PATIENT EXPERIENCE AND BARRIERS WITH FAMILY COMMUNICATION AFTER RECEIVEING GENOMNIC INFORMATION FROM A BIOBANK

By

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ABSTRACT OF THE THESIS

Patient experience and barriers with family communication after receiving genomic information from a biobank

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The purpose of this study was to examine the breadth of participant experiences communicating with family members after receiving genetic information from a biobank. Interviews were conducted with MyCode participants who had received results and with family members of participants who had undergone cascade testing. MyCode is a population-based biobank where participants consent to exome sequencing for research and the possibility that Geisinger may return genetic information important to their health. Results for pathogenic and likely pathogenic variants in clinically actionable genes are reported to MyCode participants and their providers. Sixty-three interviews were analyzed for the purpose of this study. The barriers revealed were similar to those found in the literature, with the most common being physical and emotional distance, proband perception that at-risk relatives were too old, not knowing who was at risk, and timing of the communication. Analysis of barriers to cascade testing showed that the most common reasons family members chose not to test were bad timing, thinking they were not at risk or too old for genetic testing, and disinterest in the information. Additionally, several participants and family members believed they had been tested by

other means such as direct to consumer (DTC) testing. As access to genetic testing expands, it will be necessary to ensure that consumers fully understand the implications and limitations of different types of genetic testing. Furthermore, continued efforts are needed to assist probands in how to explain their results to family members in order to overcome barriers to family communication and cascade testing.

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Introduction

Cascade testing is the genetic testing in family members of individuals diagnosed with genetic conditions. The rate at which these at risk relatives choose to test has been, historically, low. Only about 20-50% of at risk first-degree relatives of individuals found to harbor a pathogenic variant decide to seek genetic testing for themselves (Christiaans, Birnie, Bonsel, Wilde, & van Langen, 2008; Sharaf, Myer, Stave, Diamond, & Ladabaum, 2013). However, this rate can increase to as much as 99% in those relatives who receive genetic counseling (Christiaans et al., 2008). It is important for these individuals to consider genetic testing because it can have an impact on their health, medical surveillance, treatment and reproductive choices. Several studies have explored the barriers to at risk relatives pursuing genetic testing including time commitment of testing, age and education level (Gaff et al., 2007; McCann et al., 2009; Stoffel et al., 2008). One barrier that emerged consistently across several studies was family communication (Sharaf et al., 2013). Understanding the barriers to family communication is essential because the current standard of practice is for medical professionals to rely on their patients to disseminate pertinent information to at-risk family members.

Family communication of genetic test results has been studied extensively. Over time, several themes influencing family communication have emerged. One of these themes is patients' feelings about informing relatives (Chivers Seymour, Addington-Hall, Lucassen, & Foster, 2010). Some patients pursue testing to gain information for family members, to get emotional support or to ask for advice on medical treatment. Others find it emotionally demanding to be responsible for sharing this information with family (Young et al., 2017). Another theme is perceived relevance to certain family members

based on gender, age or genetic relationship (Chivers Seymour et al., 2010). Studies have found that men and women with a BRCA mutations specifically are most likely to share this information with close female relatives and least likely to share with distant male relatives (Elrick et al., 2017; Suttman, Pilarski, Agnese, & Senter, 2018). A third theme is that decreased comprehension of autosomal dominant inheritance leads to decreased family communication due to the fact that patients do not know which family members are at risk or how to explain the information (Batte et al., 2015). Closeness of relationship in the emotional and geographic sense was another theme that emerged (Batte et al., 2015; Chivers Seymour et al., 2010; Whyte, Green, McAllister, & Shipman, 2016). The theme of family structure asserts that some patients believe it is not their responsibility to tell their distantly related family members because it is the job of more closely related relatives (Chivers Seymour et al., 2010). Even within these linear family patterns however, women are more likely to take on the role of communicator within the family and communicate with more distant relatives than men (Chivers Seymour et al., 2010; Elrick et al., 2017; Suttman et al., 2018). A final theme that arose from the literature is timing. Many patients who do not share the genetic results with family members say that it was “not the right time” (Chivers Seymour et al., 2010).

While the literature on family communication is quite robust, the studies have predominantly been conducted using symptomatic patients, or patients who had strong family histories where only one or a handful of genes were tested. With recent advances in technology that have led to a decrease in the cost and turn around time of DNA sequencing, more clinicians are transitioning from the traditional single gene tests based on family history to whole exome sequencing (WES) which can be used as a diagnostic

device or for disease prevention in healthy individuals. WES has the potential to reveal genetic information unrelated to the patient's initial indication known as incidental findings. While there has been much debate about returning these results to patients, several studies utilizing focus groups and clinician experience have found that a majority of patients want to know about findings that are medically actionable (Carey et al., 2016; Faucett & Davis, 2016; Smith, Douglas, Braxton, & Kramer, 2015).

