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ARTICLE

Attitudes, knowledge, and risk perceptions of patients who received elective genomic testing as a clinical service

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ABSTRACT

Purpose: Elective genomic testing (EGT) is increasingly available clinically. Limited real-world evidence exists about attitudes and knowledge of EGT recipients.
Methods: After web-based education, patients who enrolled in an EGT program at a rural nonprofit health care system completed a survey that assessed attitudes, knowledge, and risk perceptions.
Results: From August 2020 to April 2022, 5920 patients completed the survey and received testing. Patients most frequently cited interest in learning their personal disease risks as their primary motivation. Patients most often expected results to guide medication management (74.0%), prevent future disease (70.4%), and provide information about risks to offspring (65.4%). Patients were "very concerned" most frequently about the privacy of genetic information (19.8%) and how well testing predicted disease risks (18.0%). On average, patients answered 6.7 of 11 knowledge items correctly (61.3%). They more often rated their risks for colon and breast cancers as lower rather than higher than the average person but more often rated their risk for a heart attack as higher rather than lower than the average person (all $P < .001$).
Conclusion: Patients pursued EGT because of the utility expectations but often misunderstood the test's capabilities.

Introduction

The growth of precision medicine has raised expectations about the expansion of genomic testing into all aspects of patient management, including primary care. Preemptive pharmacogenomic (PGx) testing and screening for medically actionable predispositions (MAPs) provide ways to improve treatment efficacy, reduce adverse drug responses, and target disease prevention. Early evidence on the clinical benefits of certain applications of genomic testing is growing,[1-3]

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although critical questions remain about its safety, feasibility, and value when provided preemptively. Nevertheless, a growing number of healthcare systems are implementing genomic testing as an elective clinical service for patients.[4,5]

The motivations, expectations, and concerns of patients who pursue elective genomic testing (EGT) are unclear. Most prior studies examining EGT have examined it as part of research or direct-to-consumer services.[6-10] Individuals who pursue EGT through these avenues generally report high expectations about the clinical utility of both disease predisposition screening and PGx testing and are highly motivated by the opportunity to learn about their disease risk.[6-9] Only a few studies have examined EGT as a clinical service. The University of North Carolina Lineberger Cancer Prevention and Control Program conducted a survey of the general public about a hypothetical genetic screen for cancer, finding a mix of positive and negative interest with concerns that test results may be uninteresting or unimportant, concerns about costs, and some fear about learning results.[11] Patients who participated in the NorthShore University HealthSystem's DNA-10K program, a clinical program offering EGT, were primarily motivated by the opportunity to learn about disease risks, by curiosity, and by desires to improve their health.[4] These individuals also reported low overall concerns about the implications of testing and were less expectant of how results would affect family members and life planning. Prospective data about motivations, expectations, concerns, and knowledge from patients receiving EGT as a clinical service are lacking.

This study addressed this evidence gap by examining surveys completed by patients at the time they enrolled in the Sanford Chip program, an EGT program offered to adult patients at Sanford Health.[12] As EGT offerings expand in the clinical space, understanding the reasons patients pursue testing and corresponding expectations, concerns, and knowledge will be critical for developing strategies to ensure patients are properly informed about testing capabilities and limitations, to reduce the risk of false reassurance with return of negative results,[13] and to minimize psychological distress after results disclosure.

Materials and Methods

Overview of the Sanford Chip Program

The Sanford Chip was an EGT program offered from 2018 to 2022, predominantly to adult patients at Sanford Health. Details regarding the rationale for and development of the program, including the genetic testing platform and communication of results have previously been published.[12,14-16] Briefly, the Sanford Chip provided PGx panel testing with the option of screening for MAPs, variants associated with 57 of the 59 inherited conditions in the American College of Medical Genetics and Genomics SF v2.0 secondary findings list (excluding *WT1* and *NF2*).[17] Testing was conducted at the Sanford Medical Genetics Laboratory (Sioux Falls, SD), a CLIA-certified and CAP-accredited molecular genetics laboratory.

To be eligible for EGT, patients had to be aged 18 years or older, speak and understand English, and be enrolled in Sanford's online patient portal, MyChart. In addition to eligible patients receiving unprompted invitations through MyChart, both patients and their providers could actively request an invitation be sent to the patient. Patients who were military veterans, members of underserved rural communities, and from certain primary care and specialty clinics also received tailored or in-person invites. Invitations directed patients to a web-based platform that provided education about genetics and the Sanford Chip program, collected clinical consent for testing (including the ability to opt out of screening for MAPs), and collected a $49 testing fee. Veterans, patients from underserved communities, Sanford Health providers, and select other individuals received the test for free by entering a coupon code at enrollment. A health care provider (HCP) had to approve the order for the Sanford Chip before a blood specimen was collected. Patients were encouraged to request a genetic consultation with any questions or concerns both before and after return of results.

Beginning in August 2020, as part of the clinical consent process, patients completed a survey in which they detailed their personal and family histories of disease and their reasons for pursuing the Sanford Chip, including their motivations, attitudes, and knowledge about testing.

Survey development and administration

An interdisciplinary team of genetic counselors, medical geneticists, epidemiologists, behavioral scientists, and survey design researchers collaborated to create the initial survey instrument. It was then iteratively revised during pilot testing with 11 genetic counseling students, a genetics nurse, and 6 adult patients, 3 of whom had previously received the Sanford Chip. Details on the survey measures and administration are described below and in Supplemental Appendix A. Scales assessing motivations, expectations, concerns, and knowledge included a combination of items from prior work on personal genetic testing and novel items.[8,18,19]

Motivations, expectations, and concerns

To assess motivations, patients rated the importance of 10 pre-specified reasons why they may have decided to pursue the Sanford Chip, as well as which 1 reason was the most important. To assess expectations, patients responded to 7 statements about what they expected to learn from their Sanford Chip results. To assess concerns, patients rated their level of concern about 8 topics when deciding to pursue the Sanford Chip.

Knowledge

We wrote a set of 11 items to assess knowledge specific to the Sanford Chip program based on key elements of the patient education materials and clinical consent document. We also asked whether respondents had heard of the Genetic Information Nondiscrimination Act (GINA)[20] and, if so, asked follow-up questions to measure their awareness of whether it provided protections for various types of insurance. All knowledge items included a response option of "I don't know."

Risk perceptions

We assessed risk perceptions about conditions that could be informed by Sanford Chip results: colon cancer, breast cancer, and heart attack. For each condition, participants were asked what they thought their risk of getting each condition is compared with the average person of the same age, sex, and ethnicity.

Patient characteristics

Patient age, gender, Sanford Health region, and Charlson comorbidity index score[21,22] were assessed at the time of enrollment into the Sanford Chip program from patients' electronic health record (EHR). Other patient characteristics, including prior genetic testing and family health history, were assessed via patient self-report on the survey. Patients were asked if a biological family member ever had specific conditions, including colon cancer, breast cancer, and heart attack, along with others that could be informed by the Sanford Chip. Response options included "Yes," "No," and "I don't know." The survey included patient weight and height, with data imputed if necessary from the EHR at a date closest to the time of enrollment. Details about the patients' invitation to and enrollment in the Sanford Chip program were captured from the EHR, consenting, and payment platforms. Patients were defined as enrolling in the Sanford Chip program for free if a standard patient-entered coupon code was documented within 30 days before the date of enrollment.

Different messaging was used in the Sanford Chip MyChart invitations to invite various subsets of eligible patients to enroll, which were then used to classify patients into one of the following 6 invitation cohorts: general, veteran, provider request, patient request, underserved community, or no invitation/unknown (a small subset of patients enrolled in the program without receiving a personal MyChart invitation; Supplemental Appendix B).

Data analysis

Data were deidentified by an honest broker before analysis by the study team. The use of deidentified data for this research were reviewed by the Sanford Health Institutional Review Board and approved via expedited review, and a waiver of HIPAA (Health Insurance Portability and Accountability Act) authorization and a waiver of consent were granted.

For inclusion in analyses, patients had to have completed enrollment in the Sanford Chip program and have a record of release of genetic results in the EHR data. EHR data were available on 97% of all patients who enrolled and received Sanford Chip results.

Descriptive statistics, including means with standard deviations, medians with interquartile ranges (IQR), and counts with percentages, were computed. We used data from patients' EHR to compare characteristics of patients who were administered the survey with patients who enrolled in the Sanford Chip program before the survey was administered using χ^2 tests, Wilcoxon rank-sum tests, and t tests. χ^2tests and t tests were used to examine the impact of talking to a primary care provider (PCP) before testing. We compared attitudes between invitation cohorts using $\chi^2$and 2-sample t tests to provide insight on differences between the various groups of patients invited to the Sanford Chip, from a general population to targeted subgroups of patients. We used the same approach to assess the impact of payment for the test by comparing patients who enrolled free of charge using a coupon with patients who paid full price for testing. χ^2 tests were used to examine whether patients who had not already been diagnosed with breast cancer, colon cancer, or a heart attack were more likely to rate their risks as higher rather than lower than the average person. All analyses were conducted using R version 4.3.2.

