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Huntington Disease: Disclosure and Future Decision-Making in Romantic Relationships

THESIS

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for the degree of

MASTER OF SCIENCE

in Genetic Counseling

by

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DEDICATION

To Don and Ginney

Thank you for sharing your HD journey and life experiences with me.
Your openness and interest is what shaped this thesis in its beginning stages.
Both of you are inspiring and such an encouragement
to all who know and love you.

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ABSTRACT OF THE THESIS

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Huntington's disease (HD) is an autosomal dominant progressive neurodegenerative condition which affects an individual's behavior, cognition, and movement. Since HD is typically an adult-onset condition, although a minority of cases have been observed to fall outside of this age range, most individuals are involved in romantic relationships, marriage, and reproduction, before the onset of symptoms. How and when individuals with, or at risk for, HD approach dating, relationships, disclosure, and life decisions with their romantic partners is a topic that has not been well documented in the literature. This study analyzed 160 individuals both at risk for and diagnosed with HD, as well as their romantic life partners regarding the subject of disclosure and its impact on reproductive decisions including family planning and *in vitro fertilization* with preimplantation genetic testing for monogenic disorders (*IVF*/PGT-M). The general findings of this anonymous online survey revealed that participants agreed, regardless of being at risk or diagnosed with HD or the romantic partners of these individuals, that disclosure should occur in the beginning of the relationship and should include information about HD's symptoms, the romantic partners' caregiving aspect, as well as the inheritance pattern and its impacts on family planning. Interestingly, a majority of the participants ranked altered behavior and personality as the most important component in a disclosure to a romantic

partner. The factors of inheritance as well as HD's symptoms and lifestyle were considered very important when making family planning decisions, particularly with those who reported having no children. When surveyed about *IVF*/PGT-M, a substantial proportion of respondents indicated they would not consider using these procedures. While cost was the main barrier, some individuals also stated that they would not consider having any children irrespective of other barriers, due to not wanting their children to have a parent with HD. The information collected in this study gives healthcare providers, including genetic counselors, insight into disclosure and factors considered by those affected and at risk for HD, as well as their romantic partners, as they consider their future together.

1. INTRODUCTION

1.1 Background of Huntington Disease

Huntington disease (HD) is an inherited neurodegenerative condition which mainly affects an individual's movement, cognition, and behavior. Chorea is one of the characteristic features of HD and is seen in over 90% of affected individuals (Snowden, 2017; Caron et al., 2018). The condition was originally named Huntington's Chorea after Dr. George Huntington who described the condition. In his original article published in the Medical and Surgical Reporter of Philadelphia on April 13th, 1872, Dr. Huntington outlined the typical presentation of chorea and emphasized the particularities of a rare "hereditary chorea" which included "1. It's hereditary nature. 2. A tendency to insanity and suicide. 3. Its manifesting itself as a grave disease only in adult life." (Huntington, 1872). His observations led to the designation of what is now called Huntington disease.

In addition to chorea, affected individuals' motor functions are gradually impaired and they experience clumsiness, bradykinesia, rigidity, dystonia, motor control issues, and gait issues (McColgan & Tabrizi, 2017). They also experience oculomotor disturbances including ocular saccades, slow and hypometric saccades, and issues with gaze fixation (Blekher et al., 2006; Golding et al., 2006). Dysarthria often occurs early on during the progression of HD while dysphagia usually occurs in later stages of HD.

Individuals with HD experience significant behavioral changes which affect their personality including depression, obsessive-compulsiveness, apathy, anxiety, and psychosis (McColgan & Tabrizi, 2017). Apathy is the most common behavioral symptom and occurs in approximately 28% of patients with HD, while psychosis is less common and only occurs in approximately 1% (McColgan & Tabrizi, 2017). These behavioral changes are also referred to as

psychiatric symptoms in the scientific literature. These symptoms do not tend to progress with the course of HD which differs from the movement and cognition symptoms (Unti et al., 2016). Depression is an aspect of the behavioral changes which requires specific attention. Studies have shown that the incidence of depression is more than doubled when HD is involved (Marshall et al., 2007). Suicide risk is highest when individuals first receive their HD diagnosis and when they become symptomatic up to the point of losing their independence (Eddy et al., 2016). Due to this known risk, it is imperative that individuals receive proper support especially during those times.

There is a progressive decline in cognition seen in all affected individuals including memory deficits and forgetfulness which are typically part of the first symptoms. Regarding memory deficits, there are impaired recall and recognition skills. Patients with HD have poorer recall than recognition (Snowden 2017). There is a clear distinction between these with an example of recall being the ability to answer a free response question and recognition being the ability to answer a multiple-choice question. As the condition progresses, there are markedly slower thought processes, impaired visuospatial abilities, and issues with emotional recognition (McColgan & Tabrizi, 2017). There is also a decline in executive functions which includes problems with planning, organization and sequencing, cognitive flexibility and set shifting, as well as multi-tasking (Snowden, 2017).

Individuals with HD experience a range of these symptoms throughout the course of their condition. Some of the early symptoms can include depression, mood swings, minor twitching, and lapses in judgement and memory. However, affected individuals are able to continue living independently and sometimes individuals may not even know that they are affected in the early stages. As the course of the condition progresses, the motor symptoms are the most noticeable of

HD's manifestations. Affected individuals usually require more assistance in their everyday life due to issues with their walking, balance, and swallowing as well as general weakness and speech difficulties. Once an individual is in the late stages of HD, they are typically unable to walk or talk and all the previously mentioned symptoms are very severe.

As Dr. Huntington observed, HD's symptoms occur during an individual's adult years with the average age of onset being around 40 years old with an average survival period of 15 to 20 years after onset (Snowden, 2017). Cases have also been documented where the age of onset and survival period after the onset of symptoms falls outside of these ranges (Snowden, 2017). Approximately 25% of affected individuals experience a milder course of HD with later age of onset, sometimes after age 70, and a smaller range of symptoms including chorea, gait disturbances, and dysphagia. Fewer than 10% of affected individuals fall outside the typical range due to experiencing a more severe course of HD known as Juvenile HD (Nance, 2007). This includes an earlier onset of symptoms, before age 20, and average survival of 10 to 20 years after onset.

1.2 Inheritance and Genetics of Huntington Disease

HD is an autosomal dominant condition which typically means inheriting one abnormal copy of the *HTT* gene will cause the individual to be affected. Every person has two copies for every gene, with one copy inherited from their mother and the other copy inherited from their father. When an individual carrying the abnormal copy has children, each child has a 50% chance of inheriting the abnormal copy of the *HTT* gene.

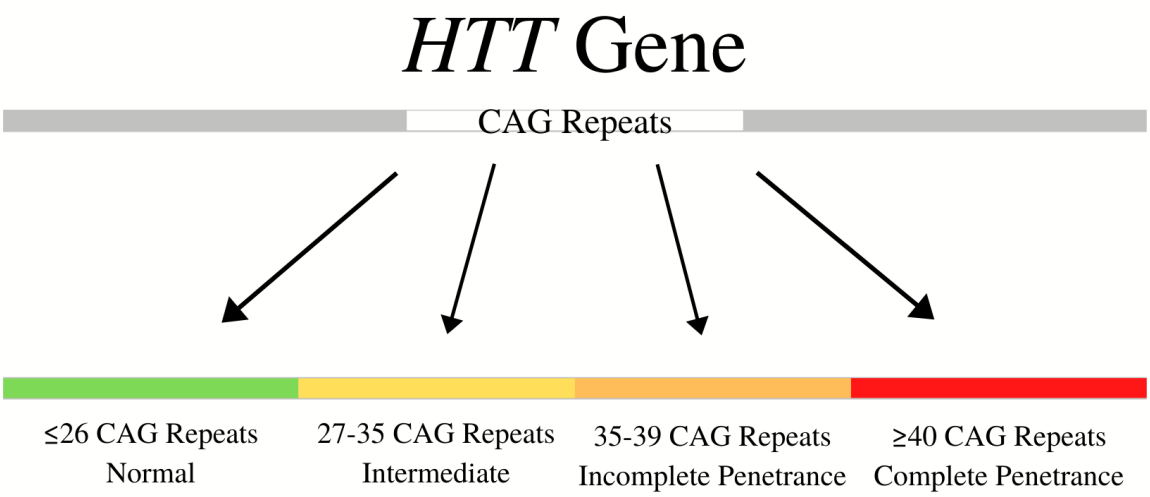
HD is inherited through a trinucleotide CAG repeat expansion within the *HTT* gene which is located on chromosome 4. This gene encodes the huntingtin protein (The Huntington's

Disease Collaborative Research Group, 1993). When the CAG expansion exceeds 39 repeats, the huntingtin protein's polyglutamine tract is expanded into disease range. The exact function of the huntingtin protein is not completely understood, although insights have emerged showing it can function as a cellular scaffold protein involved in numerous processes including oxidative DNA damage repair mechanisms, autophagy, and cancer (Thion & Humbert, 2018; Maiuri et al., 2017; Ochaba et al., 2014). CAG repeats are unstable and may expand as they are passed down through generations and are more likely to expand when passed down through an affected father rather than an affected mother (Nance, 2007). Larger CAG repeats are also more likely to expand when passed down in subsequent generations. Each of these subsequent generations may also experience an earlier and earlier age of onset in what is known as anticipation (McColgan & Tabrizi, 2017).

There is a generally accepted clinical categorization for HD that is based on the number of CAG repeats an individual carries (Figure 1). An unaffected individual carries 26 or less CAG repeats which is considered to be within the normal range (McColgan & Tabrizi, 2017; Nance, 2017). When the CAG repeat is between 27 and 35 repeats, this is considered the intermediate range where individuals will not develop HD symptoms (McColgan & Tabrizi, 2017). This range has also been referred to as the gray zone or premutation category (Nance, 2017). When the CAG repeat expands to between 36 and 39 repeats, this is considered the incomplete, or reduced, penetrance range (McColgan & Tabrizi, 2017). Some of these individuals may experience symptoms at a later age than is typical for an individual with HD, however others may never exhibit symptoms (Nance, 2017). Once the CAG repeat reaches 40 repeats, the individual will be affected by HD due to complete penetrance (McColgan & Tabrizi, 2017). In less than 10% of cases, individuals under the age of 20 years old will be affected with HD. These individuals have

juvenile-onset HD and typically have more than 50 CAG repeats (Nance 2017). There is generally an inverse relationship between the size of the CAG repeat expansion and the age of onset, accounting for approximately 56% of the variability in age of onset in individuals (McColgan & Tabrizi, 2017).

FIGURE 1. CAG REPEAT EXPANSION IN *HTT* GENE



Due to the autosomal dominant inheritance of HD, an affected individual has a 50% chance of passing the condition to each of their children. However, depending on how many CAG repeats are inherited, an individual with an intermediate expanded number of CAG repeats will not experience symptoms of HD themselves but their children may be affected. This can happen if the CAG repeat expands into the disease range when it is inherited by their children. For an individual who is within the incomplete penetrance range, their children have a 50% chance of inheriting the abnormal CAG repeat. This may remain the same repeat length as the parent, with no risk of manifesting HD, or the repeat could expand further into the incomplete penetrance range or even the full penetrance range. An individual who is within the incomplete penetrance range may have a child who inherits the same expanded CAG repeat but is not

necessarily affected by HD since those within this range do not always experience symptoms (McColgan & Tabrizi, 2017). If that CAG repeat expands further into the complete penetrance range, then they will be affected by HD (McColgan & Tabrizi 2017; Nance 2017).

1.3 Modifiers for HD

Studies have shown that there are genetic modifiers that can alter HD's age-of-onset for a given individual. As discussed above, the number of CAG repeats determines what category an individual falls into which determines approximately their HD risk and what the recurrence risks are for their children. The CAG repeat length also accounts for approximately 65% of age-of-onset (Keum et al., 2016).

One of these modifiers involves CAA interruptions within the CAG repeat itself. An individual can have zero, one, or two CAA interruptions. However, the majority (>95%) of individuals with European ancestry carry one CAA interruption (Wright et al., 2019). Research has shown that the number of uninterrupted CAG repeats acts as a modifier for the age of onset in a given individual (Genetic Modifiers of Huntington's Disease Consortium, 2019). This was supported by data that showed individuals who did not carry any CAA interruptions had an association with an earlier age of onset of 25 years on average (Wright et al., 2019). When an individual has a duplication of the CAA interruption, an association was noted that these individuals have a delayed age of onset of 4 years on average (Wright et al., 2019). These CAA interruptions can lead to a misinterpretation of the number of CAG repeats. This can be important when interpreting a CAG repeat size in a given individual when they are in less informing ranges such as the intermediate or reduced penetrance categories (Genetic Modifiers

of Huntington's Disease Consortium 2019). While these modifiers are important, it is rather rare in the general population to have either zero or two CAA interruptions (Wright et al., 2019).

Research has uncovered genetic modifiers in completely different chromosomes than chromosome 4 where the *HTT* gene is located. Two of these modifiers are located on chromosomes 8 and 15. These appear to modify the onset of HD's symptoms (McColgan and Tabrizi 2017). There is an "onset-hastening" allele modifier on chromosome 8 and both "onset-hastening" and "onset-delaying" alleles on chromosome 15 which collectively account for approximately 1.6% of the variance in the age of onset for HD (Long *et al.* 2018).

There are additional genes on other chromosomes that have been associated with affecting the age of onset, DNA mismatch repair, and DNA maintenance (Genetic Modifiers of Huntington's Disease Consortium 2019). The *MSH3* gene, one of the DNA mismatch repair genes on chromosome 5, shows that specific types of alleles affect the age-of-onset and progression of HD as well as impacting other conditions which interact with this mismatch repair gene including Myotonic Dystrophy Type 1 (Flower *et al.* 2019). Specifically, somatic expansion of the CAG repeat is associated with an earlier onset of HD symptoms (Holmans *et al.* 2017). This research shows that there are modifiers that affect multiple conditions and by understanding how modifiers affect the course of HD, researchers suggest this may lead to developments in treatments to delay the progression or prevent the onset of HD and possibly other conditions in affected individuals.

1.4 Huntington Disease-Like 2

Since individuals have been able to obtain a molecular diagnosis of HD in addition to a clinical diagnosis of HD, there has been a growing awareness of Huntington Disease-like

conditions (Schneider et al., 2007). Huntington Disease-Like 2 is one of the most common conditions with overlapping clinical features with HD and is often misdiagnosed as HD in the absence of molecular testing. Interestingly, HDL2 has been exclusively diagnosed in those of African ancestry, indicating that HDL2 may be due to an African founder mutation (Walker et al., 2018). In the South African population, HDL2 has been diagnosed in up to about 33% of individuals with suspected HD phenotype (Anderson et al., 2019). HDL2 is caused by 40 or more CTG trinucleotide repeats in the *JPH3* gene (Holmes et al., 2001). Since HDL2 is also autosomal dominant, an affected individual has a 50% chance of passing down the condition to each of their children.

As with HD, there are movement, cognitive, and behavioral symptoms which present during an affected individual's adult years with an average onset of age 41 (Anderson et al., 2017). The average survival after the onset of symptoms is between 10 to 20 years (Margolis et al., 2001). Individuals with HDL2 experience progressive symptoms, including chorea, dementia, and behavioral changes which involve depression, apathy, and irritability (Anderson et al., 2017). Due to its similar presentation, it is not possible to clinically differentiate HDL2 from HD and genetic testing is required to confirm a diagnosis.

Similar to HD, there is an inverse relationship between the size of the repeat expansion in *JPH3* and the onset of symptoms. An individual who carries 28 or less CTG repeats is considered unaffected and their offspring are not at risk for HD. When the CTG repeat expands to between 29 and 39 repeats, this is considered to be a questionable range as there are two possibilities. First, these may be similar to the intermediate range in HD, where the individual does not experience symptoms themselves but their children are at risk of inheriting HDL2 if the CTG repeat expands to more than 40 repeats. The second possibility is that these may be reduced

penetrance alleles where some of these individuals may experience symptoms at a later age, others may present with different symptoms than typical HDL2, and still others may never exhibit symptoms. Their children are at a 50% risk for also having reduced penetrance or of having HD if the repeat expands. Once the CTG repeat exceeds 40 repeats, the individual will be affected by HDL2 and their children have a 50% risk of inheriting HDL2.

There is no cure for HDL2 itself, rather there are treatments to manage HDL2's symptoms. These treatments are similar to HD and other neurodegenerative conditions which are discussed in further detail below.

1.5 Treatments

There is currently no disease modifying treatment or cure for HD. However, there are many promising research studies for treatments to manage symptoms and offer possible disease-modifying treatments for HD. The current medical management for individuals with HD involves a combination of therapies which focus on specific symptoms.

Movement is one of the characteristic symptoms of HD and is the typical target for treatment. Various therapies, such as physical therapy and occupational therapy, have proven somewhat useful for patients with HD. In some studies, physical therapy and exercise have been shown to benefit individuals with HD specifically through improvement in motor function, gait speed, and balance (Fritz et al., 2017). Additional social benefits have been seen when patients are in group-based rehabilitation including increased social interaction, self-confidence, and independence (Frich et al., 2014). There have not been a substantial amount of studies dedicated to observing the effect of occupational therapy with patients who have HD (Hawrylak et al., 2014). However, there is a perceived benefit due to occupational therapists' specialty of

providing guidance, intervention, and exercises which help patients to develop, recover, and maintain their daily activities. This differs from physical therapy that focuses solely on an individual's physical movement and abilities. According to the Huntington Disease Society Of America, occupational therapy is able to help patients with HD retain an active role in their daily activities to the best of their abilities for as long as possible and both physical therapy and occupational therapy have beneficial value for patients with HD in the early stages, mid-stages, and later stages of the condition (Imbriglio, 2010).

Other treatments alleviate the movement symptoms of HD. Dopamine-modifying drugs have been a fruitful approach for treating HD. Tetrabenazine, which was approved in 2008 by the United States' Food and Drug Administration (USFDA) as the first drug that targeted HD's chorea, is a pharmacologic agent that is specifically used as treatment for chorea by affecting dopamine levels in the brain (Claassen et al., 2019). More recently in 2017, deutetrabenazine was approved by the USFDA and it essentially modified tetrabenazine to allow for lower doses that are administered less often (Claassen et al., 2019). However, there are some potential side-effects to be considered when deciding to use dopamine-modifying drugs including slowness of movement, depression, restlessness, falls, drowsiness, and neuroleptic malignant syndrome which is a serious nervous system disorder (American Academy of Neurology, 2012 & Videnovic, 2013).

There are also treatments that target behavioral and cognitive symptoms of HD. Various antipsychotics are administered to treat various symptoms, including depression, that some patients with HD may experience (Unti et al., 2016). These antipsychotics are involved with multiple processes which have an effect on chorea including blocking dopamine transmission and monoamine depletors (Kapur et al., 2006; Unti et al., 2016). However, many of these

medications have potential side-effects including dry mouth, hypotension, dizziness, asthenia, and slowness of movement among others (Videnovic, 2013). There are also pharmacologic treatments for cognitive dysfunction that is associated with HD. These treatments often are accompanied with side-effects of diarrhea, nausea, vomiting, and dizziness among others (Videnovic, 2013).

