HGG Advances

ARTICLE

Characteristics and experiences of patients from a community-based and consumer-directed hereditary cancer population screening initiative

Veronica Greve,[1,*] Katherine Odom,[2] Susanna Pudner,[3] Neil E. Lamb,[1] Sara J. Cooper,[1,*] and Kelly East[1]

Summary

A clinical hereditary cancer population screening initiative, called Information is Power, began in North Alabama in 2015. After 4 years of the initiative, we were interested in exploring (1) the characteristics and motivations for patients who self-refer to population genetic testing, (2) how patients make decisions on testing, (3) what patients do with results, and (4) patient perceptions of benefits and limitations after undergoing population genetic testing. Patients who consented to research recontact at time of test ordering were sent an electronic survey with the option for a follow-up phone interview. Among the 2,918 eligible patients, 239 responded to the survey and 19 completed an interview. Survey and interview participants were highly educated information seekers motivated by learning more about their health. Those who were previously interested in hereditary cancer testing reported barriers were cost and insurance coverage, access to testing, and uncertainty how results could impact their health. Many participants (77%) communicated with family and friends about their decision to test and communicated about test results. Fewer participants (23%) discussed the decision to test with their healthcare providers; however, 58% of participants discussed their test results with a healthcare provider. Most people (96%) with negative results accurately recalled their results. In contrast, three out of 11 positive results for heterozygous *MUTYH*, *PALB2*, and *BRCA2* reported receiving negative results. This study contributes to knowledge on population genetic testing and may guide other population genetic testing programs as they develop enrollment materials and educational materials and consider downstream needs of population genetic testing participants.

Introduction

Hereditary cancer can have a significant burden on families and healthcare systems. Hereditary cancer genes, specifically hereditary breast and ovarian cancer and Lynch syndrome genes, are well studied and have management guidelines to avoid or reduce the significant lifetime cancer risk.[1,2] Identifying a hereditary cancer syndrome in one patient can lead to cascade screening in relatives allowing for increased opportunity for personalized screening and preventative surgeries throughout a family.[3] Currently, hereditary cancer testing is most often offered to patients who are undergoing cancer treatment or who are identified as having a strong family history of cancer meeting national guidelines for consideration of genetic testing.[1,2,4] Studies have found this model is limited by a lack of referrals for appropriate candidates,[5,6] and the structure of testing guidelines omits a significant portion of people who have an underlying hereditary cancer syndrome.[7,8] Given these limitations, more widespread implementation of hereditary cancer genetic testing is needed. For patients undergoing cancer treatment, new models of referring include automated referrals for cancer genetic counseling and/or genetic testing upon any breast or ovarian cancer diagnosis.[9,10] In recent years, population screening programs based on healthcare system and state of residence have provided limited hereditary cancer testing regardless of personal or family cancer history.[11]

Consumer-directed testing (CDT) is a genetic testing model that has the potential to reduce logistical barriers and increase access to genetic testing for patients. In CDT, patients directly request genetic testing from a laboratory, which then contacts the patient's physician to obtain test authorization.[12] This model enables patients to access genetic testing from healthcare providers who may not typically interact with genetics. Having a patient-initiated model can reduce the genetics referral barrier that has been observed in cancer genetics. It can also reduce non-genetics healthcare providers' reported genetic testing barriers of limited genetics knowledge, uncertainty with hereditary cancer testing criteria, and time limitations.[13,14] Previous research identified population genetic testing as an economically feasible way to identify high-risk hereditary cancer syndromes, given that costs for testing are low enough to outweigh the amount of the population that needs to be screened for impact.[15,16] Economic feasibility and the opportunity for intervention to reduce morbidity and mortality through increased screening or surgical interventions make hereditary cancer well suited to population screening given previously published principles.[17,18]

Examples of ongoing genetic population screening programs in the United States are the MyCode project, the Healthy Nevada project, and the Alabama Genomic Health Initiative (AGHI).[11,19,20] MyCode is conducted through the Geisinger healthcare system setting and currently performs

[1]HudsonAlpha Institute for Biotechnology, Huntsville, AL 35806, USA; [2]University of Alabama at Birmingham, Birmingham, AL 35294, USA; [3]University of South Alabama, Mobile, AL 36688, USA
*Correspondence: vgreve@hudsonalpha.org (V.G.), sjcooper@hudsonalpha.org (S.J.C.)
https://doi.org/10.1016/j.xhgg.2021.100055.

exome sequencing on patients within Geisinger who opt in to research genomic screening and biobank participation. Result returns are optional, returned by the study team via phone call or certified letter, and genes investigated include hereditary cancer, cardiovascular conditions, and genetic disorders deemed important as secondary findings by the American College of Medical Genetics (ACMG).[19,21] The Healthy Nevada project is available to residents of Nevada and the surrounding area. Medical results from the study are optional to receive, returned by genetic counselors via phone call, and include familial hypercholesterolemia, hereditary breast and ovarian cancer, and Lynch syndrome.[11] AGHI is available to residents of Alabama. In this initiative, there are no options for opt-out of research results, results are returned by genetic counselors via phone call, and genes investigated include hereditary cancer, cardiovascular conditions, and genetic disorders modeled after the secondary findings deemed important to investigate for exome and genome sequencing (ACMG SF v.2.0).[20]

Previous implementations of healthcare-wide (MyCode) or community-wide (Healthy Nevada and AGHI) genomic screening programs have been conducted in the research setting. While a research study has certain advantages, there are remaining questions of how these genomic screening programs can be implemented in a clinical setting and the willingness of non-research patients to participate and pay for these programs. In recent years, genetic testing laboratories have started offering clinical testing for proactive genetic testing.[22] With the theoretical wide-spread availability of proactive genetic testing for hereditary cancer, questions remain about who would seek out this type of proactive testing and if there are concerns with the implementation of CDT in a clinical setting.

