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ORIGINAL ARTICLE

Assessing patient readiness for personalized genomic medicine

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Abstract

The Human Genome Project and the continuing advances in DNA sequencing technology have ushered in a new era in genomic medicine. Successful translation of genomic medicine into clinical care will require that providers of this information are aware of the level of understanding, attitudes, perceived risks, benefits, and concerns of their patients. We used a mixed methods approach to conduct in-depth interviews with participants in the NCI-funded Breast Cancer Family Registry (BCFR). Our goal was to gain a better understanding of attitudes towards different types and amounts of genomic information, current interest in pursuing genomic testing, and perceived risks and benefits. We interviewed 32 women from the six BCFR sites in the USA, Canada, and Australia. In this sample of women with a personal or family history of breast cancer, we found high acknowledgement of the potential of genetics/genomics to improve their own health and that of their family members through lifestyle changes or alterations in their medical management. Respondents were more familiar with cancer genetics than the genetics of other diseases. Concerns about the testing itself included a potential sense of loss of control over health, feelings of guilt on passing on a mutation to a child, loss of privacy and confidentiality, questions about the test accuracy, and the potential uncertainty of the significance of test results. These data provide important insights into attitudes about the introduction of increasingly complex genetic testing, to inform interventions to prepare individuals for the introduction of this new technology into their clinical care.

Keywords Personalized genomic medicine · Multigene panels · Next-generation sequencing · Breast Cancer Family Registry

Introduction

The successes of the Human Genome Project and the continuing advances in DNA sequencing technology that have decreased the cost of sequencing have ushered in a new era in genomic medicine (Biesecker et al. 2009). The ability to sequence the entire human genome expands our ability to identify the contribution of genetic variation to disease (Dondorp and de Wert 2013). As the understanding of how to utilize this information evolves, genomic medicine holds the promise of using the genome to identify and quantify health threats and determine what interventions (pharmacologic, screening, behavioral) will have the greatest benefit.

Genome-informed medicine has already had a substantial impact on cancer care for many years, allowing individuals to make personal health management decisions based on single-gene tests such as mutation screening for *BRCA1* or *BRCA2*. Now, germline cancer testing has expanded with the recent

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availability of *gene panels*, which evaluate many hereditary cancer genes simultaneously, and even *whole-exome/genome sequencing*, which can assess an individual's entire genome for variants relevant to cancer and other diseases. These scientific advances, however, raise ethical, legal, and social challenges. Many of these challenges, including personal and societal benefits and risks, and privacy and confidentiality concerns, are mirrored in the current professional and public debate about the appropriate utilization of this information in clinical care (Wolf et al. 2015). It is important that the thoughts and opinions of the potential recipients of genomic results, who must consider the risks and benefits to themselves and their families, are sought and taken into consideration.

A successful translation of genomic medicine into clinical care, therefore, will require that providers of this information are aware of the level of understanding, attitudes, perceived risks and benefits, and concerns of the individuals, diverse groups, and communities who will be considering testing. Consumers of health care, however, are often poorly equipped to integrate genomic medicine into their health-related behaviors and decisions or may use the information in unexpected and unintended ways (Haga et al. 2013; McBride et al. 2010; Graves et al. 2015).

To better understand potential consumers' current attitudes and understanding of and interest in different types and amounts of genomic information and to document their perceived risks and benefits, we used a mixed methods approach to conduct in-depth interviews with participants in the NCI-funded Breast Cancer Family Registry (BCFR). As noted by Creswell and Plano Clark (2007), mixed methods focus on "collecting, analyzing, and mixing both quantitative and qualitative data" with a view that using both of these "approaches…provides a better understanding …than either approach alone." For this study, we applied an exploratory mixed methods approach using a triangulation design wherein both qualitative data collection and quantitative data collection occur at the same time. We explored how BCFR participants understand genomic medicine and what changes, opportunities, concerns, and problems they anticipate for themselves and their families as consumers of health care. Combining the qualitative data with the quantitative data allowed us to describe the frequency of the constructs being addressed. This information will help anticipate some of the challenges and opportunities as health care systems attempt to incorporate personalized genomic medicine.

