Development, user and usability testing of MyCancerGene: A digital genetic health portal for patients who have received germline cancer genetic test results

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Table of Contents

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Phillip Triue[1*]; Dominique Fetzer[1*] BA; Briana McLeod[2*] MPH; Kathryn Schweickert[1*]; Lauren Gutstein[1] MS; Brian Egleston[3*] PhD; Susan Domchek[1*] MD; Linda Fleisher[3*] PhD, MPH; Lynne I. Wagner[4*] PhD; Kuang-Yi Wen[5*] PhD; Cara Cacioppo[1] MS, LCGC; Jessica E Ebrahimzadeh[1*] MS, LCGC; Dana Falcone[1*] MS, LCGC; Claire Langer[1*] MS, LSGC; Elisabeth McCarty-Wood[1*] MS, LCGC; Kelsey Karpink[1*] BS; Shelby Posen[1*] BS; Enida Selmani[1*] BS; Angela Bradbury[6] MD

[1]The University of Pennsylvania, Abramson Cancer Center and Division of Hematology-Oncology Philadelphia US
[2]The University of Pennsylvania, Abramson Cancer center and Division of Hematology-Oncology Philadelphia US
[3]Fox Chase Cancer Center, Temple University Philadelphia US
[4]The University of North Carolina, Grillings School of Global Public Health Chapel Hill US
[5]Thomas Jefferson University Philadelphia US
[6]University of Pennsylvania Philadelphia US
[*]these authors contributed equally

Corresponding Author:
Angela Bradbury MD
University of Pennsylvania
3400 Civic Center Blvd
Philadelphia
US

Abstract

Background: The use of multigene panels in clinical practice has created an increasing likelihood that cancer genetic testing will leave many patients with uncertainties regarding test interpretation, implications and recommendations, which will change over time. We lack effective longitudinal clinical care models to provide updated information to patients regarding genetic test results or medical recommendations and to obtain personal and medical history updates.

Objective: To bridge this gap in genetic medicine, we developed a patient and provider informed digital genetic health portal, "MyCancerGene," to improve longitudinal patient understanding and responses to genetic testing, especially in an evolving landscape of evidence and risk information.

Methods: We used a 5-step process to develop the MyCancerGene digital tool. To better understand interest in and willingness to utilize a digital genetic health portal, we first surveyed 307 patients who completed genetic testing (Step 1). We completed qualitative interviews with 10 patients and a focus group with 17 providers to inform the content and function of MyCancerGene (Step 2). Next, we developed initial intervention content (Step 3) and completed user testing of intervention content with 25 providers and 28 patients (Step 4). After the prototype intervention was developed, we completed usability testing with eight patients for feedback on the final content, functions and ease of use (Step 5).

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variant reclassification upgrades or clinically significant results), genetic providers had mixed feelings on the appropriateness of sharing variant reclassification upgrades through MyCancerGene

Conclusions: MyCancerGene, a patient-centered digital genetic health portal, was developed with extensive patient and provider feedback and designed to enhance longitudinal patient understanding of and affective and behavioral responses to genetic testing, particularly in the era of evolving evidence and risk information. Clinical Trial: NCT04774445

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Authors:
Phillip Trieu[1]
Dominique Fetzer, BA[1]
Briana McLeod, MPH[1]
Kathryn Schweickert[1]
Lauren Gutstein, MS[1]
Brian Egleston, PhD[2]
Susan Domchek, MD[1]
Linda Fleisher, PhD, MPH[2]
Lynne I Wagner, PhD[3]
Kuang-Yi Wen, PhD[4]
Cara Cacioppo, MS, LCGC[1]
Jessica E Ebrahimzadeh, MS, LCGC[1]
Dana Falcone, MS, LCGC[1]
Claire Langer, MS, LCGC[1]
Beth McCarthy-Wood, MS, LCGC[1]
Kelsey Karpink, BS[1]
Shelby Posen, BS[1]
Enida Selmani, BS[1]
Angela Bradbury, MD[1,5]

Affiliations
[1] The University of Pennsylvania, Abramson Cancer Center and Division of Hematology-Oncology
[2] Fox Chase Cancer Center, Temple University
[3] The University of North Carolina, Gillings School of Global Public Health
[4] Thomas Jefferson University
[5] The University of Pennsylvania, Department of Medical Ethics and Health Policy

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Corresponding author:
Angela R. Bradbury, M.D.
Department of Medicine, Division of Hematology/Oncology
Department of Medical Ethics & Health Policy
3 West Perelman
3400 Civic Center Blvd.
Philadelphia, PA 19104
angela.bradbury@pennmedicine.upenn.edu

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Conclusions: MyCancerGene, a patient-centered digital genetic health portal, was developed with extensive patient and provider feedback and designed to enhance longitudinal patient understanding of and affective and behavioral responses to genetic testing, particularly in the era of evolving evidence and risk information.

Introduction

Basic science advances in genetics have provided great promise for improving human health and reducing the burden of cancer.[1,2] The promise of precision medicine is the ability to tailor treatment or screening of individual patients based on their genotype. With these advances, there is an increasing need for multidisciplinary translational research that focuses on how to advance precision medicine discoveries into clinical practice and to capitalize on connectivity (e.g. digital health solutions) in ways that benefit the health of entire populations.[3-5]

One of the challenges with recent advances in clinical sequencing, including hereditary cancer multi-gene panel testing (MGPT), is the increasing likelihood that genetic testing will leave many patients with uncertainties regarding interpretation, implications and recommendations, which will change over time. Many of the genes included in multi-gene panels are moderate-penetrance genes, increasing the risk of cancer by only 2-4 fold and in many cases risks estimates are based on limited data and continue to evolve over time.[6-8] There is also uncertainty regarding optimal screening given medical management recommendations, such as those published by the National Comprehensive Cancer Network (NCCN) and others, are continually evolving as new data emerges. Thus, even positive results leave many unknowns regarding cancer risks, optimal management and the value of testing unaffected relatives.[6,9,10] Additionally, multi-gene panels have been associated with higher rates of variants of uncertain significance (VUS), which are difficult for patients and providers to understand, and can be reclassified over time.[11-15]

This clinical transition from discrete (i.e. single gene) to broad (i.e. multi, whole-genome) sequencing in clinical genetic testing presents challenges that will only increase as precision medicine applications expand. With “broader” testing, an increasing number of patients will be left at risk for misunderstanding, uncertainty and evolving interpretations and recommendations.[8,16] While these uncertainties will be clarified over time, we lack clinical care models to maintain longitudinal communication with patients in order to provide updated information regarding their genetic test result or medical recommendations and to obtain personal and medical history updates.[16-19] For example, in the current standard-of-care, if a genetic variant interpretation is updated (e.g. VUS to benign or VUS to likely pathogenic result) the commercial lab contacts the ordering provider, who in turn contacts the patient.[20,21] This model is not sustainable and may not be feasible due to outdated patient contact information or change in employment of providers. Alternatively, patients can contact their provider periodically, but this places a burden on patients and has not been proven to be successful.