Moving into the research realm for HD, antisense oligonucleotide therapy is one of the treatments at the forefront of the research field for HD. In order to understand antisense oligonucleotides, the central dogma of biology needs to be explained. The central dogma of molecular biology describes the process of retrieving genetic information from DNA and creating proteins. The first step is transcription which involves decoding a segment of DNA and synthesizing a complimentary strand of RNA. The second step is translation which interprets the RNA and produces the corresponding protein. Antisense oligonucleotides are short sequences of nucleotides which bind to the RNA strands and essentially block the second step of translation. This results in no protein product from that strand of RNA (Dias & Stein, 2002; Tabrizi et al., 2019). There are currently multiple studies utilizing the antisense oligonucleotide therapy to effectively lower huntingtin protein levels. The theory is that lowering the levels of the abnormal huntingtin protein in the brain, which is seen in patients with HD, will either slow down the progression of HD symptoms or possibly prevent them from occurring at all. One study in particular has had a successful clinical trial involving 46 patients with HD (Tabrizi et al., 2019). In this study, 34 participants were chosen at random to receive the antisense oligonucleotide therapy via intrathecal injections. The remaining 12 participants received a placebo via intrathecal injections. This phase of the trial was to confirm the safety of the antisense oligonucleotide therapy. The results showed that there was no increase in major adverse effects

associated with the antisense oligonucleotide therapy during the time frame of the trial. It was noted that there were some minor adverse effects with this study. However, individuals in the control group who received the placebo were equally as likely to experience these minor adverse effects as a result of the intrathecal injections themselves rather than the antisense oligonucleotide therapy (Tabrizi et al., 2019). In addition to confirming the safety of the antisense oligonucleotide therapy, several other findings were noted. Mainly, patients who received the antisense oligonucleotide therapy had lower levels of abnormal huntingtin protein in their cerebrospinal fluid than the patients who received the placebo (Tabrizi et al., 2019). This is not a direct measurement of abnormal huntingtin protein in the brain. However, at this time, there is no direct way to safely measure levels of abnormal huntingtin protein in the brain and we must rely on the known interaction between the brain and cerebrospinal fluid. Due to the success of this trial, a Phase 3 trial is currently underway and will focus on the actual effectiveness of antisense oligonucleotide therapy.

RNA interference therapy targets the RNA to prevent abnormal huntingtin proteins from being produced. This complex gene-silencing mechanism uses small noncoding, inhibitory RNA strands to regulate gene expression by binding specific targeted strands of RNA. This recruits a gene-silencing complex which ultimately leads to specific messenger RNAs being degraded preventing that specific protein from being produced. This has proven to be an effective treatment method with other dominant disease genes. Hereditary transthyretin amyloidosis is the first RNA interference therapy approved by the USFDA and the European Medicine Agency and was approved in 2018 (Bartoszewski & Sikorski, 2019). Currently, there are numerous RNA interference therapies in various stages of clinical trials for conditions involving hepatic, renal, and ocular conditions. It is projected that in the near future there will be RNA interference

therapies in clinical trials for conditions that involve the central nervous system (Setten et al., 2019). Regarding HD specifically, RNA interference therapy has shown some promising results in rodents (Harper, 2009). However, there are several challenges that present with RNA interference therapy which point towards the need for more research and studies before trials in human patients can be conducted.

Another approach to lowering levels of abnormal huntingtin protein is by using a specific compound to selectively clear it from a cell using autophagy, a clearance mechanism the cell uses to eliminate unwanted proteins. This process allows the cell to recognize and trigger a response that engulfs then degrades unwanted proteins. Specifically addressing huntingtin protein, two specific compounds, 10O5 and 8F20, have showed some promise in allowing the cell to degrade abnormal huntingtin protein (Zoghbi, 2019).

There are associations with an impaired immune system and neurodegenerative conditions such as HD. These immune system abnormalities, including cerebral and peripheral inflammatory responses, appear years before any of the typical first behavior changes or motor symptoms of HD (Denis et al., 2018). Due to results from mouse model studies, it is understood that an impaired immune system correlates with the severity of HD symptoms. There have been advances in immunotherapies that have revealed conflicting results. However, there is hope to develop an immunotherapy treatment which may reactivate the peripheral immune system which ultimately may delay or even prevent the further progression of HD (Lee et al., 2018).

Gene editing is an exciting breakthrough in genetics, which at first seemed to be the answer and cure for all genetic conditions. Unfortunately, the truth of the complexity of gene editing became apparent when a clinical trial for gene therapy ended with Jesse Gelsinger's death due to complications with his immune system which resulted in multiple organ failure. Mr.

Gelsinger had ornithine transcarbamoylase deficiency, a rare metabolic disorder. The USFDA took immediate action and suspended the clinical trial as well as other ongoing trials at the same institution due to concern for inadequate training of the staff. In addition, the USFDA issues investigations of the other ongoing gene therapy clinical trials (Sibbald, 2001). This brought a halt to gene therapy research and dampened the excitement surrounding gene editing in general. To date, there has been further research in gene therapy with animal models which has shown promising results. There is also an ongoing clinical trial to confirm the safety of an adeno-associated virus serotype 5 vector which has completed previous studies and shown promising results in decreasing the amount of abnormal huntingtin protein (Clinicaltrials.gov). These studies involved a single intracranial injection which resulted in prevention of neuronal dysfunction in both rodents and minipigs, a long-term evaluation of mice which resulted in confirmation of the theorized improvement of HD symptoms, as well as confirming that there were lower levels of abnormal huntingtin without any unintended effects in patient-derived neuronal cultures (Keskin et al., 2019; Spronck et al., 2019).

Human stem cell research is another breakthrough and cutting-edge research area that is involved in the journey for cures and treatments for HD. Human pluripotent stem cells are a very specific type of cell that are proliferative and can replicate in culture, and have the ability to differentiate into any type of cell in the body. There are sub-types of adult stem cells which have the ability to develop into certain types of cells. Neural stem cells have the ability to develop into different types of brain cells and are currently being used in research as therapeutic candidates. Mouse model studies have shown that human neural stem cells have the capability to develop into several types of neurons in the brain and potentially form synapses (Reidling et al., 2018). In addition, these mice displayed improvement in motor deficits and showed signs that the

transplanted human neural stem cells may be capable of protecting and/or repairing damaged brain tissue and delaying the progression of HD symptoms in general. This points to a possible treatment for HD (Reidling et al., 2018). Other stem cell products, including medium spiny neuron progenitors and astrocyte progenitors, are also being tested as HD treatments (Golas, 2018; Cho et al., 2019).

1.6 Disclosure

Merriam-Webster Dictionary defines disclosure as "the act or an instance of disclosing" and defines disclose as "to make known or public." There are many types of disclosures that happen in every individual's lifetime and can occur in all types of relationships. There are disclosures that happen between family members, friends, coworkers, or romantic partners. In addition, there are different types of information to be disclosed to certain people even when dealing with the same topic. This is due to the nature of how relationships differ between people. For an individual with HD, a disclosure may be different between family members and friends. The type and level of information varies per person.

When referring to a disclosure in a romantic relationship, there is an added layer that complicates the situation since a romantic partner's relationship is unique from a friend or a family member. Romantic partners typically are not related and have a much closer connection than friends. However, there is a whole spectrum encompassing the type of relationship romantic partners have including: dating as a casual relationship that has no long-term objective, dating as a serious relationship that has a long-term objective, a committed relationship that may include co-habitation and/or children, as well as marriage. There are various factors that can contribute to a disclosure being delivered and accepted well by a romantic partner including the timing and

components of what is disclosed. Specifically concerning HD, there are many aspects to consider disclosing such as explaining what HD is, the hereditary component and inheritance pattern of HD, the consideration of care-taker role, as well as the various movement, behavioral, and cognitive symptoms. All of these have the potential to be sensitive topics to discuss with another individual, especially when that individual is a romantic partner. As with any disclosure, divulging information on HD allows the individual who is receiving the disclosure to be privy to this sensitive information and have the freedom to make an informed decision about continuing the relationship.

Previous studies have been conducted to assess how disclosing sensitive information on genetic conditions effects relationships. For the individuals who had information about a genetic condition to disclose to a romantic partner, one study observed that many individuals fear and experience being rejected which leads to anxiety concerning whether to disclose as well as what specific information to share, when to share, and how to approach sharing (Klitzman & Sweeney, 2011). This study included individuals with HD, however, the details of this study did not delve deeper into the disclosure itself or interview the romantic partners. There was a study that explored the psychological effect of pre-symptomatic testing on the at-risk individuals themselves and also focused specifically on the effect of HD pre-symptomatic testing on familial and romantic relationships. In regard to the second aim of this study, the main response from all the participants in the study was to "be open and discuss the process with your loved ones" (Voight, 2014). Another study focused on how presymptomatic testing effects a couple and what life with either the risk of HD or the reality of HD looks like for a couple (Richards, 2004). One of the main findings confirmed that there are certain core concerns for these couples including concern about how their marriage/relationship is impacted by HD, the knowledge of HD and

how romantic partners' react, as well as the decision of whether to have children or not. In addition, the complexity of these issues is compounded with the uniqueness of each couple's relationship (Richards, 2004). In a study that focused solely on different types of disclosures that happen between romantic partners when HD is involved and how they impact marriages, there were different types of disclosures that emerged which ranged from HD being kept as a "marital secret" to "marital ignorance" (Forrest et al., 2013).

This study specifically addresses disclosure between romantic partners from two perspectives. The first perspective is of an individual who is at risk or diagnosed with HD concerning how they approached disclosing this information to their romantic partner including details of when they decided the timing was appropriate and what specific information about HD was shared. The second perspective is of an individual who is received an HD disclosure from their romantic partner, how they processed the information disclosed to them and made decisions based on it. In addition to collecting information about how disclosures have happened in the past, this study presents the opportunity for all the participants to outline what they believe are components of an ideal disclosure for HD.

1.7 *In Vitro Fertilization* and Preimplantation Genetic Testing for Monogenic Disorders

Currently, medical advances have reached a point that allows couples to start a family using assisted reproductive technologies. This is especially useful when a genetic condition is a concern in a family. Through a series of fertility procedures called *in vitro fertilization* (*IVF*), a woman's eggs are retrieved and fertilized with a man's sperm outside of the woman's body. This family planning option is typically used when there is a history of infertility.

There have been several studies showing that there is an increase of adverse outcomes for both the mothers and babies when *IVF* is involved. The women are at increased risk of preeclampsia, gestational diabetes, perinatal mortality, atonic bleeding, uterine rupture, amniotic fluid embolism, and placenta issues including low-lying placenta, placenta previa, placenta accrete, and placenta abruption (Tanaka et al., 2020). The babies are at increased risk of being delivered through caesarean section as well as being born prematurely and having low birth weight (Kathpalia et al., 2016). There is also evidence that these babies have a higher risk of congenital malformations with one study observing a 2-fold increase from the general population's 2-3% chance of having a birth defect (Hansen et al., 2002).

Preimplantation genetic testing (PGT) is a procedure which extracts some of the outer cells from the embryo and examines those cells for their genetic information. There are two main types of PGT. There is genetic testing which tests for aneuploidies specifically checking the amount of chromosomes since there are known medical conditions and symptoms that result from an individual having more or less genetic material. There is also genetic testing which tests for monogenic disorders. This means that conditions which have been associated with only one gene are able to be detected through this test. HD is considered a monogenic disorder since HD has been associated with only the *HTT* gene. Couples who decide to have any type of PGT can use the results of the test to decide which embryos, if any, they would like transferred to the woman's uterus. It is important to note that not all embryos that are transferred to a woman's uterus will implant and it may take several rounds for a woman to become pregnant.

One main point with PGT is understanding that these results do not guarantee a perfectly healthy baby. It is important to understand that on top of the 2-3% general population's chance of having a child with a birth defect, the results of the test may not be an exact representation of

the baby's genetic material. This is due to the PGT being performed on the outer layer of cells. It is possible for the inner layer of cells, which develop into the baby, to have different genetic material due to mosaicism. In the case of HD, it is possible, though unlikely, for PGT to return negative and for the baby to still inherit the expanded CAG repeat in *HTT*.

In addition to all of these concerns, there is a considerable financial cost to having these procedures performed. The exact cost differs for each couple depending on how many rounds of *IVF* are needed. However, considering the involved process of medication and treatments for the extraction of the woman's eggs, the fertilization procedure itself, the PGT, the lab's costs for keeping and/or freezing embryos, the implantation procedure, and the clinic's fees, it is no surprise that this is a costly process. To date, the average insurance will not cover any part of this process. Due to this, there is a financial barrier that does not allow this family planning option to be available for everyone. In response to this financial barrier, there are certain organizations lobbying for these types of healthcare services to be covered and made available for all.

1.8 Significance for Genetic Counseling

Individuals with HD are followed by multi-disciplinary care team which typically begins with the onset of symptoms and continues as the condition progresses. These healthcare specialties include neurology, psychiatry, genetics, social work, nutrition, physical therapy, occupational therapy, and palliative care. Genetic counselors are mainly known for playing a role in the asymptomatic and/or early stages of HD. Interactions between patients and genetic counselors surround presymptomatic testing which is typically a three-appointment process. This creates the space for the patient at risk for HD to understand what knowing their HD status means for them. Genetic counselors are able to provide discussion of topics that patients may not

have thought out. These topics are usually not discussed outside of genetic counseling appointments which may include thinking through insurance situations, how different results will impact their lives, and how this information will affect their relationships with the people in their lives.

One aspect of this study inquired about how individuals approach disclosing HD, how their romantic partners process the disclosure, and how disclosing HD affects the romantic relationship. As was previously discussed, many individuals with an HD status have achieved various life milestones and may already be in or entering into romantic relationships. These individuals' perspectives are not reported in the scientific literature and it will be beneficial to report others' experiences. In addition, the results of this study may be a valuable resource for genetic counselors regarding the topic of disclosing HD to a romantic partner.

Another aspect of this study explored the reasons for family planning decisions that are made by couples who are affected by HD. Since an individual with HD has a 50% chance of passing the condition down to each of their children, the knowledge of assisted reproduction options, such as *in vitro fertilization* and preimplantation genetic testing for monogenic disorders, should be discussed with these individuals. Since this is a complex process, it is important to consider all the pros and cons of using these medical advances to have children. The perspectives and knowledge of the HD community regarding these family planning options is not reported in the literature and may be useful for genetic counselors when discussing this topic.

There are many changing aspects of HD that can affect how individuals react and absorb information about the condition. Back in 1872 when Dr. Huntington described HD, there was no treatment or knowledge of how to fight this condition. Now nearly a century and a half later, the stigma around HD is different. Today, there is a message of hope with the revolutionary research

for treatments and the groundbreaking knowledge of various modifiers. These developments should be included in genetic counseling sessions for HD. However, these developments are still on the horizon and there is the reality of the current HD situation which also needs to be discussed. The affected individuals are still progressing with their symptoms while their romantic partners, caretakers, and families are still living with the daily struggles of having a loved one with HD. The reality of living with HD and the promise of hope for the future can both have a huge impact on disclosure and decisions for family planning. These changing aspects should be considered in the field of genetic counseling as they can greatly impact an individual's perspective of HD.

2. MATERIALS AND METHODS

2.1 Participant Eligibility

Individuals were eligible to participate in this Institutional Review Board-approved study, "Huntington Disease: Disclosure and Future Decision-Making in Romantic Relationships" if they were 18 years of age or older and either diagnosed with HD or at risk for HD or the romantic partner of someone who was either diagnosed or at risk for HD. The survey was only provided in English. As such, the participants were required to read and understand English. Internet access was required in order to participate in this study.

There were 202 total responses. 34 participants did not complete any survey questions beyond the demographics page and were not included in this analysis. 14 participants completed questions from sections of the survey and were included in those sections of analysis. 76% of participants completed the survey.

2.2 Recruitment

Participants were recruited through events and online resources. The lead researcher actively recruited participants through numerous events within the HD community, including the Huntington Disease Society of America's Annual Convention located in Boston, MA, from June 27-29th, 2019, Huntington Disease Society of America Orange County Chapter's Annual HOPE Walk in Santa Ana, CA, on October 26th, 2019, Huntington Study Group's Annual Meeting in Sacramento, CA, on November 9th, 2019, and HD-CARE's Annual Symposium in Irvine, CA on November 16th, 2019. For the aforementioned events, the lead researcher had a booth and handed out flyers to those in attendance. In addition, the lead researcher was permitted to attend and distribute flyers at the Affected Huntington Disease Support Group in Irvine, CA on January

12th, 2020. The flyer included the information about the study as well as the link to the online survey and participants were encouraged to contact the lead researcher with any questions. There were several healthcare professionals who also distributed flyers in their own clinics and among their own patients. The flyer was posted to several support groups with a focus on families affected by HD on Facebook. These posts were made either with permission from the group's administrator or by the administrator themselves. The flyer and posters are available in Appendix B.

2.3 Protection of Participant Privacy and Data Collection

Participants were asked to complete an anonymous web-based survey generated through UCI REDCap, a secure web application for building and managing online surveys and databases. Participants accessed the online survey link in their own private settings. The privacy of participants was protected throughout the entirety of the data collection process. No personal identifying information was obtained in this study including name, date of birth, or medical records number. This research study did not cause any harm to the participants. All research data was stored securely and confidentially.

2.4 Consent

Implied informed consent (unwritten consent) was obtained prior to participating in the study. On the first page of the online survey, participants were prompted to a study information sheet. This page included contact information for the lead researcher and faculty sponsor, the purpose of the study, the eligibility requirements, and the contact information of the UCI

Institutional Review Board. By clicking 'Yes,' participants indicated that they consented to being a research participant.

2.5 Survey

The survey instrument was generated using UCI REDCap and was accessed through the website link: https://ci-redcap.hs.uci.edu/surveys/index.php?s=T4YKLENH7Y or through https://is.gd/HDsurvey. The survey consisted of a total of eighty-three questions, including an assortment of twelve Likert scale-based questions, thirteen multiple-choice questions, one multiple-answer question, sixteen short answer questions, and forty-one yes-or-no questions. The survey questions include seven demographics questions, three linking questions for romantic partners, thirty-five questions on disclosure, eleven questions on the ideal disclosure, seven questions on family planning, sixteen questions on in vitro fertilization and pre-implantation genetic testing – monogenic, and seven concluding questions on information that would change any of the answers. The complete survey for this study is available in Appendix C.
Branching logic was utilized to ensure that participants were not given questions that were not applicable to them. The main branching question was about the individual's HD status. The three main categories were (1) at risk or diagnosed and pre-symptomatic, (2) diagnosed and symptomatic, and (3) a romantic partner. Several questions had an "other" option which provided a short answer box for these who had additional insight to these particular questions. No single participant was offered every possible survey question.

If an individual indicated they were in a relationship, then three linking questions appeared to potentially link them to their romantic partner. These questions included "When is your anniversary?", "Location of your first date?", and "When did you move in together?". This

allowed for additional insight and analysis of couples in a relationship without obtaining personal identifying information.

This study specifically addresses disclosure between romantic partners. From the perspective of an individual who is at risk or diagnosed with HD, how they approach disclosing this information to their romantic partner including details of when they decide the timing is appropriate and what specific information about HD is shared. From the perspective of an individual who is receiving an HD disclosure from their romantic partner, how they process the information disclosed to them and make decisions based on it. In addition to collecting information about how disclosures have happened in the past, the study presents the opportunity for all the participants to outline what they believe are components of an ideal disclosure for HD.

2.6 Data Analysis

Data were analyzed using the IBM Statistical Package for the Social Sciences (SPSS) Statistics version 25. Patient demographics and responses to the survey questions were summarized using means and standard deviations for continuous variables and counts and percentages for categorical variables. Pearson's Chi-Square test, Fisher's Exact test, ANOVA Table test, and McNemar test were calculated using SPSS. P-values <0.05 were considered statistically significant.