Methods

Setting

The Breast Cancer Family Registry (BCFR) is an international resource of multi-generational families, data, and biospecimens established in 1995 for interdisciplinary collaborative research on breast cancer that is available to the entire scientific community (John et al. 2004). The BCFR sites include four US sites (Cancer Prevention Institute of California, Columbia University, Fox Chase Cancer Center, Huntsman Cancer Institute at the University of Utah), one site in Canada (Sinai Health System, University of Toronto), and one site in Australia (University of Melbourne). The six sites recruited breast cancer families either through incident breast cancer cases identified from population-based cancer registries (population-based case families) or through clinical settings and community outreach (clinic-based families). Participants have provided data and/or biospecimens with the expectation that their contributions will be used for cancer research and have demonstrated their willingness to be followed longitudinally to maintain and enhance this unique resource (Terry et al. 2016). The resource contains extensive data and biospecimens collected for 34,300 individuals from 11,900 families across a wide spectrum of breast cancer risk, including 6345 individuals who have undergone screening for *BRCA1* and *BRCA2* mutations, regardless of test outcome. The BCFR families represent a diverse racial/ethnic mix, including Caucasian, African American, Asian American, and Hispanic families.

Patient population, recruitment, and data collection

Eligible participants were women enrolled in the BCFR who were between the ages of 30 and 65 years and who spoke English. This age range represents ages when women are most likely to pursue genetic testing, to use the information to alter their screening regimens, and/or to consider prophylactic surgeries. Only one person per family was recruited for this study. Stratified purposeful sampling was used to ensure the inclusion of participants who vary on pre-selected characteristics that are thought to be important in understanding how the risks and benefits of genomic medicine are understood and how it will be used by consumers. The pre-selected variables were as follows: (1) age, (2) *BRCA1* and *BRCA2* mutation testing status, and (3) breast cancer status (affected vs. unaffected). A random sample of 20 women from each site who met eligibility criteria was selected. They were contacted by letter, phone, or email by BCFR staff at each site to invite their participation in this study. Those who expressed interest were sent a consent form to complete and return. Less than 10% of women declined participation. The main reason for not participating was that participants had not yet responded to the study team by the time recruitment at each site was complete. Once the signed consent form was received, each participant was contacted to schedule an interview. This process was continued with a plan to interview a total of approximately 42 (seven from each site) to reach saturation. We interviewed 32 women: three from Australia, seven from California, seven from Ontario, one from New York, seven from Philadelphia,

and seven from Utah. Although we did not reach seven interviewees per site, we found that we reached saturation of the themes by interviewing 26. We interviewed additional participants to be sure that no new information emerged from further interviews. Institutional Review Board approval was obtained at each site for this study. The interviews were all conducted from the Utah site.

The interviewers were two female Master of Social Work research trained assistants. These two interviewers were trained by one of the researchers (CJF), and two of the researchers (MBD, CJF) reviewed four of the interviews with the assistants as they moved through the interview process. The researchers were available to answer questions and identify solutions to any interview issues that arose. The study began in 2013 and was completed in 2014.

Content of the semi-structured interviews (see supplemental materials)

Each interview began with a general overview of the interview topic and an explanation of the aims of the study. The first set of questions was formatted as Likert items to quantify the interviewees' level of familiarity with the role of genetics in disease, their level of interest in learning more about their own genetic risks, the level of importance they assign to genetic risk information, and their perceived risks and benefits of genetic risk information.

The qualitative questions that followed were divided into questions about *cancer gene panels* and questions about *whole genome sequencing*. The interviewer prefaced each section by a description of the type of test and some possible advantages and disadvantages to the test. The open-ended questions that followed inquired about the following: level of interest in each type of genetic test, what factors would influence a decision to undergo the particular test, which components of the test results would be considered most important, how the test results would be used, and the perceived risks and benefits of having one of these tests. Finally, another set of Likert questions was used to quantify perceived advantages and disadvantages of each type of test and to measure intention, anticipated behavioral reactions to test results and perceived behavioral control. The average interview was 31 min, with a range between 24 and 55 min.

Data analysis

All interviews were completed by telephone, recorded using a digital voice recorder, and transcribed. We summarized the Likert scale data using percent response to each Likert category. For the qualitative data, we used the constant comparison method during the interview process, wherein the data are reviewed and compared to one another throughout the interview timeframe (Creswell 2013). Four of the authors (MBD, CJF, KC, EG) co-reviewed and co-coded the transcripts. Open and focused coding were used to analyze the data collected in these interviews. Coding was structured through three basic procedures. First, the researchers recognized the participants' understanding of genomic medicine and how it might be useful for them, from the qualitative data. Second, the researchers collected examples of those phenomena. Third, the researchers analyzed those phenomena in order to find commonalities, differences, patterns, and structures (Esterberg 2002; Shiloh et al. 2009). The coding process organized large amounts of text data into content areas. Once we completed open coding, we conducted focused coding wherein we read through the data again emphasizing the patterns and themes identified by the open coding. We selected the top themes and memoed (wrote down concrete ideas about the information from the transcripts) around these themes. The wealth of information from these processes provided us with the phenomena, examples of the phenomena, and links to patterns that were needed to address our study aims. In the interpretation of the data, these categories and themes were explored for relationships and relevance to the proposed domains of genomic medicine. The investigative team explored the text data in terms of how it fit with what we know from professional and clinical experiences about the process of coping with new genetic risk information and how the data can inform future studies.