The use of whole exome sequencing to return results from a biobank has been a more recent area of study (Biesecker et al., 2009; Faucett & Davis, 2016; Fossey et al., 2018; Zouk et al., 2018). Individuals consented to biobanks are not being tested because of a family or personal history of disease and may not even be expecting to get a result back at all. While family communication of genetic test results has been widely studied, it has not been looked at in the context of returning results to biobank participants. Our aim is to observe any barriers to communication that patient-participants in MyCode encounter and how those may differ from the literature surrounding traditional return of results. As this type of genetic testing becomes more widely used to improve population health it will be important to know if the way they communicate genetic information is different.

Methods

Study Design

This study involved the qualitative analysis of 63 interviews using a phenomenological experiential design to identify patient experience with communicating genetic results to their family members (van Manen, 2017).

MyCode Description

Geisinger has recently expanded their MyCode Community Health Initiative, which is their patient-participant biobank that also uses clinical data collected in their electronic health record to conduct research. This expansion includes the return of clinically actionable results that arise from genomic sequencing of biobank participants' samples (Faucett & Davis, 2016). A list of genetic variants that should be returned was created based partially on the American College of Medical Genetics and Genomics March 2013 clinical testing recommendations (Faucett & Davis, 2016).

Study Population

This study is a secondary analysis of transcripts from patient interviews collected across multiple MyCode-related studies. Interviews were conducted with individuals who fell into four categories: two months post result disclosure (N=29), participants who had received a result of Familial Hypercholesterolemia through MyCode (N=7), those who had received a result related to hereditary breast cancer or hypertrophic cardiomyopathy but did not have a personal or family history consistent with the hereditary condition (N=19), and family members of MyCode participants who underwent cascade screening (N=8).

Qualitative Data Collection

Interviews were conducted with MyCode participants at least two months after receiving results, but varied between 2-18 months post-disclosure depending on the interview sample. Interviews with family members were conducted after having cascade testing and either already received either a positive or negative result or were still waiting for test results. All interviews were conducted by telephone by team members trained to

standardize the interview process (Rahm, 2019). Regardless of original study, all interviews consisted of open-ended questions on their thoughts, feelings and opinions of the return of results process. The semi-structured format gave interviewers the opportunity to explore various topics that are expected to arise with each participant, while still gaining quality information across participants that could be developed into themes. The interviews were transcribed and uploaded into the qualitative analysis software, Atlas.ti.

Analysis

In addition to *a priori* codes derived from the literature and interview guides, the transcribed interviews were reviewed by multiple readers to develop additional *de-novo* codes and a finalized codebook. Based on the coding of ten interview transcripts, inter-rater reliability was reached for each theme. High inter-rater reliability was established for the following themes: to whom they did not communicate (K= 0.85), Why they talked to relatives (K= 0.96), why they did not talk to relatives (K= 0.93), Relatives tested (K= 1.0), relatives did not test (K= 0.85), why the relatives tested (K= 0.96), why the relatives did not test (K= 0.85), actions taken by relatives (K= 0.96), and how the information was communicated (K= 0.96). Substantial inter-rater reliability was established for the theme of whom they communicated the information to (K= 0.74)(Landis & Koch, 1977). All transcripts were then coded using the established codebook.

