Impact of Direct-to-Consumer Predictive Genomic Testing on Risk Perception and Worry Among Patients Receiving Routine Care in a Preventive Health Clinic

KATHERINE M. JAMES, MPH; CLAYTON T. COWL, MD, MS; JON C. TILBURT, MD, MPH;
PAMELA S. SINICROPE, DRPH; MARGUERITE E. ROBINSON, MAR, MA; KATRIN R. FRIMANSDOTTIR, PhD;
KRISTINA TIEDJE, PhD; AND BARBARA A. KOENIG, PhD

OBJECTIVE: To assess the impact of direct-to-consumer (DTC) predictive genomic risk information on perceived risk and worry in the context of routine clinical care.

PATIENTS AND METHODS: Patients attending a preventive medicine clinic between June 1 and December 18, 2009, were randomly assigned to receive either genomic risk information from a DTC product plus usual care (n=74) or usual care alone (n=76). At intervals of 1 week and 1 year after their clinic visit, participants completed surveys containing validated measures of risk perception and levels of worry associated with the 12 conditions assessed by the DTC product.

RESULTS: Of 345 patients approached, 150 (43%) agreed to participate, 64 (19%) refused, and 131 (38%) did not respond. Compared with those receiving usual care, participants who received genomic risk information initially rated their risk as higher for 4 conditions (abdominal aneurysm [$P=.001$], Graves disease [$P=.04$], obesity [$P=.01$], and osteoarthritis [$P=.04$]) and lower for one (prostate cancer [$P=.02$]). Although differences were not significant, they also reported higher levels of worry for 7 conditions and lower levels for 5 others. At 1 year, there were no significant differences between groups.

CONCLUSION: Predictive genomic risk information modestly influences risk perception and worry. The extent and direction of this influence may depend on the condition being tested and its baseline prominence in preventive health care and may attenuate with time.

Trial Registration: clinicaltrials.gov Identifier: NCT00782366

Mayo Clin Proc. 2011;86(10):933-940

DTC = direct-to-consumer; GWAS = genome-wide association study; PSA = prostate-specific antigen

The rhetoric of personalized medicine is omnipresent, fueled by the reduced cost and increased speed of technologies to characterize the human genome^{1,2} and a growing appetite to translate genomic information into better tools for disease prediction and prevention.³⁻⁵ Genome-wide association studies (GWASs) continue to identify small variations in the genome known as single nucleotide polymorphisms,⁶ the presence or absence of which is thought to confer risk for developing a variety of conditions.⁷

In 2008, a number of private companies began marketing direct-to-consumer (DTC) predictive genomic risk assessment products that provide information about

a person's likelihood of developing a range of diseases.⁸ Since the first DTC testing services became available, voices within the scientific and health policy communities have raised concern about the rapid translation of GWAS findings into consumer products. Although most acknowledge the likely *future* benefit of predictive genomic risk assessment,^{9,10} others emphasize the uncertain clinical utility of these products as well as the potential adverse psychological implications of predictive testing.¹¹⁻¹⁴ Concern is heightened when screening occurs outside the context of routine medical practice, a sentiment recently expressed by members of the Molecular and Clinical Genetics Panel of the US Food and Drug Administration's Medical Devices Advisory Committee, who recommended that DTC genomic tests be accessible only to patients with medical supervision.¹⁵ Others have argued that genomic risk assessment should be provided only in the context of a clinical trial.^{11,16}

Documenting the clinical utility of predictive genomic testing is an essential undertaking in translational genomics, one that will likely require longitudinal studies spanning lengthy time frames. As such, it is critical to ask how predictive genomic risk information shapes patients' understandings of their health, particularly the balance between appropriate concern and excessive worry. Individuals respond to health information through both cognitive and affective mecha-

From the Biomedical Ethics Research Unit (K.M.J., J.C.T., M.E.R., B.A.K.), Division of Preventive, Occupational, and Aerospace Medicine (C.T.C.), Division of General Internal Medicine (J.C.T.), Behavioral Health Research Program (P.S.S.), Center for Translational Science Activities (K.R.F.), and Division of Health Sciences Research (B.A.K.), Mayo Clinic, Rochester, MN; and Faculté d'Anthropologie et de Sociologie, Université Lumière Lyon 2, Lyon, France, (K.T.).