Results

The survey was initiated by 8075 patients, but 437 were excluded for incomplete enrollment, and 1718 were excluded for missing Sanford Chip results in the EHR. In total, 5920 patients (73.3%) completed enrollment, received results, and were included in analyses (Table 1). The majority of patients included were female (n = 3725, 62.9%), middle-aged (median age: 51.7 years, IQR: 25.8 years), White (n = 5573, 94.1%), and married (n = 4009, 68.6%). One thousand fifty-five patients (19.5%) used a coupon to receive testing at no out-of-pocket cost. Nearly all patients included in analyses (n = 5803; 98.0%) opted to receive MAP results. When we compared the representativeness of patients included in this analysis with those who received the Sanford Chip before administration of the baseline survey on characteristics available in the EHR, there were some statistically significant differences (Supplemental Table 1); however, there were no meaningful or substantial differences between the 2 groups.

Just over half of analyzed patients (n = 3328; 56.2%) enrolled in response to untargeted, general invitations. Differences were observed between cohorts on most patient characteristics (Supplemental Table 2), particularly between nonveterans and veterans, the latter of whom were more likely to be older, male, and married. On average, patients reported hearing about the Sanford Chip program from 1.8 sources (Supplemental Table 3). The sources that were cited

Table 1 Characteristics of survey respondents at enrollment

Characteristic	*N* (%), Unless Noted[a]
Sex	
Female	3725 (62.9%)
Male	2195 (37.1%)
Median age (IQR)	51.7 (25.8)
Self-reported race	
American Indian or Alaska Native	33 (0.6%)
Asian	31 (0.5%)
Black or African American	30 (0.5%)
Native Hawaiian or Pacific Islander	≤5 (≤0.1%)
White	5573 (95.4%)
More than one race	132 (2.3%)
Other	40 (0.7%)
Ethnicity	
Not of Hispanic, Latino, or Spanish origin	5724 (98.0%)
Hispanic, Latino, or Spanish origin	118 (2.0%)
Adopted	197 (3.3%)
Currently Married	4009 (68.6%)
Mean number of children (SD)	1.8 (1.4)
Employed full time	3473 (59.4%)
Household income	
<$50,000	1291 (27.0%)
$50,000 to $74,999	927 (19.4%)
$75,000 to $99,999	821 (17.2%)
$100,000 to $149,999	979 (20.5%)
≥$150,000	757 (15.9%)
Educational attainment	
High school graduate or less	805 (13.8%)
Post high school training / some college	2143 (36.8%)
College degree	1919 (32.9%)
Graduate or professional degree	958 (16.4%)
Mean BMI (SD)	31.7 (8.4)
Smoking status	
Current smoker	455 (7.8%)
Former smoker	1818 (31.0%)
Never smoker	3583 (61.2%)
Self-reported health status	
Excellent	319 (5.4%)
Very good	1776 (30.2%)
Good	2644 (45.0%)
Fair	957 (16.3%)
Poor	182 (3.1%)
GAD-2 score ≥3	1143 (19.5%)
Mean Charlson comorbidity score (SD)	1.77 (1.99)
PCP visit within prior 1 year	5219 (90.3%)
Prior visit with genetic specialist	600 (10.1%)
Self-reported prior genetic testing	783 (13.3%)
Self-reported personal history of genetic condition	781 (13.4%)
Self-reported family history of genetic condition	1627 (28.3%)
Self-reported personal history of cancer	535 (9.3%)
Self-reported family history of cancer	4366 (74.1%)
Sanford Region	
Sioux Falls	2789 (47.1%)
Fargo	2198 (37.1%)
Bismarck	634 (10.7%)
Bemidji	293 (4.9%)
Other/Not Reported	6 (0.1%)
Invitation cohort	
General	3328 (56.2%)
Veterans	1051 (17.8%)
Patient request	735 (12.4%)
Provider request	598 (10.1%)
Underserved	93 (1.6%)
No invitation	115 (1.9%)

BMI, body mass index; PCP, primary care provider.

[a]Percentages, means, and medians are not all based on a total of 5920 patients because of missing responses to some items. All variables were missing data from 5% or less of patients except for self-reported income, which had 19.3% missing.

most often were the Sanford MyChart patient portal (n = 3845, 65.1%), followed by patients' PCPs (n = 1320, 22.4%). Among patients who provided data about discussions with their PCP before testing, 832 of 1305 patients who learned about the Sanford Chip from their PCP reported talking to their PCP before getting testing, compared with 726 of 4495 patients who did not hear about the Sanford Chip from their PCP (63.8% vs 16.2%, respectively, $P < .001$). Only 9 patients reported that their PCPs were unsupportive of them getting the Sanford Chip.

Motivations, expectations, and concerns

Patients most frequently cited interest in learning personal disease risk (n = 2306, 39.1%) as the most important consideration when deciding to receive the Sanford Chip, followed by interest in medication response (n = 1382, 23.4%; Supplemental Table 4). When asked about how important each factor was in their decision to get the Sanford Chip, a majority of patients rated interest in medication responses, interest in personal disease risks, and providing disease risk information for children as very important considerations (71.4%, 61.5%, and 57.1% of patients, respectively; Table 2). The items least endorsed by patients as being very important considerations include the Chip being a fun opportunity, providers' recommendations, price, or family members' experiences (22.4%, 16.3%, 12.9%, and 4.7% of patients, respectively). However, the percentage that rated providers' recommendations as very important increased to 38.7% (601 of 1554 patients) among patients who reported discussing the Sanford Chip with their PCP. Overall, patients rated an average of 2.8 of the 10 motivation statements as very important.

Less than 20% of patients reported being "very concerned" about each of the potential topics of concern (Table 2). The topics that generated the most concern were the privacy of genetic information, how well results predicted future disease risk, and the potential for results to affect insurance (rated "very concerned" by 19.8%, 18.0%, and 14.1% of patients, respectively). Over 70% of patients

Table 2 Motivations, expectations, and concerns about getting the Sanford Chip

Item	
Motivations, *n* (%) who rated each reason "very important" (*n* = 5904)	
Interest in finding out how my body responds to certain medications	4214 (71.4%)
Interest in finding out about my personal disease risk	3631 (61.5%)
Providing disease risk information for my children (current or future)	3370 (57.1%)
There is a medical condition in my family that may be genetic	2808 (47.6%)
To learn more about my genetics because I lack information about my family history	1990 (33.7%)
I have a previous history of medications not working or frequent side effects to medications	1879 (31.8%)
It seemed like it would be a fun opportunity	1321 (22.4%)
My healthcare provider recommended it	961 (16.3%)
It was cheaper than other options	763 (12.9%)
Other members of my family have received the Sanford Chip	278 (4.7%)
Expectations, *n* (%) who agreed or strongly agreed (*n* = 5716 to 5849)	
Help guide my medication management	4298 (74.0%)
Help me prevent future health conditions	4023 (70.4%)
Help me learn more about the risk of passing on a disease to my children (current or future)	3810 (65.4%)
Explain a family history of disease	2532 (43.5%)
Give me information about specific diseases that I am concerned about	2036 (35.1%)
Reassure me that I am healthy	2046 (35.7%)
Help explain a condition that I have	1354 (23.1%)
Concerns, *n* (%) who rated their level of concern as "very concerned" (*n* = 5727 to 5853)	
The privacy of my genetic information	1156 (19.8%)
How well the results will predict my future disease risk	1055 (18.0%)
The results might affect my ability to get insurance	814 (14.1%)
How the results may affect family members	416 (7.2%)
The possibility that I might receive unwanted information	338 (5.9%)
The price of the Sanford Chip	178 (3.1%)
The amount of time I will have to wait to receive my Sanford Chip results	118 (2.0%)
My ability to cope with my Sanford Chip results	86 (1.5%)

The data above summarize survey responses about "how important the following were in [the patient's] decision to get the Sanford Chip," what the patient expected "to learn from [their] Sanford Chip results," and the patient's "level of concern with any of the following factors when deciding to get the Sanford Chip." Summaries that include data for all responses options are presented in the Supplemental Tables S4, S5, and S6.

reported at least some concern regarding how well results predicted risks for future disease (Supplemental Table 6), and over half of patients expressed at least some concern about the privacy of genetic results and the potential impact on patients' ability to obtain insurance. More than 75% of patients reported that they were not at all concerned about the price of the Sanford Chip (including 78.6% of patients who paid for the service), the wait time for results, or coping with results. Overall, patients rated being very concerned for an average of 0.71 of the 8 potential concerns presented.

