ORIGINAL RESEARCH ARTICLE | Genetics inMedicine

Patients' understanding of and responses to multiplex genetic susceptibility test results

Kimberly A. Kaphingst, ScD[1], Colleen M. McBride, PhD[2], Christopher Wade, PhD[2,3], Sharon Hensley Alford, PhD[4], Robert Reid, MD, PhD[5], Eric Larson, MD, MPH[5], Andreas D. Baxevanis, PhD[6] and Lawrence C. Brody, PhD[6]

Purpose: Examination of patients' responses to direct-to-consumer genetic susceptibility tests is needed to inform clinical practice. This study examined patients' recall and interpretation of, and responses to, genetic susceptibility test results provided directly by mail.

Methods: This observational study had three prospective assessments (before testing, 10 days after receiving results, and 3 months later). Participants were 199 patients aged 25–40 years who received free genetic susceptibility testing for eight common health conditions.

Results: More than 80% of the patients correctly recalled their results for the eight health conditions. Patients were unlikely to interpret genetic results as deterministic of health outcomes (mean = 6.0, s.d. = 0.8 on a scale of 1–7, 1 indicating strongly deterministic). In multivariate analysis, patients with the least deterministic interpretations were white ($P = 0.0098$), more educated ($P = 0.0093$), and least confused by results ($P = 0.001$). Only 1% talked about their results with a provider.

Conclusion: Findings suggest that most patients will correctly recall their results and will not interpret genetics as the sole cause of diseases. The subset of those confused by results could benefit from consultation with a health-care provider, which could emphasize that health habits currently are the best predictors of risk. Providers could leverage patients' interest in genetic tests to encourage behavior changes to reduce disease risk.

Genet Med 2012:14(7):681–687

Key Words: direct-to-consumer genetic tests; genetic testing; provider–patient communication; public health genomics; understanding

INTRODUCTION

Direct-to-consumer (DTC) availability of genetic susceptibility information is expected to expand as genome sequencing technologies decrease in cost and more gene–disease associations are identified.[1] Several commentaries have raised concerns that consumers will bring test feedback to their health-care providers for interpretation, creating communication challenges for providers.[2] Indeed, up to half of physicians surveyed reported having been asked by a patient about a DTC genetic test and 15% reported being asked by a patient to help interpret DTC test results.[3] Challenges expected for health-care providers arise from numerous contextual factors including the ambiguity of the genetic risk information and the limited evidence for its clinical utility.[4–6] Added to this are frequently described health-care system challenges such as time and cost constraints as well as pressure to comply with numerous evidence-based guidelines in primary-care visits.[7]

Critics of DTC genetic testing have been particularly concerned that individuals will be unable to interpret small increases in risk associated with common gene variants or other limits of genetic susceptibility tests.[6,8,9] Correcting such misunderstandings could place significant demands on clinic visits and compete with other important issues to be covered.[7] There is some evidence that this phenomenon has occurred with DTC advertising of prescription medications.[10] However, DTC genetic testing could raise unique challenges for provider–patient communication in that genetic test feedback conveys individualized risk information that, if misunderstood, could undermine motivation to adhere to accepted preventive behaviors. For example, if patients misunderstand the limits of risk information based on single-gene variants that indicate lower levels of risk for a common health condition, they may be less inclined to take actions that could lower their risk for other chronic health conditions.[6,11] Conversely, overinterpretation of risk information could lead patients to perceive themselves as at greater risk than is warranted based on results, potentially leading to negative emotional responses such as fear and requests for unnecessary screening or other tests.[6,9,11,12] However, very limited data exist to support or refute any of these concerns about patients' understanding of DTC genetic susceptibility test results.