Information is Power (IiP) is a consumer-directed hereditary cancer screening initiative in North Alabama that provides free or reduced-cost access to genetic testing. This is a community-based model with healthcare providers, funding partners, and the genetic testing laboratory residing and operating within a specific community and geographic region. IiP has over 4 years of experience offering consumer-directed hereditary cancer genetic screening in a clinical initiative. To better understand our population and more broadly those interested in seeking out hereditary cancer screening, we surveyed and interviewed the patient population to address four questions. Primary questions were: (1) Who elects hereditary cancer screening? (2) How do patients make decisions around genetic testing? (3) What do patients do with test results? (4) What are patients' perceived benefits and limitations of a CDT hereditary cancer population screening model?

Material and methods

IiP initiative

IiP targets people with a low risk for hereditary cancer based on personal and family history. Marketing and communication, genetic counseling, and fundraising are conducted by the non-profit HudsonAlpha Institute for Biotechnology. The test is subsidized for a reduced cost to residents of North Alabama (Madison, Marshall, Morgan, Jackson, and Limestone counties), and free genetic testing is provided for residents between the ages of 28 and 30 years. Age ranges have varied throughout the initiative but are focused on providing access to men and women around the age of 30 years, as advocates have recommended this age for cancer screening and decision-making impact.[23] IiP's consumer-directed model involves an electronic test requisition process where patients input their local provider for authorization. At the time of test requisitions, patients have the option to provide personal and family history of cancer, which is triaged by genetic counselors into high risk for hereditary cancer or low risk for hereditary cancer based on National Comprehensive Cancer Network guidelines for consideration of genetic testing.[1,2] This information determines the type of letter patients with negative results receive. A buccal collection kit is then mailed to patients to self-collect their DNA sample and mail to the testing laboratory. The testing laboratory, Kailos Genetics, performs next-generation sequencing of 33 genes (Table S1) associated with hereditary cancer and reports novel frameshift and protein-truncating variants in addition to likely pathogenic or pathogenic variants previously reported in ClinVar. The IiP initiative, test methods, and participant perspectives on educational aspects of IiP have been previously described.[24]

Survey

A patient survey was developed with study-developed questions addressing demographics; previous genetic testing experience and motivations for genetic testing; cancer knowledge; self-reported health literacy; test result recall; test result impact; communication with family, friends, and healthcare providers; and Likert scale questions for participant comfort with genetic terms and pretest concern for cancer. The survey also included a modified state-trait anxiety inventory (Form Y-1)[25] and a modified perceptions of uncertainties in genome sequencing (PUGS) scale.[26] A final question requested permission to recontact for a future phone interview (Supplemental methods). The survey was piloted among a small group of IiP patients (n = 3), and minor revisions were made based on suggestions. The survey and interview guide were approved by the HudsonAlpha institutional review board (IRB). A unique electronic link to the survey was deployed to IiP patients who consented to research recontact at time of test ordering (n = 2,918), which allowed clinical demographics to be linked to survey responses. Survey consent was performed electronically. Survey collection happened at two time periods: May 30, 2019 and July 28, 2020. The survey link was active for 4 weeks. Partial surveys were used and analyzed if the participant responded past demographic questions.

Interview

Follow-up interviews were conducted with survey participants from May 30, 2019 to collect in-depth information about IiP survey participants' views around hereditary cancer and population genetic testing. An interview guide was developed with questions including motivations for IiP participation, testing process, beliefs around causes of cancer, communication of test results, and views of population genetic testing (Supplemental methods). All participants with positive results who consented to interviews were recontacted. Participants with negative results who consented to

interviews were prioritized for recontact based on sex, ethnicity, age, and family history, with the goal of interviewing participants from demographics underrepresented in the survey (male, non-Hispanic white) and who may have different perspectives (e.g., young versus older participants). Interviews were conducted to reach response saturation. Nineteen semi-structured interviews were conducted by two researchers (V.G., K.O.) from October 2019 to November 2019.

Data analysis

Descriptive statistics were calculated for demographics, testing motivations, and the modified State-Trait Anxiety Inventory. R software was used to conduct significance testing.[27] Binomial and generalized linear regressions were used to identify significant characteristics associated with communication with healthcare providers and motivations for testing. McNemar's test was used to compare communication prior to and post testing. Open-ended responses to survey questions were thematically analyzed using an inductive approach.[28]

Interviews were audio recorded and transcribed. Deductive analysis was conducted for overall interview themes of primary motivations, participant knowledge of genetics, result impact, and perspectives of population genetic testing. An inductive thematic analysis was used to identify additional themes that emerged during interview of "Patients are autonomous," "Patients are curious," and "Cancer is preventable." A genetic counselor reviewed interview transcriptions for initial themes, and a coding guide was developed. Transcripts were independently coded by a genetic counselor (V.G.), genetic counseling assistant (K.O.), and genetic counseling intern (S.P.). Reconciliation with all three coders was performed to achieve consensus.

Results

Demographics

There were 239 survey respondents, with 200 full responses and 39 partial responses, for an 8% response rate. Survey demographics were skewed from overall community demographics, with a higher percentage of women (90.3%); white, non-Hispanic participants (94.5%); and highly educated, with 81.9% reporting a college degree (Table 1). The five-county average demographics are 50.6% female, 77.0% white ethnic background, and 23.4% with a bachelor's degree or higher.[29] Survey participants had an average age of 41 years and a median age of 34 years, which are both outside of the free testing range. Thirty-two percent of survey participants qualified for free genetic testing when they enrolled in the initiative, which is similar to the overall initiative rate of 37.3% eligibility for free testing. Of the 167 participants who provided their cancer family history, 21.3% were classified as a high-risk family history, 28.5% were classified as low risk, and 48.5% had either no family history provided or no history relevant to hereditary cancer syndromes tested (e.g., basal cell carcinoma, cervical cancer, etc.). Our survey participants had a 4.6% positive result rate, consistent with the overall IiP positive result rate. Sixty-one percent of IiP survey participants consented to interview contact. Interview demographics were similar to the overall survey demographics except for an oversampling for positive results (15.8%).