Results

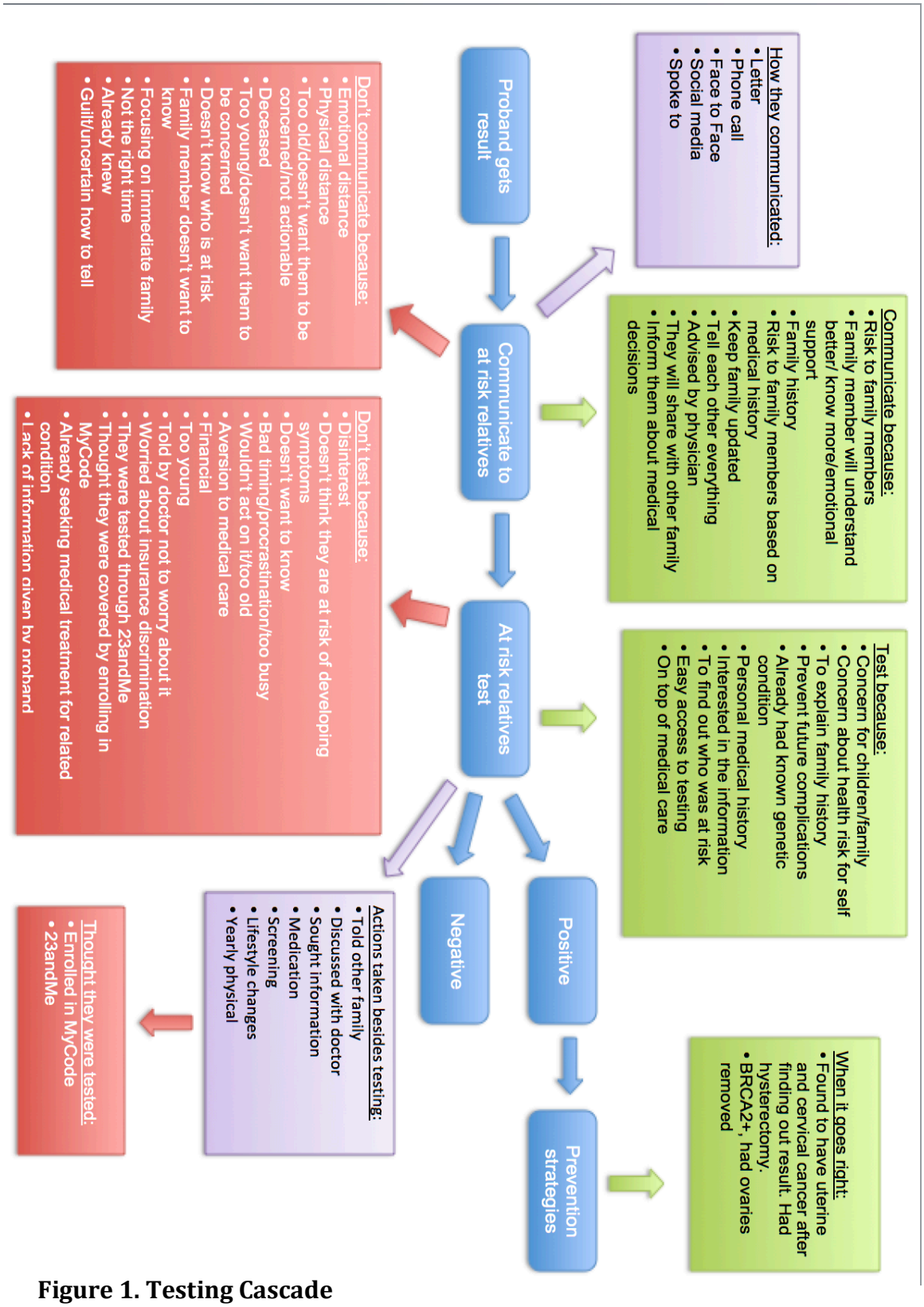

Figure 1. Testing Cascade

When pursuing genetic testing with a patient, there is an expected progression of events that follow to maximize prevention and public health benefit from genetic testing (Schwiter, Rahm, Williams, & Sturm, 2018). It begins when a proband receives a genetic test result and they share that information with their at-risk relatives, who then get tested. For relatives who are positive, preventive strategies can be pursued depending on the condition. Through the analysis of the semi-structured interviews several examples showing how this cascade can succeed emerged. However, barriers and facilitators of the testing cascade became evident at two stages in this expected process: (i) Communicating information to at risk relatives; and (ii) The at risk relatives pursuing testing. Additionally, patient-participants revealed how they communicated the genetic information to their relatives and actions their family members took in lieu of or in addition to cascade testing.

Successful Cascade Testing

When asked about their general experience receiving a MyCode result, participant's stories illustrated this expected cascade testing process. One participant with a positive result for BRCA2 said:

> *"Well, I shared the information with members of my family, and as it turns out, my daughter discovered that she had uterine and cervical cancer, and as a result had a hysterectomy and is now doing well. No further problems. So, in a way, that kind of helped to shine a light on her and get her to do her checkups more diligently."* (F_BRCA2_72_noFHx)

In these successful examples, participants noted that communication of this information came naturally to their family and that the next steps were a clear and obvious choice. When asked if hearing about her mother's BRCA2 results affected her perceptions of herself, one participant mentioned:

"*Not much really. I tested positive. I decided to have my ovaries removed. I did that, and I've gone on to have increased mammograms and an MRI every year, gone to the high-risk breast clinic and found that helpful…"* (F_BRCA2_cascade)

For this participant it seemed "*silly"* not have her ovaries removed considering she was past child-bearing age and knew that ovarian cancer was difficult to screen for. However, interviewees also expressed that for other family members this information was not as easy to handle.

