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Improving Health Education for Women Who Carry an *FMR1* Premutation

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Abstract

Women who carry an *FMR1* (i.e., fragile X) premutation have specific health risks over their lifetime. However, little is known about their experience understanding these risks and navigating their health needs. The aim of this study was to use qualitative analysis to uncover both barriers and facilitators to personal healthcare using a framework of the Health Belief Model. Five focus groups were conducted with a total of 20 women who carry the *FMR1* premutation using a semi-structured discussion guide. All sessions were transcribed verbatim and independently coded by two researchers. The coders used a deductive – inductive approach to determine the prominent themes related to the participants' experiences seeking healthcare for premutation-related conditions. Salient barriers to personal healthcare included difficult clinical translation of research findings, lack of knowledge among healthcare providers and among the women themselves, different priorities, and shortage of premutation-specific support and targeted educational materials. Facilitators included family members, national and community support organizations, research studies, compassionate physicians, and other premutation carriers. Addressing barriers to personal healthcare through up-to-date educational materials can help diminish misperceptions regarding health risks. Targeted educational materials will aid in information sharing and awareness for women who carry the *FMR1* premutation and their physicians.

Keywords

Fragile X associated disorders; *FMR1* premutation; Barriers; Facilitators; Focus groups; Health education; Educational materials; Health Belief Model; Qualitative analysis

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Conflict of Interest Whitney Espinel, Krista Charen, Lillie Huddleston, Jeannie Visootsak, and Stephanie Sherman declare that they have no additional conflict of interest.

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Animal Studies No animal studies were carried out by the authors for this article.

Introduction

Fragile X syndrome (FXS) is an inherited X-linked condition characterized by intellectual disability with a range of cognitive and behavioral deficits. Over 95 % of FXS cases are caused by an expanded, methylated CGG repeat (above 200) in the 5' untranslated region of the *FMR1* gene (Verkerk et al. 1991). Alleles with CGG repeats between 55 and 199 have the ability to expand to the full mutation in one generation and have been termed premutations (Fu et al. 1991). It is estimated that at least 1 in 260 women are carriers of an *FMR1* (i.e., fragile X) premutation, and potentially as many as 1 in 150 may be carriers (Cronister et al. 2008; Hantash et al. 2011). Women who carry the *FMR1* premutation by definition have a significantly increased chance of passing on an expansion of over 200 repeats and having a child affected by FXS (up to 50 % risk for FXS in her sons; less for daughters due to X inactivation) (Nolin et al. 2003). In addition to reproductive implications, *FMR1* premutations have specific repercussions for women's health.

One clinically significant risk associated with the *FMR1* premutation in women is for fragile X-associated primary ovarian insufficiency (FXPOI). Approximately 20–25 % of carriers will develop premature ovarian failure (POF), or cessation of menses prior to age 40 compared to 1 % of the general population (Sherman 2000; Wittenberger et al. 2007). FXPOI can manifest in a spectrum of symptoms related to early onset ovarian changes and may present distinct challenges according to stage of life (Allen et al. 2007; Rohr et al. 2008; Sullivan et al. 2005; Welt et al. 2004; Wheeler et al. 2014). Early concerns focus on family planning and decreased fertility, while later concerns shift to medical conditions associated with early estrogen deficiency, such as osteoporosis, cardiovascular health and the associated treatments (i.e., hormone replacement therapy options). Across all stages of life, women may struggle with psychological health, as research has shown that *FMR1* premutation carriers are at an increased risk for developing symptoms of depression, anxiety, ADHD, or social phobias (Hunter et al. 2012a; Hunter et al. 2012b; Kenna et al. 2013).