Sample size consideration

We chose the sample size to have sufficient power to detect themes that were common across many participants. Themes that were mentioned by over 40% of participants were of particular interest, while themes that were mentioned by fewer than 15% of the participants were of lower interest. Thirty-two participants provide 88% power to detect themes that are of concern to at least 40% of the participants. Under a null proportion of 15%, this has a type I error (one-sided) of 0.0156 (< 2%). Under this design, a theme was of high interest if it was mentioned by more than 13 participants. We set the type I error to a low level to account for the fact that we examined multiple themes in the study, and thus, we minimized the number of false positives. Power was calculated assuming an exact binomial test (Agresti 2002).

Demographics of sample population=

The mean age of the women in this sample was 52 years and ranged from 30 to 65 years. Sixty-nine percent of the women were diagnosed with breast cancer, and 31% were unaffected; 54% had undergone genetic testing for *BRCA1/2*, and 46% had not.

Results

Qualitative data

We identified ten overarching themes from the interview data. These themes were (1) impact of genetics on disease development, (2) impact of personal experiences with cancer, (3) perceived benefits of gene panel testing, (4) uses of genomic information in making health decisions, (5) concern about the use of genomic information, (6) interest in specific genomic information, (7) characteristics of genomic information, (8) issues of privacy and confidentiality, (9) concerns about pursing testing, and (10) need for professional help in understanding tests. For each theme, quotes are provided that exemplify how the participants framed the discussion about these concepts. Breast cancer status is indicated by BrCA+ or BrCA−. The information from the participants highlights overlapping ideas about genetic information for participants and thus are not quite as discrete a set of concepts as they might appear. Participants' statements connecting to these themes are discussed below.

1. Impact of genetics on disease development. Participants were asked how genetics impacted the development of disease and what the role of genetics is in cancer development. Overall, there appeared to be an appreciation of the role of genetics in the development of cancer and other diseases and a general enthusiasm for the concept of gene panels which include many diseases in addition to cancers.

> I just think it is important to see what is going on to help you make the decisions you need in your life. With all the different diseases, cancer, diabetes and epilepsy it would be really nice to learn the answers if there are genetic answers. This is to help prevention and care.(UT1, BrCa−)

> It's in the beginning stages, and being part of that helps to develop knowledge that in the future will be more positive to people, somebody else so many years down the road.(PA4, BrCa+)

> I still think it's a good idea to move forward with it. The health care provider or the person administrating the test, making sure that all of that is clearly explained… I think it would be helpful at the time of the test to know that the results may not necessarily mean a whole lot for the immediate future. (CA1, BrCa−)

2. Impact of personal experiences with cancer. Participants often cited a personal experience with cancer or other diseases, either in themselves or in other family members, as a strong motivator for interest in genomic testing.

> I think it would help just with the cancer that's in my family. Not so much for me but children and grandchildren. (ON6, BrCa−)

> …we are cancer ridden in our family so you know we are talking 3 generations so if there is something that can be a trigger that we can find out through these generations then that could only help the next generation.(AU3, BrCa−)

> Because I have cancer in my family so I would want to know if I carry the genes that would also give me cancer or whether I just have the same level of risk as the average person in the general population. (ON2, BrCa−)

> …my dad had lung cancer and I had breast cancer. So I would be interested in knowing about all …of the results and all the information it provides. (PA6, BrCa+)

> Because I have already had cancer and have been known to have the BRCA1 gene. My sister was also tested for the BRCA1 gene but thank God, has not had cancer. And so the panel may be able to give us some distinguishing factors as to what would make one more at risk that the other even with a single mutation. (PA3, BrCa+)

> I ended up with breast cancer. I am BRCA2 positive. Is this the only factor that played into that? I would like to know if anything else was present and what may or may not have been able to be done about that. And that could have an impact on my own children down the road. (UT2, BrCa+)

> I have a brother who died as a diabetic not too long ago. If we were more knowledgeable in how strong it is in our genes, maybe we'll take steps to be more in tune to what's around us. (CA4, BrCa−)

3. Perceived benefits of gene panel testing. Participants were asked about their perception of the potential benefits that panels including multiple genes would provide, both for themselves and for their family. General benefits to the individual revolved around the concept of improving their knowledge base for the purpose of improving their health.