Regarding expectations, a majority of patients agreed with statements that the Sanford Chip results would help guide medication management, prevent future health conditions, and help patients learn about the risks of passing on disease to children (endorsed by 74.0%, 70.4%, and 65.4% of patients, respectively; Table 2). Overall, patients expected the Sanford Chip to provide information about 3.4 of the 7 topics presented. Three-hundred twenty of 771 patients (41.5%) who reported that they had a known genetic condition expected results to explain a condition they had, compared with 1012 of 4993 patients (20.3%) who reported that they did not have a known genetic condition ($P < .001$). Similarly, 879 of 1604 patients (54.8%) who reported a known genetic condition in their family expected results to explain a family history of disease, compared with 1587 of 4079 patients (38.9%) who did not report a known genetic condition in their family ($P < .001$).

Important differences were identified in comparisons by cohort. Veterans were less likely than nonveterans to report interest in PGx (60.9% vs 73.7%, $P < .001$; Supplemental Figure 1) or interest in learning personal disease risk (50.3% vs 63.9%, $P < .001$) as very important motivations. Patients who had an invitation requested personally or by a HCP were more likely than other patients to report a history of medication nonresponse or side effects as a very important motivation (44.2% vs 28.2%, $P < .001$) and were more likely to report expectations that test results would guide medication management (80.9% vs 72.0%, $P < .001$; Supplemental Figure 2). Patients whose invitation was requested by a HCP were more likely than other patients to report provider recommendations as very important (39.2% vs 13.7%, $P < .001$). Some differences were also identified in comparisons by coupon status. Patients who used a coupon to enroll free of charge rated slightly fewer motivations as very important (3.1 vs 3.7, $P < .001$; Supplemental Figure 3) and endorsed slightly fewer expectations (3.3 vs 3.5, $P = .01$; Supplemental Figure 4) than patients who did not use a coupon.

Knowledge

On average, patients answered 6.7 of 11 knowledge items correctly (61.3%) and responded "I don't know" to 1.9 items (17.6%). Patients who reported talking to their PCP before testing answered fewer knowledge items correctly than those who did not report having this discussion (mean 6.6 vs 6.8, respectively, $P < .001$) and both groups responded "I don't know" to the same number of knowledge items, on average (1.9 vs 1.9, respectively, $P = .76$). The question on the meaning of an uninformative result had the highest percentage of "I don't know" responses (36.6%; Table 3). Patients were most likely to know that PGx refers to how genes affect medication processing (82.1%) and that the Sanford Chip provided information about both disease risk and medication response (85.8%). Patients were least likely to answer correctly on items about whether the Sanford Chip would provide definitive information about what medications would work or would cause side effects (answered correctly by 41.0% and 37.1% of patients, respectively). Similarly, only slightly more than half of patients (56.3%) correctly answered that genes were not the only factor that influence how one responds to medications.

Only 1745 patients (29.5%) reported that they had heard about GINA, despite it being covered in the Sanford Chip consent process. Of those who reported awareness, 1515 (86.8%; Supplemental Table 7) correctly reported that it protected against health insurance discrimination, whereas only 911 (52.2%) knew that it also protected against employment discrimination. Approximately half of patients with awareness of GINA knew that it did not protect against discrimination toward life, disability, or long-term care insurance.

Risk perceptions

Overall, patients were more likely to report their risks as lower rather than higher than an average person of the same age, sex, and ethnicity for both colon cancer (30.3% vs 22.5%, respectively, $P < .001$) and breast cancer (42.6% vs 21.7%, respectively, $P < .001$). In contrast, patients were more likely to report their risks for a heart attack as higher rather than lower than an average person of the same age, sex, and ethnicity (40.6% vs 20.1%, respectively, $P < .001$). Risk perception analyses stratified by family history status showed that patients perceived greater risk for all conditions when they reported an uncertain rather than no family

Table 3 Responses to knowledge items

Statement	Response Options				
	How Body Processes Certain Medications	**Chances to Develop Certain Genetic Conditions**	**Both Types of Information**	**Neither Type of Information**	**Don't Know**
The Sanford Chip is a genetic screening tool that may give information about	570 (9.6%)	196 (3.3%)	5072 (85.8%)[a]	5 (0.1%)	71 (1.2%)
	Lower	**Unchanged**	**Higher**		**Don't Know**
An uninformative result means my risk for a genetic condition tested by the Sanford Chip is	1005 (17.0%)	2637 (44.6%)[a]	106 (1.8%)		2,166 (36.6%)
	False	**True**			**Don't Know**
An uninformative Sanford Chip result means that I will not develop a genetic condition in the future	4476 (75.7%)[a]	215 (3.6%)			1223 (20.7%)
Pharmacogenomics refers to how changes in my genes impact how my body processes certain medications	132 (2.2%)	4855 (82.1%)[a]			927 (15.7%)
Only my genes influence how I respond to medications	3331 (56.3%)[a]	1065 (18.0%)			1518 (25.7%)
My Sanford Chip results will tell my healthcare provider what medications will definitely work for me	2422 (41.0%)[a]	2397 (40.5%)			1095 (18.5%)
My Sanford Chip results will tell my healthcare provider what medications will definitely cause side effects for me	2196 (37.1%)[a]	2246 (38.0%)			1472 (24.9%)
The Sanford Chip reports genetic changes that play a role in…	**No**	**Yes**			**Don't Know**
Increased risk for Alzheimer's disease	3260 (55.1%)[a]	1838 (31.1%)			816 (13.8%)
Ancestry	3752 (63.4%)[a]	1349 (22.8%)			813 (13.7%)
Increased risk for cancer	1942 (32.8%)	3163 (53.5%)[a]			809 (13.7%)
How I process some medications	457 (7.7%)	4690 (79.3%)[a]			767 (13.0%)

[a]Correct answer.