Who elects testing

From our surveyed population, about half of participants (52.7%) considered genetic testing for cancer risk prior to IiP but had not pursued testing due to cost or lack of insurance coverage, uncertainty in how to access testing, and perceived lack of benefit at that time. Of those with a stated interest in hereditary cancer genetic testing, 33.6% reported a personal or family history that met criteria for consideration of genetic testing.[1,2] Prior to participating in IiP, 24.0% of surveyed participants had previous experience with genetic testing. Prior genetic testing included carrier screening, prenatal screening, karyotyping, hereditary cancer testing, and neuropathy genetic testing. Participants were motivated to pursue hereditary cancer screening to know future health risks and health implications to children and family members (Table 2). Average concern of developing cancer prior to receiving test results was 2.96 (SD, 1.08) on a 5-point Likert scale consistent with being somewhat concerned. Those who reported they were quite a bit concerned about cancer were more likely to be motivated by health risks to themselves or their children ($p < 0.01$) (Figure S1).

Most interviewed participants were autonomous information seekers who felt cancer could be prevented and cancer risks controlled (Table 3). Participants reported information-seeking behaviors, with most looking up additional information before and after testing to supplement IiP educational videos. Interviews with participants revealed patients had a strong sense of their autonomy as healthcare consumers and advocated that testing and health decisions should primarily be in patient control. Participants believed cancer was due to both environmental and genetic causes. Most people interviewed had specific environmental causes they were focused on, such as diet or geography. Most interviewees also had a strong belief that cancer is preventable—largely citing a healthy lifestyle as their preventative strategy. The reason to undergo testing was often paired with preventative actions available with a positive result. "Risks like that can then be mitigated with extra monitoring or just something else for my doctors to know about in terms of managing the care" (*Interviewee 11*).

IiP result communication

Surveyed participants discussed their decision to undergo hereditary cancer screening with their friends and family more often than with healthcare providers (Figure 1). Fifty-eight percent only discussed their decision to undergo testing with friends and family, while 19% also discussed with a healthcare provider, 19% did not discuss the decision with anyone, and 4% only discussed with a healthcare provider. Post-test discussions often included both healthcare providers and family or friends (56%) or just friends and family (36%). Younger participants were

Table 1. Demographics of IiP survey participants and interview participants

	Survey (n = 239)	Interview (n = 19)	Total IiP population (n = 4,177)
Average age at testing, years	40.8 (range, 25–80)	40.1 (range, 27–80)	40.0 (range, 19–96)
Sex, n (%)			
Female	215 (90.3)	16 (84.2)	3,537 (84.8)
Male	23 (9.7)	3 (15.8)	633 (15.2)
Race/ethnicity, n (%)			
Non-Hispanic white	223 (94.5)	19 (100)	2,562 (92.8)
Asian	1 (0.4)	–	34 (1.2)
Black or African American	2 (0.8)	–	71 (2.6)
Latino or Hispanic	4 (1.7)	–	44 (1.6)
Multiracial	6 (2.5)	–	49 (1.8)
Education, n (%)			
High school/some college	43 (18.0)	6 (31.6)	NA
2/4-year college degree	111 (46.6)	7 (36.8)	NA
Graduate/professional degree	84 (35.3)	6 (31.6)	NA
Rural residence	53 (22.2)	5 (26.3)	1,377 (33.0)
Years since testing, n (%)			
< 1 year	66 (27.6)	2 (10.5)	1,098 (26.3)
1 year	48 (20.1)	7 (36.8)	941 (22.5)
2 years	49 (20.5)	5 (26.3)	766 (18.3)
3 years	76 (31.8)	5 (26.3)	1,372 (32.8)
Family history, n (%)			
Strong personal	4 (1.7)	1 (5.3)	45 (1.1)
Strong family history	51 (21.3)	5 (26.3)	913 (21.9)
Not strong family history	68 (28.5)	7 (36.8)	922 (22.1)
No relevant cancer history	44 (18.4)	2 (10.5)	738 (17.7)
Unknown or did not provide	72 (30.1)	4 (21.1)	1,559 (37.3)
Test results, n (%)			
Positive	11 (4.6)	3 (15.8)	183 (4.4)
Negative	228 (95.4)	16 (84.2)	3,994 (95.6)

Numbers may not equal total, as participants were not required to answer demographic questions. Percentages are calculated from the total answered.

more likely to report discussing results with their providers ($p < 0.05$) (Figure S2). Reasons participants did not discuss results of genetic screening with their healthcare providers were lack of a primary care provider at the time, perceived disinterest of healthcare providers, and perceived lack of necessity due to negative genetic testing results. For survey participants who discussed results with healthcare providers, there were few (n = 3) that felt healthcare providers were dismissive of results. Other perspectives around results discussions were that providers were interested in results (n = 19), had little discussion but put into the medical record (n = 12), discussed limitations of testing and continuation of cancer screening (n = 11), and changed medical management based on results or family history (n = 11). During interviews, one interviewee reported discussion of her results with her healthcare provider included a recommendation to not place genetic testing results in the medical record due to concerns for health insurance discrimination.

Survey participants reported hereditary cancer screening results most commonly left participants with a feeling of relief, and participants did not recall feeling upset upon receiving and opening their results (Table 4). Those who discussed results with families and friends also felt results provided relief to those in their life. Several participants (n = 8) reported their family or friends participated in

Table 2. IIP participant motivations for hereditary cancer population screening

IiP participant primary motivation	% (n)
Concern about future cancer risk	58.7 (132)
General curiosity	13.8 (31)
Concern about passing a genetic risk factor for cancer on to my children/grandchildren	12.9 (29)
Contribution to research	5.3 (12)
Access to testing insurance does not cover	4.0 (9)
Understand why I developed/currently have cancer	3.1 (7)
Other	2.2 (5)

testing after discussing results. Few people with negative results reported any changes to their lifestyle (5.7%) or medical management (7.5%) based on their hereditary cancer screening. Out of our participants with positive results, only four (36.4%) reported changes to either lifestyle or medical management based on results. One person with a positive result reported no management changes, as they were already proceeding with high-risk screening. The remaining six surveyed participants with positive results gave no explanation for their lack of management changes. Changes reported based on results were earlier annual cancer screenings, finding a primary care physician, and an increase in exercise or healthy diet.