Equally important, while many studies have shown limited psychosocial distress with genetic testing, robust longitudinal data on cognitive, affective and behavioral outcomes in diverse and representative patient populations and with MGPT are limited.[22,23] Recent studies suggest some subgroups are at risk for greater post-test distress with MGPT, including patients with positive results, history of cancer and lower formal education.[24-26] Patients with positive and VUS results have also demonstrated greater distress and uncertainty.[15,27,28] Further, there is an increased use of remote counseling (e.g. phone or videoconference), digital alternatives and streamlined counseling models, which may introduce additional short-term or longitudinal knowledge gaps or testing related distress.[29-33] Thus, effective, evidence-based alternative strategies for longitudinal communication and care for genetic patients are critical to realizing the promise of precision medicine.

The Institute of Medicine has highlighted the importance of patient-centered care and improved transparency to enhance the delivery and outcomes of medical care.[34-36] Data from the Pew Research Center in 2021 reports that 93% of Americans use the internet, 80% have looked online for health information and patients frequently have high interest in communicating electronically with providers.[37-41] Thus, Interactive Health Communication Applications, also known as digital health solutions or tools (apps, health care portals, educational or decision aid interventions) have been implemented to facilitate this goal of enhanced transparency and communication.[36,42-44] Digital health

tools may be particularly effective in chronic disease, where longitudinal care is crucial, informational needs change over time or vary among patients, when coping and adjustment are part of the "journey" and improved medical outcomes requires changing health behaviors.[43] Studies from a variety of chronic disease settings, but not including genetics, have shown that digital health tools can improve knowledge,[43] self-efficacy,[43,45,46] satisfaction,[45,47], clinical outcomes,[43,47-50] and unmet communication needs.[45,48] Recent randomized studies have shown reductions in distress with digital health tools.[46,49,51] Further, digital health tools may provide education in a way that is more simple, accessible and salient, resulting in better knowledge retention.[43]

Yet, many have identified limitations and knowledge gaps related to digital health tools.[36,42,44,45,52,53] Various types of digital health tools have been used and electronic patient portals with limited functions (i.e. providing access to records only) may have less impact on outcomes.[36] The majority of randomized studies involving health portals have been relatively small or report limited outcomes or benefits.[37,45,52]

Further, in some studies, participants rarely or never log on to the portal[50], which may impact outcomes and diminish power in some studies and has been associated with factors such as race, ethnicity, and level of education.[50,54-58] Additionally, studies including socioeconomically diverse patient populations are needed, as minority patients are significantly less likely to use electronic patient portals, which could exacerbate health care disparities.[37,45,59-63] Importantly, at the time we developed MyCancerGene there were no published studies evaluating longitudinal digital health tools in clinical cancer genetics, which shares many of the characteristics of chronic illness (evolving information over time, adjustment and need for behavior change and communication with relatives and other health care providers). Thus, we proposed that cancer genetic testing is an ideal clinical context to study the benefits and limitations of a theoretically and patient and provider informed patient-centered longitudinal digital health tool to optimize patients' outcomes after cancer genetic testing and clinical implementation of precision medicine.

To address this clinically significant gap in the delivery of genetic medicine, we sought to obtain patient and provider input to develop a patient and provider informed longitudinal digital genetic health portal called "MyCancerGene" to enhance longitudinal patient understanding of and affective and behavioral responses to genetic testing, particularly in the era of evolving evidence and risk information. First, we describe initial patient and genetic provider feedback and recommendations regarding the concept of MyCancerGene (**Table 1**). Next, we describe user and usability testing, which informed the final content and functionality of MyCancerGene.

METHODS

STEP 1. Evaluating Patient Interest in a Digital Genetic Health Portal

To better understand interest in and willingness to utilize a digital genetic health portal (GHP) among patients who had undergone clinical cancer genetic testing, we surveyed patients in the NIH funded COGENT (Communication of Genetic Test Results by Telephone) study. The COGENT study was a multi-center, non-inferiority randomized study of telephone disclosure (TD) compared to in-person disclosure (IPD) of cancer genetic test results, including MGPT.[29,64] All participants completed germline cancer genetic testing and surveys before and after disclosure of results. This was felt to be an ideal clinically diverse population to obtain patient feedback on the value, advantages, disadvantages and content for development of a future digital genetic health portal (e.g. MyCancerGene).

To obtain patient feedback, we develop closed- and open-ended items that were added to the COGENT post-disclosure surveys. These included 7 close-ended questions about the interest in and barriers to a GHP, as well as 9 open-ended items asking how a GHP could be helpful or not helpful, advantages and disadvantages, and what types of information and functions would be most useful.

STEP 2. Qualitative Patient and Provider Inquiry to Inform the MyCancerGene Intervention

To better inform specific content and functions of our initial GHP, we conducted additional qualitative interviews with patients and providers. Interviews were guided by Diffusion of Innovation Theory and evaluated key attributes of successful innovations (e.g. advantage, risk, compatibility, complexity).[65-68] Providers included genetic counselors and physicians (n=17) at the five COGENT sites who participated in a provider focus group (2014). Providers were asked open-ended items evaluating the perceived usefulness of a GHP for patients and providers, perceived provider challenges, comfort with different types of updates (reminders, general testing updates, upgraded and downgraded VUS results and patient family history updates). Patients included 10 randomly selected COGENT participants across sites to represent the view of sociodemographically diverse patients who had genetic testing. Patients completed individual interviews including open-ended questions (2014). These included: a) evaluating internet and health portal use in general, b) advantages and disadvantages to health portals, c) advantage and disadvantages to a GHP, d) content that would be useful and not useful, e) perceived usefulness of updates in genetic information and updates in family history, and f) other suggestions for the GHP content and function.

STEP 3. Developing the MyCancerGene Intervention

Key components and functions of our GHP (MyCancerGene) were informed by our patient and provider formative interviews. Initial screenshots were developed for patient and genetic provider feedback.

STEP 4. User Testing and Refinement of the Intervention

Initial screenshots for MyCancerGene content were developed based on patient and provider formative interviews and individual user testing feedback on these screenshots was obtained from both patients and genetic providers. We conducted individual user testing interviews with 25 genetic counselors (2018-2019). Interviews included questions about use of patient portals in general (7 items), feedback on the purpose, content and comfort with specific functions of MyCancerGene (7 items) and feedback on individual screenshots and draft messaging for updates (14 items).

We obtained feedback from patients at two time points. The first group of patients providing user testing included eight participants (2014), and the second included 20 participants (2019). In both sets of interviews, participants viewed current versions of screenshots and were asked if the content was useful, what they expected to see and why or why not for each question. Additionally, they were asked for additional recommendations to improve the content.

Feedback from patients and providers were incorporated into the initial digital version of the MyCancerGene intervention.

STEP 5. Usability Testing and Final Modifications to the Intervention

Using the initial digital version of MyCancerGene and co-browsing software, we conducted individual usability interviews with eight patients to obtain feedback on the functionality, navigation, experience and any additional comments on content. Participants were asked what they liked and disliked on each page, if the information was understandable and how it could be clarified if not. As applicable, they were asked about fonts, colors and images, how easy it was to navigate the functions, and how content or functions could be improved.

