

# Motivation vs. Hopelessness: The Well-Being Following Predictive Testing for Huntington's Disease

Ianna Lee<sup>1</sup> and Angela Bongiovanni<sup>#</sup>

<sup>1</sup>Dominican Academy, USA

<sup>#</sup>Advisor

## ABSTRACT

Predictive genetic testing for Huntington's Disease, a fatal and progressive neurodegenerative disorder with no cure, can lead to a multitude of favorable and unfavorable responses, impacts, and experiences. Utilizing many qualitative studies, participants' reactions to their gene-positive test results were categorized into the opposing psychological states of motivation vs. hopelessness. Key milestones of adulthood, such as education and career, romantic and familial relationships, reproductive choices, and financial investments, were used as metrics for the two categories. By studying the psychological well-being of at-risk individuals for Huntington's, this literature review also argues for the use and improvement of long-term, tailored genetic counseling.

## Introduction

### Defining Huntington's Disease

As quoted by George Huntington, the disease is like that of "an heirloom from generations away back in the dim past"; "when once it begins, it clings to the bitter end" (Wexler et al., 2016, para. 5-7). Huntington's Disease (HD) is a rare and fatal neurodegenerative disorder predominantly characterized by involuntary, uncontrolled movements, as well as cognitive and psychiatric disturbances (Roos, 2010). Today, there are approximately 41,000 symptomatic individuals in the United States (HDSA, 2020). The first complete medical account of hereditary chorea, described with its psychiatric and cognitive symptoms, was written by George Huntington in 1872 (McColgan & Tabrizi, 2018). His years of work describing the disease, based on his studies of the exhibited symptoms from one family's several generations, led to its official name, "Huntington's chorea" (Mandal, 2019; Roos, 2010); the word "chorea" derives from the ancient Greek word "choreia", meaning dance (Vale & Cardoso, 2015). The name remained unchanged until the nineteen-eighties, when its extensive non-motor symptoms and signs became known, and the disorder's name changed to Huntington's Disease (Roos, 2010).

Huntington's Disease is caused by the huntingtin (HTT) gene on chromosome 4, which contains repeats of the trinucleotide sequence cytosine-adenine-guanine (CAG) (McColgan & Tabrizi, 2018). While everyone has the HTT gene, only those with the mutant gene will develop Huntington's (HDSA, 2020). Huntington's Disease is an autosomal-dominant inherited disorder, meaning that an afflicted individual's offspring have a 50% risk of having HD via inheritance of the dominant allele of the mutant huntingtin gene (Lewis & Simpson, 2023; NIH, 2023). Individuals with CAG repeats below 27 are considered normal (McColgan & Tabrizi, 2018). Between 27 and 35 is considered an intermediate repeat length that does not cause HD but could expand into the pathogenic range for future generations. The gene is abnormal or expanded once it exceeds 36 (Novak & Tabrizi, 2010). The range of 36 to 39 leads to a reduced/incomplete penetrance or delayed symptomatic onset of Huntington's (Roos, 2010). CAG repeats of 40 or more guarantee the onset of Huntington's Disease (Novak & Tabrizi, 2010). The abnormal gene is transcribed into RNA and subsequently translated into the mutant huntingtin (mHTT) protein (HDSA, 2020).

The abnormal, repeated segments of CAG on chromosome 4 cause progressive degeneration of the basal ganglia nuclei, specifically the medium-sized spiny neurons in the striatum (Matz & Spocter, 2022). The basal ganglia nuclei are clusters of cell bodies found within the telencephalon of the cerebral hemispheres, which carry out a multitude of functions for the body, ranging from motor control, cognition, saccadic eye movement, and facial expressions (Matz & Spocter, 2022). As these nuclei degenerate, the basal ganglia's role as a relay center between the external stimuli and the cerebral cortex is lost (Matz & Spocter, 2022). The striatum, which controls movement, mood, and memory, is damaged over time, leading to the major symptoms of Huntington's Disease (HDSA, 2020).

The nuclear symptoms of Huntington's Disease consist of motor, cognitive, and psychiatric disturbances. The mean age of onset for symptoms is 30 to 50 years old; however, symptoms have been recorded in a complete range of 2 to 85 years (Roos, 2010). Chorea, the most characteristic motor symptom of HD, initially emerges in distal extremities like the fingers, toes, and small facial muscles (Roos, 2010). Gradually, the involuntary movement progresses to other muscles, such as all four limbs and the torso (HDSA, 2020). As the disease progresses, they become more extreme and obvious (NIH, 2023). Dystonia (unchanging movement/posture) is another key involuntary motor symptom of HD (Roos, 2010). Voluntary movements become severely impaired, especially through certain conditions such as bradykinesia (slowness of movement) and akinesia (delayed start of movement) (HDSA, 2020; NIH, 2023). This results in a slower pace of all activities, such as reduced manual dexterity and difficulties with speech, swallowing, eating, walking, and balance (HDSA, 2020; NIH, 2023). Choking and weight loss are caused by issues with eating, swallowing, and unnecessary movement (NIH, 2023). In later stages, patients can become mute with the impairment of speech (Roos, 2010). Other symptoms include insomnia, loss of energy, fatigue, and seizures (NIH, 2023).

