Two Decades of Huntington Disease Testing: Patient's Demographics and Reproductive Choices

Rebekah C. Krukenberg[1], Daniel L. Koller[2], David D. Weaver[2], Jennifer N. Dickerson[2], Kimberly A. Quaid[2]

[1]*Breast Care, Community Physician Network, Indianapolis, Indiana*

[2]*Department of Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, Indiana*

Running Title: Two Decades of Huntington Disease Testing

Correspondence to: Kimberly A. Quaid, PhD, Department of Medical and Molecular Genetics, IB130, Indiana University School of Medicine, 975 W. Walnut Street, Indianapolis, IN 46202-5251. E-mail: kquaid@iupui.edu. Telephone number: 317-278-4039. Fax number: 317-274-2390.

Journal of Genetic Counseling. 2013 Oct;22(5):643-53.
The final publication is available at: http://dx.doi.org/10.1007/s10897-013-9596-0

ABSTRACT

Predictive testing for Huntington disease (HD) has been available in the United States (US) since 1987, and the Indiana University Predictive Testing Program has been providing this testing since 1990. To date there has been no published description of those who present for such testing in the US. Here we describe demographics of 141 individuals and reproductive decision making of a subset of 16 of those individuals who underwent predictive HD testing between 1990 and 2010 at one site in the US. This study is a retrospective chart review of the "Personal History Questionnaire" participants completed prior to testing. As seen in other studies, most participants were female (64.5%), in their mid-30s (mean=34), and had at least one child prior to testing (54%). Multiple demographic datum points are described, and the reproductive decision making of these at-risk individuals was analyzed using Fisher's Exact Tests. Of those women who had children before learning of their risk to inherit HD, those who attended church more frequently, had three or more children total, or whose mother was affected with HD were more likely to be comfortable with their choice to have children. We conclude that these demographic factors influence the reproductive decision-making of individuals at risk for HD. Psychologists, clinical geneticists, and genetic counselors may be able to use this information to help counsel at-risk patients regarding current or past reproductive decision making.

Key Words: Huntington disease, reproduction, decision making, predictive testing, genetic counseling, patient demographic characteristics

INTRODUCTION

Huntington disease is an autosomal dominant, neurodegenerative disorder characterized by progressive movement, cognitive, and psychiatric disorders (Huntington 1872; Sturrock and Leavitt 2010; Walker 2007). The age of onset of symptoms is typically between 35 and 45, but symptoms have been seen as early as two years of age and have started as late as 80 (Huntington's Disease Collaborative Research Group 1993). The earliest findings of HD, which can begin years before a clinical diagnosis is made, can include problems with executive functions, increased fidgeting, apathy, restlessness, depression, obsessive behaviors, and mild chorea. These symptoms become progressively worse, usually over the course of 15 years or more, until the individual passes away, often from a recognizable infection or pneumonia. Prevalence estimates vary, but HD is thought to affect between seven and ten of every 100,000 Caucasians, with lower prevalences in other ethnicities (Sturrock and Leavitt 2010; Walker 2007). There is no cure for this devastating condition, although symptomatic management has been shown to improve and delay the progression of disease (Venuto et al. 2012).

HD is a triplet-repeat disorder caused by an increase in CAG repeats in the *HTT* gene on chromosome 4 (Huntington's Disease Collaborative Research Group 1993); greater than 40 CAG repeats leads to 100% penetrant HD, 36-39 repeats lead to incomplete penetrance and is designated as the "gray zone," and less than 35 repeats is considered unaffected (Rubinsztein et al. 1996). Predictive testing programs for HD were initiated in the late 1980's, originally using linkage analysis and progressing to direct gene testing after the gene was discovered in 1993. These programs now can provide information about an individual's risk for developing HD, although the disease severity and onset cannot be predicted with certainty. These testing

programs have strict protocols and follow guidelines set out by the United States Huntington's Disease Genetic Testing Group (2003).

Only between five and ten percent of those at risk for HD actually pursue presymptomatic testing (Dufrasne et al. 2011; Walker 2007). Now that accurate predictive testing has been available for almost two decades (Huntington's Disease Collaborative Research Group 1993), many predictive testing programs have begun to evaluate the demographics of their populations that present for presymptomatic testing. Published studies include centers in the Netherlands (van der Steenstraten et al. 1994); Germany, Austria, and Switzerland (Laccone et al. 1999); the United Kingdom (Harper et al. 2000); Victoria, Australia (Trembath et al. 2006); Mexico (Alonso et al. 2009); Montreal, Canada (Dufrasne et al. 2011); and Greece (Panas et al. 2011) but not the US. The common findings among these demographic studies are that more females request testing (64%-54.7%), with an average age of those requesting testing between 31.6 and 40.4 years. These studies have also found that most people requesting testing already have children (67%-57%), and that most have completed high school or some college (64%-43%) (Dufrasne et al. 2011; Panas et al. 2011; Trembath et al. 2006; van der Steenstraten et al. 1994).

A limited amount of research has been done on the reproductive decision making of people who carry an HD gene mutation or who are at 50% risk of HD. Richards and Rea (2005) found that after receiving their results, there was no difference in the number of pregnancies between those individuals who carried the mutation and those who did not. Decruyenaere et al. (2007) noted that over half (58%) of those who had positive presymptomatic testing had more children, while only 35% ceased having children after their positive result. In contrast, Evers-

Kiebooms et al. (2002) showed that after a predictive test, carrier individuals were significantly less likely to have more children than individuals who tested negative for the gene mutation.

