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Disclosing Research Results to Participants: Is There a Consensus?

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Abstract

Traditionally, research results have not been disclosed to participants during medical research. However, recently a debate on the ethical duty of disclosing research results to participants has emerged. In this review, three positions in the debate are outlined: first, the disclosure is deemed an ethical imperative, second, a prima facie duty, and third, a consideration only. Although the notions of respect for persons, beneficence, and reciprocity can provide strong arguments for accepting disclosure as a duty, no consensus has been concluded on this issue yet. In the lack of consensus, addressing the issue of disclosure is required from every research plan.

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Medical research; duty of disclosing research results to participants; principle of respect for persons; principle of beneficence, reciprocity.

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I. Introduction

Prior to the initiation of every medical research, detailed information is provided to prospective participants about their rights, the purpose of the study, the procedures to be undergone, the potential risks and benefits of participation, the expected duration of the study, the confidentiality of personal data, the randomisation process, etc. to promote their entirely voluntary participation [1]. This informed consent process, embedded in the principles of the Nuremberg Code and The Declaration of Helsinki, is considered as one of the most important ethical requirements of biomedical research. While pre-trial

information-giving primarily aims at supporting the autonomous decision-making of participants and ensuring safeguards for them during research, it also reveals important data on the research project itself.

In the light of this detailed, sometimes extremely voluminous, information-giving before research initiation, it can be surprising that after the completion of research, traditionally, researchers have not been expected to disclose information about the study results directly to the participants. The conventional ways of disseminating research results have included peer-reviewed journals, scientific meetings or even the lay media, but towards the study participants, the non-disclosure policy has been in effect for decades. Considerations about informing participants of research results have not comprised the part of ethical conduct during medical research.

However, in the recent medical ethics literature, a debate on the ethical duty of disclosing research results to participants has emerged. The need to breach the tradition of non-disclosure and to share research results with participants has been raised especially by cancer clinical trials, and by genetic experiments applying whole genome sequencing or exome sequencing technologies [2, 3]. These types of trials can generate results with direct consequences for the health status of the research participant, thus the non-disclosure of these results can hardly be justified. Over the years, the debate has extended, and nowadays the dispute focuses on the issue whether the disclosure of research results to participants should be assessed as a universal duty.

II. Conditions influencing the perspective of a debate on the duty of disclosing research results to participants

When studying the history of disclosing research results to participants, it is recognisable that the theoretical debate has partly been triggered by the problems occurring in the sporadic application of this idea. Seemingly, in the case of disclosing research results to participants, the steps of practical implementation have preceded the theoretical clarification.

In 2005, introducing the new disclosure policy was demanding for a research project named "North Central Cancer Treatment Group Study n9831," conducted in the United States, since the planned, interim analysis had revealed that the experimental treatment regimen for breast

cancer was significantly more effective than the standard treatment. The research constituted a randomised, phase III clinical trial to study the effect of trastuzumab on disease-free survival of women with operable, HER-2 positive breast cancer, obtaining adjuvant chemotherapy [4]. When the interim analysis explored that the disease-free survival among women who had been randomised to chemotherapy plus trastuzumab showed statistically significant improvement compared to women randomised to chemotherapy alone, a decision was made to communicate the findings in writing to all participants. The patient letter included also the recommendation that women on the control arm should be offered trastuzumab if they had completed chemotherapy within six months [5].

In the trastuzumab trial, the decision to share research results with participants was entirely governed by the principle of beneficence, meaning that promoting the well-being of women whose treatment might change based on the research findings enjoyed preference. The disclosure decision was in accordance with the recommendation of the US National Consensus Conference on Clinical Trials in 2000, which suggested that providing the results to trial participants be considered the ethical norm [6]. As no routine procedure on disclosing results had previously been worked out, the information given to participants of trastuzumab trial focused essentially on one of the main goals of biomedicine, saving lives, thus the option of rejecting results was not offered to participants. However, a study conducted four years later to examine the effect of disclosure of results in the trastuzumab trial highlighted that not all participants wanted to get the research results. Some others mentioned that they would have valued to get the offer of disclosure first, and in this way, they could have made a decision about acceptance or rejection [5]. These findings have drawn the attention of researchers that other aspects than only the principle of beneficence should be taken into account through the disclosure process.

