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What Were You Thinking?: Individuals At Risk for Huntington Disease Talk About Having Children

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Abstract

Most of the research on reproduction in those at risk for Huntington Disease (HD) has focused on the impact of genetic testing on reproductive decision-making. The main goal has been to determine whether discovering one is a carrier of the HD mutation changes an individual's or couple's decision to start a family or to have more children. The purpose of this qualitative study was to examine reproductive decision-making in a sample of individuals at risk for HD who have chosen not to pursue genetic testing. PHAROS (Prospective Huntington At Risk Observational Study) is a multi-site study that aims to establish whether experienced clinicians can reliably determine the earliest clinical symptoms of HD in a sample of individuals at 50% risk who have chosen not to pursue genetic testing. Data for this article were obtained from unstructured open ended qualitative interviews of a subsample of individuals participating in the PHAROS project. Interviews were conducted at six PHAROS research sites across the United States. In this paper, the research team used qualitative descriptive methods to construct and explore reproduction decision-making in three groups of people: 1) those who knew of their risk and decided to have children; 2) those who had children before they knew of their risk, and 3) those who chose not to have children based on their risk. We discuss the delicate balance health care professionals and genetic counselors must maintain between the benefits of providing hope and the dangers of offering unrealistic expectations about the time in which scientific advances actually may occur.

Keywords

Genetic disease; Huntington Disease; Reproduction; reproductive decision-making

INTRODUCTION

Huntington Disease (HD) is a rare, highly penetrant, dominantly inherited neurodegenerative disease with a prevalence ranging from 4.1 to 7.5 cases per 100,000 in the Caucasian population (Folstein 1989). The characteristic symptoms of HD include abnormal movements, cognitive changes leading to dementia, and a variety of psychiatric abnormalities, most notably depression. These symptoms normally appear around the age of 40 although the onset of disease has been seen in children as young as 2 and adults as old as 70 (Hayden 1981). Individuals with HD typically live between ten and seventeen years after the onset of symptoms (Harper 1991).

HD is inherited as an autosomal dominant disorder, meaning that each child of an affected parent has a 50:50 chance of inheriting the genetic mutation that causes HD, and men and women are equally likely to inherit the mutation. In 1983, genetic markers linked to the HD gene were first identified, allowing some individuals at risk to establish whether or not they would develop HD using a process called linkage analysis. Linkage analysis required blood samples from both affected and unaffected family members, sometimes from as many as three generations, to trace the inheritance of these genetic markers in a family. In 1993, the gene for HD was identified: an expanded tri-nucleotide repeat of cytosine-adenine-guanine (CAGn) on chromosome 4 is the mutation that causes the disease (Huntington Disease Collaborative Research Group 1993). This discovery meant that all individuals at risk for HD could choose to be tested for the presence or absence of the HD mutation without family cooperation. Studies done prior to the finding of the HD mutation suggested there would be high rates of uptake for predictive testing in individuals at risk for HD (Kessler et al., 1987; Markel et al., 1987; Mastromauro et al., 1987; Meissen et al., 1987; Tyler, Ball and Crauford 1992). However, current estimates indicate that only 15-20% of individuals at risk for HD have elected to pursue genetic testing (Creighton et al., 2003).

The Huntington Study Group

The Huntington Study Group (HSG) is an international consortium of basic science and clinical researchers designing and implementing clinical trials in HD. Although treatment for HD is entirely symptomatic at this time, research is progressing rapidly. In preparation for future clinical trials, the Huntington Study Group undertook a study of individuals at risk for HD. This study, the Prospective Huntington At Risk Observational Study (PHAROS) is designed to establish whether experienced clinicians can reliably identify emerging clinical symptoms that indicate the earliest signs of onset of HD in a cohort of clinically unaffected individuals at 50% risk for carrying the HD gene but who have not had genetic testing.

Between July 1999 and January 2004, 1,001 adults at risk for HD who had chosen not to undergo predictive genetic testing for the presence or absence of the HD gene were enrolled in this longitudinal study. A complete description of the PHAROS study, this sample, and baseline characteristics can be found in Shoulson et al. (Shoulson et al., 2006). In 2002, the Ethical, Legal and Social Implications (ELSI) Program of the National Human Genome Research Institute provided funds to support the conduct and analysis of semi-structured qualitative interviews on a subset of PHAROS participants. The overall purpose of the qualitative study was to gather information about the everyday experience of living with the risk of HD. One major component of living with risk is the decision whether to have children or not and questions about reproduction were explicitly asked in our interviews.