Klitzman et al. (2007) performed a series of interviews with symptomatic and asymptomatic individuals, some of whom had been tested and others who had not. They concluded that, "In making these [reproductive] decisions, individuals weighed numerous, often competing, desires and concerns." Decisions to have children or for prenatal testing are likely very difficult ones for at-risk individuals to make and are not taken lightly by these individuals who understand the implications.

While multiple groups have aimed to describe the reproductive decision making of those at-risk for HD, no research has yet been done on what demographic factors are associated with the reproductive decisions of individuals who present for predictive testing.

The Indiana University Predictive Testing Program was started in 1990 and offers presymptomatic testing for individuals at risk for HD. This testing center is the only one of its kind in the state of Indiana and, with over 20 years of experience in testing, is one of the oldest in the country. The aim of this study is to describe 30 demographic factors of those individuals presenting to our center for testing, including personal, social, and HD-related characteristics. We will then investigate the relationship of many of these demographics to individuals' reproductive decision making, aiming to determine factors that may influence reproductive decisions in those at risk for HD.

METHODS

Sample

This study is a retrospective chart review of those individuals who presented for HD predictive testing at the Indiana University Predictive Testing Center between January 1, 1990

and December 31, 2010. Personal History Questionnaires distributed by the psychologist and director of the program were completed by most participants in the program and are the means by which data were extracted.

Instrumentation

Information was obtained through the Personal History Questionnaire, a seven-page, fill in the blank survey given to patients prior to presymptomatic testing. This questionnaire documents information on age, race, gender, family history of HD, marital status, number and ages of children, education level and grades in school, occupation and occupation history, income, who lives in the home, length of time in current residence and number of residences in the last 10 years, personal medical history, insurance status, use of alcohol and illicit drugs, personal and family history of psychiatric treatment and emotional/nervous problems, religion, social involvement in the community, number of close friends, when the risk of HD was discovered, and if decisions would have been changed regarding children if risk had been discovered earlier.

Procedures

This study received approval from the institutional review board (IRB) at Indiana University – Purdue University Indianapolis under the study number 1105-53 prior to the initiation of chart review. The informed consent process was waived by the IRB for this study. Personal History Questionnaires were extracted from patient charts for data entry and analysis by the first author; this process was not audited. Charts found to be without a Personal History Questionnaire were omitted from further analysis.

Data Analysis

The data from these questionnaires were compiled into a Microsoft Access database, and descriptive analysis was completed using Microsoft Excel and SAS version 9.2, SAS Institute Inc., Cary, NC USA. Data are presented as means for continuous variables and proportions for categorical variables. Proportional measures from the Indiana census data were compared to our data using a proportion test with normal approximation, and the Wilcoxon ranked sign test was employed for comparisons of median values. Tests of independence were performed using chi-square and Fisher's Exact Tests. Statistical significance was defined as a P-value less than 0.05.

RESULTS

The total number of predictive tests completed for HD in our center between 1990 and 2010 was 212. One hundred forty one of these individuals fully completed our Personal History Questionnaire. It is impossible to know from this limited chart review which of these individuals continued through our testing protocol and received results, or what their results were; however, the number of individuals receiving testing and the number completing the survey are detailed in Fig. 1. The year with the most surveys completed (n=17) was 1990, immediately after the predictive testing program opened. Since that time, the number of surveys has varied from year to year, with relative peak years occurring in 1997 (11 surveys) and 2007-2008 (8 surveys) (Fig. 1).

Demographics

The demographics of the 141 participants are summarized in Table I. Of note, nearly 65% of the individuals completing our survey were women, and nearly half of the participants (47.5%) were between the ages of 22 and 34. The vast majority of individuals completing the survey were Caucasian (98.6%). Also, 91.8% of individuals had health insurance at the time of completing the survey, 74.8% had life insurance, and 45.2% had disability insurance.

The social demographics of this population are summarized in Table II. Notable results from this table include that just over half (54%) already had children, while the remaining 46% did not have children. Also, a slight majority of individuals reported that they attended church never, rarely, or only on holidays (53.7%), while the remainder (46.3%) reported attending often or every week.

Lastly, the HD histories of these families are described in Table III. Seventy-three individuals filling out our survey had experienced HD by seeing their mother affected (51.8%), while 64 of the individuals had an affected father (45.4%) and four were unsure or did not have an affected parent (2.8%). The average age these individuals learned of their risk was nearly 21 years, and the average age that their parents had exhibited symptoms was just over 41 years of age. For those whose parents had already passed away, their average age of death was 55.7 years of age. Most reported that they had between two and five affected relatives (62.5%), while 23 individuals (16.9%) reported that only their parent was affected with HD.

Reproductive Decision Making

In order to evaluate reproductive decision making of the at-risk cohort, we reviewed responses to a series of survey questions regarding when the individual learned of their risk to inherit HD (before or after getting married/having children), and then if they would have changed any of their decisions regarding children if they had known of their risk earlier. The logical progression of these questions is shown as a flowchart in Fig. 2. A key survey question was, “Do you think you would have had children if you had known of your risk?”. This question should only have been answered by those who reported that they were unaware of their risk for HD before they had any children (Fig. 2).

We were interested in responses to this question from individuals who: a) had one or more children, b) reported to not be aware of their risk for HD before they had any of these children, and c) completed the reproductive decision-making portion of the questionnaire according to directions. Twenty-two individuals met these criteria. Six of these individuals answered that they were unsure whether or not they would have had children if they had known of their risk, despite the only answers available to them on the survey being "yes" and "no." These individuals were omitted from further analysis. This left a sample size of only 16, which limited the power of our study to detect modest effects of the measured responses upon reproductive choices.