2.7 Institutional Review Board Confirmation

This research study was reviewed and confirmed under the category of 'self-determined exempt human subjects research' by the Institutional Review Board of the University of California, Irvine. The documentation of this study's IRB confirmation is in Appendix A.

3. RESULTS

3.1 Demographics

In total, 202 participants opened the survey between June of 2019 and February of 2020. There were nine individuals who only opened the survey and did not answer any questions in the survey. Additionally, there were other individuals who did not answer certain questions in the demographic section. 12 individuals did not indicate their gender, 13 individuals did not indicate their age, 10 individuals did not indicate their ethnicity, 11 individuals did not indicate their relationship status, 33 individuals did not indicate their HD status, and 9 individuals did not indicate their current self-reported understanding of HD. These individuals were indicated however, not included in the frequency comparisons (Table 1).

There were a total of 190 participants who submitted their gender with a majority (83%) being female (Table 1). 189 participants submitted their age with a mean age of 36 years old and a standard deviation of about 13 years (Figure 2). The majority (60%) of individuals were in the younger age group (36 years old or younger). Out of the 192 participants who indicated their ethnicity, a majority were Caucasian (83%) and only a handful identified as being of non-Caucasian ethnicity. These included Hispanic (6%), Asian (1%), African (1%), or Native American (1%). There were also some individuals (7%) who indicated they were of either mixed ethnicity or an "Other" ethnicity which was not included in the survey options. There were 191 participants who indicated their relationship status. Slightly less than half of the participants (49%) indicated they were "Single". When further delineated, over half of those in the "Single" subpopulation indicated they considered themselves to be "Single – In a Serious Relationship" which may include being in a long-term relationship, engaged, or cohabitating. However, this differentiation between "Single" and "Single – In a Serious Relationship" was left to the

participants' interpretation. A majority (42%) of the remaining individuals indicated they were "Married" and there were some individuals who indicated they were "Separated" (2%), "Divorced" (4%), or "Widowed" (3%).

An individual's HD Status was an important demographic for analyzing the data in this study (Table 1). There were four categories which were presented to all the participants. The "At Risk" subpopulation indicated the participants who had a family history of HD but have not yet been diagnosed themselves. The "Diagnosed and Presymptomatic" subpopulation indicated the participants who have been diagnosed with HD and are not yet experiencing symptoms. The "Diagnosed and Symptomatic" subpopulation indicated the participants who have been diagnosed with HD and are already experiencing symptoms of HD, whether that be early on or later in the progress of the condition. It is important to note that the individuals who indicated they have a diagnosis of HD did not specify if they received a clinical or molecular diagnosis of HD. This was merely by patient report. The "Romantic Partner" subpopulation indicated the participants who are unaffected themselves but have a romantic partner who is either considered at risk, diagnosed and presymptomatic, or diagnosed and symptomatic. There were 169 participants who indicated their HD Status in this study. The "At Risk" subpopulation was the largest proportion (40%), followed by the "Romantic Partner" subpopulation (30%), then the "Diagnosed and Presymptomatic" subpopulation (19%), and finally the smallest proportion was the "Diagnosed and Symptomatic" subpopulation.

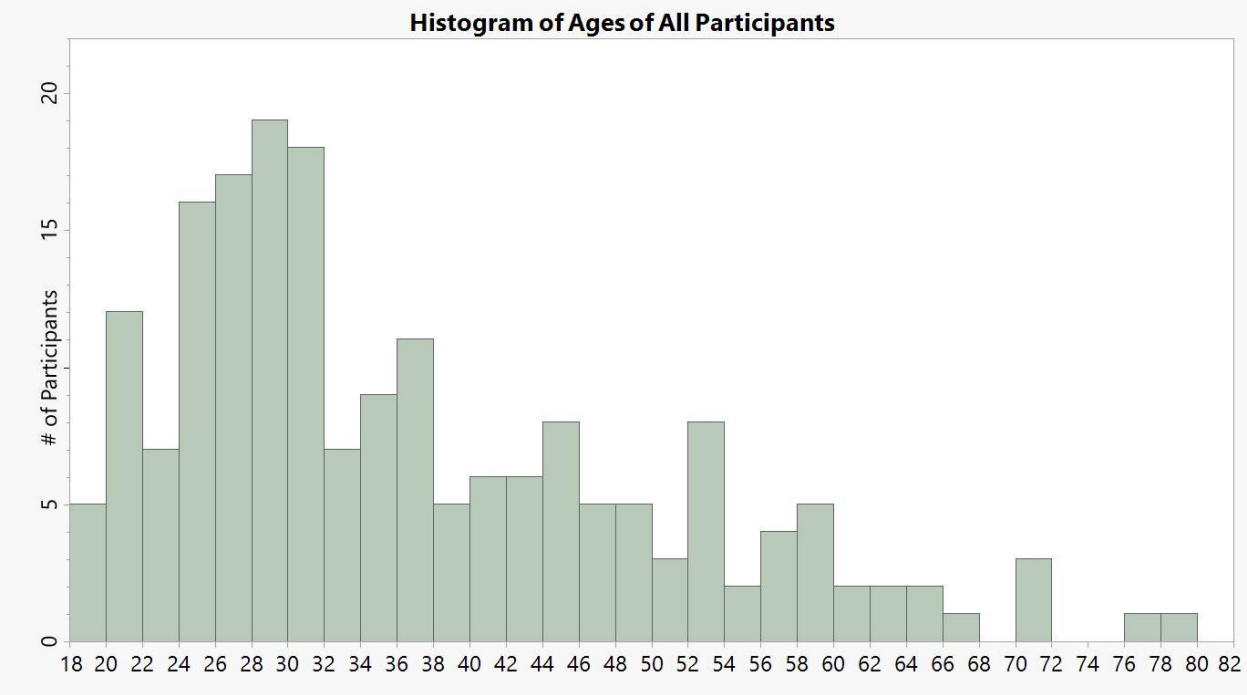
There was a final question in the demographic portion of the survey which asked all participants to indicate their current level of understanding of HD on a Likert scale of one to three with the assigned values of "Very Well", "Somewhat Well", and "Not Well". Out of 193 respondents, a majority (73%) indicated they understood HD "Very Well" (Table 1). There was

an additional question posed to the "Romantic Partner" subpopulation which addressed their understanding of HD prior to the disclosure.

TABLE 1. DEMOGRAPHICS OF TOTAL PARTICIPANTS (N=202)

Demographics	N	%
Gender		
Male	31	16
Female	157	83
Prefer Not to Answer	2	1
Did Not Answer	12	
Age (mean = 36)		
36 Years Old or Younger	113	60
Older than 36 Years Old	76	40
Did Not Answer	13	
Ethnicity		
Caucasian	160	83
Hispanic	11	6
Asian	5	2
African	1	1
Native American	1	1
Other/Mixed Ethnicity	14	7
Did Not Answer	10	
Relationship Status		
Single	40	21
Single – In a Serious Relationship	54	28
Married	80	42
Separated	4	2
Divorced	8	4
Widowed	5	3
Did Not Answer	11	
HD Status		
At Risk	67	40
Diagnosed and Presymptomatic	32	19
Diagnosed and Symptomatic	19	11
Romantic Partner	51	30
Did Not Answer	33	
Understanding of HD (Self Report)		
Very Well	141	73
Somewhat Well	50	26
Not Well	2	1
Did Not Answer	9	

FIGURE 2. DISTRIBUTION OF AGES OF TOTAL PARTICIPANTS



3.1.1 Demographics by HD Status

To further understand the demographics of the study, the demographics were compared by HD Status subpopulations (Table 2). For each demographic, the smaller proportion categories were combined in order to analyze the differences between the majority proportions for each of the HD subpopulations. There were two individuals who did not answer for gender, two individuals who did not answer for age, one individual who did not answer for ethnicity, and one individual who did not answer for relationship status. These individuals were excluded from this demographic analysis.

For statistical analysis, those who identified as "Male" and "Prefer Not to Answer" were combined into "Male/Prefer Not to Answer" due to the small proportion of individuals (Table 2). When gender was analyzed by the participants' HD status, there was no significant differences in the proportion of genders with the majority being female (p=0.098). There was no significant

difference with the proportion of ethnicities, either Caucasian or non-Caucasian (included "Hispanic", "Asian", "African", "Native American", "Mixed Ethnicity" and "Other Ethnicity" options), between the HD Status subpopulations ($p=0.931$). For comparing the Relationship Status between the HD Status subpopulations, the categories of "Separated", "Divorced", and "Widowed" were combined into "Other" due to the number and similarity of these participants' perspectives on their romantic relationships. There is a significant difference in the Relationship Status of the proportions of individuals who indicated their HD Status ($p=0.024$). Furthermore, the "At Risk" and "Diagnosed and Presymptomatic" subpopulations were more likely to indicate they were "Single" while the "Diagnosed and Symptomatic" and "Romantic Partner" subpopulations were less likely to indicate they were "Single". The "Diagnosed and Symptomatic" subpopulation was less likely to indicate they are "Single – In a Serious Relationship" and the "Romantic Partner" subpopulation was more likely to indicate they are "Single – In a Serious Relationship". The "Diagnosed and Presymptomatic" subpopulation was less likely to indicate they are "Married" and the "Diagnosed and Symptomatic" and "Romantic Partner" subpopulations were more likely to indicate they are "Married". The "Diagnosed and Presymptomatic" and "Diagnosed and Symptomatic" subpopulations were more likely to identify with the "Other" category.

The analysis for "Understanding of HD" required the "Somewhat Well" and "Not Well" to be combined into one category due to the small proportion and similar perspectives of these individuals (Table 2). There was no significant difference among the HD Status subpopulations when comparing their self-reported levels of "Understanding of HD" ($p=0.081$).

TABLE 2. DEMOGRAPHICS BY HD STATUS (N=169)

Demographic	At Risk (n=67)	Diagnosed/ Presymptomatic (n=32)	Diagnosed/ Symptomatic (n=19)	Romantic Partner (n=51)	Fisher's Exact P-Value
	N (%)	N (%)	N (%)	N (%)	
Gender					0.098
Male/Prefer Not to Answer	11 (17)	4 (12)	7 (39)	7 (14)	
Female	55 (83)	28 (88)	11 (61)	44 (86)	
Did Not Answer	1	0	1	0	
Ethnicity					0.931
Caucasian	56 (84)	26 (81)	16 (89)	43 (84)	
Non-Caucasian	11 (16)	6 (19)	2 (11)	8 (16)	
Did Not Answer	0	0	1	0	
Relationship Status					0.024
Single	21 (32)	11 (34)	3 (16)	4 (8)	
Single – In a Serious Relationship	18 (27)	8 (25)	4 (21)	17 (33)	
Married	23 (35)	8 (25)	9 (47)	26 (51)	
Other	4 (6)	5 (16)	3 (16)	4 (8)	
Did Not Answer	1	0	0	0	
Understanding of HD (Self Report)					0.081
Very Well	50 (75)	29 (91)	12 (63)	36 (71)	
Somewhat/Not Well	17 (25)	3 (29)	7 (37)	15 (29)	

"Did Not Answer" Responses Excluded From Percentages

The 167 participants who indicated their age were further analyzed by their HD Status (Table 3). One participant from the "At Risk" subpopulation did not indicate their age and was excluded from this analysis. The "At Risk" subpopulation (n=66) was found to have a mean age of 31 years old with a standard deviation of about 10 years (Figure 3). The "Diagnosed and Presymptomatic" subpopulation (n=32) had a mean age of 33 years old with a standard deviation of about 14 years (Figure 4). One participant from the "Diagnosed and Symptomatic" subpopulation did not indicate their age and was excluded from this analysis. The "Diagnosed and Symptomatic" subpopulation (n=18) had a mean age of 45 years old with a standard deviation of about 13 years (Figure 5). "Romantic Partner" subpopulation (n=51) had a mean age of 40 years old with a standard deviation of about 15 years (Figure 6).