In addition to symptoms related to a low ovarian reserve, women who carry an *FMR1* premutation have an 8–17 % chance of developing fragile X-associated tremor/ataxia syndrome (FXTAS) in their lifetime. FXTAS can present with an array of symptoms that include progressive gait ataxia, tremor, Parkinsonism, and executive function deficits (Hagerman et al. 2004; Rodriguez-Revengea et al. 2009). Recent studies suggest that women may have different manifestations of FXTAS as compared to males, with higher presentation of muscle pain, thyroid problems, hypertension, neuropathy, seizures, deficits in cognitive functioning, or fibromyalgia (Coffey et al. 2008; Hagerman and Hagerman 2013; Hall et al. 2014; Wheeler et al. 2014). Differences in symptom manifestation may also include older age of onset and milder phenotypic expression as compared to males (Grigsby et al. 2008; Hagerman and Hagerman 2013).

While there is currently no specific treatment for FXPOI or FXTAS, early diagnosis and early intervention for estrogen deficiency or neurological deficits may improve symptoms and decrease secondary health effects (R. J. Hagerman et al. 2008; Mann et al. 2012; Opinion 2014; Singer et al. 2011). Screening of ovarian reserve using follicle stimulating hormone (FSH) or anti-Müllerian hormone (AMH) can be done prior to symptom

development to provide anticipatory guidance and possibly allow for earlier symptom management (Leader and Baker 2014; Opinion 2014; Spath et al. 2011; Visser et al. 2012). Premutation carriers with early information regarding a low ovarian reserve can be given the option of early hormonal treatments or fertility preservation by freezing eggs. In addition, information on AGG interruptions can give premutation carriers improved risks for expansion to the full mutation (Nolin et al. 2014). Finally, early diagnosis and treatment of depression and anxiety in premutation carriers is important to overall well-being of the patient and family.

One model that has been used to predict uptake of preventative or treatment behaviors is the Health Belief Model (HBM). First proposed by Hochbaum in the 1950s, it was developed to explain the health behaviors of an individual under conditions of uncertainty (Becker and Maiman 1975; Rosenstock 1974). The HBM has received widespread use to predict health behaviors across psychology and public health domains, but there is a relative paucity of research on the HBM and genetic conditions. A high level of ambiguity in understanding the diagnosis and interpreting risks accompanies many genetic conditions, including *FMR1*-associated conditions. This makes them a good candidate for application of the HBM. According to the HBM, an individual's willingness to engage in health behaviors is determined by multiple factors including: 1) the perceived susceptibility and severity of the condition, 2) the potential benefit of action vs. barriers faced by the patient, and 3) cues to action that trigger appropriate health behaviors (Rosenstock 1974). There is currently a lack of attention on all three HBM factors for *FMR1* premutation carriers, which may be contributing to a low uptake and understanding of positive health behaviors.

A meta analysis by Janz and Becker (1984) looked at a total of 46 studies over a 10 year period to determine which HBM factors were determined to be significant predictors of health behaviors related to a variety of conditions. While each factor influenced health behaviors, perceived barriers proved to be the most powerful dimension of the HBM. This study was designed to use qualitative analysis of data from focus group discussions to uncover both barriers and facilitators to health behaviors for women who carry the *FMR1* premutation from a framework of the HBM.

Methods

Participants

Participants were recruited through the Fragile X Syndrome Clinic and Fragile X Center research studies at Emory University and through the National Fragile X Foundation's Community Support Network in Atlanta. A total of 120 women met initial eligibility criteria and were contacted for study enrollment. An initial invitation was sent to eligible participants and follow up phone calls were made to determine interest if no response had been received. Once interest was determined, questions were asked to establish eligibility and availability.

Eligible participants were women between the ages of 18 and 80 who lived near the Atlanta area and were carriers of the *FMR1* premutation confirmed in either a clinical or research setting. Prior knowledge of premutation-associated health risks was considered a criterion

for enrollment because focus group discussions were targeted toward current barriers to personal healthcare and experience with educational materials. This was assessed through an open-ended question asking what participants knew about the health risks to female premutation carriers. Women who had little to no knowledge were excluded from participation and referred to a genetic counselor for more information. The goal was to recruit a diverse group of women to gather information based on different experiences and life stages.

