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When to Tell and Test for Genetic Carrier Status: Perspectives of Adolescents and Young Adults From Fragile X Families

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We report here on our findings from adolescent and young adult females (ages 14–25) with a family history of fragile X syndrome regarding their perceptions of the optimal ages for (1) learning fragile X is inherited, (2) learning one could be a carrier for fragile X, and (3) offering carrier testing for fragile X. Three groups were enrolled: those who knew they were carriers or noncarriers and those who knew only they were at-risk to be a carrier. Only 2 of the 53 participants felt that offering carrier testing should be delayed until the age of 18 years. Participants who knew only that they were at-risk to be a carrier provided older optimal ages for offering carrier testing than those who knew their actual carrier status. Participants did not express regret or negative emotions about the timing of the disclosure of genetic risk information regarding their own experiences. Participants' reasoning behind reported ages for informing about genetic risk and offering carrier testing varied depending on what type of information was being disclosed, which carrier status group the participant belonged to, and the preferred age for learning the information. Study findings suggest that decisions regarding the timing to inform about genetic risk and offer testing should be tailored to the individual needs of the child and his/her family.

Key words: carrier testing; minors; adolescent; genetic risk communication; fragile X syndrome; X-linked disorders

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INTRODUCTION

Genetic testing in childhood presents as a complex medical, ethical, and social concern for families diagnosed with genetic disorders as well as their health care providers. A recent review of the literature on guidelines and policy for carrier testing in minors found 14 position papers written on the subject from 1994 to 2003, each of which recommends either that carrier testing should not be performed in children or that it should be deferred until the child is old enough to give informed consent [Borry et al., 2006]. Current practice guidelines regarding the timing of carrier testing for genetic disorders in children and adolescents emphasize a respect for the autonomy of the minor, as well as concerns for the minor's psychosocial well-being, stigmatization or discrimination (including insurance discrimination), family relationships, and self-concept [Andrews et al., 1994; Clarke, 1994; Wertz et al., 1994; ASHG and ACMG, 1995; Fryer, 2000; Ross and Moon, 2000]. Many of these concerns are rooted in theories or principles of ethics, and few use empirical evidence to support their conclusions.

Previous Research

Much of the research on timing of offering carrier testing in childhood has focused on the opinions of parents, health care professionals, and adults who were either tested for carrier status as children or had siblings with genetic disorders; few studies have reported the views of adolescents and young adults with a family history of a genetic disorder. Studies on the attitudes of health care

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professionals regarding carrier testing in minors have shown that genetic counselors and clinical geneticists are less willing to provide carrier testing to a child based on a parent's request than pediatric physicians [Rosen et al., 2002; Borry et al., 2007]. McConkie-Rosell et al. [1999] found that parents, on the other hand, felt they should have a right to choose when to test their child. Similarly, Balfour-Lynn et al. [1995] found that while most parents felt it was their right to learn their child's carrier status, almost half of the directors of regional genetics service centers surveyed thought parents had no right to this knowledge. Finally, McConkie-Rosell et al. [2002] investigated the opinions of adult women before and after undergoing carrier testing for fragile X syndrome themselves, and found that the majority of the participants favored disclosing genetic risk and carrier testing prior to 18 years of age in order to provide the child with time to adjust to the information.

Studies involving preferences about age to offer testing including the opinions of adolescents and young adults are limited. Järvinen et al. [1999] surveyed young adult women with a family history of Duchenne muscular dystrophy and hemophilia A who had undergone carrier testing as minors and found that the majority felt that carrier testing should be performed in the childhood or teenage years. Although Sparbel et al. [2008] do not advocate offering genetic testing to teens at-risk for Huntington disease, they found that teens ages 14–18 years were actively thinking about their future options regarding learning their genetic status. However, not all teens view genetic testing in a positive light. James et al. [2003] interviewed a small sample of adolescent females with a sibling affected by chronic granulomatous disease and found that many of these girls felt carrier testing for this disorder should not be offered until 18 years of age or older.

The purpose of this study was to explore perceptions regarding age to inform about genetic risk, self-concept, and coping in adolescents and young adults growing up with knowledge of their genetic risk for fragile X syndrome. Fragile X is an X-linked disorder affecting approximately 1/4,000 individuals in a mixed ethnic population [Turner et al., 1996]. The disorder is caused by CGG trinucleotide repeats in the fragile X mental retardation 1 (FMR1) gene that disrupts gene function, causing a range of phenotypic effects, including cognitive disabilities and autistic-like behaviors [Rogers et al., 2001]. The carrier incidence of the premutation is estimated to be 1/260 females and 1/755 males [Rousseau et al., 1995]. We have previously reported our findings on self-concept [McConkie-Rosell et al., 2008], which suggest that learning about the possibility of "being a carrier" is a threat to self-concept, and for some girls, may be as threatening as actually learning one is a carrier. We report here our findings on young females with a family history of fragile X syndrome regarding their opinions of the optimal age of risk disclosure and offering carrier testing as well as their reflections on their personal experiences with learning genetic risk information.

