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Optimizing communication strategies and designing a comprehensive program to facilitate cascade testing for familial hypercholesterolemia

Gemme Campbell-Salome^{1,2*} , Laney K. Jones^{1,3}, Nicole L. Walters¹, Kelly M. Morgan¹, Andrew Brangan¹, Ilene G. Ladd¹, Mary P. McGowan^{4,5}, Katherine Wilemon⁴, Tara J. Schmidlen⁶, Emilie Simmons⁶, Marci L. B. Schwartz⁷, Megan N. McMinn¹, Eric Tricou¹, Alanna K. Rahm¹, Catherine D. Ahmed⁴ and Amy C. Sturm^{1,3}

Abstract

Background This project aimed to optimize communication strategies to support family communication about familial hypercholesterolemia (FH) and improve cascade testing uptake among at-risk relatives. Individuals and families with FH provided feedback on multiple strategies including: a family letter, digital tools, and direct contact.

Methods Feedback from participants was collected via dyadic interviews ($n = 11$) and surveys ($n = 98$) on communication strategies and their proposed implementation to improve cascade testing uptake. We conducted a thematic analysis to identify how to optimize each strategy. We categorized optimizations and their implementation within the project's healthcare system using a Traffic Light approach.

Results Thematic analysis resulted in four distinct suggested optimizations for each communication strategy and seven suggested optimizations that were suitable across all strategies. Four suggestions for developing a comprehensive cascade testing program, which would offer all optimized communication strategies also emerged. All optimized suggestions coded green ($n = 21$) were incorporated. Suggestions coded yellow ($n = 12$) were partially incorporated. Only two suggestions were coded red and could not be incorporated.

Conclusions This project demonstrates how to collect and analyze stakeholder feedback for program design. We identified feasible suggested optimizations, resulting in communication strategies that are patient-informed and patient-centered. Optimized strategies were implemented in a comprehensive cascade testing program.

Keywords Familial hypercholesterolemia, Cascade testing, Chatbots, Direct contact, Implementation, Health communication

*Correspondence:

Gemme Campbell-Salome
Gcampbell3@geisinger.edu

Full list of author information is available at the end of the article



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Background

Familial hypercholesterolemia (FH) is one of the most common genetic disorders, causing increased risk of premature atherosclerotic cardiovascular disease (ASCVD) [1, 2]; however, early diagnosis and treatment can significantly improve prognosis and be lifesaving [3]. Individuals with FH can be diagnosed through genetic testing of the main genes associated with FH (*LDLR*, *APOB*, *PCSK9*) and through clinical methods including low density lipoprotein (LDL) cholesterol testing, physical exam, and collection of a family health history [1, 4, 5]. Cascade testing, or the stepwise and systematic screening of at-risk relatives in the family, is an effective method of identifying additional individuals with FH, as most individuals with FH have an autosomal dominant form of the condition [6, 7]. However, FH cascade testing is not routinely performed in the U.S. and the burden of sharing risk information about FH and motivating family to pursue testing is left to the proband, or first person diagnosed with FH.

Probands report a myriad of challenges trying to communicate with their family about FH including difficulty recalling and sharing complex risk information, navigating geographic and emotional distance with at-risk relatives, and inability to motivate relatives to pursue diagnosis and treatment [8, 9]. Probands may be provided Dear Family Letters to share with at-risk relatives that aim to support family communication and cascade testing, but such passive methods remain suboptimal [10]. Recently, a systematic review found passive methods resulted in <1 new relative with FH identified per proband on average [11]. Comparatively, more active methods such as clinicians directly contacting relatives resulted in a higher rate of new relatives with FH identified per proband [11]. Further, individuals with FH have expressed interest in receiving assistance from clinicians to share FH-related health risks with family [8, 9, 12].

Innovative, active communication strategies such as digital tools and direct contact are potential solutions to reduce the communication burden on probands and improve FH cascade testing uptake [13, 14]. Digital tools like chatbots can support patient activation by delivering standardized medical information designed by clinicians at the user's pace and by increasing access to genetic counseling and testing resources [15, 16]. Chatbots are digital conversational agents that communicate in ways mirroring human dialogue and have been implemented in healthcare systems to scale the delivery of genetic information [15]. Direct contact is another novel, active method that has the potential to reduce proband burden and improve cascade testing uptake. Historically, programs outside the U.S. in which a clinician directly contacts at-risk relatives with a proband's permission have

been highly effective in identifying additional individuals in the family with FH [7, 11].

Chatbots and direct contact strategies can also help at-risk relatives navigate to cascade testing resources. Recent evidence found individuals with FH and clinicians described these novel communication strategies as both acceptable and appropriate as well as feasible to implement in current practice [17]. Moreover, there is evidence suggesting offering a combination of passive and active communication strategies to probands sharing an FH diagnosis with at-risk relatives can lead to a higher proportion of relatives being tested [18]. However, more research is needed to inform the development of a patient-centered program offering multiple communication strategies to FH probands to facilitate cascade testing [19].

This project aimed to gather perspectives from individuals and families with FH to optimize existing communication strategies (i.e., Dear Family Letter, chatbots) and design a new communication strategy (i.e., a direct contact program) to improve FH cascade testing uptake. We document feedback from participants on how to (re) design communication strategies and create a comprehensive cascade testing program offering the strategies to probands to facilitate their family communication and improve FH cascade testing uptake. We also describe how the transdisciplinary team with expertise in FH, pharmacy, genomic medicine, health communication, and implementation science incorporated participants' feedback and what suggested optimizations the team could or could not feasibly incorporate. Results may inform other healthcare systems on how to develop, optimize, and incorporate innovative, patient-centered communication strategies to facilitate cascade testing uptake.

Methods

Setting

The Identification Methods, Patient Activation, and Cascade Testing for FH (IMPACT-FH) research study took place at Geisinger, a central Pennsylvania-based integrated healthcare delivery system. The Geisinger healthcare system consists of multiple hospitals and outpatient facilities, serving approximately 1.5 million patients annually. Additionally, Geisinger offers a health insurance plan, which is synchronized with clinical decisions made within the healthcare system to ensure high-quality care is accessible and affordable to plan members (approximately a third of Geisinger patients). The (re) designed communication strategies were targeted to individuals with FH identified through Geisinger's MyCode[®] Community Health Initiative (MyCode) [19]. MyCode is a population-based genomics project that includes electronic health records (EHRs) data as well

as genomic data generated from exome sequencing [20]. MyCode also includes a genomic screening initiative that returns actionable genetic results (including FH results) to patient-participants, called the MyCode Genomic Screening and Counseling Program (GSCP) [21]. The MyCode GSCP is equipped with 14 genetic counselors, 2 medical geneticists, 4 genetic counseling assistants, administrative leadership support, and study support staff, all at varying levels of funded time and effort. Additionally, MyCode GSCP offers genetic counselling and provides patient-facing resources such as chatbots and detailed summaries of genomic findings as well as provider-facing resources to help explain results and next steps. Finally, Geisinger has a multidisciplinary lipid clinic (MDLC), staffed with a lipidologist, genetic counselor, and pharmacist [22]. The MDLC cares for individuals with severe lipid disorders, such as FH, within the health system. Qualitative findings from this study were applied to create a comprehensive cascade testing program (i.e., IMPACT-FH Cascade Testing Program) to offer the optimized communication strategies to probands receiving an FH result from MyCode to facilitate family communication and cascade testing uptake.