LITERATURE REVIEW

Past literature on reproductive decision-making in Huntington disease focused mainly on the effects of predictive testing on reproduction. Decruyenaere and her colleagues evaluated 53

individuals (31 gene-negative individuals and 22 gene positive individuals) requesting genetic testing to learn whether knowing one's genetic status reduced anxiety and uncertainty and whether it facilitated decision making about reproduction (Decruyenaere et al., 1996). They found that mean anxiety and depression levels were significantly decreased one year after receiving a gene negative result (i.e. "a good test result"), and not significantly changed after "a bad test result" or learning that one was gene positive. Testing did appear to alter reproductive decision making for both gene positive and gene negative individuals alike. Among gene negative couples, one year after receiving their test results, five couples had a newborn baby and three couples were pregnant. Of these eight couples, five already had children prior to testing. One woman became pregnant prior to the disclosure of her test results. Three married and two single participants said that they planned to have children in the future. One couple with fertility problems decided not to have children and two persons remained undecided about reproduction. For gene positive individuals, four of the 13 couples who had considered procreation before the test had chosen to refrain from (further) reproduction, a choice consistent with their pretest choice should they prove to be a gene carrier. Two of these couples had no children yet, the other couples had two and three children respectively. Four couples had a pregnancy with prenatal diagnosis for HD or were pregnant and planned a prenatal test. Before testing, three of these couples had planned to have children with prenatal diagnosis in the case of carrying the gene, while the other couple had been undecided about reproduction at that time.

The authors concluded that learning one's gene status confronts persons with new dilemmas in their reproductive decision-making. To refrain from having children or to pursue prenatal testing with a 50% chance of a positive test can be a difficult decision. The fact that one woman became pregnant prior to receiving her test results suggests that reproductive decisions are very complex and may be subject to emotional and unconscious psychological processes.

An early collaborative European study asked whether a predictive test result for HD has an effect on subsequent reproduction by comparing 180 gene positive individuals and 271 gene negative individuals. Data were collected in the five years following the discovery of the HD mutation (1993-1998) in seven European cities. The data showed that 54% of gene positive individuals and about 48% of gene negative already had children prior to testing. There was a 50% reduction in subsequent pregnancies among gene positive individuals after testing (14% of the gene positive individuals carriers had one or more subsequent pregnancies vs 28% of the gene negative individuals). A prenatal test was carried out in about two thirds of the gene positive pregnancies, and one child was born after pre-implantation diagnosis. A more refined analysis looked at those who were in a subgroup ($n= 171$) followed for at least three years and who had in the pretest period reported "family planning" as a motivation for testing. In this subgroup, 69% of the gene negative individuals and 39% of the gene positive individuals had subsequent pregnancies. The percentage of gene positive individuals using prenatal diagnosis was slightly higher than the percentage of gene positive individuals not using it.

The authors cite three possible motivations for using testing as an aid to making reproductive decisions: 1) the desire for children along with the desire not to transmit the HD gene to the next generation, 2) a desire not to have children who may be exposed to an affected parent in their childhood or adolescence, or 3) the need to know in terms of planning the exact number of children or timing of pregnancies. Several participants became pregnant in the pretest period prior to receiving their test results, despite the stated desire to have testing for the purpose of reproductive decision making. This further emphasizes the emotional factors that may be at play (Evers-Kieboom, et al., 2002).

An Australian study (Richards and Rea 2005) retrospectively examined the reproductive decision-making for 281 people during both the pre and post test period. The sample had undergone testing between 1990 and 2002, thus including those tested using both linkage analysis and direct gene testing. The results of this study confirmed those of other studies that found a low uptake of prenatal testing and alternative reproductive options both for those at risk for HD and for those found to be gene carriers as a result of genetic testing. The reasons for this low uptake are unknown. Reasons may be related to greater hope for the future since the discovery of the gene in 1993, or the impact of genetic counseling to explore options: prenatal testing, learning the fetus' carrier status, and potential termination of the pregnancy. Pursuing prenatal testing and considering pregnancy termination may heighten the meaning of a positive genetic test. For example, two women who terminated a pregnancy following a high-risk prenatal result became clinically depressed and required both hospitalization and medication.

A second study by Decruyenaere and her colleagues (2007) examined reproductive decisions in gene carriers after predictive testing for HD in an attempt to identify factors that play a role in decision-making. Those who had been tested between 1987 and 2004 were asked about their reproductive decision-making during a five-year follow-up study. Qualitative data about reproductive decision-making were collected through semi-structured interviews. For 46 gene positive individuals (51% of gene carriers in this study) and 2 persons with equivocal genetic marker results, family planning was one of the stated motives for pursuing predictive testing. In this group, slightly more than half of the gene carriers (58%) chose to have prenatal testing or pre-implantation genetic diagnosis. After learning their positive gene carrier status, 35% chose to have no children. Factors in the decision to not have children were the person's gender (female), personal experiences growing up in a family with HD, and ethical issues about prenatal diagnosis and pre-implantation genetic diagnosis. Factors related to not using prenatal testing were an unwillingness to terminate a pregnancy and optimism for future treatments and cures (Decruyenaere et al., 2007).

In the large European study of reproductive decision-making after testing, a positive test result appeared to reduce the number of subsequent pregnancies in the gene carrier group and increase the number of individuals and couples using prenatal testing (Evers-Kiebooms et al., 2002). The Australian study (Richards and Rea 2005) found a relatively low uptake of prenatal testing, but the reason for this difference between these two studies is unclear.