RESULTS

STEP 1. Evaluating Patient Interest in a Digital Genetic Health Portal

Three hundred and seven COGENT participants completed the GHP patient items (see **Table 2**). The majority of patients reported a GHP would be useful and that they would use a GHP (**Table**

3). Those with a positive result were significantly more likely to report that a GHP would be helpful (OR=10.9, 95% CI 2.2-54.0, p=0.003) and that they would use a GHP (OR=7.2 compared to true negatives, 95% CI 2.1, 25.0, p=0.002). Nonetheless, over 75% of those with a VUS or uninformative negative results reported a GHP would be helpful. Another factor associated with likely GHP use was history of prior health care portal use (OR=2.5, 95% CI 1.4-4.4, p=0.001). Age, gender, education, cancer history and baseline cognitive and affective measures (e.g. knowledge, anxiety, etc.) were not significantly associated with interest in a GHP or likelihood of using.

In response to open-ended questions (**Table 4**), the most frequently reported advantages of the GHP were increasing accessibility, convenience and efficiency (46.0%), keeping genetic information organized (24.1%) and to increase or maintain patient understanding of the information (17.0%). Patients also reported it could be helpful for sharing genetic information with others, downloading and/or printing documents, security and reducing anxiety.

A subset of patients (15.63%) reported that a GHP would not be helpful (**Table 4**), citing the lack of human interaction, potential access challenges and concerns regarding privacy and the potential to cause anxiety. When asked specifically about potential disadvantages to a GHP, most participants (36.4%) reported no disadvantages but some reported concerns about privacy, that information could be distressing, trouble remembering login information, technical challenges and the lack of human interaction (**Table 5**).

When asked what components or functions should be offered in a GHP, the most frequently reported included access to results (49.3%), medical recommendations (20.7%), easy to understand review of results (12.8%), access to providers and additional resources, appointment details, screening results, and family history (**Table 6**). Some participants also endorsed the value of a summary page, updates in information and the ability to print and share materials with relatives or providers.

STEP 2. Qualitative Patient and Provider Inquiry to Inform the MyCancerGene Intervention

Qualitative Genetic Provider Focus Group

The primary potential benefits of a GHP, as reported by providers, included a mechanism to improve patient sharing of accurate information with relatives and providers, and a mechanism for genetic providers to update patients with new risk or test information. Most genetic providers felt a GHP would be useful to patients as they already expect providers to update them (“call them”) with new information, although providers admitted this is not always feasible in practice and over time. Many endorsed a GHP as a way for patients to maintain genetic records electronically in a specific location instead of in paper files. At the same time, providers indicated that many patients already have electronic access to these records in the Electronic Health Record (EHR) and asked how the GHP would be different from the access already provided.

Providers acknowledged that they were not sure that a GHP would alleviate day-to-day challenges for providers as they already communicate with some patients via the EHR. Other concerns with a GHP included ensuring that patients receive and understand updates shared through the GHP, and that many patients don’t log on or use ancillary platforms. Genetic providers asked if there could be an alert to providers if their patient logged on and reminders to patients when new information is available. Other concerns regarded the burden on providers to update a GHP, maintaining current information and the potential to create additional work for providers.

Genetic providers had different levels of comfort with updates provided through a GHP. They all felt that a GHP could be a good method to alert patients to update their family history (suggested once or twice a year). They were less comfortable with updates to screening recommendations as these could change overtime and could conflict with other information or recommendations patients’ were receiving. In general, most were comfortable with new general information about testing (e.g. new testing available) and downgraded VUS reclassifications. At the time, VUS downgrades were

communicated via letter and a GHP could provide a good alternative to mail communication, although they raised concerns that some patients may not log in. Most genetic providers were less comfortable with upgraded VUS reclassifications being shared through a GHP. They felt these needed to be communicated by a genetic counselor and felt a message (“please call your genetic provider”) was a more appropriate method for notification through a GHP.

Qualitative Patient Interviews

Patients (n=10) were 29-69 years old, and included two men, two patients with less than a college degree, one non-white patient and a range of test results (positive, VUS, negative and results pending). Most participants (n=9) thought that a GHP could be useful in referencing immediate results, concise information, and accessing reports and documents. Suggestions from participants included the addition of content and documentation (results, recommendation letter, family history), information about individual risk compared to the general population, ability to track screening and medical management, and updates in the field. Most participants (n=8) supported receiving updated test results through a GHP. Participants also felt that a GHP could help support communication with relatives. They also suggested that a GHP could be more useful if it provided tailored educational resources, more billing and security information, a medical history summary, opportunities to connect with other patients, and if it were designed to be user-friendly.

STEP 3. Developing the MyCancerGene Intervention

Patient Facing Content

Components of our GHP (MyCancerGene) were informed by our patient and provider interviews (details in **Table 7**). Components include: 1) Log in (**Figure 1**) and Landing Page (**Figure 2**), 2) Summary of Care page (**Figure 3),** 3) My Genetic Test Result page (**Figures 4**), 4) My Family History page (**Figure 5**), 5) Provide an Update page, 6) Review Updates page**,** 7) Resources page, and 8) Screenings Tracker.

Engagement Strategies

As endorsed by patients, reminders and engagement functions were designed to remind patients about the portal (**Table 8**). These include initial activation reminders to encourage patients to activate their MyCancerGene portal. We also designed general reminders sent every 6 months to remind patients to update their family or personal history and any new testing in the family. We also designed educational engagement reminders, which are short educational messages regarding cancer genetics or family risk and are sent every 6 months, alternating with general reminders (**Table 8**).

Patient and Provider Updates

As outlined above, a main purpose of the MyCancerGene intervention is to provide a mechanism for patients to provide updates to their personal and family history to the genetics team and for genetic providers to send updates to patients.

Patient driven updates

MyCancerGene was designed so that patients can provide updates at any time on the “Provide an Update” page. They may also provide an update in response to general engagement messages sent every 6 months. All updates were designed to be reviewed by their genetic provider to determine if their update prompts a change in medical management or new genetic testing in them or their relatives. Given integration challenges and concerns about burden on genetic providers, research staff reviewed updates, drafted responses when appropriate, and obtained a final approved response from the genetic provider. Genetic provider responses to updates were then sent to patients through the MyCancerGene portal. It is intended that this could be better automated in the future

after efficacy is established.

Provider driven updates

MyCancerGene was designed for two specific genetic provider updates. First, to provide updates in VUS classifications (e.g. VUS reclassification to benign or VUS reclassification to pathogenic or likely pathogenic). When genetic providers received a lab update on a patient enrolled in the MCG portal, they contacted the research team with the update. The genetic provider and research team created updated content for Summary of Care, My Summary Note and My Genetic Test Results. These changes were then programmed by the Clinical Research Computing Unit (CRCU) and, when completed, would generate a message to be sent to the patient. Example: “Your Variant of Uncertain Significance Result has been reclassified. To view the details of your reclassification now, please log onto your MyCancerGene portal.” The message provided login information and the option to speak with a provider to receive the updated information. Example: “If you would rather speak with your Genetic Counselor to discuss this update, please contact a member of the research study team who will help you set up a telephone call.”