This study was funded jointly by Navigenics, Inc. and Mayo Clinic. Navigenics had no role in the design of the study or in data analysis. The views expressed in this study are those of the authors; Navigenics did not review the manuscript before submission.

Address reprint requests and correspondence to Clayton T. Cowl, MD, MS, Division of Preventive, Occupational, and Aerospace Medicine, Mayo Clinic, 200 First St SW, Rochester, MN, 55905 (cowl.clayton@mayo.edu).

© 2011 Mayo Foundation for Medical Education and Research

nisms, depending on whether that information is salient with existing representations of a threat.^{17,18} A number of theories include risk perception or perceived vulnerability as a predictor in models of preventive health behavior (eg, the health belief model, self-regulation theory).^{19,20} Health information can be managed in both positive and negative ways, especially in the context of genomic risk information. For example, if an individual is told that he or she is at increased genetic risk of developing heart disease, that person might decide that engaging in risk-reducing activities such as weight loss or exercise would have no bearing on his or her chance of developing the disease.

In predictive genomics, the need is great not only to understand how individuals perceive and react to their genomic risk information—especially given the uncertainty surrounding the state of the science²¹⁻²⁴ and concerns that we not cause undue harm^{12,25,26}—but also to examine whether and how this information is used. Thus, a logical first step in understanding the effects of receiving predictive genomic risk information is to evaluate whether such information influences perceptions of disease risk and levels of worry.

To our knowledge, this study is the first of its kind to focus on the introduction of predictive genomic risk information in a clinical setting. We report on the impact of receiving genomic risk results from a commercially available predictive genomic testing product on patients' perceptions of risk and levels of worry for 12 conditions, including several cancers and cardiovascular, metabolic, and autoimmune diseases. We hypothesized that patient ratings of perceived risk and worry would not significantly differ between a group receiving estimates of genomic risk and a group not receiving such information.

PATIENTS AND METHODS

This study was conducted using a sequential mixed methods design, in which an initial phase of qualitative data collection and analysis provided the basis for a subsequent study in which quantitative data were collected and analyzed. After initial approval from the Mayo Clinic Institutional Review Board, we piloted the delivery of genomic risk results from a DTC product with 20 patients and their physicians to assist in the design of a larger trial (reported here) and to ensure the safety and feasibility of the approach. In-depth follow-up interviews with patients and physicians, including video recordings of office visits and qualitative analysis

of interview data, provided information for the design of the larger trial and the development of a survey.

SETTING AND PARTICIPANTS

The trial was implemented in a preventive medicine outpatient clinic that specializes in comprehensive executive health care and is located at a major medical center. To ensure optimal patient safety, we identified an ambulatory clinical environment with an educated, well-insured patient population as an appropriate clinical context in which to introduce an uncertain medical technology (ie, DTC genomic testing) that has not been validated. This clinic annually provides more than 7000 individuals (primarily executives in leadership positions and/or their spouses) with comprehensive preventive medical assessments during the course of a 1- to 3-day expedited visit.

Twelve staff physicians (of 20 eligible) in this preventive medicine practice agreed to participate in the study. Patients were eligible to participate if they were established patients of one of these 12 physicians; had routine, annual appointments scheduled during a predetermined 2-week block of time; resided in the continental United States; and were younger than 70 years. We invited all eligible patients to participate by mailing them an introductory cover letter and informed consent document, and we followed up with a telephone call. To ensure adequate human participants protection, a study coordinator (trained by a genetic counselor) reviewed with each patient the uncertain nature of genomic risk information, noting that although the predictive genomic testing provided by the DTC company was being offered directly to consumers via the Internet, its clinical efficacy was not established. Our procedures were modeled after pretest genetic counseling; a genetic counselor was available to speak to patients before consent as needed.

INTERVENTION AND PREDICTIVE GENOMIC TESTING PROCESS

The trial was implemented between June 1 and December 18, 2009. After providing informed consent, eligible patient participants were randomly assigned to receive either the study intervention in addition to usual care (intervention group) or usual care alone (control group). Usual care includes a comprehensive medical and family history review, a physical examination, a full range of age-appropriate preventive screening tests, a cardiovascular fitness evaluation, a review and update of medications and immunizations, and an in-depth discussion of all preventive screening test results.