When asked about their results, almost all participants surveyed who received negative test results had accurate recall (96.5%) (Table 5). One person with negative results incorrectly recalled results as positive, and six people with negative results were unsure and did not select positive or negative. Three out of the 11 people surveyed with positive test results had incorrect recall. All participants with positive results and inaccurate recall reported receiving negative test results, but their actual test result revealed heterozygous *MUTYH*, *PALB2*, or *BRCA2*.

Demographics of those who mis-recalled positive results were two females and one male who were aged 31–57 years at testing, were between 1 year and 3 years out from receiving results, and reported having at least a 4-year degree. All three positive participants with inaccurate recall had a phone conversation with a genetic counselor at the time of results disclosure to review results and next steps for result management. However, survey responses found two reported they did not receive this phone call, and one was unsure. Two of the three reported discussing their results with a primary care physician. None of the three reported making lifestyle or medical management changes. Unfortunately, none of the survey participants who inaccurately recalled their positive results responded to phone interview invitations.

Fourteen of the 19 interviewees reported they felt relief, including all three of those with positive results (*BRCA1*, *RAD51C*, and heterozygous *MUTYH*). Interviewees who reported no changes to their lifestyle emphasized they already felt they had a healthy lifestyle and cited diet and exercise patterns. Interviewees with negative test results were resistant to lifestyle changes, although they still planned to continue appropriate cancer screening. About half of interviewees were uncertain what a negative genetic test result meant for their cancer risk. One interviewee felt that negative results were inaccurate with a high-risk family history, despite their theoretical knowledge around limitations of genetic testing.

> I said, well, it's probably not accurate, but cool. There is a strong history of cancer in my family, and since I came negative it seems it's likely that there are genetic predispositions for me given my family history of cancer, and so saying no seems counterintuitive. (*Interviewee 7*)

Benefits and limitations of IiP

Interviewees felt benefits to population hereditary cancer screening were convenience, empowerment, and patient privacy. Many cited free testing as a benefit to IiP specifically. On a broader scale, they cited a benefit of CDT testing is the ability to receive test results quickly without waiting for an appointment or physician call. Empowerment was noted as well, with interview participants feeling their ability to learn about the initiative and decide information was useful for their health as a benefit to self-referred population testing. Three of our interviewees reported privacy to receive test results and the ability to process information before discussing with a healthcare physician as their preferred way to receive good and bad news. Interviewees did not directly cite increased knowledge and interest in genetics as a benefit; however, we feel overall awareness was a benefit of IiP. Some people looked up further information on the genes tested, hereditary cancer syndromes, and other types of genetic testing, such as prenatal testing.

> Making me more aware of how genetics can play a role in your risk. For me, just kind of diving more into family and what types of cancer they had. When I had my baby, I chose to do genetic testing then just to explore other risk factors for other conditions, so it made me more aware of genetic testing in general. (*Interviewee 14*)

Interviewees felt limitations of population hereditary cancer screening were risks of misinterpretation, adverse psychological events, and data safety. Five interviewees did not feel that patients should be able to order hereditary cancer testing through CDT methods. Although interviewees themselves did not report problems using CDT methods, they felt the risk was too high for patients in general to misunderstand results and take inappropriate action, and having a doctor deliver results could reduce psychosocial concerns. Overall, 7.9% of survey participants did not feel comfortable with a CDT method of testing, although we cannot determine if that was due to their

Table 3. Interview themes and representative quotes

Category	Theme	Description	Representative quote
Participant characteristics	patients are autonomous	can make decisions on their own	"It's information that pertains to your health, and you're in charge of your health and not your physician." (*Interviewee 13*)
	patients are communicators	discussion of decision to test and results with friends, family, or HCP	"I talked to my husband, and I also talked to a couple of my sisters about it…just to let them know that I was doing it, and that I could let them know the results." (*Interviewee 12*)
	patients are information seekers	wanted to learn about health or genetic testing	"I felt like the more information I would have about it the better I could be prepared in the event that something like that [cancer] were to happen." (*Interviewee 10*)
Cancer beliefs	large genetic influence	genetics plays a big role in cancer development	"Pretty big risk factor there [DNA]. I can't tell you in percentage what I think, I'm not sure, but I certainly say over 50%." (*Interviewee 4*)
	specific environmental influence	mentioned one large environmental contributor to cancer risk	"I just think most of it's environmental…I'm gearing more toward organics." (*Interviewee 3*)
	preventable	there are measures patients can take to prevent or manage cancer risk	"The healthier someone is and how they treat themselves can really reduce their likelihood of cancer." (*Interviewee 7*)
	uncertainty around negative genetic testing	unsure what negative genetic testing means for their risk or inaccurate understanding	"There was some level of I'm pretty sure this is good but maybe not." (*Interviewee 6*)
Impact on life	neutral	results did not impact life significantly	"Being that my results were negative…I don't feel like it has a huge impact on me." (*Interviewee 9*)
	relief	results made them relieved or gave peace of mind	"I felt relieved…it has made me less concerned when I go get my mammograms…" (*Interviewee 6*)
	resistance to lifestyle changes	did not feel lifestyle changes were necessary	"I wasn't going to change anything I did regardless of the results." (*Interviewee 7*)
	continuation of appropriate screening	wanted to continue cancer screening	"I still get my mammogram…it did not influence me continuing to get my regular, normal screening." (*Interviewee 12*)
Population model benefits	convenience	mentioned process was easy, fast, or cost-effective	"I think that the benefits are definitely easier and faster access." (*Interviewee 11*)
	empowerment	CDT process put participants in charge of their own health	"I think taking charge of your own healthcare, making those decisions for yourself are the positives…" (*Interviewee 8*)
	increased knowledge	increased understanding of cancer or genetic testing due to process	"It did get me thinking about things…I think I investigated other testing options." (*Interviewee 5*)
	other	option not to share information with third parties, receive results alone, increased access	"I just feel like if you were going to get good or bad news, I'd rather do it in the comfort of my own home." (*Interviewee 2*)