The cognitive decline of individuals with HD is the other main sign of the disease. It can be present long before motor symptoms appear, or it can be very mild in the advanced stages of the disease. Cognitive and motor behavior is goal-directed, and individuals are typically able to distinguish priorities and make decisions. However, patients with Huntington's lose these abilities (Roos, 2010). They are no longer able to organize, plan, judge, prioritize, and decide as simply as they used to (NIH, 2023). Paying attention, learning new things, remembering the past, expressing oneself, and answering questions become difficult (HDSA, 2020; NIH, 2023). Language is somewhat spared (Roos, 2010). These cognitive symptoms get more severe as the disease progresses, until many with Huntington's are not able to drive, work, or care for themselves. Once an individual experiences extreme cognitive changes and cannot function in daily life, the condition is acknowledged as dementia (NIH, 2023).

The psychiatric symptoms are frequent in the early stages of Huntington's Disease. Depression is the most commonly occurring psychiatric symptom. However, diagnosis is difficult as inactivity, apathy, and weight loss, all signs of clinical depression, occur as symptoms in Huntington's as well (Roos, 2010). There is also a wide variety of neuropsychiatric symptoms, such as low self-esteem, obsessive compulsive behavior, guilt, and mania (McColgan & Tabrizi, 2018; Roos, 2010). Some of the more frequent psychiatric symptoms are apathy, anxiety, and irritability. In contrast, the more extreme and rare psychiatric symptom of psychosis appears in the later stages of the disease and often coincides with cognitive decline (McColgan & Tabrizi, 2018; Roos, 2010). Overall, these mental disorders and behaviors can have potentially severe consequences on an individual's well-being (HDSA, 2020). The second most common cause of death in those with HD is suicide. Around the time of the gene test and of diminished independence are the most high-risk periods for suicide (Roos, 2010). The debilitating symptoms of HD have a rare level of interconnectedness in comparison to other diseases, as the motor, cognitive, and psychiatric changes affect each other and all aspects of the individual's life (HDSA, 2020). Psychiatric symptoms have been especially recognized for their inherent nature in Huntington's Disease. However, many continue to suffer from under-diagnosis and under-treatment. These symptoms are considered the most disabling yet most treatable of HD; their treatment and care heavily influence the quality of life for an individual afflicted with Huntington's (HDSA, 2020).

While very limited treatment for symptomatic management exists, Huntington's Disease is a fatal condition with no cure (McColgan & Tabrizi, 2018). After a demonstration of clinical symptoms, the individual will have approximately 10 to 20 years of remaining life (Matz & Spocter, 2022). In the last decade, there has been a great increase

in potential therapies and clinical trials aimed at lowering levels of the mutant huntingtin protein (McColgan & Tabrizi, 2018). Research is currently being conducted through biomarkers, stem cells, imaging technology, and brain development (NIH, 2023). Hopefully, we are approaching significantly improved treatment and the potential cure to this devastating disease for which over 200,00 individuals are at-risk of in the United States (HDSA, 2020).

## Defining Predictive Genetic Testing

Genetic testing is used to determine an individual's chances of developing a suspected genetic condition (NIH, 2023). Genetic testing for the mutant huntingtin is performed through diagnostic or predictive testing (McColgan & Tabrizi, 2018). Predictive testing is for asymptomatic/presymptomatic individuals to predict future risk of a genetic condition (Novak & Tabrizi, 2010). The usual objective for predictive testing is early identification of risk potential for certain genetic conditions, eventually leading to reduced morbidity through prevention methods, symptomatic treatments, and lifestyle changes (Evans et al., 2001). While predictive genetic testing has relatively accurate risk assessment, the tests can carry uncertainty in confirmation of condition development, time of onset, and the severity of the condition. Testing also heavily depends on the nature of the condition, resulting in varied accuracy, treatment efficacy, cost, and accessibility (Evans et al., 2001).