FIGURE 3. DISTRIBUTION OF AGES OF AT RISK SUBPOPULATION

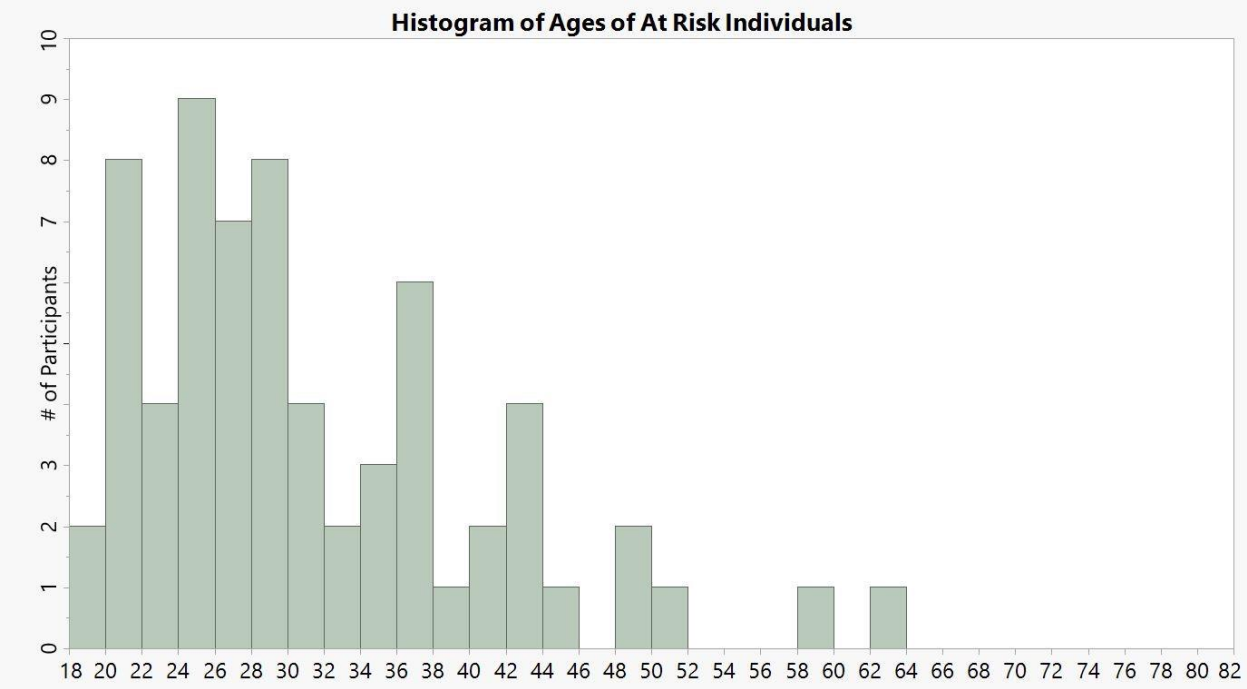


FIGURE 4. DISTRIBUTION OF AGES OF DIAGNOSED AND PRESYMPTOMATIC SUBPOPULATION

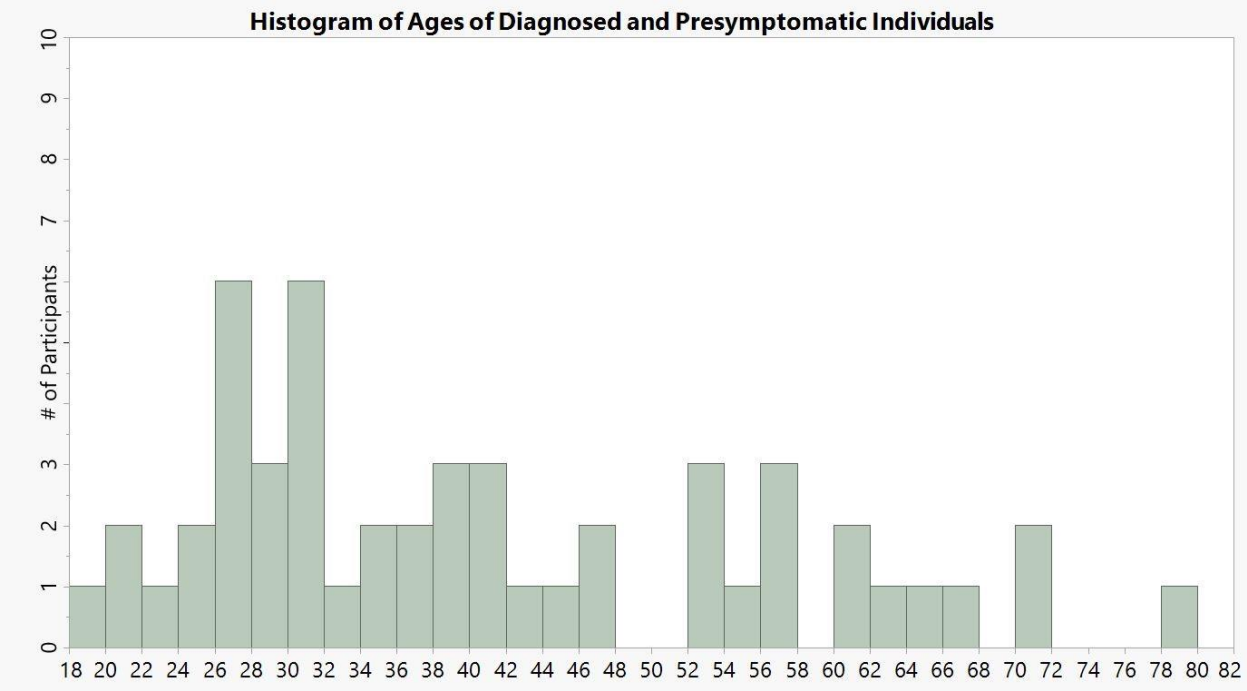


FIGURE 5. DISTRIBUTION OF AGES OF DIAGNOSED AND SYMPTOMATIC SUBPOPULATION

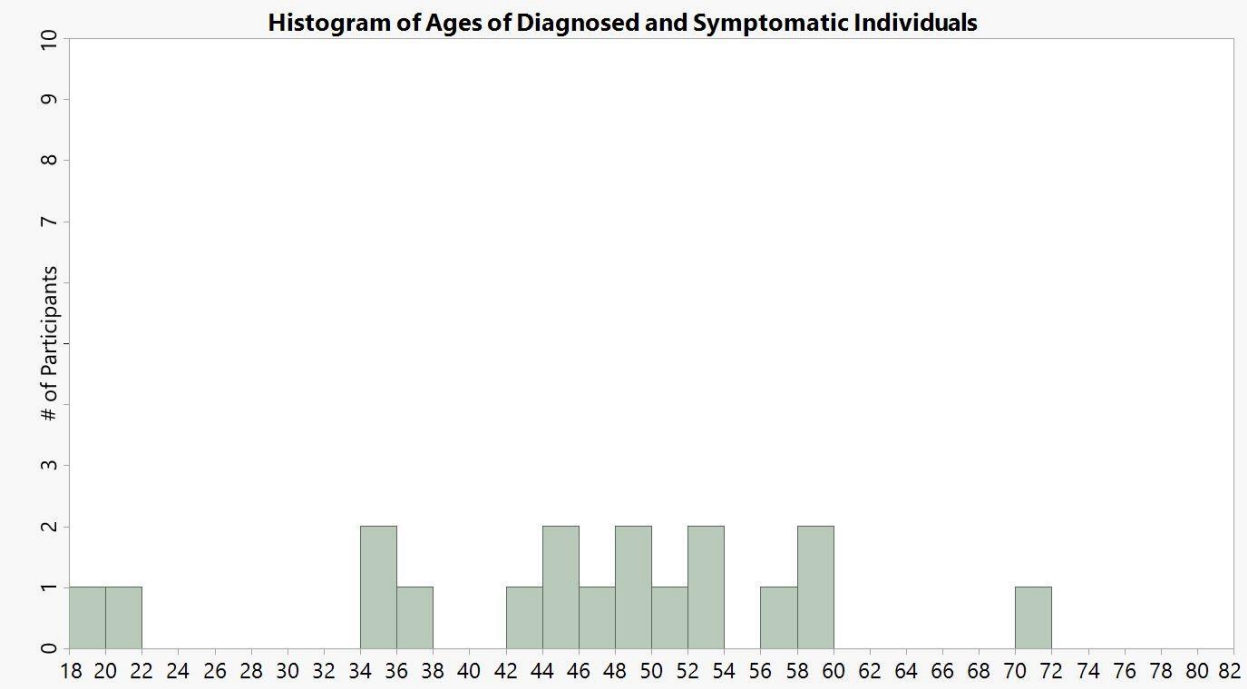
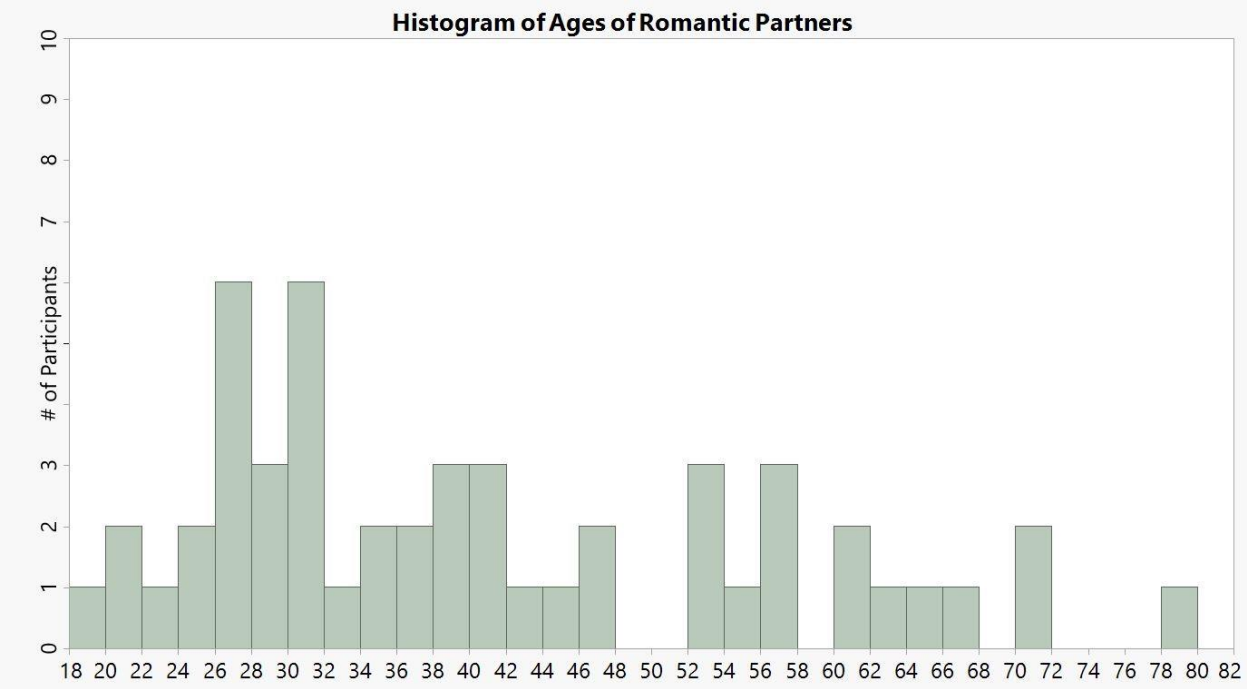


FIGURE 6. DISTRIBUTION OF AGES OF ROMANTIC PARTNER SUBPOPULATION



Furthermore, there were three significant associations when the ages of the participants were compared by HD status (Table 3). There were significant differences between the mean ages of the "At Risk" subpopulation and the "Diagnosed and Symptomatic" subpopulation ($p<0.0005$) as well as the "Romantic Partner" subpopulation ($p<0.0005$). There was also a significant difference between the mean ages of the "Diagnosed and Presymptomatic" and "Diagnosed and Symptomatic" subpopulations ($p=0.009$). There were no other significant differences between the mean ages of the other subpopulations.

TABLE 3. AGE ANALYSIS BY HD STATUS (N=167)

HD Status	N	Mean	Standard Deviation	Tukey P-Value
At Risk	66	30.86	9.65	
Diagnosed/Presymptomatic				0.782
Diagnosed/Symptomatic				<0.0005
Romantic Partner				<0.0005
Diagnosed/Presymptomatic	32	33.44	13.53	
At Risk				0.782
Diagnosed/Symptomatic				0.009
Romantic Partner				0.070
Diagnosed/Symptomatic	18	45.44	13.11	
At Risk				<0.0005
Diagnosed/Presymptomatic				0.009
Romantic Partner				0.482
Romantic Partner	51	40.47	15.23	
At Risk				<0.0005
Diagnosed/Presymptomatic				0.070
Diagnosed/Symptomatic				0.482
Total	167	35.86	13.62	

ANOVA P-Value = <0.0005

3.1.2 Additional Demographics for Romantic Partners

In order to understand the situation and experience of the "Romantic Partner" subpopulation, they were presented with a couple additional demographic questions in a branched section of the survey (Table 4). For reference, the previously described demographics

(Table 2) are included below. Most of these individuals had partners who are "Diagnosed and Symptomatic" (39%), followed by partners who are "At Risk" (35%), and finally partners who are "Diagnosed and Presymptomatic" (26%). The majority (80%) of individuals reported that they had no prior knowledge of HD before their disclosure and relationship with their partner.

TABLE 4. DEMOGRAPHICS FOR ROMANTIC PARTNERS (N=51)

Demographic	N	%
Gender		
Male/Prefer Not to Answer	7	14
Female	44	86
Did Not Answer	0	
Ethnicity		
Caucasian	43	84
Non-Caucasian	8	16
Did Not Answer	0	
Relationship Status		
Single	4	8
Single – In a Serious Relationship	17	33
Married	26	51
Other	4	8
Did Not Answer	0	
Understanding of HD (Self Report)		
Very Well	36	71
Somewhat/Not Well	15	29
Partner's HD Status		
At Risk	18	35
Diagnosed and Presymptomatic	13	26
Diagnosed and Symptomatic	20	39
Prior Knowledge of HD		
None	41	80
Some	9	18
A lot	1	2

3.1.3. Demographics of Participants Who Did Not Proceed Past the Demographic Section

It is important to note that out of the 202 total individuals, there were nine individuals who only opened the survey and did not answer any questions. There were also 25 individuals who only responded to the demographic section of the survey. When combined, there was an approximate 21% drop rate of participants after the demographic section of the survey (Table 5).

Of these participants, the majority indicated they were “Female” (59%) and “Caucasian” (59%). Most individuals indicated they are “Married” (44%) as well as being “Older than 36 Years Old” (44%). Aside from the nine (28%) individuals who did not answer any questions, there were only one or two individuals who did not answer any given question in the demographic section. The overwhelming majority (94%) of these individuals did not indicate their HD Status.

TABLE 5. DEMOGRAPHICS OF PARTICIPANTS WHO DID NOT PROCEED PAST THE DEMOGRAPHIC SECTION (N=34)

Demographic	N	%
Gender		
Male	3	9
Female	20	59
Prefer Not to Answer	1	3
Did Not Answer	10	29
Age (mean = 36)		
36 Years Old or Younger	9	27
Older than 36 Years Old	15	44
Did Not Answer	10	29
Ethnicity		
Caucasian	20	59
Hispanic	1	3
Asian	1	3
African	1	3
Native American	0	0
Other/Mixed Ethnicity	2	6
Did Not Answer	9	26
Relationship Status		
Single	1	3
Single – In a Serious Relationship	7	21
Married	15	44
Separated	0	0
Divorced	1	3
Widowed	0	0
Did Not Answer	10	29
HD Status		
At Risk	1	3
Diagnosed and Presymptomatic	1	3
Diagnosed and Symptomatic	0	0
Romantic Partner	0	0
Did Not Answer	32	94

3.2 Disclosure

The second section of the survey presented individuals with questions about disclosure regarding HD. As mentioned previously, there was a drop rate of approximately 21% after the demographic section and these individuals did not proceed with the remaining sections of the survey. Therefore these participants were excluded from subsequent analysis and the remaining 160 participants were analyzed for the disclosure section.

3.2.1 Experienced Disclosure

The beginning part of the disclosure section of the survey inquired if participants have experienced, either giving or receiving, a disclosure. There were 28 participants (17%) who answered "no" and were branched forward to the latter part of the disclosure section. There were 132 participants (83%) who answered "yes" and were branched to a set of questions which inquired specific details about their experienced disclosure. There was one respondent who did not specify if a disclosure was experienced however, continued on to answer the latter part of the disclosure section as those individuals who answered "no".

Out of the 160 participants, a majority (83%) reported experiencing disclosure (Table 6). When the participants were grouped into HD subpopulations of "At Risk", "Diagnosed and Presymptomatic", "Diagnosed and Symptomatic" and "Romantic Partners", the majority (78% to 89%) of individuals in each HD Status subpopulation reported they experienced either giving or receiving disclosure. There was no significant difference found in the proportion of individuals who reported they had experienced disclosure between the HD Status subpopulations ($p = 0.627$).

TABLE 6. ASSOCIATION OF EXPERIENCED DISCLOSURES TO HD STATUS (N=160)

Disclosure Experienced	At Risk (n=63)	Diagnosed/ Presymptomatic (n=28)	Diagnosed/ Symptomatic (n=18)	Romantic Partner (n=51)	Total (n=160)
	N (%)	N (%)	N (%)	N (%)	N (%)
Yes	51 (81)	25 (89)	16 (89)	40 (78)	132 (83)
No	12 (19)	3 (11)	2 (11)	11 (22)	28 (17)

Fisher's Exact Test P-Value = 0.627

Individuals in the "At Risk", "Diagnosed and Presymptomatic", and "Diagnosed and Symptomatic" were presented with an additional question which inquired if they have already disclosed or would plan to disclose their HD status to their romantic partner (Table 7). This wording was chosen to encompass the participants who may not have given a disclosure about HD at the time of taking the survey however, they would plan to disclose to their romantic partner if they were in a relationship or situation they deemed appropriate.

There is no significant difference among the "At Risk", "Diagnosed and Presymptomatic", "Diagnosed and Symptomatic" subpopulations who have already given or would plan to disclosure to a romantic partner (p=0.242) (Table 7). The majority (>89%) indicated "Yes", they have given or would plan to disclose.

TABLE 7. ASSOCIATION OF THOSE WHO HAVE GIVEN OR WOULD PLAN TO DISCLOSURE WITH HD STATUS (N=109)

Given Disclosure or Would Plan to Disclose	At Risk (n=63)	Diagnosed/ Presymptomatic (n=28)	Diagnosed/ Symptomatic (n=18)
	N (%)	N (%)	N (%)
Yes	61 (97)	26 (93)	16 (89)
No	2 (3)	2 (7)	2 (11)

Fisher's Exact Test P-Value = 0.242

3.2.1.1 Sources of Disclosure for Romantic Partners

100% of the "Romantic Partner" subpopulation indicated they experienced disclosure and were presented with branched sections of the survey which included added details about the disclosure they received.

To understand the situation surrounding the disclosure they experienced, the "Romantic Partner" subpopulation indicated the source(s) of the disclosure and were allowed to include all that applied (Table 8). A majority (69%) of individuals reported disclosure was by their partner, followed by them finding out about HD together with their partner (43%), and individuals who indicated they were friends or acquaintances with their partner before the relationship and therefore had knowledge and awareness of HD from the beginning of the relationship (26%). There were equal proportions of individuals who indicated their partner's family member(s) disclosed HD to them (24%) as well as those who indicated they noticed the symptoms in their partner themselves (24%). There were some individuals who reported disclosure was by their partner's friend (4%) or that they preferred not to answer the question (2%). Finally, there were other sources of disclosure indicated which some individuals expanded upon through the free response section. The most notable of these was an individual who reported noticing the symptoms in her mother-in-law (see Appendix D).

TABLE 8. SOURCES OF DISCLOSURE (N=51)

Source of Disclosure	N	%
Partner Disclosed Their HD Status	35	69
Friends/Acquaintances Before the Relationship, so Knowledge of HD from the Beginning	13	26
Partner's Family Member(s) Disclosed HD Status	12	24
Partner's Friend Disclosed HD Status	2	4
You Noticed Changes/Symptoms in Your Partner	12	24
You and Your Partner Found Out Together	22	43
Prefer Not to Answer	1	2
Other	3	6

Do not add up to total of "Romantic Partner" subpopulation because respondents were able to select multiple answers.

3.2.1.2 Components of Disclosure

The 133 participants who have experienced either giving a disclosure or receiving a disclosure indicated which components about HD were included in the disclosure. They were presented with the following options of "Movement", "Behavior/Personality", "Cognition", "Late Onset (Yet Still a Range of Ages of Onset)", and "Inheritance: 50%". Participants were then asked to indicate whether each component was included in the disclosure or not. They had the option to choose all the components that applied.

Each component was indicated as being included by the majority (>65%) of participants in each of the HD Status subpopulations (Table 9). Specifically, the components which were included in the disclosure most often were "Inheritance" (88%) and "Movement" (83%). The "Diagnosed and Presymptomatic" subpopulation was the most likely to report including these two components while the "Romantic Partner" subpopulation were the least likely to report these two components were included in the disclosure. There were no significant differences found in four of the five component options that were reported as being included in the disclosure among the HD subpopulations ($p>0.054$). These include "Movement", "Behavior/Personality", "Cognition", "and Inheritance". However, since these components were close to statistical

significance ($p<0.2$), this suggests that the HD Status subpopulations may differ with which components were included in disclosure. The proportion of individuals who reported that "Late Onset" was included in the experienced disclosure differed significantly between HD Status subpopulations ($p=0.021$). Further, the "Diagnosed and Presymptomatic" subpopulation was more likely to report they included "Late Onset" in the disclosure and the "Romantic Partner" subpopulation was less likely to report that "Late Onset" was included in the experienced disclosure.

TABLE 9. ASSOCIATION OF COMPONENTS EXPERIENCED IN DISCLOSURE OF HD STATUS (N=133)

Components Included in Disclosure	At Risk (n=52)	Diagnosed/ Presymptomatic (n=25)	Diagnosed/ Symptomatic (n=16)	Romantic Partner (n=40)	Total (n=133)	Fisher's Exact Test P-Value
	N (%)	N (%)	N (%)	N (%)	N (%)	
Movement						0.119
Yes	45 (87)	25 (100)	15 (94)	33 (83)	118 (89)	
No	7 (13)	0 (0)	1 (6)	7 (17)	15 (11)	
Behavior/ Personality						0.161
Yes	44 (85)	24 (96)	14 (88)	30 (75)	112 (85)	
No	8 (15)	1 (4)	2 (12)	10 (25)	21 (15)	
Cognition						0.054
Yes	44 (85)	24 (96)	13 (81)	28 (70)	109 (82)	
No	8 (15)	1 (4)	3 (19)	12 (30)	24 (18)	
Late Onset						0.021
Yes	40 (77)	24 (96)	11 (69)	26 (65)	101 (76)	
No	12 (23)	1 (4)	5 (31)	14 (35)	32 (24)	
Inheritance						0.126
Yes	51 (98)	25 (100)	14 (88)	37 (93)	127 (95)	
No	1 (2)	0 (0)	2 (12)	3 (7)	6 (5)	

3.2.1.3 Timing of Experienced Disclosure

The other element of disclosure is its timing. Specifically, in relevance to the timeline of their romantic relationship (Table 10). There were 131 participants who indicated the timing of

their experienced disclosure and two individuals who did not specify the timing of their disclosure. They were presented with four options. The majority (71%) of individuals report experiencing the disclosure in the "Beginning of Relationship". Followed by those who indicated the disclosure occurred "After Certain Milestone(s)" (19%). These individuals were given the option to expand on their answer in the free response section. Slightly over half (56%) of these free responses referred to milestone(s) that would indicate being in a committed or serious relationship with some explicitly stating "engaged". Some individuals indicated that the timing of their disclosure occurred "After Marriage" (3%) and "After Children" (6%).

TABLE 10. TIMING OF EXPERIENCED DISCLOSURE (N=133)

Timing of Disclosure	N	%
Beginning of Relationship	94	71
After Certain Milestone(s)	25	19
After Marriage	4	3
After Children	8	6
Did Not Specify	2	1

3.2.1.4 Romantic Partners' Reactions to Disclosure

The "Romantic Partner" subpopulation was presented with a separate branch of questions regarding their reaction to their partner's disclosure about HD. Participants were allowed to choose all that applied for the following reactions which were available in the survey's choices: "Shock", "Confusion", "Anger", "Denial", "Sadness", and "Understanding".

A majority of participants indicated their reaction included "Understanding" (82%) and "Sadness" (76%), and "Shock" (53%), with the remaining reactions experienced by smaller proportions (24%-45%) of the "Romantic Partner" subpopulation (Table 11). In addition, 11 individuals indicated experiencing some "Other" reaction. Participants who indicated "Other" were offered the option of expanding their answer in more detail through a free response box (see Appendix D). Among these were acceptance, motivation, stress, sympathy, worry, and

irritation at their partner's family for "pretending it [HD] wasn't happening". Two individuals also included concern as their reaction to their partner's disclosure.

TABLE 11. ROMANTIC PARTNERS' REACTIONS TO THE DISCLOSURE (N=51)

Reaction	N	%
Shock	27	53
Confusion	23	45
Anger	12	24
Denial	19	37
Sadness	39	76
Understanding	42	82
Other	11	22

Do not add up to total of "Romantic Partner" subpopulation because respondents were able to select multiple answers.

These 51 participants all received different levels of disclosure in terms of which components were included (Table 12). In order to understand how that may affect their reaction to the disclosure, the "Romantic Partner" subpopulation was analyzed by whether they received a partial disclosure or full disclosure. Partial disclosure is defined as a disclosure which included zero to four of the component options ("Movement", "Behavior/Personality", "Cognition", "Late Onset", and "Inheritance") in any combination. Full disclosure is defined as a disclosure which included all five of the component options.

There were some associations between the "Romantic Partner" subpopulation's reactions and whether they reported experiencing a partial or full disclosure (Table 12). Individuals were more likely to experience "Shock" when given a partial disclosure (60%) than a full disclosure (43%). They were also more likely to experience "Understanding" when given a full disclosure (90%) than a partial disclosure (77%). However, these differences in the reactions reported by the "Romantic Partner" subpopulation when a partial disclosure or full disclosure was given were not found to be significant ($p > 0.277$).

