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Valuations of Genetic Test Information for Treatable Conditions: The Case of Colorectal Cancer Screening

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ABSTRACT

Background: The value of the information that genetic testing services provide can be questioned for insurance-based health systems. The results of genetic tests oftentimes may not lead to well-defined clinical interventions; however, Lynch syndrome, a genetic mutation for which carriers are at an increased risk for colorectal cancer, can be identified through genetic testing, and meaningful health interventions are available via increased colonoscopic surveillance. Valuations of test information for such conditions ought to account for the full impact of interventions and contingent outcomes. **Objectives:** To conduct a discrete-choice experiment to elicit individuals' preferences for genetic test information. **Methods:** A Web-enabled discrete-choice experiment survey was administered to a representative sample of US residents aged 50 years and older. In addition to specifying expenditures on colonoscopies, respondents were asked to make a series of nine selections between two hypothetical genetic tests or a no-test option under the premise that a relative had Lynch syndrome. The hypothetical genetic tests were defined by the probability of developing colorectal cancer, the probability of a false-negative test result, privacy of the result, and out-of-pocket cost. A model specification identifying necessary interactions was derived from assumptions of risk behavior and the decision context and was estimated using random-parameters logit. **Results:** A total of 650 respondents were contacted, and 385 completed the survey. The monetary equivalent of test information was approximately $1800. Expenditures on colonoscopies to reduce mortality risks affected valuations. Respondents with lower income or who reported being employed significantly valued genetic tests more. **Conclusion:** Genetic testing may confer benefits through the impact of subsequent interventions on private individuals.
Keywords: colorectal cancer, discrete choice experiment, genetic testing, Lynch syndrome.

Introduction

Recent advances in molecular genetic testing technology provide individuals with opportunities to acquire information about predispositions to cancers and other diseases. Despite its promise, the merit of such information is not unequivocal, especially when well-defined clinical responses to test results are lacking [1,2]. Ideally, test results aid health care professionals and individuals to predict the risk of developing genetic conditions and to begin effective health interventions earlier.

Although the information may be valuable in itself [3], it is worthwhile for economic evaluations to account for the effects of health interventions on individuals contingent on the final test result. Lynch syndrome, or hereditary nonpolyposis colorectal cancer (CRC), provides a demonstrative example. The condition is caused by a genetic mutation characterized by a high risk of developing CRC. Carriers of the mutation may have up to 80% probability of contracting CRC, usually before the age of 50 years. Clinical studies indicate that increased colonoscopic surveillance yields significant reductions in mortality risk [4]. Clinical guidelines recommend frequent colonoscopies, especially in families in which the mutation has been previously observed, to detect CRC earlier [5–9]. The advent of genetic testing makes it possible to identify whether a particular individual in a family with Lynch history has the mutation. The information may not only lead to earlier detection and treatment of CRC but also spare noncarriers from needlessly undergoing additional colonoscopies. Although the incidence of the mutation in the general population is relatively low (~0.10%) [4], several members of the affected families can avoid prolonged surveillance and the discomfort and expense associated with this erroneous path.

The role of genetic testing is examined at both the policy and individual levels. Policy and reimbursement authorities are concerned with costs relative to the quantifiable clinical benefits of genetic screening for the general population and specific subpopulations, as well as the overall effect of screening on health care expenditures. A review of several economic evaluations of genetic testing by Rogowski [10] and Rogowski et al. [11] reveals skepticism for whether publicly funded screening poses an acceptable burden on health care budgets and even for whether the costs of most screening programs exceed the potential savings from early prevention.

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An appraisal of genetic testing at the individual level is quite different. For conditions such as Lynch syndrome, for which meaningful interventions are possible, the potential clinical benefits of genetic tests for individuals are apparent but costs depend on a number of factors such as the expenses of the tests and colonoscopies and the discomfort and inconvenience of undergoing procedures. In the United States, costs of genetic tests are paid either by insurance or by the patient (out of pocket). The test result itself may raise privacy concerns or negative psychological responses, such as a fear of discrimination from positive test results or complacency from negative test results [12,13]. False positives and false negatives may further aggravate individuals. Foster et al. [14] propose a generic, composite measure of the "personal" utility of genomic information that includes all informational effects on individual patient behavior in addition to all other costs and benefits. A complete account, although not considered herein, would even include changes in lifestyle, human capital, and reproductive decisions [15].