MATERIALS AND METHODS

Participants

This study was reviewed and approved by the Duke University Hospital System (DUHS) Institutional Review Board. For a detailed description of study participants refer to McConkie-Rosell et al. [2008]. Briefly, the participants were adolescents and young adults age 14–25 years who had knowledge they were either (1) a carrier, (2) a noncarrier, or (3) at-risk for being a carrier (~50% chance, not yet tested) for fragile X syndrome. All participants were recruited through the Fragile X Clinic of the DUHS, family support groups affiliated with the National Fragile X Foundation, or postings on the FRAXA listserv. After prescreening to ensure participants met study inclusion criteria such as age and length of time with knowledge of risk status, all participants were interviewed by the principal investigator of this study, AMR.

Interview

The structured interview was adapted for adolescents from one used in a previous study involving adult women [McConkie-Rosell et al., 2002]. The interview was piloted with 10 adolescents who knew they were carriers of fragile X syndrome. Interviews consisted of both open and closed-ended questions which were followed by prompts asking participants to provide their reasoning. The interview was audio recorded and transcribed verbatim. Three specific stages of participants' knowledge were explored: (1) learning the disorder was inherited (i.e., that fragile X runs in the family); (2) learning about the possibility of being a carrier (i.e., that the participant could have a child with fragile X syndrome); and (3) learning one's actual carrier status. Participants were asked about their opinion of the optimal timing of disclosure of these three stages of knowledge and encouraged to provide an exact age or an age range as well as a rationale in support of their opinion. In addition, we explored with the participants their knowledge about genetic terminology and their own preferences related to their experiences in learning about fragile X syndrome.

Quantitative Analysis

The relevant age responses were extracted from the interviews for use in statistical analyses. Data were assessed to evaluate (1) group differences based upon carrier status, (2) differences in preferred ages related to the three stages of knowledge, and (3) whether the age the participant remembered being informed was related to the age preferences she gave (i.e., to determine whether the girls were giving the same age as they remembered for themselves). Group differences were evaluated using ridit analysis [Bross, 1958; Fleiss et al., 2003] to account for the ordinal nature of the age range preferences. Ridit ("relative to an identified distribution") analysis is a parametric test used to detect statistical differences between groups on an ordered categorical scale by comparing the probability that a randomly selected individual in one group will be higher on the scale than a randomly selected individual from the other(s) group(s) [Fleiss et al., 1979; Jansen, 1984]. Ridit analysis is valid for comparison of subgroups and pairwise comparison of subgroups is possible in order to detect where specific differences in groups reside. Additionally, if the responses in any one group resulted in the sample size falling below 15 we confirmed the Ridit analysis using an exact test (Kruskal–Wallis test or Mann–Whitney/Wilcoxon Rank Sum) [Fleiss et al., 1979]. Differences in preferred age ranges reported for the three stages of knowledge were com-

pared using the exact version of the sign test. Kendall's tau-b [Agresti, 1984] was used to assess whether there was an increasing or decreasing relationship between the remembered age range and preferred age range for each of the three stages of knowledge. Fisher exact tests and extensions [Mehta and Patel, 1983] were also performed to assess whether there was evidence of other types of association between reported and preferred age. All tests were two-tailed and a *P*-value less than 0.05 was considered significant. All statistical analyses were performed using SAS version 9 (SAS Institute, Inc., Cary, NC).

Qualitative Analysis

Transcribed interviews were uploaded into ATLAS Ti 5.0. A directed content analysis approach [Potter and Levine-Donnerstein, 1999] was used to develop a series of categorical codes based on concerns expressed in published position papers regarding the timing of carrier testing, as well as results from a previous study with adult women [McConkie-Rosell et al., 2002]. The interview transcripts were repeatedly read and key questions were reviewed. The targeted questions were then coded using the predetermined codes and new codes developed as indicated. The targeted questions were first independently coded by AMR, GAS, and RMW and then jointly reviewed until a consensus was reached.

RESULTS

Participants

Fifty-three adolescent girls and young adult women (20 carriers, 18 noncarriers, and 15 at-risk for being a carrier) from 13 different states in the US were enrolled from 2003 to 2006 (Table I). The majority of participants were in high school at the time they were in the study and had at least one sibling affected by fragile X syndrome. Approximately half had multiple relatives affected with fragile X syndrome. There were no significant differences in age or sample demographics among the three groups.