TABLE 12. ROMANTIC PARTNERS' REACTIONS TO DISCLOSURE BY AMOUNT OF COMPONENTS INCLUDED IN DISCLOSURE (N=51)

Reaction	Partial Disclosure (0-4 Components) (n=30)	Full Disclosure (5 Components) (n=21)	Chi-Square Test P-Value
	N (%)	N (%)	
Shock			0.227
Yes	18 (60)	9 (43)	
No	12 (40)	12 (57)	
Confusion			0.788
Yes	14 (47)	9 (43)	
No	16 (53)	12 (57)	
Anger			0.518
Yes	6 (20)	6 (29)	
No	24 (80)	15 (71)	
Denial			0.917
Yes	11 (37)	8 (38)	
No	19 (63)	13 (62)	
Sadness			1.000
Yes	23 (77)	16 (76)	
No	7 (23)	5 (24)	
Understanding			0.277
Yes	23 (77)	19 (90)	
No	7 (23)	2 (10)	

To understand how other various factors affect the "Romantic Partner" subpopulation, their reactions were compared with the reported timing of the disclosure (Table 13). For statistical analysis, the "After Certain Milestone(s)", "After Marriage", and "After Children" subpopulations were combined into "Later in Relationship" due to the small proportion of individuals in each subpopulation and the similar perspectives of these individuals. The general associations found were that those who reportedly experienced the disclosure "Later in Relationship" were more likely to experience "Anger", "Denial", and "Sadness" and less likely to experience "Confusion". Regardless of the timing of the disclosure being in the "Beginning of Relationship" or "Later in Relationship, individuals seem to be equally as likely to experience

"Shock" and "Understanding". However, these associations were not found to have statistical significance (p>0.120).

TABLE 13. ASSOCIATION OF ROMANTIC PARTNERS' REACTIONS TO DISCLOSURE TIMING (N=51)

Reaction	Beginning of Relationship (n=26)	Later in Relationship (n=14)	Unspecified (n=11)	P-Value
	N (%)	N (%)	N (%)	
Shock				*0.323
Yes	12 (46)	7 (50)	8 (73)	
No	14 (54)	7 (50)	3 (27)	
Confusion				**0.194
Yes	15 (58)	4 (29)	4 (36)	
No	11 (42)	10 (71)	7 (64)	
Anger				**0.314
Yes	4 (15)	5 (36)	3 (27)	
No	22 (85)	9 (64)	8 (73)	
Denial				**0.146
Yes	6 (23)	8 (57)	5 (46)	
No	20 (77)	6 (43)	6 (54)	
Sadness				**0.229
Yes	17 (65)	12 (86)	10 (91)	
No	9 (35)	2 (14)	1 (9)	
Understanding				**0.892
Yes	22 (85)	11 (79)	9 (82)	
No	4 (15)	3 (21)	2 (18)	

*Chi-Square Test and **Fisher's Exact Test

The final aspect of exploring what may affect a romantic partner's reaction was their reported understanding of HD before experiencing the disclosure (Table 14). For statistical analysis, the "A Lot of Prior Knowledge" and "Some Prior Knowledge" subpopulations were combined due to the small proportion of individuals in each subpopulation and the similar perspectives of these individuals.

The majority (>70%) of all individuals, regardless of their prior knowledge level of HD, report experiencing "Sadness" and "Understanding" (Table 14). There are no significant differences in five of the six reactions reported by the "Romantic Partner" subpopulation when

they reportedly had either “A Lot/Some Prior Knowledge” of HD or “No Prior Knowledge” of HD (p>0.238). These reactions include “Shock”, “Confusion”, “Denial”, “Sadness”, and “Understanding”. However, there was a significant difference in the proportion of Romantic Partners who reported they experienced “Anger” after the disclosure (p =0.042). Individuals who reported having “A Lot/Some Prior Knowledge” about HD were more likely to experience “Anger” while those who reported having “No Prior Knowledge” of HD were less likely to experience “Anger”.

TABLE 14. ASSOCIATION OF ROMANTIC PARTNERS' REACTIONS WITH THEIR PRIOR KNOWLEDGE OF HD (N=51)

Reactions	A Lot/Some Prior Knowledge (n=10)	No Prior Knowledge (n=41)	Fisher's Exact Test P-Value
	N (%)	N (%)	
Shock			0.444
Yes	6 (60)	21 (51)	
No	4 (40)	20 (49)	
Confusion			0.500
Yes	4 (40)	19 (46)	
No	6 (60)	22 (54)	
Anger			0.042
Yes	5 (50)	7 (17)	
No	5 (50)	34 (83)	
Denial			0.334
Yes	5 (50)	15 (37)	
No	5 (50)	26 (63)	
Sadness			0.249
Yes	9 (90)	30 (73)	
No	1 (10)	11 (27)	
Understanding			0.238
Yes	7 (70)	35 (85)	
No	3 (30)	6 (15)	

3.2.1.5 Effect on Relationship (n=127)

This survey also explored whether there were any factors that had a reported effect on the couple's relationship. Respondents of all HD status groups were given the option of indicating

whether their relationship changed after their disclosure by either becoming closer, becoming further apart, or if there was no noted change in the relationship. There were 127 participants who answered this question. The participants who did not answer were excluded from analysis.

Timing of the experienced disclosure was the first factor used to determine if there was an association with individuals who reported the disclosure's effect on their relationship (Table 15). There was no significant difference on proportion of individuals who reported the effect the disclosure had on the relationship when disclosure was given at the "Beginning of Relationship", "After Certain Milestone(s)", or "After Marriage/Children" (p=0.927).

TABLE 15. ASSOCIATION OF TIMING OF DISCLOSURE WITH EFFECT ON RELATIONSHIP (N=127)

Effect on Relationship	Beginning of Relationship (n=92)	After Certain Milestone(s) (n=25)	After Marriage/Children (n=10)
	N (%)	N (%)	N (%)
Became Closer	40 (43)	12 (48)	4 (40)
No Change	44 (48)	10 (40)	5 (50)
Became Further Apart	8 (9)	3 (12)	1 (10)

Fisher's Exact Test P-Value = 0.927

The next factor explored was seeing if the source of the disclosure had any effect on the romantic partners' relationships (Table 16). There were 40 individuals from the "Romantic Partner" subpopulation who answered both the questions regarding the source of the disclosure as well as reported the effect of the disclosure on their relationship and were therefore analyzed. Most romantic partners had their own partner give the disclosure. Slightly over half (53%) of the individuals who reported their "Partner Disclosed" also indicated they felt they became closer with their partner afterwards. However, there is no significant difference when the partner disclosed or did not disclose on the effect of the relationship after disclosure (p=0.360).

TABLE 16. EFFECT ON RELATIONSHIP WHEN PARTNER DISCLOSED (N=40)

Effect on Relationship	Partner Disclosed (n=32)	Partner Did Not Disclose (n=8)
	N (%)	N (%)
We Became Closer	17 (53)	2 (25)
No Change	12 (38)	5 (63)
We Became Farther Apart	3 (9)	1 (12)

Fisher's Exact Test P-Value = 0.360

A majority (67%) of the individuals who reported they were "Friends/Acquaintances Before the Relationship" also indicated they felt there was no change to the relationship (Table 17). It was assumed that if individuals were friends or acquaintances before the relationship then there was an awareness of HD prior to the relationship. There is no significant difference whether the individuals were friends or acquaintances before the relationship and the reported effect on the relationship after disclosure (p=0.119)

TABLE 17. EFFECT ON RELATIONSHIP WHEN FRIENDS/ACQUAINTANCES BEFORE THE RELATIONSHIP (N=40)

Effect on Relationship	Friends/Acquaintances Before the Relationship (n=12)	Not Friends/Acquaintances Before the Relationship (n=28)
	N (%)	N (%)
We Became Closer	3 (25)	16 (57)
No Change	8 (67)	9 (32)
We Became Farther Apart	1 (8)	3 (11)

Fisher's Exact Test P-Value = 0.119

Over half (60%) of the individuals who reported their "Partner's Family/Friend Disclosed" also indicated they felt they became closer with their partner afterwards (Table 18). However, there is no significant difference when a partner's family or friend disclosed or did not disclose on the effect of the relationship after disclosure (p=0.584).

TABLE 18. EFFECT ON RELATIONSHIP WHEN PARTNER'S FAMILY/FRIEND DISCLOSED (N=40)

Effect on Relationship	Partner's Family/Friend Disclosed (n=10)	Partner's Family/Friend Did Not Disclose (n=30)
	N (%)	N (%)
We Became Closer	6 (60)	13 (43)
No Change	4 (40)	13 (43)
We Became Farther Apart	0 (0)	4 (14)

Fisher's Exact Test P-Value = 0.584

The majority (67%) of the individuals who reported they "Noticed Symptoms" in their partner also indicated they felt they became closer with their partner afterwards (Table 19). However, there is no significant difference when the romantic partner noticed symptoms in their partner or not on the effect on the relationship after disclosure (p=0.473)

TABLE 19. EFFECT ON RELATIONSHIP WHEN ROMANTIC PARTNER NOTICED SYMPTOMS (N=40)

Effect on Relationship	You Noticed Symptoms (n=9)	You Did Not Notice Symptoms (n=31)
	N (%)	N (%)
We Became Closer	6 (67)	13 (42)
No Change	3 (33)	14 (45)
We Became Farther Apart	0 (0)	4 (13)

Fisher's Exact Test P-Value = 0.473

Over half (57%) of the individuals who reported they "Found Out Together" with their partner also indicated they felt there was no change to the relationship (Table 20). However, there is no significant difference when the romantic partner and their partner found out about HD together or did not find out together on the effect on the relationship after disclosure (p=0.495).

TABLE 20. EFFECT ON RELATIONSHIP WHEN ROMANTIC PARTNER AND PARTNER FOUND OUT TOGETHER (N=40)

Effect on Relationship	You and Partner Found Out Together (n=14)	You and Partner Did Not Find Out Together (n=26)
	N (%)	N (%)
We Became Closer	5 (36)	14 (54)
No Change	8 (57)	9 (35)
We Became Farther Apart	1 (7)	3 (11)

Fisher's Exact Test P-Value = 0.495

3.2.1.6 Romantic Partners' Decision Factors

The main decision that all individuals in the "Romantic Partner" subpopulation faced after disclosure was the choice to stay with their partner and continue in the relationship with the knowledge of HD or to leave their partner and end the relationship. To gain a better understanding of this decision, the "Romantic Partner" subpopulation was presented with a branched section of the survey.

Respondents were asked to indicate if they needed time to make a decision about the relationship (Table 21). In order to understand what may influence whether an individual required time to make a decision, the factor of an individual's level of prior knowledge HD was analyzed. These levels consisted of a Likert Scale of "A Lot of Prior Knowledge", "Some Prior Knowledge", and "No Prior Knowledge". Regardless of an individual's reported level of prior understanding of HD, the majority indicated they did not need time to decide to stay with their partner and continue the relationship (p=0.484).

TABLE 21. ASSOCIATION OF PRIOR KNOWLEDGE WITH TIME NEEDED TO DECIDE ON RELATIONSHIP (N=51)

Time Needed to Decide	A Lot of Prior Knowledge	Some Prior Knowledge	No Prior Knowledge
	N (%)	N (%)	N (%)
Yes	0 (0)	3 (33)	7 (17)
No	1 (100)	6 (67)	34 (83)

Fisher's Exact Test P-Value = 0.484

In addition, the "Romantic Partner" subpopulation was presented with a set of factors which may have influenced their decision for the relationship and asked to rate each factor on a Likert scale of "Very Important", "Somewhat Important", and "Not Important" (Table 22). These options included "Late Onset Symptoms", "Inheritance: 50%", "Role of Caretaker", and "Faith/Religion". There were 3 participants from the "Romantic Partner" population who did not answer this question and were excluded from the analysis.

The "Role of Caretaker" had the largest proportion (35%) of the "Romantic Partner" subpopulation indicate it was "Very Important" when making their decision about the relationship while a majority (77%) indicated that "Faith/Religion" was "Not Important" (Table 22). However, in general, the "Romantic Partner" subpopulation indicated that all the given factors, except for "Faith/Religion", were "Somewhat Important" (40% to 48%). There were some individuals who reported "Other" factors that were "Very Important" and "Somewhat Important" and expanded on their answer in the free response box (see Appendix D). One individual indicated that the "advances in research would find treatments" and this was a "Somewhat Important" factor when deciding to stay in the relationship.

TABLE 22. DECISION FACTORS FOR THE RELATIONSHIP (N=48)

Factor	Very Important	Somewhat Important	Not Important
	N (%)	N (%)	N (%)
Late Onset Symptoms	6 (12)	23 (48)	19 (40)
Inheritance: 50%	13 (27)	19 (40)	16 (33)
Role of Caretaker	17 (35)	20 (42)	11 (23)
Faith/Religion	8 (17)	3 (6)	37 (77)
Other	3 (6)	4 (8)	41 (86)

Do not add up to total of "Romantic Partner" subpopulation because respondents were able to select multiple answers.

3.2.2 Ideal Disclosure

All participants were presented with this section of the survey which consisted of questions on the individual's opinion of the ideal disclosure. There were 153 individuals who responded to this section due to some of the "At Risk" and "Romantic Partner" subpopulations not continuing past this point of the survey. These individuals were excluded from analysis.

3.2.2.1 Components of Disclosure

Participants were presented with the same five components of disclosure as was presented in the experienced disclosure section and asked to indicate their opinion of the importance of each component on a Likert scale of "Very Important", "Somewhat Important", and "Not Important" (Table 23). Additionally, there was a free response box for participants to indicate any other components they believe should be included in disclosure (see Appendix D). The most common (43%) component being caregiving.

In order to account for the different perspectives of individuals by their HD Status, these responses were analyzed by HD Status subpopulations (Table 23). There is no significant difference among the HD subpopulations and how they ranked each component's importance ($p=0.230$). The majority (>50%) of all participants, regardless of HD subpopulation, indicated

that each of the components were "Very Important". Furthermore, the "Behavior/Personality" component was considered "Very Important" by the largest proportion of individuals (>89%), followed by "Inheritance" (>83%), "Cognition" (>80%), "Movement" (>62%), and finally "Late Onset" (51%).

TABLE 23. ASSOCIATIONS OF IDEAL COMPONENTS FOR DISCLOSURE WITH HD STATUS (N=153)

Component	At Risk (n=60)	Diagnosed/ Presymptomatic (n=28)	Diagnosed/ Symptomatic (n=18)	Romantic Partner (n=47)	Fisher's Exact Test P-Value
	N (%)	N (%)	N (%)	N (%)	
Movement					0.327
Very Important	40 (67)	21 (75)	15 (83)	29 (62)	
Somewhat Important	19 (31)	7 (25)	2 (11)	15 (32)	
Not Important	1 (2)	0 (0)	1 (6)	3 (6)	
Behavior/Personality					0.322
Very Important	56 (93)	25 (89)	17 (94)	43 (92)	
Somewhat Important	4 (7)	3 (11)	0 (0)	2 (4)	
Not Important	0 (0)	0 (0)	1 (6)	2 (4)	
Cognition					0.981
Very Important	48 (80)	23 (82)	16 (88)	39 (83)	
Somewhat Important	9 (15)	4 (14)	1 (6)	6 (13)	
Not Important	3 (5)	1 (4)	1 (6)	2 (4)	
Late Onset					0.230
Very Important	38 (63)	17 (61)	15 (83)	24 (51)	
Somewhat Important	19 (32)	10 (36)	2 (11)	17 (36)	
Not Important	3 (5)	1 (3)	1 (6)	6 (13)	
Inheritance					0.239
Very Important	57 (95)	24 (86)	15 (83)	40 (85)	
Somewhat Important	2 (3)	4 (14)	2 (11)	4 (9)	
Not Important	1 (2)	0 (0)	1 (6)	3 (6)	

One factor that may influence an individual's opinion of what components should be included in an ideal disclosure is their own experience (Table 24). In order to understand if there is an association between an individual's ideal disclosure and their experienced disclosure, the components aspect was analyzed. For statistical analysis, the "Somewhat Important" and "Not

Important" subpopulations were combined due to the small proportion of individuals in each subpopulation and the similar perspectives of these individuals.

There is an association of the proportions of participants who indicated "Movement" as being "Very Important" when it was included in their disclosure (73%) versus when it was not (50%) (Table 24). However, there was no statistically significant difference between these proportions (p=0.106). The overwhelming majority of participants indicated "Behavior/Personality" as "Very Important" regardless of whether the component was included in the disclosure (92%) versus when it was not (93%) (p=1.000).

There were significant differences found with the remaining three components: "Cognition" (p=0.013), "Late Onset" (p=0.002), and "Inheritance" (p=0014) (Table 24). Individuals who indicated "Cognition" as being "Very Important" were more likely to have the component included in their disclosure (89%) versus when it was not (65%). Individuals who indicated "Late Onset" as being "Very Important" were more likely to have the component included in their disclosure (72%) versus when it was not (39%). Individuals who indicated "Inheritance" as being "Very Important" were more likely to have the component included in their disclosure (92%) versus when it was not (50%).

TABLE 24. ASSOCIATION OF COMPONENTS' IMPORTANCE WHEN INCLUDED IN EXPERIENCED DISCLOSURE (N=127)

Component Included	Component Very Important	Component Somewhat/Not Important	P-Value
	N (%)	N (%)	
Movement			*0.106
Yes (n=115)	84 (73)	31 (27)	
No (n=12)	6 (50)	6 (50)	
Behavior/Personality			*1.000
Yes (n=109)	100 (92)	9 (8)	
No (n=18)	17 (94)	1 (6)	
Cognition			*0.013
Yes (n=107)	95 (89)	12 (11)	
No (n=20)	13 (65)	7 (35)	
Late Onset			**0.002
Yes (n=99)	71 (72)	28 (28)	
No (n=28)	11 (39)	17 (61)	
Inheritance			*0.014
Yes (n=121)	111 (92)	10 (8)	
No (n=6)	3 (50)	3 (50)	

* Fisher's Exact Test and **Chi-Square Test

3.2.2.2 Timing of Disclosure

An additional aspect of understanding the details about an ideal disclosure is the timing for it to occur within a relationship's timeline (Table 25). Among the 160 respondents who answered this question, the majority (71%) indicated the "Beginning of Relationship" as their ideal time to disclose HD.

TABLE 25. THE IDEAL TIMING TO HAVE DISCLOSURE (N=160)

Timing of Disclosure	At Risk (n=48)	Diagnosed/ Presymptomatic (n=23)	Diagnosed/ Symptomatic (n=16)	Romantic Partner (n=37)	Total (n=160)
	N (%)	N (%)	N (%)	N (%)	N (%)
Beginning of Relationship	36 (75)	19 (83)	14 (88)	27 (73)	113 (71)
After Certain Milestone(s)	12 (25)	4 (17)	1 (6)	10 (27)	37 (23)
After Marriage/Children	0 (0)	0 (0)	1 (6)	0 (0)	2 (1)
Not Specified	0 (0)	0 (0)	0 (0)	0 (0)	8 (5)

One factor that may influence an individual's opinion of when disclosure should occur is their own experience (Table 26). For statistical analysis, the "After Certain Milestone(s)", "After Marriage", and "After Children" subpopulations were combined into "Later in Relationship" due to the small proportion of individuals in each subpopulation and the similar perspectives of these individuals. The majority (87%) of individuals indicated that their ideal timing for disclosure is the same as the timing as their experienced disclosure. Furthermore, most participants (69%) both experienced the disclosure at the beginning of the relationship and considered this timing ideal. There was a small proportion (13%) who indicated their ideal timing is different from the timing they experienced. However, there is no specific significance of one timing being preferred over the other (p=0.210).

TABLE 26. ASSOCIATIONS WITH IDEAL TIMING WITH THE TIMING EXPERIENCED (N=124)

Timing Experienced	Ideal Beginning of Relationship	Ideal Later in Relationship
	N (%)	N (%)
Beginning of Relationship	85 (69)	5 (4)
Later in Relationship	11 (9)	23 (18)

McNemar Test P-Value = 0.210

3.2.3 Importance of Understanding Disclosure

The final question regarding disclosure asked participants to indicate the importance of the romantic partner's understanding of the disclosure (Table 27). The "At Risk", "Diagnosed and Presymptomatic", and "Diagnosed and Symptomatic" HD Status subpopulations were combined into "At Risk/Diagnosed" due to the similar perspectives of these individuals. The overwhelming majority, as well as equal proportion, of the "At Risk/Diagnosed" subpopulation (94%) and the "Romantic Partner" subpopulation (94%) indicated it was "Very Important" for the romantic partner to understand what was discussed in any given disclosure.