In order to determine possible relationships between responses to this question and demographic factors for these specific 16 participants, including personal, social, and HD-related factors (Tables I-III), we conducted a series of Fisher's exact tests. Significant relationships were found for frequency of church attendance (p=0.016), number of children (p=0.018), and which of the participant's parents is/was affected with HD (p=0.025) (Table IV). The Fisher's exact scores for these datum points were 0.034, 0.036, and 0.044, respectively. We found that a greater percentage of individuals who reported they still would have had their children even if they had known of their risk for HD at the time of conception attended church more frequently, had three or more children, and/or had an affected mother. Conversely, a greater percentage of individuals who reported they would not have had any children had they known of their risk attended church less frequently or not at all, had only one or two children, and had an affected father (Table IV). The remainder of the datum points analyzed did not correlate significantly with reproductive decision making.

Comparisons

We compared the demographic data of our population (n=141) both to other published populations of individuals seeking predictive HD testing as well as the general population in the state of Indiana (Tables I & II). To compare our data to the Indiana population data, we used both proportion tests with normal approximation to the binomial as well as Wilcoxon ranked sign tests.

We found that our population that presented for testing (n=141) is overall similar to other populations of individuals who have pursued predictive testing for HD (Alonso et al. 2009; Dufrasne et al. 2011; Harper et al. 2000; Laccone et al. 1999; Panas et al. 2011; Trembath et al. 2006; van der Steenstraten et al. 1994), although we also studied new categories of data that we were unable to compare to other centers. Our proportion of females (64.5%) was slightly higher than in the Australian, British, Canadian, Eastern European, and Greek groups (57.8%, 58%, 57%, 58%, and 54.7%, respectively) (Dufrasne et al. 2011; Harper et al. 2000; Laccone et al. 1999; Panas et al. 2011; Trembath et al. 2006), but nearly the same as the Dutch and Mexican findings (64% and 63%) (Alonso et al. 2009; van der Steenstraten et al. 1994). Our average age (34.4) is similar to many other studies that have shown average ages of those requesting testing in their 30s (Alonso et al. 2009; Dufrasne et al. 2011; Harper et al. 2000; Laccone et al. 1999; Panas et al. 2011; van der Steenstraten et al. 1994). The number of individuals in our group with children (54%) is somewhat similar, although slightly lower, compared to studies in Australia and Canada, where 67% and 57%, respectively, had children (Dufrasne et al. 2011; Trembath et al. 2006).

We also compared much of our data to the Indiana state census from 2000 or 2010 (Tables I & II) (U.S. Census Bureau, 2000; 2010). Our population is significantly different from Indiana in that our population has a higher proportion of women and a higher proportion of white

individuals than Indiana. The age groups between the two populations are significantly different in that our population has an increased number of younger individuals (18-44) and Indiana has more of the older age groups (55 and older). Our proportion of those never achieving high school graduation (5.9%) is significantly lower than Indiana's proportion (17.9%), but the rest of the education levels are consistent between Indiana and our population. The unemployment rate in our population (4.4%) was not significantly different from unemployment rate in Indiana in 1999, which was 3.3%.

In addition, the type of relationship these individuals were in was also similar to the general population in Indiana, with the only discordant relationship status being those who were widowed. This is likely related to the age distribution of those presenting for testing versus the general population in Indiana. The proportion of individuals in our sample with health insurance (91.8%) is significantly increased from the proportion of individuals in Indiana who are insured (85.2%) (U.S. Census Bureau, 2000; 2010).

DISCUSSION

The purpose of this study was to describe the personal and social demographics, as well as the family histories of HD, of those who presented for predictive testing at our center. We also wanted to better understand how at-risk individuals viewed reproductive decision making in light of their risk for developing HD.

Overall, we found these data were similar to other studies analyzing those who presented for predictive HD testing. Our group, similar to other studies, showed a general predominance of females requesting testing, and we had more females present for testing than would be expected based on the general population. Multiple potential reasons for this predominance have been proposed, including that women are more invested in the reproductive decision-making process

and the rearing of children, women are more willing to make difficult decisions and deal with the consequences of those choices, and women may be better able to cope with negative results (Simpson et al. 1992; Taylor 2005). The reason for the predominance of Caucasians in our sample and the significantly increased proportion versus what would be expected in Indiana is most likely due to the fact that HD is primarily a Caucasian disease (Harper 1992).

Considering the average age of our population, the proportion of people in Indiana with health insurance, and the proportion of our group with chronic health concerns, our population appears over insured. Because these tests were not billed to insurance and individuals were not counseled to have health insurance in place prior to their appointment, the high insurance coverage could indicate concern over the ability to acquire insurance after receiving test results. Although the Genetic Information Nondiscrimination Act (GINA) (2008) now protects against health insurance prejudice, this was not the case before 2008, when most of these predictive tests were completed and when these concerns were more valid. These concerns may have been more likely to influence decision making regarding insurance coverage.

Regarding their family history of HD, more people presented for testing when their mother had been affected with HD than when their father had been affected. The reason for this difference is unknown, but could correspond with the fact that over 55% of this group learned of their risk for HD before they turned 18. It may be that living in a home with an affected mother may lead one to learn of their risk at a younger age, when the mother is first becoming affected.

Regardless of which parent was affected, the average age that a parent was affected was just over 41 years of age. This age of onset is similar to the average age of onset of HD, which has been found to be around 40 years of age (Foroud et al. 1999). These parents' average age of death, if they were deceased, was nearly 56 years, which corresponds to around a 15-year

survival rate, similar to the 10 to 20 year survival rate that has been previously reported (Roos et al. 1993). The vast majority of participants knew of more affected family members than just their parent, which could indicate that individuals were more likely to present for testing when they understood their own extended family history of this condition and had witnessed more than one example of the effects HD can have on an individual.