Design

This project used a parallel mixed method design (interviews and surveys) to gather feedback from individuals and families with FH to optimize communication strategies to improve FH cascade testing uptake. The combination of methods ensured the project team could identify different perspectives on FH and cascade testing, characterize family dynamics relevant to offering optimized strategies, and triangulate findings that capture the breadth and depth of stakeholder feedback [23, 24]. Employing multiple methods to collect feedback also enabled wider recruitment and participation than solely conducting interviews.

The current project is part of a larger mixed-method study, “Identification Methods, Patient Activation, and Cascade Testing for Familial Hypercholesterolemia (IMPACT-FH)”, that aims to examine the optimized communication strategies’ effectiveness in facilitating FH cascade testing uptake in a prospective, pragmatic trial [19]. This project follows the Standards for Reporting Qualitative Research (SRQR) [25]. The interview guide and survey were developed for this study by the transdisciplinary research team and have not been published elsewhere (see Supplementary Materials for interview guide and surveys).

Data collection

We used a combination of purposive and snowball sampling to recruit participants. To be eligible, participants

had to be (a) English speaking, and (b) diagnosed with FH through genetic testing or clinical criteria, (c) an at-risk family member, and/or (d) a family member (i.e. spouse) of someone with FH [26]. Eligible participants were invited to either complete a dyadic interview or respond to an online survey. Eligible participants were allowed to only participate in one method (either dyadic interview or survey).

Participants were recruited from Geisinger’s MyCode (MyCode) [20, 21], Geisinger’s MDLC [22], and via the Family Heart Foundation. The Family Heart Foundation is a national patient-centered research and advocacy organization that works to improve identification and care of genetic lipid disorders including FH and elevated Lipoprotein(a).

To complete dyadic interviews, the participant with an FH diagnosis was invited to and asked to recruit a family member to join. Participants who completed interviews received a \$20 Amazon gift card. Participants were invited to complete surveys via email and through posts on the Family Heart Foundation’s social media accounts. Survey participants could also invite their family members to complete a survey. Survey participants recruited from Geisinger were entered into a raffle to win one of five \$50 Amazon gift cards.

Participants of each method were asked to review existing communication strategies including a Dear Family Letter (Supplemental Fig. 1a), a Family Sharing Tool (FST) [27] for the proband to utilize, [27] and a Cascade Chatbot for relatives to receive and use. The FST is a flat webpage for probands to encourage communication of their FH result to family and allows them to send a Cascade Chatbot to their relatives (Supplemental Fig. 2a). The Cascade Chatbot is received by relatives and discusses the proband’s result, associated health risks for relatives, and recommended care for at-risk relatives (Supplemental Fig. 3a) [16]. Participants were provided a description on how clinicians could directly contact at-risk relatives with the proband’s permission. Questions among both methods focused on gathering participants’ perspectives on (1) how to optimize the letter, FST, and Cascade Chatbot, (2) how to design the direct contact strategy, (3) how to offer low-cost genetic testing options, (4) what strategy or combination of strategies they would use and why, and (5) additional suggestions for how to facilitate cascade testing for at-risk relatives.

Dyadic interviews were conducted by phone and audio-recorded. Transcripts were de-identified, checked for accuracy, and analyzed by the team. Responses to demographic questions and open-ended survey responses were exported from the survey, de-identified, and checked for accuracy by ensuring there was only one response per IP address, before inclusion in the full data set. Open-ended

survey responses were moved to a spreadsheet to organize responses to each survey question on how to improve and design the strategies. Open-ended survey responses were then segmented by the type of strategy they gave feedback on. Interview transcripts and open-ended survey responses were iteratively read and analyzed concurrently. Descriptive statistics for participant demographics were analyzed using SPSS version 26.

Data analysis

Two authors (G.C.S., N.L.W) kept operational memos and de-briefed after each interview to discuss emergent themes, refine probes, and discuss when saturation was being reached. The two authors noted that saturation was being reached after the ninth dyadic interview as no new data was surfacing from interviews about using the strategies with family and feedback on how to optimize the strategies became repetitive of previous interviews. At this time two more dyadic interviews were scheduled and conducted as planned to ensure saturation of concepts and feedback was reached for interviews. Before closing the survey, open-ended survey responses were reviewed by the two authors, who determined that saturation had been achieved and responses added to insights from dyadic interviews [26, 28].

Interviews and open-ended survey data were thematically analyzed using the constant comparative method to identify key points of participant feedback on how to optimize each communication strategy and develop a comprehensive program offering the strategies to support FH cascade testing uptake [29]. The two authors engaged in first-cycle coding by independently open-coding three interview transcripts. The two coders met to review one another's coding, discuss discrepancies, iterate on the coding approach, and develop a codebook [30]. They proceeded to secondary-cycle coding by iteratively reviewing transcripts and survey responses and meeting to discuss codes to identify patterns, organize, and synthesize codes [28]. To ensure rigor, the coding team was expanded during axial coding to iteratively define and refine themes, descriptions, and examples and systematically group themes under hierarchical categories [29]. All coders had access to independently review transcripts and open-ended survey data in each phase of coding. The transdisciplinary coding team (G.C.S., N.L.W., L.K.J., C.D.A., K.M.M., A.C.S) included experts in genomic and precision medicine, pharmacy, implementation science, FH diagnosis and care, and an individual with FH. The diversity of the coding team ensured credibility of analysis that represents multi-faceted, crystallized qualitative findings [31].

The final data analysis step was to demonstrate how participant feedback was incorporated to optimize

communication strategies for patient-participants receiving an FH result from MyCode. The transdisciplinary team utilized a Traffic Light approach to categorize how feasible participants' suggested optimizations were within the context of the project and healthcare setting [32]. Green lights represent optimizations that fully addressed the participants' feedback and could successfully be made (were feasible) within our setting. Yellow lights represent optimizations that partially incorporated the participant feedback. Red lights represent optimizations that could not be incorporated.

Results

Overall, 120 participants were included in the project (see Table 1 for participant demographics). Eleven family dyads ($n=22$) completed joint phone interviews between July–August 2020. Additionally, 98 separate participants responded to surveys conducted August–September 2020. Qualitative data between interviews and surveys provided consistent feedback on topics reported below. Of note, survey participants tended to express more hesitancy about whether genetic testing was necessary compared to clinical methods for identifying FH. Most survey participants reported being diagnosed with FH via clinical methods (cholesterol/lipid testing, physical exam, and family history), with about 32% having had FH genetic testing.

Optimizing the Dear Family Letter resulted in a Family and Healthcare Professional Packet

Participants described finding the letter useful overall but recommended making printed and digital copies of the letter available, clarifying how to use the genetic testing report provided as part of the letter, incorporating edits to make the letter more personal so it might grab a relative's attention, and eliminating jargon (Table 2). Using the Traffic Light approach, all suggested optimizations were categorized as green and incorporated except for the recommendation to remove logos. This suggestion was categorized as yellow because the letter still needed to identify the participating organizations. Based on these participant responses and recommendations to clarify the genetic testing report and make the letter more personal, we expanded the Dear Family Letter into a Family and Healthcare Professional Packet (Supplemental Figs. 1a and 1b).