In addition to patient specific updates to results, the MCG intervention was designed to permit other updates based on changes in the field that might apply to a group of individuals. Examples include new screening recommendations for patients with a specific genetic mutation (e.g. new screening recommendations for *PALB2* carriers), changes to risk estimates for particular genes or new genetic testing options for patients with specific personal or family history. Thus, MyCancerGene was designed to allow edits to all patient-facing content to allow for these updates and a mechanism to message patients that updates had been made. In practice, updates were classified as “informational”, with a message notifying patients that there were changes made to their genetic information but that it likely did not change their current care. In contrast, other updates were classified as “potentially actionable” and messages suggested that they access MyCancerGene to review the updates and contact their genetic provider if they had questions.

Provider Interface and Functionality

At the time of development, there was not an easy pathway for this intervention to integrate with the existing EHR. Further, at the time of development, the use of MyPennMedicine, the institutional patient portal, was relatively limited and for messaging only. Given that the intervention could not be integrated with EPIC at the time of development, and genetic provider concerns about the burden of operating in two separate systems, we elected to not develop a provider facing functionality. Rather, case report forms for research staff to enter messages and submit content to programmers were employed. We planned that if the intervention had proven efficacy (e.g. after a randomized trial), an integrated provider facing interface would be developed. For the randomized trial, we planned that research staff would act as facilitators to populate the genetic information in MyCancerGene (e.g. testing performed, copies of reports and letters). Additionally, to reduce human error, a second verification step was included to ensure accuracy (e.g., a study genetic counselor or second research staff member verifies that there is accurate information in MyCancerGene prior to participant access). It was expected that these steps would be reduced over time as systems permitted greater integration, or at the time of wider dissemination after efficacy of the intervention has been proven.

Programming and Technology Specifications

The MyCancerGene Participant Portal is based on Oracle database tools that reference tables, functions and procedures in an Oracle database. The participant is provided with a URL link that they enter into a standard web browser. The link invokes an Oracle REST Services call that connects to the appropriate database and schema to call a stored procedure that implements the login process. The participant is provided credentials by the MyCancerGene staff to complete the login. The login

procedure passes the credentials to a registration procedure that checks the credentials and creates an active session if the login is valid. The active session includes an expiration time for security purposes. Once a session is established, a page rendering procedure is invoked to read content from database tables and dynamically generate HTML code for display on the browser. All content for the portal is maintained in tables in the database. Study research staff use a separate application that was built using Oracle ApEX to enter participant specific information into Oracle tables that is used by the portal procedures to build the web screens. The page rendering procedure handles page navigation as well as screen display. A logout option on the main portal screen is used to terminate the session.

STEP 4. User Testing and Refinement of the Intervention

Patient User Testing

Participants for the first eight user testing interviews were from four of the COGENT sites. They were all female, 39-57 years old, included one Hispanic and one Black patient, and three participants with less than a college degree and a range of results (5 negative, 1 positive, 2 VUS results). Most participants reported the content to be both what they expected and useful. Key feedback from initial interviews included adding a landing page to be seen prior to the summary of care, reducing text, and suggestions for descriptive text, colors and fonts. Participants were evenly divided on presenting family history information as a list versus as a pedigree. They also reported that general reminders and notifications when MyCancerGene information was updated would be important to increasing use of the intervention. Other recommendations included the addition of educational resources, details on care providers, and dates of visits and other events.

Participants for the second set of patient user testing interviews (N=20) were identified from recent clinical encounters. They were 29 – 72 years old, included five men and one participant with less than a college degree and a range of results (3 negative, 10 positive and 7 VUS results). Participants had limited feedback for most content, with most suggestions for the Landing Page, My Family History page, messages about updates, and general suggestions to increase use. Suggestions for the Landing Page included clarifying the organizational affiliation and changes to design, fonts and images. Suggestions on the Family History page included the option to enter relatives and their test results, inclusion of third and extended generations and the option to view a pedigree. Other general suggestions included: replace pie charts with numerical risks, include a glossary and define terms, clarify the type of update and a link to the portal in messages, add educational resources, make MyCancerGene accessible on mobile devices, integrate MyCancerGene into the existing medical record and patient portal, and to provide reminders about availability of MyCancerGene. Some participants expressed concerns about privacy and security and provided recommendations to reassure participants (e.g. use a secure site, authentication strategies).

Participants in the second set of interviews also reviewed several options for messaging for updates to their test results. In contrast to provider opinions, they strongly preferred the option to receive a message and directly access their updates in MyCancerGene, with the option to speak with a genetic provider (participant choice), as opposed to options which alerted them of an update, but then required that they speak with a genetic provider first before having access to their update (provider disclosed).

Genetic Provider User Testing

Of the 25 genetic counselors who completed user testing interviews, 88% were female, 8 were affiliated with the University of Pennsylvania, 17 were from external practices from 5 states (PA, NJ, TX, CA, FL). Genetic provider reported benefits to patients included providing a centralized area for information and a tool to communicate updates (**Table 9**). Providers also identified benefits for

providers, including optimizing communication and saving provider time. They also reported potential challenges for providers including creating extra work and potentially leading to inefficiencies (**Table 9**). Genetic providers also had recommendations for changes to the Summary of Care, Landing Page, My Family History, and VUS reclassification pages, including simplifying text, changes to graphics and pictures, adding screening recommendations/care plans, changes to identify relatives on the family history page and accounting for multiple VUS results. Providers reported variable comfort with different types of updates being provided through MyCancerGene (**Table 9**). There was high comfort with updates to general testing information, reminders, and downgrades to VUS results. However, genetic providers varied in their comfort with upgraded VUS results being provided through MyCancerGene. Some were comfortable providing patients the option to directly access their updates in the portal with the option to speak with a genetic provide instead if they preferred. Others felt that changes in VUS classification (particularly upgrades) could be sent as a message, which alerted patients of the update, but felt patients should be required to speak with a genetic provider before having access to their update in MyCancerGene.