(*Continued on next page*)

Table 3. ***Continued***

Category	Theme	Description	Representative quote
Population model limitations	misinterpretation	concerns people would misunderstand meaning of results	"The average person is not really going to know what all this means." (*Interviewee 3*)
	psychosocial	concerns people would be distressed due to results or take inappropriate action	"Some people, especially if they would get a bad report would fall apart…" (*Interviewee 4*)
	data safety	information would be shared with third parties without patient knowledge	"Really the only concern [was] why a company would want to do that for free." (*Interviewee 5*)

experiences or concerns for the broader population. Despite hesitancy from interviewees around widespread population screening, they had no concerns about recommending IiP, and 99% of survey participants would recommend others consider testing through the initiative. Data safety concerns cited by interviewees involved possible breaches to the lab and ulterior motives a free population screening initiative may have. There were also concerns around insurance discrimination and genetic privacy from health insurance companies. These protections were discussed in pre-test educational videos; however, interviewees continued to cite concerns for genetic discrimination.

Discussion

IiP research participants surveyed and interviewed provided information on who elects hereditary cancer screening, how they make that decision, and how they communicate and use test results. As anticipated with a self-referral initiative, participants for our hereditary cancer screening initiative were highly educated, information seekers, and motivated by improving health outcomes. Despite interests in hereditary cancer genetic testing, 17.7% of surveyed participants had not previously undergone genetic testing prior to IiP testing despite a reported personal or family history meeting guidelines for genetic testing consideration.[1,2] This demonstrates limitations in access to hereditary cancer genetic testing even among a highly educated and self-motivated patient population, and a lack of patient awareness of genetic services available for hereditary cancer has been previously described as a barrier to care.[30]

Results of genetic testing had little reported impact on participants' lives or medical management. Having negative results from cancer genetic testing has been previously reported as stress relieving and lowering cancer risk perceptions, and this appears to hold true for our hereditary cancer population screening participants.[31] IiP interviewees perceived cancer as preventable and cited lifestyle factors as a way to control risk. These sentiments have previously been observed in other studies with patients who are at high risk for hereditary cancer undergoing cancer genetic testing, and we also observed this in participants who were low risk for a hereditary cancer syndrome.[32] Genetic testing may improve participants' sense of control over their cancer risk similar to their sense of control over lifestyle factors.[33]

Importantly for cascade screening, survey participants were likely to communicate with family members about their decision to test and test results (77% and 92%, respectively). Participant communication with relatives and the ease of access to IiP compared to traditional models of in-person genetic testing address multiple barriers to cascade screening.[3] Thirty-nine percent of survey participants who received negative results through IiP did not discuss negative results with healthcare providers. Another qualitative interview study with elective genetic testing participants found that most intended to share negative results with healthcare providers with participants who received results within 2 months of interviews.[34] This difference between our study and previous studies may be due to a difference between intention to discuss results in the short term versus long-term action. Not discussing negative results may be a missed opportunity for reinforcement of residual risks and discussion of cancer screening management based on family history. Twenty-three percent of survey participants reported a personal or family history during the test-ordering process that could warrant additional hereditary cancer testing or management changes based on family history. While participants acknowledge the personal utility of negative results provided a sense of relief, further education around the value of negative results for both IiP patients and healthcare providers should be emphasized. Thirty percent of participants who discussed genetic testing results perceived positive outcomes from discussing genetic testing results with their non-genetics healthcare providers. This is encouraging, as previous studies have focused on healthcare provider perceived low self-efficacy in discussing genetic testing results.[14]

Interviewees reported a CDT model for population genetic testing was convenient and allowed participants to be more proactive in their healthcare. In addition, it increased broader interest in genetics, family history, and hereditary cancer. These reported benefits can be linked to two tenets of education and support for patient autonomy in the reciprocal engagement model of genetic testing.[35] Some felt a CDT model better fit their psychosocial needs to learn about results and process them before

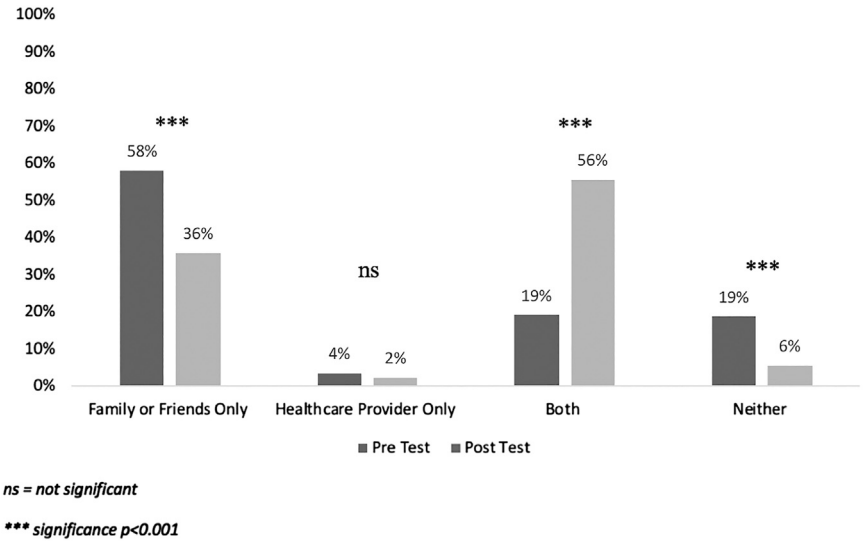

Figure 1. IiP survey participant communication about pre-testing decision and results

IiP survey participants had significantly more communication with their healthcare providers about results than the decision to undergo genetic testing. More participants reported discussing results with friends, family, or a healthcare provider than discussing the decision to undergo genetic testing.