Demographic and clinical data were collected at either study enrollment or focus group attendance. These included: premutation repeat length, age and setting of diagnosis (e.g., diagnosed through a child with FXS, through prenatal screening, etc.), race/ethnicity, current age, number of children with FXS, and current premutation-associated health complications. Participants were compensated with a \$20 gift card at the conclusion of the focus group. Verbal consent was received from all individual participants before focus group participation. This study was submitted to the Institutional Review Board at Emory University but considered exempt from further review.

Procedures

A total of five focus groups, each taking about 90 min to complete, were held over a two-week period utilizing a semi-structured discussion guide. Each focus group consisted of a moderator, note taker, and three to five study participants, scheduled based on participant availability. The focus group approach was chosen to allow for more in-depth and personal discussion compared with a quantitative approach and for more participant interaction compared with in-depth interviews (Stewart et al. 2007). All sessions were audiotaped. The moderator followed a detailed focus group discussion guide along with follow-up probes to explore issues in greater depth. The moderator's guide, developed by the research team in consultation with an outside specialist on focus group research, was divided into three main sections including analysis of current educational materials, discussion of clinical vignettes, and questions about personal experiences and health behaviors. Content areas for discussion included motivators and barriers to receiving personal healthcare and experience with or opinions on current educational materials specific to female *FMR1* premutation carriers.

Data Analysis

Descriptive statistics (mean and standard deviation or frequencies and percentages) were used to analyze participant demographics and characteristics. All focus group sessions were transcribed verbatim. Prior to data analyses, four members of the research team met to develop and define deductive codes based off the moderator's guide and research question. Two of the four members of the research team then independently coded each of the five focus group transcripts to identify predefined deductive codes and to identify and define inductive codes based on the transcripts. Following themes analysis, reliability was established by inter-coder agreement of 80 %. Codes were also discussed and clarified between the two coders and adjustments were made until intercoder consensus was achieved. The transcripts were then electronically coded using Atlas.Ti (version 1.0.16) software and themes, trends, and patterns were identified (Atlas.ti 2011). Quotations illustrating main themes were identified during the coding process.

Results

Study Sample

Thirty-five women were screened for enrollment. Fourteen women (40 %) were not scheduled due to distance or scheduling conflicts. Only one woman (2 %) was excluded based on lack of prior knowledge. Twenty eligible women were ultimately scheduled for focus group participation (mean age [SD] 48.05[11.3] years, range 33–77 years, 15 Caucasian, five self-identified as African American).

Table 1 displays demographics for the twenty women who participated in the focus groups. All women had at least an associates degree and 12 (60 %) had a family income over \$100,000. A majority (15 of 20) of the women had children and of the women with children eight of the 15 had a child with FXS. Table 2 displays diagnostic and premutation characteristics for participants. All women had been diagnosed for over five years from the start of our study. Fifteen of the 20 (75 %) were diagnosed after a family member's FXS diagnosis, two (10 %) in a research study, two (10 %) following personal symptoms, and one (5 %) after a family member's FXTAS diagnosis. Only seven women (35 %) had met with a genetic counselor either for a family member or for themselves around the fragile X mutation. Thirteen (65 %) women thought they were experiencing symptoms related to the premutation.

Identified Themes

Results from the qualitative analyses were organized into two broad themes: barriers to personal healthcare and facilitators to personal healthcare. For each broad category a number of subthemes were identified. Identified themes are outlined in Fig. 1.

Barriers to Personal Healthcare

Participants identified six barriers to healthcare for premutation-associated health risks which include: difficult clinical translation of research findings, negative experiences with healthcare providers, feeling uninformed, different priorities, lack of support, and lack of targeted materials.

Difficult Clinical Translation of Research Findings—Study participants felt confused by ambiguity in the research field, especially around premutation-associated health conditions like FXPOI and FXTAS. Many of the women in this study had been diagnosed as carriers when research on premutation-associated conditions was in its early stages. They reported firsthand experience with researchers and doctors providing contradictory results about their health risks.