TABLE 27. IMPORTANCE OF THE ROMANTIC PARTNER'S UNDERSTANDING OF DISCLOSURE (N=153)

Importance	At Risk/Diagnosed (n=106)	Romantic Partner (n=47)
	N (%)	N (%)
Very Important	100 (94)	44 (94)
Somewhat Important	6 (6)	3 (6)
Not Important	0 (0)	0 (0)

3.3 Family Planning

The third section of the survey presented individuals with questions about family planning. After the disclosure section, there were seven participants who did not proceed with the remaining sections of the survey. Therefore these participants were excluded from subsequent analysis and the remaining 152 participants were analyzed for the family planning section.

3.3.1 Family Plans

Respondents were asked to indicate their family plans in whether they "Already Have Children", "Currently Have No Children but Want to Have Children", or "Currently Have No

Children and Have No Plans to Have Children" (Table 28). A large proportion (74%) of participants indicated they currently have no children. When further delineated, over half of these individuals indicated that they would like to have children.

The "Already Have Children" subpopulation was given a free response box to provide details about their children (see Appendix D). A majority (93%) of these individuals indicated they have between one to five children. There was a small proportion (5%) of the "Already Have Children" who indicated they have non-biological children through adoption. There was also one individual who indicated they had their children through *in vitro fertilization* and preimplantation genetic testing for HD.

TABLE 28. FAMILY PLANS (N=152)

Family Plans	N	%
Already Have Children	55	36
Currently Have No Children but Want to Have Children	58	38
Currently No Children and Have No Plans to Have Children	39	26

3.3.2 Factors for Family Planning

Participants were then asked about which factors they considered when making their family planning decisions (Table 29). They were presented with three factors and asked to indicate their importance on a Likert scale of one to three with the assigned values of "Very Important", "Somewhat Important", and "Not Important". There were five participants who were not included in the analysis as they did not indicate the importance of these factors due to their specific situations of not wanting children for reasons unrelated to HD, being beyond child-bearing age, or they had their children before knowing about HD (see Appendix D). Participants had the option to expand their answer about additional factors with a free response box (see Appendix D). Some of the common responses included having children before knowledge of HD

in the family, not wanting children for other reasons unrelated to HD, cost, and not wanting their children to have a parent who has HD.

Most (79%) of respondents indicated "Inheritance: 50%" was a "Very Important" factor when making their decision to have children or not (Table 29). Additionally, "Inheritance: 50%" was an overall important factor for the majority (90%). This was followed by the "Symptoms/Lifestyle" factor as being both a "Very Important" factor (67%) and an overall important factor (87%). In general, the "Faith/Religion" factor was considered to be the least important (30%).

TABLE 29. FACTORS CONSIDERED FOR FAMILY PLANNING (N=145)

Factors	N	%
Inheritance: 50%		
Very Important	115	79
Somewhat Important	16	11
Not Important	14	10
Symptoms/Lifestyle		
Very Important	97	67
Somewhat Important	29	20
Not Important	19	13
Faith/Religion		
Very Important	31	21
Somewhat Important	13	9
Not Important	101	70

These factors may influence an individual's, or couple's, decision to have children. In order to understand the importance of these factors, the responses were analyzed by the subpopulations of individuals who "Already Have Children" with the subpopulations who have "No Children" and indicated either the desire to have children or not.

Individuals who "Already Have Children" are less likely (58%) to indicate "Inheritance" as being a "Very Important" factor then the "No Children but Want Children" (90%) and "No Children and Do Not Want Children" (92%) subpopulations (Table 30). This difference in the

importance of "Inheritance" is statistically significant (p<0.0005). Likewise, the "Already Have Children" are less likely (42%) to indicate "Symptoms/Lifestyle" as being a "Very Important" then the "No Children but Want Children" (71%) and "No Children and Do Not Want Children" (94%) subpopulations. This difference in the importance of "Symptoms/Lifestyle" is also statistically significant (p<0.0005).

There was no significant difference for the "Already Have Children" subpopulation compared to the "No Children But Want Children" and "No Children And Do Not Want Children" in regards to the importance of "Faith/Religion" as a factor for family planning (p=0.150) (Table 30).

TABLE 30. ASSOCIATION OF FACTORS FOR FAMILY PLANNING WITH FAMILY PLAN STATUS (N=145)

Factor	Already Have Children (n=50)	No Children but Want Children (n=37)	No Children and Do Not Want Children (n=58)	Fisher's Exact Test P-Value
	N (%)	N (%)	N (%)	
Inheritance				<0.0005
Very Important	29 (58)	52 (90)	34 (92)	
Somewhat Important	10 (20)	4 (7)	2 (5)	
Not Important	11 (22)	2 (3)	1 (3)	
Symptoms/Lifestyle				<0.0005
Very Important	21 (42)	41 (71)	35 (94)	
Somewhat Important	12 (24)	16 (27)	1 (3)	
Not Important	17 (34)	1 (2)	1 (3)	
Faith/Religion				0.150
Very Important	15 (30)	12 (21)	4 (11)	
Somewhat Important	6 (12)	5 (8)	2 (5)	
Not Important	29 (58)	41 (71)	31 (84)	

3.3.3 *In Vitro Fertilization* and Preimplantation Genetic Testing for Monogenic Disorders

The last set of questions for the Family Planning section of the survey inquired about *in vitro fertilization* and preimplantation genetic testing for monogenic disorders (*IVF*/PGT-M). An explanation of *IVF*/PGT-M was included in the survey as seen below:

> "*IVF* is when the egg is fertilized by the sperm outside of the body. PGT-M, also known as preimplantation genetic diagnosis (PGD), is a procedure to identify which ones have a genetic condition, such as HD, prior to implanting the fetus."

There were 150 participants who continued with this set of questions about *IVF*/PGT-M and those who did not respond were excluded from analysis (Table 31). Respondents were asked to indicate if they already had prior knowledge about *IVF*/PGT-M and a majority (88%) responded "Yes".

TABLE 31. TOTAL PARTICIPANTS' KNOWLEDGE OF IVF/PGT-M (N=150)

Knowledge of *IVF*/PGT-M	**N**	**%**
Yes	132	88
No	18	12

Participants were then asked if they are considering or would consider utilizing *IVF*/PGT-M in their own family plans (Table 32). Under half (41%) reported they would not consider *IVF*/PGT-M.

TABLE 32. TOTAL PARTICIPANTS WHO WILL CONSIDER IVF/PGT-M (N=150)

Consider *IVF*/PGT-M	**N**	**%**
Yes	88	59
No	62	41

3.3.3.1 Factors for Choosing Not to Use IVF and PGT-M

The 61 respondents who reported they would not consider *IVF*/PGT-M were presented with a branched section of the survey which delved into the reasoning behind their decision (Table 33). Participants were asked to indicate all factors that applied in their decision from the presented five of "Cost", "Faith/Religion", "Uncertainty/Not Enough Information", "Time", and "Experience". Additionally, participants had the option to include "Other" factors with a free response box (see Appendix D). Of these additional factors submitted, the common themes included individuals who already had children, did not want children for other reasons unrelated to HD, did not want children to have a parent with HD, as well as the emotional and physical stress that *IVF*/PGT-M may cause.

Of the 62 participants who reported they would not utilize *IVF*/PGT-M, most (44%) indicated "Cost" was a factor in that decision (Table 33). This was followed by a general even spread of proportions for the other presented factors of "Faith/Religion" (21%), "Uncertainty/Not Enough Information" (29%), "Time" (26%), and "Experience" (24%).

TABLE 33. FACTORS FOR NOT CHOOSING IVF/PGT-M (N=62)

Factors	N	%
Cost	27	44
Faith/Religion	13	21
Uncertainty/Not Enough Information	18	29
Time	16	26
Experience	15	24
Other	25	40

Do not add up to total of population because respondents were able to select multiple answers.

3.3.3.2 Educated About *IVF* and PGT-M

The 150 participants were then asked how they were educated about *IVF*/PGT-M (Table 34). They were presented with five sources and specified all that applied to their experience. There was a free response box for individuals to include additional sources of education (see

Appendix D). The two most common additional sources were by "word of mouth" from their family members, friends, or members of their support groups taking the time to share information about these procedures or through various HD organizations such as the Huntington's Disease Society of America.

Most (59%) of the respondents indicated they were educated about *IVF*/PGT-M through the "Internet" (Table 34). This was followed with being told about *IVF*/PGT-M from their "Genetic Counselor or Geneticist" (31%), "Neurologist" (19%), and then "Primary Care Physician" (11%). There were some (18%) individuals who indicated they were made aware of *IVF*/PGT-M from the survey's explanation. Additionally, compared from the free responses for this question, some individuals reported they were educated about *IVF*/PGT-M through "word of mouth" from their family or friends (10%) and through various HD organizations (8%).

TABLE 34. EDUCATION SOURCES FOR IVF-PGT-M (N=150)

Source	N	%
Primary Care Physician	17	11
Neurologist	28	19
Genetic Counselor or Geneticist	46	31
Internet	88	59
This Survey	27	18
Other	44	29

Do not add up to total of population because respondents were able to select multiple answers.

3.4 Reflections

The fourth and final section of the survey presented individuals with a set of reflective questions. After the family planning section, there were two participants who did not proceed with the final section of the survey. Therefore, these participants were excluded from subsequent analysis and the remaining 148 participants were analyzed for the reflection section.

3.4.1 How a Cure Changes Perspectives on Disclosure or Family Planning

The 148 remaining participants were presented with the hypothetical scenario of the existence of a cure for HD (Table 35). Respondents were then asked to indicate which, if any, sections of the survey they would have answered differently. The disclosure section had the lowest proportion (38%) of participants indicate they would have changed their answers for this part of the survey. The highest proportion of participants (57%) responded that they would have answered the family planning section differently and less than half of the participants (43%) specified it would have changed their answers to the *IVF*/PGT-M section.

TABLE 35. PERSPECTIVES WHICH WOULD CHANGE WITH CURE FOR HD (N=148)

Perspective	N	%
Disclosure	56	38
Family Planning	84	57
IVF/PGT-M	64	43
Other	4	3

Do not add up to total of population because respondents were able to select multiple answers.

3.4.2 Information that Would Change the Decision to Disclose to Romantic Partner

The HD Status subpopulations who are in the position of giving disclosure (n=102) were asked if there was any additional information that would change their decision to disclose to their romantic partner. This question was asked in a free response format to allow participants to expand upon their answer. The general consensus for this question was "No", there is no additional information that would change their decision for disclosure. Furthermore of the "At Risk" subpopulation (n=56), there was one individual who responded "Yes" and expanded their answer with their own personal HD status being a reason to change their decision about disclosing to their romantic partner. Of the "Diagnosed and Presymptomatic" subpopulation (n=28), there was one individual who responded "Yes" and expanded their answer with the information of HD's effect on insurance and employment status being a reason to change their

decision to disclose. Of the "Diagnosed and Symptomatic" subpopulation (n=18), there were three individuals who responded "Yes" and expanded their answer with the age of onset being information that change their decision to disclose.

3.4.3 Information that Would Change the Romantic Partner's Decision About the Relationship

The "Romantic Partner" subpopulation (n=46) was presented with a similar question of whether there was any information which would change their decision to stay with their partner and not end the relationship. This question was asked in a free response format to allow participants to expand upon their answer. The majority (85%) indicated "No", there is no additional information which would change their decision about the relationship and their partner. One individual stated they were "unsure". There were six individuals who responded "Yes" and expanded their answers with information about a cure or way to delay the onset of symptoms, adopting children versus having biological children, awareness of the emotional/cognitive symptoms of HD and particularly the aspect of the spouse's anger being affected, as well as knowledge of *IVF*/PGT-M and understanding that these procedures do not always work, the partner's family "pretending it [HD] wasn't happening". Finally, one individual responded that the timing of disclosure would have changed their decision to stay. Furthermore, they would have chosen to leave their partner and end the relationship if they had "found out sooner".

4. DISCUSSION

Huntington Disease (HD) has several unique characteristics that set it apart from many other genetic conditions since it typically has an adult-onset of symptoms, affects multiple aspects of an individual's life, and currently has no disease modifying treatment or cure. Patients with HD benefit from receiving counseling from genetics healthcare providers, such as genetic counselors, who can guide and counsel them through complex topics including educational aspects as well as emotional and psychological aspects. One of the complex educational topics to address is the new information about HD that continues to be discovered through the ongoing research. Recent discoveries include variations to the age of onset due to genetic modifiers other than an individual's CAG repeat size. In this study, various emotional and psychological topics regarding disclosing to romantic partners and family planning were identified by participants.

4.1 Disclosure

One complexity that arises with the adult-onset of symptoms of HD is the absence of symptoms during certain key phases of life. This allows individuals to achieve typical life milestones such as establishing careers, bonding with romantic partners, and making family plans, before they are affected by symptoms of HD. When an individual has a family history of HD and/or a diagnosis of HD that is already known, there is a disclosure that eventually happens with a romantic partner. This study explored the importance of including certain components as well as when the disclosure occurs within the timeline of the relationship.

4.1.1 Disclosure Components and Timing

The majority of respondents, regardless of their personal HD status, indicated that each given component of movement, behavior/personality, cognition, late onset of symptoms, and inheritance were very important and should be included in a disclosure to a romantic partner. When considering what to include in the disclosure, individuals may want to prioritize different components in their conversation with their romantic partner.

The aspects about HD that were considered the most important to be aware of were the effects on an individual's behavior and personality. These behavior and personality features may include changes to an affected individual's temperament, depression, and anxiety. One individual expressed their concern about these potential behavioral and personality changes:

> "… people with HD can be mean and they do not know that they are. When the time comes I fear if I'm mean and he leaves not being aware it's my brain and not me. There are always more to talk about in what symptoms look like besides the obvious."

Since the autosomal dominant inheritance pattern of HD is an important factor that affects the romantic partners' children as well, respondents indicated that it is imperative for this component to be included in disclosure. Romantic partners should be made aware that an affected individual has a 50% chance of passing down the expanded CAG repeat to each of their offspring. Inheritance was also a factor that was deemed important for family planning and was discussed by individuals in that section of the study. However, some individuals also specified that disclosure should include some discussion about the family planning options that are available. Currently, this includes *in vitro fertilization* with preimplantation genetic testing for monogenic disorders (*IVF*/PGT-M) which are procedures that can identify and implant the offspring who did not inherit HD. The other components of cognition and movement followed in importance which

include memory deficits as well as the physical changes which are more "obvious." These include chorea, rigidity, and impaired motor control. Late onset of symptoms was considered to be the least important of the five components for disclosure. This component refers to an individual being able to live a majority of their life unaffected and experiencing the onset of the previously described symptoms in their adult years.

A majority of individuals, regardless of their HD Status, deemed the ideal time to disclose HD as being identical to the timing of their own experienced disclosure. It's interesting to note that this timing for disclosure was in the beginning stages of the relationship for most of the participants in the study. There was a proportion of individuals who indicated that their ideal time for disclosure was after certain milestone(s) with the majority of these responses indicating this to be after the relationship is considered serious.

Importantly, the romantic partners reported that there are no significant factors which affect how they receive their partner's disclosure of HD. This was measured by the reported reactions following disclosure. There were some general trends such as individuals were more likely to experience anger, denial, and sadness when disclosure was given later in the relationship. However, in comparison to the individuals who reported disclosure was given in the beginning of the relationship, the difference was not found to be significant. Overall, the perspectives of the romantic partners after disclosure were similar regardless of disclosure timing, depth, or partner's prior knowledge level.

4.1.2 Descriptive Analysis of At Risk and Diagnosed's (Presymptomatic and Symptomatic) Free Response Answers For Disclosure

There were some very specific points that the individuals who disclosed HD discussed in greater detail when considering decisions about disclosure. These were described in their free response answers to certain questions in the survey (see Appendix D).

A significant proportion (47%) of participants who expanded their answer indicated the importance of including the caregiving aspect as a component of disclosure since it may not be obvious from the discussion of HD's symptoms. As individuals with HD, particularly those who are symptomatic, clearly have experienced or observed, it is imperative for them to have someone in their life who will care for them as the condition progresses. One individual, who identified as being at risk, stated that it is important for romantic partners to be aware of "the burden of being in a family that has HD (caretaking, etc) even if you test negative." Essentially, acknowledging that HD is a condition which is bound to affect the entire family unit regardless of an individual's HD status.

In regards to the timing of disclosure, the majority of participants indicated that the ideal time to disclose HD to a romantic partner is in the beginning stages of the relationship. However, approximately a quarter of these individuals indicated the ideal time for disclosure was later in the relationship. A significant proportion (63%) of these individuals expanded their answer to specify that disclosure should occur once the relationship is considered to be serious, whether this be once marriage is being considered or the relationship is decidedly "long-term." It's important to note that the definition of a serious relationship varied between individuals within this study and this variation most assuredly exists outside of it. One individual also specified that the romantic partner must be ready for disclosure stating, "You know they are understanding and

capable of understanding what this is." Another qualified their answer by including the aspect that everyone's relationship is different and timing will vary from couple to couple.

One respondent shared the experience which caused her to disclose to her romantic partner and solidified her position of its importance:

> "My mom was trying to get me to lie and not tell anyone I was with until we were engaged because she thought it made me undatable (sic), which is why I went straight home that night and told my partner after 3 months of dating. I think it's actually better, because if they're going to run off because of HD then you don't want them anyways. You need someone who stays despite it, not to trap someone into the problem."

4.1.3 Descriptive Analysis of Romantic Partners' Free Response Answers for Disclosure

Some romantic partners discussed additional specific points to consider in decisions concerning disclosure in greater detail. These were described in their free response answers to certain questions in the survey (see Appendix D).

Similar to the population who disclose HD, a significant proportion (43%) of romantic partners also expanded their answer with the importance of the caregiving aspect as a component of disclosure. This was reported by individuals who had partners who are either at risk or already diagnosed and symptomatic. Since the main burden of caregiving typically falls onto the romantic partner, this should be clearly communicated in the disclosure. One individual emphasized "the need to have support," though whether this was intended as the romantic partner needing support or the individual with HD needing support was not clear. However, it is true that both the individual and their romantic partner require support throughout the progression of HD. A different individual also included this idea while expressing frustration at

the lack of the family's support through denial of HD as part of their personal reaction to their partner's disclosure.

Of the individuals who indicated the ideal timing of disclosure was later in the relationship and specified when it should occur, it was unanimous that disclosure should ideally happen once the relationship is considered to be serious. Three of these individuals also included the definition of a serious relationship to be anywhere from 6 months to a year of dating.

Several romantic partners included additional factors that they considered when making their decision to stay with their partner. Two individuals brought up that the aspect of having their own family and children as important when making their decision to continue the relationship. There was also an individual who reported considering "advances in research [that] would find treatments" and the impact this would make on their relationship in the future. These factors along with the components included in disclosure may be helpful for romantic partners to take into consideration when deciding to continue the relationship.

4.2 Family Planning

In general, the decision to start a family is monumental for couples. However, when a genetic condition such as HD is involved, this decision is decidedly more complicated due to its inheritance pattern. Several individuals stated their concern, worry, and heartache over family planning decisions. One individual wondered "would I be around and well enough to raise the child" and another individual shared that she "tied my tubes to not have sick babies."