> "*…She, my daughter, kind of freaked out about it. Because I think some of this is going to really more affect her than how it was going to affect me. I thought she would understand it better. Unfortunately, she understood it too well, and she kind of took a little bit of a panic attack on it, but after she went and talked to some of your counselors or genetic research…you know, they gave her some insight, and then she has lined herself up with taking these, whatever types of exams for like mammograms…"* (M_61_noFHx)

Stage 1: Communicating Information to At-Risk Relatives

Facilitators

Risk to relative

One of the reasons expressed as to why interview participants chose to communicate their MyCode results with their family members was because of the risk to their relatives' health. They expressed wanting their relatives to pursue testing or begin screening and surveillance. One interviewee found it "*very very important"* to tell her family so they could get tested as well:

"*…I encouraged my brother and sister to do it so at least we knew, you know, they could be on the watch list to whatever cancers they are prominent to."* (F_45_noFHx)

Interview participants also expressed concern for their children or grandchildren; one interview participant described her communication with her son by saying:

> "*…I stressed the fact that he had a son and that it would be more important for him to find out also in light the fact that medical advances are made every day, that, you*

> *know, this is not something that you need to necessarily be depressed about or upset about, but it would be helpful to know about."* (F_MYBPC3_65_noFHx)

Positive family history of condition

Another reason interview participants expressed why they chose to tell their family members this information was because of their family history. For those who received BRCA1/2 results this was a family history of cancer. For Familial Hypercholesterolemia (FH) results, a history of high cholesterol or heart attacks was the family history reported by participants interviewed who received this result. When speaking to her daughter about her BRCA mutation one woman said,

> *"I gave her all that and literature that I had gotten and impressed upon her because of our family history. My mother had cancer and as a result died from either uterine or cervical cancer…but I think when I got my result, it made me be a little more adamant about her making sure that she did her checkups."* (F_BRCA2_72_noFHx)

While there were interview participants who had a very clear family history of the condition for which they received a result, other interview participants expressed that their results explained a previously ambiguous family history. One participant with strong history of sudden death in his family described how this affected his family by saying:

> *"…so it opened up the whole family to it because there were young deaths in my grandmother's… My grandmother lost 3 of her sons, and one of them died, and they never knew why he died, and then I had a grandmother who was 37, and she died. They said it was stroke, but sometimes I really wonder if it was a stroke and it wasn't that because she was so young."* (F_55_noFHx)

Desire for understanding

Other interview participants said they shared the information with their family members in hopes that those relatives may be able to understand the information better than they could. These participants were looking to their family members to explain the

information to them, either because the family member was in the medical field or was perceived as being more knowledgeable about health information. One participant who reached out to his daughter for information because of her work said:

> *"…When I actually shared it with my daughter, I figured, You know what, she's the one who's gonna be able to tell me a little more about what it means than what I can tell, because that's somewhat in her field."* (61_noFHx)

While this was the reason for the MyCode patient-participant to communicate with his family member, this did not always go over well with the family member being communicated to as this interviewee reported his daughter started "freaking out" about the information.

Other facilitators

Other reasons interviewees noted for why they chose to tell their family members included: the risk to family members based on the family member's medical history, a tendency to keep their family updated on life events, to inform family members about their own medical decision, and in hopes that the relatives they tell will tell other relatives.

Breakdowns

Distance (physical and emotional)

A reason interview participants expressed as to why they chose not to tell certain family members about their genetic results was emotional and/or physical distance. A portion of participants indicated they had never met or had not spoken to some of their relatives in a number of years. Such interview participants described how it would be difficult or even

impossible to contact these relatives because they did not have addresses or phone numbers. One participant left the decision of whether or not to reach out to her paternal cousins to her father:

"He has not spoken to his family because they are not close. So, therefore, they do not speak, you know…So, it is not something he can feel comfortable enough to call and say, hey, guess what." (F_BRCA_Cascade)

"Too old"

Interview participants also reported they chose not to tell certain relatives because they felt certain relatives were too old. They said they did not want to worry these relatives and did not believe the information would be of much "*use"* to them at their age. One participant shared:

"*I find it very unlikely they will get it. I don't know if I'm just wishful thinking, but they're that elderly that I just thought maybe I don't need to share."* (F_BRCA2_55_noFHx)

Other interview participants reported they did not want their parents to be concerned, but noted that because they did not tell their parents, they could not tell which side the mutation came from and therefore chose not tell either side.

