recommended to go through the list in order to specify the generic indications of the international research ethical codes.

CONCLUSION

Based on the principles of beneficence and distributive justice, provision of potential benefits for study participants should be a key criterion in planning and assessing health research projects involving humans. Yet, whereas the majority of international research ethical codes deal with informed consent in great detail, benefits are often referred to in more general terms and without addressing the many practical dilemmas. The issue is especially conspicuous in projects comprising participants from both developing and developed countries. We have introduced a list of questions that allows a systematic analysis of benefits and facilitates a more elaborate and practical description.

It comprises three main analytic dimensions: 1) the target groups *(who?)*, 2) the period of time during which the services are planned to be rendered *(when?)*, and 3) the nature of the benefits provided *(what?)* – all of which are continua along which the potential benefits can be perceived and organised. How the various points on the checklist are eventually assessed in relation to a given project depends on factors such as the type of research, the context in which it is implemented and the parties involved.

Thus, we provide a tool that may facilitate an evaluation, but we do not conduct the evaluation ourselves. It is our hope that the views presented here will initiate a discussion on standards for benefit assessment, and that the checklist will assist both researchers in the planning phase of a study and RECs in dealing with ethical reviews.

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