Two recent studies have examined reproductive decision making in persons at risk for HD (Downing 2005). In the first investigation, three case studies of reproductive decision making among persons at risk for HD were explored, and two reproductive dilemmas were identified. The first dilemma is whether to have children who later in life may develop a highly penetrant and dominantly inherited neurodegenerative disorder for which there is no treatment or cure. The second is whether it is justifiable to have children given the uncertainty about whether the at-risk parent would be able to fulfill the role of parent if symptoms were to develop in the future. This study emphasized the importance of responsibility toward others. The manner in which that responsibility is defined is considered a key factor in reproductive decision-making. These case studies however, were gathered in the period of time when only linkage analysis was used for both predictive and prenatal testing. As previously stated, this method required the cooperation of numerous family members in as many as three generations in order to have an informative test result. In many cases, this method required extensive negotiation with family members in order to obtain blood samples and medical records. The advent of direct gene testing may serve to mitigate responsibility to other family members while lending more focus to the issue of what parents owe to their children (Downing 2005).

Klitzman (Klitzman et al., 2007) explored reproductive decision-making in 21 individuals, 9 of whom had not been tested. Of the 12 tested, 8 were gene carriers and faced difficult decisions regarding adoption, pre-implantation genetic diagnosis, amniocentesis or chorionic villus sampling and the possibility of pregnancy termination. The authors did not clearly identify issues that differed between those who had been tested and those who had not.

In summary, in the two studies looking at reproductive decision-making in individuals at risk for HD, one was very small and occurred during the period when linkage analysis was the method used for testing (Downing 2005). The second looked at both tested and at risk individuals without differentiating motivations and decisions between the two groups (Klitzman et al., 2007). Thus, we know next to nothing about reproductive decision-making in individuals at risk for HD who have had the option of direct gene testing since 1993, but have chosen not to be tested. This paper focuses on reproductive decision-making but is part of a larger study that examined the everyday experience of living with the risk of HD. That larger study encouraged participants to describe freely their personal experiences with HD, their relationships with affected family members, their involvement in care-giving, their attitudes about telling others about their risk for HD, their motivation to participate in research and, finally, reproductive decision-making. This paper focuses on the participants who fell into one of three groups: 1) those participants who knew they were at risk and had children; 2) those who had children prior to knowing they were at risk and 3) those who decided not to have children based on their risk for HD.

METHODS

Design and Procedures

A full description of our study design, procedures, and analysis can be found in Quaid et al. (Quaid et al., 2008). We developed an unstructured interview guide and conducted five pilot interviews in the homes of PHAROS participants from the Indiana site. We reviewed these interviews and revised our interview questions. We then invited PHAROS investigators and coordinators from the sites enrolling the largest number of participants to volunteer as interviewers. Five experienced clinicians from various PHAROS study sites attended a two-day training session in Indianapolis to learn unstructured interview techniques from two experienced qualitative interviewers (M.S. and S.S.). Training focused on active listening, minimal direction for answers, conversational initiators, and summarizing techniques. Interviewers practiced during this training and received feedback on their approaches. The interviewers then returned to their sites with the goal of completing 10 interviews within the next 12 months.

We asked these interviewers to identify individuals from their PHAROS cohorts whom they thought would be “narratively active” and to invite them to participate in the interview process. IRB approval was obtained for this study at Indiana University and at the five institutions with which our interviewers were affiliated: Emory University in Atlanta, Columbia University in New York City, Ohio State University in Dublin Ohio, Hereditary Neurological Disease Centre in Wichita, Kansas and the Hennepin County Medical Center in Minneapolis, Minnesota. Interviews occurred either in a place convenient for the participant or at the PHAROS research site, usually at the time of the scheduled PHAROS research visit. The open-ended conversational interviews lasted at least one hour and usually longer. Interviewers encouraged participants to describe freely their personal experiences with HD, their relationships with affected family members, their involvement in care-giving, their attitudes about telling others about their risk for HD, their reproductive decision-making, and their motivation to participate in research.

Thematic Analysis

We used qualitative descriptive research methods as the foundation for the analysis in this study. Qualitative description uses naturalistically acquired data such as unstructured, open-ended interviews to increase the understanding and explanation of a social situation by vividly and conceptually describing it (Sandelowski 2000). The analysis aims at the identification and discussion of themes and patterns in order to understand and to describe complicated situations.

Participants

Informed consent for participation in the study was obtained from participants after the nature of the study had been fully explained to them. This purposive sample of 55 participants (including the 5 pilot interviews) consisted of 38 women and 17 men, reflecting the 2:1 ratio of women to men in the larger PHAROS study. Their average age was 42 with an education level of 15.6 the equivalent of over three years of college. Participants were 87% White, 7% Black, 4% Hispanic and 2% other. Of the 55 participants, 78% were married, 16% were single, and 5% were divorced. Thirty had affected mothers and 25 had fathers affected with HD. The average age of parental onset was 47.6 for affected fathers and 48.7 for affected mothers.

We compared this group of 55 participants to the larger PHAROS cohort and found no significant differences in the distribution of our sample by gender or marital status or the gender of their affected parent. There was a significant difference in the percentages of Black and Hispanic participants when compared to the larger cohort owing to our deliberate over-sampling of minority participants to interview.

This study considers a sub-sample of 51 transcripts, chosen because they contained references and stories related to reproduction and reproductive decision-making in the context of being at risk for Huntington disease. Twenty-six participants knew of their risk, and decided to have children. Fifteen had children before they knew of their risk, and ten knew of their risk and decided not to have children.