"Too young"

Participants interviewed also reported they chose not to tell certain family members, usually children, because they were too young. One participant described her reasoning for not telling her 5 and 6 year old daughters about her test results by saying:

"We haven't gone into any detail with them just because I haven't had, it really hasn't been of importance right now, I don't want them to stress or worry about it right now." (F_BRCA_Cascade)

Unclear about who is at risk

Other interview participants seemed unsure which relatives were at risk. This appeared to be either due to a misunderstanding of the condition or a misunderstanding of genetics and inheritance. One participant found to have a TNNT2 mutation said:

> *"We don't really have heart issues within our family, so I have not been real concerned about that, and actually have not—I told some of the siblings, but I did not pursue sending the letter to everybody…I sent it out to a few of them…The ones that I thought might have some sort of, you know, issue in the future…"*
> (TNNT2_54_noFHx)

When asked why he chose not to tell his son about his BRCA2 mutation, one man said,

> *"…because I really do not know if it's genetic…that's the thing. I don't know if a gene that is in my…from within my family or like I said whether it's chemically induced."*
> (M_BRCA2_62_noFHx)

Other barriers to informing relatives

Other interview participants expressed that it was not the "*right time"* to tell certain family members because of personal or health issues that person was facing; noting they did not want to burden these individuals with information that may add to their stress. Two interview participants mentioned that they did not tell certain relatives because that relative did not want to know if they were at risk. Another reason interview participants expressed was that they were unsure how to go about telling certain relatives, especially ones they were not close with. One interview participant stated that they were focusing on immediate family first and did not want to involve extended family in their business.

Stage 2: Cascade testing of at-risk relative

Facilitators

Concern for children

A reason reported by interview participants why family members decided to pursue genetic testing was because of concern for their children. One participant expressed:

"*I wanted to know and that they could start getting watched if they needed to be, if they had it."* (F_45_noFHx)

Concern for personal health

Individuals interviewed because they had cascade testing expressed having done so out of concern for their own health; stating they wanted to know if they had any major health risks and if they could prevent further health complications. One cascade interview participant, who had a relative receive a result for FH, pursued testing because she had already been diagnosed with high cholesterol. She noted, "*the one thing I'm very much trying to avoid is have open heart surgery."* (F_FH_49_Cascade). Another cascade interview participant, who did not have children, explained that her biggest concern was for her own risk for ovarian cancer after finding out a relative received a result for a BRCA2 mutation.

To explain family history

Interview participants noted their relatives decided to get testing to explain their family history. A participant whose brother died suddenly of a cardiac event explained that his nieces and nephews were:

"*Glad to hear that, you know, they definitely had their hearts checked after that for the cardiomyopathy."* (F_FH_55_noFHx)

He also mentioned that this result gave them some *"closure"* around his brother's death. For another interview participant's family, she stated the BRCA2 result gave some insight into their family history of prostate cancer.

" ...It's a good thing to know and also they let me know that there could be a prostate problem and there are prostate problems in the men in the family, it's just telling us something we already knew." (F_BRCA2_ 55_noFHx)

Other facilitators of cascade testing

Other reasons interview participants reported for why relatives sought out testing were because of their personal medical history, because they were interested in the information, because they wanted to find out who else might be at risk, because they had easy access to testing because of their work, or because they are usually on top of all their medical care. One participant interviewed from a family that had already been through genetic testing for Lynch Syndrome stated that testing for a newly found BRCA2 mutation was important for them rule out any other screening they may need.

Breakdowns

Disinterest

Interview participants reported that their family members who did not want to test were not interested in the information; stating that their relatives *"didn't care"*, or *"weren't interested in getting testing".* Along the same lines, interview participants also reported that their relatives didn't want to know the information for themselves. One interview participant reported his son reacted by saying he:

"...doesn't need to know something to worry about that they can't fix." (M_MYH7_ 51_noFHx)

It's fate/wouldn't change anything

Interview participants also reported relatives who state that when it's *"their time to go"*, they are okay with that and do not believe having this information about themselves would change anything for them.

Relatives believe they're not at risk

Interview participants reported family members who chose not to test because they did not believe that were at a great risk for developing symptoms. One participant described his nephew's attitude towards receiving genetic information that could impact his health as:

"…Yeah I am superman, nothing is going to touch me unless they like it with kryptonite." (M_66_noFHx)

Other interview participants reported experiencing this same reaction from some of their relatives because of age. A participant with a 23 year old son described him as being, *"at the age where he's invincible."* Other participants reporting these reactions stated they believed that these family members might reconsider testing when they get older and lose their child-like sense of invincibility. Interview participants also reported other relatives who believed they were not at risk because they did have other medical issues that they had addressed and so were no longer at risk. One participant summarized why her daughter did not believe the genetic information would be useful to her as:

" Well, I think since my daughter had the hysterectomy, she probably is thinking that there is no, you know, need for any more." (F_BRCA2_72_noFHx)

In this case, because the participant's daughter had a hysterectomy for an unrelated reason and did not think that testing for a BRCA2 mutation would impact her health or management.