It's important to note that approximately one third of participants indicated they had children before knowing about HD in their family. There was also a considerable proportion of individuals who indicated they did not want to have children for reasons unrelated to HD. These

individuals were included in the statistical analysis; however, they were excluded from the descriptive analysis of the decision-making for having children or using *IVF*/PGT-M.

4.2.1 Considerations for the Decision to Have Children or Not to Have Children

The majority (66%) of participants in this study, regardless of HD status, indicated they did not have children at the time they submitted their survey. Of the proportion who indicated they do not currently have children, over half of these individuals specified they also did not want to have children. In the decision of whether or not to have children, the autosomal dominant inheritance pattern of HD as well as the symptoms and lifestyle for those affected by HD were both considered to be more important factors for those who do not have children than for those who already have children.

Some individuals elaborated upon additional factors that they took into consideration when deciding whether to have children or not. There was a considerable proportion (25%) who factored finances into their decision. This included, cost of living with HD such as healthcare care or insurance as well as the elective cost of using procedures like *IVF*/PGT-M. In addition, several individuals (17%) indicated that the progress of research and possible cure for HD in the future was an important factor in their decision. For some participants, this progress of research included advancements in the prenatal field such as “the ability to have children that wouldn’t be at risk” for HD through *IVF*/PGT-M.

4.2.2 Considerations for *In Vitro Fertilization* and Preimplantation Genetic Testing for Monogenic Disorders

Currently, genetic testing for HD during pregnancy is available through prenatal procedures such as chorionic villus sampling or amniocentesis. One relatively newer area of progress in the prenatal field is the development of *IVF*/PGT-M. These procedures allow for the birth of biological children who will not be at risk for HD. An area of interest in this study was to understand the HD community's knowledge and opinion of *IVF*/PGT-M. A majority (88%) of the participants were previously aware of *IVF*/PGT-M. The most common source of education or awareness about these procedures was through the internet (59%), followed by being counseled by either a genetic counselor or geneticist (31%). There were also some participants (18%) who indicated they were educated about *IVF*/PGT-M through this study.

There was a substantial proportion (41%) of participants who stated they would not choose to use *IVF*/PGT-M in their own family planning. In exploring why these individuals would not choose to utilize these procedures, the most common barrier (44%) was cost. Some individuals included additional barriers in the free response section. The most notable of these were the individuals (16%) who specified they did not want their children to grow up with a parent who has HD. One respondent detailed her conflict of "already [having] one child at risk, feel unfair to give future children risk free status."

4.3 Descriptive Analysis of Paired Participants

This study included three linking questions to potentially pair participants as couples. Though a considerable proportion of individuals answered these questions, only three pairs were identified. This is not a sufficient sample size for statistical analysis of the paired responses.

However, because a goal of this study was to understand the dynamics of couples in addition to the responses from individuals, a descriptive summary of these data is included here.

Overall, each couple was in agreement that all the components considered in the survey were important and should ideally be included in disclosure. One romantic partner added in their free response that it is important to include the discussion of family planning and the option to have children through *IVF*/PGT-M in the disclosure. There were some minor differences between the couples anout when the ideal timing of disclosure should occur. However, the majority indicated this to be the beginning of the relationship.

In general, both members of a couple had similar responses in their desire to have children and which factors were of importance when making their family planning decisions. The majority of individuals and couples indicated that the autosomal dominant inheritance of HD was a very important factor in their decisions. However, for some couples there were some dissimilarities in their responses for the *IVF/*PGT-M section of the survey including whether they would consider using these procedures.

None of the romantic partners in these couples indicated that there was any information that would change their decision to stay with their partner. One romantic partner stated, “I'm happy as can be, regardless of whether or not my significant other is going to develop the disease. True love will triumph anything in its way.”

4.4 Summary of Recommendations for Practice

The goal of this study was to explore the process of disclosure and family planning decisions when HD is involved. By understanding the perspectives of individuals either at risk or diagnosed with HD and their romantic partners, healthcare providers may be able to better

address the concerns and questions that patients and their romantic partners convey. There may also be additional topics that patients may not be aware of and would benefit from discussing. Genetic counselors are considered an integral part of patients' HD care, particularly with individuals who are at risk and elect presymptomatic genetic testing to confirm if they inherited HD. Due to the nature of genetic counseling appointments, patients may be more inclined to discuss these topics with a genetic counselor. Some of the findings were expected, however, the participants of this study also revealed some surprising and unexpected information. This would be informative for counseling patients regarding disclosure to romantic partners and family planning decisions.

4.4.1 Counseling Points for Disclosure

As one of the healthcare providers on the HD multidisciplinary team, genetic counselors are well-suited to discuss patients' concerns and questions about disclosing HD to their romantic partner. The findings of this study may help shape the conversation around disclosure and provide guidance for patients approaching this decision in their own relationship.

The overall consensus of the study was that disclosure to a romantic partner should include more information rather than less information. The symptoms of HD including movement, behavior and personality, cognition changes, and the late onset of symptoms, as well as the autosomal dominant inheritance of the condition were the components presented in the survey. Each of these components were deemed very important to include in disclosure by over half of all participants. However, the most important components reported were changes in an affected individual's behavior and personality as well as the inheritance pattern where 50% of an affected individual's offspring may inherit HD. A notable number of individuals alluded to the

effect on an affected individual's temperament and how HD can affect someone's propensity for anger. Since the caregiving aspect may not be obvious from the previously mentioned components and it was reported as being very important, many individuals reported that the role of being a caretaker should be included explicitly in disclosure since it affects the romantic partner specifically. Additionally, some other important components to consider including in disclosure are the complexities of how HD affects insurance and employment as well as the various family planning options that are available such as adoption or *IVF*/PGT-M.

Another aspect of disclosure which may be a cause for concern is when to give disclosure. For a majority of the study, the timing the participants indicated to be ideal was when they either disclosed or received disclosure themselves. The major proportion reported that they both experienced their disclosure at the beginning of the relationship and believe the ideal timing for disclosure is at the beginning of the relationship. There were some individuals who indicated that though it is more ideal to disclose earlier in the relationship rather than later, it is also important to confirm the relationship is serious and has a future before doing so.

4.4.2 Counseling Points for Family Planning

While the discussion of family planning may not be appropriate for all patients, it may be beneficial for some patients who are in that specific phase of life. Particularly, if they and their romantic partner are looking towards a future together. The findings of this study may assist in addressing the common concerns the HD community carries when considering whether to have children or not.

Specifically, in regards to making the decision to have children, two important topics to consider are the autosomal dominant inheritance of the condition and the effects of HD on the

affected individual as well as the family's lifestyle. One unexpected yet very valuable point that was brought up by several participants was the aspect of children, affected or unaffected, having an affected parent. Even if there was a guarantee that they would not inherit HD, their children would be raised by a parent who has HD. This carries its own emotional and physical burden regardless of their personal HD status. Furthermore, the romantic partners would be assuming multiple roles including the primary caregiver for their children, as well as their partner after the onset of their symptoms.

One of the relatively new advancements in the prenatal field of genetics is the ability to fertilize embryos and have them undergo genetic testing outside of the woman's body. This enables a viable yet costly option to have children who will not inherit HD. While a referral to a fertility clinic may be appropriate, it may be helpful to address some concerns surrounding *IVF*/PGT-M. A majority of the participants in this study indicated cost being a major barrier for them as well as concern over the emotional and physical stress of these procedures. One individual included the important life experience of undergoing "two rounds of *IVF* [which] didn't work for us." This elucidates the inclusion of unsuccessful *IVF*/PGT-M in counseling these patients. The rate of complications with these procedures is equally important to include in counseling.

4.4.3 Counseling Points for Couples

Due to the very limited population of paired participants, these findings carry no statistical significance. However, certain aspects of the descriptive analysis may reveal specific points of discussion for some couples and can benefit genetic counselors in understanding how to approach couples through the counseling of HD topics.

Often, it is easier to appreciate the full scope by including various perspectives of a situation. While most of the time the individuals in a couple agreed upon the same factors which were important to them when making certain decisions, there were some individuals who commented on additional factors which were not originally included in the survey. This added perspective allowed a more comprehensive understanding for the study's population as whole. Though couples tend to have the same, or very similar, opinions of what values and factors are most important to them, there may be additional thoughts that set these individuals apart. This finding contributes to our ability of understanding that couples may be in agreement overall yet have slightly varied opinions which are important to discuss.

While it is less complicated for a couple to be in agreement and not in conflict regarding all issues, this is not always realistic. A genetic counselor may be able to provide guidance to couples who hold differing opinions by helping navigate these topics or even identifying such topics. This study revealed that one such possible subject is the decision or consideration of using *IVF*/PGT-M. It can be helpful for both members of the couple to receive accurate information from a genetic counselor about these procedures so they are able to make fully informed decisions together.

4.5 Limitations

This study was limited by its sample size and due to the majority of participants being female, younger than 36 years old, and of Caucasian ethnicity, the results from this study may not be representative of the HD community as a whole. Particularly for the romantic partners, the majority of female respondents may be indicative of a biased perspective in this study. A 21% drop rate after the demographic section of the survey excluded a noteworthy proportion of

individuals from the analysis of the study. While the reasons for why these individuals did not progress further in the survey are not explicitly known, it is interesting that a majority (94%) refrained from indicating their HD status. It could be speculated that a reason for this may be that individuals felt this survey was inquiring about sensitive topics and felt vulnerable when asked to indicate their HD status of being at risk, diagnosed, or a romantic partner. Additionally, they may have had doubts about the survey's confidentiality and had concerns about possible effects on insurance and employment. There were some other participants who submitted certain sections of the survey and did not complete the survey in its entirety. This may be due to individuals disregarding specific sections that they did not believe applied to them such as not answering the family planning section since they do not have children.

While the total sample size was still considered significant, each HD subpopulation was significantly impacted by the percentage of individuals who did not proceed past the demographic questions. The smallest HD subpopulation consisted of the individuals who identified as being diagnosed and symptomatic. There are various possible factors for this impact including the format of the survey. Individuals who are further in the progression of HD and experiencing symptoms may have been less inclined to join this study. It is possible that the online format may have been a barrier which made taking this survey more difficult and served as a limitation for affected individuals.

One unique limitation to this study was the patient report of having a diagnosis of HD. There are differences between a clinical diagnosis and molecular diagnosis as well as the added complexity of HD-like conditions. A neurologist may perform an evaluation and series of tests which can result with a clinical diagnosis of HD based off of symptoms and imaging. A patient may also pursue genetic testing which reveals the number of CAG repeats in the *HTT* gene. This

confirms whether an individual actually inherited the expanded CAG repeat and can result in a molecular diagnosis of HD. Due to the nature of analyzing the *HTT* gene rather than examining an individual's symptoms, it is possible for individuals to be diagnosed with HD years before they become symptomatic. This survey did not inquire how individuals were diagnosed and also relied solely on the patient's interpretation of whether they consider themselves as presymptomatic or symptomatic.

There is a slight possibility that some participants of the study identified being both a romantic partner as well as another HD status such that they were also being part of the at risk subpopulation. This survey only allowed participants to identify with one HD Status subpopulation. In the analysis of the answers to the free response questions, there were no individuals who indicated this situation of identifying with multiple HD Status subpopulations. Therefore this type of situation was not accounted for in this study.

Though this study offers a substantial amount of understanding into how the HD community has been handling decisions concerning disclosure and family planning, there is still much to be explored. Some limited aspects to this study include data that was not gathered which may have offered additional insight into the participants and their responses. This includes information on when the affected individual was diagnosed with HD, whether the affected individual was symptomatic at the time of disclosure, and whether there were romantic partners who left their partner and ended the relationship after disclosure. These aspects may change the way an individual views HD, from their knowledge about the condition to their hope surrounding research for a cure and treatments.

Another key limitation of this study was the lack of linked participants. Though many individuals responded to the linkage questions, there were only three couples who were linked

with confidence and therefore qualitatively analyzed in this study. This may have been due to unclear or missing responses from individuals which led to couples not being recognized. Additionally, this may have been the result of some partners choosing not to participate or not completing the survey. It is also possible that the two individuals of a couple may be less likely to both take part of this study if they have conflicting opinions. If there had been more data available from couples for analysis, then this may have allowed for significant findings, additional understanding, and context for the responses from the affected individual and their romantic partner.

4.6 Future Studies

The purpose of this study was to explore how individuals approach romantic relationships and the factors considered when making future life decisions with HD. Furthermore, this study sought to understand if and how the perspectives of those either at risk or diagnosed with HD may differ from the romantic partners of these individuals.

This study had a small population of individuals who identified as being diagnosed and symptomatic. One aspect which may have limited the sample size of these individuals is the online survey format. Because of this limitation, there is possibly more informative data that could be collected from this subpopulation. A future study may benefit by collecting data about this subpopulation through a different means such as an interview format. This may lend itself to a more qualitative analysis. Since this population has advanced the furthest in the progression of HD, it is imperative that their opinions be taken into consideration.

A substantial proportion of respondents in this study indicated that a cure for HD would change their answers to particular sections of the survey. However, this question was not

structured in a way that allowed participants to expand upon how this would affect their answers. There is potential to explore the details of this indication of change for a future study such as understanding the nuances of an HD cure and how this would influence factors and decisions. It would be particularly interesting to learn about disclosure and whether the components of disclosure or timing of disclosure would be considerably different or not.

Several participants brought up the aspect of having a parent with HD which lends an entirely new perspective to many of the data analyses in this study. Specifically, some individuals stated they would not have any children, even with the guarantee their children would not have HD, because they will not subject their children to the experience of having a parent with HD. This raises an interesting question for future study. How does having a parent with HD and therefore having the experience of living life with HD and witnessing the symptoms of HD first-hand, make a significant difference in their answers to the topics of this survey? It may be informative to further understand how this life experience influences an individual's perspective on disclosure and especially family planning decisions.

Throughout the family planning section of the survey, some individuals indicated they had children prior to knowing about HD or having access to various family planning options such as *IVF*/PGT-M. Therefore, they did not submit their opinions and thoughts for certain questions. A fascinating area of future research would be a retrospective study on these couples to inquire about any relief or guilt surrounding their personal history of having children.

This study revealed the common barriers that prevent the HD community from utilizing *IVF*/PGT-M with cost being the most common one. This raised the question of whether these barriers are common across other families facing other genetic conditions or unique to the HD community. While this future study would fall outside of the realm of solely HD, understanding

what factors typically lead to the choice of not using *IVF*/PGT-M would be particularly beneficial information for the prenatal setting of genetic counseling. In addition, there are other research areas regarding *IVF/*PGT-M which could be explored as well. These include the ethical considerations of whether cost should even be allowed to prevent some couples' access to these family planning options and whether it should be available to all individuals' regardless of socioeconomic status. There are also the risks associated with the *IVF*/PGT-M procedures themselves including the chance of being unsuccessful or the increased likelihood of having a child with other genetic conditions.

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APPENDIX A: Confirmation of Exempt Self-Determined Research Status by UCI Institutional Review Board

SECTION 10: LEAD RESEARCHER ASSURANCE

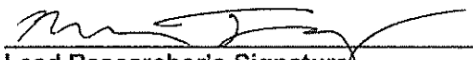
The Lead Researcher (and Faculty Sponsor – if applicable) assure the following.

As Primary Lead Researcher and Faculty Sponsor, we have ultimate responsibility for the performance of this study, the protection of the rights and welfare of the human subjects, and applicable UCI policies, as well as state statutes for research involving human subjects.

We hereby assure or acknowledge the following:

1. The information provided in this application is accurate to the best of my knowledge.
2. All named individuals on this project have read and understand the procedures outlined in the protocol and their role on the study.
3. All named individuals on this project have completed the required electronic educational research tutorials and have been made aware of the "Common Rule" (45 CFR Part 46) and acknowledge the importance of the Belmont Principles - Respect for Persons, Beneficence and Justice in conducting research involving human participants. Also UCI has signed the Federalwide Assurance (FWA) that is available for review on the Human Research Protections (HRP) website.
4. Minor changes to the research that do not increase risk to participants, or significantly alter the study aims or procedures, such as the addition or removal of students researchers, do not require additional self-confirmation of exemption or approval from the IRB. Major changes that increase risk or constitute substantive revisions to the research including procedural changes will require a new self-confirmation of exemption or approval from the IRB.
5. When conducting research off-site or collaborating with an investigator at another institution (e.g., another UC, CHOC, CSUF, or a local school district), Lead Researchers must comply with the requirements and policies of the site, including securing Confirmation of Exempt Status from the IRB.
6. The Self-Determination of Exemption, consent documents including recruitment materials and data collection materials will be maintained by the Lead Researcher or Faculty Sponsor for 10 years beyond the completion of the research.
7. This research study is subject to routine monitoring by the Human Research Protections (HRP) unit of the Office of Research. Through the Education Quality and Improvement Program (EQUIP) program, HRP staff conduct periodic quality improvement monitoring and educational outreach.

Please sign below, indicating that you agree with the above.

Lead Researcher's Signature	**Date**
	5/13/2019

Faculty Sponsor's Signature (if applicable)	Date
	5/13/2019

HUMAN RESEARCH PROTECTIONS CONFIRMATION OF EXEMPTION (OPTIONAL)

Researchers: You may request that the HRP staff review and confirm the self-determination of exemption. You may submit a completed Self Determination Tool signed by the LR / FS and any relevant supporting documents (i.e., grant, consent forms, study materials) to the HRP staff at IRB@research.uci.edu. You should receive a response within 10 business days.

FOR IRB ONLY – researchers do not complete this section.

☒ **The proposed activity is exempt research. IRB review is not required.**

This determination only applies to the activities described in this request. Please review Item #4 under Section 10: Lead Researcher Assurance. If there are any changes that may alter this determination the investigator may request another written determination.

☐ **The proposed activity does not qualify as exempt research. Submission of an IRB Application IS REQUIRED.**

IRB Approval must be obtained before the research can begin. Please complete and submit an IRB Application with the appropriate Protocol Narrative. All forms are available on the Applications & Forms web page under Human Research Protections.

HRP Staff or IRB Member	Date
M Camarena	6/18/19

APPENDIX B: Posters and Flyer

The following posters were on display and the following flyer was distributed for active recruitment by the lead researcher during events in the HD community as outlined in the Methods and Materials section. The posters and flyer were created by Courtney Bishop Design.

HUNTINGTON'S DISEASE:

Disclosure and Future Decision-Making in Romantic Relationships

Huntington's Disease (HD) is an inherited neurodegenerative condition in which an affected individual gradually loses control over their behavior, cognition, and movement. Typically, onset of symptoms is in the 30s or 40s, although there are some cases which fall outside of this age range. This means most individuals often achieve early to mid-life milestones, including romantic relationships, marriage, and reproduction, before the onset of symptoms. An individual with HD has a 50% chance of passing down the condition to each child. If an individual decides to disclose to a potential romantic partner their HD history, communicating the symptoms and inheritance aspects of the condition may help the couple make informed decisions regarding their possible future life together. How and when individuals with, or at risk, for HD approach dating, relationships, disclosure, and life decisions with a potential romantic partner is a topic that has not been well documented in the literature. This information can give healthcare providers important insight into this aspect of life for their patients.

This study will survey individuals both at risk for and diagnosed with HD, as well as their romantic life partners regarding issues surrounding discussion of the diagnosis of HD. The survey will include both multiple choice and free response questions on the subject of disclosure and its impact on reproductive decisions including family planning and in vitro fertilization with preimplantation genetic testing (PGT-M). The information collected in this study will provide insight into disclosure and factors considered by those affected and at risk for HD and their romantic partners as they consider their future together.