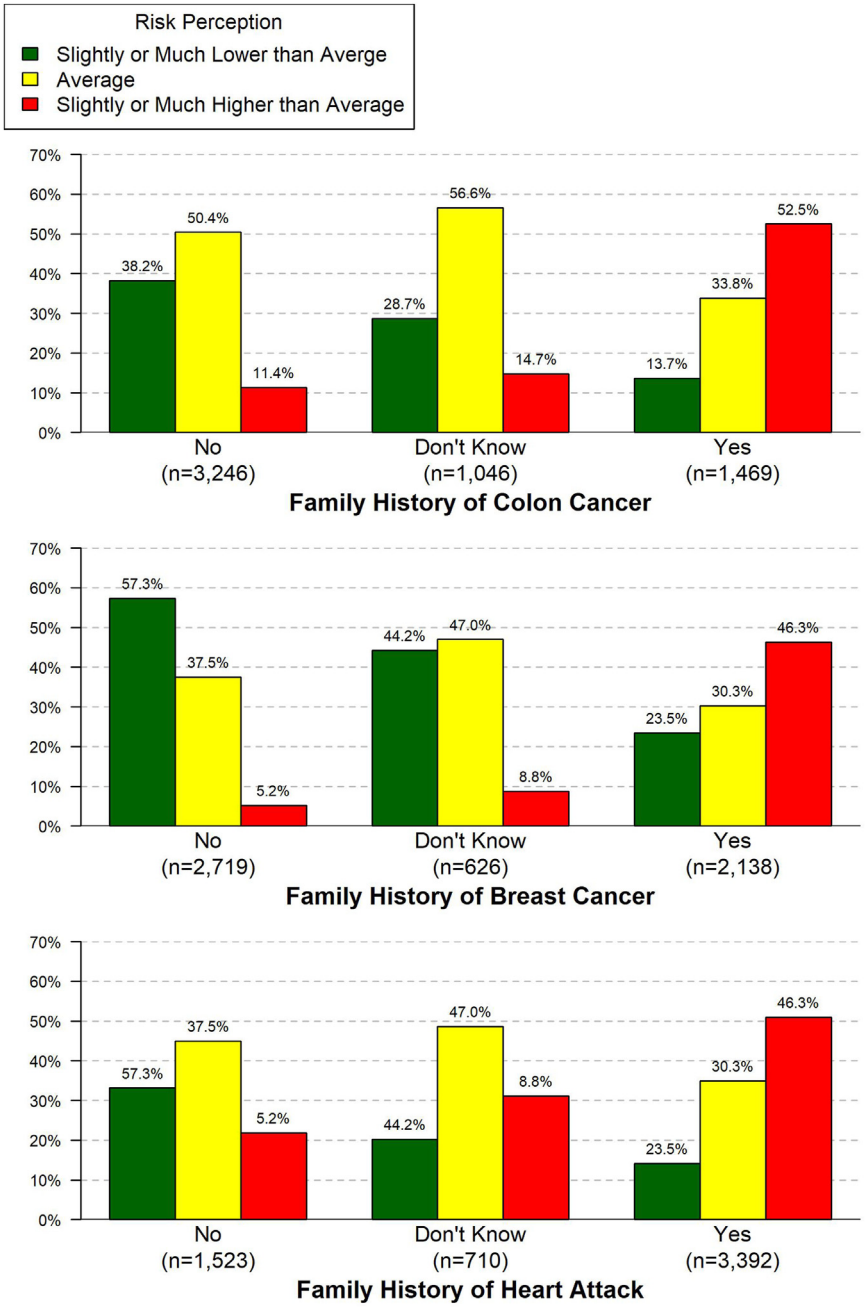

Figure 1 Risk perceptions for colon cancer, breast cancer, and heart attack, stratified by family history of the condition. Patients were asked to rate their risk for 3 conditions compared with the average person of the same age, sex, and ethnicity.

history of the condition (all P <.001; Figure 1) and also perceived greater risk when they reported a definitive rather than uncertain family history of the condition (all P <.001).

Discussion

This study provides real-world data about the motivations, expectations, concerns, knowledge, and risk perceptions of adult patients undergoing EGT as a clinical service. Our data show that nearly all patients opted to be screened for MAPs, and that patients were largely motivated by and were expectant of the clinical and personal utility that EGT could provide for themselves and their children. Concerns about testing tended to be low. Overall, findings show strong enthusiasm toward EGT among those who pursued testing; however, some show relatively poor understanding of the capabilities of EGT, especially overestimating its ability to definitively predict medication efficacy and side effects.

Our results provide important prospective data about perceptions of patients who pursue EGT as part of clinical programs. Results are largely consistent with retrospective findings from the DNA-10K program,[4] in which patients showed similar levels of motivation toward learning their

disease risks and similar levels of concerns toward privacy and insurance risks, as well as a lack of familiarity with GINA. The elective nature of testing likely explains the relative lack of concerns among patients who underwent testing because patients with significant concerns may avoid testing before or following test education. However, although few patients here reported concerns at enrollment, follow-up studies assessing anxiety and distress after results are received will provide more insight. Differences between our data and findings from the DNA-10K program were greatest with respect to PGx testing. Over 70% of Sanford Chip recipients reported learning about their medication response as a very important motivation, compared with less than half of DNA-10K participants who rated learning about their medication response as influencing their enrollment "to a great extent." These discrepancies likely reflect the strong emphasis on PGx testing at Sanford Health and its investments in developing the infrastructure and clinical decision support to support these applications.[14,23-25]

Findings on the knowledge and awareness items raise some concerns. Clinics offering EGT may need to integrate robust steps to ensure patients who follow through with testing are making well-informed choices. Patients answered only about 60% of knowledge items correctly, and only 30% were aware of GINA, despite having finished the web-based education, which included information on GINA. The high percentage of patients unsure of the meaning of an uninformative result, the most likely MAP result for a patient to receive, could lead to confusion or false reassurance once results are received. The meaning and implication of both positive and negative MAP results should be clearly explained with results disclosure to ensure patients fully understand their results.

Knowledge about PGx testing was also concerning, given that the genes examined by the Sanford Chip are just some of the many factors that affect drug response.[26] Just over half of patients correctly reported that medication responses were determined by more than genes. As many patients responded "true" as responded "false," however, to statements that Sanford Chip results would tell health care providers what medications would definitely work and definitely cause side effects. Discussing the Sanford Chip with their PCP before testing did not result in higher knowledge compared with those who did not report having a discussion, although providers may not have been well prepared to discuss the Sanford Chip with patients, and we do not know the content of these discussions. Web-based patient education about genetics has produced mixed results in prior studies.[27-29] In implementing web-based education for a scalable EGT program, knowledge check questions with correct answer reinforcement may be considered in the future to improve information retention and comprehension. In addition, our findings highlight the potential for patients to have deterministic beliefs about drug response. Although most studies to date show that patients appreciate that genetics are just one of many factors that determine disease risk,[30-32] few studies have examined beliefs about genetic determination and drug response.

Interestingly, attitudes toward PGx information may not have been as important to patients as attitudes toward screening for MAPs when deciding to pursue the Sanford Chip. Learning about PGx was rated as a very important motivation by the greatest number of patients, but learning about disease risks surpassed this as the most important factor in their decision to enroll in the Sanford Chip program. Yet, anecdotal evidence from Sanford Health and a cross-site study of the IGNITE Network suggest that general practice providers may have more favorable attitudes toward PGx testing than genetic testing for disease risk.[33] Emphasis on MAP screening by patients may be explained by the high percentage in our analyses who reported a personal or family history of a genetic condition. Although prior studies of population screening programs have found that they attract patients with higher a priori risks of genetic conditions,[13] based on patients' limited genetics knowledge and overestimation of test capabilities, this self-report may not accurately reflect diagnoses of established genetic conditions nor those relevant to the Sanford Chip. Health systems offering EGT will need to be sensitive to the potential for patients to be focused on test results that HCPs have more reservations about to avoid misunderstanding and false reassurance.

Our study also provides insight about the generalizability of findings from investigational studies of EGT in which patients may be receiving testing at low or no cost. Patients who enrolled in the Sanford Chip program using a coupon appear to be less motivated toward testing and expected less from test results than patients who paid full price for testing. Given the low likelihood of identifying a monogenic disease risk during testing,[12] it is possible that patients who pay for EGT out-of-pocket are more likely to report dissatisfaction with the experience than patients who receive complimentary EGT. It is also possible that the lower motivation among patients receiving complimentary EGT will result in them being less likely to use results to make lifestyle changes or changes to life planning.[34]

Limitations

Strengths to our study include a real-world population, prospective design, and mandatory survey completion to receive testing. Limitations include data from a single health system with predominantly White patients. Data were not available to compare the characteristics of program participants and survey respondents with the characteristics of eligible patients. Survey data were not collected from patients who enrolled in the program before August 2020. Additionally, novel survey items were not validated, and cognitive interviews were not conducted to ensure that survey items were interpreted as intended or that prepopulated response options were inclusive and relevant to this patient population. Data collected after disclosure of the genetic results on the impact of testing on patient and provider outcomes are not yet available.

Conclusion

EGT is increasingly available in an expanding number of health systems. Patients who pursue such testing are likely to appreciate the potential benefits of this testing but are also likely to overestimate its capabilities. Health systems and HCPs will need to be sensitive to patients' understandings and ensure that their expectations are realistic.

Data Availability

Data and code will be made available on request. Inquiries can be directed to the corresponding author.

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Ethics Declaration

This study was approved by the Sanford Institutional Review Board, and a waiver of HIPAA authorization and a waiver of consent were granted.

Conflict of Interest

Robert C. Green, Kurt D. Christensen, Emilie S. Zoltick, Madison R. Hickingbotham, Jessica L. LeBlanc, and Lauren N. Galbraith were supported by a research grant from Sanford Health. Madison R. Hickingbotham, Madison R. Hickingbotham, Ann Chen Wu, Lauren N. Galbraith, and Jessica L. LeBlanc have been funded by National Center for Advancing Translational Sciences (NCATS), National Heart, Lung, and Blood Institute (NHLBI), and National Institute of Child Health and Human Development (NICHD). Ann Chen Wu has received grants from NICHD, NHLBI, and GlaxoSmithKline. Catherine Hajek is an employee of Helix OpCo. Christine Y. Lu undertook contract work with Illumina Inc outside the submitted work and has received research grants and contracts from National Human Genome Research Institute (NHGRI), NIMH, NICHD, National Cancer Institute, and Centers for Disease Control and Prevention. Emilie S. Zoltick has been funded by NIMHD. Hadley Stevens Smith has been funded by NHGRI and NICHD, has consulted for Illumina, Inc and received compensation, and has received compensation from Elsevier and the Eastern Society of Pediatric Research. Kurt D. Christensen has received research grants from NHGRI, NCATS, NHLBI, and NICHD. Lauren N. Galbraith is an employee of Pfizer, Inc. Robert C. Green has received compensation for advising the following companies: AIA, Allelica, Atria, Fabric, Genome Web, Genomic Life, Verily, and VinBigData; is cofounder of Genome Medical and Nurture Genomics; and has received research grants from NCATS, NHLBI, the Danaher Foundation, the Southcentral Foundation, GRAIL, and Beaumont Health. All other authors declare no conflicts of interest.