STEP 5. Usability Testing and Final Modifications to the Intervention

Usability participants were all white women, ages 24- 70 years old, with a range of education levels (high school only to graduate level). Participants had a range of genetic test results (6 positive, 1 VUS, 1 negative). Overall, many participants reported that icons and features were easy to understand, useful and what they expected. Participants reported greatest interest in the Genetic Test Results and Family History pages and additional resources. While they reported the summary letter was useful to have, several mentioned that they may not use it. Some were not clear what it was, even though they should have received a copy after their genetic counseling disclosure visit. Most found the Summary of Care and Summary of Updates useful and most felt the Updates page was easy to understand. There were several typos or spacing recommendations to make text easier to understand and these were generally adopted. Recommendations for changes to fonts, pictures or colors were made when recommendations were not conflicting or were mentioned by more than one participant. Key recommendations included: making pages available as a printable format, summaries under the videos, a note that if something does not appear accurate (e.g. personal or family history) to go to share an update, and the ability to provide more notes on the family history page (e.g. dates of diagnosis). Another recommendation was to add the My Screenings page, which had been a prior recommendation that was not included due to the challenge of keeping it updated with the electronic medical record when MyCancerGene was not yet integrated. However, given the repeated patient feedback, this page was created in the final version so that participants could self-track screening and data. Other recommendations that were considered but not possible at the time included: providing access to relatives, access to providers, syncing a screenings tracker with their calendar, making this available within their existing portal and creating a repository where patients could keep articles and websites they found personally useful. These were not included because they were either suggested by a single participant or were technically challenging at the time, but they were recorded as potential future considerations.

DISCUSSION

With the advent of multigene panel testing in clinical genetic testing, an increasing number of patients are left at risk for misunderstanding, uncertainty, and evolving interpretations and recommendations after receipt of cancer genetic test results.[6,69,70] Thus, longitudinal follow-up to update risk estimates and recommendations for positive results, update of VUS results and updates due to changes in family history are needed. Yet, cancer genetic testing is often a one-time encounter with a genetic counselor, as opposed to an ongoing relationship with continuity of care. This leaves the responsibility for follow-up, updates, and longitudinal care to patients, who can contact their

genetic provider as needed, or to their other health care providers, who may not be equipped to provide genetic-specific updates. To address this clinically significant gap in cancer genetic care, we developed a patient-centered longitudinal digital genetic health portal to support longitudinal care after receipt of cancer genetic test results. MyCancerGene was directly informed by patient and genetic provider feedback directing both the content and functionality of the intervention. The initial prototype was then refined through extensive user and usability testing with patients who had received a range of genetic test results.

Patient and provider interviews identified high interest in a patient-centered longitudinal digital genetic health portal to support longitudinal care. Over 90% of patients with positive results reported interest in a patient-centered digital genetic health portal, and over 75% of participants with a VUS or uninformative negative results reported similar interest. The primary advantages of this type of tool, according to patients, included increased accessibility, convenience and efficiency of accessing their genetic test reports and other documentation from the genetic visits, keeping genetic information organized, and increasing and maintaining patient understanding through easy to-understand materials and educational resources. Patients also felt that such a digital health tool could help with communication and sharing of materials with relatives or other providers. Patient were also in favor of receiving electronic updates through a patient-centered digital genetic health portal and highlighted that the intervention would need to address privacy concerns and be easy to use. Similar to patients, genetic providers reported that a patient-centered digital genetic health portal could help patients share information with relatives and other health care providers and help patients to update the genetics team about new health information (i.e., personal or family history or new test results in the family). Patients and providers also felt the portal may help provide a mechanism to update patients with new information about genetic results. While many providers endorsed this tool as a place to electronically store documents for patients, some noted that this could be redundant to what is already provided in the electronic health portal and the added value was unclear.

A key component of this formative work was to determine, from the patient and provider standpoint, what content and functions this patient-centered digital genetic health portal (MyCancerGene) should include. Patient and provider input identified eight key components of the tool and most were endorsed by both patients and providers as useful for longitudinal care. These included a Landing Page, Summary of Care, My Genetic Test Results, My Family History, Provide an Update, Review an Update, Resources and a Screenings Tracker. Patients and providers also addressed several key functions, including the ability to download and print materials and the inclusion of reminders and engagement functions. The iterative user and usability testing helped inform changes to increase ease of access by making the layout and design more intuitive, changes to content to increase understanding, the inclusion of a glossary with defined terms, the addition of educational resources, and changes to pictures/colors to help with patient understanding and overall experience. Integrating MyCancerGene into other health portals, providing access to relatives, syncing screening trackers with personal calendars were unable to be incorporated at the time, but were identified as future content or functions that could be helpful.

While most patients and genetic providers endorsed advantages and benefits of a patient-centered digital genetic health portal, some identified potential challenges. Some participants had privacy/security concerns, and a minority anticipated that reviewing past or updated information regarding genetic risk electronically could be upsetting/distressing. A minority also commented that MyCancerGene would be yet another health portal that could create additional login credentials, which can be hard to recall. Patient and provider comfort levels also varied with the return of updated VUS results in MyCancerGene. While patients were comfortable with updates (even VUS reclassification upgrades or clinically significant results), genetic providers had mixed feelings on the appropriateness of sharing upgraded VUS results through MyCancerGene. After sharing the overwhelming support among patients to make a choice for themselves if they are ready for updated information about their results, genetic providers were more open to this option although some still

had reservations. This will be an important outcome to evaluate in future longitudinal studies given the variable opinions from patients and genetic providers.

Another primary challenge identified by both patients and genetic providers is the strong desire to have such a genetic portal integrated with the existing EHR. Technological challenges in integrating the Oracle based system with the existing EHR and long queues and prioritization for already existing EHR modifications were barriers to developing MyCancerGene initially as an integrated component of the EHR. Further, it was felt that establishing efficacy would be important to establishing prioritization, value and investment in future integration. Another concern was that there are a variety of different EHR platforms available and institutions may vary in which EHR platform is used, which could limit future implementation. For these reasons, the intervention was built as a proof of concept for a randomized trial with plans to engage an IT integration committee throughout the trial to consider how MyCancerGene could be integrated with the EHR in the future. Of note, the provider-facing component of MyCancerGene would need to be developed and tested at the time of future integration.

Some limitations to our formative research and development are acknowledged. First, hypothetical query may not align with future use and benefits. Thus, a randomized trial of the intervention compared to usual care is planned and may better define real-world benefits and outcomes. As noted above, some desired components and functions could not be included and may limit the benefits, although these could be developed for future version of MyCancerGene. Additionally, while there is demographic diversity in the initial group of patients interviewed, the user testing evaluations were more limited and could have benefited from a more diverse patient population. Recruiting a diverse patient population in the future RCT will be critical to assessing the real-world benefits to a genetic health portal and to ensure it doesn't contribute or exacerbate existing digital disparities.[5,44,71]

Randomized Trial

The efficacy of MyCancerGene is being compared to usual care after receipt of genetic testing in real-world clinical patients in a randomized study (NCT04774445). In this ongoing study, we hypothesize that the intervention will be associated with short-term and longitudinal increases in knowledge, decreases in distress, increases in communication with relatives and health care providers, and increases in performance of risk-reducing health behaviors.

Conclusion

In summary, the MyCancerGene digital genetic health portal was developed with extensive feedback from patients and genetic providers and may be a useful digital health tool to enhance longitudinal patient understanding of and affective and behavioral responses to genetic testing, particularly in the era of evolving evidence and risk information. Evaluation of MyCancerGene in a randomized trial in real-world clinical settings will determine real-world uptake and clinical risks and/or benefits of this portal, which will ultimately contribute to the integration and promise of personalized genetic medicine.