RESULTS

We identified three groups of participant responses: Group 1) those who had children despite knowledge of HD risk, Group 2) those who did not know the risk before having their children, and Group 3) those who knew the risk and chose not to have children. Within these three groups, we identified themes that characterized the participants' thinking about having, or not having, children. Table 1 summarizes the participant groups and the emergent themes:

Group 1:

Four major themes emerged in Group 1 (the group of respondents who knew of their risk and chose to have children). We have identified these themes as: 1) Hoping for a Cure; 2) Feeling Guilty 3) Magical Thinking; and 4) Just Another Something. Eight people in Group 1 (the group who knew their risk prior to having children) stated explicitly that they based their decision to have children on the hope for a cure in the near future, a cure that would come in time to save their children. This pattern reinforces the findings of our previous paper which found that choosing not to be tested and living with the uncertainty of being at 50% risk was a way to preserve hope in this population (Quaid et al., 2008). The second theme reflects the feeling of guilt that some participants felt about the decision to have children despite their genetic risk. The third theme reflected "magical thinking" on the part of some participants, in which they discussed their belief that they simply would not get Huntington Disease. We titled the fourth theme "just another something," a direct quotation

from one of the participants. In this theme, respondents maintained their lives as usual, refusing to let the risk of HD affect any decisions, including those about having children. These participants equated their risk of having or passing on HD with all other risks in their lives (“you could have this disease or you could get hit by a Mack truck someday”).

Hoping For A Cure—Hoping for a cure, Matthew (all names mentioned have been disguised) and his wife had their first child prior to his mother’s diagnosis of HD and without thinking too much about HD. After the diagnosis, however, the decision to have a second child was complicated by the now-known risk. However, the appeal of bringing a child into the world was greater than the risk of having a child who might someday develop HD. Matthew described their decision-making process this way:

So when Briana was born we didn’t really have, we didn’t really discuss it very much. But after my mom was diagnosed, and we discussed it more, we kind of came to the agreement that we thought it was more important to bring a child into the world and give them 50 years of life. And then by that time, with the dramatic things that are happening in today’s world, that they will have a cure for our children. So we thought it was best for us to, we wanted to have another child, at least one more. And that’s what we did and that’s all we’re going to have.

Similarly, Marcia said that the hope of a cure figured into her decision to have children. She placed her hope for a cure firmly in the realm of rapidly expanding scientific progress, progress “they” will make in time for her children to be cured. She thinks that technology will triumph, and soon.

When I was younger is that the statistic I heard is, well in the last ten years they’ve made more progress, or in the last five years they have made more progress with this disease as they have in over a century. Some statistic like that. How they had really found ...had really done a lot of research. And so I guess we kind of had that in the back of our mind too you know. That maybe they would find something before I became symptomatic. Or surely there would be something available before our children would ever have to worry about it. So it [a cure] was kind of always in the back of my mind anyway.

Cynthia and her husband discussed whether or not to have children prior to marriage. Cynthia’s first impulse was to consider adopting a child, but her husband’s optimism overtook her concerns.

Eileen (a sister) had adopted a child, and I said “I think that’s the better thing to do.” And he said, “Well if that’s what we have to do, that’s what we’ll do. If you feel strongly that that’s the way to go. But by the time you get it or they (our children) get it ...” We were pretty confident by that time that there would be more research and there would be getting closer to a cure or better treatment. So by the time it would affect me or the time it would affect them for sure, we would, you know, we felt pretty confident that there would be an answer. So we wouldn’t have to worry about it for them.

Joan, at age 53, with both children and grandchildren, believed that she was showing no symptoms herself. Her son was born before Joan’s own mother was diagnosed with HD, but she said that she does not think that it [her mother’s diagnosis] would have gotten in the way of her having children even if she had known of her risk. This hope for a cure may even be communicated through generations as a reason to have children.

I just feel like, and the way I look at it with my own children (particularly my own child and his children) is that I’m just hopeful for a cure. I’m so hopeful that that is just, I think that’s the only way we fight it. We can’t fight it by sitting around

worrying about it and you know focusing on what could have been or what should have been or what isn't. We just have to deal with the fact that you know there's research out there and we're going to support it and we're going to do what we can. I would say about that is that the information that we have been able to gather about it in recent years in the research, wonderful research that's going on, it's so positive and so hopeful, allows us to be hopeful, that has helped me. Because I feel I have been able to pass that information along to my own children, to my child, for him to make decisions about having children.

Some participants used the hope of a cure as a way of "allowing themselves" to decide to have children. In some cases, though, this rationale was not enough to completely remove the guilt or remorse they felt about possibly passing on the HD mutation. For example, Lisa and her husband had been thinking about children. Lisa was in favor of adoption but her husband was pressing her to have their own biological children. She then said this about her husband,

He was a psychologist and felt that there were other things just as difficult as Huntington's and that he also was very hopeful that there would be research and a cure was very [close]. I was thinking in that direction and of course, I really would have liked to have had children. So when he started talking about it it really pulled at me because I had felt that this was the right thing to do, [not to have children] but it was a huge decision. And we decided to go ahead and see about getting pregnant. But I really struggled with a lot of guilt about that and it was a very hard thing for me.