Additional Information

The online version of this article (https://doi.org/10.1016/j.gim.2024.101200) contains supplemental material, which is available to authorized users.

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SUPPLEMENTARY MATERIAL

Attitudes, Knowledge, and Risk Perceptions of Patients who Received Elective Genomic Testing as a Clinical Service

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Contents

Appendix A. Description of survey measures and administration

Survey Measures

Motivations, expectations, and concerns

To assess motivations, patients rated the importance of ten pre-specified reasons why they may have decided to pursue the Sanford Chip. Response options included “not at all important,” “somewhat important,” “very important,” and “not applicable.” Participants also indicated which of the ten reasons were most important to them. To assess expectations, patients responded to seven statements about what they expected to learn from their Sanford Chip results on 5-point scales, from “strongly disagree” to “strongly agree.” To assess concerns, patients rated their level of concern about eight topics when deciding to pursue the Sanford Chip. Response options included “not at all concerned,” “somewhat concerned,” and “very concerned.”

Knowledge

We wrote a set of eleven items to assess knowledge specific to the Sanford Chip program based on key elements of the patient education materials and clinical consent document. The knowledge questions included two multiple choice items, five true/false items, and an item that asked respondents to indicate whether the Sanford Chip provided four types of genetic results. We also asked whether respondents had heard of the Genetic Information Nondiscrimination Act (GINA)[1] and, if so, the respondent was asked a series of true/false questions to measure their awareness of whether it provided protections about health insurance, employment, life insurance, disability insurance, or long-term care insurance. All knowledge items also included a response option of “I don’t know.”

Risk Perceptions

We assessed risk perceptions about conditions that could be informed by Sanford Chip results: colon cancer, breast cancer, and heart attack. For each condition, participants were first

asked, “Compared to the average person of your age, sex, and ethnicity, what do you think your chance of [getting colon cancer/getting breast cancer/having a heart attack] is?”. Response options included, “much lower than average,” “slightly lower than average,” “average,” “slightly higher than average,” “much higher than average,” and “I already have/had [colon cancer/breast cancer/a heart attack].” Next, participants who did not indicate already experiencing the condition were asked, “What do you think your chance of [getting colon cancer/getting breast cancer/having a heart attack] in your lifetime is?” Response options included, “not at all likely to happen,” “not very likely to happen,” “somewhat likely to happen,” “very likely to happen,” and “certain to happen.”

Survey Platform

From August 2020 to December 2020, the survey was administered during the Sanford Chip program consent process through a third party survey platform created by Pryzm Health (https://www.pryzm.health/). From January 2021 to April 2022, the consent and survey were administered on a platform developed by Sanford Health.

Supplemental References

1. The Genetic Information Non-Discrimination Act. Public Law 110-223. https://www.govinfo.gov/content/pkg/PLAW-110publ233/pdf/PLAW-110publ233.pdf. Accessed Jan 10, 2024.

Appendix B. Details of Sanford Chip cohort assignment based on invitation messages

Sanford Chip invitation subject lines were specific to each subset of eligible patients, though patients could receive multiple invitations of different types. These invitation messages were used to classify patients into one of six invitation cohorts. Based on the patient experience, including the time between receiving an invitation and enrolling, the following algorithm was used for assigning a cohort to patients who received more than one invitation. Any patient who ever received an invitation specific to military veterans was categorized in the veteran cohort. If a patient received an invitation requested by a provider (defined using the invitation subject line and the presence of a provider order requesting an invitation), requested by the patient, or as a member of an underserved community within six months of their last invitation prior to enrollment, then the patient was categorized into that respective cohort. All other cohort assignments were defined based on the last invitation received prior to enrollment.

***Table S1*. Characteristics of Sanford Chip recipients prior to enrollment, by survey administration status**

Characteristics of patients who received the Sanford Chip, from electronic health records data, stratified according to whether or not they enrolled after August 2020 and were administered the baseline survey.

Characteristic	Not administered the survey (n=11,470)	Administered the survey (n=5,920)	p
Sex			0.876
Female	7,231 (63.0%)	3,725 (62.9%)	
Male	4,239 (37.0%)	2,195 (37.1%)	
Median age (IQR)	55.8 (25.4)	51.7 (25.8)	<0.001
Race[a]			<0.001
African American or Black	40 (0.3%)	50 (0.8%)	
American Indian or Alaskan Native	78 (0.7%)	57 (1.0%)	
Asian	78 (0.7%)	37 (0.6%)	
White	11,204 (97.7%)	5,733 (96.8%)	
Other	12 (0.1%)	5 (0.1%)	
Declined or data were unavailable	58 (0.5%)	38 (0.6%)	
Ethnicity[a]			
Hispanic or Latino	85 (0.7%)	91 (1.5%)	
Not Hispanic or Latino	11,262 (98.2%)	5,768 (97.4%)	
Not reported	123 (1.1%)	61 (1.0%)	
Smoking status[a]			0.128
Current smoker	697 (6.1%)	394 (6.7%)	
Former smoker	3,531 (30.8%)	1,746 (29.5%)	
Nonsmoker	7,187 (62.7%)	3,744 (63.2%)	
Not reported	55 (0.5%)	36 (0.6%)	
Mean Charlson comorbidity score (sd)	1.9 (2.0)	1.8 (2.0)	<0.001
PCP visit within prior 1 year	10,391 (92.9%)	5,219 (90.3%)	<0.001
Prior visit with genetic specialist	1,083 (9.4%)	600 (10.1%)	0.142
Sanford Region			<0.001
Bemidji	602 (5.2%)	293 (4.9%)	
Bismarck	1,225 (10.7%)	634 (10.7%)	
Fargo	4,650 (40.5%)	2,198 (37.1%)	
Sioux Falls	4,986 (43.5%)	2,789 (47.1%)	
Other/Not Reported	7 (0.1%)	6 (0.1%)	

[a] Results for these characteristics may differ slightly from those presented in Table 1, as all patient characteristics in this table are from EHR data only.

***Table S2*. Characteristics of survey respondents, by cohort**

		Cohort					
Characteristic	**General**	**Veterans**	**Patient Request**	**Provider Request**	**Underserved**	**No invitation**	**p**
Sex							<0.001
Female	2409 (72.4%)	197 (18.7%)	539 (73.3%)	425 (71.1%)	70 (75.3%)	85 (73.9%)	
Male	919 (27.6%)	854 (81.3%)	196 (26.7%)	173 (28.9%)	23 (24.7%)	30 (26.1%)	
Median age (IQR)	50.0 (24.4)	61.6 (24.9)	50.0 (25.7)	45.9 (26.5)	54.6 (25.1)	48.9 (21.7)	<0.001
Non-Hispanic White	3107 (93.4%)	988 (94.0%)	670 (91.2%)	543 (90.8%)	85 (91.4%)	107 (93.0%)	0.057
Adopted	102 (3.1%)	46 (4.4%)	28 (3.9%)	17 (3.0%)	2 (2.2%)	2 (1.8%)	0.272
Currently Married	2249 (68.1%)	792 (76.8%)	460 (63.6%)	379 (65.1%)	69 (75.0%)	60 (53.1%)	<0.001
Mean number of children (sd)	1.8 (1.4)	2.0 (1.3)	1.8 (1.4)	1.6 (1.3)	1.9 (1.3)	1.7 (1.4)	<0.001
Employed full time	2087 (63.2%)	499 (48.1%)	429 (59.4%)	343 (58.8%)	48 (52.2%)	67 (59.3%)	<0.001
Household income							<0.001
<$50,000	718 (26.2%)	195 (22.9%)	189 (33.7%)	140 (30.6%)	20 (25.6%)	29 (32.6%)	
$50,000 to $74,999	499 (18.2%)	189 (22.2%)	103 (18.4%)	98 (21.4%)	18 (23.1%)	20 (22.5%)	
$75,000 to $99,999	462 (16.9%)	171 (20.1%)	92 (16.4%)	70 (15.3%)	12 (15.4%)	14 (15.7%)	
$100,000 to $149,999	589 (21.5%)	184 (21.6%)	99 (17.6%)	70 (15.3%)	21 (26.9%)	16 (18.0%)	
≥$150,000	470 (17.2%)	112 (13.2%)	78 (13.9%)	80 (17.5%)	7 (9.0%)	10 (11.2%)	
Educational attainment							0.003
High school graduate or less	436 (13.2%)	124 (12.0%)	126 (17.5%)	92 (15.9%)	10 (11.0%)	17 (15.0%)	
Post high school training / some college	1163 (35.3%)	429 (41.7%)	265 (36.9%)	206 (35.6%)	28 (30.8%)	52 (46.0%)	
College degree	1132 (34.4%)	309 (30.0%)	214 (29.8%)	193 (33.3%)	38 (41.8%)	33 (29.2%)	
Graduate or professional degree	563 (17.1%)	168 (16.3%)	113 (15.7%)	88 (15.2%)	15 (16.5%)	11 (9.7%)	
Mean BMI (sd)	32.0 (8.7)	31.5 (7.5)	31.1 (8.4)	30.8 (8.1)	32.4 (9.7)	30.8 (7.6)	
Smoking status							<0.001
Never smoker	2094 (63.4%)	508 (49.0%)	482 (66.4%)	383 (65.4%)	51 (55.4%)	65 (57.5%)	
Former smoker	977 (29.6%)	455 (43.9%)	180 (24.8%)	141 (24.1%)	29 (31.5%)	36 (31.9%)	
Current smoker	232 (7.0%)	73 (7.0%)	64 (8.8%)	62 (10.6%)	12 (13.0%)	12 (10.6%)	
Self-reported health status							0.336
Excellent	173 (5.2%)	68 (6.5%)	33 (4.6%)	32 (5.5%)	5 (5.5%)	8 (7.0%)	
Very good	1024 (30.9%)	324 (31.0%)	203 (28.0%)	172 (29.3%)	27 (29.7%)	26 (22.8%)	
Good	1494 (45.0%)	471 (45.1%)	320 (44.1%)	256 (43.6%)	44 (48.4%)	59 (51.8%)	
Fair	531 (16.0%)	151 (14.5%)	141 (19.4%)	106 (18.1%)	11 (12.1%)	17 (14.9%)	
Poor	95 (2.9%)	30 (2.9%)	28 (3.9%)	21 (3.6%)	4 (4.4%)	4 (3.5%)	
GAD-2 score ≥3	618 (18.7%)	109 (10.6%)	181 (25.1%)	192 (32.9%)	16 (17.4%)	27 (23.9%)	<0.001