Bad timing

Another reason stated by interview participants was that their family was too busy or had *"too much on their plate"* to get testing done at the time the information was disclosed to them. Some of these relatives were in school, had other medical issues, or were just too busy with work and family. One cascade interview participant who had procrastinated cascade testing for herself described her reaction to learning about her aunt's result:

> *"...But like I'm going to all these doctor appointments, all these things are wrong, I just couldn't handle anything else, even though I know I want to go, but I felt like all I'm doing are these appointments, you now, going to the hospital, going to the hospital, going to the hospital...I just felt overwhelmed and I'm like I can't take another thing and just with my osteoporosis, osteopenia and the fibromyalgia how it has knocked me down so much and changed who I was because I was very active and so forth, and just changed my life that I just thought what else could possibly pile up..."* (F_FH_49_Cascade)

While this participant eventually pursued testing, other interview participants did not state that any relatives who gave this reason ever went on to test.

Too old

Participants also reported relatives who said they would not get tested because of their age. These relatives were reported as saying that they were too old and therefore would not act on the information. Some interview participants said they had relatives who believed that if any symptoms were going to present, they would have done so already. When asked about her mother's response to a BRCA2 result one participant said, *"she doesn't want to know because at her age, won't do anything about it anyway."* (F_BRCA2_59_noFHx) Another cascade participant's mother was reported by the interviewee as saying:

> *"Oh I'm not worried about it, I'm not going to get tested, I don't care. You know, I'm going to be 69 years old."* (F_FH_49_Cascade)

Participants who received this response from their family member often expressed they were not pleased and still saw a benefit to those relatives being tested.

Cost

Participants also reported relatives who were concerned about the cost of getting the testing done. One interview participant described her son's reservation by saying,

> *"…He doesn't have a regular doctor, so I think this why he has hesitated and because of the cost of having a blood test done."* (F_MYBPC3_65_noFHx)

Along these lines, several interviewees reported they had family members who were worried that their insurance might not cover the cost of the testing.

Other barriers to cascade testing

Additional reasons reported by interview participants as to why relatives chose not to test included an aversion to medical care in general, they were too young, they worried about insurance discrimination, or they were not given enough information. A few interview participants believed a family member had been correctly tested by other means. For example, one participant's daughter believed she had been tested for her father's PMS2 mutation through 23andMe. Two different interview participants stated that their relatives were also enrolled in MyCode when asked if other relatives had tested for their familial variant.

Additional information gathered

Table 1. How result was communicated to at-risk relatives

Mode of Delivery	Representative Quote
Face to face	*"Well, basically what happened, we all went out to dinner. My brother, sister-in-law, and the 3 kids and we kind of went out to dinner and stuff and I kind of brought up the subject and stuff and was mentioning it to them."* (66_M_FHxNeg_10)
Family sharing letter	*" I gave them the letter and told them to read it 2 or 3 times because that's what it took for me to comprehend it…"* (65_M_FHxNeg_29)
Phone call	*"… she called me on the phone. She gave me the information that she found out, and she gave me the genetics phone number and stuff…"* (FH_neg_F_49_Cascade)

Table 2. Actions reported as taken by family members besides cascade testing

Action	Representative Quote
Told other family	*"… um as far as my aunt, my aunt contacted everybody in the family, and I know some are just still in the process of getting that."* (FH_neg_F_Cascade)
Discussed with doctor	*" My daughter said she would follow up with her doctor, and that's what they all pretty much said."* (65_M_FHxNeg_29)
Screening	*"… whoever she talked to, you know, they gave her some insight, and then she has lined herself up with taking these, whatever type of exams for like mammograms."* (61_M_FHxNeg)
Lifestyle changes	*"… Right now I'm just trying to lose some weight. I'm getting back slowly to exercise."* (FH_neg_F_49_Cascade)
Yearly Physical	*"My son, he did not, and that's sort of based on our counseling as well. He just is going to get regular checkups and keep in mind the things he needs to keep an eye out for."* (BRCA1_61_M_FHxNeg_22)

Discussion

To our knowledge, this is the first study to examine family communication in the context of returning results from a biobank. By analyzing transcripts across multiple projects where biobank participants were interviewed, we found that there are many similarities between family communication of results from a biobank and results from testing based on family or personal history of disease. Additionally, we analyzed interviews from individuals who had cascade testing, which revealed some similarities to the literature, but also illuminated new barriers that will likely become more prevalent as technology advances and genetic testing becomes more widespread. Our findings should be taken into account moving forward when considering ways to overcome barriers to family communication and cascade testing.