Lisa and her husband eventually had two children, partly so that her first son would not be alone if she were to fall ill. She was foreseeing her possible future with HD. Nevertheless, she then continued

I can't say that my rationale for deciding to go ahead and have children was really thought out. It went through phases and I made the decision best I could with what was happening to me at the time. But I struggled with it and even after I decided to, it wasn't that I felt like it was necessarily the right thing to do. It was more something I just did. And sometimes I thought it was because I wasn't strong enough in certain ways to fight with my husband not to go ahead. So it was quite hard.

However, after HD was diagnosed in both of her sisters, and after she experienced two near-fatal heart attacks (which she attributed to stress), Lisa eventually pursued testing. One of her main reasons for being tested was to be able to tell her two children whether or not she carried the HD mutation before she died of something else. Knowing her genetic potential, she hoped would make their reproductive decision-making easier than hers had been.

Joy got pregnant soon after her marriage. She states that she "probably should have gotten tested before I did that and didn't do it." She considered abortion, but rejected the idea partly because the onset of the disease in her family was fairly late. She played the odds and let herself be heartened by the promise of research success.

I was really kind of encouraged by people saying that possibly there may be a cure in this child's lifetime, the way things are moving. Fifty-fifty for you, fifty fifty for her. And so we had our child and then we had another one. And I feel guilt over that probably every day.

While some people in our cohort do not appear to struggle much with the decision to have children, for many it is a difficult decision filled with uncertainty and guilt. For some, this guilt and "second guessing" was quite pronounced. As Carolina told us "My brother and his

wife have one son, and his wife said to me that she wished (and she told her son this), that she wished she would not have had any children.”

Magical Thinking—Magical thinking is a clinical term used to describe a wide variety of nonscientific and sometimes irrational beliefs. In this context, it describes an almost willful denial of any potential to develop HD. This theme is most clearly stated by Violet:

My view is that I don't have it and therefore I am going to live with the hope that I don't rather than find out for sure that I do. So, and you know, I think over the years I admit that I have used denial to its advantage so that I can live my life and like it's useful.

For Wesley, the fact that his wife was at risk for HD did not outweigh his desire to have children and his belief that they would be good parents.

I thought she was tough and strong and I felt that we could with, you know that we would be good parents and I thought that HD would take care of HD.

When Thomas's wife approaches the subject of HD, at the urging of ,

Thomas's mother, he shrugs it off and, apparently, does not discuss it again for 18 years.

[My wife] said well your mom wanted me to know before we got married in case you know if you ever had kids that there was this possibility. And I said well no big deal. We just kind of just shrugged it off like there was nothing to it. And it was, that was in '73 and I never heard anything about the word Huntington's again until '91

For Diana, she just “decided” that she did not have HD and went on with her life. Her children have gotten older and have begun to think about having families of their own. Now the possibility of getting HD and the need to be tested to let her children know of their own risk, has been put firmly back on the table.

Having children, I don't think it ever really did [affect my decision]. Because like I said in my mind I had already decided that I didn't have Huntington's but if now, if my girls were to marry if they wanted to be, to know if they have the Huntington's gene, I would get tested if they wanted

Joan and her siblings had somehow developed the idea that the age of fifty was some kind of a magical cutoff date, and that if you did not develop HD by that age, you were, in effect, safe.

All of us knew that grandmother had had Huntington's but we thought, we were under the impression in those days that when she was diagnosed that fifty was kind of the cut-off date that they talked about. If you didn't develop symptoms before you were fifty then perhaps, you know then you weren't, you were set so we all, my mother included, just assumed that since she was not so symptomatic before she was fifty that we were all out of the woods.

Just Another Something—In this theme, those at risk minimize the threat of HD by putting it in the context of all the other health problems that could potentially materialize and might be as bad, or worse, than HD.

If HD wasn't in our lives certainly we would of, it might have been something else. That's what the kids tell us. They made the decision to go ahead and have children based on the fact that there are a lot of things out there you know that could be you know and a lot of things in their blood line that could be you know create problems for them and this is just another something.

Liz had already had one son before her mother was diagnosed. After the diagnosis, she felt that maybe they should not have another child but her husband disagreed:

And when we first started talking about having another child, I said you know maybe we shouldn't [have another child] because mom has Huntington's and such. And he said, you know, we do not know what's in the future and anything could happen to us and so I don't think that that's a reason that we need to decide that we're not going to have another child.

Group 2

In this group, (those who had children before they knew of their risk), we have identified two major themes. The first, "Too Little, Too Late" reflects a lack of information about HD and its manner of inheritance. The second, "Getting it Wrong," characterizes some participants who had inaccurate information about the actual risk of HD. We are aware that some of this misinformation occurred far in the past (sometimes 30 years or more ago), and families (as well as health professionals) may have provided guidance based on the minimal understanding of HD at the time.

Too Little, Too Late—Martina's family did not readily discuss the presence of HD. It was not until her Aunt Ann died, that she learned about the disorder.

Aunt Ann was 42 and she died of Huntington's. But we, I heard it at the funeral. That is the first time. And by then my uncle who was probably 35 was starting to act weird and be bizarre and my mom was a little bit on the weird and bizarre side. But we didn't know. I mean I remember this was probably when I was about 25. I had not heard of Huntington's Disease till I was married and had a baby.