Mean Charlson comorbidity score (sd)	1.5 (1.7)	2.7 (2.4)	1.7 (2.0)	1.6 (2.0)	1.6 (1.6)	1.5 (1.9)	<0.001
PCP visit within prior 1 year	2903 (89.7%)	933 (90.8%)	649 (90.5%)	553 (92.5%)	77 (91.7%)	104 (92.0%)	0.357
Prior visit with genetic specialist	376 (11.3%)	37 (3.5%)	76 (10.4%)	86 (14.4%)	12 (12.9%)	13 (11.3%)	<0.001
Self-reported prior genetic testing	487 (14.7%)	100 (9.6%)	101 (13.9%)	70 (11.9%)	8 (8.6%)	17 (15.0%)	<0.001
Self-reported personal history of genetic condition	454 (13.8%)	103 (10.0%)	118 (16.5%)	81 (14.0%)	10 (10.8%)	15 (13.5%)	0.004
Self-reported family history of genetic condition	958 (29.4%)	204 (20.1%)	246 (34.7%)	163 (28.6%)	26 (28.3%)	30 (27.0%)	<0.001
Self-reported personal history of cancer	298 (9.2%)	189 (18.3%)	106 (14.8%)	80 (13.8%)	6 (6.6%)	14 (12.4%)	<0.001
Self-reported family history of cancer	2914 (87.6%)	863 (82.1%)	625 (85.0%)	526 (88.0%)	79 (84.9%)	102 (88.7%)	<0.001
Sanford Region							<0.001
Bemidji	163 (4.9%)	47 (4.5%)	30 (4.1%)	22 (3.7%)	25 (26.9%)	6 (5.2%)	
Bismarck	351 (10.5%)	126 (12.0%)	76 (10.3%)	66 (11.0%)	0 (0.0%)	15 (13.0%)	
Bozeman	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	0 (0.0%)	0 (0.0%)	
Fargo	1334 (40.1%)	323 (30.7%)	237 (32.2%)	273 (45.7%)	2 (2.2%)	29 (25.2%)	
Sioux Falls	1475 (44.3%)	555 (52.8%)	392 (53.3%)	236 (39.5%)	66 (71.0%)	65 (56.5%)	
Other/Not Reported	5 (0.2%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	0 (0.0%)	0 (0.0%)	

***Table S3*. How patients heard about the Sanford Chip**

Source	n (%)
MyChart Message	3845 (65.1%)
Patient's primary care provider at Sanford Health	1320 (22.4%)
Sanford Flyer or Advertisement	483 (8.2%)
Family Member	394 (6.7%)
Provider other than PCP	275 (4.7%)
Friend	155 (2.6%)
Other	489 (8.3%)

***Table S4*. Patients' ratings of motivations for getting the Sanford Chip: all response options**

Patients' rated "how important the following were in [their] decision to get the Sanford Chip." "Not applicable" was a response option to all statements. Patients also specified "the MOST important in [their] decision to get the Sanford Chip."

	Rated Importance, n (%)				Rated as
Motivation	**Not at all**	**Somewhat**	**Very**	**Not Applicable**	**Most Important**
Interest in finding out how my body responds to certain medications	94 (1.6%)	1,567 (26.5%)	4,214 (71.4%)	29 (0.5%)	1,382 (23.4%)
Interest in finding out about my personal disease risk	111 (1.9%)	2,100 (35.6%)	3,631 (61.5%)	62 (1.1%)	2,306 (39.1%)
Providing disease risk information for my children (current or future)	268 (4.5%)	1,564 (26.5%)	3,370 (57.1%)	702 (11.9%)	526 (8.9%)
There is a medical condition in my family that may be genetic	427 (7.2%)	2,253 (38.2%)	2,808 (47.6%)	416 (7.0%)	637 (10.8%)
To learn more about my genetics because I lack information about my family history	916 (15.5%)	2,317 (39.2%)	1,990 (33.7%)	681 (11.5%)	363 (6.2%)
I have a previous history of medications not working or frequent side effects to medications	1,043 (17.7%)	1,833 (31.0%)	1,879 (31.8%)	1,149 (19.5%)	425 (7.2%)
It seemed like it would be a fun opportunity	1,481 (25.1%)	2,306 (39.1%)	1,321 (22.4%)	796 (13.5%)	108 (1.8%)
My healthcare provider recommended it	646 (10.9%)	1,110 (18.8%)	961 (16.3%)	3,187 (54.0%)	92 (1.6%)
It was cheaper than other options	1,461 (24.7%)	1,069 (18.1%)	763 (12.9%)	2,611 (44.2%)	33 (0.6%)
Other members of my family have received the Sanford Chip	1,318 (22.3%)	453 (7.7%)	278 (4.7%)	3,855 (65.3%)	23 (0.4%)

***Table S5*. Patients' expectations about the Sanford Chip: all response options**

Patients rated how strongly they agreed with seven statements about "what [they] expect to learn from [their] Sanford Chip results."

Expectation	Strongly Disagree	Disagree	Neither Agree nor Disagree	Agree	Strongly Agree
Help guide my medication management	80 (1.4%)	89 (1.5%)	1,342 (23.1%)	3,179 (54.7%)	1,119 (19.3%)
Help me prevent future health conditions	50 (0.9%)	130 (2.3%)	1,513 (26.5%)	3,258 (57.0%)	765 (13.4%)
Help me learn more about the risk of passing on a disease to my children (current or future)	209 (3.6%)	153 (2.6%)	1,651 (28.4%)	2,899 (49.8%)	911 (15.6%)
Explain a family history of disease	181 (3.1%)	330 (5.7%)	2,778 (47.7%)	2,148 (36.9%)	384 (6.6%)
Give me information about specific diseases that I am concerned about	108 (1.9%)	339 (5.8%)	3,315 (57.2%)	1,699 (29.3%)	337 (5.8%)
Reassure me that I am healthy	117 (2.0%)	394 (6.9%)	3,178 (55.4%)	1,756 (30.6%)	290 (5.1%)
Help explain a condition that I have	306 (5.2%)	559 (9.6%)	3,630 (62.1%)	1,021 (17.5%)	333 (5.7%)

***Table S6*. Patients' concerns about the Sanford Chip: all response options**

Patients rated their level of concern about certain factors "when deciding to get the Sanford Chip."