Identification of the huntingtin gene on chromosome 4 in 1983 allowed for predictive testing and diagnosis through linkage analysis, a tool used to detect chromosomal location of mutant genes (Dufasne et al., 2011; Pulst, 1999). A predictive testing program was established and the first test for Huntington's was offered in 1986. Due to the autosomal-dominant inheritance pattern of Huntington's, a predictive test will wholly confirm or dismiss whether an individual carries the expanded mHTT gene and will face onset of HD. A positive test result ensures development of HD but does not ensure time of onset and what the symptoms may be (Novak & Tabrizi, 2010). International guidelines for predictive testing of HD were established soon after the HTT gene's identification in 1993 (McColgan & Tabrizi, 2018). Predictive testing for HD is currently a globally accepted clinical application and is carried out in specialist genetic centers (Dufasne et al., 2011; Novak & Tabrizi, 2010).

The official testing process begins with a confirmation of confidentiality by the testing center, as well as suggestions of a support system and a counselor in the local area. A pre-test counseling session informs the candidate of all aspects of the genetic testing process including costs, limitations, risks, and benefits (HDSA, 2016). The session is followed by a psychological screening for mental health assessment, especially for individuals who are high-risk for suicide (HDSA, 2016). After the participant's blood is drawn, genetic counseling is conducted with a review of the individual's genetic history, explanation of their risk status, the individual's personal experiences with HD, and the potential burden of the results. Once a signed document of informed consent is given to the testing laboratory with the blood sample, an optional neurological exam is offered, followed by a second counseling session (HDSA, 2016). Finally, disclosure of the test result is given in-person, which the individual has the right to postpone or cancel (HDSA, 2016). Post-test counseling must also be available to monitor the impact of test results, especially for gene-positive individuals, and should be used to develop further support (McColgan & Tabrizi, 2018; Novak & Tabrizi, 2010).

In 2019, the Huntington's Disease Society of America certified 47 centers of excellence (COE), i.e. clinics that provide "comprehensive multidisciplinary services to families affected by HD" (HDSA, 2020; Massey et al., 2021, para. 1). The test's average cost at the COE's was approximately \$1,157 USD, ranging from \$275 to \$3,640 USD. The average costs included the genetic test itself, counseling, psychological and neurological assessments, neurology, social work, and miscellaneous fees (Massey et al., 2021). The reasons, benefits, and limitations of predictive testing for HD differ in comparison to those of testing for other genetic conditions due to the lack of cure for HD and its autosomal-dominant inheritance pattern. For example, the typical benefits of predictive testing, lifestyle changes and prevention treatment, are not available for HD. The typical limitation of predictive testing, the relatively accurate risk potential, becomes a benefit as the gene-positive result for HD definitively confirms or denies future onset. Thus, the pros in testing for HD at-risk individuals become future planning and relief from uncertainty. Most of future planning involves decisions regarding education, career, finances, marriage, reproduction, and health care (HDSA,

2016). The cons of testing for HD are the potential psychological and social risks, such as changes in self-perception, harmful impact on relationships, genetic discrimination, difficulty in retaining insurance, issues with privacy and confidentiality, and extremely adverse psychological and emotional responses (HDSA, 2016). Despite the availability of centers for predictive genetic testing for HD, a relatively small portion of the at-risk population undergoes testing, possibly due to the costs or cons of testing (HDSA, 2016).

## Defining Motivation vs. Hopelessness

Motivation, as defined in “The Behavioral Neuroscience of Motivation”, is the energizing of behavior in pursuit of goal, as well as a fundamental property of deliberate behavior (Simpson & Balsam, 2016, para. 3). Motivation is derived from the Latin word *motivus*, “a moving cause”, suggesting the psychological activation in motivation (Cofer & Petri, 2023). Motivation is typically deduced by the result of behavioral change in response to internal or external stimuli (Cofer & Petri, 2023). Motives are categorized into two forms: primary and secondary motives. Primary is for inherent and common motivations aimed at survival in animals and humans alike. Secondary motives, e.g. achievement or wealth, are learned and studied singularly in humans and depend on social and cultural influences (Cofer & Petri, 2023). Motivation is often framed by a cost-benefit analysis, each cost and benefit’s value calculated by the individual and their internal physiological state, environment, and past (Simpson & Balsam, 2016). The costs can include physical or mental effort, time, discomfort, and danger involving risk of pain and potential death. The benefits can include fulfillment of physiological and psychological needs, safety from danger, or avoidance of the aforementioned costs (Simpson & Balsam, 2016).