If I had more knowledge about it, I would be more in tune to raise my children and how I value the disease. If we were more knowledgeable in how strong it is in our genes, maybe we'll take steps to be more in tune to what's around us. (PA4, BrCa+)

Because I think the knowledge of knowing far outweighs the knowledge of not knowing. I think it would give some benefits that I can change my lifestyle or – it would help me in some way, the more information that I have. (CA1, BrCa−)

An increased conscientiousness about overall health and making healthy choices. …awareness allows you to keep an eye on your own personal health better and keep an eye out for possible symptoms that might otherwise go unnoticed. So that you can be treated earlier, which increases the possibility of a cure. (UT2, BrCa+)

It just gives you a good game plan moving forward. It would not change anything but it would give you at least a little bit of your history, so if anything does pop up you would have an idea of what it could be or where to go from there. (UT4, BrCa−)

I think having some ability to anticipate potential problems more accurately with the ability to plan for it. (PA1, BrCa−)

Well they would know how to better help themselves with better health in regards to high blood pressure heart problems that their dad has and to learn to, you know, eat properly, exercise properly and just lead a good life. (ON4, BrCa+).

They would have more control. They can decide if they want to start some type of regimen plan because they would have more information. (CA2, BrCa−)

I think the more information that you have, even if it's hasn't been studied out, I think that'll still benefit you, still benefit the family. Sometimes it might not benefit that particular person, like it might not benefit me, but later down the line it can benefit my family. (CA1, BrCa−)

4. Use of genomic information in making health decisions. Participants were asked how their genomic information would be used in decision-making about their health behaviors. One of the benefits offered by many of the participants was the opportunity to make lifestyle changes that would impact the risk conferred by the test findings. There was a sense that genomic risk knowledge would provide a mechanism to have some control over their health.

I think if we knew we had weaknesses in genes in certain areas that there is maybe something that we could investigate and kind of take control of our life. And go okay, this is something that if we are not careful and watching about we can help it along in a negative way, or maybe we can alter our habits and lifestyle choices and kind of give us a fighting chance. (UT3, BrCa−)

The most important benefit would be the knowledge to make the decisions that I need to make, the knowledge that would help me to make better decisions for my quality of life. If I find out I got something bad, that would alter my future, I would alter some plans. (CA1, BrCa−)

If you know we are more susceptible to a type of cancer you know you would take a little more control of your surroundings, your lifestyle and your habits. (ON6, BrCa−)

I think we are like computers with our genetic makeup. I think we have so little control over who we are because I feel like our genes mean so much, so if we can map out our genes, I would love that. (ON7, BrCa7)

I would use it to structure my life. That way I can gain help, be it nutrition, physical exercise, medications or whatever is needed to keep me from getting that disease. (UT1, BrCa−)

I would take the options for early treatment more seriously if I knew I had a genetic predisposition for a specific disease. (ON2, BrCa−)

5. Concern about the use of genomic information. However, some participants expressed concern about their ability to utilize genomic data to control their fate and some uncertainty about the actual value of the test results.

It does not matter what you do in your lifestyle because you are going to get it anyway….There are some cancers that if it has your number it is going to get you no matter what. (UT4, BrCa−)

I think if there are things that would be improved by lifestyle changes, that would allow me some-a little more sense of control, but if there are not, then I think that they might add to the sense of lack of control. (PA1, BrCa−)

I guess my level of worry that I would be told something is indicated in your genetic makeup and is going to develop something horrible, nothing can be done about it. And so I would be just sitting and waiting. (ON1, BrCa+)

I would probably have a breakdown. I am such a worrier, no I would absolutely not want to be told [about the information on the gene test]. (ON1, BrCa+)

That's the thing if there is nothing I can do don't tell me. If there is something I can do then I will turn my life upside down, but if there is nothing I can do then sometimes ignorance is bliss. (AU3, BrCa−)

I am concerned that with understanding our genes and what we are potentially at risk for could cause us to be so hyper concerned that we do not live a normal life… and we freak out and do things that are not necessary to prevent a disease that we may or may not actually get just because it is a possibility. (UT7, BrCa+)

6. Interest in specific genomic information. Despite general enthusiasm for the use of both multi-gene panels and a whole genome testing, when participants were asked more specifically about which information would be useful to them, there was more interest in learning about the diseases which have occurred in their family, although some expressed interest in any gene.