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TABLES

Table 1: Development of MyCancerGene informed by patient and genetic provider feedback

Steps	Methods	Outputs
1. Inquire	Surveyed patients (n=307) who have completed genetic testing in the multi-center COGENT study	• Evaluated participants interest in, and barriers to a digital health portal • Explored GHP advantages, disadvantages, and usefulness and potential content
2. Determine	Individual qualitative interviews with patients (n=10) and a provider focus group (n=17) to better understand key intervention components and functions	• Informed by Diffusion of Innovation Theory, evaluating key attributes (e.g. relative advantage, risk compatibility, complexity). • Evaluated patient and provider preferences for content and functionality, including comfort with updates in test results
3. Develop	Incorporate feedback into MyCancerGene	• GHP (MyCancerGene) informed by formative interviews. • Key components from patient and provider input. • Initial screenshots were developed for user testing.
4. User Testing and Refinement of the Intervention	Provider (n=25) and patient (n=28) feedback on the specific drafted content and functionality	• Feedback on the purpose, content and comfort with specific functions • Recommendations for changes
5. Usability Testing and Final Modifications to the Intervention	Patient feedback (n=8) on the initial digital version of the intervention	• Feedback on content, presentation and functionality of the initial digital intervention

Table 2: Characteristics of patients who completed COGENT stakeholder questions (n=307)

	N (%)
Mean Age (SD)	47.60 (12.86)
Gender	
Female	286 (93.16)
Male	21 (6.84)
Education	
College	107 (34.85)
Post College	104 (33.88)
Refused to answer	1 (0.33)
Some College or less	95 (30.94)
Race	
White	282 (91.86)
Black/African American	16 (5.21)
Asian	5 (1.63)
Mixed	4 (1.30)
Ethnicity	
Hispanic/Latino	4 (1.30)
Non-Hispanic/Latino	303 (98.70)
Married	226 (73.62)
Disclosure method	
In-person^	173 (56.35)
Telephone	134 (43.65)
Site	
University of Pennsylvania	105 (34.20)
Fox Chase Cancer Center	110 (35.83)
University of Chicago	50 (16.29)
Stroger Hospital at Cook County	7 (2.28)
MD Anderson Cancer Center at Cooper	35 (11.40)
Known Mutation in the Family	11 (3.58)
History of cancer	153 (49.84)
Result	
Positive	52 (19.64)
True Negative	32 (10.42)
Uninformative negative	189 (61.56)
Variant of Uncertain Significance	34 (11.07)

Table 3: Patient Interest in a Genetic Health Portal					
	All N (%)	Positive (n=50-52)	Uninformative Negative	True Negative	VUS (n=32-34)

		N (%)	(n=179-188) N (%)	(n=30-32) N (%)	N (%)
Would a Genetic Health Portal be helpful?[a] (n=303)	249 (82.2)	48 (96.0)	154 (81.9)	22 (68.75)	25 (75.8)
Any barriers to using a Genetic Health Portal?[b] (n=291)	60 (20.6)	13 (26.0)	36 (20.1)	6 (20)	5 (15.6)
Would use a Genetic Health Portal[c] (n=305)	227* (74.4)	48* (92.3)	135* (72.2)	20* (62.5)	24* (70.6)

A range is included as some participants did not answer all items.

[a] "Now that you have received your results, do you think it would be helpful to have access to a secure, password protected electronic Genetic Health Portal (similar to other health portals you might have used in the past) with the information you received from your genetic provider (genetic counselor, physician, nurse practitioner, physician assistant)? (Yes/No)"

[b] "Do you think there would be any challenges with and/or barriers to using a Genetic Health Portal?"

[c] " How likely is it that you would use a Genetic Health Portal?

*Indicates somewhat or very likely on a 5 point Likert scale.

Table 4: Why a Genetic Health Portal would be helpful or not helpful^ (n=224)

Themes	
Reasons a Genetic Health Portal would be helpful	
Accessibility --Convenience or accessibility including access at any time. --For efficiency (fast or quick) “So that the information is readily accessible.” “Again, it's just more convenient to have access to information whenever I choose.” “Because I would be able to refer back to the results. It would also be good to be able to see anything that I might have missed.”	103 (46.0%) 85 18
Organization “Paper records can be misplaced and this is a way to access the information” “I would like to be able to electronically see my results so I don't have to keep track of the printout” “Having access to electronic records alleviates having to keep track of paper records.”	54 (24.1%)
Maintaining understanding “A Genetic Health Portal would be a central information resource for information related to my specific results and general genetic information. A portal could provide a central source for information and resources.” “Access to information is always helpful, especially when details are important and the information is sensitive.”	38 (17.0%)
Ability to share results with others --Ability to download and/or print results	26 (11.6%) 6
Helpful (NOS)	13 (5.8%)
For security (benefit of keeping results secure) “No one else should have access to my genetic information” “[This] would be a safe way to communicate with genetic provider”	7 (3.1%)
Emotional benefit “I feel like it would empower me more to be in control of my own health information for my future.”	7 (3.1%)
Ability to update information	1
Reasons a Genetic Health Portal may not be helpful	
Lacks human interaction	14 (6.3%)

“I think it would be worrisome to see this information without the assistance of someone knowledgeable explaining it to me… The genetic information is so sensitive and in some cases, unclear as to its significance regarding the individual and family members and really requires assistance to understand it.”	
Not helpful if you lack access to/comfort with technology “However, those that are not internet savvy will have difficulties." “I haven't used (or care to use) health portals because, quite frankly, creating accounts/ passwords for so many varied things has become too frustrating for me (personally).”	9 (4.0%)
No benefit or advantage “I prefer meeting in person so I can receive a thorough explanation and have the opportunity to ask questions.”	7 (3.1%)
Concern for security breach/privacy “Might be nice. Concerned about security of personal information”	7 (3.1%)
Could cause anxiety “But I always worry about finding bad news this way [through GHP] and then having to wait to see doctor.	5 (2.2%)
Not helpful because not combined with other portals	1
^ Now that you have received your results, do you think it would be helpful to have access to a secure, password protected electronic Genetic Health Portal (similar to other health portals you might have used in the past) with the information you received from your genetic provider (genetic counselor, physician, nurse practitioner, physician assistant)? Why or Why not (coded responses).	

Table 5: Disadvantages of a Genetic Health Portal^ (n=206)

Theme	**N (%)**
None	75 (36.4%)
Not secure enough/ privacy (risk of breach) “Data could be hacked and used against for insurance or employment purposes” “The only disadvantage would be if the site was breached.” “I suppose digital security is always a concern.”	67 (32.5%)
Upsetting/distressing “Genetic testing that could prove to be more anxiety-provoking than beneficial” “Finding out some life changing news without the comfort or clarification from a person” “For some, upsetting way to get bad news, perhaps misunderstanding information”	20 (9.7%)
Difficulty recalling login information or too many health care sites “One more password to remember/forget”	12 (5.8%)
Technical challenges --Hard for those who lack technical skills --Some may lack of access to technology --Glitches, website malfunctioning and maintenance “It would not be so beneficial for people who do not have access to online portals or do not know how to use the system.” “If I didn't have a computer and had no access to a computer.” “Any possible glitches with the system.”	10 (4.9%) 6 2 2
May not use (too much time or no benefit) “Not referred to often enough” “The time to sit down and look up/use the portal.”	7 (3.4%)
Lack of human interaction “Less personal than talking to someone...”	5 (2.4%)
^ What do you feel would be the disadvantages to having access to the Genetic Health Portal?	