Despite the fundamental (inherent and learned) motivation of the human being, the otherwise devastating circumstances and struggles of life, such as Huntington’s Disease, can deter an individual from this typical behavior. Hopelessness is the subjective psychological state in which an individual lacks hope, tending to overestimate the probability of unfavorable events while underestimating the probability of favorable occurrences, and having a pessimistic attitude towards their condition, self, or future (Drinkwater et al., 2023). Hopelessness often coincides with a variety of adverse emotions and behaviors, such as low self-esteem, feelings of futility, lack of energy, major depression, demoralization, and suicidal ideation (Drinkwater et al., 2023, Marchetti et al., 2023). Dismal expectations are a key feature of hopelessness, as favorable future thinking is significantly reduced. Hopelessness also arises from the irremediable obstruction of goals the individual is strongly committed to (Marchetti et al., 2023). The perceived loss of control and pursuit over important goals often associates hopelessness with helplessness, i.e. the expectation that an outcome is independent of one’s actions and ability (Marchetti et al., 2023). Hopelessness is the result of several complex emotions and does not exist in a vacuum, often facilitated by many contextual factors in an individual’s life, such as loneliness and reduced social support (Marchetti et al., 2023). The well-known consequence of hopelessness is increased suicidal ideation, tendencies, attempts, and suicidal death.

Motivation and hopelessness are two opposing psychological states. The gene-positive result of an asymptomatic individual of Huntington’s Disease, a fatal and progressive neurodegenerative disorder, presents the afflicted with an irreversibly informative life sentence. With a defined future, no disease-modifying treatment, and no cure, the gene-positive result opens up a world of intricate feelings, perceptions, and ideas about oneself and their life. I have categorized these varied responses under the dichotomous psychological relationship: motivated vs. hopeless. The individual will ultimately feel favorably or unfavorably towards their remaining limited years and studying these psychological states can aid in the further development of research and counseling for the affected individuals.

## Defining Decisional Regret

The decision to take a predictive genetic test for Huntington’s Disease is ultimately an irreversible life sentence, defining the end that the afflicted individual may face. Choosing to face the knowledge of a future with motor, cognitive, and psychiatric disturbances and death will have a great impact on the individual. Unable to walk away from an

unfavorable reality may lead to adverse consequences, such as decisional regret. Decisional regret is defined as the “distress or remorse after a (health care) decision” (O’Connor, 1996). Regret in health care implies the desired mental or physical aspects unable to be regained following medical intervention. Unwanted results often lead to regret in the individual’s decision-making process (Xu, 2021).

## Literature Review (Thematic)

This literature review will summarize qualitative studies of individuals who opted to undergo predictive genetic testing for Huntington’s Disease and their experiences as confirmed mutation carriers. With a focus on young adults, I will examine the dichotomous psychological states of motivation vs. hopelessness that occur in presymptomatic participants following testing. I will also advocate for tailored, flexible, and long-term genetic counseling.

**Table 1.** Information of Main Studies

Author(s) & Year	Name of Study	Participants	Summary
Duncan et al., 2007	“Holding Your Breath”: Interviews with Young People Who Have Undergone Predictive Genetic Testing for Huntington Disease	Eight participants, 17 to 25-years-old, four females and four males, two carriers and eight non-carriers	Qualitative interviews were conducted to explore the experiences and impacts of predictive testing for HD on young adults. Predictive testing was observed as having the potential to create harms and benefits for at-risk young individuals.
Gargiulo et al., 2009	Long-term outcome of presymptomatic testing in Huntington Disease	119 participants, 21 to 66-years-old, 62% female (73.78) and 38% male (45.22), 57 carriers and 62 non-carriers, mean time of 3.7 years between result and interview	Interviews were conducted comparing the psychological well-being and social adjustment of carriers and non-carriers following predictive testing for HD. Psychological support and psychiatric care were recommended to both carriers and non-carriers with a particular focus on psychiatric illnesses.
Gong et al., 2016	Impact of Huntington Disease Gene-Positive Status on Pre-Symptomatic Young Adults and Recommendations for Genetic Counselors	14 participants, 18 to 35-years-old, 12 females and two males, all carriers, mean time of 4 years between result and interview	A qualitative study conducted on young adults and their outlook on the future since discovering their gene-positive results for Huntington’s Disease. Results found that knowledge of one’s gene-positive status led to adjustments and urgencies to reach key milestones of adulthood, with young adults desiring flexible and tailored genetic counseling.
Hagberg et al., 2011	More Appreciation of Life or Regretting the Test? Experiences of	10 participants, 34 to 62-years-old (median: 51), six females and four	10 interviews were conducted to explore the long-term experiences of being a mutation carrier. Results showed a broad variety of positive