I think a focus on cancers that have been present [in the family] makes more sense than just any cancer at all. It might not be meaningful to look at any type of cancer in my own family situation if certain cancers have never presented themselves. (UT2, BrCa+)

If they wanted to say genetic testing for Parkinson's and no, it doesn't run in my family, no I wouldn't waste any bodies' time, but all the illnesses that my husband and I have yes, I would be very interested. (ON4, BrCa+)

Cancers that we had in the family would be higher priority, but I would want to know about all cancers. (ON2, BrCa−)

I guess if there was a family history of something that was debilitating or something that could be prevented if you knew ahead of time based on your family's genetic generations. I think that would be when I would want something done like that. (UT7, BrCa+)

7. Characteristics of genomic information. Other participants based their level of interest on the severity of the diseases, their level of risk, and their ability to alter their risk associated with the information provided by the panels.

For me personally, if the risk was in that 30-50 % range or higher, definitely I think it would be valuable to know. (UT2, BtCa+)

If there is a 50% chance or more, it would be something that I would be more interested in. If it came back and I had a 10% risk for lung cancer, I do not know if that is necessarily information that would be as helpful for me. (UT6, BrCa−)

I guess depends on what the diseases are, because like you said, if they are untreatable diseases, they might be a little bit better not to know than to feel a sense of hopelessness.(UT4, BrCa−)

I'd consider the most important benefit is the fact that I would know if I was at risk for some other diseases other than cancer on the other testing that they'll do. (PA3, BrCa3)

Test results that I can do something about I would want to know. If it were something I could not do anything about I would not want to know. (ON1, BrCa+)

If the risk is low, then I would take that into account, but still use it to try to reduce the risk and easy ways of my lifestyle. If it was uncertain I probably would not rely upon the results at all and not make any changes in my lifestyle. (ON2, BrCa−)

Whether it's risky or whether you're low risk or high risk or whatever; I think having the information really outweighs the not knowing or closing your eyes and sticking your head in the sand. (CA7, BrCa−)

8. Issues of privacy and confidentiality. Participants were generally aware of the issues of privacy and confidentiality associated with genetic information.

I wouldn't have concerns about my privacy or confidentiality because I would have that in place before. I would understand what the guidelines are for that before I would get into the test. (CA7, BrCa−)

I would be interested in privacy systems that are in place with regard to sharing the information obtained about myself. (UT 2, BrCa+)

I do have some concerns on privacy and confidentiality specifically as it relates to being insurable and information being made available to people who might have a financial interest in my health. (PA1, BrCa−)

I do have some concerns about whether I would be able to afford to seek treatment based on test results, particularly with the insurance system that we have. (PA1, BrCa−)

Everything is supposed to be under confidentiality. But I know records get out there. (UT7, BrCa+)

I would be concerned that it could either be used to discriminate against folks that have certain predisposition or that it could potentially be a financial burden because there would be some…applied insurance cost based on a person's genetic makeup. (PA2, BrCa−)

9. Concerns about pursuing testing. Participants were asked about their concerns about the practical aspects of obtaining genomic tests.

It's the money, the price. To me, it's definitely worth knowing, but is it something that would – could I fit in my budget? That's a big factor. (CA1, BrCa−)

Well I would have to know what it entails, number one. I mean I don't know if you have to spend the day in the hospital or if you have to travel. It would depend on the logistics of it. (CA7, BrCa−)

Cost, insurance, I guess another thing that would really bother me is the time. Waiting between a test and getting results. If it is going to be done, I do not want to be in limbo. (UT3, BrCa−)

First of all, I just would not even know where to go to get one done. And second, the cost. I am not sure what the cost would be. And insurance probably would not pay for those at this point. And so just the difficulty of just hassle and cost. (UT7, BrCa+)

"I'd want to know where the test came from, who's administering it, and who is interpreting it and what their qualifications are,…I'd want to make sure that the person who developed the test and are administrating it have some credibility." (PA1, BrCa−)

I think the certainty is somewhat important, if it's sort of 75% accurate and helpful, but if it's 25% accurate then it is not very helpful. (ON2, BrCa−)

10. Need for professional help. Many participants expressed the need for professional help in understanding the meaning of the tests.