The aim of this report is to bring data to the ongoing debate over individuals' comprehension of, and responses to, genetic

[1]Division of Public Health Sciences, Department of Surgery, Washington University School of Medicine, St. Louis, Missouri, USA; [2]Social and Behavioral Research Branch, National Human Genome Research Institute, Bethesda, Maryland, USA; [3]Nursing Department, University of Washington Bothell, Bothell, Washington, USA; [4]Henry Ford Hospital, Detroit, Michigan, USA; [5]Group Health Research Institute, Seattle, Washington, USA; [6]Genome Technology Branch, National Human Genome Research Institute, Bethesda, Maryland, USA. Correspondence: Kimberly A. Kaphingst (kkaphingst@gwbmail.wustl.edu)

Submitted 30 November 2011; accepted 24 January 2012; advance online publication 5 April 2012. doi:10.1038/gim.2012.22

susceptibility information when provided using a DTC model. Specifically, we examine (i) whether individuals can recall and accurately interpret a battery of personal genetic test results; (2) whether results unduly alarm individuals in ways that could prompt increased demands on health-care providers; and (3) which individuals are most likely to misrecall and misinterpret test feedback. This report is based on data from the Multiplex Initiative, which developed and evaluated a "multiplex" test (i.e., a test that assayed 15 genetic variants for susceptibility to eight common health conditions) taken by healthy adults insured through a large managed care organization.[13,14] The study presented genetic susceptibility test feedback that was based on best practices in health literacy and health communication and examined patients' responses.

MATERIALS AND METHODS

Study participants

The Multiplex Initiative has previously been described in detail.[14,15] Briefly, the multiplex genetic susceptibility test used in this study included 15 genetic variants associated with increases in risk for diabetes, heart disease, high cholesterol, high blood pressure, lung cancer, colon cancer, skin cancer, and osteoporosis.[14,15] Study participants were selected from a large health maintenance organization. Selection criteria included being age 25–40 years, being enrolled in the plan for at least 2 years, and not having the health conditions assayed through the Multiplex test. Groups traditionally underrepresented in genetics research (i.e., men, African Americans, and those with lower educational attainment) were oversampled.[14] All procedures were approved by the institutional review boards of the National Human Genome Research Institute and the Henry Ford Health System. These analyses are based on 199 patients who agreed to test and completed a baseline telephone assessment, a call with a research educator about 10 days after receiving the test results by mail, and a 3-month follow-up telephone assessment.

Feedback content

Mailed test results. Patients received a folder by mail containing their test results, as well as three supplementary one-page enclosures that described important caveats about the results, outlined behavioral strategies to reduce disease risk, and prepared them for the research educator call (see **Supplementary Figure S1** online, which presents an example test results report). The test results booklet presented the risk-increasing variants that a patient carried; the patient was told that people carrying this type of variant were at increased risk for the associated health condition as compared with those who did not carry the variant. We did not present quantitative disease risk estimates due to wide variability in available estimates and lack of evidence concerning the effect of carrying multiple variants.

Feedback materials were developed by an interdisciplinary team, drawing on prior research and best practices in health literacy and health communication. We used plain language, limiting the use of jargon (e.g., using "risk version" instead of "risk-increasing gene variant") and defining jargon where it was used. We organized the feedback around health conditions rather than genes because of patients' greater familiarity with the health conditions. Other practices employed included limiting the scope of content to essential information, reviewing or summarizing the information at the end of sections, and highlighting key information with visual and typographic cues.[16,17]

Research educator call. A trained research educator attempted to contact the participants within 10 days of receipt of mailed test results. This call was scripted and integrated data collection assessments along with discussion of test results. Calls were recorded and reviewed for quality assurance by a study manager. Study materials included contact information for a medical geneticist or genetic counselor, but no participant requested this or reported extreme responses to the feedback.

MEASURES

Measures were collected during the baseline survey, research educator call, and 3-month follow-up survey.

Recall. Free recall (e.g., "Please tell me which health conditions you had any risk versions for") and prompted recall (i.e., "Please tell me if you have any genes with risk versions for each of these health conditions") for each of the eight assayed health conditions were assessed during the research educator call. We summed the number of health conditions for which participants correctly recalled their risk status based on both free and prompted recall to create an overall recall score (range 0–8).

Interpretation. We developed a set of four items for use as part of the 3-month follow-up survey to examine whether participants interpreted the test results as deterministic (e.g., "Your health habits such as poor diet, smoking, and too little exercise are important factors that raise your chance of getting the health conditions"; "Having a risk version of a gene is one of many factors that raises your chance of getting common health conditions"). Patients were asked to what extent they agreed with the statements on a scale from 1 (strongly disagree) to 7 (strongly agree). Scores were averaged across items; lower values reflected a more deterministic interpretation of test results.