One woman in her forties had already had her daughter before her own mother was diagnosed. Well-meaning health professionals gave her advice that would never be given today:

Because I had had my daughter by then. So by that time we were bringing Mom here to the Huntington's Clinic, but she hadn't been diagnosed and [they told us] "we decided your mother has Huntington's disease so you girls might want to consider sterilization" or something like that came up in the meeting. I can just see us all sitting around that table. It was awful.

Getting It Wrong—For Carolina seriously inaccurate information came from her family:

In the 1970s, my granddad's sister (which would be my great aunt), she had this disease and that maybe his brothers had it too and so it was kind of shoved away for a number of years that we just really didn't talk about it. And then I do remember when my older brother, they were getting married and wanted to have a family and they talked to my grandparents. Was there any risk of granddad having this disease?. And at the time [the grandparents] said no. So they chose to have a child.

Unfortunately, this lack of information can have drastic consequences as it did for Carolina's brothers:

My brothers don't believe that mother has it, even though she had the gene test showing she has it, and she has the clinical symptoms. They're devastated. They have one child and the last I talked to my brother's wife she's just devastated about it and so is he. And he has gone into a depression and she doesn't understand depression. He's, he's depressed because he is so scared, not for himself but for his son. That he has passed this gene down to his son.

Group 3

This group consisted of individuals who knew and understood the risks, and as a result, decided not to have children. In the main theme “Vigilant Witness,” participants shared some of the most poignant stories about being there to see the decline and death of family members because of HD. Some participants were actual caregivers; all witnessed HD in multiple generations. In the second theme in this group, “Stopping HD”, participants were told, sometimes by members of their own family, not to have children. In the third theme, “Being Alone”, participants describe how they have lived their lives avoiding intimate relationships, or denied themselves having children, in order to avoid harm to others should they become ill.

Vigilant Witness—Monica was a Vigilant Witness whose experience providing direct care for her mother greatly influenced her decision to not have children.

My main decision on not to have children was because of what I went through with my mother. I just, there were just so many things that went on there. There's so many stories I could tell you that you don't even have time to hear. But, that was why...It was not like I had to sit there and think about it and think about it and struggle with it. It was like I'm just not gonna have kids and I went and had my tubes tied when I was twenty just before my twenty-first birthday and the doctors did it because of the circumstances

Kathy had her tubes tied at the age of 19 because she felt so strongly that she did not want to pass on the HD gene.

I realized the gravity of all this when I got to be of childbearing age and was having a serious relationship and that was at the age of 19. Of course back then most people didn't wait until their thirties to get married. So I decided to have my tubes tied and when I was 19 years old... I just made a decision that I just couldn't. If I had it, I didn't want to pass it on. And now they know so much more about it than they did then.

Adrienne took care of her mother who had HD for a very long time before she finally died. Now her sister is ill and Adrienne again finds herself in the role of care-taker.

My mother was ill for so many years and now my sister. So I mean a little bit of a respite in-between but it's always a thought that is there. It's not something that I dwell on. There's not much I can do about it but deal with it as it comes but yet my decision not to have children certainly was directly related to the fact that Huntington's was in the family.

Stopping HD—In our second theme, “Stopping HD,” some participants were specifically told not to have children, sometimes by their own parents. Sherry's parents told her that the only way to stop the disease was to stop having children. She took this advice to heart:

I don't know what kind of a person I am but I decided back when I was a kid that due to HD in our family I would never have children. I mean I knew that back then. And that was pre-test and pre-everything. I had been told by my parents that the only way to stop this disease is to stop having children. You know that stops the line of the illness. So I had decided as a child I'm not ever going to have children.

Frederick had his own reasons for not wanting to have children of his own.

And [my fiancée] is worried that I don't want to have children. She asked me whether I don't want to have children because of the HD gene, whether I don't want to pass it on or because I don't want the kids to see me the way I see my

dad? . It's not just the fact that I don't want to pass on the gene. I just don't want another generation going through the same thing we do.

Being Alone—The third theme in this group is “Being Alone.” This theme represents participants who have isolated themselves because of their risk for HD. These respondents may also be afraid that, having had no children, there will be no one to take care of them if they develop HD. Rudy not only decided not to have children, he also avoided relationships altogether.

So I've lived my life as if, I've built this bomb shelter just in case the big one falls. I've kind of prepared myself. No emotional relationships. No romantic relationships. This is my bunker. This is my little cold war protection in the back yard. I have no involvement, no children. I've lived my life as if I'm going to be alone for the rest of my life because I don't know.

For another woman, not having children was a source of regret as well as fear. She describes this paradox:

I have a fear of being alone that, if I get to the point where I can't take care of myself, there won't be anybody there. I'll just be by myself.