discussing with a healthcare provider. This has been reported previously as a benefit to patient-facing reports.[36] From a genetic counseling perspective, a benefit to the population genetic testing model was a broader increased interest in genetics, family history, and hereditary cancer. Although CDT can improve patient access, the concern for widening healthcare disparities by providing an advantage to patients who already have high genetic and health literacy needs to be addressed.[12]

Interviewed participants had concerns about the acceptability of hereditary cancer population genetic testing for all patients and concerns about privacy. The interviewees' concerns that hereditary cancer population genetic testing is not acceptable for all patients is important, given the growing evidence for disparities in hereditary cancer genetic testing based on racial/ethnic group and socioeconomic status.[37] Although IiP reduced financial and logistical barriers for some participants, there may still be gaps in educational outreach and engagement with all members of the initiative's community, which is recommended to reduce disparities in genetic testing and genetic research.[38,39]

Interviewees' specific concerns for broad population genetic testing were that people would have adverse psychological effects or misinterpret results without physician or genetic counselor disclosure. Few patients have long-term elevation of depression or anxiety due to genetic testing.[9,40] However, the concern for misinterpretation mirrors genetics professionals' concerns about misinterpretation from genetic testing leading to inaccurate management and discontinuation of cancer screening.[41] Participants with negative results had 99.5% accuracy in recall of their results. There were no participants from our study who indicated they ceased routine cancer screening due to results of IiP, which has been seen in interviews with other elective proactive genetic testing participants.[13] In contrast, 27.3% of surveyed participants with positive results did not accurately recall their results status, with actual test results ranging from low risk (heterozygous *MUTYH*) to high risk (*BRCA2*). This misinterpretation could have large implications for inaccurate cancer risk management. IiP materials have been updated to improve information on written materials for positive results, as written materials can increase result recall.[42] As this is a new intervention, adequate time has not passed for assessment. Inaccuracy with genetic information recall has been reported before; in one study assessing recollection of *BRCA1/2* genetic counseling sessions, 47% of patient statements showed inaccurate recall of genetic information 2 years after result disclosure.[43]

Limitations of study

Our data are limited by patient self-referral into the IiP initiative and convenience sample of IiP patients interested in research recontact. By the nature of their participation, they are likely more familiar with genetics and view population genetic testing as acceptable. We did not verify actions reported by survey participants and can only comment on their perceived medical management impact from results. In addition, IiP participants were surveyed between 1 year and 3 years from return of results. Those who recently received results may be limited by a shorter amount of time to discuss with a healthcare provider; those who received results multiple years ago may be limited by their detail of recollection. Our participant demographics, while reflective of early adopters of genetic testing and technology,[44] do not reflect the overall demographics of the IiP geographic area. This is a limitation for the generalizability of the study and requires more exploration of non-participators and decliners to assess if this lowered rate of participation in certain demographics is due to non-interest or if they have barriers to access that remain unaddressed.

We recommend future research investigate perspectives from more diverse patient populations and include patients who decline population genetic testing to understand their perspectives of utility, result communication, and data safety. The current initiative goal is to broaden participation in rural counties and minority populations. Community engagement events through IiP with diverse populations have indicated an interest in hereditary cancer population screening; however, actual uptake remains low.

Table 4. Participant emotional recall upon viewing genetic test results

	Average rating (SD)
Calm	2.30 (1.10)
Tense	4.04 (1.03)
At ease	2.47 (1.21)
Upset	4.78 (0.66)
Worried	4.24 (0.94)
Frightened	4.63 (0.78)
Self-confident	2.92 (1.25)
Confused	4.75 (0.74)
Nervous	3.96 (1.14)
Relaxed	2.73 (1.24)

Likert scale with 1 = extremely and 5 = not at all.

Future research from IiP is planned to address physician perspectives of IiP through a companion survey and interview guide that will explore physician experiences with the initiative and how results do or do not affect patient care.

Conclusions

Hereditary cancer screening through a CDT population testing model engaged information-seeking individuals who were largely motivated by knowing their disease risks. Patients often reported feeling relieved after receiving screening results and feeling supported even without direct genetics professional interaction, and they reported high levels of communication with family and friends. Recall of negative test results was largely correct, although inaccurate recall in positive screening participants suggests additional efforts may be needed to maximize long-term management and cascade testing. IiP is an ongoing initiative, and insights from this research will be used to address these concerns. In addition, IiP's model is like other clinical CDT genetic testing models, and these results, especially the inaccurate recall of positive results, should be monitored in other CDT and population-screening initiatives. The perceptions of hereditary cancer screening participants are important to identify gaps in recall, educational concepts, and patient communication for current and future implementations of genetic screening programs.

Data and Code Availability

The datasets supporting this study have not been deposited in a public repository due to concerns full dataset information could reasonably de-identify a participant, given the narrow geographic region and open-text responses. Datasets are available from the corresponding author on request.

Supplemental information

Supplemental information can be found online at https://doi.org/10.1016/j.xhgg.2021.100055.

Table 5. Participant result recall versus actual results

		Perceived results	
Actual Results		Positive	Negative
	Positive	7	3
	Negative	1	191

Acknowledgments

Information is Power and V.G. are supported by the Russel Hill Cancer Foundation, Jane K. Lowe Foundation, and the City of Decatur. S.J.C. receives support from the State of Alabama Cancer Fund and the Center for Clinical and Translational Sciences (1UL1TR003096).

Declaration of interests

The authors declare no competing interests.

