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Opportunities, Risks, and Limitations of Genetic Testing: Looking to the Future From Patients' Point of View

In this issue of *Mayo Clinic Proceedings*, 2 contributions discuss the present and future challenges of innovative genetic testing services. An original research article by Lindor et al¹ presents an exploratory enquiry on the clinical implementation of whole-exome sequencing in a group of medically trained volunteers. A commentary by Oliveri et al² focuses on direct-to-consumer genetic testing, providing a critical discussion of the implications of this practice on downstream patient experiences.

Genome- and exome-sequencing technology has advanced at an extremely fast pace, from a mere futuristic prospect, to early implementations in case studies, to the verge of mainstream commercialization.³ Such rapid developments have also raised considerable ethical and regulatory concerns regarding access to and use of these services.⁴ There is no doubt that these techniques have greatly improved the accessibility of information regarding individuals' pathogenic gene mutations that may lead to future health conditions. Widespread availability of such information might radically change preventive medicine, allowing patients and health care professionals to anticipate certain diseases years before their potential onset. A current limitation of this kind of services is the small number of known disease-causing and disease-modulating mutations^{5,6}; however, the number is very likely to increase greatly in the coming years, as genetic and clinical research continue accumulating new evidence. Other limitations, such as the need for highly resource-intensive curation and analysis of raw data (and the associated costs), are also likely to be addressed by technological innovations and incremental refinements of the procedures.

As contributions by Lindor et al¹ and Oliveri et al² correctly point out, however, this field of research and clinical practice faces another crucial, yet currently underestimated, challenge. Advances in genetic testing services should be not only a way to increase our knowledge of individuals' susceptibility to future health conditions, but also a way to empower health care professionals and prospective patients, facilitating their decisions regarding their future welfare and quality of life. Deepening our understanding of patients' decision-making processes might therefore be as useful as finding new ways to scrutinize their genome. To do so, we have to consider several factors that constitute what Oliveri et al define as the patient's "individual experience,"² which reflects his or her individual characteristics, family history, and social and personal backgrounds.

Given the novelty of genetic testing procedures and results interpretation, formal studies of patients' experiences with genetic testing, and their corresponding reactions to test results, are still limited.⁷ Furthermore, there is an important qualitative difference between patients' experiences and decision making when confronted with the results of "traditional" diagnostic testing versus whole-exome sequencing and direct-to-consumer genetic testing. In the former case, patients seek the guidance of a medical expert or specialist to interpret test results regarding an existing condition or, alternatively, to investigate susceptibility to specific diseases they are already aware of (eg, due to familiarity). In the latter case, on the contrary, healthy individuals can test for a wide range of gene mutations that are associated with several conditions that they may have never

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suspected or even heard about before. Furthermore, patients may or may not be aware that—given the evolving understanding of gene-disease associations—test results that are deemed unimportant or inconclusive today may in the future be linked to increased disease risks. Although we know reasonably well how patients deal with the results of traditional diagnostic testing results, in the case of both positive and negative results, we know far less about their impressions and responses to genetic testing results.⁸

Psychological research on decision making in several different contexts might shed some light on what individuals experience in this situation and, most importantly, it might provide us with some very useful insight into individuals' medical decision-making processes.

We know, for instance, that individuals' understanding of basic concepts related to genetic risk often deviates from ideal rationality.⁹ The mere fact of presenting results in different formats, for example, as percentages or frequencies, can result in more optimistic or pessimistic interpretations of the same data. In addition, as Oliveri et al² stress in their commentary, any numeric representation of risk is often overshadowed by personal or familiar history of disease.¹⁰ Individuals tend to read genetic test results in light of their experiences, often assimilating present situations with their own or some close relative's not necessarily similar conditions.

It is also possible that emotions play a greater and more complex role in medical decision-making processes than currently believed. Since early studies on the emotional consequences of genetic testing,^{11,12} research has focused on the psychological dimensions of well-being, anxiety, and depression as the outcomes of the decision to undergo genetic testing and of later access to results. To date, the available research has identified little or no negative emotional effects in the case of genetic testing for specific diseases (eg, Huntington disease, hereditary breast and ovarian cancer, and other types of cancer).¹³ Most current psychological models of health-related behavior, however, consider emotions not only as the *outcomes* of decisions but also as sometimes very powerful *motivating factors* in the decision-making process. Emotions can therefore influence individuals' intention to undergo testing and their willingness to

adopt the necessary therapy regimens or lifestyle changes once the results are known. Therefore, we should not always assume that increased knowledge of one's susceptibility to future conditions is a sufficient motivation to undergo genetic testing.

In the study by Lindor et al,¹ most participants reported being motivated to participate by scientific curiosity and perceived professional duty to contribute to research in this area. Individuals in the general population, however, probably have very different priorities when they contemplate the possibility of having genetic tests performed on themselves. Laboratories and medical facilities will often have to deal with prospective patients motivated by preoccupation, apprehension, and fear, rather than mere curiosity. These emotions might lead some individuals to undergo unnecessary diagnostic procedures or, conversely, can lead others to avoid appropriate ones. A perceived lack of control over the wide range of conditions detectable by genetic tests can induce certain individuals to miscalculate the potential costs associated with exploring the meaning of positive genetic testing results, as well as the potential benefits and detriment of those explorations (eg, disease confirmation vs the costs and adverse effects of unnecessary testing and procedures). Research on health communication, however, has provided extensive evidence of how cost-benefit assessments can be influenced by several external factors, for instance, by the way messages promoting diagnostic and preventive behaviors are framed.¹⁴ Effective communication and counseling can therefore contribute to patients' ability to make informed decisions, formulate realistic expectations, and use the information obtained through genetic testing to prepare for future health conditions and adapt their lifestyle accordingly. In this sense, the new genetic testing techniques paired with carefully adjusted and developed counseling protocols can really advance preventive medicine, not only telling patients what to expect from the future but also putting them in the position to actively improve their health.

Contributions from Lindor et al¹ and Oliveri et al² in this issue of *Mayo Clinic Proceedings* provide a critical point of view on the future of this innovative research area. As genetic testing techniques will likely become increasingly

accessible to the general public, medical and psychological researchers will have more and more opportunities to collect data on actual patients' experiences with them. Well-established theories and hypotheses emanating from the disciplines of cognitive and health psychology may be tested in this specific context, and they may be refined as a result of observations made in the field by physicians, genetic counselors, and medical geneticists. An increased availability of empirical data may, in turn, help health care professionals in their practice. Interviews and open-ended responses of participants in the study by Lindor et al clearly stressed the importance of appropriate counseling in all the phases of genetic testing, from initial interest in the procedure, to discussion of one's expectations regarding the results, to their final disclosure and dissemination (particularly to relatives and family members who may take part in, or be affected by, patients' decisions regarding their health). In the case of direct-to-consumer genetic testing, as Oliveri et al² argue, counseling is further complicated by the lack of a proper face-to-face interaction between the patient and a specialist. In general, these kinds of services should be designed in a way that allows individuals accessing them to receive all the information they need to understand the results and make informed decisions regarding their potential implications on their health and lifestyle. There have already been some efforts to regulate in this sense the developing genetic testing market, but once again we should not forget the importance of the users' point of view. Realistic and responsible communication about the opportunities, limitations, and risks of genetic testing services can effectively shape potential users' expectations regarding them. If we take these perspectives into consideration when researching, designing, discussing, and administering these new types of genetic tests, potential users will expect them to be not only extremely sophisticated (and expensive) fortune-telling machines, but also powerful and empowering tools to prevent

diseases and improve their future health and well-being.

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