Patients randomly assigned to the intervention group were mailed a saliva sample collection kit to be returned to Navigenics, Inc (Foster City, CA). At the investigators' request, Navigenics, Inc offered a modified version of its DTC product to intervention group participants, one that provided genomic risk information for just 12 conditions of the 28 typically included in this company's product. These 12 conditions were selected by a panel of physicians (each with expertise in the condition of interest) as potentially "actionable," that is, diseases for which an individual could potentially benefit from early diagnosis or could alter his or her risk by making behavioral modifications (eg, increased physical activity) or undergoing additional preventive screening tests (eg, colonoscopy). The 12 conditions included abdominal aneurysm, atrial fibrillation, breast cancer (women only), celiac disease, colon cancer, type 2 diabetes mellitus, Graves disease, myocardial infarction, lung cancer, obesity, osteoarthritis, and prostate cancer (men only). Predictions of drug response were not included.

After following the instructions in the kit, patients mailed their saliva sample to the company's Clinical Laboratory Improvement Amendments (CLIA)-certified laboratory for analysis using the Affymetrix Genome-Wide Human SNP Array 6.0 (Santa Clara, CA). Five participants (7%) in the intervention group were sent a second testing kit because saliva volume in their initial sample was insufficient or the cap on the saliva collection tube was not adequately secured. After successful DNA analysis and 1 week before their scheduled preventive medicine appointment, participants in the intervention group were sent an electronic notification containing their unique user name and password granting them access to view their predictive genomic testing results on the company's secure Web site. (An example of the results viewed by participants is included in Appendix A of the Supporting Online Material.) All patients were offered genetic counseling according to the company's standard practice, but none made contact with the company to request this service.

All patients then attended their previously scheduled appointments. Physicians were notified 1 day before each patient's appointment that they would be evaluating a study patient. For those patients randomly assigned to the intervention group, physicians were also given access to each patient's results (both electronically and in hard copy) to review before the patient's appointment if they chose. To better approximate a "real-world" DTC experience, physicians were not provided

with special training in interpreting the genomic risk profiles. Intervention group participants were told that they had the option of discussing their genomic testing results with their physician. Participants in the control group received usual care as previously described.

DATA COLLECTION

All patient participants were sent by e-mail a link to complete an online survey within 1 week of their final preventive health appointment. Up to 3 reminder e-mails or telephone calls were made to nonresponding participants in the 3 weeks after the initial e-mail. Survey responses were collated in SurveyTracker (Training Technologies, Inc, Lebanon, OH).

Participants completed a follow-up survey containing our outcomes of interest approximately 1 year later. Responses to this survey were collected and managed using the secure, Web-based application Research Electronic Data Capture (REDCap).²⁷ Reminder e-mails were sent to nonresponding participants 2 and 4 weeks after initial contact.

OUTCOME MEASURES

We measured patients' self-reported perceptions of risk for the 12 previously described conditions using a modified version of a widely used risk perception measure developed by Lerman et al.²⁸ Participants in both the intervention and the control groups were asked, "Compared to other people of your same age, sex, and race, how likely do you think you are to develop the following health conditions some time in your life?" They rated their perception of risk for each of the 12 conditions on a 3-point Likert scale ranging from "very likely" to "not at all likely" and were also given the option to answer "do not know/unsure," "currently have this condition," or "does not apply."

We also measured patients' self-reported levels of worry for developing each of the 12 conditions included in the predictive genomics testing panel, an item also adapted from the work of Lerman et al.²⁸ Participants were asked, "How worried are you about developing the following health conditions?" They answered using the same ordinal rating scale as described in the previous paragraph. We included the same 2 items assessing perceived risk and worry in the 1-year follow-up survey.

STATISTICAL ANALYSES

Analysis of outcome measures was conducted using SAS version 9.1 (SAS Inc, Cary, NC). Comparisons between intervention and control groups for our outcomes of in-

FIGURE 1. Flow diagram of trial methodology.

terest were made using Pearson χ^2 or Fisher exact test, when appropriate. All reported P values are 2-sided and were declared significant at the $\alpha=.05$ level. For ease of presentation, risk perception and worry measures are presented in a dichotomized fashion unless otherwise noted. Specifically, we collapsed the response categories “very likely” and “somewhat likely” into one category and compared it with “not at all likely.” Those who rated “do not know/unsure,” “currently have this condition,” or “does not apply” were not included in analyses.