Received: March 25, 2021
Accepted: August 17, 2021

Web resources

Information is Power consumer-facing site, https://www.hudsonalpha.org/information-is-power/

References

1. National Comprehensive Cancer Network. Genetic/Familial High-Risk Assessment: Colorectal.
2. National Comprehensive Cancer Network. Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic.
3. Roberts, M.C., Dotson, W.D., Devore, C.S., Bednar, E.M., Bowen, D.J., Ganiats, T.G., Green, R.F., Hurst, G.M., Philp, A.R., Ricker, C.N., et al. (2018). Delivery Of Cascade Screening For Hereditary Conditions: A Scoping Review Of The Literature. Health Affairs *37*, 801–808.
4. Owens, D.K., Davidson, K.W., Krist, A.H., Barry, M.J., Cabana, M., Caughey, A.B., Doubeni, C.A., Epling, J.W., Jr., Kubik, M., Landefeld, C.S., et al.; US Preventive Services Task Force (2019). Risk Assessment, Genetic Counseling, and Genetic Testing for BRCA-Related Cancer: US Preventive Services Task Force Recommendation Statement. JAMA *322*, 652–665.
5. Armstrong, J., Toscano, M., Kotchko, N., Friedman, S., Schwartz, M.D., Virgo, K.S., Lynch, K., Andrews, J.E., Aguado Loi, C.X., Bauer, J.E., et al. (2015). Utilization and Outcomes of BRCA Genetic Testing and Counseling in a National Commercially Insured Population: The ABOUT Study. JAMA Oncol. *1*, 1251–1260.
6. Alberty-Oller, J.J., Weltz, S., Santos, A., Pisapati, K., Ru, M., Weltz, C., Schmidt, H., and Port, E. (2021). Adherence to NCCN Guidelines for Genetic Testing in Breast Cancer Patients: Who Are We Missing? Ann. Surg. Oncol. *28*, 281–286.
7. Beitsch, P.D., Whitworth, P.W., Hughes, K., Patel, R., Rosen, B., Compagnoni, G., Baron, P., Simmons, R., Smith, L.A., Grady, I., et al. (2019). Underdiagnosis of Hereditary Breast Cancer: Are Genetic Testing Guidelines a Tool or an Obstacle? J. Clin. Oncol. *37*, 453–460.

8. Neben, C.L., Zimmer, A.D., Stedden, W., van den Akker, J., O'Connor, R., Chan, R.C., Chen, E., Tan, Z., Leon, A., Ji, J., et al. (2019). Multi-Gene Panel Testing of 23,179 Individuals for Hereditary Cancer Risk Identifies Pathogenic Variant Carriers Missed by Current Genetic Testing Guidelines. J. Mol. Diagn. *21*, 646–657.
9. Høberg-Vetti, H., Bjorvatn, C., Fiane, B.E., Aas, T., Woie, K., Espelid, H., Rusken, T., Eikesdal, H.P., Listøl, W., Haavind, M.T., et al. (2016). BRCA1/2 testing in newly diagnosed breast and ovarian cancer patients without prior genetic counselling: the DNA-BONus study. Eur. J. Hum. Genet. *24*, 881–888.
10. Plaskocinska, I., Shipman, H., Drummond, J., Thompson, E., Buchanan, V., Newcombe, B., Hodgkin, C., Barter, E., Ridley, P., Ng, R., et al. (2016). New paradigms for BRCA1/BRCA2 testing in women with ovarian cancer: results of the Genetic Testing in Epithelial Ovarian Cancer (GTEOC) study. J. Med. Genet. *53*, 655–661.
11. Grzymski, J., Elhanan, G., Smith, E., Rowan, C., Slotnick, N., Dabe, S., Schlauch, K., Read, R., Metcalf, W., Lipp, B., et al. (2019). Population Health Genetic Screening for Tier 1 Inherited Diseases in Northern Nevada: 90% of At-Risk Carriers are Missed. BioRxiv, 650549.
12. Ramos, E., and Weissman, S.M. (2018). The dawn of consumer-directed testing. Am. J. Med. Genet. Part C Semin. Med. Genet *178*, 89–97.
13. Lynn, B., Hatry, A., Burnett, C., Kan, L., Olatunbosun, T., and Bluman, B. (2018). Identifying Primary Care Physicians Continuing Education Needs by Examining Clinical Practices, Attitudes, and Barriers to Screening Across Multiple Cancers. J. Cancer Educ. *33*, 1255–1262.
14. Hamilton, J.G., Abdiwahab, E., Edwards, H.M., Fang, M.L., Jdayani, A., and Breslau, E.S. (2017). Primary care providers' cancer genetic testing-related knowledge, attitudes, and communication behaviors: A systematic review and research agenda. J. Gen. Intern. Med. *32*, 315–324.
15. Manchanda, R., Sun, L., Patel, S., Evans, O., Wilschut, J., De Freitas Lopes, A.C., Gaba, F., Brentnall, A., Duffy, S., Cui, B., et al. (2020). Economic Evaluation of Population-Based *BRCA1/BRCA2* Mutation Testing across Multiple Countries and Health Systems. Cancers (Basel) *12*, 1929.
16. Guzauskas, G.F., Garbett, S., Zhou, Z., Spencer, S.J., Smith, H.S., Hao, J., Hassen, D., Snyder, S.R., Graves, J.A., Peterson, J.F., et al. (2020). Cost-effectiveness of Population-Wide Genomic Screening for Hereditary Breast and Ovarian Cancer in the United States. JAMA Netw. Open *3*, e2022874.
17. Wilson, J.M.G., and Jungner, G. (1968). Principles and Practice of Screening for Disease (World Health Organization).
18. Khoury, M.J., McCabe, L.L., and McCabe, E.R.B. (2003). Population screening in the age of genomic medicine. N. Engl. J. Med. *348*, 50–58.
19. Carey, D.J., Fetterolf, S.N., Davis, F.D., Faucett, W.A., Kirchner, H.L., Mirshahi, U., Murray, M.F., Smelser, D.T., Gerhard, G.S., and Ledbetter, D.H. (2016). The Geisinger MyCode community health initiative: an electronic health record-linked biobank for precision medicine research. Genet. Med. *18*, 906–913.
20. East, K.M., Kelley, W.V., Cannon, A., Cochran, M.E., Moss, I.P., May, T., Nakano-Okuno, M., Sodeke, S.O., Edberg, J.C., Cimino, J.J., et al.; AGHI Consortium (2021). A state-based approach to genomics for rare disease and population screening. Genet. Med. *23*, 777–781.
21. Kalia, S.S., Adelman, K., Bale, S.J., Chung, W.K., Eng, C., Evans, J.P., Herman, G.E., Hufnagel, S.B., Klein, T.E., Korf, B.R., et al. (2017). Recommendations for reporting of secondary findings in clinical exome and genome sequencing, 2016 update (ACMG SF v2.0): a policy statement of the American College of Medical Genetics and Genomics. Genet. Med. *19*, 249–255.
22. Invitae (2019). Invitae introduces new service to make it easier for consumers to receive the medical genetic testing that experts trust.
23. King, M.-C., Levy-Lahad, E., and Lahad, A. (2014). Population-Based Screening for BRCA1 and BRCA2: 2014 Lasker Award. JAMA *312*, 1091–1092.
24. Greve, V., Garner, M., Odom, K., Cooper, S.J., and East, K.M. (2021). Experiences and attitudes of hereditary cancer screening patients in a consumer directed testing model. Patient Educ. Couns. *104*, 473–479.
25. Spielberger, C.D. (1983). Manual for the State-Trait Anxiety Inventory (STAI) (Palo Alto, CA: Consulting Psychologists Press).
26. Biesecker, B.B., Woolford, S.W., Klein, W.M.P., Brothers, K.B., Umstead, K.L., Lewis, K.L., Biesecker, L.G., and Han, P.K.J. (2017). PUGS: A novel scale to assess perceptions of uncertainties in genome sequencing. Clin. Genet. *92*, 172–179.
27. R Core Team. (2017). R: A language and environment for statistical computing. (R Foundation for Statistical Computing).
28. Silverman, D. (1993). Interpreting Qualitative Data: Methods for Analyzing Talk, Text, and Interaction (London, UK: Sage).
29. U.S. Census Bureau. (2018). QuickFacts Madison County, Alabama.
30. Shaw, J., Bulsara, C., Cohen, P.A., Gryta, M., Nichols, C.B., Schofield, L., O'Sullivan, S., Pachter, N., and Hardcastle, S.J. (2018). Investigating barriers to genetic counseling and germline mutation testing in women with suspected hereditary breast and ovarian cancer syndrome and Lynch syndrome. Patient Educ. Couns. *101*, 938–944.
31. Gill, G., Beard, C., Storey, K., Taylor, S., and Sexton, A. (2020). "It wasn't just for me": Motivations and implications of genetic testing for women at a low risk of hereditary breast and ovarian cancer syndrome. Psychooncology *29*, 1303–1311.
32. Kelly, K., Leventhal, H., Andrykowski, M., Toppmeyer, D., Much, J., Dermody, J., Marvin, M., Baran, J., and Schwalb, M. (2005). Using the common sense model to understand perceived cancer risk in individuals testing for BRCA1/2 mutations. Psychooncology *14*, 34–48.
33. Gooding, H.C., Organista, K., Burack, J., and Biesecker, B.B. (2006). Genetic susceptibility testing from a stress and coping perspective. Soc. Sci. Med. *62*, 1880–1890.
34. Hoell, C., Aufox, S., Nashawaty, N., Myers, M.F., and Smith, M.E. (2021). Comprehension and personal value of negative non-diagnostic genetic panel testing. J. Genet. Couns. *30*, 418–427.
35. Veach, P.M., Bartels, D.M., and Leroy, B.S. (2007). Coming full circle: a reciprocal-engagement model of genetic counseling practice. J. Genet. Couns. *16*, 713–728.
36. Solomon, I.B., McGraw, S., Shen, J., Albayrak, A., Alterovitz, G., Davies, M., Del Vecchio Fitz, C., Freedman, R.A., Lopez, L.N., Sholl, L.M., et al. (2020). Engaging Patients in Precision Oncology: Development and Usability of a Web-Based Patient-Facing Genomic Sequencing Report. JCO Precis. Oncol. *4*, 307–318.