	Living as a Mutation Carrier of Huntington's Disease	males, all carriers, median time of 8.5 years between result and interview	and negative impacts on the carriers' lives.
Keenan et al., 2015	Help or hindrance: young people's experiences of predictive testing for Huntington's disease	12 participants, 17 to 26-years-old (mean: 21), all female, all described ethnicity as white	The study conducted pre- and post-test interviews with the aim of exploring young adults' prospective and retrospective experiences of predictive testing for HD and the impact of results. A qualitative thematic analysis demonstrated that, regardless of test results, young adults experienced: "a journey of empowerment", "an ambivalent process", or "a poor experience".
MacLeod et al., 2014	Experiences of predictive testing in young people at risk of Huntington's disease, familial cardiomyopathy, or hereditary breast and ovarian cancer	36 participants, 15 to 31-years-old (median: 25), 27 females and 9 males, mean time of 3.8 years between result and interview	The study focused on young people testing for later onset genetic conditions, aimed at exploring their motivations and experiences. Majority of the participants adjusted to their test results, with a noted resilience in gene-positive experiences.
Tillerås et al., 2020	Psychological reactions to predictive genetic testing for Huntington's disease: A qualitative study	33 participants, 13 to 65-years-old, 24 females and 9 males, seven carriers and 12 non-carriers	In-depth, semi-structured interviews were conducted to explore predictive testing experiences for individuals at risk for HD. With a focus on pre-testing experiences, the study identified three main themes: life in preparation for HD, factors influencing the testing decision, and the test result.

### Presymptomatic Young Adults with Huntington's Disease

Young adults make up approximately half of the population undergoing predictive genetic testing for Huntington's Disease (Gong et al., 2016). This significant portion of the at-risk population for an incurable, fatal disease have much future planning to do. Their limited healthy years entail many decisions in milestones of adulthood, such as completing one's education, starting a career, entering long-term relationships, family planning, and establishing investments. There is limited data on the impact of testing for HD on young adults, rarely highlighting how it affects these key milestones (Gong et al., 2016; Keenan et al., 2015; MacLeod et al., 2014). Thus, further study conducted on young adults' psychological state following their gene-positive result would greatly contribute to the improvement of genetic counseling techniques and quality of life for this seldomly studied population.

Before testing, children of individuals with the mutated gene are aware of their 50% chance of inheriting Huntington's Disease. Testing for HD ensures certainty of disease upon receiving the gene-positive result. A prominent theme of the studies was young adults holding a high level of awareness that their future was limited by the later onset of HD (Gong et al., 2016). The knowledge of one's gene-positive result, a temporary lack of symptoms, and

limited healthy years provide this population the ability to manage their future plans in a way that others, with different genetic conditions, cannot.

Gene-positive results for HD had a profound impact on the young adults' perspectives of their future. Gong et al. cites a study in which young adulthood, 18 to late 20s, is described as "a time of possibilities, exploration, and optimism about the future." When young adults are faced with the reality of their mutation carrier statuses, a need to expedite this time emerges (2016, p. 1189). Testing young during the early phases of career advancement, gave the adults opportunities to make adjustments to their developing career path. In romantic relationships, while older gene-positive individuals often considered the need for a caretaker in their relationships, young adults did not emphasize this intention as their dependency on a caretaker was far into the future. Young adults were also observed to have an overall decrease in their desire to have children after testing gene-positive (Gong et al., 2016). All of these decisions were made with the knowledge of one's medical future in mind. Thus, testing was described as an empowering experience for young adults, granting a perception of control over future events (Duncan et al., 2007; MacLeod et al., 2014)

The test results had prominent, varied effects that were particular to young adults. Other than future planning and motivation, predictive testing helped some establish personal identities and improve interpersonal and family relationships (Gong et al., 2016; Keenan et al., 2015). While testing for young adults can have extreme benefits, it can have its extreme disadvantages as well. Youth and lack of life experience were common factors for unfavorable reactions in young adults: a lack of emotional experience made preparing for the test results' impact difficult (MacLeod et al., 2014); a lack of personal experience caused failure in anticipating results' impact on family dynamics and relationships (Keenan et al., 2015); and the newfound independence the majority of young adults experience from previously constant parental support may have led to the acute isolation they experience prior and following testing (Keenan et al., 2015).

## Motivated Mutation Carriers

Due to the current lack of literature focusing on predictive testing for Huntington's in young adults, this literature review encompasses a wider age range of presymptomatic mutation carriers while maintaining a highlight on young individuals. This section of the review covers *Successful Adjustment to "Bad News," Relief from Uncertainty, the Limited Healthy Years, An Optimistic Future, No Regret, the Metrics of Motivation, and the Ultimate Hope.*

### *Successful Adjustment to "Bad News"*

After an individual undergoes the testing process and receives a gene-positive test result, or "bad news," their ability to adjust or cope sets the stage for the overall experience of motivation vs. hopelessness. Despite much speculation in past literature, predictive testing for Huntington's has not led to significantly increased rates of suicide or psychiatric illness (Keenan et al., 2015). While carriers may experience initial shock and difficulty regarding their test results, adjustment usually occurs within one year; however, anxiety levels may rise in the long-term as individuals approach onset (Keenan et al., 2015). Adjustment was typically achievable through certain means of coping. In a study by MacLeod et al. in 2014, most participants discussed focusing on the favorable aspects of their situation, such as the many years before onset or the advantage of being informed about their gene-status unlike those who hadn't been tested. In addition, a study completed by Hagberg et al. in 2011, the majority of participants stated that as the years went by, the difficulty of the knowledge decreased despite approaching onset. A possible explanation could be the acceptance and integration of their mutation carrier status into their lives. However, it is important to note that this was not the case for most of the studies, with many others reporting increasing hopelessness and distress caused by approaching onset. Considering the external sources facilitating successful adjustment, participants were able to cope through the support of friends and family (Hagberg et al., 2011).