Ratings of test results information. Patients were asked to rate the believability, reliability, completeness, helpfulness, difficulty, and accuracy of the test results information during the research educator call using seven-point Likert scales from "strongly disagree" to "strongly agree" (e.g., "How much do you agree with the following statement: the information in the report was believable").

Psychological reactions. We assessed patients' positive and negative psychological reactions to the test results during the research educator call using seven-point Likert-scale items adapted from the Positive and Negative Affect Scale[18–20] (e.g., "To what extent did your test results make you feel confused") answered on a scale from "not at all" to "a great deal."

Discussion of results. At the 3-month follow-up, we asked patients: "Have you discussed your results with anyone?" and "Who did you talk to about your results?"

Information-seeking behaviors. At the 3-month follow-up, we used two yes/no items adapted from a national survey[21] to examine whether patients had looked for additional information about the effects of health habits and family history on risk of developing the assayed health conditions (e.g., "Have you looked for any information about how your personal health habits, such as your diet and how much you exercise, affect your chances of getting the health conditions that were on the Multiplex Genetic Test?").

Covariates. Participants self-reported having a family history of the health conditions. A six-item measure of genetic self-efficacy (i.e., confidence in ability to use genetic information) was adapted from Parrott *et al.*[22] The health literacy measure was adapted from a subjective screener.[23,24] Health information seeking was assessed with one item used in a national survey.[21] Self-reported importance of genetic information was assessed with one item (i.e., "How important is it to you to learn more about how your genes affect your chance of getting certain health conditions?") rated on a seven-point Likert scale. Patients were asked what health habits they thought they should try to improve. We also assessed gender, age, educational attainment, race, and marital status.

Analysis

Descriptive statistics were examined for all variables in the analytic sample. As compared with those who completed all study components, participants who did not complete at least one component were generally similar but reported a positive family history of significantly fewer health conditions and had significantly higher health literacy. We examined possible predictors of recall and interpretation (i.e., number of risk-increasing variants carried, family history, health information seeking, importance of genetic information, genetic self-efficacy, health literacy, amount of information read, and ratings of and psychological reactions to test results), all of which were identified based on theory[25] and prior empirical research.[13,14,20] Bivariate relationships were assessed using χ^2 tests and univariate linear regression models. We then built multivariate linear regression models to examine the independent contributions of predictor variables, employing forward-checking and backward-elimination methods to determine which covariates to include in the final models.[26–28] Statistical significance was assessed as $P < 0.05$. Data were analyzed using SAS, version 9.2 for Windows (Cary, NC).

RESULTS

Patient characteristics

Over half of the patients who completed all study components (henceforth called "testers") were college educated (52%), female (57%), and white (62%; **Table 1**). Testers reported high importance for learning about genetic information (mean (M) = 5.8 out of 7, s.d. = 1.3). They reported a positive family history for more than three (M = 3.6, s.d. = 1.4) health conditions. On average, testers carried at least one variant associated with increased risk for six (M = 5.9, s.d. = 0.9) of the eight health conditions; they carried a mean of 9.2 risk-increasing variants (s.d. = 1.7) out of the possible 15.

Table 1 Characteristics of 199 health maintenance organization patients who received Multiplex genetic susceptibility testing

Characteristic	Mean (s.d.) or *n* (%)
Age	34.9 (4.2)
Female	114 (57%)
White	124 (62%)
Married/partnered	136 (68%)
Education	
High school or less	20 (10%)
Some college	75 (38%)
College degree or higher	104 (52%)
Family history	
Hypertension	164 (82%)
Heart disease	130 (65%)
High cholesterol	130 (65%)
Diabetes	118 (59%)
Cancer	107 (54%)
Osteoporosis	45 (23%)
Total number of diseases	3.6 (1.4)
Carry at least one genetic variant associated with increased risk for	
Diabetes	195 (98%)
Osteoporosis	195 (98%)
Heart disease	193 (97%)
Colon cancer	185 (93%)
High cholesterol	172 (86%)
Lung cancer	120 (60%)
High blood pressure	64 (32%)
Skin cancer	42 (21%)
Importance of genetic information	5.8 (1.3)

Recall and interpretation of test result information

Almost half (47%) of testers reported that they had read all of the test results information and another 38% said that they had read most of it. Testers' unprompted recall of increased risk ranged from 40% to 70%, with highest recall for diabetes and lowest for high cholesterol (**Table 2**). With prompting, >80% correctly recalled their risk status for each of the eight health conditions.

