Reporting actionable genetic findings to research participants

Recommendations developed by the Swiss Personalised Health Network

ELSI Advisory Group – February 2020

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1. Background

This document contains recommendations to ensure ethically responsible handling of primary and secondary genetic research findings that have potential medical relevance for individual research participants involved in SPHN-funded studies.
This document only addresses findings in genetic research. Findings of medical relevance to research participants are also common in other types of health research. For incidental findings in imaging, the swissethics report “Richtlinie zum Umgang mit Zufallsbefunden in der medizinischen Forschung” can be consulted.1

The aim of these recommendations is to raise awareness in SPHN-grantees about the medical and ethical importance of defining a clear strategy for reporting of research findings to research participants. At the same time, they offer concrete indications about how to meet the ethical obligations of researchers towards research participants. Adherence to the recommendations presented here will promote more harmonized and accountable decisions in this ethically sensitive issue and will increase public trust in SPHN as well as in SPHN-grantees.

These recommendations align with existing regulatory provisions on this subject. They also have taken into account the current template of the General Consent (version 2.0 of February 2019). While these guidelines suggest specific measures on reporting genetic findings, they do not prescribe specific implementation strategies nor do they serve as a compliance tool. Funded institutions and research groups will be responsible for effective implementation of the recommendations by asking researchers to adhere to these recommendations. Institutions can decide themselves if they wish to develop additional tools to enable and monitor compliance with these guidelines.2

[1] Guidelines for reporting research findings not stemming from genetic or imaging techniques are focus of another report in the future.
[2] As a reference for the consent template, swissethics can be consulted.

2. Ethical Principles

Responsibilities of medical researchers are laid down in professional codes of conduct, such as the World Medical Association's Helsinki Declaration (1964, revised for the 7th time in 2013) or CIOMS' International Ethical Guidelines for Health-related Research Involving Humans (1982, 4th version 2016). Those professional responsibilities and moral duties of medical researchers partly overlap with those of physicians – because oftentimes those who conduct health research are also medical doctors, and those who participate in research studies are patients.

In both medical ethics and research ethics emphasis is on not doing harm (often referred to as non-maleficence) to patients or research participants respectively. When it comes to the moral obligation to actively promote health (or beneficence), it is not only physicians who have the medical duty to promote the wellbeing of patients – as enshrined in medical ethics codes since antiquity – but also researchers have a general human responsibility towards their research participants. Specifically, with regard to reporting research findings, the moral principle of duty to rescue applies: It stipulates that one should be held responsible for failing to prevent injury or death of another party when this could be achieved without disproportionate effort or unreasonable risk. Failing to provide life-saving information to research participants that is easy to generate or has been accidentally generated clearly configures a violation of such principle.

Providing general research results, as well as individual findings to research participants, is moreover regarded as a way of acknowledging their fundamental role in scientific research, to reward their participation, and especially their propensity to face risks and discomfort out of an altruistic motivation to contribute to medical knowledge for the benefit of future patients. The underlying ethical virtues of this aforementioned view are reciprocity, respect, transparency and trust.

A last ethical rationale for communicating individual findings to research participants is that it promotes their autonomy and considers them to be in charge of their health-related choices.

3. Recommendations

1. General research results should be sufficiently disseminated through both academic publications and lay summaries in accessible language. Newsletters, flyers or leaflets (including in electronic form) can be used to effectively communicate general results.

2. Research participants have the right to decline information about their individual genetic findings (primary or secondary, incidental or non-incidental). This right is based on the principle of autonomy, and is often called the “right not to know”. However, whether the right not to know applies should be determined by carefully evaluating the possible consequences people could incur if they do not receive the relevant findings. A tension arises in these instances: on the one hand, the duty to promote the health and best interest of the research participant; on the other hand, the duty to accept the participant’s autonomy-based wish to decline medically relevant information. SPHN-grantees should promote health for participants by communicating to them all medically relevant genetic findings (see Point 19 on page 7). For this reason, SPHN recommends excluding prospective participants who do not want to receive individual, medically-relevant information. Since participants do not benefit directly by participating in a research study (at least not in studies generally envisaged by SPHN), it is justified and not discriminatory to exclude prospective participants who do not want to receive individual genetic findings. Exceptions can be made, however, on a case-by-case basis.

3. Informed consent forms shall carefully explain the possibility that medically relevant findings could be generated during the study and fully disclose the options that research participants have in terms of receiving such findings, including the possibility to forego such information and the consequences of such decisions.

4. Preferences expressed through informed consent by research participants as to how they want to be recontacted with medically relevant information produced in the course of an SPHN-funded study should be respected. However, exceptions could be envisaged as in the case of findings that are of relevance to third parties, for instance, family members or population health.

5. Informed consent forms shall also explain the impact that disclosure of medically relevant information can have for the individual beyond the management of their health. For instance, it should be explained that such information may need to be disclosed when applying for private insurances such as life insurance, complementary health insurance or daily sickness allowances.
6. Appropriate measures shall be taken to ensure that all information regarding reporting of individual genetic findings is clearly explained to prospective research participants during the consent process.