Optimizing the Family Sharing Tool resulted in a Family Sharing Chatbot and Cascade Chatbot with new functionality

Participants described the FST and Cascade Chatbot as easy-to-use tools that could help at-risk relatives learn about FH in a non-threatening format. Participants

Table 1 Participant demographics

Overall Sample (N=120)	
Sex	Female (75%) Male (25%)
Highest Educational Attainment	Some high school/high school/GED (14.2%) Some college/trade/technical degree (15.8%) Associate's degree (6.7%) Bachelor's degree (35%) Post-graduate degree (27.5%) Prefer not to answer (0.8%)
FH Diagnosis/Risk Status	Diagnosed (90.8%) At-risk (5%) Spouse/Caregiver (4.2%)
Dyadic Interview (N=22)	
Age Ranges	25 – 34 (18.2%) 35 – 44 (13.6%) 45 – 54 (22.7%) 55 – 64 (13.6%) > 65 (31.8%)
Dyadic Relationships	Sisters (n=3) Spouse (n=2) Mother-Daughter (n=3) Mother-Son (n=2) Father-Daughter (n=1)
Survey Responses (N=98)	
Participant Type	Individual with FH from Geisinger (n=19, 19.4%) Individual with FH from the Family Heart Foundation (n=72, 73.5%) Family member of an individual with FH (n=7, 7.1%)
Age	14–80 years old (M=55.94, SD=13.45)

recommended expanding the FST to be more interactive. They also recommended including a genetic testing ordering module in the Cascade Chatbot. These recommendations would enhance the technical capabilities of both tools. Participants also discussed their perceptions of the ideal types of users for chatbots (Table 3). Using the Traffic Light approach, four suggested optimizations were categorized as green (i.e., expand the FST, include an ordering module in the Cascade chatbot, offering additional options for sending a Cascade chatbot, and describing the chatbots as easy to use despite age/comfort with technology), two were yellow (i.e., Cascade chatbot reminders and overcoming perceptions that younger family members would prefer a chatbot), and one was red (i.e., offering a live chat function). The FST was expanded into a Family Sharing Chatbot (FSC) based on participants' feedback on making the FST more interactive, similar to the Cascade Chatbot (Supplemental Figs. 2a and 2b). A genetic testing ordering module was added to the Cascade Chatbot based on participants' recommendations to make it simple and accessible for

at-risk relatives to pursue cascade testing for FH (Supplemental Fig. 3b).

Designing the FH Outreach and Support Program for direct contact

Participants described how a clinician directly contacting their at-risk relatives to share information about FH and cascade testing could potentially motivate their family members to act. To create an acceptable direct contact strategy, participants recommended that an expert in FH who has a connection to the proband conduct the direct contact, relatives should be primed via a letter before direct contact takes place, clinicians within the same healthcare system of the proband and at-risk relative(s) should automatically coordinate contact without consent from the proband, and probands should be given the opportunity to partner with clinicians for direct contact (Table 4). Using the Traffic Light approach, two participant recommendations were categorized as green (i.e., having an expert with a connection to the proband and good communication skills perform direct contract,

Table 2 Optimizing the Dear Family Letter resulted in a Family and Healthcare Professional Packet

Theme		Participant Feedback	Optimization	Exemplar Quotes
Provide both printed and email version of the letter	GREEN	<ul style="list-style-type: none"> Desired an electronic version of the letter in addition to a printed version Suggested electronic versions could be in their patient portal and/or emailed to them 	<ul style="list-style-type: none"> Gave probands the option to receive the Family and Healthcare Professional Packet via secure message within the patient portal Gave probands the option to receive the packet via secure email Continued to mail a print version of the packet to probands 	<p><i>"Both e-mail and printed. Not everyone checks their e-mail."</i> (FH-Dx, S-26)</p> <p><i>"Allow to download and save."</i> (FH-Dx, S-78)</p>
Clarify how to use the genetic testing report	GREEN	<ul style="list-style-type: none"> Expressed confusion over the purpose of the genetic testing report Described difficulty not understanding instructions on what to do with the report 	<ul style="list-style-type: none"> Separated the genetic testing report from the relative's letter within the packet and included it with a Dear Healthcare Provider letter that relatives can give to their clinician Included frequently asked questions (FAQs) for clinicians with their Dear Healthcare Provider letter to describe how to use the genetic testing report Explained in FAQs for relatives that the report is from the proband's genetic test, but that the relative does not need to understand the details on the report to use it 	<p><i>"The second page is far too much medical gobbledegook for the average person to understand."</i> (FH-Dx, S-53)</p> <p><i>"So, I don't really think my lab report is going to mean anything to them. It's not even going to mean anything to their doctor because it's mine, it's not theirs."</i> (FH-Dx, DI-5)</p>
Grab relatives' attention by making the letter personal	GREEN	<ul style="list-style-type: none"> Explained that the letter needs to emphasize that the proband is the sender, but materials were written by clinicians Recommended opening with the proband's result, why this information is relevant to the reader, and sharing facts about FH to hold the reader's attention 	<ul style="list-style-type: none"> Added a more personal greeting and used the proband's name in the second sentence Added the phrase, "My healthcare provider gave me this letter to help share this information with you..." to the beginning of the letter Wrote a detailed yet simple description of FH and the proband's genetic result at the beginning of the letter 	<p><i>"I would say to put as much information about us, the test result and the fact that it comes, you know, from our healthcare providers and the fact that, [my wife] is sharing the information with them out of a keen interest in their good health. I would say the more that could be put in the letter and impress this upon them, the better."</i> (FM-NAR, DI-2)</p>
Eliminate jargon and define terms	GREEN	<ul style="list-style-type: none"> Expressed confusion over organization names (e.g., the healthcare system's name) Recommended less technical language for the genetic result Suggested defining institutions later in the letter 	<ul style="list-style-type: none"> Wrote a detailed, yet simple description of FH as a serious genetic disorder when explaining the genetic result Institutional names were introduced and briefly defined after the letter's purpose had been introduced Added an FAQ to define the organization names 	<p><i>P7: I'm looking at the letter right now, "[the LDLR gene] does not work correctly through the [healthcare system's study], and I would be like, "What the hell is this?" You know, I just think it's too technical. I have it and I don't even know what "LDLR gene" stands for."</i> (FH-Dx, DI-6)</p>
	YELLOW	<ul style="list-style-type: none"> Described confusion over logos for the healthcare system, the study, and the lab 	<ul style="list-style-type: none"> Removed logos for the healthcare system and study on packet documents except for the Dear Relative and Dear Healthcare Provider letters 	

priming relatives before direct contact), while the other four recommended optimizations were categorized as yellow (i.e., having a PCP perform direct contact, giving a specific timeline for direct contact, automatically contacting an at-risk relative's clinician within the same healthcare system as the proband, active proband involvement in direct contact). The direct contact strategy was designed based on participant recommendations and formally named the FH Outreach and Support Program. As part of the program, genetic counselors who worked with the original FH proband were the clinicians performing direct contact. First, probands received a flyer describing the program to help them consider whether to choose direct contact to help inform their at-risk relatives about their FH result (Supplemental Fig. 4). If probands chose direct contact, a primer letter was sent to alert the proband's relative that they would be contacted by a clinician (Supplemental Fig. 5).

Cross-cutting optimizations among strategies

Participants provided suggested optimizations that applied across strategies. Participants recommended providing credible, informative resources on FH for further information-seeking, including resources among strategies to help at-risk relatives navigate next action steps. This included clarifying the costs for cascade genetic

testing and lipid testing, providing at-risk relatives with an option to connect directly with a clinician about their FH risks, stressing that the strategies are from a credible source and are trustworthy, improving strategies to get through the noise of spam/scams relatives may receive, and encouraging probands to give relatives a "heads up" before the strategy reaches the relative. Using the Traffic Light approach, seven participant recommendations were categorized as green, four recommendations were yellow, and one recommendation was red (Table 5). We implemented the green and yellow suggested optimizations across strategies, such as providing links to the Family Heart Foundation's website for more information and resources, providing detailed instructions and multiple resources to help at-risk relative navigate next action steps, and using clear, transparent language comparing costs across options for cascade testing.