SURVEY LINK: https://is.gd/HDsurvey

This study will explore the process of disclosing Huntington's disease (HD) to romantic partners by surveying both the individual at risk or diagnosed with HD and their romantic partner. In addition to disclosure, this study will discover what factors are considered in a couple's reproductive decision.

You are eligible to participate in this survey if you are over 18 years old and:

- At risk for Huntington's disease

OR

- Diagnosed with Huntington's disease

OR

- The romantic partner of someone who is at risk for Huntington's disease

OR

- The romantic partner of someone with Huntington's disease

De

The survey should take approximately 15-20 minutes to com Dear Happy of your responses will be kept anonymous. This survey is voluntary and there is no cost to you for participating. There are no harms or discomforts associated with this survey beyond those encountered in normal daily life. There are no direct benefits associated with taking this survey. However, the results of this study may provide a greater understanding of how individuals approach romantic relationships and decisions when HD is a factor.

This study is being conducted by Marian Tsang, Moyra Smith, Leslie Thompson, and Katherine Hall of the University of California, Irvine. Please contact Marian Tsang with any comments, concerns, or questions regarding the conduct of this study by email at [redacted]

HUNTINGTON'S DISEASE:

Disclosure and Future Decision-Making in Romantic Relationships

SURVEY LINK: https://is.gd/HDsurvey

Has Huntington's disease affected the way you approach dating, relationships, and/or family planning?

This study is exploring the process of disclosing a diagnosis or family history to a romantic partner and which factors couples consider for reproductive decisions. The information gathered from this study can give healthcare professionals, such as genetic counselors, deeper insight into this important aspect of life for the Huntington's disease community.

Please visit the link above to participate in a short confidential survey! To be eligible for this survey you must be at least 18 years old and:

- At risk for Huntington's disease

OR

- Diagnosed with Huntington's disease

OR

- The romantic partner of someone who is at risk for Huntington's disease

OR

- The romantic partner of someone with Huntington's disease

Please feel free to contact me with any questions or concerns!

CONTACT INFORMATION
Attn: Marian Tsang
[redacted]

APPENDIX C: Survey

The following document consists of the survey as it appeared to the participants who viewed and responded to the questions online. This survey was developed via REDCap.

Huntington's Disease: Disclosure and Future Decision-Making in Romantic Relationships

This study that will explore the process of disclosing Huntington's disease (HD) to romantic partners by surveying both the individual at risk or diagnosed with HD and their romantic partner. In addition to disclosure, this study will discover what factors are considered in a couple's reproductive decision.

You are eligible to participate in this survey if you are over 18 years old and:

At risk for HD

Diagnosed with HD

The romantic partner of someone who is at risk for HD

The romantic partner of someone with HD

The survey should take approximately 15-20 minutes to complete and all of your responses will be kept anonymous. This survey is voluntary and there is no cost to you for participating. There are no harms or discomforts associated with this survey beyond those encountered in normal daily life. There are no direct benefits associated with taking this survey. However, the results of this study may provide a greater understanding of how individuals approach romantic relationships and decisions when HD is a factor.

This study is being conducted by Marian Tsang, Moyra Smith, Leslie Thompson, June-Anne Gold, and Katherine Hall of the University of California, Irvine. Please contact Marian Tsang with any comments, concerns, or questions regarding the conduct of this study by email at mjtsang@uci.edu.

Please contact UCI's Office of Research by phone, (949)824-6662, or by email at IRB@research.uci.edu if you are unable to reach the researchers listed and have general questions or concerns.

Basic Information	
Gender	◯ Male ◯ Female ◯ Prefer not to answer
Age	_____
Ethnicity	☐ Caucasian ☐ Hispanic ☐ Asian ☐ African ☐ Native American ☐ Other

How would you rate your understanding of Huntington's disease?	◯ Not well ◯ Somewhat ◯ Very well
Relationship Status	◯ Single ◯ Single - in a serious relationship ◯ Married ◯ Separated ◯ Divorced ◯ Widowed

Linking Questions for Romantic Partners	
When is your anniversary?	_____
Location of your first date?	_____
When did you move in together?	_____

Huntington's Disease (HD) Status	
Are you:	◯ At risk ◯ Diagnosed and presymptomatic ◯ Diagnosed and symptomatic ◯ Romantic partner
What is your romantic partner's HD status?	◯ At risk ◯ Diagnosed and presymptomatic ◯ Diagnosed and symptomatic

How did you find out about your partner's HD status?		
	Yes	No
Partner disclosed their HD status	○	○
Friends/acquaintances before the relationship, so knowledge of HD from the beginning	○	○
Partner's family member(s) disclosed HD status	○	○
Partner's friend disclosed HD status	○	○
You noticed changes/symptoms in your partner	○	○
You and your partner found out together	○	○
Prefer not to answer	○	○
Other	○	○

If other, please specify: _____

How much did you know about HD before being in a relationship with your partner?

○ None
○ Some
○ A lot

Disclosure	
Was there a conversation disclosing HD?	◯ Yes ◯ No
Have you disclosed or would you plan to disclose HD to your romantic partner?	◯ Yes ◯ No

Which of the following were included in the explanation of HD?		
	Yes	No
Movement	◯	◯
Behavior/personality	◯	◯
Cognition	◯	◯
Late onset (yet still a range of ages of onset)	◯	◯
Inheritance: 50%	◯	◯

What was the timing of the disclosure?

◯ Beginning of relationship
◯ After certain milestone(s)
◯ After marriage
◯ After children

If after certain milestone(s), please specify here: _____

Which of the following were part of your reaction to the disclosure?		
	Yes	No
Shock	◯	◯
Confusion	◯	◯
Anger	◯	◯
Denial	◯	◯
Sadness	◯	◯
Understanding	◯	◯
Other	◯	◯

If other, please specify: _____

Do you feel that your relationship with your partner changed after disclosure?

◯ We became closer
◯ We became further apart
◯ No change

Did you need time to make your decision about the relationship after the disclosure?

◯ Yes ◯ No

How important were these factors when making your decision about the relationship after disclosure?			
	Not important	Somewhat important	Very important
Late onset symptoms	○	○	○
Inheritance: 50%	○	○	○
Role of caretaker	○	○	○
Faith/religion	○	○	○
Other	○	○	○

If other, please specify: _____

Which of the following do you think should be included in the explanation of HD and how important are they?			
	Not important	Somewhat important	Very important
Movement	◯	◯	◯
Behavior/personality	◯	◯	◯
Cognition	◯	◯	◯
Late onset	◯	◯	◯
Inheritance: 50%	◯	◯	◯
Other	◯	◯	◯

If other, please specify: _____

What would you consider to be ideal timing for this disclosure?

◯ Beginning of relationship
◯ After certain milestone(s)
◯ After marriage
◯ After children

If after certain milestone(s), please specify: _____

How important do you feel it for you to understand these aspects of HD?

◯ Not important
◯ Somewhat important
◯ Very important

How important is it to you that your partner understands these aspects of HD?

◯ Not important
◯ Somewhat important
◯ Very important

Family Planning	
What are your future family plans regarding children?	◯ Currently have no children and have no plans to have children ◯ Currently have no children but want to have children ◯ Already have children
If you already have children, how many?	_____

How important were each of the following factors when making your decision about having or not having children?			
	Not important	Somewhat important	Very important
Inheritance: 50%	○	○	○
Symptoms/Lifestyle	○	○	○
Faith/Religion	○	○	○
Other	○	○	○

If other, please specify: _____

IVF and PGT-M

IVF is when the egg is fertilized by the sperm outside of the body. PGT-M, also known as preimplantation genetic diagnosis (PGD), is a procedure to identify which ones have a genetic condition, such as HD, prior to implanting the fetus.

Have you heard of IVF/PGT-M (in vitro fertilization and preimplantation genetic testing - monogenic)?	◯ Yes ◯ No
Is IVF/PGT-M something you would consider?	◯ Yes ◯ No

If not, is it because:		
	Yes	No
Cost	○	○
Faith/religion	○	○
Uncertainty/not enough information	○	○
Time	○	○
Experience	○	○
Other	○	○

If other, please specify: _____

Who did you hear about IVF/PGT-M from?		
	Yes	No
Primary Care Physician	○	○
Neurologist	○	○
Genetic counselor or geneticist	○	○
Internet	○	○
This survey	○	○
Other	○	○

If other, please specify: _____

If there were a definitive cure/therapy available for HD, would this knowledge change any of your answers to this survey in:		
	Yes	No
Disclosure components	○	○
Family planning	○	○
IVF/PGT-M	○	○
Other	○	○

If other, please specify: _____

Is there any piece of information that if you had known, would have changed your mind in your decision to disclose to your romantic partner? _____

Is there any piece of information that if you had known, would have changed your mind in your decision to stay in the relationship? _____

APPENDIX D: Free Response Answers

The participants who expanded upon their responses to the survey questions with free response answers are included with the associated question. Answers are copied here exactly as the participant submitted them. All typographical errors and misspellings have been left as is.

How did you find out about your partner's HD status? If other, please specify:

My partner has a family history, is showing symptoms but has not been diagnosed yet. We have an appointment on 11/9/19 with the genetics clinic to join the HD Enroll
Noticed symptoms in Mother in law
My husband told me he was at risk when we were just friends, I was in the appt with him when he got his results after we had been dating for 1-2 years

What was the timing of the disclosure? If After certain milestone(s), please specify here:

Engagement
After meeting my father about a year in when I knew we were serious
Once we were talking about becoming official/exclusive
Early on but not the first couple dates. Once I knew this could be serious
Family members were gene-tested
After 1 month of dating
During the relationship when I decided to be tested after finding out my family history. My partner went with me.
After I fully understood it myself, my mom was diagnosed in the middle of our relationship. We had broken up afterwards, when I fully understand I asked him if this is what he wants his life to look like. We have been learning together and preparing for if I am positive.
Age
After we said I love you
After the dating phase
After a few weeks.
Dating about a year
Knowing that person would want a long term relationship that leads into marriage
3 years into relationship
Engage
6 months together
Engagement
More serious relationship
before I met his father who was already diagnosed for 10 years
after mother was diagnosed in 1995

Which of the following were part of your reaction to the disclosure? If other, please specify:

Faith
Worry
irritation at my partners family at pretending it wasn't happening. We wouldn't be ignoring cancer!
acceptance
Concerned and scared
What steps to take
Motivation
Concerned but also interested to learn more
Sympathy
Stress
This is difficult to say because it was more of a realization rather than a disclosure, but along the way I've experienced most of those feelings.

How important were these factors when making your decision about the relationship after disclosure? If other, please specify:

Children
we were already well into our relationship before he told me of his fathers illness
Advances in research would find treatments.
ability to have a family
Very young so didn't take it seriously enough
Nursing home

Which of the following do you think should be included in the explanation of HD and how important are they? If other, please specify:

mate would become caregivier
Family planning
they had to agree that I was unwilling to pass it on, and be ok with the fact we wouldn't be able to have kids in a normal way.
Also the burden of being in a family that has HD (caretaking, etc) even if you test negative there are too many to list!
That HD can be scary and cause irrational situations to occur, some people with HD can be mean and they do not know that they are. When the time comes I fear if I'm mean and he leaves not being aware it's my brain and not me. There are always more to talk about in what symptoms look like besides the obvious.
Long term care
Emotional toll
Current research and clinical trials
Not any HD patient is the same
caregiving/ length of time between diagnosis/symptom onset and death - these are the worst
Caregiver responsibilities and emotional well-being
Caretaking
My CAG repeat is 43; a neurogist said, "That's not so bad."
Caretaking
How it effects the people around you
Speech changes, grimacing
Symptoms can be many years before considered symptomatic
Children's risk
Discussion of having kids, with regards to being able to select offspring that are not affected in attempts to halt the disease.
na
The need to have support
Have an early discussion about getting life insurance too- while young; and talking about it is so much different than someone seeing the disease. My (now) husband has seen the disease with my grandmother, now my dad. I hope I'm not next - but we have always lived within 15 minutes from each other and are very close so the disease has just always been there.

What would you consider to be ideal timing for this disclosure? If after certain milestone(s), please specify:

After it becomes more of a serious relationship
Serious relationship
Have fun, if it starts getting serious then sit down and talk about it
You know you could be serious with this person
After getting serious
After making an ongoing commitment to this person
I don't think it needs to be discussed on a first date. But it does need to be discussed somewhat early on.
When you decide that this is the right person for you.
You know they are understanding and capable of understanding what this is.
When moved from dating to relationship
Seriously dating (moving in, making future plans together)
After the dating phase
When planning future together
when you know the relationship is serious
Dating longer than 1year
it's dépends from people
when the relationship seemed to be getting serious
Declaration of love for a long term relationship
Before becoming exclusive.
Before kids
50
6 months to a year of being together
More serious
6 months
When it feels serious
relationship becoming long-term
After spending at least one year together and feeling farly certain that it's a long term relationship with the possibility of marriage and/or children
when things become long term
When a couple feels the relationship could get serious
after knowing relationship will last
Whan the relationship becomes serious

What are your future family plans regarding children? If you already have children, how many?

3
2
1
2
1
4, but not biological. Do not intend to have biological children.
2
2
2
3
3
1
2
2
1
3
4
2
1
1
2
1
2
2
1
3
2
1
3
2
2
2
1
2
2
2
3
1
2
1
2
3

What are your future family plans regarding children? If you already have children, how many? Continued:

2
1
2
3
1
5
1
3
2
Two, but both are adopted
Two, but they are both adopted
2 (twins), through IVF w/ PGD

How important were each of the following factors when making your decision about having or not having children? If other, please specify:

Didn't know then
I don't like children
Money
heathcare cost over their lifetime, the fact it's a pre-existing condition and coverage for that might change, the fact there is no cure or real treatment, that nursing homes don't often let in people with HD, that the healthcare system isn't that great at helping with people with HD
late onset of the disease in my family, with mild symptoms
hopefully by the time that the onset is for my boys there will be a cure.
I will never create a kid if it means they have to know what being at risk and taking care of their mother with HD feels like. Everyone is different and there is no judgement in the HD community but that is my own personal choice. I will adopt or do PGD IVF when the time comes and it happens to work.
Research and cure options
I didn't want children to begin with
Money- PGD-IVF
Had kids prior to knowing about HD
Would I be around and well to raise the child
Children were adults at time of disclosure
Knowing what I know now I would have acted differently
Found out only this last year I was HD positive from my sperm donor. So we weren't able to talk about this before hand
I tied my tubes to not have sick babies
Risk of passing the disease on/ cost of IVF
Father deceased at 35 Huntington's unknown
The ability to have children that wouldn't be at risk (ie artificial insemination)
No one in my husband's family knew that HD was in the family until one sibling was diagnosed at age 30. By that time, other siblings already had partners and had kids.
Too old
Little understanding of disease
I never wanted to have children for various reasons. And I kept telling myself "maybe I'll want one next year." It never changed. And then once dad was diagnosed - that sealed the deal.
Timing, finances for IVF

Is *IVF*/PGT-M something you would consider? If not, is it because: If other, please specify:

No more kids
No desire to have children
Don't want kids
I don't want them without HD
I not think I could handle the letdown if IVF didn't initially work.
Additional emotional stress of going through IVF
I have already had my children and am not planning any more
Heart ache
I have never wanted children
Already have one child at risk, feel unfair to give future children risk free status
Already have children did not know my risk status then
Don't want to raise kids and have HD.
Doesn't apply
Our current age.
If I were positive for HD or untested, the possibility of a kid having an HD parent was unacceptable to me
disclosure was After Children were adults
We had no idea hd was in the family until we already had kids
Already have children
stress on body and relationship
never wanted children
Too old for children now
Do not want children
I don't want to have children while being symptomatic. It is not fair to them.
i may have considered it when i was younger
I was pregnant (by accident) in 2016- and from what I understand even if we decided to go down this route- there's no way to do this and not find out if I myself have HD. or perhaps you could - but I can't remember. I didn't want to do it. I didn't think it was right to have a healthy baby born with a job to do which would be (likely 50%) taking care of me one day. HD may not be in that baby's gene's but if I still had it, HD would still consume that child as it has me.

Who did you hear about *IVF*/PGT-M from? If other, please specify:
hdsa
HD conventiin
My boyfriend who has tested positive for HD
Hd convention
HDYO camp. Jeff carroll
HDSA's NYA
My partner
Convention
My Sister
My dad who has HD and saved up money for me to be able to access it
Family member
Looked into it myself
Education. I am a primary healthcare provider.
a couple in our support group has used this service
My sibling who has already been through it.
Facebook group and hunts association
HDSA Activities
My dad and an HDSA article.
My daughter is aNeurologit. She and her husband did genetic testing. She was negative
Family
HDSA, support groups
I have a degree and experience in reproductive assistance technologies in animals/livestock - and news articles
Brother
College Course
HD Convention
my wife told me
Research
School
Cousin
Medical training
research scientific publications
Spouse
Today show
from my husband's brother who was diagnosed at around age 30
TV
In biology class
In school
My background is in biotech, I had already heard of it.
Science background
A woman in one of my dad's support groups had just had a baby through IVF. The baby was HD free but the mother was 29 and stuck in a wheel chair. She seemed as advanced my grandmother.
No conversation with healthcare professional

Who did you hear about *IVF*/PGT-M from? If other, please specify: Continued:
HDSA and HD news/research

If there were a definitive cure/therapy available for HD, would this knowledge change any of your answers to this survey in: If other, please specify:

I would be more relieved! Not sure if my answers would change.
Commitment
anger at finding out his status
My husband got a vasectomy already so any future HD developments will not help us.

Is there any piece of information that if you had known, would have changed your mind in your decision to disclose to your romantic partner?

No
No
nothing. My mom was trying to get me to lie and not tell anyone I was with until we were engaged because she thought it made me undatable, which is why I went straight home that night and told my partner after 3 months of dating. I think it's actually better, because if they're going to run off because of HD then you don't want them anyways. You need someone who stays despite it, not to trap someone into the problem.
My personal HD status
No
Yes
No
No. HD is a huge part of my life.
No
Date of onset
No, HD is not something to hide or be ashamed of, but it is important for a partner to know about when making life decisions. I told my partner when we were both 18 on our third date together. He would be meeting my dad who was symptomatic soon anyway, it was important for him to know about before meeting him. I did tell him that it was genetic. Since then he has been able to see first hand the progression of HD.
No.
No
No
When I found out I waws 60, had been married for 21 years
No
No
no
no
No
No
No
No
No but I think it's important to note that we didn't know I was at risk until after we were married. We found out about my father's HD diagnosis after 4 years of marriage.
no
No
No
No
No
HD's effect on insurance and employment status

Is there any piece of information that if you had known, would have changed your mind in your decision to stay in the relationship?

I'm not sure?
No
my partners family pretend its not happening! I wish that they had been more open about the disease
No
Two rounds of IVF didn't work for us.
I probably would have stayed in the relationship, but I would have adopted children instead of having my own. The burden of potentially passing this along to my children is overwhelming guilt. Praying for a cure/treatment soon.
No
No
No
No
He's my best friend I knew before we started dating.
No
None
No I don't think so
no
No
Nope
if I'd found out sooner, I wouldn't have stayed
N/a- I'm happy as can be, regardless of whether or not my significant other is going to develop the disease. True love will triumph anything in its way.
no
No
No
No
A cure or delay in symptoms beyond the usual 30-50 years. That's too young!
no
No
No
No
If I had known that it would bring out my husband's anger, that would have given me pause at least. He's experiencing early emotional and cognitive symptoms just in the last year.