What we know is so evolving...if you talked to someone a year ago it could be different today... how do you get information?

Although a majority of the participants tried to stay updated with research findings through different media like the Internet or attending conferences, they stated that information was difficult to understand especially when written in scientific language.

It would say ... researching the protein of the FMR1 and I'm like...it's not English for me.

Some women expressed that the cautious and disciplined nature of research has resulted in a lack of translation to their health concerns as quickly as they hoped. One woman expressed:

I have two daughters who are both carriers and they are in their very early 50s so I want you all to hurry up and figure out FXTAS... I try to keep up with the journals just to see if there is anything new, and there hasn't been anything new that I know about. I mean I'm sure they can't just publish you know, 'we think this.' They have to wait until all the tests [come back] and all that kind of stuff, but it's hard to sit and wait.

A number of participants attested to the difficulty of waiting for research findings to be implemented, especially when it came to their own health.

Negative Experiences with Healthcare Providers—As expected, the women in this study reported a wide variety of experiences with healthcare providers. While many had positive experiences, several also had experiences they felt hindered them from seeking further healthcare. The most common statements dealt with a lack of understanding or lack of up-to-date information about premutation carrier health issues.

She said, 'No children?' And I said, 'No, I'm a fragile X carrier, so no children' and she got this look for a second like she almost didn't know what I was talking about and I thought, 'Really? You're a gynecologist and an OB!'

I've been dealing with menopausal stuff, I'm 47 now, and it's been the past 4 years... 'It can't be night sweats, it can't, you're too young. The average age of menopause is 51.' If I hear that one more time! (laughs)

For some women, the lack of knowledge among healthcare providers lengthened their diagnostic odyssey after symptoms had presented.

Most doctors thought, 'Oh you're just fine' ... so it took a couple doctors to actually get that. Cause I was 25 when I went through, um, menopause.

Acting as an advocate for their personal health needs came naturally to some participants, but for others it was a more difficult process. While they recognized the importance of being a self-advocate, there was a range of opinions on how and what information to share with healthcare providers. Many felt that providing educational materials or journal articles was helpful in the process.

I think it's good to have stuff to give to your doctor. Because I, I don't know, maybe not all doctors are as unaware as the ones I've come across but you know if I start having short term memory problems or troubles with balance I'm going to immediately think... this is one thing they could think about.

Feeling Uninformed—While lack of healthcare provider knowledge was of great concern, many of the women also pointed out that they felt uninformed when it came to their own health risks and potential symptoms. Many participants felt that they did not have the

knowledge to recognize relevant symptoms in themselves or in their family members. One woman expressed the following regarding a family member experiencing hot flashes in her twenties:

We thought she was really hot, and we bought her extra fans.

Participants also expressed confusion about the resources that were available to them. Some were unsure about where to find specific types of support and others did not know appropriate next steps after developing symptoms.

Would this be something you would follow up with your gynecologist about or your primary care doctor, or do you need to see an endocrinologist... Like who do I talk to about this particular issue?

For some, a personal lack of understanding hindered health behaviors because they did not feel adequately prepared to explain premutation health risks to their doctor.

Well I can't say that I fully understand it enough to even be able to explain it to others.

While the focus groups were not meant to be an informational session, even among a group of women selected for prior knowledge of health risks, it was necessary to stop and clarify premutation carrier risks in each group. A majority of participants expressed learning new information from the focus groups sessions.

Different Priorities—Many women expressed that their reception to personal health information and their motivation for seeking medical care was dependent on personal factors. For some women, making themselves a priority was difficult.

I don't make myself a priority because I'm always worried about everybody else and it's not until something starts to happen to me that I think, oh maybe it's something I should get checked out.

Other women expressed feeling overwhelmed and preoccupied with children who were diagnosed with FXS to the point that they overlooked their own health needs.

I'm already dealing with all the medical issues with my son and I mean it's a full time job just about keeping prescriptions in the house, you know. So just the idea of having to get another medical professional involved in your life.