…genetic counseling is really helpful. I spoke with a genetic counselor on several occasions and I think that is an essential part. Cause everybody is going to handle it differently. (UT2, BrCa+)

I think that is where the people designing these tests need to make sure that things are in place to help people understand. Understand what the numbers mean, understand what to do about it. (UT2, BrCa+)

I would want to talk to someone who could interpret the test results and could explain to me what the issues were. I would not want to do it myself. (ON2, BrCa−)

I think having someone very clearly explain the reasons why and how it would be beneficial and also the reasons why not and why you really do not need it. (UT7, BrCa+)

Results of the quantitative data

The quantitative data is complementary to the themes which emerged from the interview data and provided an estimate of the frequency of each construct (Table 1).

Table 1 Percent distribution of responses to Likert questions

1. How familiar are you with the role of genetics in causing diseases like cancer?		
Very familiar or somewhat familiar, 94%	Not very familiar or definitely not familiar, 6%	Not sure, 0%
2. How familiar are you with the role of genetics in causing diseases other than cancer?		
Very familiar or somewhat familiar, 81%	Not very familiar or definitely not familiar, 16%	Not sure, 3%
3. How interested are you to learn about what genetic abnormalities might put you at increased risk for cancer?		
Very interested or somewhat interested, 100%	Not very interested or definitely not interested, 0%	Not sure, 0%
4. How interested are you to learn about what genetic abnormalities might put you at increased risk for diseases other than cancer?		
Very interested or somewhat interested, 88%	Not very interested or definitely not interested, 3%	Not sure, 9%
5. How important do you think your genetic risks for cancer are for your family members?		
Very important or somewhat important, 97%	Not very important or not important at all, 0%	Not sure, 3%
6. How important do you think your genetic risks for diseases other than cancer are for your family members?		
Very important or somewhat important, 91%	Not very important or not important at all, 0%	Not sure, 9%
7. Do you think that learning more about your genes would improve your sense of control of your health?		
Very much or somewhat, 90%	Not very much or not at all, 3%	Not sure, 6%
8. Do you think that learning more about your genes would leave you feeling hopeless: that you could not control your future health?		
Very much or somewhat, 31%	Not very much or not at all, 53%	Not sure, 16%
9. Do you think that learning more about your genes would improve your health?		
Very much or somewhat, 91%	Not very much or not at all, 3%	Not sure, 6%
10. Would knowing more about your genes benefit your family?		
Very much or somewhat, 97%	Not very much or not at all, 0%	Not sure, 3%
11. Would you feel guilty about the possibility of passing a genetic mutation onto your child?		
Very much or somewhat, 56%	Not very much or not at all, 31%	Not sure, 13%
12. How would you weigh the advantages and disadvantages to you of having a *gene panel* test?		
Disadvantages outweigh advantages greatly or disadvantages outweigh advantages somewhat, 16%	Disadvantages and advantages are the same, 16%	Advantages outweigh disadvantages somewhat or advantages outweigh disadvantages greatly, 68%
13. How would you weigh the advantages and disadvantages to you of having a test that looks at all of your genes? (Full gene panel)		
Disadvantages outweigh advantages greatly or disadvantages outweigh advantages somewhat, 25%	Disadvantages and advantages are the same, 19%	Advantages outweigh disadvantages somewhat or advantages outweigh disadvantages greatly, 56%
14. I plan to have a gene panel in the next year/12 months.		
Extremely unlikely or moderately unlikely or a little unlikely, 34%	A little likely or moderately likely or extremely likely, 53%	Neither unlikely nor likely, 13%
15. How likely or unlikely is it that you will have a gene panel test in the next year/12 months?		
Extremely unlikely or moderately unlikely or a little unlikely, 41%	A little likely or moderately likely or extremely likely, 53%	Neither unlikely nor likely, 6%
16. For me to have a gene panel test in the next year/12 months is:		
Extremely difficult or moderately difficult or a little difficult, 28%	A little easy or moderately easy or extremely easy, 47%	Neither difficult nor easy, 25%
17. I plan to have a *full* gene panel test in the next year/12 months.		
Extremely unlikely or moderately unlikely or a little unlikely, 50%	A little likely or moderately likely or extremely likely, 38%	Neither unlikely nor likely, 12%
18. How likely or unlikely is it that you will have a full gene panel test in the next year/12 months?		
Extremely unlikely or moderately unlikely or a little unlikely, 53%	A little likely or moderately likely or extremely likely, 38%	Neither unlikely nor likely, 9%
19. For me to have a full gene panel test in the next year/12 months is:		
Extremely difficult or moderately difficult or a little difficult, 47%	A little easy or moderately easy or extremely easy, 28%	Neither difficult nor easy, 25%

Level of familiarity with and interest in genetics was high in this sample, with slightly more familiarity and interest in cancer genetics than in genetics related to other diseases.