Direct elicitation of individual willingness to pay for a genetic test is one approach to assessing the contribution of personal utility to benefits and costs associated with genetic testing. Neumann et al. [16] recently elicited willingness to pay for test results from a general population sample in the United States via a contingent-valuation survey. Depending on both the possible disease and the accuracy of the testing procedure, the estimated values for test information varied from $100 to $300. Given that prices for current genetic tests fall outside this range, it is difficult to claim that individuals would indeed pay for a test themselves [17]. Grosse et al. [18] are skeptical of such cost-benefit analyses in general because studies commonly include only morbidity and mortality outcomes, neglecting other informational effects. The authors recommended more indirect approaches, such as discrete-choice experiments (DCEs) or choice-format conjoint analysis [18]. These approaches may accommodate conceptually based measures of individual responses to new genomic information [19,20]. DCEs are not the only reasonable method for understanding individuals' decisions to mitigate mortality risk via genetic tests—for example, stochastic decision trees have been used for Lynch syndrome in addition to contingent-valuation methods for cancer risks [16,21]. In addition to accommodating valuations of risk and information, DCEs can simultaneously incorporate valuations of other test features (e.g., the privacy of test results).

Thus, the objective of this study was to motivate DCEs as a viable method for measuring the "personal utility" of genomic information, specifically for treatable conditions with meaningful interventions. We intend to show that DCEs can accommodate the elicitation of preferences for the features of genetic tests and can control for the potential recourse actions of individuals in response to genetic test results. Exploiting the flexibility of DCEs, however, requires careful consideration of the model specification, particularly when multiple health interventions are available in response to results from genetic testing. For Lynch syndrome, individuals' evaluations of genetic test information depend on the perceived likelihood of having the mutation, the accuracy and features of the test, and the cost and efficacy of colonoscopic surveillance. Ignoring the heterogeneity of the perceived value of test results on the basis of an individual's expected behavioral response to genetic information may bias the evaluation. We implement a DCE study for a representative US sample and derive an empirical choice model specification that incorporates the evaluations of subsequent interventions for Lynch syndrome; calculate individuals' evaluations of the test information; and determine specific groups of individuals that may have stronger preferences for genetic testing.

Methods

DCE Survey

We used a DCE to elicit individuals' stated preferences for genetic testing for elevated CRC risks. Using clinical-expert recommendations and seven focus groups (42 respondents total), we identified salient features for genetic testing. Each focus group featured an open-ended discussion of genetic testing and a structured discussion of specific factors that influenced the decision to test. The transcripts of the interviews were coded and analyzed by three experienced qualitative researchers using a content analysis approach [22]. We identified four genetic testing features to describe genetic testing alternatives for Lynch syndrome (Table 1): the probability of developing CRC because of a genetic mutation, the likelihood of a false-negative test result, who else observes the test result, and the personal cost not covered by insurance [23].

After the focus groups, 10 face-to-face general population interviews were conducted to test a draft survey and make necessary revisions. The choice-format conjoint survey instrument was developed and tested using best-practice methods [24]. Survey development included careful face-to-face pretesting of the instrument to ensure that attribute definitions and choice tasks were explained in simple, understandable language. A simple risk tutorial and graphical representation of probabilities ensured sufficient comprehension of risk trade-offs [25]. False positives were also initially included, but interviewees in the face-to-face interviews often confused false positives with false negatives when presented together in the same choice question. Moreover, false positives are more likely to invite follow-up procedures and monitoring that can correct test errors and previous studies have found that the likelihood of a false negative is more important to patients [18]. Therefore, our application accounted for potential false-negative genetic test results only. For autosomal-dominant disorders such as Lynch syndrome, the probability of having the mutation may be inferred by the presence of the mutation in an individual's relative. The levels of the risk attribute were designed with this

Table 1 – Attributes and levels used in discrete-choice experiment.

Attributes	Levels
Chance that you will get colorectal cancer*	10 out of 100 (10%) 25 out of 100 (25%) 50 out of 100 (50%)
Chance of a false-negative test result (the test result says people do not have the gene when people actually do have it)	0 out of 10 times (0%) 1 out of 10 times (10%) 2 out of 10 times (20%)
In addition to you, who else sees the test results	Your primary care doctor Your genetics health professionals Your life insurance and health insurance companies
Personal cost to you not covered by insurance	$250 $500 $1000 or $1500†

* Risk of colorectal cancer, given the presence of the genetic mutation.

† Half the participants saw $1000, and half the participants saw $1500.