	Level of Concern		
Concern	**Not at All**	**Somewhat**	**Very**
The privacy of my genetic information	2,655 (45.5%)	2,020 (34.6%)	1,156 (19.8%)
How well the results will predict my future disease risk	1,686 (28.8%)	3,112 (53.2%)	1,055 (18.0%)
The results might affect my ability to get insurance	2,731 (47.3%)	2,232 (38.6%)	814 (14.1%)
How the results may affect family members	2,976 (51.8%)	2,348 (40.9%)	416 (7.2%)
The possibility that I might receive unwanted information	3,248 (56.7%)	2,141 (37.4%)	338 (5.9%)
The price of the Sanford Chip	4,604 (79.6%)	1,000 (17.3%)	178 (3.1%)
The amount of time I will have to wait to receive my Sanford Chip results	4,803 (82.5%)	900 (15.5%)	118 (2.0%)
My ability to cope with my Sanford Chip results	4,433 (77.0%)	1,235 (21.5%)	86 (1.5%)

***Table S7*. Patients' responses about the protection GINA provides**

Analyses include only patients who reported awareness of GINA.

Type of Insurance	Yes	No	Don't Know
Health insurance discrimination	1,515 (86.8%)	113 (6.5%)	117 (6.7%)
Employment discrimination	911 (52.2%)	703 (40.3%)	131 (7.5%)
Life insurance discrimination	743 (42.6%)	870 (49.9%)	132 (7.6%)
Disability insurance discrimination	681 (39.0%)	928 (53.2%)	136 (7.8%)
Long-term care insurance discrimination	668 (38.3%)	940 (53.9%)	136 (7.9%)

***Figure S1*. Motivations, by cohort**

Bars indicate the percentage of each cohort who rated motivations as “very important” in their decision to get the Sanford Chip.

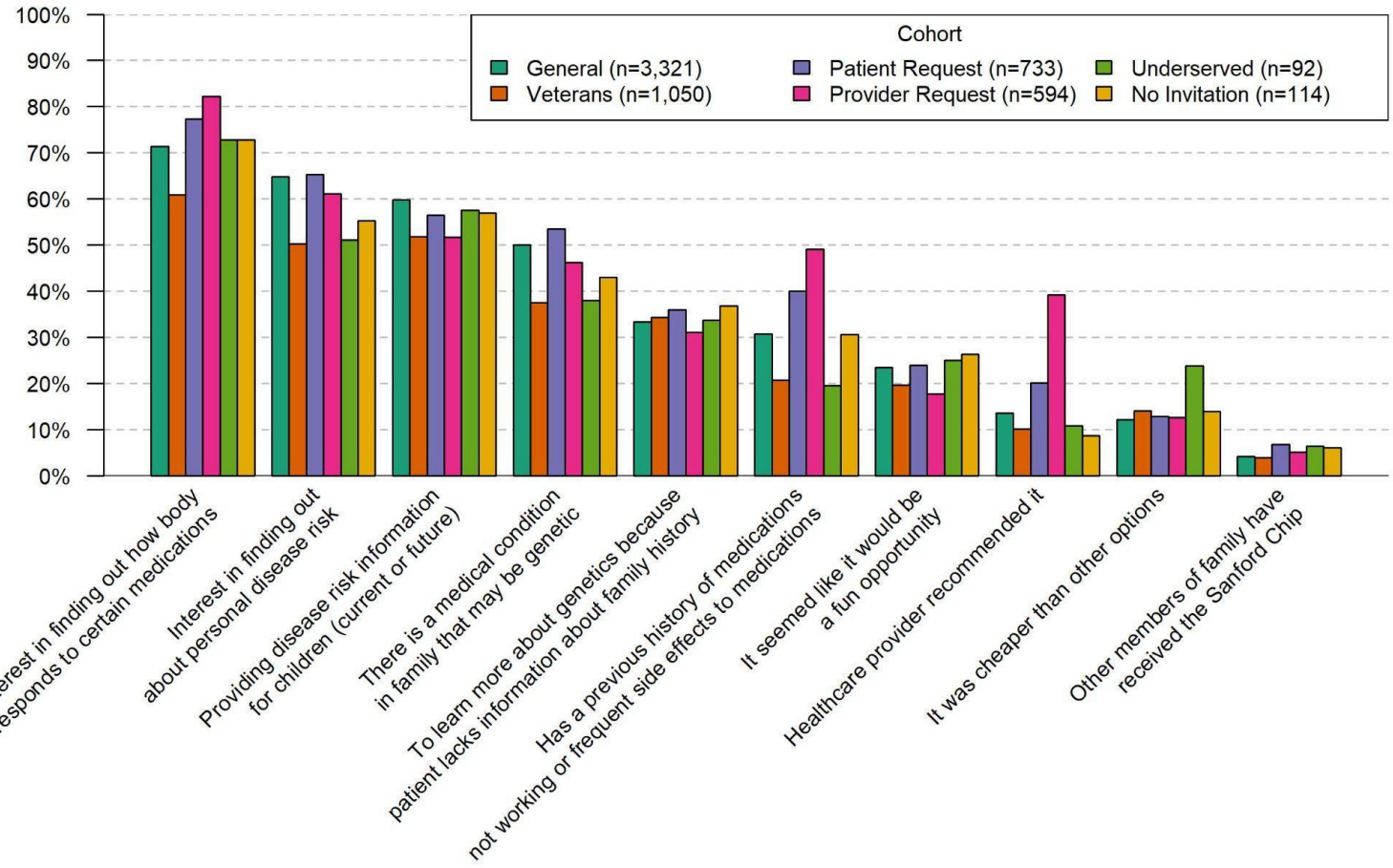


***Figure S2*. Expectations, by cohort**

Bars indicate the percentage of each cohort who agreed or strongly agreed with statements about information they expected "to learn from [their] Sanford Chip results.

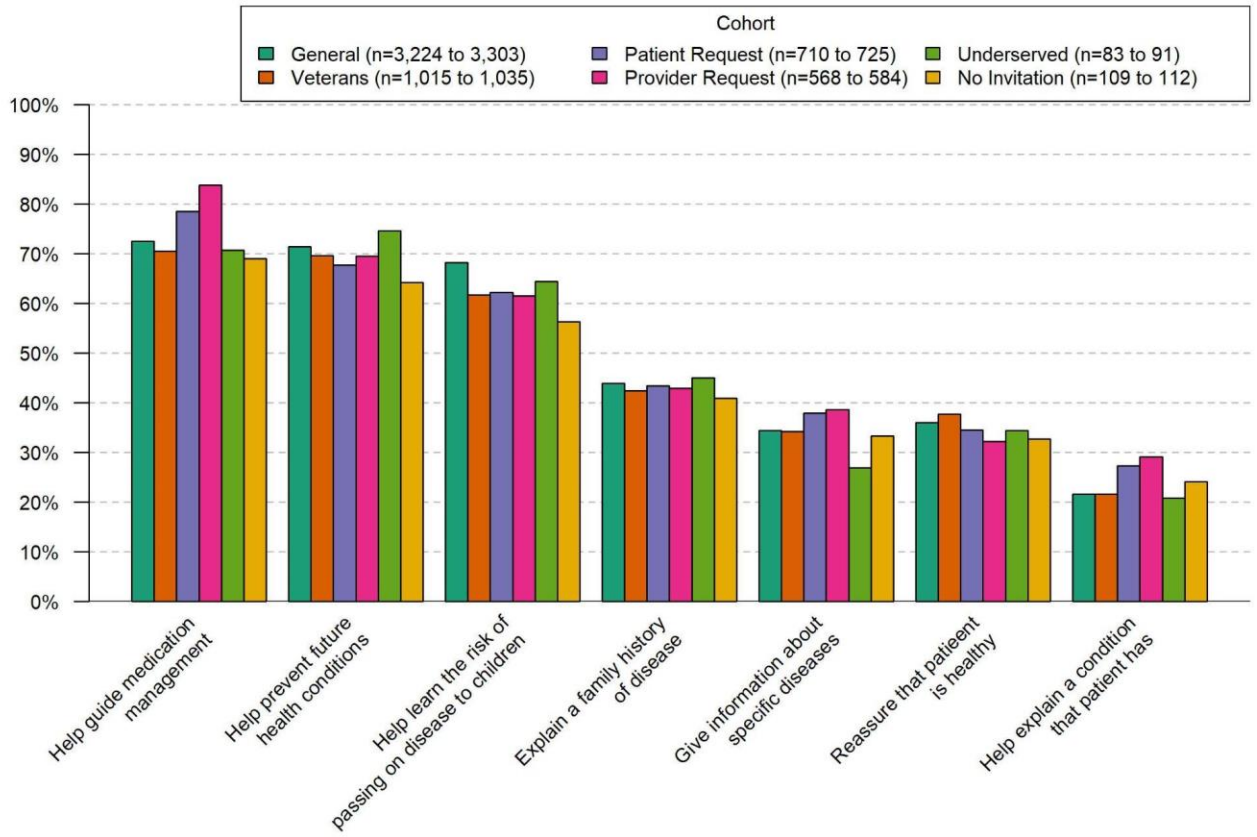


***Figure S3*. Motivations, by coupon status**

Bars indicate the percentage of patients who rated motivations as “very important” in their decision to get the Sanford Chip, stratified by whether or not they used a coupon to enroll fee of charge.

