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Estimating Preferences for Complex Health Technologies: Lessons Learned and Implications for Personalized Medicine

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ABSTRACT

We examine key study design challenges of using stated-preference methods to estimate the value of whole-genome sequencing (WGS) as a specific example of genomic testing. Assessing the value of WGS is complex because WGS provides multiple findings, some of which can be incidental in nature and unrelated to the specific health concerns that motivated the test. In addition, WGS results can include actionable findings (variants considered to be clinically useful and can be acted on), findings for which evidence for best clinical action is not available (variants considered clinically valid but do not meet as high of a standard for clinical usefulness), and findings of unknown significance. We consider three key challenges encountered in designing our national study on the value of WGS—layers of uncertainty, potential downstream consequences with endogenous aspects, and both positive and negative utility associated with testing information—and potential solutions as strategies to address these challenges. We conceptualized the decision to acquire WGS information as a series of sequential choices that are resolved separately. To determine the value of WGS information at the initial decision to undergo WGS, we used contingent valuation questions, and to elicit respondent preferences for reducing risks of health problems and the consequences of taking the steps to reduce these risks, we used a discrete-choice experiment. We conclude by considering the implications for evaluating the value of other complex health technologies that involve multiple forms of uncertainty.

Keywords: choice behavior, discrete-choice experiment, genetic testing, patient acceptance of health care, patient preference, personalized medicine.

Introduction

Genomic testing, such as whole-genome sequencing (WGS), can be used to predict future disease risk or inform treatment for present disease and for which there is growing demand from patients. Genomic testing provides an excellent example of the challenges of measuring the value of personalized health technologies in general, and WGS is an example of a test that provides more than one result for multiple diseases. As the costs of genomic testing decrease, it is possible that it will become more routine and eventually be used for general population screening. It is, however, unclear whether the benefits of the information received from genomic testing outweigh the potential harm from anxiety, unnecessary follow-up testing, and overtreatment (Table 1) [1–4].

Whether genomic testing can achieve its potential to improve patient outcomes will ultimately depend on what information patients receive and how patients and providers value and respond to test information. As noted in the Institute of Medicine report on genomic diagnostic testing [5], there is a need to evaluate how such technologies and the information they generate can best be integrated into the clinical setting to maximize patient benefit and minimize harm. Phillips et al. [6] suggest that there is a need for evidence on the value of personalized medicine technologies to inform decision making. Furthermore, the value of genomic testing needs to consider health and nonhealth benefits and the impact on downstream health services [7].

Neumann et al. [8] found that people value information from predictive tests for both medical and nonmedical decision making. People also value test information if it can alter their behavior [8]. Research in the area of diagnostic tests has found that there are multiple types of value to consider when evaluating diagnostic testing, such as value of knowing, medical value, and psychological value [9]. Lee et al. [9] suggest that methods such as discrete-choice experiments (DCEs) would be useful in isolating the value of knowing versus medical value. The value of knowing may, however, encompass other values, such as the value for the option to do something in the future when new health technologies are available. Furthermore, the value of

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Table 1 – Definitions [1–4].

Genome is the full DNA sequence of an individual (coding, noncoding, and mitochondrial DNA).
Whole-genome sequencing involves sequencing the whole genome (coding, noncoding, and mitochondrial DNA).

knowing is likely disease-specific [9], which highlights the challenges faced with tests that provide more than one result for multiple diseases, such as WGS testing.

The objective of this article was to examine key study design challenges of using stated-preference methods to estimate the value of WGS. We use WGS as a specific example of genomic testing and other personalized medicine technologies more broadly, in which the study design challenges we explore are inherent in the complexity of the decision problem. We start with a brief overview of stated preferences and methods for measuring preferences in health. We then describe how we conceptualized the problem of measuring the value of WGS as a decision, how we designed a DCE considering three challenges posed by the problem complexity, and our proposed solutions. We conclude with the limitations of our solutions, and the implications and consequences of these limitations for evaluating the value of other complex health technologies.