Designing a comprehensive program—The IMPACT-FH Cascade Testing Program

As participants described their feedback on each communication strategy, they also described that they would like to use one or more of the strategies for each of their relatives as part of a comprehensive program. Participants recommended designing a multi-pronged

Table 3 Optimizing the family sharing tool resulted in a family sharing chatbot and cascade chatbot with new functionality

Theme		Participant Feedback	Optimization	Exemplar Quotes
Expand the Family Sharing Tool (FST) into an interactive Family Sharing Chatbot (FSC)	GREEN	<ul style="list-style-type: none"> Explained that the FST did not give much information beyond who to send and how to send the Cascade Chatbot Described wanting the information provided in the Cascade Chatbot in the FST 	<ul style="list-style-type: none"> Optimized the simple FST with limited information into an interactive FSC Provided guidance on why and how to share the Cascade Chatbot with relatives Retained function for probands to skip additional information to share the Cascade Chatbot link with relatives 	<p>"So first the Family Sharing [Tool], I didn't really like that one...it just didn't seem to go anywhere." (FH-Dx, DI-5)</p>
Develop an easily accessible, patient-initiated, cascade testing module within the Cascade Chatbot	GREEN	<ul style="list-style-type: none"> Explained that ordering a genetic test via a chatbot could be convenient and easy Discussed liking the ability for relatives to order testing now or later on via the Cascade Chatbot Suggested explaining how the result would be returned 	<ul style="list-style-type: none"> Developed integration with chatbot, genetic testing laboratory, and third-party physician service for patient review and genetic testing ordering Added an ordering module with pre-populated genetic testing information and choice to skip down to ordering Provided the option to leave the Cascade Chatbot and come back to order any time Explained how results will be returned after placing the order 	<p>"I mean, is this a possibility to just say, 'Hey, order your test right here?' The more convenient, the better. Um, so, I think that would be a cool option." (FH-Dx, DI-1)</p> <p>"I'd probably [order a genetic test via the Cascade Chatbot]. I know that people do that stuff all the time where they send out their DNA in the mail and all that." (FM-AR, DI-11)</p>
Enhance the technical capabilities of the chatbots	GREEN	<ul style="list-style-type: none"> Recommended providing additional options within the FSC for sending the Cascade Chatbot 	<ul style="list-style-type: none"> Specified that the link provided at the end of the FSC can be copy/pasted into other messaging applications 	<p>"[Add options for sharing via] GroupMe, WhatsApp." (FH-Dx, S-27)</p>
	YELLOW	<ul style="list-style-type: none"> Suggested providing Cascade Chatbot reminders to improve recall and nudge relatives to return for genetic test ordering 	<ul style="list-style-type: none"> Reminders are already sent to the proband for the FSC and One Month Chatbots Cannot currently send relatives reminders for the Cascade Chatbot 	<p>"Maybe give people a choice [for when and how to receive Cascade Chatbot reminders]." (FH-Dx, DI-8)</p>
	RED	<ul style="list-style-type: none"> Described wanting a live chat function 	<ul style="list-style-type: none"> Could not feasibly incorporate a live chat function 	<p>"Possibly have live chat instead of pre set answers." (FH-Dx, S-82)</p>
Overcome misperceptions about age and being "tech-savvy"	GREEN	<ul style="list-style-type: none"> Explained how they may not share the Cascade Chatbot with certain family members based on age and the assumption that a relative was not "tech-savvy" 	<ul style="list-style-type: none"> Provided anticipatory guidance in the FSC about how the Cascade Chatbot is easy to use, not just for "tech-savvy" family members, and older individuals have used it successfully 	<p>"I liked how simple it was, like even if you're not text savvy, you could use it. You know, like if you are an older person that doesn't have a smart phone or doesn't use a computer very often, you can definitely figure out how to use it and navigate it, which I think is a huge deal." (FH-Dx, DI-3)</p>
	YELLOW	<ul style="list-style-type: none"> Described assuming younger family members would prefer the Cascade Chatbot instead of talking to a person 	<ul style="list-style-type: none"> Have not yet developed this language to address this assumption beyond anticipatory guidance above 	

program that provides options for probands regarding which strategies they could select to communicate their FH result with different family members. They also recommended offering the Cascade Chatbot to relatives within other strategies (i.e., QR code within packet), providing something tangible relatives could review and store (i.e., printed materials such as the packet, a transcript from the chatbot, direct contact primer letter), and encouraging future probands to tailor their strategy choices for each at-risk relative (Table 6). Using the Traffic Light approach, all suggested optimizations were categorized as green except for the suggestion that probands should contact family members to check their preferences to choose their preferred strategy, which was yellow. Based on this feedback, the team designed the IMPACT-FH Cascade Testing Program to provide the optimized, patient-centered strategies and provide probands choices among strategies over time. For the IMPACT-FH Cascade Testing Program, the team designed a workflow organizing how optimized strategies could function independently or in concert to facilitate family communication and cascade testing uptake (Supplemental Fig. 6).

Discussion

Developing a comprehensive program including patient-centered, innovative communication strategies can potentially overcome the challenges probands and their relatives face as they manage complex risk information about FH and pursue cascade testing [33]. Findings from this project identify key recommendations from individuals and families with FH to (re)design communication strategies and build a comprehensive cascade testing program. Using a Traffic Light approach [32], this project described how optimizations were mapped on to participant feedback and how optimizations could be feasibly incorporated within the study's healthcare system. Finally, the process of analysis utilized in this project can inform similar approaches to collect critical feedback from the populations similar programs seek to serve. This approach also illustrates how to translate feedback to implement optimizations both in genomic and precision health as well as more broadly to areas of equity and inclusion efforts or community-based programs.

Incorporating feedback for optimizing the Dear Family Letter into a Family and Healthcare Professional Packet was relatively straightforward as most participant suggestions were to adjust the language and expand the