Testers did not generally interpret the test results as deterministic (**Table 3**). When asked four agree–disagree statements about their perceptions of the meaning of a test result that showed an increased risk for a health condition, highest levels of agreement were with the statement "Your health habits such as poor diet,

Table 2 Free and prompted recall of Multiplex test results among a sample of 199 patients who received testing

Health condition	Correct recall of being at increased risk[a] (free recall; %)	Correct recall of test results[b] (prompted recall; %)
Diabetes	70	94
Heart disease	62	90
Skin cancer	56	92
Colon cancer	53	86
High blood pressure	53	83
Lung cancer	49	86
Osteoporosis	44	81
High cholesterol	40	83

[a]Proportion of those carrying at least one risk-increasing variant associated with the condition. [b]Proportion of all testers (patients who completed all study components).

Table 3 Interpretation of and reactions to Multiplex test results among a sample of 199 patients who received testing

Interpretation of increased risk result	Mean (s.d.)[a]
Can lower chance of getting health condition	5.3 (1.6)
Other factors affect chance of getting condition	5.8 (1.5)
Can still lower chance of getting condition	6.3 (1.2)
Health habits increase chance of getting condition	6.6 (1.0)
Overall score	6.0 (0.8)
Psychological reactions to test result	**Mean (s.d.)[b]**
Positive psychological reactions	
Determined	4.1 (1.8)
Hopeful	3.6 (1.9)
Relieved	3.0 (1.8)
Negative psychological reactions	
Nervous	2.6 (1.7)
Afraid	1.8 (1.5)
Confused	1.7 (1.3)
Regretful	1.3 (0.9)
Behavioral reactions to test result	***n* (%)**
Discussed test results	154 (77%)
Spouse	31 (20%)
Family	28 (18%)
Health-care provider	2 (1%)
Information seeking about risk of health conditions	
Effect of health habits	130 (65%)
Effect of family history	72 (36%)

[a]Scale from 1 (strongly disagree) to 7 (strongly agree). [b]Scale from 1 (not at all) to 7 (a great deal).

smoking, and too little exercise are important factors that raise your chance of getting health conditions" (M = 6.6, s.d. = 1.0). The lowest agreement was with the statement "There's really nothing you can do to lower your chance of getting that health condition" (reverse-scored, M = 5.3, s.d. = 1.6).

Responses to test results

Testers generally found the information believable (M = 6.5 out of 7, s.d. = 1.0), reliable (M = 6.4, s.d. = 1.1), and complete (M = 5.6, s.d. = 1.7). They generally did not agree that they expected to receive more information than they had (M = 2.6, s.d. = 1.9), that the information raised more questions than it answered (M = 2.3, s.d. = 1.5), that it required a lot of information to understand (M = 2.0, s.d. = 1.5), or that they had concerns about its accuracy (M = 1.9, s.d. = 1.6). In addition, test feedback generally did not evoke strong positive or negative psychological responses (Table 3). On average, patients reported feeling "somewhat" positive emotions (e.g., determined, hopeful, relieved) and "a little bit" of negative emotions (i.e., nervous, afraid, confused, or regretful). Psychological reactions were not associated with number of risk-increasing variants carried (data not shown). At 3 months, most testers had discussed their test results with someone (77%), but only 1% reported having talked about their results with a health-care provider.

Predictors of recall and interpretation

Of tested variables, only ratings of reliability were associated with testers' overall recall in bivariate analyses (P = 0.02; data not shown). In multivariate linear regression analyses, higher reliability ratings were associated with higher recall (i.e., for each unit increase in reliability rating, recall score increased by 0.23 points, on average (P = 0.025); Table 4). Gender was also a significant predictor of recall in the model, with women having recall scores 0.53 points higher than men, on average (P = 0.023).