37. Parikh, D.A., Dickerson, J.C., and Kurian, A.W. (2020). Health Disparities in Germline Genetic Testing for Cancer Susceptibility. Curr. Breast Cancer Rep. *12*, 51–58.
38. Smith, C.E., Fullerton, S.M., Dookeran, K.A., Hampel, H., Tin, A., Maruthur, N.M., Schisler, J.C., Henderson, J.A., Tucker, K.L., and Ordovás, J.M. (2016). Using Genetic Technologies to Reduce, Rathar Than Widen, Health Disparities. Health Aff. (Millwood) *35*, 1367–1373.
39. May, T., Cannon, A., Moss, I.P., Nakano-Okuno, M., Hardy, S., Miskell, E.L., Kelley, W.V., Curry, W., East, K.M., Acemgil, A., et al. (2020). Recruiting diversity where it exists: The Alabama Genomic Health Initiative. J. Genet. Couns. *29*, 471–478.
40. Hirschberg, A.M., Chan-Smutko, G., and Pirl, W.F. (2015). Psychiatric implications of cancer genetic testing. Cancer *121*, 341–360.
41. Brothers, K.B., Vassy, J.L., and Green, R.C. (2019). Reconciling Opportunistic and Population Screening in Clinical Genomics. Mayo Clin. Proc. *94*, 103–109.
42. Watson, P.W.B., and Mckinstry, B. (2009). A systematic review of interventions to improve recall of medical advice in healthcare consultations. J. R. Soc. Med. *102*, 235–243.
43. Jacobs, C., Dancyger, C., Smith, J.A., and Michie, S. (2015). Accuracy of recall of information about a cancer-predisposing BRCA1/2 gene mutation among patients and relatives. Eur. J. Hum. Genet. *23*, 147–151.
44. Lewis, K.L., Han, P.K.J., Hooker, G.W., Klein, W.M.P., Biesecker, L.G., and Biesecker, B.B. (2015). Characterizing Participants in the ClinSeq Genome Sequencing Cohort as Early Adopters of a New Health Technology. PLoS ONE *10*, e0132690.