The majority of the adolescents and young adults reported they learned that fragile X was an inherited disorder and that they were possibly a carrier by 13 years of age (Table II). Forty-two percent of participants who had been tested knew their actual carrier status by age 13 years. Some have no memory of not knowing and felt that they have just always known.

Age Preferences for Stages of Knowledge

Forty-three percent of all study participants felt that early childhood (0–10 years) was the preferred age to inform a child that fragile X syndrome is an inherited disorder (Table III). In addition, the majority endorsed the preteen (11–13 years) to teen years (14 to <18 years) as the preferred age to learn about the possibility of being a carrier (Table IV). The only significant difference among the groups regarding preferred age was for when to offer carrier testing. Participants who are carriers and noncarriers endorsed offering testing at a younger age than participants who had not been tested (Table V).

Additionally, we considered whether the stated age range preferences given in response to each of the questions differed for each of the three stages of knowledge, by stage as well as carrier status group. There was strong evidence that participants tended to state older age preferences for learning that one could be a carrier (could have a child with fragile X) than for learning that fragile X runs in one's family ($p < 0.0001$, exact Sign test). This pattern persisted within each of the carrier status groups, with $p < 0.008$ in all instances. Participants also tended to state older age preferences for offering carrier testing than for learning that fragile X is inherited ($p = 0.0290$, exact Sign test), and this pattern was found within each carrier status group, although no individual test was significant ($p > 0.07$ in all instances). However, the data suggested that participants who are carriers and noncarriers tended to state younger ages for offering carrier testing than for learning that one could have a child with fragile X. This pattern was not seen in the participants who knew only that they were at-risk. However, the small sample size limits our ability to explore or confirm this suggested finding.

We also assessed for an association between the ages the participants remembered learning each of the three stages and the age preferences given for each stage to help determine if the participants were providing unique responses or mirroring their own remembered experiences. We found no evidence ($p > 0.05$ in all instances) of an association between remembered age and reported age preference at any of the three stages of knowledge, either overall or by carrier status group.

TABLE I. Demographics of Study Participants

Age	18.02 years (s.d. 2.74)
Ethnicity	
Caucasian	50 (94.4%)
African American	2 (4%)
Hispanic	1 (2%)
Religion	
Baptist	8 (15%)
Protestant/Christian nondenominational	27 (52%)
Catholic	9 (17%)
Jewish	2 (4%)
No formal affiliation	6 (11.3)
No religious beliefs	1 (2%)
Year completed in school at the time of the interview	
7–8th grade (middle school)	6 (11.4%)
High School (9–12th)	31 (58%)
Some College	16 (30%)
Closest relative affected by fragile X syndrome	
Sibling/parent[a]	36 (68%)
1st Cousin	9 (17%)
niece/nephew	5 (9.%)
Uncle/aunt	1 (2%)
Greater than 3rd degree	2 (4%)
Multiple relatives affected	29 (55%)

There are no significant differences among the three groups ($p > 0.1$ Pearson Chi-Square).
[a]One girl had an affected mother.

TABLE II. Participants Remember Age of Learning Each of the Three Stages of Genetic Risk

	Carrier	Noncarrier	At-risk
Learned fragile X was an inherited disorder			
0–10 years	3/15%	7/39%	7/47%
11–13 years	6/30%	2/11%	5/33%
14–< 18 years	6/30%	3/17%	0
≥18 years	2/10%	0	1/7%
Don't know/can't remember	3/10%	6/33%	2/13%
Learned could be a carrier (could have an affected child)			
0–10 years	1/5%	6/33%	3/20%
11–13 years	7/35%	6/33%	7/47%
14–< 18 years	8/40%	3/17%	2/13%
≥18 years	3/15%	0	1/7%
Don't know/can't remember	1/5%	3/17%	2/13%
Learned actual carrier status			
0–10 years	2/10%	3/17%	na
11–13 years	5/25%	7/39%	na
14–< 18 years	7/35%	4/22%	na
≥18 years	4/20%	1/6%	na
Don't know/can't remember	2/20%	3/17%	na

Ages are the remembrances of the participants. There is no significant difference in mean ages of the girls ($p = 0.72$, Kruskal–Wallis test) or remembered stages of knowledge ($p > 0.1$ Pearson Chi-Square) among the three groups.

Rationales for Age Preferences for Stages of Knowledge

Based on the ages provided by the participants as optimal for disclosing the three stages of knowledge, four distinct age categories were developed that corresponded to developmental stages: early childhood (0–10 years), preteen (11–13 years), teen (14 to <18), and adult (≥18). We assessed for thematic patterns based on the preferred age range and rationale given for each stage of knowledge.