Table 6: Types of information desired for Genetic Health Portal^ (n=227)	
Theme	N (%)

Genetic Test Result	112 (49.3%)
Educational or informational resources --Resources and education --Statistics, cancer risks or other numerical information --Current research or updates in research --Results of this research	62 (27.3%) 26 20 19 2
Medical recommendations	47 (20.7%)
Easy to understand explanation of results	29 (12.8%)
Provider information and notes --Access to clinicians or contact information --Provider notes --Medication details	24 (10.6%) 14 7 3
Appointment information --Appt details (dates seen, who did I see, location of visit) --upcoming appts or reminders for upcoming appts	22 (9.7%) 18 6
Everything	18 (7.9%)
Results of screening/procedures results	16 (7.1%)
Family history	14 (6.2%)
Genetic test description	14 (6.2%)
Summary (quick overview, snapshot)	10 (4.4%)
Updates to recommendations, new information or research	9 (4.0%)
Print and share function (to share with relatives or providers)	6 (2.6%)
Ways to share/engage with others (other patient experience or patient forum)	3 (1.3%)
Recommendations for relatives	1
Billing/Insurance	1
^**“What type of information or documents do you think would be most useful to include in the Genetic Health Portal?”**	

Table 7: Components of the MyCancerGene Genetic Health Portal

Component	Patient Endorsement	Provider Endorseme
1. **Landing Page** – includes eight icons for intervention components and a list of learning links in the left side bar. There is a summary statement regarding any new updates and a reminder to provide an update if there is new family information.	"First page shouldn't include any medical information. Users should be able to click and navigate to what they want to see and when."	
2. **Summary of Care** – includes location and date of service, testing lab, date and provider, test result statement (e.g. positive for a BRCA1 mutation) and link to result page.	"Would make things easier to recall when it is organized like this."	
3. **My Genetic Test Result** – includes type of test, test result statement and pdf to the test report. There is a patient-centered simple explanation (summary) of the results, a table of lifetime risks associated and general medical recommendations for positive results.	"Would be likely to refer to this when sharing results, especially by phone." "It's like having an electronic file cabinet!"	"Could be an easier w patients to share r with family and providers."
4. **My Family History –** includes family history obtained at the medical visit and updated by the patient in the portal. There is a link to the pdf of the last provider-generated pedigree and a link to update family history.	"Super useful section. New doctor always asks for this." "Big improvement than when [patient] had to fill it out by hand."	"Some patients migh recall which rela history they have or ha shared. Being able to to verify before they out would be helpful."
5. **Provide an Update –** includes icons to provide a family update (family history or genetic testing in relatives), personal update (medical history of genetic testing) and other updates (contact information, other).	"Feels there is a higher chance of 'success' in conveying updates or contact this way over a 'standard' telephone approach. With a portal, there is a way to track who has been told what and when. With the phone/mail, who can say?"	"Many patients are the impression we wi them when new testi other information bec available. This is ofte feasible."
6. **Review Updates –** provides a chronological list of updates with dates, provider involved and summary of the update.	"[I] like this, but would probably be more inclined to update as needed when reminded."	"Currently, certain up are handled by letter verification that updat been received is avai some updates may be this way."
7. **Resources** – a list of 8 links for organization	"[Would want] a section for	

that provide information regarding emotional and/or additional education resources. There is also a tool bar on the home screen with "Learning Links" including 3 videos and 3 text screens.	recommendation links and resources"	
8. Screenings Tracker – including the ability to enter the details of upcoming screening appointments including date, description and comments. These are self-entered and self-monitored.	"Medical management recommendations for the patient specifically would be ideal…perhaps a way to track what screening/med. management had been done – a timeline."	
There is a home icon on all component screens to return to the home screen. There is "Have a question?" ic every page.		

Table 8: MyCancerGene Engagement Reminders		
Type	**Frequency and timing**	**Examples**
1. Initiation reminder	4 reminders. On days 5, 9, 15 and 30	
2. General reminders (to update personal and family history and new testing in the family)	No end date, every 6 months. At 6, 12, 18 months, etc.	-Have you updated your family history: cancer status? -Have you updated your family history: testing status?
3. Engagement reminders (including educational messages and reminders about genetic and familial risk)	No end date, every 6 months. At 3, 9, 15 months, etc.	-Have you shared your results with your relatives? - Have you had your recommended screening?