Individuals who understand their risk for HD and the autosomal dominant inheritance pattern of the disease are often faced with the difficult decision of whether or not to have children. There are several factors that influence this decision, and we attempted to quantify some of those factors in this study. First, we found that frequency of church attendance was the strongest factor associated with these individuals being comfortable with their decisions to have children. That is, a significantly greater percentage of individuals who attended church often or every week reported that even if they had known they were at risk when they had their children, still would have had them. Increased religious involvement has been shown to correspond with better coping mechanisms, improved stress control, better quality of life, less psychological distress, and an increased feeling of stability, while decreasing the rates of depression, suicide, anxiety, and substance abuse (Koenig 2009; Puchalski 2001). Also, higher levels of spirituality in individuals at risk for HD lead them to be more likely to report benefits from a family history of HD and undergoing testing for HD (Williams et al. 2010). At-risk individuals who attend church more frequently may be more prone to have an optimistic outlook on life and better coping mechanisms, leading them to be at peace with having children who could inherit the lethal condition for which they are also at risk. Further research is needed to investigate this hypothesis.

Another factor that was significant in reproductive decision making was the number of children an individual had. A greater percentage of participants who had three or more children reported they still would have had their children even if they had known of their risk, versus those individuals who had two children or less. This decision could be because those individuals who have three or more children may have been more likely to have decided they wanted many children long before they knew of their risk for HD, and the value they place on having children is a significant part of their identity. Those with fewer children may be more likely to consider the fact that they could have refrained from having children and thereby ceased the disease from spreading into the next generation of their family. These reasons are speculative and warrant further investigation.

Lastly, which parent was affected with HD was significantly related to whether or not those at risk reported they would have still decided to have children. A greater percentage of individuals whose mothers were affected with HD reported they would have decided to have children if they had known of their risk than those whose father was affected. It is known that growing up in a family with HD does not render solely negative effects on a child (Forrest Keenan et al. 2007); however, very little research has been done on the effects mothers versus fathers with HD have on the development, coping, and adjustment of their children. It has been shown that, regardless of which parent in a family is affected, frequently both parents in families with HD are dysfunctional (Vamos et al. 2007), and also that children raised by a parent with HD are less likely to be able to establish close bonds with their own children (Van der Meer et al. 2005). More research should be done to investigate gender differences in HD and the role gender plays in the dynamics of families with HD.

Study Limitations

While these data are novel and significant, there are multiple limitations to this study. We asked asymptomatic individuals to decide whether they would have had children if they had known of their risk for HD prior to having children. This decision is obviously not an easy one, and asking people what they *would* have done has its limitations. There is no way to know what these individuals actually would have done regarding children had they known of their risk earlier in life. This is merely what they *reported* they would have done. When a person is faced with hypothetical decisions, it is often impossible for them to predict how they will feel, what factors they will consider, and ultimately what decision they will make. Also, we analyzed only those who presented for presymptomatic testing. There is no way of knowing if the demographic factors that reached significance in our sample are the same factors that affect the decisions made by those at risk for HD who do not pursue predictive testing. It is also possible that if our cohort showed symptoms of HD at the time of the survey they would have made different statements about whether or not they still would have had their children.

Along with limitations based on the population of people we surveyed, there were also functional limitations. We had a limited sample size of individuals who presented for predictive testing, who did not know of their risk before they had children, and who filled out the rather complexly worded survey correctly and in its entirety. This left our sample size at only 16. The statistical relationships we report from this exploratory sample in Table IV ($p=0.016$ or greater) do not achieve stringent alpha levels consistent with a full multiple comparison correction, but this is not surprising given the sample size available. In addition, there may have been more individuals who felt unsure in response to the question regarding whether or not they would have had children (which would have omitted them from our analysis), but chose either “yes” or “no” because there was no “unsure” option on the questionnaire. Also, because of the low uptake of

predictive testing for HD in general, there is no way of knowing if these data are representative of all individuals at risk for HD who had children before learning of their risk. Also, these results were collected from one center in Indianapolis, Indiana. There is a possibility that in other parts of the world, or even in the United States, people would have made their reproductive decisions based on very different criteria than were found in this study.

There is also the possibility that not all of these individuals were fully aware their children were at a 50% risk of inheriting the condition. Quaid et al. (2010) recently described that those who have children before they know of their risk for HD often do not understand their risk fully until after they have children or have inaccurate information regarding inheritance, either from other family members or an uninformed healthcare provider. This survey was filled out before the individuals received counseling regarding the condition and its inheritance pattern; people may have answered differently if they had been previously unaware of the exact risk to their children.

Research Recommendations

We believe that there is a need for more studies on the factors that influence these individuals' reproductive decisions. Further studies to confirm our tentative findings should include a wider geographical area in order to compare those at risk in different areas of the United States and the world. Also, in order to truly characterize which factors are significant, similar studies should be done of those at risk who decide against testing as well those who have completed testing. Longer-term or follow-up studies could be done to analyze the proportion of individuals who go on to have more children even if it contradicts what they reported at the time of testing.

Practice Implications

The implications of this study are twofold. First, it has been demonstrated that knowing some basic demographic information about individuals at risk for HD may aid researchers and medical professionals in deciphering how these patients may be feeling about having children. While individuals should never be stereotyped or assumed to be feeling a certain way, these data may help practitioners to better understand the factors that contribute to an individual's decisions and may also help an individual come to terms with aspects of their life that may have a role in their decision making. Second, while genetic counselors and psychologists should always respect individuals' reproductive decisions, these data further indicate that there are many demographic and social factors that may impact these decisions. These data may help supply healthcare providers with potential questions or issues to consider while they are discussing reproductive decision making with those at risk for HD.