The perspective of the debate has further been widened by those theoretical articles that discuss the ethical problems of the disclosure of research results by using a framework different to the beneficence-based assessment. Conrad Fernandez, in his often-cited article, gives an interpretation of the issue [7], which goes far beyond the scope of the four principles of biomedical ethics (respect for autonomy, beneficence, non-maleficence and justice) [8], as he evaluates the lack of disclosure

of results to research participants as "betrayal". In the hypothetical case history of Fernandez, a 33-year-old woman noticed a slowly growing mass in her breast. Medical examination confirmed she had breast cancer, which had formed metastases to lungs and bone. The patient had Hodgkin's disease at age 14 and received radiation therapy as part of medical research. After reaching her maturity, she had no further contact with the paediatric clinic where her follow-up had happened. Long-term follow-up studies showed that there was an approximately 30-fold increase in risk of breast cancer in those who had received radiation therapy in the research. The patient became upset and angry that she had never been informed of these findings and felt "betrayed" [7].

In the analysis of this case history, the author refers not only to the rational part of ethics e.g. that non-disclosure can cause harm and disseminating medical knowledge only among professionals may limit the maximisation of good produced by biomedical research, but to the emotional aspect of morality as well. By addressing non-disclosure as betrayal, the extremely vulnerable nature of trust between participants and researchers, and between patients and doctors is also highlighted. The inclusion of the aspects of emotion and social relationship into the debate is again questioned the exclusive relevance of the beneficence-based approach, which promotes the disclosure of only those clinical trial findings that can directly benefit the health of the participant. Owing to practical experiences and theoretical efforts, the scope of the debate has widened, and the question has been raised whether disclosing research results to participants is a universal duty.

III. Different positions in the debate on disclosure

The articles dealing with the problem of returning research results to participants embrace three large fields of biomedical research, such as fundamental, translational and clinical research. Researchers belonging to these divergent territories of scientific research are expected to take a stand on the issue whether similarly to informed consent prior to research, disclosure of results to participants after the completion of research should be regarded as an essential part of biomedical trials. The post-trial information can be provided in the form of aggregate research result, which is a summary of overall study findings drawn from the population of research participants, or in the form of

individual research result, which is a research finding regarding the person herself. When the individual research result contains information having direct consequences on the health of the participant herself, it is required to provide it through a face-to-face communication [9, 10].

A. Disclosure as an ethical imperative

One position in the debate of disclosure contends that disclosing research results to participants should be considered as an ethical imperative, which derives from the principle of respect for persons. The most prominent representative of this view is the above-mentioned Conrad Fernandez, who believes that the disclosure of research results can uphold the requirement that participants should be treated as more than a means to a scientific end. By disclosure, it is possible to diminish the chance that participants may feel exploited during the research process [7]. As respect does not end with pre-trial informed consent, sharing results with participants comes from the commitment of showing respect for persons through the whole research process.

In this approach, the duty of disclosure is deemed universal also in the sense that not only investigators of clinical trials but all investigators are expected to offer to provide a summary of research results on completion of their study. Investigators owe a debt to research participants since, for example during clinical trials, participants are exposed to risks that they must assume; in genomic trials, participants provide tissues that possess their personal and private characteristics [11]. For their altruistic contribution, all participants deserve the possibility of getting information on research results because the disclosure can demonstrate reciprocity and effectively express appreciation [12]. Fernandez and his colleagues declare: "There are no conditions under which an offer of disclosure of research results should not be made" [7]. This opinion is objected by experts of medical genetics, who point out that fundamental research results in the field of genetics are not understandable or significant for participants since exploratory genetic factors have not yet reached the point of general clinical acceptance [3]. However, it should be mentioned that in this conception special attention is paid for those who cannot benefit directly from research (e.g. participants of fundamental research), claiming that the gesture of returning research results can help

acknowledge their contribution to the development of scientific knowledge and can raise their self-esteem.