### *Relief from Uncertainty*

The at-risk individual for Huntington's Disease lives with a 50% chance of affliction, which can cause much anxiety. Therefore, a key benefit for participants who undergo predictive testing is to be able to relieve themselves from the coin-flip uncertainty of HD. The majority of participants in the studies reported this relief from uncertainty, allowing for a sense of security in their expectations for the future (Hagberg et al., 2011; MacLeod et al., 2014). As observed by Duncan et al., the uncertainty of young adults' genetic status represented a barrier in their lives, preventing them from moving forward (2007).

### *The Limited Healthy Years*

For many of the mutation carriers in these studies, the knowledge of their existing healthy, presymptomatic years motivated them. Eight of the 10 participants for Hagberg et al. acknowledged the opportunity to be able to live their lives in finite health (2011). 11 of the 14 young adults in Gong et al. reported a greater appreciation for their limited healthy years after receiving their gene-positive result (2016, p. 1190).

### *An Optimistic Future*

In many of the studies, clear motivation to continue living fulfilled lives was expressed through key themes of a greater appreciation for life, a newfound sense of maturity, and a chance to plan and move forward (Duncan et al., 2007; Gong et al., 2016; Hagberg et al., 2011; MacLeod et al., 2014; Tillerås et al., 2020). For Hagberg et al., a majority of the participants described life and family becoming more precious with knowledge of their mutation carrier status. This shift in mentality was illustrated by the referenced aphorism, "When you learn to die, you learn to live" (2011, p. 74). Test results also affected the participants' notions of self, many expressing that the knowledge made them mature faster and become a better human being (Gong et al., 2016; MacLeod et al., 2014). Results served as a positive motivator or catalyst for many, pushing participants to plan their lives in positive and practical ways (Duncan et al., 2007; Hagberg et al., 2011; MacLeod et al., 2014). One study, as reported by Meiser & Dunn, utilized a control group to compare the effects of test results. In a 12 month follow-up, at-risk people who didn't receive a genetic test result had higher levels of depression and lower levels of well-being compared to carriers who did; the authors concluded that the acquiring of a test result, even if indicating a gene-positive status, was beneficial through the reduction of uncertainty and a given opportunity for future planning (2000).

### *No Regret*

While decisional regret is addressed later on in this review, some of the studies observed that none of the participants expressed regret for their decision to undergo predictive genetic testing, with an emphasis on young participants (Duncan et al., 2007; Gong et al., 2016; MacLeod et al., 2014). Regretting the test or not, eight of the 10 participants in the study of Hagberg et al. acknowledged the favorable aspects of predictive testing (2011).

### *The Metrics of Motivation*

The *Metrics of Motivation* utilizes the aforementioned aspects of young adulthood, i.e. career and education, familial and romantic relationships, and reproductive choices, to measure the motivation for the participants in multiple studies.

Career Path and Education: The alterations of one's career and educational path, without the specific details involved in such a decision, can either be regarded as beneficial or harmful. For example, changing to a more stable occupation for financial and security reasons can be perceived as motivated preparation for onset of HD or as an unfortunate obligation. While it can be difficult to ascertain the cause between a motivated vs. hopeless response in career and education, the provided explanations for these decisions were used to determine which emotional state they were associated with. In the study conducted by Gong et al., eight of the 14 participants made minor changes to their pursuit of higher education and careers in response to their gene-positive result. These participants' reasons were a desire to



earn money during their limited healthy years, a fear of onset leading to career loss, and preparing financially for future onset of symptoms. However, personal interest persisted throughout these decisions, and test results did not deter them from their original goals (2016).

Thriving Familial, Friendly, and Romantic Relationships: Huntington's Disease can be extremely isolating for the afflicted individual. Thus, a fundamental feature of a mutation carrier's optimistic response is having a strong support system. Many of the participants in these studies with a successful adjustment, a positive outlook towards their future, and an appreciation for life shared a theme of persisting healthy relationships (Gong et al., 2016; Hagberg et al., 2011; Keenan et al., 2015; Tillerås et al., 2020). For some of the studies, participants stated that after their gene-positive result, the quality of their relationships with friends and loved ones remained unchanged or grew stronger (Gong et al., 2016; Hagberg et al., 2011; Keenan et al., 2015). In the study conducted by Tillerås et al., some felt closer to their family due to the enhanced understanding of their affected parents' experiences (2020). Limited healthy years also motivated individuals to become more particular in choosing fulfilling, romantic relationships. In one study, eight of the 14 unmarried participants became more selective of romantic partners after receiving their results (Gong et al., 2016).