ACKNOWLEDGEMENTS

We thank the patients who presented for HD predictive testing for their time and effort to complete this survey, along with the HD community at large for their support of ongoing research.

REFERENCES

Alonso, M.E., Ochoa, A., Sosa, A.L., Rodriguez, Y., Chavez, M., Boll, C., Yescas, P., Macias, R., & Rasmussen, A. (2009). Presymptomatic diagnosis in Huntington's disease: The Mexican experience. *Genetic Testing amd Molecular Biomarkers, 13,* 717-720.

Decruyenaere, M., Evers-Kiebooms, G., Boogaerts, A., Philippe, K., Demyttenaere, K., Dom, R., Vandenberghe, W., & Fryns, J.P. (2007). The complexity of reproductive decision-making in asymptomatic carriers of the Huntington mutation. *European Journal of Human Genetics, 15,* 453-462.

Dufrasne, S., Roy, M., Galvez, M., & Rosenblatt, D.S. (2011). Experience over fifteen years with a protocol for predictive testing for Huntington disease. *Molecular Genetics and Metabolism, 102,* 494-504.

Evers-Kiebooms, G., Nys, K., Harper, P., Zoeteweij, M., Dürr, A., Jacopini, G., Yapijakis, C., & Simpson, S. (2002). Predictive DNA-testing for Huntington's disease and reproductive decision making: A European collaborative study. *European Journal of Human Genetics, 10,* 167-176.

Foroud, T., Gray, J., Ivashina, J., & Conneally, P.M. (1999). Differences in duration of Huntington's disease based on age at onset. *Journal of Neurology, Neurosurgery, and Psychiatry, 66,* 52-56.

Forrest Keenan, K., Miedzybrodzka, Z., van Teijlingen, E., McKee, L., & Simpson, S.A. (2007). Young people's experiences of growing up in a family affected by Huntington's disease. *Clinical Genetics, 71*, 120-129.

Genetic Information Nondiscrimination Act of 2008 § 42 U.S.C. §1635 (2008).

Harper, P.S. (1992). The epidemiology of Huntington's disease. *Human Genetics, 89,* 365-376.

Harper, P.S., Lim, C., & Craufurd, D. (2000). Ten years of presymptomatic testing for Huntington's disease: The experience of the UK Huntington's Disease Prediction Consortium. *Journal of Medical Genetics, 37*, 567-571.

Huntington's Disease Collaborative Research Group. (1993). A novel gene containing a trinucleotide repeat that is expanded and unstable on Huntington's disease chromosomes. *Cell, 72*, 971-983.

Huntington, G. (1872). On chorea. In Yudofsky, S.C. *The Journal of Neuropsychiatry and Clinical Neurosciences, 15,* 109-112. (Reprinted from *The medical and surgical reporter: A weekly journal, 26,* 317-321).

Klitzman, R., Thorne, D., Williamson, J., Chung, W., & Marder, K. (2007). Decision-making about reproductive choices among individuals at-risk for Huntington's disease. *Journal of Genetic Counseling, 16,* 347-362.

Koenig, H.G. (2009). Research on religion, spirituality, and mental health: A review. *Canadian Journal of Psychiatry, 54,* 283-291.

Laccone, F., Engel, U., Hollinski-Feder, E., Weigell-Weber, M., Marczinek, K., Nolte, D., Morris-Rosendahl, D.J., Zühlke, C., Fuchs, K., Weirich-Schwaiger, H., Schlüter, G., von Beust, G., Vieira-Saecker, A., Weber, B.H.F., & Riess, O. (1999). DNA analysis of Huntington's disease: Five years of experience in Germany, Austria, and Switzerland. *Neurology, 53,* 801-806.

Panas, M., Karadima, G., Vassos, E., Kalfakis, N., Kladi, A., Christodoulou, K., & Vassilopoulos, D. (2011). Huntington's disease in Greece: The experience of 14 years. *Clinical Genetics, 80,* 586-590.

Puchalski, C. (2001). The role of spirituality in health care. *Baylor University Medical Center Proceedings, 14,* 352-357.

Quaid, K.A., Swenson, M.M., Sims, S.L., Harrison, J.M., Moskowitz, C., Stepanov, N., Suter, G.W., & Westphal, B.J. (2010). What were you thinking?: Individuals at risk for Huntington disease talk about having children. *Journal of Genetic Counseling, 19,* 606-617.

Richards, F.H., & Rea, G. (2005). Reproductive decision making before and after predictive testing for Huntington's disease: an Australian perspective. *Clinical Genetics, 67,* 404-411.

Roos, R.A.C., Hermans, J., Vegter-van der Vlis, M., van Ommen, G.J.B., & Bruyn, G.W. (1993). Duration of illness in Huntington's disease is not related to age at onset. *Journal of Neurology, Neurosurgery, and Psychiatry, 56,* 98-100.