Estimating Patient Preferences

Patient preferences are increasingly relevant in the era of personalized medicine and patient-centered care. Patients who know and understand their preferences may experience less decisional regret, increased satisfaction, and improved communication with their health care provider [10]. Stated-preference studies quantify trade-offs that respondents are willing to accept among multiple characteristics of alternative health care interventions or technologies and can be used to estimate the value or utility of the characteristics of these interventions or technologies. Quantifying stated preferences can identify differences among individuals, or groups of individuals, and can be applied in samples of patients, care providers, or the general population. Aggregate or mean preference estimates are used to inform resource allocation or health policy decisions. Individual- or group-level preferences are relevant to clinical decision making.

Estimating Preferences for Complex Health Technologies—The Case of WGS

Although methods for measuring preferences in health have developed considerably [11–13], there remain significant study design challenges, particularly in estimating preferences for complex health technologies that could simultaneously affect multiple disease conditions, include multiple sequential or conditional risks, and occur over different time periods with varying levels of uncertainty. WGS results can include actionable findings (variants considered clinically useful and can be acted on, i.e., variants for which there are medical treatment guidelines or that are associated with preventable diseases), findings for which evidence on effective clinical action is not available (variants that are considered clinically valid but do not meet as high a standard for clinical usefulness, i.e., variants for which there is unclear medical treatment), and findings of unknown clinical significance (variants considered to have unknown or no clinical significance) [14,15]. Furthermore, elective interventions to reduce or avert the risk of health problems have their own risks (e.g., potentially serious side effects). Assessing the value of WGS information must jointly consider the potential benefits, harms, and costs associated with the findings and their short- and long-term downstream sequelae.

We consider three key challenges encountered in designing our study [16] on the value of WGS—positive and negative utility associated with testing information, layers of uncertainty, and potentially downstream consequences with endogenous aspects—and potential solutions to address these challenges. We conclude by considering the limitations of our solutions, and the implications and consequences of these limitations for evaluating the value of other complex health technologies.

The Decisions to Acquire and Act on WGS Information

We conceptualized the decision to acquire WGS information as a series of sequential choices that are assumed to be resolved separately. Untangling the decisions that link the acquisition of WGS information to outcomes is facilitated by the use of various preference-elicitation formats, each selected to deal with study design challenges related to specific decision points.

In genomics, *personal utility* is defined as the meaning and worth an individual gives to a genomic or genetic test from his or her personal perspective [17,18]. Previous research suggests that individuals, regardless of health status, value having choices about the WGS information they receive [19–22]. The initial decision to acquire WGS information involves assessing whether a broad set of uncertain outcomes, including both the WGS findings and the willingness to act on the information received, is likely to offer enough benefit to justify the cost of sequencing. We used contingent valuation (CV) questions to determine the value of WGS information at the initial decision to undergo WGS. CV is a method used to value commodities or services for which there are no market data or for which market data are uninformative about values to consumers, such as health and health care. CV surveys elicit the money-equivalent value (willingness to pay) of a specified commodity or service [23,24] and thus can be used to estimate the perceived benefit of WGS information. Figure 1 illustrates the bid structure of the CV questions in our survey to elicit willingness to pay for WGS information (experimental design and analysis details in the study by Marshall et al. [16]). The findings from our CV analysis (see Results section) highlight that a substantial proportion of the respondents did not value obtaining WGS testing information even if it were free, and for those who were interested, they were willing to pay more for actionable findings from WGS than for findings for which treatment is presently unavailable. In contrast, our DCE findings reported here focus on whether a person is willing to act on the information received.

We considered the final decision in the sequence of choices to be whether a person is willing to act on the information received—specifically, to what degree is a person willing to accept medical interventions with risks and costs, given the likelihood and severity of the health problems exposed by WGS results. There are many actions people could take in response to WGS findings. For example, they could share the information with family members, move to a location with better access to specialized health services, or alter education, employment, saving, reproductive life, or other plans. We focused on the medical actionability of WGS information to evaluate the trade-offs people are willing to accept among factors related to their genetic predisposition for health problems, and the potential downstream consequences.

We used a DCE to elicit respondent preferences for reducing risks of health problems and the consequences of taking the steps to reduce risks. Using DCEs is a systematic approach for eliciting stated preferences to quantify the relative importance that respondents assign to various characteristics of a health care service or treatment [25]. The options are described by a set of