Editorial

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Personalized Medicine

Family-level impact of genetic testing: integrating health economics and ethical, legal, and social implications

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"We discuss approaches to considering family impacts in genetics and genomics and suggest ways to achieve the more meaningful integration of ELSI and health economics that is required to understand the full value of clinical genetic testing interventions."

Tweetable abstract: Health economics and ELSI can be better integrated to consider the family impacts of genetic and genomic testing.

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Family-level implications are important to consider when assessing the health and economic outcomes of genetic testing and while examining the ethical, legal and social implications (ELSI) of genetics and genomics [1–3]. Health economics and ELSI are two distinct yet complementary fields of research that aim to understand the impact of genetic testing on patients, families, the healthcare system, and society. The field of ELSI research is primarily used to guide clinical decision-making and ethical implementation of genetic testing, while health economics is used to inform resource allocation decisions and policy. Given the significance and nuance of familial considerations in genetic testing, collaboration between these two fields is necessary to accurately evaluate the full range of costs, benefits, and harms. We discuss approaches to considering family impacts in genetics and genomics and suggest ways to achieve the more meaningful integration of ELSI and health economics that is required to understand the full value of clinical genetic testing interventions.

Family impacts from an ELSI perspective

ELSI is a multidisciplinary research field, bringing together expertise in philosophy, medicine, law, social sciences and public health. Lines of ELSI research employ normative analysis to determine which impacts of genetic testing should be evaluated [4], as well as qualitative and survey research to understand and measure psychosocial impacts of testing from the patient's and/or family's perspective [5].

ELSI scholars use the term utility to refer to the balance of benefits and harms associated with a clinical intervention. In the context of genetic testing, the term utility is used to convey the usefulness of test results to the clinician, patient or family. Discussions of the value of genetic testing have centered around clinical utility, meaning the establishment of a diagnosis leading to improved health outcomes. However, more recently, the concept of clinical utility has been expanded to recognize the value of the full range of impacts of a genetic test. For example, the American College of Medical Genetics and Genomics now defines clinical utility broadly to include both health and psychological benefits for the patient and family, as well as an accounting of the "value a diagnosis can bring to the individual, the family and society in general" [6]. This expanded definition of clinical utility may

include aspects of what has been referred to as the personal utility of genetic testing, meaning the well-documented non-clinical effects on patients and families. Examples of non-clinical impacts include enhanced peace of mind and ability to cope, increased self knowledge, ability to use information gained from testing to plan, and potential for discrimination [3,7,8].

Family impacts from a health economics perspective

Health economists weigh the costs versus benefits of genetic testing to assess its economic value to the healthcare system and society. When assessing the benefits of genetic testing, economic evaluation guidelines recommend that studies include all health effects that accrue to both patients and family members [9]. However, this is rarely done in practice. When family effects of genetic testing have been considered in economic evaluations, it has typically been through the inclusion of cascade screening effects. Cascade screening is the process of testing patients' biologic relatives to determine whether they carry the same genetic variant that increases disease risk. Based on the hypothesis that targeted screening of relatives is more cost-effective than population-wide screening and allows for early detection and intervention to avert downstream health costs, cascade screening has figured prominently into the value proposition for genomic medicine [10,11].

Effects of cascade screening on relatives' health can be incorporated using standard approaches to utility measurement in health economics. Health economists have traditionally defined utility in a narrow way, focusing only on health-related quality of life (QoL). For both patients and tested relatives, impacts on QOL and survival can be incorporated into evaluations through quality-adjusted life years (QALYs). QALYs reflect the number of years a person lives, with each year assigned a health-related QOL weight or utility value. For example, genetic testing that detects a *BRCA1/2* variant in a patient might lead to earlier breast cancer screening and detection in the patient's relatives and increased QALYs in both groups [12]. There is a great deal of variability in cascade screening uptake in reality, however, based on features like insurance coverage [13] that makes it challenging to include in analyses.