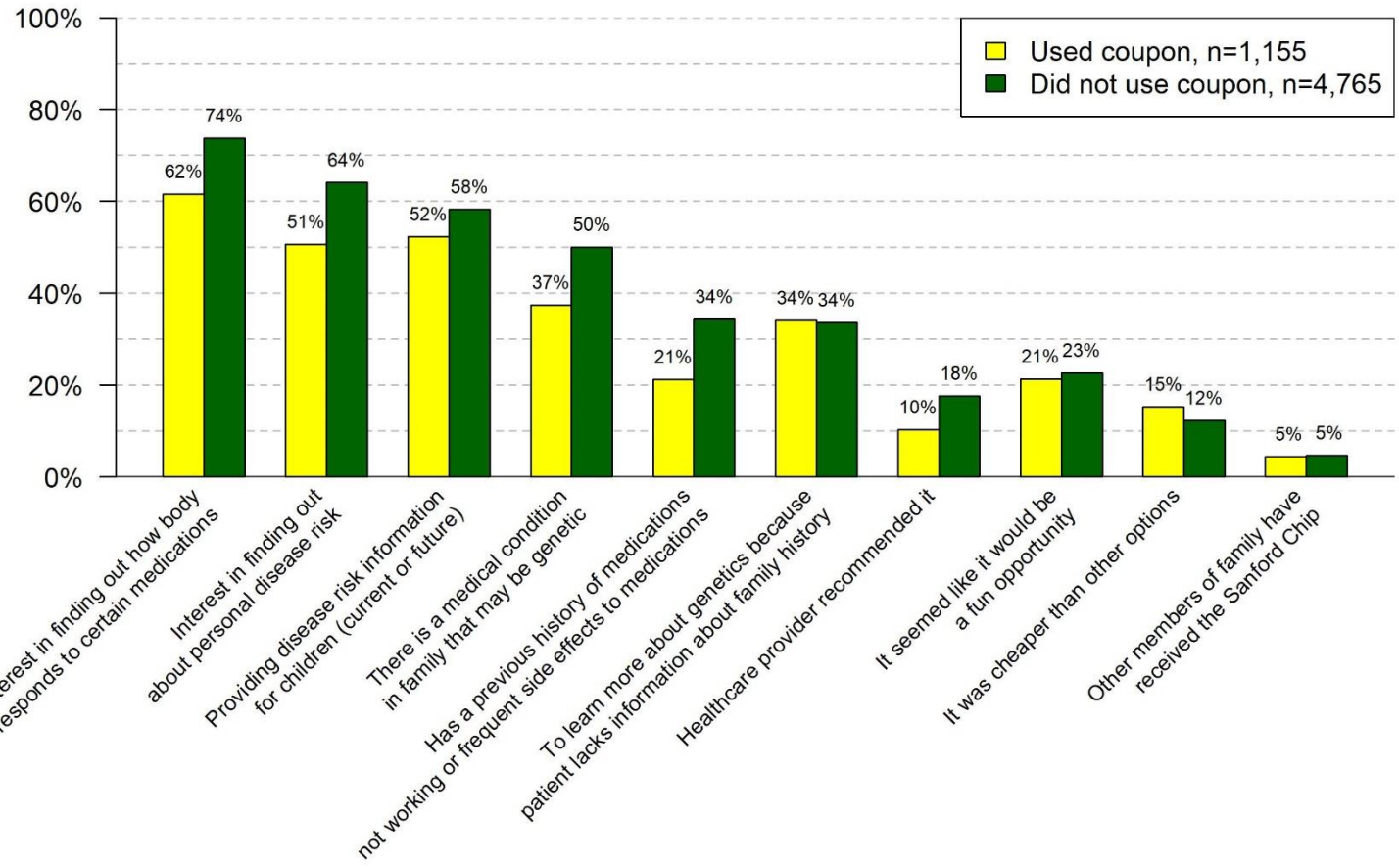
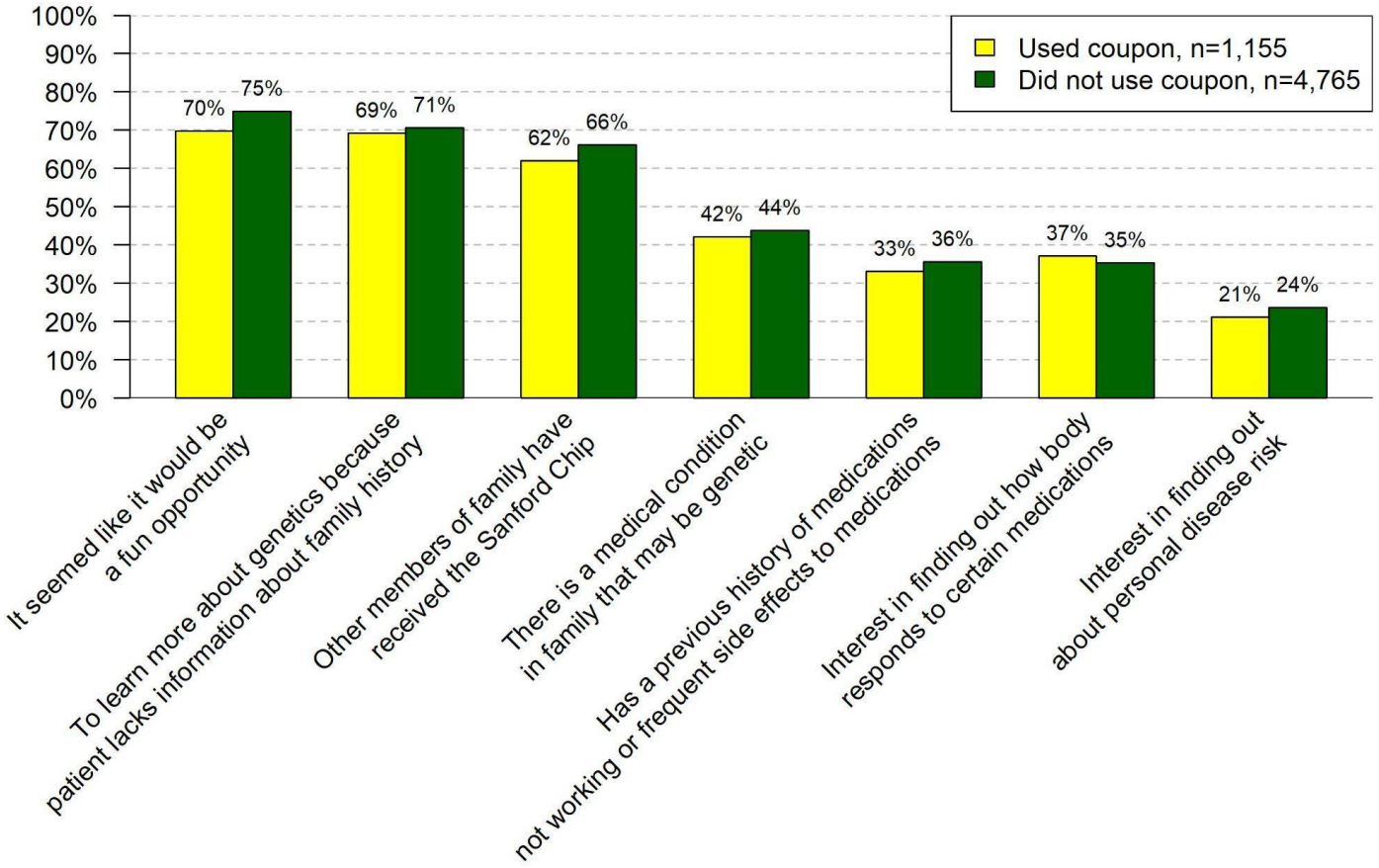


***Figure S4*. Expectations, by coupon status**

Bars indicate the percentage of patients who agreed or strongly agreed with statements about information they expected "to learn from [their] Sanford Chip results, stratified by whether or not they used a coupon to enroll free of charge.



Appendix C. Members of the Imagenetics METRICS team

Members of the Imagenetics Medical/Economic Impact and Reactions to the Sanford Chip Study (METRICS) team include:

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