It is noteworthy that, in this concept, universal duty refers to the offer of disclosure of research results and not to the disclosure itself. Making a distinction between the offer of disclosure and the realisation of disclosure is demanded by the principle of respect for persons, which claims that the decision of participants about the rejection of getting results should be accepted. Thus, in this view, it is mandatory for the researcher to offer the disclosure of results, but it is not mandatory for the participant to accept this offer.

Besides the principled approach, utilitarian arguments can also justify the duty of disclosing research results as disclosure can provide benefit for the individual (increased self-esteem, improved health), for the community (raised public awareness of science), and for the researcher (enhanced public trust). Although the possible negative psychological, social and economic impacts of disclosure and the logistic problems (what, when, who, by whom to be informed) have been revealed, the supporters of this view assess these problems as pragmatic, which can be overcome by well-designed research projects. As David Resnik notes, the demand of respect for persons outweighs the obligations of preventing harm or saving financial resources. However, in well-designed research projects investigators are aware of the possibility of negative consequences and this awareness helps them to develop strategies to minimise risk. This precautionary approach includes counselling, psychological support and medical follow-up strategies [13].

B. Disclosure as a prima facie duty

Another approach, elucidated mainly by Annelien Bredenoord and her colleagues, accepts the disclosure of research results as a moral duty, but this duty is perceived as *prima facie*, i.e. a duty that must be fulfilled unless it conflicts with an equal or a stronger duty [14]. The idea of prima facie duty, elaborated by W. D. Ross, is not unknown in biomedicine as the four principles of biomedical ethics represent this type of obligation [8]. Prima facie duties are always binding if they constitute single duties, but in the case of their conflicts, it is possible to choose the most stringent among them. However, the infringement of a prima facie duty leaves guilty conscience. By interpreting disclosure as

a prima facie duty, researchers can gain a middle position between the universal duty of disclosure and the total rejection of the duty to disclose, which makes them possible to adjust disclosure policy to the context [15].

To justify the duty of disclosure, this position alludes to the principles of respect for autonomy and beneficence. Respect for autonomy obligates researchers to return research data if participants wish to receive these. Respect for autonomy is defined in a broad sense, not only non-interference is included in its meaning but also the idea of fostering individuals' capacity of being capable of controlling their own lives and living according to their own values. It is recognised that if beneficence is completed with respect for autonomy, these principles together can give ground for the disclosure of wide range of research results, not only to data of immediate clinical relevance [14].

However, the richness of research results may cause difficulties for both participants and researchers. For example, selecting among the wide range of research findings can be too demanding for participants. They need counselling to make their decision and later they need psychological support or follow-up to cope with the awareness of research results. Result disclosure may have negative consequences and can cause harm for participants. Furthermore, the disclosure of huge amount of data can be too demanding for researchers as well since they should make efforts to communicate the findings in an understandable way, to help participants comprehend the information, and to promote the participants' adequate selection among research data. The practical problems of disclosing research results may impose unmanageable burden on researchers and on the research infrastructure. The financial, occupational, psychosocial burdens posed by the duty of disclosing wide range or the full spectrum of research results can be so enormous that it threatens the execution of the original aim, the conduction of research [14].

Perceiving disclosure of research results as a prima facie duty offers solution for the problem as the duty of disclosing results can be subordinated to the more stringent duty, to the duty of performing research, which constitutes the fundamental professional obligation of a researcher. First, it is possible to take into consideration the circumstances (capabilities of researchers, limits of financial resources, capacities of laboratories, etc.) and then make a selection about what

research results to be disclosed [16]. Bredenoord notes that "In the ideal world, researchers would offer disclosure of all data if participants wish so, but in reality, individual benefits have to be balanced against societal benefits" [14]. Since offering full data disclosure is currently not realistic, in research programs where the disclosure policy is applied, generally life-saving data and data of immediate or potential clinical utility are communicated. Future contextual changes can make possible to widen the scope of result disclosure, e.g. to share data of reproductive, personal or recreational significance with participants.