The vast majority (94%) reported being very or somewhat familiar with the role of genetics in causing cancer. Participants were slightly less familiar with the role of genetics in causing diseases other than cancer (81% very or somewhat familiar).

All (100%) expressed interest in learning about genetic abnormalities that would put them at increased risk of cancer. Interest in learning about genetic abnormalities that would put them at risk for other diseases was slightly lower at 88%.

The acknowledgement of the importance of genetic risks for cancer and other diseases for family members was high.

The vast majority (97%) thought that genetic risk for cancer was important for their family, and 91% thought that genetic risk for other diseases was important for their family.

Overall, the impact of knowing more about their genes was positive, but some concerns were identified.

The vast majority (90%) reported that learning more about their genes would improve their sense of control over their health and would improve their health. An even higher percentage (97%) felt that knowing more about their genes would benefit their family.

On the other hand, 31% felt that knowing more about their genes would leave them feeling hopeless about control over their future health, and over half (56%) believed that they would feel guilty about the possibility of passing on a genetic mutation to their child.

The advantages of having genetic information outweighed the disadvantages; however, there was a substantial subset of women who felt negatively about having genetic testing, especially for whole genome sequencing.

Most (68%) participants felt that the advantages of having genetic cancer panel testing outweighed the disadvantages; however, 16% felt that the disadvantages outweighed the advantages. When asked about whole genome sequencing, a higher percentage (25%) felt that the disadvantages outweighed the advantages.

Likelihood of having genetic testing was variable. Likelihood was higher for a cancer gene panel than for whole genome sequencing.

When asked about intention to have a cancer gene panel test in the next year, 53% of participants reported that it was likely that they would plan to have a cancer gene panel test; 34% said that it was unlikely that they would plan to have a gene panel test, and 13% were unsure. When asked about the likelihood of actually having a cancer gene panel test, the same percentage (53%) said that it was likely, and more (43%) said that it was unlikely. Only 6% were unsure. Similarly, 47% felt that having a cancer gene panel test in the next year was easy, while 28% felt it would be difficult, suggesting that there are potential barriers to pursuing testing. Intention to and likelihood of having whole genome sequencing was lower (38%), as was the anticipated ease of having whole genome sequencing (28%).

Discussion

We have applied a mixed methods approach to understanding changing or novel health-related issues because of its ability to delve deeply into the thought processes underlying beliefs about the issues and to gain insight into the frequency of those beliefs. From this sample of women with a personal or family history of breast cancer, we found interest in and acknowledgement of the potential of genetics/genomics to improve their own health and that of their family members through lifestyle changes or alterations in their prevention or medical management. Concern about the next generation was a common theme. Respondents were somewhat more familiar with cancer genetics than the genetics of other diseases, which most likely reflects their own experience with cancer and the degree of media attention directed to this area. Actionability has emerged as an important consideration in placing value on the personal use of genomic information. Our data support this concept as a theoretical motivation for behavior change. Our participants expressed the intention to alter lifestyle factors based on genomic information. They also perceived that the genomic information would benefit other family members. Concerns about the testing itself included a potential sense of loss of control over health, feelings of guilt on passing on a mutation to a child, loss of privacy and confidentiality, questions about the test accuracy, and the potential uncertainty of the significance of test

results. The concepts expressed by the interviewees in the qualitative portion of the survey were similar in affected and unaffected women. However, given the constraints of qualitative data and the small sample size, no definitive conclusions can be reached about the impact of cancer status.

Over 90% of participants in this small sample linked better knowledge of their genetic risks to the ability to improve control over their health. On the other hand, there was a minority of participants who expressed concern about a perceived inevitability of genetic risk and the possibility that knowledge of their genetic risk may lead to a feeling of anxiety, a sense of hopelessness, and a feeling of guilt about having passed on a genetic risk to their offspring. In this regard, several participants were aware of the benefit of and need for professional help in understanding the genetic information and counseling to allow them to address and manage their concerns and areas of potential distress. Practical aspects of the testing process, including type of test, type of biospecimen, amount of travel involved, and cost all emerged from the interviews as important considerations.