The ages and situations in which women were diagnosed as carriers differed greatly. For some, timing was simply not right to hear and comprehend their results.

A 22 year old isn't thinking about personal health risks. They're looking at ... going out and getting jobs and meeting up with friends.

Lack of Support—Most women expressed the desire to have additional support available specifically aimed at premutation carriers. Often participants felt that family, friends, and healthcare providers made light of symptoms related to the premutation and that it was difficult to find people who understood what they were experiencing. Some felt that while

there were support groups available in the community, most were aimed at women who have children with FXS rather than all premutation carriers.

I feel like the stuff that I get invited to, it's always, you know, family type things. It's not you know, women who got a diagnosis before they had children and chose not to.

Lack of Targeted Materials—Women expressed the need to have materials available to help educate women on their health risks; however they acknowledged that women have different informational needs depending on their personal situations.

I think it's good just to have tools to empower the patient ... what I'm hearing, with all these wonderful stories, is, there's no cookie cutter way, but if people are empowered with information they can at least make decisions.

When asked to compare different educational materials currently available, many women voiced that their informational needs changed over time. Both stage of life and stage of acceptance of the diagnosis helped to determine the preferred amount of information. A common suggestion was that a summary handout was initially preferred with a more comprehensive review to follow.

A progression...What you need to know when you first get a diagnosis might be totally different than what you need after you've had the diagnosis.

So I think if I was only going in to maybe consider getting pregnant, and I was getting counseling on that, I would want to know all the genes, and what is going on, and what I can pass on to folks. If I was maybe a teenager and just trying to figure out what the heck's going on I'd want a different set of information.

Participants wanted different educational materials available to share with others including healthcare providers or family members. They also felt that having access to information from many different media sources was important, such as videos, websites, phone applications, social media, or speaker sessions.

Facilitators to Personal Healthcare

Focus group discussions identified a number of resources that have facilitated health behaviors for premutation-associated health risks. Four subthemes were identified which include: national or community organizations, family members, research studies, and healthcare or experiential experts.

National or Community Organizations—Many of the participants, especially those who have family members with FXS, identified the National Fragile X Foundation and other community groups as a first line for new information about their health. Some expressed that these groups were a way to feel connected.

One of the first things we did was we were reading and one of the things said for more information call the Foundation you know my thought was, 'Oh, there's a Foundation, there must be more people.'

Family Members—For many women family members were a source of support and provided a significant way to disseminate new health information. Others identified with this theme by stating that family members were the first to encourage them to seek personal healthcare.

He's [husband] the one always reminding me, 'You know this affects you, too... you need to take time for yourself'... I think I'm blessed because [my husband] does...push me...'you need to make sure you're taken care of.'

Research Studies—For others, a significant source of information was obtained through involvement in research studies. Several of the women in this study had been enrolled in a number of research studies in the past. Many participants stated that for questions regarding fragile X-associated risks a first line of information would be study coordinators or principal investigators involved in the research studies. While this facilitated obtaining updated information among carriers, for some, it replaced seeking care from traditional medical sources.

We've also been in every single trial for everything that's ever happened...We flew out to California for trials. We went to Chicago for trials. But I've never talked to... my personal physicians. It's always been for a study for someone else.

Healthcare or Experiential Experts—Some women discussed how positive experiences with healthcare providers encouraged them to seek care or to learn more about their personal risks. Many expressed that a well-informed healthcare provider was important, but equally note-worthy was a willingness to learn about premutation-associated conditions and expressions of validation toward the patient.

Doctors vary, at least in my experience... My OB/GYN I mean I gave a... scientific publication and she took it and read it and came back to me and was...grateful. I mean, so that to me is a sign of a good doctor, who wanted to learn...So, she's still my doctor.

A subset of participants relied on other premutation carriers for information and support about their own health risks. As is true for many genetic conditions, often the first line of information is an individual who has experienced a similar course.

It's really interesting to know that there are people out there that have experience, not that they are the experts, but they are certainly experiential experts as far as what has happened in their family.