Rubinsztein, D.C., Leggo, J., Coles, R., Almqvist, E., Biancalana, V., Cassiman, J.J., Chotai, K., Connarty, M., Craufurd, D., Curtis, A., Curtis, D., Davidson, M.J., Differ, A.M., Dode, C., Dodge, A., Frontali, M., Ranen, N.G., Stine, O.C., Sherr, M., Abbott, M.H., Franz, M.L., Graham, C.A., Harper, P.S., Hedreen, J.C., Jackson, A., Kaplan, J.C., Losekoot, M., MacMillan, J.C., Morrison, P., Trottier, Y., Novelletto, A., Simpson, S.A., Theilmann, J., Whittaker, J.L., Folstein, S.E., Ross, C.A., & Hayden, M.R. (1996). Phenotypic characterization of individuals with 30-40 CAG repeats in the Huntington disease (HD) gene reveals HD cases with 36 repeats and apparently normal individuals with 36-39 repeats. *American Journal of Medical Genetics, 59,* 16-22.

Simpson, S.A., Besson, J., Alexander, D., Allan, K., & Johnston, A.W. (1992). One hundred requests for predictive testing for Huntington's disease. *Clinical Genetics, 41,* 326-330.

Sturrock, A., & Leavitt, B.R. (2010). The clinical and genetic features of Huntington disease. *Journal of Geriatric Psychiatry and Neurology, 23,* 243-259.

Taylor, S. (2005). Gender differences in attitudes among those at risk for Huntington's disease. *Genetic Testing and Molecular Biomarkers, 9,* 152-157.

Trembath, M.K., Tassicker, R.J., Collins, V.R., Mansie, S., Sheffield, L.J., & Delatycki, M.B. (2006). Fifteen years of experience in predictive testing for Huntington disease at a single testing center in Victoria, Australia. *Genetics in Medicine, 8,* 673-680.

U.S. Census Bureau. (2000). *Indiana Summary Tables*. Retrieved 2012 from http://factfinder2.census.gov.

U.S. Census Bureau. (2010). *American FactFinder Sheet: Indiana.* Retrieved 2012 from http://factfinder.census.gov.

United States Huntington's Disease Genetic Testing Group. (2003). *Genetic testing for Huntington's disease: Its relevance and Implications (Revised).* United States of America: Huntington's Disease Society of America.

Vamos, M., Hambridge, J., Edwards, M., & Conaghan, J. (2007). The impact of Huntington's disease on family life. *Psychosomatics, 48,* 400-404.

Van der Meer, L., Timman, R., Trijsburg, W., Duisterhof, M., Erdman, R., Van Elderen, T., & Tibben, A. (2006). Attachment in families with Huntington's disease a paradigm in clinical genetics. *Patient Education and Counseling, 63,* 246-254.

van der Steenstraten, I.M., Tibben, A., Roos, R.A.C., van de Kamp, J.J.P., & Niermeijer, M.F. (1994). Predictive testing for Huntington disease: Nonparticipants compared with participants in the Dutch program. *American Journal of Human Genetics, 55,* 618-625.

Venuto, C.S., McGarry, M., Ma, Q., & Kieburtz, K. (2012). Pharmacologic approaches to the treatment of Huntington's disease. *Movevment Disorders, 27,* 31-41.

Walker, F.O. (2007). Huntington's disease. *Seminars in Neurology, 27,* 143-150.

Williams, J.K., Erwin, C., Juhl, A., Mills, J., Brossman, B., & Paulsen, J.S. (2010). Personal factors associated with reported benefits of Huntington disease family history or genetic testing. *Genetic Testing and Molecular Biomarkers, 14,* 629-636.

Table I Basic Demographics

Variable	Number	Percentage	Indiana Census (2000)
Gender (N=141)			
Women	91	64.5%	51.0%*
Men	50	35.5%	49.0%*
Age (N=141)[a]			
18-24	23	16.3%	10.1%*
25-34	56	39.7%	12.8%*
35-44	40	28.4%	12.9%*
45-54	17	12.0%	14.6%
55-64	2	1.4%	11.9%*
>65	3	2.1%	13.0%*
Average Age (N=141)			
Male	34.78		
Female	34.15		
Overall	34.38		Median = 35.2
Race (N=141)			
Caucasian	139	98.6%	87.5%*
Black	1	0.7%	8.4%*
Other	1	0.7%	4.1%*
Education (N=135)[b]			
Did not complete high school	8	5.9%	17.9%*
Graduated high school	61	45.2%	37.2%
Some college	30	22.2%	25.5%
Bachelor's degree	19	14.1%	12.2%
Master's degree	14	10.4%	7.2%
Doctorate degree	3	2.2%	
Grades Received (N = 135)			
Honor Roll – A's	29	21.5%	
Above Average – B's	64	47.4%	
Average – C's	36	26.7%	
Below Average – D's	4	3.0%	
Poor – F's	1	0.7%	
Average Length of Occupation (years) (N=115)	7.13		
Number of Jobs in Last Five Years (N=123)			
0	9	7.3%	
1	52	42.3%	
2	38	30.9%	
3	15	12.2%	
4	3	2.4%	
5	0	0%	
6	3	2.4%	
7	2	1.6%	
8	1	0.8%	
Occupation (N=134)			
Academic	9	6.7%	
Professional	61	45.5%	
Clergy	1	0.7%	
Skilled	23	17.2%	