The barriers to family communication we identified across these interviews are consistent with what has been reported in the literature for clinically tested populations. We found that physical and/or emotional distance was a common reason for not informing relatives. Participants reported that they had not relayed genetic information to relatives who lived far away because they were not in regular contact with these family members. If they would not contact those family members about other life events, they did not feel like it would be important to contact them about this result. They did not feel comfortable sharing that information with those relatives or did not feel it was important enough to share. This is similar to other studies, which have found that patients have difficulty communicating this type of information to relatives with whom they only have sporadic contact because of emotional or physical distance (Chivers Seymour et al., 2010(Whyte et al., 2016). Others interviewees reported they did not communicate the

information because of logistical reasons like not having a phone number or address for the relative or relatives. Some interview participants reported they chose not to tell relatives because of a rift in the family or general lack of an emotional relationship.

One study noted that emotional ties, rather than a genetic relationship, can have more influence over who participants tell (Chivers Seymour et al., 2010). While we did not ask about this specifically, our analysis of these interviews suggest this holds true for unexpected genetic information as well. Interviewees in data analyzed for this study said that they had shared the information with their spouse, close friends or coworkers, but not with certain family members. Interestingly, in transcripts where the interviewer asked if they would be comfortable allowing the research team to reach out to relatives they were not comfortable contacting on their own, almost all of these interviewees declined. While some of the interviewees reported the logistical reasons mentioned above, others stated they did not feel that they wanted this information shared with those relatives or that it was appropriate for the team to be the ones to share the information.

Two other barriers that we noticed in these transcripts were participants not telling relatives because they are too old or because they do not know who is at risk, which could be encompassed by a broader theme of misunderstanding or miscomprehension of the information by the participant. It appeared to us that participants believed that because of their relative's age, the information was not relevant to them. They either didn't think there would be anything for their older relative to do about it or that if the older relative was unaffected to this point, they would probably remain healthy. This could be attributed to a lack of understanding of the genetic information or risk associated with different genetic mutations, as medically, many of these relatives would still be able

to benefit from the information. Additionally, testing these older relatives gives more insight into other family members who may be at risk. Some participants reported not knowing if extended family members were at risk or thought that only those family members who were already symptomatic were at risk. This finding could indicate a lack of understanding of either the condition or the genetics behind it. This is consistent with other findings that individuals with less comprehension of inheritance patterns are less likely to know who is at risk and less likely to relay the information to their relatives (Batte et al., 2015). Additionally, other studies have found that while the general public perceives their knowledge of genetics to be high, misconceptions are common (Haga et al., 2013; Lanie et al., 2004).

We also found that timing was a barrier for some participants, which has been mentioned in the literature (Chivers Seymour et al., 2010). Across these interviews, participants reported that it was either not the right time for them to tell extended relatives or not the right time for the relative to receive the news. This could have been because they were focusing more on their immediate family at the time, the relative was already dealing with a medical issue, or there had been a recent death in the family. Some participants mentioned that they only speak to certain relatives at big family gatherings, and they did not feel that was an appropriate time to share the information. It is unclear from our data if these participants have real intentions of ever telling these relatives about their genetic test results.

Because we had access to transcripts of interviews with individuals who had pursued cascade testing after a relative receive a MyCode result, we were able to explore cascade individuals and their motivations for testing or not testing. Some barriers to

cascade testing cited in the literature include time commitment, age and education level (Sharaf et al., 2013). Time commitment was a theme that we identified in our transcripts as well. Cascade individuals interviewed and family members of participants put off testing because they had too much going on in their lives with big life events, illnesses, work or school. While some individuals noted bad timing as a reason they or their family member delayed testing, only a small portion could be determined from the transcripts to ever have went on to test when the timing was better. However, this may be a product of when then interviews were conducted, as we do not have extended follow-up with all of the interviewed individuals. Alternatively, these individuals may have no intention of testing and could be using timing as a defense.

Two themes that emerged in our analysis that could be attributed to lack of understanding were at-risk cascade individuals not believing they were at risk or thinking they were too old for testing. Participants' family members who fell into these themes may have a false sense of security because of their age or previous medical history. Some individuals were also reported who seemed to believe they were too young to be affected by any major medical issue. We know that for several of the results returned through MyCode, this is not the case as many have implications for pre-symptomatic individuals (e.g. FH). There were family members reported who believed they were too old to need testing. These individuals were reported as saying that even if they were to be found positive, they wouldn't do anything about it because of their age. While it is possible that these individuals fully understand the risks, it is also possible that they do not completely comprehend what can be done at their age.