Discussion

The HBM has been used to predict health behaviors by measuring factors including perceived susceptibility and severity of the condition, barriers vs. benefit to action, and available cues to action. This study used focus group discussions to ascertain factors that contribute to health behaviors in women who carry an *FMR1* premutation. Barriers and facilitators to personal healthcare were identified and then used to develop educational materials that can serve as a cue to action. Barriers were divided into six subthemes

including: difficult clinical translation of research findings, negative experiences with healthcare providers, feeling uninformed, different priorities, lack of support, and lack of targeted materials. Facilitators were divided into four subthemes including: national or community organizations, family members, research studies, and healthcare or experiential experts.

Research continues to focus on characterizing the phenotype associated with the *FMR1* premutation and to identify the related mechanisms. However, a common theme identified in this study was that the slow pace by which research findings are translated to clinical utility makes it difficult to stay informed. As a consequence participants had received conflicting sources of information regarding health risks. For example, initial research studies showed that women had little to no risk for FXTAS, but current research has identified that there is a risk (up to 17 %) for relevant symptoms, although exact risk are still being defined (R. J. Hagerman et al. 2004; Hall et al. 2014). An additional consequence of continual research into *FMR1* premutation outcomes in women is that educational materials with patient friendly language quickly become outdated.

All participants identified negative experiences with healthcare providers as a barrier to health behaviors and some found that providers' lack of knowledge lengthened their diagnostic odyssey. These findings complement a study by Groff et al. (2005) where participants with primary ovarian failure (POF) from the general population reported a lack of sensitivity, knowledge, and helpful suggestions from their physicians regarding POF. In that study 71 % of women reported being unsatisfied with how they received their diagnosis and 53 % felt that their physician had very limited knowledge of POF. This is especially concerning as another study cited health professionals as a main source of information for primary ovarian insufficiency (Singer et al. 2011). Many other studies have confirmed the importance of the patient-doctor relationship in coping and encouraging health behaviors across conditions (Bertakis et al. 1991; Kaplan et al. 1989). Our participants also expressed that health professionals were important to their health behaviors and felt frustrated by the lack of knowledge from medical specialists. Some familiarity with *FMR1* premutation-associated conditions is important from a number of specialties given the wide variety of diagnostic scenarios. Kemper and Bailey (2009) found that most pediatricians knew FXS was associated with intellectual disability but only 28 % of respondents knew that carriers could have health problems as adults. This study also reported that 75 % of pediatricians knew of a genetic counselor in their community to whom they could refer patients. While this study focused on pediatricians, many women are being diagnosed as premutation carriers following a child's diagnosis of FXS and may not be receiving appropriate counseling regarding personal health risks upon diagnosis. In our study of 20 premutation carriers, only seven women (35 %) had received genetic counseling. However, genetic counseling was not necessarily specific to the woman's premutation. Most cited seeing a genetic counselor for a family member's FXS diagnosis where premutation risks were also mentioned. Given that our population was selected from an area with access to a fragile X syndrome clinic, it could be hypothesized that the number of women who receive genetic counseling for premutation-associated risks in the general population would be lower than 35 %.

Participants also felt that their own lack of confidence in understanding their personal risks was a barrier to health behaviors. In our sample, under-recognition of symptoms, management, and knowledge of available resources hindered women from initiating discussions with their healthcare providers. The lack of confidence to discuss preventative care or treatments with a healthcare provider can significantly impact care especially in combination with low provider knowledge. Participants with POF have also acknowledged similar problems communicating with a healthcare provider and expressed that it caused them a great deal of distress (Groff et al. 2005). That study also found that the lack of available knowledge about POF seemed to decrease the participant's sense of control and diminish their ability to function with the diagnosis. Comparably, Kroll et al. (2000) demonstrated that women who had higher ratings of self-efficacy were more likely to seek medical care for menopausal symptoms. Because *FMRI*-associated disorders are not as familiar to the medical community, obtaining accurate health information may require additional effort on the part of the patient and therefore higher self-efficacy. Education and appropriate materials are important to address patient knowledge regarding their own risk factors, to improve self-efficacy, and increase positive health behaviors.