Learning fragile X is inherited. The majority of the girls who endorsed early childhood as an optimal time to learn about the inheritance of fragile X syndrome stressed the importance of learning this information early to help with the child's adjustment to the information. There was also an appreciation that even though a young child might not understand the information, it was important to start the process.

Many felt that the information should be staged by revealing that fragile X is inherited early and subsequently discussing the other stages of knowledge over time so as not to overwhelm a child.

> Noncarrier (21 years)
> I think that you should talk about . . . just go in baby steps, you don't have to just say when a child is 4 years old, "Well, Cindy Lou" (laugh) You know, "You have this really terrible thing, and you could give it to your children." I think just saying . . . just taking baby steps and identifying that someone has fragile X in your family, and then mommies and daddies give their children this. So, I think at a very early age, 5, 6, start talking about it.

Additionally, participants thought early disclosure might help a young child understand an affected relative's abnormal behavior and therefore attenuate confusion or frustration that might otherwise arise. Several of these participants felt that deciding when to reveal this information should be based on whether or not the child has a direct relationship with an affected individual.

TABLE III. Preferred age for Learning Fragile X Is Inherited

	All participants, N = 53	Carrier, n = 20	Noncarrier, n = 18	At-risk, n = 15
Early childhood (0–10 years)	23/43%	8/40%	10/56%	5/33%
Preteen (11–13)	18/34%	7/35%	6/33%	5/33%
Teen (14–< 18)	11/21%	5/25%	2/11%	4/27%
≥18 years	0	0	0	0
Unable to give a specific age	1/2%	0	0	1/7%

There was no significant differences among the three groups in the age response provided ($p = 0.36$, ridit analysis). The two responses "unable to give a specific age" were excluded from the analysis.

TABLE IV. Preferred Age for Learning About the Possibility One Could be a Carrier (Could Have a Child With Fragile X Syndrome)

	All participants, N = 53	Carrier, n = 20	Noncarrier, n = 18	At-risk, n = 15
Early childhood (0–10 years)	4/8%	0	3/17%	1/7%
Preteen (11–13)	28/53%	11/55%	10/56%	7/47%
Teen (14 to <18)	20/38%	9/45%	5/28%	6/40%
≥18 years	1	0	0	1/7%
Unable to give a specific age	0	0	0	0

There was no statistical difference found in the age provided for learning about the possibility of being a carrier ($p = 0.23$, ridit analysis).

Noncarrier (15 years)

I really don't know, probably fairly young, um not too young I guess. Before they are in middle school, I think, especially if they're not, if they have other family members are affected. If they have family members that are affected because they should know about why their family members are affected, how they can be affected, and how to deal with it.

Participants who felt that the information should be provided during the preteen or teen years were more concerned that the child be cognitively mature enough to "understand."

Carrier (18 years)

I think they'd be able to understand it more, understand it better than they did when they were younger.

Approximately one-third felt that it was important to know by the preteen years because the child is starting to become more socially and self aware.

At-risk (16 years)

That is just a time of self-exploration for girls especially, so they're probably wondering how their sibling got it or whatever anyway, so they probably either find out that they could be a carrier by their selves and want to know or someone could tell them, you know.

Learning could be a carrier for fragile X. Only a few of the participants felt that a child should learn that she could be a carrier in early childhood. The majority endorsed the preteen or teen years as the optimal time to learn about the possibility of being a carrier. These ages were perceived as a time in which a child would be able to understand the information.

Noncarrier (16 years)

Because I mean you can actually understand it, and it's more known to you, like, you realize what it means and stuff.

Many participants thought that preteens needed to know because this age was a time of physical maturation. Some also felt a preteen should be informed of her risk so as to avoid an unplanned or unwanted pregnancy.

Carrier (22 years)

I think that a girl should know before she ever, you know, starts dating or anything. I really think that she should know before then, just for the simple reason, you know, if she'll know what she's getting herself into if she happens to you know (have sex).

Those who endorsed the older teen years felt that it would be important to inform a minor of her risk of being a carrier at this age to aid in decisions about life and future family planning.

Carrier (18 years)

Because that's when she'll start thinking, I mean, you think about being married for a long time. That's when she really starts thinking about marrying and how many, you know if she wants a family and her job and all that, you know, the life stuff.

Also, many felt that a teen would be better able to understand than a younger child.

TABLE V. Preferred Age for Offering Carrier Testing

	All participants, N = 53	Carrier, n = 20	Noncarrier, n = 18	At-risk, n = 15
Early childhood (0–10 years)	16/30%	7/35%	8/44%	1/7%
Preteen (11–13)	10/19%	3/15%	6/33%	1/7%
Teen (14 to <18)	16/30%	6/30%	3/17%	7/47%
≥18 years	2/4%	0	0	2/13%
Unable to give a specific age/whenever ready	9/17%	4/20%	1/6%	4/27%

Carrier/at-risk: $p = 0.012$, ridit analysis; noncarrier/at-risk: $p = 0.0016$, ridit analysis; no difference carrier/noncarrier: $p = 0.48$, ridit analysis.