7. SPHN-funded researchers are responsible for ascertaining whether any of their research has generated medically relevant information about any individual research participant. For cases in which the medical relevance of the finding is not obvious, when the research participant is a minor or an incapacitated person, or when the findings are of relevance to third parties, the research team should consult with a Multidisciplinary Expert Panel (MEP) (see point 17 below). Some institutions that could potentially receive SPHN funding already avail themselves of such bodies.

8. Application templates for SPHN funding should include a section in which the Principal Investigator discusses the likelihood that the project will generate medically relevant findings (both primary and secondary), how they will be documented, and how they plan to report them to participants and/or relatives.

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What?

This section of the recommendations offers clarifications regarding specific types of individual genetic findings.

9. From an ethical standpoint, it is equally compelling to report findings of medical significance, independently of the way in which, or the reason why, they have been generated. Therefore, the recommendations apply to both primary and secondary genetic findings. Primary genetic findings are genetic variants uncovered by means of any type of genotyping or sequencing technique (such as for instance PCR, microarray analysis, genome sequencing) that are related to the primary purpose of the research protocol. Secondary genetic findings are genetic variants uncovered in a study participant but unrelated to the primary purpose of the research protocol.

10. Pathogenic variants for which preventive or therapeutic measures are available are said to have clinical utility. They present the strongest ethical rationale for being reported to research participants.

11. There is a very strong ethical (beneficence-based) rationale for reporting highly penetrant genetic variants associated with a disease or pathological condition, so that affected individuals can receive appropriate medical care and take personal decisions regarding the medical as well as practical management of their condition.

12. Knowledge about a given genetic mutation, such as carrier status for a recessive Mendelian disorder, while not affecting the health of carriers themselves, is likely to affect third parties, for example, their progeny (third-party utility). Since this information can be taken into account in the course of reproductive decisions, there is an ethical rationale to disclose this type of information to research participants.

13. Information about variants linked to conditions that are not preventable or curable, does not have clinical utility, but it still has personal utility. Individuals may be able to make practical arrangements to better cope with such conditions.

14. Variants of unknown significance should not be reported to research participants unless the participant explicitly requests to know about them. In such cases clear information about the uncertainty of the variant should be provided.

15. Current techniques, such as exome or genome sequencing, consider large numbers of genes in the course of one single study. As a result, these techniques are likely to generate potentially useful information about pathogenic DNA variants for a fraction of study participants. Whenever any such variant is detected, research participants are entitled to be informed if they choose to be informed during informed consent. However, researchers are not expected to actively look for medically relevant variants.

16. Specific decisions as to which genetic variants should be reported shall take into account the severity of the condition; the existence of preventive, therapeutic and palliative options; the relevance of the variant for the progeny of the research participant; and the personal utility of knowing about a given mutation, even if this is linked to a non-curable disease.

How?

Research institutions hosting SPHN-funded projects should establish clear procedures for reporting medically relevant genetic findings to research participants. This should involve all necessary organizational arrangements. The following points need to be considered:

17. Applications for SPHN funding should indicate the composition and the mandate of an MEP whenever a project is expected to generate genetic findings that could be medically relevant. Members of such MEPs shall cover relevant scientific and medical specialties, e.g. a specialist of the disease(s) of interest, a patient representative, a medical geneticist, if possible a genetic counsellor, and an expert in bioethics among others.

18. Findings should be communicated as soon as possible to research participants following validation by an officially certified clinical-grade laboratory. Only such laboratories can ensure the accuracy of the test result. Validation costs for findings should be covered by the research budget or by an independent hospital fund. If researchers anticipate reporting of findings, the validation costs of such findings have to be budgeted for in the proposal for SPHN funding.

19. Communication of individual research findings should be performed by either a physician designated upon enrollment by the research participant (at the moment of informed consent), or by specialized medical personnel.

20. The following communication best practices should be followed:
    - SPHN researchers will communicate individual genetic findings to a designated physician or medical professional. The designated physician or medical professional will then report the findings to the research participant. Given that a research participant's life circumstances or preferences might have changed with time, the medical personnel should always ask the participant if he or she still wants the content of the findings to be disclosed to him or her.

    - The communication process should take into due account both the psychological and the social consequences of receiving genetic information (e.g. anxiety, risk of stigmatization); the significance and consequences of the information should be presented in an understandable way; privacy and confidentiality should be ensured; instructions and appropriate medical advice regarding any available therapeutic option, as well the availability of psychological support should be clearly communicated.

        - In case of minors: if information is actionable during childhood, it must be reported to the parents or legal guardians. For adult onset or any other findings, the MEP should specify a plan for disclosing these findings to parents or legal guardians and the patient.

        - In case of incapacitated participants: access to their data should be granted when they recover capacity. For durably incapacitated participants, individual genetic findings should be communicated to their authorized representative. The authorized representatives should receive the same information that the research participant would have received, and an effort should be made to ensure that recipients understand the meaning of such information.

        - In case of deceased participants: if individual genetic findings related to a deceased participant are relevant for family members, such information shall be communicated to family members if they consent.