Additionally, families are often the caregivers for patients with suspected or diagnosed genetic conditions, a role that can negatively impact a family member's own health and wellbeing. These family spillover effects can be quantified through preference-based utility measures of either health-related or care-related QOL. However, they are rarely measured [14] or included [15] in economic evaluations, despite methodological guidance to do so [16]. Family spillovers are especially important to consider in economic evaluations of pediatric genetic testing applications, when parents typically serve as the child's primary caregiver and decision maker [17]. Yet the impact that the diagnostic odyssey and caring for a child with a genetic condition has on a parent has not been quantified or included in in previous economic evaluations of genetic testing.

Finally, despite ELSI's focus on personal utility, these effects are not conventionally included in economic evaluations. Health economists view personal utility as reflecting non-health related effects of testing, and outside of the realm of traditional economic evaluation. Their omission, however, prevents economic evaluations from reflecting the full value of genetic testing. Only a handful of studies have used methods from health economics to quantify personal utility in metrics that could be used in economic evaluation [18]. Adapting health economic valuation methods to estimate the personal utility of testing to patients and families is an important area for future research.

Integrating health economics & ELSI to better capture family-level impacts of genetic & genomic testing

While the evidence base on genetic testing is rapidly building, gaps remain in the quantification of family health effects and non-health effects, including ELSI-related considerations suitable for inclusion in economic evaluations [18]. The fields of health economics and ELSI must be better integrated to accurately account for, and assign value to, the full range of impacts of genetic testing on patients and families. There are three key aspects of moving ELSI-informed economic evaluations forward.

First, there must be more meaningful cross-disciplinary collaboration between ELSI scholars and health economists. This requires understanding how concepts of risk versus benefit have historically been conceptualized, defined and assessed in each field, including the disciplinary-specific orientations toward the construct of utility. Economic evaluation could benefit from the patient perspective on which much of ELSI scholarship has focused, and ELSI researchers could benefit from increased appreciation of the goals and methods of economic evaluation.

Second, better understanding of which genetic testing impacts are of interest to which stakeholders is required. While health economic utility assessment methods involve stakeholder preference elicitation, the far-reaching impacts of genetic testing call for broader stakeholder involvement, which has been a longstanding research emphasis within ELSI. ELSI research can inform value assessment at the family level, allowing health economists to better account for elements of value that patients and their families perceive as important. Patient and family engagement would also help shape the family-level aspects of economic evaluation design. For example, it would illuminate the genetic testing contexts in which family spillovers are substantially important enough to measure and include. Additionally, while the focus of economic evaluation is to inform population-level decision-making, inclusion of more dimensions of patient/familial preferences can increase its clinical decision-making relevance. This is key as the field of genomic medicine strives for a future with more diverse research participation and more accurate clinical application in historically under-represented populations.

Third, the full range of impacts of genetic testing must be considered in evaluations of its use. The narrow approach to utility measurement in health economics that focuses on health related QOL could be broadened to better capture dimensions of value that are important to patients and families in the context of genetic testing, including concepts associated with personal utility. This would not require development of new approaches, but rather application of existing valuation approaches to capture the full range of relevant outcomes – both within and outside of the context of medical care. Benefits and risks traditionally within the purview of ELSI could be measured using methods from health economics, allowing for inclusion of effects that would otherwise be omitted under the narrow definition of utility in health economics. This would allow ELSI considerations to be quantified and presented in a way that meets the informational needs of various decision-makers when they otherwise might not be.

Greater integration of ELSI and health economics, especially to consider family-level impacts, is crucial to strengthen the design of genetic testing evaluations. The outcomes of these evaluations have implications for access to testing through their influence on decisions about clinical uptake and insurance coverage. ELSI-informed economic evaluations that include broader dimensions of value that are important to stakeholders can support ethical clinical implementation and patient-centered evaluation of genetic testing.

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