At-risk (16 years)
Just because then I understood more I think and when you're really young, you're, like, it's going to go in one ear and out the other. And when you're that age, it's like it sinks in a little bit and then as you get older, it'll sink in even more.

Offering carrier testing. Responses for the optimal timing of offering carrier testing were much more varied than for the other two stages of knowledge, and similarly, so were the reasons given for these reported ages. Many of the participants who were carriers (45%) and noncarriers (77%) endorsed the childhood to preteen years. Only two participants who were at-risk endorsed such an early age (Table V).

Among those who felt that testing should be offered in childhood to the preteen years, several felt that presenting this information early gave the child time to adjust to his/her genetic status or to avoid "shocking" moments later in life.

Carrier (18 years)
I don't know. It seems like that would be better to do that earlier, you know even before, just so that it was always. Cause for me the information was always there so it's not like I've had any shocking moments. No I wouldn't want to have that. That would be terrible. It's like if you're like adopted. It seems like it would be better to know that you're adopted your whole life than to just have a day when you're 13 and your parents sit you down and tell you you're adopted. That would be terrible.

Additionally, many felt that parents should have the right to choose the timing of carrier testing, often feeling that parents had the right to test their child as early as birth. These participants stressed the importance of parental choice in learning their child's genetic status so that parents could be better prepared to relate this information to their child. Many also felt that parents should know to alleviate their own anxiety about their child's status. None of the participants who were at-risk advocated parents' choice in the decision of when to offer carrier testing.

Noncarrier (15 years)
I think it's, I think when a child is very young, a parent should have them tested so they know. So they can make sure they get treated if they have it, or so the parents can figure out what they need to do. And they can be more educated also before they tell their children.

Carrier (17 years)
I think if parents know that, if they know that one of them is a carrier, they should just test their child as soon as possible at birth even, just so that they know and so that they don't have to be worried or wondering.

The majority of the participants at-risk for being a carrier felt that minors should wait until the teen years, as this age was seen as a time of planning for the future, including thinking about childbearing.

At-risk (14 years)
Just because then she's, I mean you're getting ready to start high school and I think that it's time that you should start to think about your life and what you want to do and everything that is going to come with it.

The participants who were carriers and noncarriers and endorsed the teen years provided more varied responses. These included concerns for social maturity, intellectual maturity, autonomy, and a desire to have this information disclosed concurrently with other stages of knowledge.

Carrier (22 years)
Um, again, I'd say 14–15, thereabouts, because if they're old enough to know that, okay, you potentially carry it, probably the first thing they're going to say is well do I, and then if they are able and mature enough and able enough to deal with the potential yes of that answer, then say, okay, well, you know, you can think about this for a while and make a decision then.

Approximately one-fourth of participants who were carriers and at-risk for being a carrier and one participant who was a noncarrier would not provide a specific age for offering carrier testing. These participants felt that the decision should be made by the child and they did not want to give an age for anyone other than themselves.

Noncarrier (18 years)
Whenever the person feels ready. Whenever they are ready to know. When they are ready to know that it could be them.

Understanding of Genetic Terminology (Carrier/Noncarrier)

All participants were asked what it means to "be a carrier." Eighty-six percent understood that the major implication of being a carrier is the risk of passing the mutation for a genetic disorder to their child. Four of the participants' responses suggested a limited understanding of this term; that being a carrier meant the individual carries an altered allele, but not that being a carrier has implications for an individual's children. Only three individuals (one noncarrier and two at-risk) were unable to answer the question.

Carrier (18 years)
It means that you could pass . . . pass on the gene to your child or they could be affected and then if, I don't know how I'm going to say this, I'm not affected like physically or mentally, but it could be passed on to my kids. Like, it's in my genes, but it's not shown, I guess.

Reflections on Participants' Personal Experiences

When asked how they might feel if they were just learning of their genetic status (for carriers and noncarriers) or their risk of having a child with fragile X (for at-risk), the majority (75–80%) of the participants in all three carrier status groups expressed a negative emotion in response to the idea that they would not have been informed. These negative emotions included feeling angry, scared, upset, or overwhelmed.

Carrier (18 years)
That would stink. No that would be terrible. I don't know how I'd feel. Probably kind of angry.

Noncarrier (19 years)
Um, I think I would feel like I should have been told before, and I think I'd maybe be a little angry, like "why haven't you told me this" because, I don't know, I like to just know things. I don't like being sat down and told like too late or something like that. I like just knowing.