Personal priorities and responsibilities other than personal healthcare were identified as a barrier to health behaviors. Many female *FMRI* premutation carriers have significant stressors in their lives beyond their personal health risks. This feeling was compounded by the age and situation when the woman was diagnosed as well as whether or not they had children with FXS for whom they had to give extra time and care. For many participants who have a child with FXS the thought of having to get additional healthcare providers involved in their life was overwhelming. This barrier speaks to the first aspect of the HBM. For many participants in our study, the severity and susceptibility to personal health risks including FXPOI and FXTAS fell secondary to that of other family members. For some, it may also be a product of a lack of understanding personal health risks as demonstrated by the previous barrier. An increase in appropriate education regarding risks and cues to action may improve willingness to seek healthcare.

The last two barriers identified in this study were lack of support and lack of targeted materials focused on premutation carriers. While some support is available to premutation carriers, the majority is targeted to women who have children with FXS rather than to premutation carriers more broadly. This finding holds true for support groups as well as written materials for premutation carriers. A similar concern has also been expressed by patients in the general population with POF who felt that the lack of available support around POF decreased their own sense of control. Groff et al. (2005), reported that 89 % of participants felt that accurate information regarding POF helped them feel better emotionally. All women in our study expressed the need to have effective and targeted educational materials addressing premutation carrier health risks. They expressed interest in a variety of types educational materials based on stage of life, proximity to diagnosis, and intended recipient of the materials. Singer et al. (2011) found that participants felt informational needs changed over time with regards to POF. Concern was lower for women in their twenties but became more distressing as women entered their thirties. A parallel pattern according to stage of life was seen in our study where initial concerns focused on low ovarian reserve and reproduction and later concerns moved to tremor and ataxia. Based

on these findings it could be hypothesized that educational materials would be most effective if they targeted concerns by stage of life or if they used language that emphasized changing priorities over time.

In addition to barriers, this study also identified facilitators to health behaviors for women who carry an *FMR1* premutation. While not a factor associated with the original HBM, facilitators can contribute to improved understanding of severity, susceptibility, and can contribute to overcoming barriers to personal healthcare. Participants mentioned that family members were a source of support and that they received encouragement to prioritize themselves from family members. In addition to family members, healthcare providers and other premutation carriers were a significant source of information and support. While close family and supportive healthcare providers can be a significant source of support, sometimes individuals who suffer from a similar diagnosis can be more effective at understanding feelings and expressing needed emotional support.

Other women found support in the availability of research studies. While national organizations and research studies provided information, they also may have replaced the typical physician patient relationship and often emphasized the relative with FXS over *FMR1*-associated disorders. Similar findings have been seen in studies on FXS as well as women in menopause, who felt that national organizations and supportive healthcare providers who could provide information were crucial to their care (Bailey et al. 2003; Clinkingbeard et al. 1999). Improving access and encouraging use of these resources for women who are both symptomatic and asymptomatic may be one step to facilitate appropriate health education and behaviors.

Study Limitations

Focus group participants were a homogeneous group with respect to education and income, although they varied based on ethnicity, age, and how they were diagnosed. This may have limited discussion on barriers and experiences with premutation-related healthcare. All women were recruited from the greater Atlanta area and most had access to Emory University, a large academic healthcare center that offered opportunities to participate in studies about *FMR1*-associated disorders. Women were also required to have some prior knowledge of premutation related health risks to participate. Both of these make their experiences unique as compared to women without these resources and with little to no knowledge of the premutation and may limit the ability to draw wider conclusions for other groups of women.