DISCUSSION

When predictive genetic testing using linkage analysis was first offered in 1986, many health professionals believed that one major use of this technology would be to allow individuals at risk to learn whether or not they carried the HD gene, and use further testing and reproductive technologies to prevent passing on the HD gene to their offspring. Health professionals believed that people would use the test to make decisions about childbearing, because that was what individuals at risk for HD reported. In one study conducted soon after the introduction of testing using linkage, 79% of individuals said that they would use a pre-symptomatic test if it were available. Nearly 2/3 said they would use the test for prenatal diagnosis, and of these, 71% would terminate a pregnancy if the fetus were found to carry the HD gene (Kessler et al., 1987). Currently, however, the number of individuals at risk choosing to be tested remains low, and the number choosing prenatal testing is lower still.

The sparse literature on reproductive decision making by individuals at high risk for passing on a genetic disorder tells us little about how they make that complex and critically-important decision. The purpose of this paper was to explore this topic in a group of individuals at risk who have chosen not to be tested. In our interpretation, participants fell naturally into three separate groups: Group 1) those who knew they were at risk and chose to have children, Group 2) those who were unclear or misinformed regarding their risk for HD at the time they were starting their family; and Group 3) those that knew of their risk for HD and decided not to have children.

For the first group, we identified four main themes, Hoping for a Cure, Feeling Guilty, Just Another Something, and Magical Thinking. Participants convinced themselves that it would be safe to have children, because they believed that research is progressing rapidly and a cure, or at least a treatment, would be found in the near future. One factor influencing their thinking is the belief that “science will save us.” The paradox is that if people at risk base their decision to have children on the promise of current and future breakthroughs in HD research, an unintended consequence may be the creation of more people at risk. Research progress, or even just the promise of progress, could inadvertently promote the proliferation of the gene and increase the incidence of the disease.

Once the decision has been made, however, participants were not without a measure of remorse about their decision. This re-thinking is reflected in the themes, Feeling Guilty and Magical Thinking. We think these two co-occur because magical thinking along the lines of “I just don’t have it” is in part motivated by feeling guilty over what some consider a “selfish” choice regarding children. Our fourth theme, Just Another Something, is also an attempt to normalize HD by putting it on a continuum with all the other ways that one could die, thus reducing its importance as a factor that needs to be considered in making decisions about procreation. This reframing ignores the large difference in the real probabilities between the risk of getting HD (50%) and the risk of being hit by a truck (very low).

Group 2, those for whom the risk of HD was unclear at the time they had their children, expressed little regret in reference to their childbearing. What was done was done; they loved their children dearly. However, in a few cases, realizing that they may have already unknowingly passed on the gene did have a negative impact on family members. Some participants expressed regret that they did not have the option of testing or the choice whether or not to pass the gene onto their children.

The most complicated situation occurs when a couple learns about their risk after they have already had one child but have not yet completed their family. In addition to grasping the fact that one is now at risk, the parent must grapple with the fact that they may have already passed on the gene. If parents still desire more children, they must decide whether to be tested first, whether to undergo prenatal testing if positive, or whether to simply have another child.

For us, it is the third group that is the most poignant. This group was aware of their risk and deliberately and consciously made the decision to have no children. In the extreme case, the decision extended to self-imposed restrictions on all relationships of any intimacy, in case the “H-Bomb” went off. Members of this group based their decision on personal experiences with an affected parent. As a result, they either did not want to pass on the gene, or did not want to have their own children go through what they had gone through. Some of the stories they told were horrific, a veritable nightmare of shame, abuse, alcoholism, suicide, and loss. A few made the irrevocable decision not to have children at a very young age through sterilization. One consequence of the decision to shun relationships and forego children is that if these participants were to become affected, they do not know who would care for them.

James March, a scholar in the field of decision theory, offers this insight into the thinking of people making decisions under conditions of real or supposed uncertainty: “Decision makers tend to exaggerate their control over their environment, overweighting the impacts of their actions and underweighting the impact of other factors, including chance. They believe things happen because of their intentions and their skills (or lack of them) more than because of contributions from the environment. As a result, “there is a strong tendency to treat uncertainty as something to be resolved rather than estimated” (1994, pp. 37-38). He suggests that we treat uncertainty as a problem to be removed, as a way to control what is essentially uncontrollable. The stories of participants in Group 3 reveal an emphatic resolution of uncertainty through permanent solutions.

John Steinbrunner’s work in decision-making offers other possibilities for understanding the thinking processes used by participants as they made their choices about childbearing. This theory provides a template for examining how individuals at risk, and their spouses, make complex and emotional decisions under conditions of uncertainty. His model critiques analytic theories of decision making, theories that assume that people are capable of understanding and using probabilities. These theories also suggest that people integrate their

values, measuring different values on the same numerical scale, in everyday decisions and under conditions of uncertainty. He proposed that instead we tend to structure decisions around single values and to limit our search for information to a few variables. People also try to manage uncertainty by making “inferences of transformation (magical thinking), inferences of impossibility, and the use of simple analogies to anchor our logic, independent of evidence. (p. 116)

These quotations from HD research participants, especially those in Group 1, (the group who knew of their risk and decided to have children anyway, illustrate Steinbruner’s description of inferences of transformation (Steinbruner 1974). In transformation inference, decision-makers appear to be managing the uncertainty of their situations by projecting the risks of HD far into the future where surely lies the cure. This method of dealing with uncertainty in a complicated decision is a way of protecting participants’ belief that having children is a normal and a right thing to do from a negative interpretation that they and their children are at risk for Huntington’s disease.