Approximately one-third reported they would feel a sense of betrayal if this information had been withheld from them, and expressed a concern for potentially harmful family secrets.

Noncarrier (17 years)
I guess I'm glad they told us when they did cause I didn't want them to wait too long. I would be kind of mad at my parents if they waited too long because it's my brother. I kind of felt that they were keeping something from me. I just had this feeling, but I'm glad they told us pretty much upfront, or when they did because I wouldn't want them to keep something, especially about my brother. I would be like, that's pretty wrong. I don't know why they would not want to tell me that.

At-risk (16 years)
Um, probably, maybe not shocked, but a little, um, apprehensive at the idea, because if you didn't know before it is like why wouldn't someone have told me before now, you know. It seems like it would be right for someone to tell you before you've reached this age.

Many of the participants who were carriers or noncarriers felt that it was important to stage the information so as to not overwhelm a child.

Carrier (16 years)
I think it all, it'd be really hard to understand and comprehend. I think it'd just be like one big hit of information and I kind of like that I have like the time to really learn about it gradually.

Participants who had been tested and knew they were noncarriers or carriers were more likely than the girls at-risk to feel either that the information was easier to accept when young or that it would have been emotionally harder to learn if they had been older.

Noncarrier (16 years)
It would be a, more shocking now. It would be more like, it wouldn't be as easy to take, I don't think. Well, I mean, it wouldn't be hard to take, but it wouldn't be as, now I just knew like when I was little. I'm 16 and have known for 16 years that there's like a possibility that I could've had it and I know for a fact that I'm not a carrier, but if I was just 16 and have to worry about taking all these tests, it wouldn't, knowing that, I mean, I'm a junior in high school and I have to worry about my kids might have it. It would be harder to take. It would be harder to get everything, make life stressful and confusing.

Only five individuals (three carriers, one noncarrier, one at-risk) said they would feel no different about learning their genetic status at the time of the interview.

When asked if they could choose for themselves whether or not they would still want to know their carrier status (for carriers and noncarriers) or their risk of being a carrier (for at-risk), all but two (one carrier, one noncarrier) of the 53 participants responded that they would still want to know in order to be better informed and to prevent family secrets.

Carrier (18 years)
Just because if I didn't know and I found out later, I would feel like my family lied to me.

For the participants who were carriers and noncarriers a major reason for wanting to know was future decision making regarding parental role enactment. This concern was expressed by only two of the participants who were at-risk.

Carrier (17 years)
Um, just like again so I know and that when I'm ready to have kids, I can do whatever I need to do so that I don't have a child with fragile X.

Finally, when asked whether they would change anything about how or when they learned their genetic status (for carriers and noncarriers) or about their risk of having a child with fragile X (for at-risk), the majority of participants responded that they would not change anything. Those that would change something either wished they had learned earlier, they had paid more attention to the information when it was given, they had had more involvement in the process or were better informed, or that the knowledge had been disclosed in stages.

Carrier (16 years)
Just so I know now so I can deal with it. I mean, I wouldn't want to find out when I was in college and then have to, you know, then have to deal with all the stuff at the same time, I'd want to know, like I think piece by piece is a good thing.

Noncarrier (20 years)
Yeah, I would have been given more information, so I could have known exactly what it meant when she said, "You don't have it."

Carrier (14 years)
Um, I wish I knew a little bit more what was going on with that. I'm kind of nervous and scared of the future. I don't really know what's going to happen to my kids. If I had any kids one day, I would want to know as much as possible.

DISCUSSION

Many of the discussions about genetic testing in minors have focused on respect for the minor's future autonomy in the decision-making process and the appropriate age to offer testing.

Thus, it is important to consider the preferences of minors themselves and their views of the optimal ages for revealing genetic risk status and offering carrier testing. This study reports the unique perspective of a cohort of adolescents and young adults who are growing up with knowledge of their actual carrier status or the knowledge that they are at-risk to be a carrier for fragile X syndrome. The adolescents and young adults in this study not only endorsed younger ages for learning risk status and being offered carrier testing than those typically recommended in the genetic testing guidelines [Borry et al., 2006], but they also provided their insights into why and how this information should be presented to children.

It is important to note that the individuals in this study were knowledgeable about the life implications of their genetic risk status. In fact, the overwhelming majority recognized that the major future implication of ''being a carrier'' for fragile X syndrome was the risk of having an affected child. They also reflected on their own experiences, and although their responses were informed by these experiences, they did not necessarily mirror them, as there were no significant correlations between the ages they remembered learning the different stages to the ages they recommended.

Regardless of their carrier status, the majority of the adolescent and young adults in this study felt that a child should learn that fragile X syndrome is an inherited disorder in early childhood and no later than the preteen years. Participants felt that it was important to learn this information early, often endorsing staging of the information in a developmentally appropriate manner. They also stressed the importance of being informed about fragile X syndrome in order to help them to understand their family and their affected relatives.