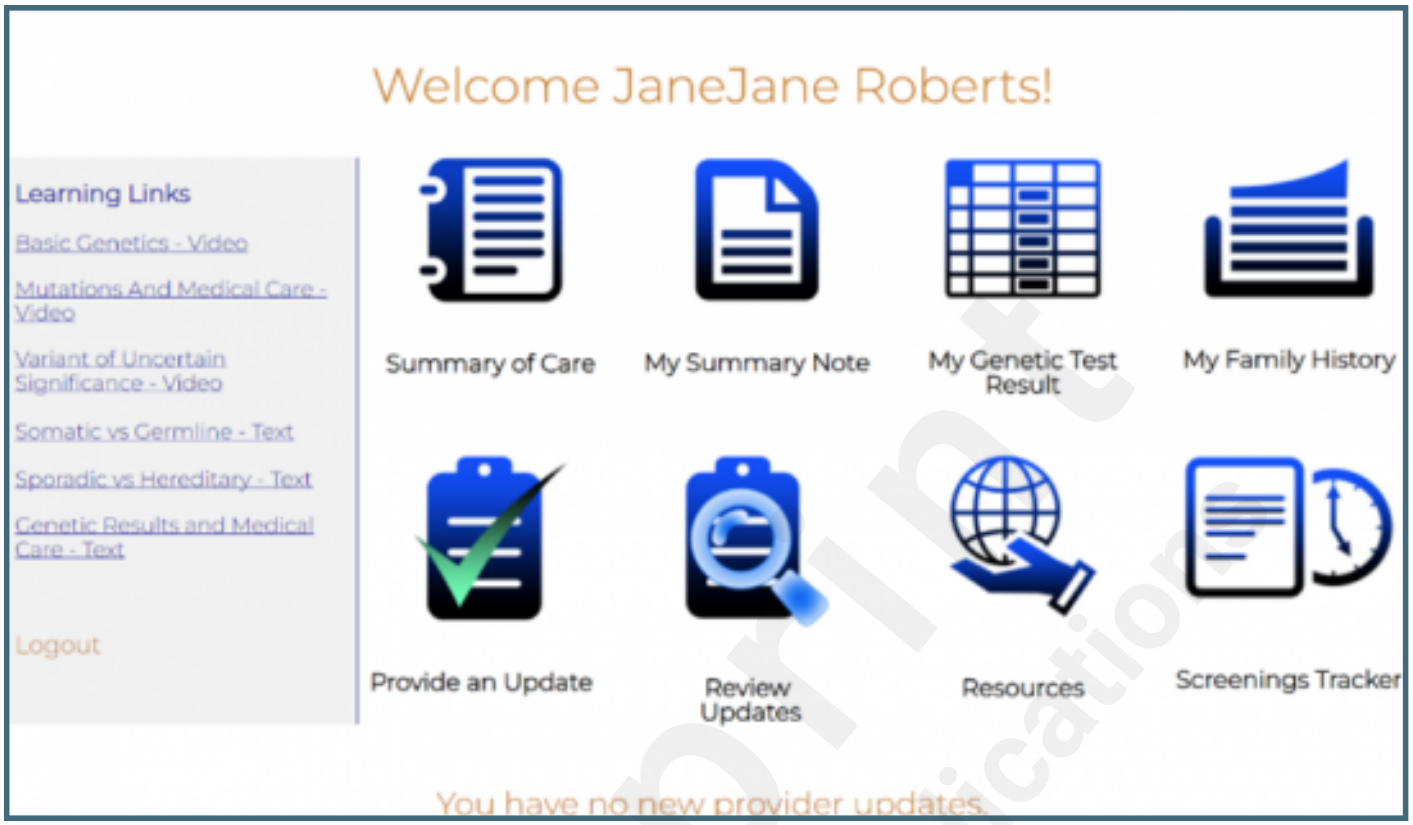
Table 9: Key findings from provider stakeholder interviews and user testing (n=25)		
Questions	**Most common themes (n, %)**	**Examples**
When thinking about your patients, how do you think this patient portal (MyCancerGene) would benefit them**?**	Centralized Information (13, 59%) Clearer updates (8, 36%)	"All documentation wou be easy to locate. Fami history and VUS updat which are typical cumbersome would streamlined."
What types of challenges could MyCancerGene alleviate for genetic counselors?	Centralized information (8, 33%) More efficient communication (8, 33%) Saves provider's time (7, 29%)	"Could increase efficien (less back and forth phon calls/sending letters that ma or may not get to where the need to, etc…)" "Could end up saving much as 30 minutes wi each interaction sinc instead of having to scaveng through chart notes, all t pertinent points a highlighted for each patient
What types of challenges could MyCancerGene create for genetic counselors?	Extra work (15, 63%) Inefficient communication (5, 20.8%)	"More work (double t work if not integrated wi the EMR). Also potential f more work if patients hav an easier means communication."
Comfort with different types of updates:		
General Testing Information	Comfortable (23, 92%)	"Comfortable. Thinks this so much better than the "ca us to follow up to see if the are any updates."
Reminders	Comfortable (24, 96%)	"Comfortable - and patien would appreciate this."
Downgraded VUS	Comfortable (22, 88%)	"Comfortable wi confirmation."
Upgraded VUS	Comfortable (11, 44%) Not comfortable (11, 44%)	"Comfortable as long follow-up with GC is not ju suggested but strong encouraged if n mandatory." "Not comfortable; prefers call patients directly."

Supplementary Files

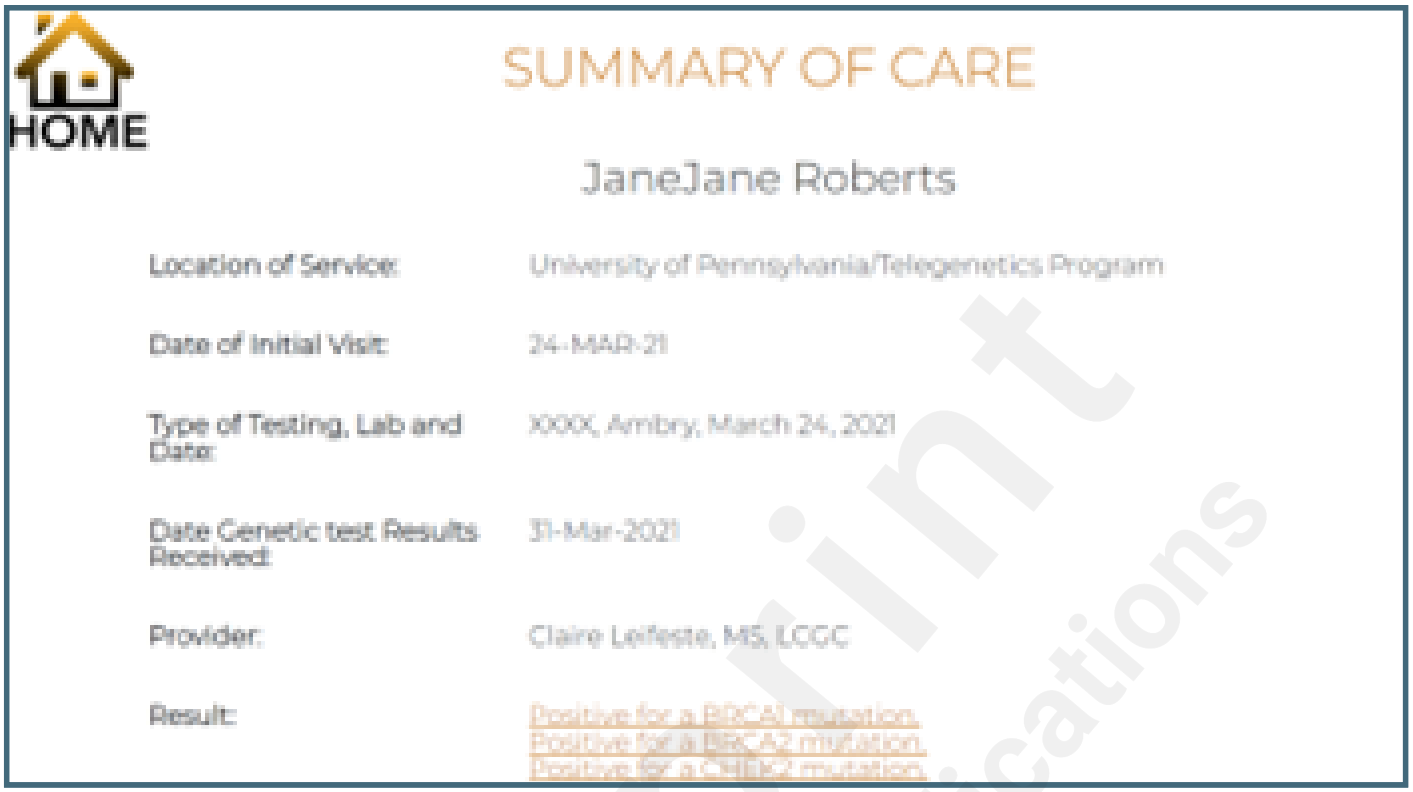
Figures

Log in Page.

Landing Page.



Summary of Care Page.



My Genetic Results Page.

My Family History Page.