These stories illustrate another feature of Steinbruner’s model of decision making: the complicating effect of involving more than one decision maker. He states, “It is very clear that one of the prime characteristics of human beings under uncertainty is that they bolster their judgments by the concurring opinions of other people.” (Steinbruner 1974 p.121). If the other person—the spouse in these stories—makes the same inferences about the situation, that a cure is in the near future, this concurrence strengthens the belief of the decision-maker. For example, in Lisa’s story, though she wanted children, she initially decided to adopt. However, her husband wanted biological children and influenced her with his belief that a cure would soon be found. This influence, intended or not, caused her to give in to her husband’s desire for children of his own. Despite her original misgivings, they had two children.

Ironically, while writing the final draft of this paper, the primary author received a phone call from a woman tested in 1991. The author describes the phone communication:

She had tested positive and had been diagnosed with HD in 2004. The purpose of her call, in her own words, was “to vent.” She said to me “I was given a lot of hope in 1991 when I was tested and I felt that not even I myself would have to deal with this disease.” She already had two children at the time of testing: a son, now 30, and a daughter, now 22. Neither of them is interested in testing nor is planning to have children, thus “depriving” her of grandchildren. She continued, “I don’t tell people I am on disability. I tell them I am retired. I am embarrassed and ashamed for my family and I don’t know how to tell people I have HD.” In essence, she called to express the fact that she felt she had been misled at the time she was tested to the point where she believed that a cure or treatment would be found to allow her, even though gene positive, to escape having to deal with developing HD. Curiously, even though the HD gene was found in 1993, (after her positive test), the fact that no treatment or cure had materialized diminished the importance of that major breakthrough in her eyes (Quaid, personal communication 2009).

All these stories demonstrate features of a complex decision made under conditions of great uncertainty. Their faith in the benevolence of science, reliance on what “they” will discover, sureness that cures will be forthcoming, and awaiting the miracles science will engineer, gives them permission to overlook the daunting odds enmeshed in decisions about having children. The combination of hope and trust in sophisticated technology provides these men and women a cognitive and emotional refuge as they make these terribly difficult decisions.

Significance And Implications For Practice

We think these stories illustrate a fine line to walk between offering hope to patients and families about the possibility of a treatment or cure, and making easy, and perhaps unfounded, predictions about when a treatment or cure might actually be found. In the face of the reality of the inexorable slowness of good science, we must try to encourage people facing a life-threatening illness like HD to support and trust genetic research while maintaining a realistic expectation about the availability of a cure or treatment in their lifetime or the lifetime of their children. At heart, many, if not most, genetic counselors share a love of science. We must pay close attention to the manner in which we frame our own beliefs in the power of research. We must attend carefully to messages sent by us, our research colleagues, dedicated fundraisers and family members who may have their own agendas. Only then can we more fully participate in helping families engage in mindful decision-making in a world of uncertainty, threat, and hope.

Limitations

One of the limitations of a study such as this is that there is, simply, too much information. To present the identified themes in a coherent manner, we made conscious decisions about which voices to include and which interviews to highlight. As a result of our choices, some data, by necessity, were not addressed. For this paper, we focused on stories about reproductive decision-making, which was only one question of many on our interview guide. Given the poignant narratives quoted here, these decisions are critically important to the participants.

PHAROS study participants are also likely to be a select subgroup of the population at risk for HD and choosing not to be tested. Individuals we interviewed were those who chose not to be tested but were comfortable enough with that decision, comfortable enough with their risk, and with themselves, to subject themselves to a neurological examination every nine months, some for as long as eight years. They were also comfortable enough to discuss such extremely personal decisions with a known health care professional.

We consider it a strength of this study that the interviewers were experienced clinicians who had known these participants for years and had, in many cases, taken care of their affected relatives. The interviewers were well-known and, we believe, trusted. We think that these ongoing relationships led to better interview data than a one-time experience with a stranger but these relationships may have influenced the interviews in unknown ways.

Research Recommendations

While childbearing and reproductive decision-making were not the sole focus of our original study, they were clearly important topics of conversation for our participants. Given the age of our participants, many would have been at least 30 years old when genetic testing (using direct gene testing) became available. Many already had their children by that age, making the issue of testing, at least for reproductive purposes, less salient. Today, genetic testing is rapidly moving into mainstream healthcare practice. It is uncertain whether the next generation of those at risk for HD and similar disorders will become more comfortable with the idea of testing, and with using that information to inform their childbearing decisions. Researchers should construct prospective, longitudinal, qualitative studies of young adults at risk as they begin to face important life choices. Such inquiry would make an invaluable contribution to the understanding of how individuals at risk use, or do not use, available technology. Studying young adults would provide insight into how their attitudes and choices about having their own children may change over time thus increasing awareness about which information is most helpful in maintaining the ability to hope for the future while understanding the realities of the present.

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Table 1

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Themes		
Group 1	Group 2	Group 3
Knew their risk, had children N=26	Didn't know their risk, had children N=15	Knew their risk, didn't have children N=10
Hoping for a Cure	Too little, too late	Vigilant Witness
Feeling Guilt	Getting it Wrong	Stopping HD
Magical Thinking		Being Alone
Just Another Something		