RESULTS

Of the 345 patient participants we approached, 64 (19%) refused, 131 (38%) did not respond after 2 follow-up telephone calls, and 150 (43%) agreed to participate. These 150 individuals were randomly assigned to either the intervention ($n=74$) or the control ($n=76$) group. Of the 74

patients in the intervention group, 61 (82%) completed the 1-week follow-up online survey; 54 (73%) completed the 1-year follow-up survey. Of the 76 patients randomly assigned to the control group, 57 (75%) completed the 1-week follow-up survey; 54 (71%) completed the 1-year follow-up survey (Figure 1). Characteristics of patients in the intervention and control groups did not differ significantly (Table 1). Within the intervention and control groups, respondents and nonrespondents to the survey did not differ with respect to age (intervention, $P=.49$; control, $P=.10$) or sex (intervention, $P=.24$; control, $P=.55$). Unless otherwise noted, results reported are from the survey administered to participants 1 week after their executive health appointments.

RISK PERCEPTION

For most conditions (7/12), a greater proportion of patients in the intervention group rated their perceived

TABLE 1. Characteristics of Patient Participants Who Completed a Survey at 1-Week Follow-up^a

Characteristic	Intervention (N=61)	Control (N=57)	P value ^b
Sex			.23
Female	20 (33)	13 (23)	
Male	41 (67)	44 (77)	
Age, y			.14
<40	0 (0)	1 (2)	
40-49	10 (16)	5 (9)	
50-59	27 (44)	19 (33)	
60-69	24 (39)	32 (56)	
Education ^c			.61
8th grade or less	0 (0)	0 (0)	
Some high school	1 (2)	0 (0)	
High school graduate or general equivalency diploma	1 (2)	2 (4)	
Vocational, technical, or business school	0 (0)	1 (2)	
Some college or associate degree	8 (13)	6 (11)	
4-y college graduate	24 (39)	18 (32)	
Graduate or professional school	25 (41)	30 (53)	
Employment status ^c			.07
Working full-time for pay	33 (54)	39 (68)	
Working part-time for pay	6 (10)	8 (14)	
Not working for pay	5 (8)	0 (0)	
Retired	16 (26)	10 (18)	

^a Values are number (percentage) unless otherwise indicated.

^b All *P* values are 2-sided and were calculated using Pearson χ^2 tests (or 2-sided Fisher exact test where cell counts are less than 5).

^c Numbers may not add up to the total for each column because of missing data.

risk for developing those conditions as “somewhat” or “very likely” compared with the control group (Table 2). For 4 conditions (abdominal aneurysm, Graves disease, obesity, and osteoarthritis), a significantly greater proportion of patients in the intervention group rated their likelihood of developing the condition as “somewhat” or “very” likely compared with the control group. This was not the case, however, for prostate cancer; patients who received genomic risk information rated their risk significantly lower than did those

who did not receive genomic risk results. One year later, however, the proportion of intervention group participants who rated their perceived risk as “somewhat” or “very” likely did not differ significantly from risk perceptions made by those in the control group for any of the 12 conditions (Table 3).

WORRY

In the 1-week and 1-year follow-up surveys, participants in both the intervention and the control groups reported similarly high levels of worry for myocardial infarction, colon cancer, and prostate cancer, with between 40% and 70% of participants in these groups rating themselves as being “somewhat” or “very” worried about developing these conditions (Tables 2 and 3).

Responses from the 1-week follow-up survey suggest that receiving predictive genomic risk information had only a slight effect on levels of worry (Table 2). For 6 of the 12 conditions (abdominal aneurysm, atrial fibrillation, breast cancer, celiac disease, Graves disease, and obesity), participants in the intervention group reported slightly higher but nonsignificantly different levels of worry about developing those conditions compared with controls. For 4 conditions (colon cancer, type 2 diabetes, myocardial infarction, and lung cancer), the intervention group reported lower levels of worry compared with controls, but these differences were also not significant. In 2 instances, differences in worry approached statistical significance. Levels of worry about developing osteoarthritis were greater among patients receiving genomic risk information than among controls ($P=.05$) but were lower for prostate cancer ($P=.05$). At 1 year, participants receiving predictive genomic information

TABLE 2. Comparison of Ratings of Risk Perception and Levels of Worry Between Intervention and Control Groups for 12 Conditions Approximately 1 Week After Participants' Executive Health Appointments