For interpretation, multivariate linear regression analyses showed that those who rated the information as confusing were most likely to interpret the test feedback as deterministic. Indeed, for each unit increase in reported confusion, testers' interpretation score decreased by 0.15 points (P = 0.001), on average (Table 5). As compared with those with a college degree or higher, testers with some college (0.34 points lower; P = 0.0093) or a high-school degree or less (0.40 points lower; P = 0.047) interpreted the test feedback more deterministically. In addition, those testers who were not white were more likely to interpret feedback deterministically (0.32 points lower, P = 0.0098) as compared with those who were white.

DISCUSSION

Most patients who participated in multiplex genetic susceptibility testing recalled their results correctly, did not interpret results in an overly deterministic way, and appreciated that genetics and behavior both contribute to disease risk. These results are consistent with national surveys indicating that only 25–33% of the public holds deterministic beliefs about genetic causation of disease.[29,30]

Table 4 Predictors of correct recall of test results in a multivariate linear regression model (*n* = 199)

Predictor variable	β Estimate[a]	*P* value
Reliability rating[b]	0.23	0.025
Male gender	–0.53	0.023
Race[c]		
White	0.61	0.13
African American	0.68	0.12

[a]Recall score was the number of health conditions for which patients correctly recalled their risk status (possible range 0–8). [b]Reliability rated on seven-point Likert scale from 1 (strongly disagree) to 7 (strongly agree). [c]Compared with "other" category.

Table 5 Predictors of test result interpretation in a multivariate linear regression model (*n* = 199)

Variable	β Estimate[a]	*P* value
Test results confusing[b]	–0.15	0.0010
Expected more information than received[c]	–0.033	0.32
Interest in changing exercise habits[d]	–0.080	0.54
Family history of cancer[e]	0.20	0.096
White[f]	0.32	0.0098
Couple married/living as married[g]	0.22	0.10
Educational attainment[h]		
High-school degree or less	–0.40	0.047
Some college	–0.34	0.0093

[a]Interpretation score was average of four 7-point Likert scale items scored from 1 (strongly disagree) to 7 (strongly agree). Lower scores reflected greater genetic determinism. [b]Rated on seven-point Likert scale from 1 (not at all) to 7 (a great deal). [c]Rated on seven-point Likert scale from 1 (strongly disagree) to 7 (strongly agree). [d]Compared with those with "no" response. [e]Compared with those without a positive family history of cancer. [f]Compared with non-white. [g]Compared with those not married/living as married. [h]Compared with college degree or higher.

It is noteworthy that few testers reported having talked with their health-care providers about the results up to 3 months after receiving test feedback. This may be a function of the time interval. It may also be attributed to their minimal emotional responses to results, a finding consistent with existing research in the context of other genetic susceptibility testing.[31–34] A recent study conducted in a preventive medicine clinic showed only modest effects on disease-risk perception and worry, which attenuated over time.[35] Although our study materials indicated that we would not share test results with their provider, patients may have been concerned about privacy and potential discrimination should discussions of test results with their provider be entered into the medical record. Our findings also suggest that there may be considerable differences in provider and patient perceptions of the frequency of DTC test discussions, a finding that warrants further exploration.

Several features of the Multiplex Initiative must be considered in interpreting these results. We relied upon best practices in clear health communication and health literacy[16,17] in developing test feedback materials, and other DTC feedback materials may be substantively different. Patients' responses to DTC test results are likely to differ substantially based on the content of test feedback. Our prior work evaluating 29 health-related DTC websites indicated wide variability in the quality of informational content, showing gaps in information about test limitations and little use of explanations for technical terms.[36] In addition, the results of a recent Facebook survey of 141 members of the general public indicated the potential for misinterpretation of DTC test results.[37] This prior research, therefore, suggests that patients will have different outcomes to DTC test results generated by different sources. One specific area in which patient responses may differ is related to genetic nondeterminism. Our test feedback emphasized the role of health habits in the causation of the health conditions on the Multiplex test, which may have led, at least in part, to the finding that patients did not interpret the results in an overly deterministic way. However, if test feedback from DTC companies focuses only on the role of genes in disease causation, patients might have a more deterministic interpretation of their results.