Table 4 Designing the FH outreach and support program for direct contact

Theme		Participant Feedback	Optimizations	Exemplar Quotes
Direct Contact should be made by an expert in FH who has a connection with the proband or family	GREEN	<ul style="list-style-type: none"> Discussed how an expert in FH would have authority Suggested clinicians explain their connection to the family Explained the tone and conversational skills of the clinician as important for establishing trust 	<ul style="list-style-type: none"> Genetic counselors, who are experts in FH, perform direct contact Developed a script for genetic counselors to use when performing direct contact that includes an introduction explaining how they are connected to the proband and their expertise in genetics and FH Genetic counselors are well-trained in communication skills and bedside manner 	<p>"I see value in having a genetic counselor explain to relatives potentially affected what the condition is and how to get tested." (FH-Dx, S-79)</p> <p>"I would say a primary care provider [to reach out for direct contact] ... Because I think they know the case, you as a person, better and be better to relate it to the family member." (FH-AR, DI-11)</p>
	YELLOW	<ul style="list-style-type: none"> Described wanting the proband's clinician, especially a PCP, to perform direct contact 	<ul style="list-style-type: none"> The genetic counselor who discloses the FH result to the proband and/or provides genetic counseling to the proband also performs the direct contact for the family It is not feasible to ask PCPs to add direct contact to their workload 	
Prime relatives for Direct Contact	GREEN	<ul style="list-style-type: none"> Described wanting a primer letter to be sent to relatives Suggested sending this primer digitally via the patient portal Suggested that the letter alert relatives that they will receive a phone call from a clinician 	<ul style="list-style-type: none"> Developed a primer letter to be sent to relatives via secure email, the patient portal, or by mail at the direction of the proband Primer letter names the proband and FH result, explains FH, and informs that a genetic counselor will contact the relative Included clinical program phone number and email address to potentially opt out 	<p>"I think getting a letter first would be better than having just a doctor call out of nowhere." (FH-Dx, DI-6)</p> <p>I would say maybe a brief note through [the patient portal], saying, "Hey, one of your family members has this [genetic result]. I'd like to talk to you more about it." (FH-Dx, DI-5)</p>
	YELLOW	<ul style="list-style-type: none"> Recommended providing a timeline for when the relative would be contacted 	<ul style="list-style-type: none"> Indicate the relative will be contacted soon, but we do not communicate a specific timeline for direct contact Genetic counselors receive an automated notification to perform contact at two weeks post-primer being sent to at-risk relatives 	
Coordinate within the healthcare system	YELLOW	<ul style="list-style-type: none"> Recommended automatically contacting a relative's clinician if they and the proband are in the same health care system without explicit permission 	<ul style="list-style-type: none"> Provided the option for the genetic counselor to directly contact the relative's clinician if the proband and/or relative provides contact information Made option available even if proband and relative were not in the same healthcare system 	<p>"It would be easy for like my doctor, if [my relative's] doctor was a doctor [in my healthcare system] to just shoot them a message in Epic." (FH-Dx, DI-5)</p>
Provide opportunity for the proband to be a part of direct contact outreach	YELLOW	<ul style="list-style-type: none"> Expressed desire to review what the clinician will say during direct contact Described wanting to help the clinician tailor conversations to relatives 	<ul style="list-style-type: none"> Provided a flyer to describe the FH Outreach and Support Program to probands to review in advance Described the topics of the direct contact conversation the genetic counselor will have with a relative Genetic counselors do tailor and personalize care based on information about the relative provided by the proband, but this is not a systematic approach for the entire program The advice based on the proband's perception about their relative may be inaccurate 	<p>"[The proband] know how [to] get [their relatives] to listen and if it's someone who doesn't do well with statistics to say, "Hey, they're not going to want to hear the numbers, they're just going to want to hear how to help themselves or prevent it." (FH-AR, DI-11)</p>

single-page letter into a more comprehensive resource for relatives and their clinicians. Optimizations geared toward the relative's clinician included a letter from a genetic counselor and an FAQ sheet notifying the clinician of the proband's FH result, describing what the result could mean for the relative's health, and providing simple steps for how the clinician could order cascade testing. Future research should examine how at-risk relatives and their clinicians respond to and use this type of resource. Recently, a web-based tool to enhance family communication by providing a digital letter for probands to share with relatives and educational modules was evaluated positively by individuals with FH and genetic counselors [14], which shows further promise for the optimizations made in this study. Additionally, while participants recommended expanding the letter into a packet, the additional information and length may seem overwhelming to some individuals and warrants further research. Overall, optimizations made to the letter alone may still face persistent limitations as it is a passive, proband-mediated strategy for family communication about FH and may need to be combined with other strategies to improve cascade testing uptake [10, 11].

Participants' recommendations to expand the FST into a FSC and design a cascade test ordering module in the Cascade Chatbot were incorporated in partnership with the project's healthcare system, a genetic testing laboratory, and a third-party physician ordering company [16, 19]. Incorporating a module within the Cascade Chatbot for a patient-initiated genetic testing order/mail-in genetic testing kit can improve access and ease of cascade testing uptake for at-risk relatives and improve FH diagnosis. With these optimizations chatbots can increase access to genetic testing and counseling resources [15]. However, some participant recommendations were not feasible to fully incorporate, such as reminders for relatives to return to the Cascade Chatbot if they start but do not complete the chat and including a live chat function with a human. For instance, developing a live chat would require an expert in FH be available any time a proband or relative opens the chatbot, which would significantly increase the workload of clinicians and their extenders (e.g., nurse, physician assistant). While our healthcare system and MyCode program cannot support a live chat due to limited availability of staff and experts in FH, other settings or environments equipped with larger staff