Unskilled	14	10.4%	
Unemployed	3	2.2%	3.3%
Homemaker	10	7.5%	
Student	11	8.2%	
Retired	2	1.5%	
If Unemployed, Current Status (N=134)			
Looking for work	3	2.2%	
Student	10	7.5%	
Disabled	2	1.5%	
Temporarily laid off	1	0.75%	
Full-time homemaker	10	7.5%	
Other (summer job)	1	0.75%	
N/A	107	79.8%	
Approximate Total Household Income (N=120)		Average=$43,926	Median = $41,567
$10,000 or less	6	5%	
$10,001 - $20,000	16	13.3%	
$20,001 - $30,000	29	24.2%	
$30,001 - $40,000	16	13.3%	
$40,001 - $50,000	15	12.5%	
$50,001 - $60,000	9	7.5%	
$60,001 - $70,000	6	5%	
$70,001 - $80,000	15	12.5%	
$80,001 - $90,000	3	2.5%	
$90,001 - $100,000	2	1.7%	
More than $100,000	3	2.5%	
Length of Time in Residence (years) (N=132)[a]		Average = 6.59	
Less than 1 year	16	12.1%	15.4%
1-2 years	10	7.6%	
2-3 years	18	13.6%	
3-4 years	15	11.4%	
4-5 years	9	6.8%	
5 years or more	64	48.5%	
Number of Moves in Last Ten Years (N=133)		Average = 3.02	
0	25	18.8%	
1	34	25.6%	
2	11	8.3%	
3	28	21.0%	
4	13	9.8%	
5	12	9.0%	
6	4	3.0%	
7 or more	6	4.5%	
Other Health Concerns (N=120)			
Reported	44	36.7%	
None reported	76	63.3%	
Insurance Status (N=135)[a]			
Health insurance	124	91.8%	85.2%*
Life insurance	101	74.8%	
Disability insurance	61	45.2%	

a – 2010 Indiana census data used; 2000 Indiana census data unavailable or formatted in categories which were unusable.
b – In the 2000 Indiana census these data were only collected on individuals 25 years of age and older.
* - $P<0.05$, indicating that the study population and the Indiana population are significantly different

Table II Social Demographics

Variable	Number	Percentage	Indiana Census (2000)
Marital Status (N=136)			
Single, never married	38	27.9%	24.8%
Married	83	61.0%	56.3%
Separated	1	0.7%	1.3%
Divorced	13	9.6%	10.9%
Widowed	1	0.7%	6.6%*
Average Length of Marriage in Years (N=82)	12.45		
Avg. Number of Previous Marriages (N=30)	1.2		
Number of Children (N=137)			
0	63	46.0%	
1 or more	74	54.0%	
Currently Residing with (N=133)			
Parents	10	7.5%	
Spouse	79	59.4%	
Opposite-sex partner	13	9.8%	
Other relative(s)	9	6.8%	
Roommate(s)	9	6.8%	
Alone	11	8.3%	
Other	2	1.5%	
Frequency of Alcohol Consumption (N=136)			
Never	51	37.5%	
Once a week or less	69	50.7%	
Several times per week	11	8.1%	
Once per day	4	2.9%	
Several times per day	1	0.7%	
Number of Drinks per Session (N=82)			
1 or less	15	18.3%	
2	33	40.2%	
3	17	20.7%	
3.5	2	2.4%	
4	4	4.9%	
5	4	4.9%	
6	4	4.9%	
7	2	2.4%	
“very little”	1	1.2%	
Ever Seen for Nervous/Emotional Issues (N=136)			
Yes	57	41.9%	
No	79	58.1%	
Ever Seen a Therapist/Counselor (N=135)			
Yes	40	29.6%	
No	95	70.4%	
Frequency of Church Attendance (N=132)			
Never	27	20.4%	
Very rarely	28	21.2%	
Only on holidays	16	12.1%	
Often	22	16.7%	
Every week (or more often)	39	29.5%	
Number of Close Friends/Confidants (N=128)			

0	4	3.1%
1-5	75	58.6%
6-10	34	26.6%
11-15	9	7.0%
>15	6	4.7%

* - P<0.05, indicating that the study population and the Indiana population are significantly different

Table III - Huntington Disease Demographics

Variable	Number	Percentage
Parent with HD (N=141)		
Mother	73	51.8%
Father	64	45.4%
Other relative	4	2.8%
Age when Learned of Risk (N=132)		Average = 20.93
18 or younger	73	55.3%
19-30	29	22.0%
31-50	29	22.0%
Over 50	1	0.8%
Affected Parent's Age of Onset (N=133)		Average = 41.33
21-30	22	16.5%
31-40	42	31.6%
41-50	37	27.8%
51-60	18	13.5%
61-70	3	2.3%
Unsure or N/A	11	8.3%
Affected Parent's Age of Death (N=131)		Average (70) = 55.7
21-30	1	0.8%
31-40	4	3.0%
41-50	20	15.3%
51-60	21	16.0%
61-70	14	10.7%
71-80	6	4.6%
Over 80	1	0.8%
Unsure	3	2.3%
N/A	61	46.6%
Number of Known Affected Relatives (N=136)		Average = 3.81
1 (parent only)	23	16.9%
2-5	85	62.5%
6-10	26	19.1%
Over 10	2	1.5%