Condition	Risk perception, No. (%) Somewhat or very likely to develop condition			Worry, No. (%) Somewhat or very worried about developing condition		
	Intervention	Control	P value ^a	Intervention	Control	P value ^a
Abdominal aneurysm	12 (35)	1 (3)	.001	5 (13)	4 (9)	.73
Atrial fibrillation	14 (42)	7 (26)	.18	10 (27)	8 (22)	.63
Breast cancer	8 (21)	4 (10)	.19	7 (16)	7 (15)	.82
Celiac disease	4 (11)	0 (0)	.13	2 (5)	0 (0)	.49
Colon cancer	20 (54)	12 (55)	.97	18 (42)	22 (54)	.28
Diabetes, type 2	21 (54)	11 (35)	.13	14 (33)	18 (44)	.28
Graves disease	7 (18)	0 (0)	.04	5 (12)	0 (0)	.06
Lung cancer	9 (25)	6 (17)	.42	9 (20)	9 (21)	.91
Myocardial infarction	29 (73)	24 (83)	.32	32 (70)	32 (73)	.74
Obesity	23 (56)	11 (28)	.01	13 (27)	9 (21)	.57
Osteoarthritis	26 (70)	10 (43)	.04	16 (42)	7 (21)	.05
Prostate cancer	23 (39)	23 (68)	.02	14 (41)	28 (64)	.05

^a *P* values are based on Pearson χ^2 tests (or 2-sided Fisher exact test where cell counts are less than 5) in which participants who rated their perception of risk for developing one of the 12 conditions and levels of worry as somewhat or very likely/worried were compared with those who rated their perception of risk and levels of worry as not at all likely/worried.

TABLE 3. Comparison of Ratings of Risk Perception and Levels of Worry Between Intervention and Control Groups for 12 Conditions Approximately 1 Year After Participants' Executive Health Appointments

Condition	Risk perception, No. (%) Somewhat or very likely to develop condition			Worry, No. (%) Somewhat or very worried about developing condition		
	Intervention	Control	<i>P</i> value ^a	Intervention	Control	<i>P</i> value ^a
Abdominal aneurysm	8 (25)	3 (9)	.11	6 (15)	2 (5)	.16
Atrial fibrillation	13 (52)	12 (43)	.51	10 (30)	9 (21)	.43
Breast cancer	3 (9)	6 (15)	.72	9 (25)	9 (20)	.59
Celiac disease	2 (8)	3 (18)	.63	2 (8)	1 (3)	.59
Colon cancer	18 (56)	12 (48)	.60	19 (50)	17 (50)	>.99
Diabetes, type 2	13 (42)	12 (40)	.88	18 (49)	17 (46)	.81
Graves disease	1 (4)	2 (10)	.57	0 (0)	0 (0)	>.99
Lung cancer	8 (27)	6 (19)	.46	12 (34)	10 (26)	.42
Myocardial infarction	20 (69)	20 (69)	>.99	29 (81)	27 (75)	.57
Obesity	17 (44)	14 (37)	.55	15 (38)	18 (39)	.88
Osteoarthritis	23 (74)	15 (60)	.39	22 (63)	14 (41)	.07
Prostate cancer	17 (50)	16 (50)	>.99	21 (54)	18 (51)	.84

^a *P* values are based on Pearson χ^2 tests (or 2-sided Fisher exact test where cell counts are less than 5) in which participants who rated their perception of risk for developing one of the 12 conditions and levels of worry as somewhat or very likely/worried were compared with those who rated their perception of risk and levels of worry as not at all likely/worried.

had ratings of worry similar to those of the control group for all conditions (Table 3).

DISCUSSION

The results of the current study suggest that receiving predictive genomic risk information influences patients' perceptions of risk and levels of worry for developing a variety of conditions, but does so in different ways and to varying degrees for different conditions. Compared with participants who received usual care, patients who received genomic information had higher initial ratings of perceived risk and levels of worry for more than half of the conditions for which they received results. However, not all differences were statistically significant or in the same direction, nor did these differences persist over time.