The majority of the study participants endorsed the preteen or teen years as the optimal time to learn about the possibility of being a carrier. Study participants felt that it was important for a girl to be old enough to have the necessary level of intellectual maturity to understand the implications of what ''being a carrier for fragile X syndrome'' means for future reproduction. Many were concerned that a younger child might not be able to understand this information. Additionally, some participants felt that information regarding risk status should be timed concurrently with physical maturity, expressing concerns for an unplanned pregnancy and/or reproductive decision making during this time. In fact, physical maturity factored more heavily in the reasoning behind the timing of this stage than in offering carrier testing. This suggests that guidelines purporting that testing should be delayed until a minor needs to make reproductive decisions might be more applicable to learning one's risk of being a carrier or having a child with fragile X than to offering testing.

Responses regarding the optimal ages for offering carrier testing varied among the three groups. Those participants who knew only they were at-risk and had not been tested and who were willing to provide an age preference, gave older ages for offering carrier testing than participants who had been tested. This finding is in part reflective of those girls who advocated offering carrier testing in the early childhood, even at birth, and suggested that the decision to test should be left to the parents of the child or that growing up with knowledge of one's carrier status might allow the child to incorporate this information into his or her self-concept early and avoid harm caused by learning carrier status later in life. In contrast, only one girl in the at-risk group supported such a young age. The majority of participants in the at-risk group supported either offering carrier testing during the teen years or felt strongly that they could not give an age as the decision should be made by the individual.

An interesting pattern emerged regarding the perceptions about optimal age to learn one could be a carrier and when to offer carrier testing. The participants in the at-risk group tended to provide sequentially older ages for each stage, learning about the inheritance, possibility of ''being a carrier,'' and then offering carrier testing. However, while the majority of the study participants felt that children should be in their preteen or teen years to learn about the possibility of being a carrier, many of the girls who were carriers and noncarriers endorsed offering testing in early childhood or by the preteen years. Thus, some of the participants who had been tested felt that a girl needed to be older to be told about the implications of being a carrier, but that carrier testing could be done at a younger age.

Participants who endorsed early childhood as an age to offer testing also supported parents making the decision so as to be informed and take an active role in preparing their child. The preferred ages and support of parental decision making regarding testing contrasts sharply to the current guidelines for clinical practice that recommend offering testing only after a minor is old enough to give consent and actively participate in the decision-making process. Still, approximately one-fourth of all participants expressed a need to respect the autonomy of the child or his/her ability to participate in the decision making regarding being tested.

In the discussions regarding timing of offering testing there is a focus on of the tension between a parent's right to choose when to have a child tested versus preserving the rights of the child [McConkie-Rosell and Spiridigliozzi, 2004]. Our results indicate that many of the adolescents and young adults in this study endorsed an approach that is tailored to the needs of the family, respecting both parents' and child's opinions. Those that advocated parents' choice gave much earlier ages for offering carrier testing than those that advocated autonomy. However, we did not specifically ask participants who had the ''right'' to make the decision regarding testing. Statements including autonomy or parental choice were spontaneously included in the responses to the questions regarding timing of offering testing. The frequency of these responses suggests that both the minor's autonomy and respect for the parents' right to choose are indeed significant concerns among our participants for the timing of offering carrier testing.

It is important to note that the majority of those who felt the minor's autonomy should be respected did not express a concern that the minor be an appropriate age to give ''informed'' consent. Rather, they emphasized the minor's choice and active involvement in the process, regardless of age. Indeed, almost half of the study participants with this view refused to provide an exact age. They felt strongly that the individuals involved should ultimately make this decision for themselves based on their own preferences.

Most guidelines regarding carrier testing and risk disclosure in minors cite potential psychological harm as a major concern, and therefore advocate delaying testing until a child is emotionally

mature enough to handle the implications of the information presented to him/her. Interestingly, very few of our participants noted the emotional maturity of the minor as an important factor in the timing of learning fragile X is inherited, learning the risk of being a carrier for fragile X, or offering the option to undergo carrier testing. Instead they emphasized the importance of staging and being able to understand the genetic risk information. They also highlighted the personal nature of the information for themselves, future life planning, and for understanding their own families. These findings suggest that minors may put less emphasis on the potential emotional harm and instead focus on the importance of understanding and personalizing this information. It is striking that only two participants (both in the at-risk group) suggested waiting until after 18 years of age to offer testing.