Practice Implications

Over the past decade, there has been an increased effort to educate medical providers and the public about FXS; however, *FMR1* premutation-associated conditions have lagged behind in awareness efforts. Receiving a FXS diagnosis has widespread, complex, and often unanticipated implications for extended family members. Related health risks can place stress on women from multiple aspects. It is not unusual for a woman who carries the premutation to be caring for one or more of her children with intellectual disability and behavioral problems associated with FXS, caring for a parent who may be displaying

symptoms of FXTAS, and possibly dealing with her own reproductive symptoms. Historically, many women have been diagnosed as premutation carriers following their child's diagnosis of FXS. However, *FMR1* carrier screening in the general population is quickly becoming more commonplace. ACOG guidelines (American College of Obstetricians and Gynecologists Committee on Genetics 2010) state that screening is appropriate for anyone with a relevant family history as well as any women who request testing, regardless of age. In addition, most autism and intellectual disability panels now test for FXS and newborn screening is being considered in a number of states. Even though testing is becoming more commonplace, genetic counseling for health risks specific to women may not be offered or available at the time of diagnosis. In our sample of well-informed women, only 35 % had received some form of genetic counseling for a family member or for themselves about fragile X-associated conditions. Addressing the barriers that can deter women from placing significance on their personal health is a first step in improving healthcare for women who carry an *FMR1* premutation.

The HBM can be used to predict health behaviors in a given health setting; however, the model is grounded on the fact that there are appropriate and available cues to action. In order to address this aspect of the HBM we developed a comprehensive guide to women's healthcare and the premutation. Materials are meant to complement currently available resources and will include detailed information on current research findings and medical practices in patient-friendly language (Wheeler et al. 2014). The created materials are designed to facilitate appropriate and tailored discussion between patient and provider at diagnosis as well as at different stages of life. They are aimed to prepare and encourage positive health behaviors for women who carry the premutation. Materials will be distributed to premutation carriers or healthcare providers through the National Fragile X Foundation. Future research will involve evaluating the effectiveness of these materials in the education of women and physicians.

This qualitative study gave greater insight into the experiences of female *FMR1* premutation carriers. Based on the results, it can be hypothesized that appropriate educational materials could increase self-efficacy in premutation carriers and improve health behaviors. Future studies quantifying knowledge of patients as well as usefulness of educational materials are important. In addition, our results uncovered a number of needs to be addressed to improve premutation-associated care. Future studies addressing healthcare provider knowledge of *FMR1* premutation-associated risks will be important to identify gaps and create interventions to improve care. Finally, as health risks are constantly evolving through new research findings, this study highlights the need to develop effective and creative means of communicating to both healthcare providers and premutation carriers.

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Fig. 1.
Themes identified through focus group discussions

Table 1Demographics of study participants ($n=20$)

Demographic	
Age (years)	
Mean (SD)	48 (11.3)
Range	33–77
Ethnicity	
Caucasian	15 (75 %)
African American	5 (25 %)
Marital status	
Married	14 (70 %)
Single	6 (30 %)
Level of education	
Associates	2 (10 %)
Bachelors	9 (45 %)
Post graduate	9 (45 %)
Income	
<\$50,000	2 (10 %)
\$50,001–\$100,000	5 (25 %)
>\$100,000	12 (60 %)
Not reported	1 (5 %)
Children	
Yes	15 (75 %)
No	5 (25 %)
Child with FXS	
Yes	8 (40 %)
No	12 (60 %)

Table 2Diagnostic and premutation characteristics ($n=20$)

Characteristic	
Premutation Length	
55–79	4 (20 %)
80–100	11 (55 %)
101–200	5 (25 %)
How diagnosed	
Family member with FXS	15 (75 %)
Family member with FXTAS	1 (5 %)
FXPOI symptoms	2 (10 %)
Research study protocol	2 (10 %)
Years diagnosed	
<5	0
5–9	4 (20 %)
10–19	10 (50 %)
>19	6 (30 %)
Received genetic counseling where premutation-associated risks were discussed	
Yes	7 (35 %)
No	13 (65 %)
Experiencing premutation related symptoms	
Yes	13 (65 %)
No	5 (25 %)
Unsure	1 (5 %)
Not reported	1 (5 %)