In contrast to concerns raised in the scientific literature^{9,12,29} and by organizations such as the American Society of Human Genetics,³⁰ the American College of Medicine Genetics,³¹ and the Secretary's Advisory Committee on Genetics, Health, and Society,³² we found no significant differences in levels of worry for 10 of the 12 conditions tested comparing patients who received predictive genomic risk information with those who received usual care; differences merely approached statistical significance for the remaining 2 conditions (prostate cancer and osteoarthritis). These findings are not unlike those recently reported by Bloss et al,³³ who found that genome-wide testing in a non-clinical setting had no measurable impact on psychological health or behavior. Although a large percentage of patients rated themselves as being "somewhat" or "very" worried about developing conditions such as colon cancer and myocardial infarction, these percentages were similarly high

for both groups of patients in our study, suggesting that the baseline level of worry for more widely known conditions is neither diminished nor enhanced by knowledge of one's genomic risk for developing those conditions. Additionally, the relatively modest impact of predictive genomic risk information on levels of worry may be explained in part by the context in which our participants were able to discuss and interpret their risk results, namely, with the guidance of a trusted physician.

The differences in risk perception we observed between those who received predictive genomic testing and those who did not were more pronounced for diseases that are less common or are not as likely to be discussed routinely in preventive health examinations. Our results for Graves disease provide a particularly striking illustration of this point: of the patients who received predictive genomic risk information, 18% rated themselves as somewhat or very likely to develop Graves disease and 12% as somewhat or very worried about developing it, whereas none of the patients who received usual care alone had similar ratings of risk and worry. This suggests that predictive genomic testing may have a stronger impact on perceived risk of lesser-known conditions in which baseline knowledge about the disease (including its severity or likelihood) is apt to be low and information about an individual's personalized risk of developing a *rare* disease is hence likely to be influential. However, because these differences disappeared with longer-term follow-up, the impact of predictive genomic testing on perceived risk of developing even lesser-known conditions appears to be temporary.

In addition, contrary to our hypothesis, we found that ratings of risk perception and worry for prostate cancer were actually lower in patients who received predic-

tive genomic testing than in those who received usual care. The comparatively high levels of baseline risk perception and worry observed among participants who received usual care might be explained by widespread public awareness about prostate cancer and the availability of a widely used screening test (prostate-specific antigen [PSA]). This suggests that men who received a genomics-based estimate of their lifetime risk of developing prostate cancer—in addition to a negative PSA test—may have been reassured by this information and consequently lowered their ratings of perceived risk and worry. Whether altered risk perception and worry would ultimately result in fewer or less frequent requests for conventional screening tests such as PSA is an important question that our study does not address.

Several limitations of the current study deserve mention. First, the clinic population from which our sample was drawn includes primarily insured, well-educated individuals with ready access to high-quality preventive health services—characteristics that significantly limit the generalizability of our findings. Given the relatively high price of these services and the fact that they are not covered by health insurance, this is precisely the socioeconomic group being targeted by companies offering DTC predictive genomic testing products. Although our study findings are by no means conclusive in the ongoing debate regarding the impact of DTC genomic testing on patients' perceived risk and worry, they are still salient to current policy debates. Second, given the breadth and comprehensiveness of preventive health services offered to participants in both the intervention and the control groups, effects of predictive genomic information on worry or risk perception could have been masked by what is likely, overall, a reassuring experience for patients seen in the executive health clinic. How individuals from diverse socioeconomic backgrounds might respond if they were offered such results in the context of routine primary care is unknown. For these reasons, our findings would need to be confirmed in a more representative sample of the US population before clinical practice recommendations could be made.

Finally, the largely nonsignificant results in this small study may be due in part to low statistical power or incomplete follow-up. Between 20% and 25% of participants in both arms of the study did not complete surveys at either the 1-week or 1-year follow-up period and are therefore considered "lost to follow-up." Although unmeasured outcomes in this subsample of participants could have possibly altered our findings, the lack of significant demographic (ie, age and sex) differences between nonresponders and those who completed a survey

gives us little reason to suspect that these differences would have changed our inferences.

The principal concern when translating a GWAS into preventive health care practice is establishing the accuracy of risk estimates. However, definitive data on the clinical utility of individualized genomic risk prediction—whether offered via a pure DTC approach or in the context of clinician-guided preventive care—may not be available for many years. The key ethical concern in translational genomics is managing the inevitable uncertainty that results when initial associations between genetic markers and a disease are introduced in a clinical setting before validation. Given the ambiguity and continued controversy surrounding oversight of the introduction of new genetic tests in the United States,³⁴⁻³⁶ the ultimate uncertainty about these risk estimates and their clinical importance could persist for years. Nonetheless, clinicians must now begin preparing to offer guidance for patients who purchase DTC genomics products, mixing due caution with full transparency about clinical utility.