Although our sample was drawn randomly from a large insured population, like most early adopters of health innovations, those who sought genetic testing had higher educational levels than the underlying patient population.[14] The Multiplex test assayed only 15 genetic variants, whereas current DTC tests that include far larger numbers of variants may be more difficult to comprehend fully, particularly in the instance of pleiotropy. One recent study indicated that recall was low for 14 participants with advanced training in genetics who underwent genomic profiling.[38] Considered together, it is likely that our results underestimate the proportion of individuals who might be confused by multiplex genetic tests results. Indeed, if, as forecast, DTC tests become less costly and more broadly available, misinterpretation and confusion likely will occur among some target groups and health-care providers would be credible sources of information to reduce such misunderstandings.

Our results indicated that a more deterministic interpretation was associated with testers being confused by the information, having lower educational attainment, and being members of racial and ethnic minority groups. Additional prior research has shown that having limited educational attainment or being members of racial and ethnic minority groups with experiences of discrimination may influence interpretation of genetic test feedback.[6,39] Health-care providers could use brief screening questions (e.g., "What could you do to lower your chance of getting those health conditions?") to identify patients who may be misinterpreting results from genetic susceptibility testing. Patients whose responses suggest deterministic interpretations or other misconceptions could benefit from health-care providers re-emphasizing that although our current knowledge indicates that genes slightly increase susceptibility for common health conditions like adult onset diabetes, health habits currently are the best predictors of disease risk.

Although our data does not lend insight into the expectations of patients who discussed test results with health-care

providers, prior research suggests that such patients may expect the provider to take the results into account when providing care, despite their lack of clinical validity and utility.[13] In addition, qualitative reports indicate that patients can be frustrated when health-care providers disregard results or actively denigrate DTC tests.[40] Our prior work indicated that those patients who seek testing tend to be highly motivated to change health habits.[13] Thus, health-care providers could take advantage of patients' interest in their disease risk as a teachable moment to promote engagement in evidence-based health behavior change programs that can reduce risk. For health-care providers asked to respond to DTC genetic susceptibility test results, augmenting these results with a comprehensive family history assessment may also be advised.[41]

Conclusion

Despite the unique features of the Multiplex Initiative, our findings lend insight into challenges and opportunities for patients and health-care providers as DTC testing becomes more widely available. At a time of considerable debate of regulation about DTC genetic testing, these findings begin to suggest that using evidence-based communication strategies with patient populations about the limits of genetic testing can do two things: (i) result in accurate interpretation of risk associated with common gene variants for the majority of patients and (ii) minimize impact on scarce provider visit time. Going forward, it is critical to examine the impact of DTC genetic information on provider–patient interactions, particularly if patients are being tested but are not seeking out follow-up advice from health-care providers. In addition, as health-care providers engage with patients about genetic susceptibility test results, either at the patients' or health-care providers' initiative, there will be a growing need for strategies health-care providers can use in the context of short health visits to address patient needs. Concerns about the competencies of health-care providers to interpret and apply genetic information in practice have been a major thread in the debate about availability of DTC genetic susceptibility tests.[6,42,43] To maximize the potential benefit of genetic susceptibility information for patients' health, it is critical for health-care providers to be aware of potential areas of misinterpretation of results and to gain skills needed to maximize the benefit of these interactions to promote the health and well-being of their patients.

SUPPLEMENTARY MATERIAL

Supplementary material is linked to the online version of the paper at http://www.nature.com/gim

ACKNOWLEDGMENTS

This research was supported by the Intramural Research Program of the National Human Genome Research Institute, National Institutes of Health. In addition, this research was made possible through a collaboration with the Cancer Research Network, funded by the National Cancer Institute (U19 CA 079689). Additional resources were provided by Group Health Research Institute and Henry Ford Hospital. K.A.K. was supported by funding from the Barnes-Jewish Hospital Foundation. Genotyping services were provided by the Center for Inherited Disease Research (CIDR). CIDR is fully funded through a federal contract from the National Institutes of Health to The Johns Hopkins University (HHSN268200782096C). We thank Cristofer Price and Yeqin He for their assistance with statistical analysis, and the members of the Multiplex Steering Committee who provided their critical review of this article. We also thank Andrea Kalfoglou for her assistance. Our thanks also go to the study participants who were all members of the Henry Ford Health System.

DISCLOSURE

The authors declare no conflict of interest.

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