C. Disclosure as a consideration

In the third type of view, the universal duty of disclosing research results to participants is questioned by researchers contending that respect for persons, beneficence, reciprocity and justice can be served by other means than disclosure. Some alternative actions are mentioned such as conducting formal ceremonies, arranging post-trial access to new medication, or planning experiments to study the special problems of the group from which participants have been recruited [17]. Based on the conviction that the above-mentioned principles cannot effectively justify disclosure as a universal duty, in this opposing view, disclosure is perceived only as a consideration [17-19].

A further element of criticism refers to the phenomenon that the ethically relevant distinction between research practice and clinical care may be blurred if the full disclosure or the individualised disclosure of research results are universally required. The disclosure practice can strengthen the therapeutic misconception, the mistaken belief that therapy and research are governed by the same primary purpose: to promote the best interest of the individual [20]. Therapeutic misconception leads to a major ethical problem in biomedical research because some participants join a research project with the false belief that it will benefit them personally. However, the goal of research is to create generalisable knowledge, and research does not focus on the optimal health care of individuals [21]. During research, participants can justifiably be exposed to risks, for example when the efficacy and side effects of an experimental therapy are not fully known, while during medical care, causing this type of risk is hardly acceptable. The therapeutic misconception can result in the overestimation of the clinical significance of research findings, which can lead to participants'

disappointment and erosion of trust in research, namely, to the very contrary for which the disclosure of research results has been implemented.

Another difference between research and clinical care appears in the access of health data. While in clinical care, respect for autonomy mandates patients to have a high-level access to their own health data, in research, the participants' access to their health data explored by the researcher is not only influenced by the wishes of the participants but also by the special features of the research process itself. Since disclosure of results is regarded as a part of research, plans about what and how to disclose should be submitted to a research review board that can give an ethical approval for the outset of a research project. Thus, ethics review boards have the authority to control individuals' access to information about themselves, but this kind of authority cannot exist in relation to clinical care [22]. The divergent nature of research data, compared to health care data, has made profoundly important to determine what to disclose after the completion of research. Fiona Miller, a strong opponent of treating disclosure as universal duty, poses the more generic issue of what counts as a precise definition of research results. To eliminate the confusion about the notion of research results, she demands to make "clearer conceptual distinctions between aggregate and individual results, amongst different types of research, and across different degrees of result veracity". In her view, without a clear definition of what counts as a research result, no consensus can be reached on what should be disclosed [23].

Currently, various types of research results are communicated to participants e.g. aggregate or individual, targeted or incidental, peer-reviewed or non-peer-reviewed, clinically valid or scientifically valid, clinically actionable or clinically non-actionable, etc. The inconsistent practice and the lack of theoretical clarification have motivated some scholars to declare that the implementation of disclosing research results as a universal duty is premature [23, 24].

IV. Consequences of the lack of consensus - Concluding remarks

Although no consensus has been reached in the debate yet, owing to the rapidly increasing number of publications on the duty of disclosing research results to participants, it seems unavoidable to address the

issue of disclosure in every research project. In research plans, where the disclosure policy is not accepted, good reasons should be given for its rejection.

The need to close the debate on the duty of disclosure and to begin to elaborate an adequate disclosure practice has been expressed by researchers [25]. Over the years, a strong agreement has been formed on the key elements of disclosure practice. The main points of agreement comprise that 1) the issue of disclosure should be involved in the pre-trial informed consent process; 2) disclosure should include a two-step procedure (offer plus disclosure) with the opportunity of refusal; 3) research review boards should make decisions about what to disclose; 4) sponsors and patient support groups should be involved in the implementation; 5) educational and psychosocial support may be necessary for participants [26, 27]. In sum, the avoidance of intuitive decision-making and the execution of careful planning are required from researchers through the implementation of disclosure.

The decade-long debate on disclosing research results has efficiently directed the attention of researchers to the importance of maintaining respect for participants through the whole research process. It has also helped scientists recognise the role of disclosing research results to participants in the process of democratising scientific knowledge. Although, the debate has remained unsettled, the aspects of disclosure cannot be ignored by researchers in the future.

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