CONCLUSION

To our knowledge, this is the first clinical trial to assess the use of predictive genomic risk assessment in a real-world preventive care setting. We found little evidence to suggest that predictive genomic risk information consistently influences risk perception or worry in the manner or degree that has been posited by some scientific critics and commentators, although our findings do suggest a possible transient effect in less common diseases. Because patients and physicians are most likely to make decisions about further screening or preventive recommendations in the period immediately following receipt of genomic risk information, this effect, even if temporary, may be relevant to policy debates. Our findings suggest that oversight of emerging genomic technologies should be targeted toward diseases and conditions in which the potential for harm is greatest. Because the impact of DTC predictive genomic testing on patients' risk perception and worry appears to be neither predictable nor enduring, policy makers must adopt a nuanced approach to oversight as data about the clinical validity and utility of predictive genomic risk assessments become available in the coming years.

We thank Abigale L. Ottenberg, MA, for assistance with participant recruitment and survey development and Ellen L. Goode, PhD, Carrie A. Zabel, MS, CGC, Devin Oglesbee, PhD, and Victor M. Montori, MD, for assistance with study design.

REFERENCES

1. Bonetta L. Whole-genome sequencing breaks the cost barrier. *Cell*. 2010;141(6):917-919.
2. Lifton RP. Individual genomes on the horizon. *N Engl J Med*. 2010;362(13):1235-1236.
3. Hamburg MA, Collins FS. The path to personalized medicine [published correction appears in *N Engl J Med*. 2010;363(11):1093]. *N Engl J Med*. 2010;363(4):301-304.
4. Kalb C. Study: Americans want to know their genetic codes. *Newsweek*. Published June 9, 2010. <http://www.newsweek.com/2010/06/09/inside-information.html>. Accessed June 1, 2011.
5. McGuire AL, Diaz CM, Wang T, Hilsenbeck SG. Social networkers' attitudes toward direct-to-consumer personal genome testing. *Am J Bioeth*. 2009;9(6-7):3-10.
6. Visscher PM, Montgomery GW. Genome-wide association studies and human disease: from trickle to flood. *JAMA*. 2009;302(18):2028-2029.
7. Wray NR, Goddard ME, Visscher PM. Prediction of individual genetic risk to disease from genome-wide association studies. *Genome Res*. 2007;17(10):1520-1528.
8. Lenzer J, Brownlee S. Knowing me, knowing you. *BMJ*. 2008;336(7649):858-860.
9. Foster MW, Sharp RR. Out of sequence: how consumer genomics could displace clinical genetics. *Nat Rev Genet*. 2008;9(6):419.
10. Toner B. Though wary of DTC testing, some clinical geneticists see opportunity for education. *GenomeWeb Daily News* Web site. Published March 17, 2009. <http://www.genomeweb.com/dxpgx/though-wary-dtc-testing-some-clinical-geneticists-see-opportunity-education>. Accessed June 1, 2011.
11. Hunter DJ, Khoury MJ, Drazen JM. Letting the genome out of the bottle—will we get our wish? *N Engl J Med*. 2008;358(2):105-107.
12. McGuire AL, Burke W. An unwelcome side effect of direct-to-consumer personal genome testing: raiding the medical commons. *JAMA*. 2008;300(22):2669-2671.
13. Ormond KE, Wheeler MT, Hudgins L, et al. Challenges in the clinical application of whole-genome sequencing. *Lancet*. 2010;375(9727):1749-1751.
14. US Government Accountability Office. Testimony Before the Subcommittee on Oversight and Investigations, Committee on Energy and Commerce, House of Representatives. Direct-to-consumer genetic tests: misleading test results are further complicated by deceptive marketing and other questionable practices. <http://www.gao.gov/new.items/d10847t.pdf>. Published July 22, 2010. Accessed June 1, 2011.
15. Zwillich T. FDA panel urges caution on genetic test kits. *WebMD* Web site. Published March 9, 2011. <http://www.webmd.com/heart-disease/news/20110309/fda-panel-urges-caution-on-genetic-test-kits>. Accessed June 1, 2011.