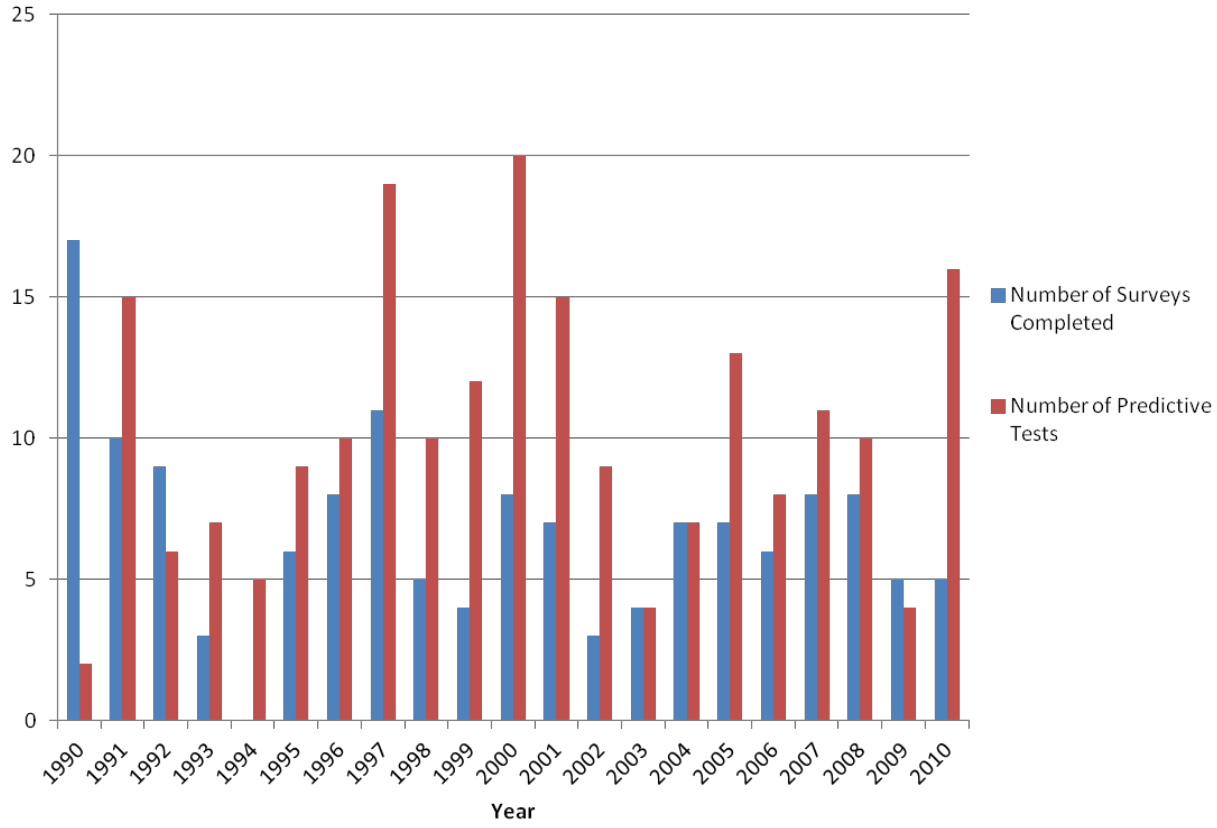
Table IV – Segregation of Demographic Factors with Reproductive Decisions with Regards to the "Key Question"

Variable (n, out of 16)	Those who still would have had their children (% of total yes [6])	P-value (n=16)
Frequency of Church Attendance		
Never/Rarely/Holidays (6)	0 (0%)	0.016
Often/Weekly (10)	6 (100%)	
Number of Children		
1 or 2 (11)	2 (33%)	0.018
3 or more (5)	4 (67%)	
Which Parent Affected[a]		
Mother (10)	6 (100%)	0.025
Father (5)	0 (0%)	
Seen a Therapist/Counselor		
Yes (4)	0 (0%)	0.074
No (12)	6 (100%)	
Insurance Status		
Health (3)	1 (17%)	0.149
Health/Life (6)	4 (67%)	
Health/Life/Disability (7)	1 (17%)	
Frequency of Alcohol Consumption		
Never (7)	4 (67%)	0.152
Once per week or more (9)	2 (33%)	
Sex		
Male (5)	1 (17%)	0.329
Female (11)	5 (83%)	
Type of Occupation		
Academic/Professional (8)	3 (50%)	0.419
Skilled/Unskilled (5)	1 (17%)	
Unemployed/Homemaker (3)	2 (33%)	
Grade of School Completed		
≤12 (6)	3 (50%)	0.424
12-18 (10)	3 (50%)	
Date of Survey		
1991 – 1995 (3)	2 (33%)	0.515
1996 – 2000 (6)	2 (33%)	
2001 – 2005 (5)	1 (17%)	
2006 – 2010 (2)	1 (17%)	
Average Grades in School		
As and Bs (12)	4 (67%)	0.551
Cs and Ds (4)	2 (33%)	
Yearly Income[b]		
<$40,000 per year (9)	4 (67%)	0.667
>$40,000 per year (6)	2(33%)	
Age when Parent Affected with HD[c]		
<50 (5)	2 (33%)	0.690

>50 (9)	4 (67%)	
Unsure (1)	0 (0%)	
Age when Learned of Risk for HD		
<35 (7)	3 (50%)	0.696
≥35 (9)	3 (50%)	
Number of Close Friends		
1 through 5 (10)	4 (67%)	0.789
6 through 10 (6)	2 (33%)	
Age		
18-44 (10)	4 (67%)	0.789
45 and older (6)	2 (33%)	
Affected Parent Living[c]		
Yes (7)	3 (50%)	0.833
No (8)	3 (50%)	
Number of Affected Relatives		
1 – 4 (13)	5 (83%)	0.869
5 – 8 (3)	1 (17%)	
Seen for Emotional/Nervous Issues		
Yes (6)	2 (33%)	0.889
No (10)	4 (67%)	
Age of Parent's Death[c]		
<65 (3)	1 (17%)	0.961
>65 (5)	2 (33%)	
Alive (7)	3 (50%)	

a – one individual was unsure which parent was affected
b – only 15 responses received for this question
c – one individual was adopted and unsure of this information

Figure 1



Number of individuals who completed the personal history questionnaire during each year of the study period.

Figure 2

Flowchart of reproductive decision-making questions asked. ┼ indicates our key question, which was used to analyze how people made their reproductive decisions.