One of the themes we identified that has not been previously described in the literature was disinterest in the information. This was often a vague answer given by participants as to why their relatives chose not to test. However, transcripts from some participants were able to give more insight. It is possible that family members who report not being interested because there was nothing they could do about it, it is because they do not believe there is any benefit to them. However, this could also be attributed to an avoidance of medical information in general.

Our analysis of these interview transcripts also included reports of family members who did not pursue genetic testing because they believed that they were already being screened appropriately or had already been tested via one of two different means. There were participants who mentioned that their relatives didn't get tested because they were already getting mammograms, getting their cholesterol checked, or going for annual physicals. This could suggest a lack of understanding about the conditions by the family member, or a lack of information given to the family member by the participant. Many of these variants have increased screening recommendations that individuals are likely unaware of.

There were two transcripts where the interviewee seemed to believe that signing up for MyCode was equivalent to cascade testing for their relative. While, they may eventually receive a result from the MyCode team, this is not the same as familial variant testing. If a MyCode participant is negative, they will never hear from the team and therefore, be unaware of their mutations status. It was explained to MyCode participants who receive a result that their relatives should seek genetic counseling to have appropriate testing and determine if they are positive or negative for the familial variant.

Interestingly, one participant reported a family member had been tested for their familial mutation via 23andMe. For that participant, the relevant gene is one that is not currently included in 23andMe's reports. This finding supports concerns that 23andMe is providing false reassurance to consumers. Particularly, there has been controversy over the addition of BRCA1 and BRCA2 reports to 23andMe as they are only testing for the three most common Ashkenazi Jewish mutations (Gill, Obley, & Prasad, 2018). Consumers who receive a negative test may believe they are negative for all BRCA mutations and not seek out further testing. Additionally, 23andMe has recently added reports for Familial Hypercholesterolemia (FH). However, they are only reporting on 24 variants associated with FH (23andMe, 2019), possibly causing the same problem. Although we only had one individual who reported this misconception, it corroborates the concern with these direct-to-consumer tests.

Access to genetic testing is rapidly growing and with it expands the need for education. It is important that patients and consumers are educated on what the purpose of each kind of testing is and their limitations. Our findings support the idea that patient education has the potential to increase cascade testing outcomes. One of the barriers to family communication revealed in our data was that participants did not know how to tell their family or what to tell them. Additionally, it appeared that a lack of understanding of inheritance patterns led some participants not to tell relatives. Exploring different educational strategies could impact several barriers our study and other studies have observed in family communication and cascade testing. Future studies should assess what educational material and/or techniques are most effective in increasing successful family communication and cascade testing.

One of the limitations of this study is that interview participants were not asked about family structure. Other studies have found that some participants believe it is the job of their parents to tell their aunts and uncles or the job of aunts and uncles to tell their cousins (Chivers Seymour et al., 2010). This could contribute to reasons why participants were less likely to tell extended family. While we did not assess for this, we did notice this as a general finding among our cohort. Additionally, the goal of the interviews as conducted was to assess the breadth of experiences of patients receiving results from biobank. The majority of what we saw was consistent with the literature on family communication, but we may not have illuminated all barriers or facilitators as family communication was not the primary goal of every interview group. Interviews were conducted between two and eighteen months after receiving a result, however, there was no follow up with patient-participants after their interview. For those who had given the reason of timing for not telling certain relatives or certain relatives not being tested, we cannot be certain of the ultimate outcome. There is also the possibility of selection bias because there may be some difference in those who agreed to be interviewed and MyCode participants who received a result but declined to be interviewed for the different projects. Additionally, the interviews collected were purposively sampled in an iterative process as unanswered questions were revealed in each population of interviews. Specifically, it was found that the first 29 interviews all had a family history related to the genetic mutation and so to diversify the sample patient-participants without a family history were purposively selected for interviews after more results were returned and a sample of individuals without relevant family history reported were found. Afterwards, once a group of family members had been seen in clinic for cascade testing, a sample of

cascade tested individuals was available to invite to be interviewed. As such, this is a secondary analysis of interviews conducted over the course of a natural experiment with a subset of Geisinger patients who received MyCode results, which may not be representative of the global population. These results give valuable insight into the barriers to family communication and cascade testing in an unselected population receiving unsolicited genetic information from a biobank, but should not be over generalized.

In summary, we found that family communication of results from a biobank does not differ greatly from family communication of results received after testing based on family or personal history of disease. Additionally, barriers to the uptake of genetic testing by family members were identified. Future research should focus on strategies and techniques for overcoming these family communication as well as cascade testing barriers to increase the overall patient understanding and communication.

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