Table 5 Cross-cutting optimizations among strategies

Theme/Participant Feedback	Optimization	Exemplar Quotes
<p>Provide more credible, informative resources on FH</p> <ul style="list-style-type: none"> Recommended including multimedia sources of information for different learning styles to improve engagement and understanding Described wanting strategies to provide links to reputable sources of information on FH 	<p>GREEN</p> <p>Dear Family Letter</p> <ul style="list-style-type: none"> Provided links to the FH Foundation's website and the healthcare system's FH webpage Added an infographic created by the FH Foundation Provided information to request a Cascade Chatbot <p>Chatbot</p> <ul style="list-style-type: none"> Developed multimedia information sources (e.g., videos, gifs) Provided links to the FH Foundation's website and the healthcare system's FH webpage <p>Direct Contact</p> <ul style="list-style-type: none"> Offered the chatbot as an additional resource that the genetic counselor can send directly to the relative Provided links to the FH Foundation's website and the healthcare system's FH webpage 	<p>"I like the [FH Foundation's] fast fact flyer and feel that should also be included in the letter. It hits on important information and catches the eye so people will read it." (FH-Dx, S-80)</p> <p>"List of educational and medically sound resources like the FH Foundation website that can answer their questions and help them moving forward." (FM-AR, S-97)</p> <p>"Video to share to explain FH." (FH-Dx, S-7)</p>
	<p>GREEN</p> <p>Dear Family Letter</p> <ul style="list-style-type: none"> Created an FAQ page to outline genetic and lipid testing options within and outside of the state and/or healthcare system Replaced the term "provider" with "healthcare professional" and provided examples Added the option to request a Cascade Chatbot for genetic test ordering Provided a Dear Healthcare Professional letter for relative's clinician with instructions for ordering genetic testing <p>Chatbot</p> <ul style="list-style-type: none"> Provided option to order genetic testing within the Cascade Chatbot Provided links to find a genetic counselor Added messaging about the importance and benefits of lipid and genetic testing The chatbot provides explanations and instructions on both genetic and lipid testing, but only provides a genetic testing ordering module. The links to an expert in FH are only for genetic counselors and not for other types of FH specialists. <p>Direct Contact</p> <ul style="list-style-type: none"> Described the importance and benefits of lipid and genetic testing Offered to place a genetic testing order or to send a link to the Cascade Chatbot to order genetic testing at-home by mail Provided links to find a genetic counselor and the FH Foundation's "Find a Specialist" webpage Although genetic counselors are describing both testing options, they can only provide genetic testing orders 	<p>"It might be helpful early on to note whether out of [state] residents will be given other appropriate sites to connect with." (FH-Dx, S-29)</p> <p>"If there was a way to get genetic testing, to me [a mail order genetic test] sounds like the easiest way to do it. I mean, we did it for Ancestry.com. It's nothing. You do a little swab. You put it in the envelope and off it goes." (FH-Dx, DI-6)</p>
	<p>YELLOW</p> <p>Direct Contact</p> <ul style="list-style-type: none"> Described the importance and benefits of lipid and genetic testing Offered to place a genetic testing order or to send a link to the Cascade Chatbot to order genetic testing at-home by mail Provided links to find a genetic counselor and the FH Foundation's "Find a Specialist" webpage Although genetic counselors are describing both testing options, they can only provide genetic testing orders 	
<p>Navigate Next Action Steps</p> <ul style="list-style-type: none"> Suggested providing information about testing options for at-risk relatives outside of the state and/or healthcare system Expressed confusion over who "provider" referred to in follow up instructions Recommended presenting both lipid testing and genetic testing options for next steps 		
<p>Clarify the costs</p> <ul style="list-style-type: none"> Explained that the current description of the low-cost genetic testing program was confusing in text-based strategies Recommended giving the date deadline for pursuing genetic testing within the low-cost program Suggested adding more information on potential costs and insurance coverage for genetic and lipid testing 	<p>GREEN</p> <p>Dear Family Letter</p> <ul style="list-style-type: none"> Included a breakdown of costs with testing options, including language around lipid testing based on insurance coverage Provided the deadline date for pursuing genetic testing within the low-cost program Clarified what is covered by the low-cost program for genetic testing <p>Chatbot</p> <ul style="list-style-type: none"> Added messaging about the associated costs (\$20) of ordering a genetic test via the Cascade Chatbot Added messaging about the average costs of lipid testing Described the low-cost genetic testing program and provided the deadline date Provided instructions on how to pursue genetic testing and costs if outside the low-cost program deadline <p>Direct Contact</p> <ul style="list-style-type: none"> Described genetic and lipid testing options and associated costs for each option Counsel on costs of genetic testing options if the relative is outside the low-cost testing program deadline 	<p>"Just say, 'free genetic testing for family members is offered through,' and have the date. Have the [deadline] calculated... They just want to know what the deadline is." (FH-Dx, DI-5)</p> <p>"Assurance of costs involved. Length of time to receive results of testing." (FH-NAR, S-98)</p> <p>"The information is correct, but incomplete. Some people can be diagnosed with FH based on testing their cholesterol and looking at their family history. This should be discussed..." (FM-AR, S-92)</p>
<p>Provide at-risk relatives with an option to connect directly with a clinician</p> <ul style="list-style-type: none"> Discussed the desire to connect directly with a clinician about testing and care for FH after being alerted to the result in the family 	<p>GREEN</p> <p>Dear Family Letter</p> <ul style="list-style-type: none"> Provided information to call or email the FH Foundation and/or the healthcare system <p>Chatbot</p> <ul style="list-style-type: none"> Provided the option to call or email the healthcare system instead of proceeding with the Cascade Chatbot to order testing <p>Direct Contact</p> <ul style="list-style-type: none"> This is the purpose of the program 	<p>"[The chatbot is] easy to do, and it seems friendlier than the letter. I would likely want to follow up with a person though, because I might have more questions." (FH-Dx, S-93)</p>
<p>Stress that strategies come from a credible source</p> <ul style="list-style-type: none"> Recommended adding messaging that these strategies were developed by clinicians and experts from a medical center Described the importance of naming the proband as the one sending the strategy to improve trust 	<p>GREEN</p> <p>Dear Family Letter</p> <ul style="list-style-type: none"> Added verbiage clarifying the proband was the sender, but clinicians and experts in FH created the packet <p>Chatbot</p> <ul style="list-style-type: none"> Added introductory text in the Cascade Chatbot that it was developed by experts in genetics and FH The chat already identified the proband as sending the chatbot and asking GIA to share this information on their behalf <p>Direct Contact</p> <ul style="list-style-type: none"> Primer letter states that the proband asked the clinician to reach out to discuss the relative's FH related health risks Developed script guiding clinicians to explain connection to the proband and their expertise in genetics and FH 	<p>"Depends [whether I send the chatbot] on if they would be worried it was not from reliable source." (FH-Dx, S-3)</p> <p>"Explain their credentials and why I should trust them." (FM-AR, S-97)</p>
<p>Get through the noise of spam/scams</p> <ul style="list-style-type: none"> Expressed concern over whether relatives would engage with each of the strategies when phone lines and inboxes are already saturated Suggested improving the look and messaging of strategies so they would not be seen as spam or scams 	<p>RED</p> <p>Dear Family Letter</p> <ul style="list-style-type: none"> It is up to the proband to share the packet in a way that can get through the noise <p>Chatbot</p> <ul style="list-style-type: none"> Gave instructions within the FSC for probands to write a personalized message when sending a Cascade Chatbot <p>GREEN</p> <p>Direct Contact</p> <ul style="list-style-type: none"> Did not require probands to ask for their relative's permission to share relative's contact information Provided option to call back later to collect contact information of relatives if the proband needed more time to gather information and/or ask permission Gave relatives the option to opt out of direct contact The primer letter is sent in a healthcare system branded envelope or in a healthcare system secure email or in patient portal to relatives. The genetic counselor introduces themselves as an expert in FH, affiliated with the healthcare system. However, this contact may still come off as a cold call if the proband did not prepare their relative. <p>YELLOW</p> <p>Direct Contact</p> <ul style="list-style-type: none"> Coached probands at multiple touchpoints to give a "heads up" before sending the packet to family We cannot control if probands give a "heads up" or when they send the packet. <p>Chatbot</p> <ul style="list-style-type: none"> Communicated tips for probands in the FSC on how to best give a heads up to their relative before sending a Cascade Chatbot Provided an example of how to write a personalized message when sending the Cascade Chatbot to a relative We cannot control if probands give a "heads up or when they send the chatbot. 	<p>"Yeah, I think, um, if [if this letter came out of nowhere, I think it would be concerning to people, and with so much, the way of trying to figure out with so many scams and everything these days, how do you know if this is really true or not." (FH-Dx, DI-6)</p> <p>"[Direct contact is] not very helpful. My family doesn't usually answer calls of unfamiliar numbers especially being skeptical of scam calls." (FH-Dx, S-78)</p>
<p>Encourage probands to give a "heads up" across strategies</p> <ul style="list-style-type: none"> Explained how the proband should give a "heads up" to relatives before any strategy is deployed Recommended allowing the proband enough time to gather relatives' contact information and get permission from family members before sharing their information with clinicians and choosing a strategy 	<p>YELLOW</p> <p>Dear Family Letter</p> <ul style="list-style-type: none"> Coached probands at multiple touchpoints to give a "heads up" before sending the packet to family We cannot control if probands give a "heads up" or when they send the packet. <p>Chatbot</p> <ul style="list-style-type: none"> Communicated tips for probands in the FSC on how to best give a heads up to their relative before sending a Cascade Chatbot Provided an example of how to write a personalized message when sending the Cascade Chatbot to a relative We cannot control if probands give a "heads up or when they send the chatbot. <p>GREEN</p> <p>Direct Contact</p> <ul style="list-style-type: none"> Coached probands at multiple touchpoints to give a "heads up" before sending the packet to family Sent primer letter to relative before direct contact Genetic counselors provide time in between when the primer letter is sent and the first attempt at direct contact in case the relative wishes to opt out 	<p>"Yeah, maybe like a letter kind of like the one you already have but from the family member or an email from the family member saying, you know, 'We have gotten this diagnosis about a genetic condition and we would like a doctor to contact you to give you more information.' You know, what would be a good contact number, time, day whatever. Just, you know, 'cause that would give them just that little bit of a heads up, too." (FH-AR, DI-3)</p> <p>"Yeah, just like give [your family] a heads up. I mean you should ask anyway. 'Is it okay if I give your phone number to, you know, these people to contact you so they can help you have more information about the possibility of you being a carrier or having FH?' I think that like in our family, I think everyone would be okay with that." (FH-Dx, DI-3)</p>

