Genome sequencing in research requires a new approach to consent

A one-off paper-based consent form is not necessarily the best solution when it comes to obtaining consent from research participants for genome sequencing.

A dynamic consent process that allows continuous interaction between researchers and research participants is preferable, particularly in scenarios where it may be appropriate to inform participants about the results of genetic testing.

Genome sequencing technologies make it possible to map the entire genetic make-up (DNA sequence) of a human being. Such technologies are used increasingly in medical research, including to study cancer (1). There is debate over the extent to which research participants should be informed about individual results from genetic research (2, 3). In projects where such feedback might be appropriate, modernisation of the consent process may be required.

Informed consent in research

As specified in the EU's Data Protection Directive (4), the use of health-related and other personal data requires consent or an alternative legal foundation, such as statutory authorisation. In accordance with the Declaration of Helsinki (5), the Health Research Act (6) and in some cases also the Biotechnology Act (7), the subject on whom research is conducted must consent to participation in the research.

This consent must be informed, voluntary, explicit and verifiable (6). The consent form is typically accompanied by paper-based patient information that provides insight into the purpose of the project, possible benefits and drawbacks of participation, and procedures for the use of research data. Usually, the consent process is a one-off procedure that takes place during recruitment of research subjects. Healthcare professionals review the information and consent form together with the research participant, explain any difficult concepts, answer any questions, and allow the research participant thinking time before s/he signs the consent form.

The use of one-off paper-based consent forms is an integral part of current research practice and is accepted by ethical approval authorities. There are, however, at least five reasons why this type of traditional consent is inadequate for research projects involving genome sequencing, especially when feedback of research results may be appropriate.

Complex information

Research participants may have difficulty understanding the content of the consent form, or be unable to remember what they have consented to, especially when the form is several pages long (8). This can be particularly challenging for patients with poor mastery of Norwegian and for individuals such as cancer patients, who already struggle to understand the complex information they are given about their disease and the personal consequences it may have. For the research participant to gain a real understanding of what she or he is agreeing to, the consent form must be short, clear, simple and concisely formulated.

In projects using genome sequencing, the challenge lies in the fact that complex information, which could be of great importance for the research participant, must be conveyed. For example, concepts that cannot be regarded as common knowledge, such as «genome», «gene variant», «biomarker» and «genetic predisposition to disease», must be explained. In addition, the consent form must provide information about which types of genetic findings it may be appropriate to inform the participant about, and the possible implications of these findings for the participant's health. Even though some genetic variants may convey a high risk of developing a disease, whether this risk will become a reality will remain uncertain. It is challenging to convey such uncertainty in the consent form in a concise and also precise manner without creating unnecessary anxiety for the participant.

«Dynamic consent can lead to greater participant engagement»

Need for regular information exchange

Although health professionals can explain some of these issues to the research participant during the consent conversation, there is often not enough time available to obtain a satisfactory picture of the participant's understanding of health-related information (9).

Furthermore, it is likely that both this understanding of the implications and their possible consequences will change over time. It may be necessary to repeat information, provide more or less detailed information at different stages of the project, or adjust the information in line with the research participant's needs and health status and changes to the project. This may be difficult to achieve when the consent process takes place only at recruitment and is based on conveying all relevant information on a piece of paper and through a brief conversation.

Resource-intensive collection

It may be necessary to obtain renewed consent from the research participant in the course of the project. This could occur, for example, if the researcher has information about genetic variants that were of unknown significance at the start of the project, meaning that there was no reason to inform participants about them, but which are subsequently shown by new research to have health implications.

It may also be necessary to check whether the research participant's views regarding the feedback of individual genetic results have changed over time, for example as a consequence of their health status. Obtaining new paper-based consent whenever such needs arise can be cumbersome and costly for researchers.

Because of the costs involved in genome sequencing, it is also likely that researchers will want to reuse genetic information obtained in research to answer new questions that they could not foresee at the start of the project. Obtaining renewed paper-based consent for new project goals and keeping an administrative overview of the consents may consume increasingly scarce research resources.

Desire for more user engagement

Traditionally, research participants have had a rather passive role in the research process. They agree to the use of their blood or tissue sample for research, and can usually expect little further involvement in the project. Such a scenario is not very consistent with the health authorities' desire to increase user engagement in health research (10).

Lack of oversight

It is difficult to have institutional oversight over consents when they are collected on paper at the start of the project, and then stored in cupboards or boxes for years, although forms are now increasingly being scanned and stored electronically. At the same time, it can be difficult for research participants to remember what they have consented to,

and how their health information and biological material are being used in research.

Dynamic consent

Dynamic consent is a new approach to the consent process that aims to place the research participant at the centre of the decision-making process (11). Dynamic consent entails two-way digital communication that enables the research participant to regularly make new choices, for example agreeing to new uses of research data or feedback of new types of genetic results, and to change these choices over time (11). The information content can be tailored to the research participant's needs regarding issues that s/he wishes to have explained more thoroughly, and results that s/he wishes/does not wish to be informed about. Basic information can be provided at the start of the project, and more detailed information added as meaningful genetic data are obtained (12).

The purpose of such a solution is not to replace human contact or deny participants the opportunity to discuss the consent process with and receive genetic counselling from health professionals face to face. It is rather to make the consent process straightforward and more interactive and ongoing, thereby leading to better dialogue and greater reflection. Dynamic consent can help to maintain participants' interest and willingness to participate over time because they feel they are being treated as fully-fledged partners rather than reduced to one-off contributors.

National solution

Use of dynamic consent is being tested in several research projects (11, 13, 14), also in Norway (15). There is a need to determine which models of dynamic consent may be appropriate for Norwegian health research, and also to identify the ethical, legal and economic implications of adopting dynamic consent, preferably in dialogue with the research ethics committees. For example, it is unclear whether electronic consent is legally sufficient in cases where the law stipulates that written consent is required (7). It is also important to consider under what conditions dynamic consent solutions can satisfy the informational requirements for valid consent. Furthermore, we must work out how to ensure that dynamic consent is used as intended, and not misused to render the consent process a mere formality.

One possible strategy for the future may be to create a national IT-based system for dynamic consent that offers a basic structure that conforms to legal requirements and that includes practical solutions for withdrawing consent. It should also include essential links, such as to the Regional Committees for Medical and Health Research Ethics (REK) and to registers by which patients can express preferences regarding the use of their biological material in research («Biologisk forskningsreservasjon» in Norway). Such a national system could provide a single portal for the research participant and simultaneously be tailored to the needs of each and every project, in line with their aims, participant group and plans regarding feedback of genetic findings.

In the Norwegian Cancer Genomics Consortium (16), work is underway to identify

«The information content can be tailored to the research participant's needs»

appropriate models for dynamic consent. There is little doubt that the time is ripe for innovation regarding consent procedures in medical research, especially when new technologies such as genome sequencing are used. Dynamic consent can lead to greater participant engagement, better oversight for all parties, and a new form of long-term partnership between researchers and research participants.

We wish to thank Professor Dag Wiese Schartum (Dr.juris), Norwegian Research Centre for Computers and Law, Faculty of Law, University of Oslo, for his comments.

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Received 7 September 2015, first revision submitted 21 October 2015, accepted 6 November 2015. Editor: Kari Tveito.