Reflections of Participants' Own Experiences on the Timing of the Stages of Knowledge

The majority of all participants did not express regret regarding their own experience of learning their genetic risk status. This suggests that they felt a sense of ownership over their own experiences with each stage of knowledge. Many participants indicated how important the process of gaining information about their genetic risk and carrier status was for them. In fact, very few would change their own experience with the stages of knowledge if given the chance, regardless of the timing in their own lives.

The overwhelming majority of participants responded negatively when asked how they might feel if they were just learning information related to their genetic risk or carrier status at the time of the interview. Many individuals cited harmful family secrets as a significant concern. Family secrets, although often meant to protect a child from harm, can cause harm themselves once revealed [Brown-Smith, 1998]. Our results support this finding, as many of the adolescents and young adults felt strongly that fragile X syndrome and the related genetic risk should be told and not kept as a "family secret," only to be revealed when the children are older. Many expressed a feeling of betrayal or being left out of something that was not only of importance to their family but also directly involved them, had they not been informed.

Finally, while the majority of all participants would still want to know their carrier status (for carriers and noncarriers) or their risk of being a carrier (for at-risk), the reasons for wanting to know differed between participants who were at-risk and those who had already been tested. Reproductive decision making was a predominant concern among participants who were carriers and noncarriers but was cited less often by those who had not been tested. This may reflect a tendency of participants who were carriers and noncarriers to have considered the consequences of their status in more depth than at-risk participants. Alternatively, this may be a result of the slight difference in the question asked to those who had been tested and those who had not, as participants who were at-risk were asked if they would still want to know that they could be a carrier rather than their actual genetic status. However, considering that reproductive decision making seemed to factor heavily in the responses provided as reasoning for the timing of both disclosure of the risk of being a carrier and offering carrier testing, the latter explanation seems less likely.

Study Limitations

We urge caution when interpreting the data presented here due to certain study limitations. This is a study focused on the perceptions of adolescent girls and young adult women with a family history of fragile X syndrome and should not be generalized to other genetic disorders due to differences in inheritance patterns and associated risk. The participants in this study had personal knowledge and experiences with fragile X syndrome through their affected relatives and their responses may have been influenced by these experiences. Because this study did not include a control sample of individuals without a family history of fragile X syndrome, it is impossible to determine the effect of these personal experiences on responses. The qualitative data and sample size also limits the ability to generalize study findings. Additionally, in this study, we did not include questions regarding the phenotype of the premutation. We plan to include exploration of specific concerns regarding possibly reduced reproductive lifetime and FXTAS in a future study.

CONCLUSIONS

Much of the literature regarding genetic testing in minors does not make a distinction between learning that a disorder is inherited, learning one's risk of being a carrier or that one could actually have a child with the disorder, and offering carrier testing. We feel that these three stages of knowledge are important and valuable discriminations. Our data indicate that the adolescents and young adults in this study advocate disclosing these aspects of genetic risk at significantly different ages. In addition, the reasoning they provide for timing their disclosure differs as well. Overall, our data suggest that the adolescents and young adults in our study would prefer to be informed that a disorder runs in their family in early childhood to allow time to adjust to this information. They would prefer to be informed in the preteen and teen years that they could have children with the disorder concurrently with being offered the option of carrier testing to determine actual status. Additionally, the adolescents and young adults who are carriers and noncarriers, highlighted the importance of being old enough to understand the implications of "being a carrier." They stressed that girls should be older to learn this aspect of genetic risk information rather than focusing on when to offer testing.

The considerations discussed above highlight several implications for healthcare professionals involved with counseling and providing care to minors who are at-risk for being a carrier of fragile X syndrome or related disorders:

- Most of the participants in this study felt that offering carrier testing in minors may be appropriate for fragile X syndrome.
- There is no one "correct" age to tell or offer genetic testing for carrier status.
- Communication of genetic risk information should be tailored to the individual needs of the family and the child and should take into account that the different stages of knowledge may have different implications. There is a need for ongoing family discussion and genetic counseling tailored to both the age of the child as well as stage of knowledge.

- The three stages do not have to occur sequentially. In fact, many of the participants in this study advocated offering carrier testing to an individual prior to informing the individual about his/her risk of being a carrier (having an affected child).
- The majority of participants in this study also felt that offering carrier testing should not be delayed long after disclosing the risk of being a carrier to a minor.
- The outcome of the carrier test should not be the end-point in the process of learning about one's risk for being a carrier.
- A health care professional should balance considerations of the minor's autonomy as well as a respect for the parents' right to choose when counseling a family on the timing of carrier testing.

These perspectives of adolescent and young adult females are a valuable addition to the limited data available regarding the timing of disclosing risk related information and offering carrier testing to minors. When to tell and offer testing? Our findings suggest that the relevant concern for participants involved in this study was not *if* a minor should be informed of risk status and offered carrier testing, but rather *when* the minor and his/her family feel that learning this information is appropriate.

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