Table 6 Designing a comprehensive program—the IMPACT-FH Cascade Testing Program

Theme		Participant Feedback	Optimizations	Exemplar Quotes
Design a multi-pronged program that gives probands choices	GREEN	<ul style="list-style-type: none"> Recommended using strategies in concert together and adjusting what is sent and when for each relative Described liking that they had multiple options for sharing this information with relatives 	<ul style="list-style-type: none"> Provided probands with descriptions of each strategy and option to use one or more strategies per relative After re-designing the Family and Healthcare Professional Packet, it was offered as its own strategy independent of the chatbot or direct contact It was always a part of the IMPACT-FH Cascade Testing Program to re-approach probands at 6 months post disclosure if their relatives have not pursued screening to offer other strategies not yet used 	<p><i>"I think that the most effective way to do it is to have some sort of combo like you, you get the Dear Family Letter in a way that you can send that out first, so you're hearing from someone you know and trust, and then it's either the call or the chatbot, and maybe even give an option of whether you would rather hear from a person or work through the chatbot on your own. I think the combo of everything is absolutely the way to go."</i> (FH-AR, DI-6)</p>
Offer the Cascade Chatbot in the Dear Family Letter and the Direct Contact script	GREEN	<ul style="list-style-type: none"> Recommended offering a link to the Cascade Chatbot within the other strategies Explained how the Cascade Chatbot could provide additional information for relatives to review in their own time with less pressure Discussed how the Cascade Chatbot may not be able to stand alone as a strategy 	<ul style="list-style-type: none"> Added QR code in the Family and Healthcare Professional Packet for the option for the relative to receive a Cascade Chatbot to get more information and order their genetic test Added the option to be sent a Cascade Chatbot in the script that genetic counselors use for Direct Contact 	<p><i>"If it were me going to talk to my kids...I would be like, "I want to share this you. So, this letter outlines exactly what the genetic problem is that I have, and you are at risk, and if you're interested, here's the contact information." Then finally I would end it with like, "If you are really not ready to commit, the chatbot is a nice way that you can have a safe conversation without a commitment."</i> (FH-AR, DI-7)</p>
Provide something tangible for review	GREEN	<ul style="list-style-type: none"> Explained that although they liked the chatbots or talking with a clinician, they would still want something physical they can review and store 	<ul style="list-style-type: none"> Probands had the choice to send the Family and Healthcare Professional Packet to a relative on its own or in combination with other strategies The Cascade Chatbot generates a transcript that is emailed to relatives, which they can print The FH Outreach and Support Program sends a primer letter that relatives can keep 	<p><i>"Well, because you can have [the letter] in your hand. You know, it's something physical that you can look at and see."</i> (FH-Dx, DI-8)</p>
Encourage probands to tailor communication strategy choices for each relative	GREEN	<ul style="list-style-type: none"> Described probands as knowing relatives the best to choose among strategy options 	<ul style="list-style-type: none"> Gave probands the choice among strategies for each relative as described above in the "Develop a multi-pronged program that gives probands choices" theme 	<p><i>"So, I think it would be more from the person with the diagnosis to talk about it within the family and then for people that are interested, then you can have options: Do you want to do the chatbot? Are you more interested in going to a website? Would you like some written literature? Do you want to see a video? You know, like I think the starting point needs to be the family."</i> (FH-AR, DI-7)</p>
	YELLOW	<ul style="list-style-type: none"> Suggested probands contact family to check relatives' preferences to determine the right strategy or combination of strategies 	<ul style="list-style-type: none"> Encourage probands to tailor options for relatives Probands are not required to contact relatives about their preferences 	

trained by experts in FH may be able to feasibly facilitate a live chat with probands and relatives.

Although chatbots are more interactive strategies and can include direct access to genetic testing ordering, using the FSC to send a Cascade Chatbot to relatives still represents challenges inherent with proband-mediated communication strategies [11]. Probands may choose not to open or complete the FSC and not to send the Cascade Chatbot to relatives. Limitations to the reach and engagement with chatbots may also be due to technology access barriers. Although implementation of digital and mobile health tools are steadily increasing to fill gaps in healthcare, these tools can also increase disparities limiting their use to individuals who have technology skills and access to broadband connection to the Internet (i.e., the digital divide) [34]. It is promising that chatbots have been successfully integrated into the MyCode GSCP and participants in this study expressed interest in using and improving the chatbots [16, 35]. However, the digital divide and probands assumptions about relatives' comfort with technology may limit the impact of the Cascade Chatbot to improve cascade testing uptake [11]. To address this limitation, our team added language to the FSC to combat these misperceptions. Relatives also can directly access the Cascade Chatbot as part of the

IMPACT-FH Cascade Testing Program by requesting a Cascade Chatbot via contact information provided in the packet and/or when a genetic counselor performs direct contact.

Participant feedback on designing a direct contact program was implemented as much as feasibly possible to create the FH Outreach and Support Program. While participants often described wanting their primary care provider (PCP) to perform direct contact, they ultimately explained that the two most important characteristics were for the clinician to be an expert in FH and have a connection to the family. Asking PCPs to perform direct contact presents several key challenges including the lack of feasibility to incorporate direct contact into PCPs' already full workload, lack of reimbursement for PCPs' time, and limitations in their knowledge and confidence discussing genetic conditions and treating FH [17, 36, 37]. As such, genetic counselors were chosen to perform direct contact. Genetic counselors' expertise is in line with qualities that participants desiring for the clinician performing direct contact, as genetic counselors are extensively trained in discussing genetic disorders, applying communication skills to disclose genetic risk information, and psychological support provision to patients and families. Other types of clinicians could

perform direct contact if they are seen as experts and trusted sources of FH information and have strong communication skills, which could improve the feasibility of implementing direct contact programs widely [17]. Participants also recommended coordination of care within the healthcare system so the proband's clinician could automatically share the FH diagnosis with at-risk relatives' clinicians seamlessly, without first gaining permission from the proband. This suggested optimization represents ethical and legal challenges related to sharing private health information, as some clinicians may feel uncomfortable directly contacting a relative's provider without the proband's express permission, although it may be acceptable based on HIPAA requirements depending on state law [38, 39]. Beyond ethical and legal questions, system level barriers to clinician communication also limit wider implementation of this suggested optimization as not all clinicians and healthcare systems use EHRs that are interoperable to facilitate sharing risk information. Methods from implementation science can be utilized to design strategies for these complex care coordination programs that involve clinician to clinician communication regarding genetic information and to evaluate their effectiveness.

The Traffic Light approach is a method used in implementation science settings to explain how suggested adaptations have been incorporated into other projects [32, 40]. Utilizing the Traffic Light approach to describe suggested optimizations in this project improves the generalizability to other healthcare settings [32]. This approach facilitated the categorization of suggested optimizations based on their feasibility. Further, this approach demonstrates how to incorporate stakeholder feedback to optimize strategies and design healthcare programs. By assigning colors to suggested optimizations and describing the decisions for making and incorporating optimizations, other healthcare settings can decide what may be feasible for their patients, clinicians, and system.

A final key contribution of this work is the development of a comprehensive, multi-pronged program, the IMPACT-FH Cascade Testing Program, consisting of multiple optimized communication strategies to be utilized by probands receiving an FH result. Participants not only provided feedback on how to (re)design each communication strategy, but also provided recommendations on how to offer the strategies to probands, enable probands to choose a combination of strategies over time, and allow probands to customize their strategy choice(s) for each relative. Thus, the IMPACT-FH Cascade Testing Program was developed to describe and offer the optimized strategies to probands with FH, with the key tenet of allowing probands to tailor their

choices for each at-risk relative and to switch strategies if the first choice did not work (Supplemental Fig. 6). Future research should examine how relatives respond to the proband's strategy choices and use these optimized strategies to make decisions about their FH risk. Participant recommendations for offering a combination of passive and active communication strategies supports previous findings that offering multiple communication methods and types of clinical support can improve cascade testing uptake [18]. Future research should pragmatically test how such a program can improve cascade testing uptake and examine how probands and relatives use the optimized communication strategies [19] and what additional improvements can be made to these strategies.