Reproductive Choices: For many of the young adults, reproductive decisions were recalled as a key possibility of the future. In the study of MacLeod et al., many of the young individuals perceived the information of a test result as useful in the proactive planning of future children (2014). For Gong et al., 10 gene-positive female participants still wanted to have children, but all wanted to avoid having at-risk children. Thus, they generally preferred pre-implantation genetic diagnosis (PGD) with in vitro fertilization (IVF) (2016). Another study observed similar findings of three individuals who reported that they would like to have children in the future if they had the chance (Hagberg et al., 2011).

### *The Ultimate Hope*

While the devastating motor, cognitive, and physical disturbances and fatality of Huntington's can steer an individual away from a favorable outlook towards their life and future, the factor that drives many afflicted individuals into a state of hopelessness is the lack of cure. Some who struggle with this reality cope through denial-avoidance, a defense mechanism of dismissing uncomfortable thoughts, feelings, and situations of an external reality, such as the affliction of Huntington's Disease (Bailey & Pico, 2023). For instance, denial-avoidance involved steering away from physicians, Huntington's support groups, and research (Hagberg et al., 2011). However, some afflicted individuals are able to remain optimistic through advancing science and the HD community. In MacLeod et al., faith in medicine strongly emerged among the young adults as they believed in the ability of their physicians and hoped for better treatments in the future (2014). A 24-year-old female participant was hopeful about the future and the possible gains of clinical trials "in the next 5-10 years" (Keenan et al., 2015, p. 565). A few participants in the study of Tillerås et al. said that they coped with the difficult news of being gene-positive by hoping for the development of a cure for HD in the near future (2020). After testing positive, a 30-year-old female participant felt that she needed to help others who were going through her situation. She now volunteers with a local chapter of the HDSA in order to aid those living through the knowledge of their mutation carrier status (Gong et al., 2016).

### Ambivalent Mutation Carriers

While the literature review mainly focuses on the dichotomous psychological states of motivation vs. hopelessness, it is important to acknowledge the few participants who felt no dramatic impact from the test result on their lives. One mutation carrier in the study of Keenan et al. described seeking testing as an ambivalent experience (2015). In the study of Hagberg et al., several participants reported that test results hadn't contributed to any important life changes;

one mutation carrier was surprised at the absence of a negative reaction following results, wondering, “Am I strange for not being more depressed?” (2011, p. 73).

## Hopeless Mutation Carriers

Hopelessness is used as an umbrella term to include all adverse reactions and impacts on the participants’ lives in response to a gene-positive test result for Huntington’s Disease. This section of the review covers *Struggling to Cope with “Bad News,” New Uncertainties Arise, Discrimination, Loneliness, the Heights of Hopelessness, and Adverse Impacts on Well-Being*.

### *Struggling to Cope with “Bad News”*

Similarly to well-adjusted mutation carriers, the coping process following test results can heavily indicate one’s long-term impacts and perception of the future. Many of the participants initially struggled with their results. For MacLeod et al., the initial period of shock and acute distress varied in duration, lasting weeks or months (2014). The longest period of difficulty with coping was observed in the study of Hagberg et al.; participants struggled with the results for at least the first two years (2011). For most of the studies, increasing hopelessness and distress was caused by approaching onset. Pertaining to young adults, participants found that receiving “bad news” was especially hard to cope with when living with a recently diagnosed parent (Keenan et al., 2015). Keenan et al. detailed two young female participants who experienced initial difficulty with their gene-positive results. As one of them grappled with the result, an issue of immense pressure along with a lack of motivation, or hopelessness, emerged, “With the result, I feel like I need to do something quick...because I know that I am going to develop it...But just now, I don’t really have the motivation to do anything...” (Keenan et al., 2015, p. 567).

A distinct coping mechanism admitted by several participants in the study of Hagberg et al. was denial-avoidance behavior. Three participants said that they avoid regular contact with physicians, one stating that it was just another “unpleasant reminder about being a mutation carrier” (2011, p. 75). For these individuals, seeing others affected by HD showed what was in store for them. Thus, many did not seek support and contact with the HD lay organization (Hagberg et al., 2011).