16. Khoury MJ, McBride CM, Schully SD, et al. The Scientific Foundation for Personal Genomics: recommendations from a National Institutes of Health—Centers for Disease Control and Prevention multidisciplinary workshop. *Genet Med*. 2009;11(8):559-567.
17. Marteau TM, Lerman C. Genetic risk and behavioural change. *BMJ*. 2001;322(7293):1056-1059.
18. Leventhal H, Leventhal EA, Contrada RJ. Self-regulation, health, and behavior: a perceptual-cognitive approach. *Psychol Health*. 1998;13(4):717-733.
19. Carver CS, Scheier MF. Themes and issues in the self-regulation of behavior. In: Wyer S Jr, ed. *Advances in Social Cognition*. Vol 12. Mahwah, NJ: Lawrence Erlbaum Associates; 1999:1-105.
20. Strecher V, Rosenstock I. The health belief model. In: Glanz K, Marcus-Lewis F, Rimer B, eds. *Health Behavior and Health Education*. 2nd ed. San Francisco, CA: Jossey-Bass; 1997:41-59.
21. Eng C, Sharp RR. Genomic testing: bioethical and clinical dilemmas of direct-to-consumer personal genomic testing: the problem of misattributed equivalence. *Sci Transl Med*. 2010;2(17):17cm15.
22. Offit K. Genomic profiles for disease risk: predictive or premature? *JAMA*. 2008;299(11):1353-1355.
23. Paynter NP, Chasman DI, Buring JE, Shiffman D, Cook NR, Ridker PM. Cardiovascular disease risk prediction with and without knowledge of genetic variation at chromosome 9p21.3. *Ann Intern Med*. 2009;150(2):65-72.
24. Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group. Recommendations from the EGAPP Working Group: genomic profiling to assess cardiovascular risk to improve cardiovascular health. *Genet Med*. 2010;12(12):839-843.
25. Janssens AC, Gwinn M, Bradley LA, Oostra BA, van Duijn CM, Khoury MJ. A critical appraisal of the scientific basis of commercial genomic profiles used to assess health risks and personalize health interventions. *Am J Hum Genet*. 2008;82(3):593-599.
26. Samuel GN, Jordens CF, Kerridge I. Direct-to-consumer personal genome testing: ethical and regulatory issues that arise from wanting to 'know' your DNA. *Intern Med J*. 2010;40(3):220-224.
27. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377-381.
28. Lerman C, Rimer BK, Engstrom PF. Cancer risk notification: psychosocial and ethical implications. *J Clin Oncol*. 1991;9(7):1275-1282.
29. Kuehn BM. Risks and benefits of direct-to-consumer genetic testing remain unclear. *JAMA*. 2008;300(13):1503-1505.
30. Hudson K, Javitt G, Burke W, Byers P. ASHG Statement* on direct-to-consumer genetic testing in the United States. *Obstet Gynecol*. 2007;110(6):1392-1395.
31. American College of Medicine Genetics Board of Directors. ACMG statement on direct-to-consumer genetic testing. *Genet Med*. 2004;6(1):60.
32. Department of Health and Human Services (HHS). Direct-to-consumer genetic testing: report of the Secretary's Advisory Committee on Genetics, Health, and Society. Published April 2010. http://oba.od.nih.gov/oba/sacghs/reports/SACGHS_DTC_Report_April2010.pdf. Accessed June 1, 2011.
33. Bloss CS, Schork NJ, Topol EJ. Effect of direct-to-consumer genome-wide profiling to assess disease risk. *N Engl J Med*. 2011;364(6):524-534.
34. FDA Panel gets varied opinions on DTC Genomics. *GenomeWeb Daily News* Web site. Published March 10, 2011. <http://www.genomeweb.com/dxpgx/fda-panel-gets-varied-opinions-dtc-genomics>. Accessed June 1, 2011.
35. Pollack A. FDA faults companies on unapproved genetic tests. *New York Times*. June 11, 2010. <http://www.nytimes.com/2010/06/12/health/12genome.html>. Accessed June 1, 2011.
36. Shuren J; US Food and Drug Administration (FDA). Direct-to-consumer genetic testing and the consequences to the public. <http://www.fda.gov/NewsEvents/Testimony/ucm219925.htm>. Accessed June 1, 2011.

Supporting Online Material

www.mayoclinicproceedings.com/content/86/10/933/suppl/DC1AppendixA