Generalizability of this project is limited as the sample reported relatively high educational attainment, did not include non-English-speaking participants, and survey participants needed Internet access [41]. Further, all dyadic interview participants identified as Caucasian, and ethnicity and race were not collected in surveys. More diverse participants and those with lower educational attainment may experience meaningful differences when managing information about FH and pursuing cascade testing and could provide different suggested optimizations. As participants were recruited via Geisinger's MyCode[®], MDLC, and the Family Heart Foundation, they may have represented a group that is more active in pursuing information and testing for FH. Additionally, it is possible that some family members of interview participants completed survey responses, which may have created few instances with similar feedback due to a shared family communication experience or preferences. Although this is possible, authors took care during recruitment and data refinement to ensure survey responses were unique and that interview participants were not included in survey recruitment. Further, while our final optimized program and strategies are based on what was feasible within our healthcare system, others can review our data and utilize the Traffic Light approach to re-categorize suggested optimizations based on the resources available in their own system. For instance, Geisinger had genetic counselors return FH results to probands via MyCode[®] [21] and perform direct contact to at-risk relatives, and had certain facilitators (e.g., well-established genetic counseling program, previously established chatbot integration) that set the healthcare system up well to support optimizations. Finally, there may be other ways to establish a comprehensive cascade testing program outside of any one healthcare system, such as non-profit patient advocacy groups, that may address some of the implementation barriers encountered by this project.

Conclusion

Overall, findings demonstrate the importance of offering choices to probands when providing patient-centered, innovative communication strategies to facilitate family communication about FH and cascade testing uptake. This project documents participant feedback to (re) design communication strategies and build a comprehensive patient-centered program to facilitate cascade testing uptake. Further, we demonstrate how feedback was implemented within the healthcare system and describe why some feedback could not be fully incorporated into the final optimized program. Other healthcare systems can learn from the Traffic Light approach to determine what feedback from participants can be feasibly implemented at their site to support family communication and FH cascade testing uptake. These learnings may inform family communication and cascade testing approaches for other genetic conditions.

Abbreviations

FH	Familial Hypercholesterolemia
ASCVD	Atherosclerotic cardiovascular disease
LDL	Low density lipoprotein
IMPACT-FH	Identification Methods, Patient Activation, and Cascade Testing for Familial Hypercholesterolemia
SRQR	Standards for Reporting Qualitative Research
GSCP	Genomic Screening and Counseling Program
MDLC	Multi-disciplinary lipid clinic
FST	Family Sharing Tool
FSC	Family Sharing Chatbot
FAQ	Frequently Asked Questions
PCP	Primary care provider

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12913-023-09304-y>.

Additional file 1: Supplemental Figure 1a. Original Dear Family Letter. The original Dear Family Letter template with lab report for probands to share with at-risk relatives. **Supplemental Figure 1b.** Optimized Family and Healthcare Professional Packet. The optimized Dear Family Letter template with a flyer on FH, FAQs for relatives, a letter for the relative's Healthcare Professional, and FAQs for the healthcare professionals.

Additional file 2: Supplemental Figure 2a. The original Family Sharing Tool (FST). The original FST with questions and answers for probands. The FST included a separate page to facilitate sharing of the Cascade Chatbot to at-risk relatives. **Supplemental Figure 2b.** The Family Sharing Chatbot (FSC). The FST was optimized into a FSC to be conversational and interactive chat to encourage probands to share information about their FH result with at-risk relatives.

Additional file 3: Supplemental Figure 3a. The Cascade Chatbot. The Cascade Chatbot is designed to share information about the proband's FH result with at-risk relatives, provide the relative information about FH, and connect them with resources for cascade testing. **Supplemental Figure 3b.** The genetic testing ordering module addition to the Cascade Chatbot. The optimized Cascade Chatbot includes a module for at-risk relatives to order family variant testing through a mail-order genetic testing kit.

Additional file 4: Supplemental Figure 4. Flyer for the FH Outreach and Support Program. The flyer is sent to probands in a packet they receive

after receiving their FH result from MyCode and describes important points related to the direct contact program.

Additional file 5: Supplemental Figure 5. Primer Letter for the FH Outreach and Support Program. The Primer Letter template for relatives the proband chooses to be contacted directly by a genetic counselor as part of the FH Outreach and Support Program.

Additional file 6: Supplemental Figure 6. IMPACT-FH Cascade Testing Program Workflow. Probands can choose multiple strategies for each of their at-risk relatives. All probands are provided with the Family and Healthcare Professional Packet and a flyer describing the FH Outreach and Support Program for direct contact after they receive their FH result even if they choose other communication strategies.

Additional file 7.

Additional file 8.

Additional file 9.

Additional file 10.

Additional file 11.

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Authors' contributions

All authors have read and approved the manuscript. Conceptualization: G.C.S., L.K.J., N.L.W., A.B., A.K.R., A.C.S., Data curation: N.L.W., A.B., Formal analysis: G.C.S., L.K.J., N.L.W., K.M.M., C.D.A., A.C.S., Funding acquisition: A.C.S., A.K.R., L.K.J., Investigation: G.C.S., L.K.J., N.L.W., A.B., K.M.M., C.D.A., A.K.R., A.C.S., Methodology: G.C.S., L.K.J., N.L.W., A.B., K.M.M., C.D.A., A.K.R., A.C.S., Project administration: A.B., N.L.W., I.G.L., Resources: N.L.W., C.D.A., T.J.S., E.S., Writing – original draft: G.C.S., L.K.J., N.L.W., K.M.M., C.D.A., A.C.S., Writing – review & editing: G.C.S., L.K.J., N.L.W., C.D.A., K.M.M., A.B., I.G.L., M.P.M., M.N.M., A.K.R., T.J.S., E.S., M.L.B.S., E.T., K.W., A.C.S.

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Availability of data and materials

The qualitative data that support the findings of this project are available on request from the corresponding author (G.C.S.). The data are not publicly available due to them containing information that could compromise participant privacy/consent.

Declarations

Ethics approval and consent to participate

Upon review, the Geisinger IRB determined that this project was not a systematic investigation designed to develop or contribute to generalizable knowledge as defined at 45 CFR 46.102(1), and was therefore not research. All procedures performed in studies involving human participants were in accordance with the ethical standard of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Participants agreed verbally to participate in interviews and in writing to complete surveys.

Consent for publications

Before interviews, researchers reviewed the goals of the project and asked participants if they wished to participate and agreed to be recorded. When participants gave verbal consent, interviews were conducted. This was appropriate as participants were given information about the study ahead of the interview, which was reviewed before interviews and participants were given time to ask questions and consider if they wished to participate. Although,

the Geisinger IRB determined that this project was no research, authors did consult the Geisinger IRB on the ethical conduct of the project. For surveys, the first webpage described the goals and procedures of the project for participants and participants had to give written consent.

Competing interests

Tara Schmidlen is an employee and shareholder of Invitae. Emilie Simmons was an employee and shareholder of Invitae at the time the project was conducted. Amy Sturm has been a consultant for Invitae.

Author details

¹Department of Genomic Health, Geisinger, Danville, PA, USA. ²Department of Population Health Sciences, Geisinger, Danville, PA, USA. ³Geisinger Heart and Vascular Institute, Geisinger, Danville, PA, USA. ⁴The Family Heart Foundation, Pasadena, CA, USA. ⁵Geisel School of Medicine at Dartmouth, Dartmouth Hitchcock Medical Center, Lebanon, NH, USA. ⁶Invitae, San Francisco, CA, USA. ⁷Cardiac Genome Clinic, Ted Rogers Centre for Heart Research, The Hospital for Sick Children, Toronto, ON, Canada.

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