Despite a high level of interest in genetic information and anticipation of benefit from having this information, responses to questions about specific scenarios revealed that participants made several distinctions about the kind of information they would want to receive. Participants' personal experiences with cancer and other diseases informed their choice of testing. This suggests that an approach which allowed for customized gene panels, depending on the individual's level of interest, might be responsive to their perceived needs. They expressed interest in specific domains of genomic risk, including as follows: the magnitude of risk associated with a genomic finding, the severity of the disease, and the potential for prevention or treatment. Personal intention and concrete plans to have a genetic test, on the other hand, reflected substantial skepticism. These findings suggest that there clearly are nuances in the individual perceptions of personal benefit and risk, and significant gaps in understanding of often abstract genomic concepts. More intensive efforts to educate and counsel potential candidates for testing, as well as practical information about the cost and logistics of testing, will be needed. Intention to have a cancer gene panel test was higher than that for whole genome sequencing which may reflect less familiarity with the latter or a more focused interest in the diseases experienced in their family.

What can we learn from these data?

Before realizing the benefits of personalized genomics, it is important to understand public perceptions of genomic medicine, anticipated patterns of utilization, preferences for genetic testing, and potential public health benefits (Phillips et al. 2008). Several qualitative studies indicate that there is a general anticipation of benefit from the receipt of actionable information about personal risk (Wright et al. 2014; Hitch et al. 2014; Seo et al. 2016). Our data are consistent with these findings, but also suggest that in reality, individuals vary in the specific conditions regarding what information they want and how they want to receive it.

Genetic information is complicated, and the growing availability of increasingly complex testing options challenges clinicians' ability to translate the genomic findings into practice. As next-generation sequencing moves from large academic centers to the community health care setting serving populations of diverse ages, health experiences, educational levels, and cultural heritages, health care providers will be called upon to inform their patients about the use of genomics in multiple health contexts (Lea et al. 2010). A challenge will be to present complex information in simple and familiar ways that match the health needs of individuals and communities (Lubitz et al. 2007). The National Human Genome Research Institute has called for research to evaluate the impact of personalized genomic information on behavior change (McBride et al. 2010). Consistent with this and other literature, the findings of this study clearly illustrate the need for genomic information to be relevant to health behaviors that can alter risk and thus provide individuals greater control over their health. We found considerable variation in attitudes towards the usefulness of genomic information, particularly with regard to their usefulness in guiding lifestyle behaviors, in the ability to cope with potentially negative information, in concerns about privacy and confidentiality, and in uncertainly about the practical logistics of being tested. Concerns expressed about the negative consequences of genomic information indicate a need to assure the protection of individuals' privacy, confidentiality, and emotional well-being, while efforts to extend societal benefits of genomic information continue.

Perhaps, one of the most enlightening findings of this study is the contrast between high levels of overall interest in and support of genomic testing and the significantly lower levels of individual intention to pursue it. This finding may in part be a function of the expressed uncertainty regarding practical considerations about having access to testing, but may also reflect an incomplete knowledge of the utility of genomic information. The contrasting opinions about several of the issues related to the usefulness of genomic information suggests that differences in attitudes may vary by a variety of factors such as age, race/ethnicity, or cultural values.

Strengths and limitations

These data provide important insights into current attitudes about the recent introduction of next-generation sequencing technologies which can inform personalized models to prepare individuals for the inevitable introduction of this new

genomic information into their clinical care. Participants in this study are women with a personal and/or family history of cancer. They have a relatively high level of general knowledge about genetic risk and interest in knowing more about genetic risk for themselves and their family members, and thus may not be representative of the public in general and may limit the generalizability of the findings. The sample did not include men, who may have a different view of genomic data. Ultimately, the power of genomic medicine to improve health will only be realized when it is accessible to all.

Next steps

The effective translation of genomic medicine "to the bedside" depends on an educated public that understands the benefits and risks of genomic data, and also has the ability to use the information appropriately. Currently, the expectations for the benefit of genomic medicine are high, both within the medical profession and among the lay public. A next step is the recognition that acceptance of this new technology will be subject to the beliefs and values of individual groups that make up our communities (Cornwall et al. 2014). In order to address individual preferences, it is becoming clear that there is a need to better understand the unique needs of personal, social, and cultural groups to guide clinical decisions. The results of this pilot study have informed the development of a survey instrument that is being administered to the entire BCFR Cohort to enable researchers to expand our understanding of similarities and differences in the potential application of genomic medicine to groups differing in age, education level, race/ethnicity, geography, cancer status, and prior genetic testing experience.

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Compliance with ethical standards

Conflict of interest All the authors declare they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

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