For some, struggling to cope often coincided with adverse psychological behaviors and disorders. While depression was frequent prior to testing, the results caused an increase of 7% in carriers. Even after a mean of 3.7 years after the gene-positive result, depression was frequent, overall affecting 58% of mutation carriers (Gargiulo et al., 2009). In the psychiatric department for major depression, Gargiulo et al. reported one suicide attempt and one hospitalization after carriers tested (2009). In the study by Tillerås et al., most participants with a gene-positive result shared that it was very emotionally and psychologically difficult to handle. For some, the mutation carrier status led to powerfully negative thoughts; one participant’s overwhelming emotions led to suicidal ideation (2020).

As the onset of symptoms for HD approaches, concern and difficulty coping can emerge for many as the reality of the disease can no longer be ignored. For Hagberg et al., most presymptomatic participants felt uneasy discussing disease onset during the study. Some were worried about a future of improper care and understanding at onset due to the rarity of Huntington’s as a condition (2011). Studies reported that distress levels may arise in gene-positive individuals as disease onset advances (Gong et al., 2016; Keenan et al., 2015; MacLeod et al., 2014). In another study, two participants reported that the burden of the test result combined with other life problems contributed to a need for long-term professional support outside of the testing program (Hagberg et al., 2011). Gargiulo et al. revealed that a long-term follow-up of seven to 10 years after results showed an increase of hopelessness (2009).

### *New Uncertainties Arise*

An often recited benefit for predictive testing of HD is relief from uncertainty, pushing an individual to live their life confidently with the knowledge of their mutation carrier status. However, the test result does not ensure a life without uncertainty. Predictive testing cannot anticipate when onset of the disease occurs or how severe symptoms may be.

Some of the participants in the study by Hagberg et al. mentioned that knowledge of their result gave way to new uncertainties and anxieties about the future, especially in regards to when and how Huntington's will present itself later in life (2011).

### *Discrimination*

Genetic discrimination is the unequal treatment of individuals based on an aspect of their genetic code or genome, such as the risk of genetic disorders (Bonham, 2023). Eight of the 14 young participants in the study conducted by Gong et al. felt a major challenge they constantly faced, following their test results, was the disclosure of their genetic status. The main reason for this concern stemmed from fear of discrimination in social, employment, and insurance settings (2016). MacLeod et al. also recognized the possibility of participants experiencing discrimination at home, in the workplace, or with insurance (2014). Another study, referenced by Gong et al., reported that although genetic discrimination is experienced by all age groups, younger adults are more likely to experience discrimination in the insurance setting (2016). While several state and federal laws protect people against genetic discrimination, such as the Genetic Information Nondiscrimination Act (GINA), it is important to protect the presymptomatic individuals for whom GINA and other laws do not include (MedlinePlus, 2021).

### *Loneliness*

Huntington's Disease, compared to cancer or Alzheimer's, is a relatively rare disease. The smaller population of individuals affected by Huntington's means fewer resources and organizations, less research, and little awareness. A lack of knowledge and understanding regarding Huntington's can lead to many individuals feeling isolated in their struggle. Three participants in the study by Gong et al. experienced loneliness after receiving their gene-positive test result due to a lack of sufficient peer support and understanding (2016). For MacLeod et al., many participants felt that others would not understand the complexities of the testing decision or trivialize their feelings about the result (2014). An example of this can be seen in another study where two participants felt that the people in their surroundings did not understand the choice of testing (Hagberg et al., 2011).

### *The Heights of Hopelessness*

The *Heights of Hopelessness*, similarly to the *Metrics of Motivation*, utilizes the aforementioned aspects of young adulthood, i.e. career and education, familial and romantic relationships, reproductive choices, and financial investments, to measure the hopelessness of the participants in multiple studies.

Career Path and Education: As previously stated in the *Metrics of Motivation*, career and educational choices can be regarded as either beneficial or harmful without proper context. The unfavorable impacts of a mutation carrier status on one's career and education were determined by the explanations provided by participants in the study. Two participants in the study of Hagberg et al. discussed their contrasting reactions to individuals who were motivated to invest in their careers and education. One participant explained her feelings of futility in starting an educational training program with the growing skepticism towards her cognitive ability. The other participant quit her job as a business leader, feeling as though there was no point in working when she was so uncertain about disease onset (2011).

Trouble in Familial, Friendly, and Romantic Relationships: Lack of a strong support system, through friends, family, and romantic partners, can heavily influence the isolation and hopelessness that a mutation carrier may experience following test results. For Gong et al., seven of the 14 participants felt that their gene-positive status and future HD symptoms were "burdens" or "deficits" in relationships, making them feel less romantically desirable. Over time, most of them were able to overcome or lessen the feeling of their status being a "deficit" or "burden" (2016, p. 1191). In the same study, participants reported fears and experiences of rejection by dating partners following disclosure of mutation carrier status (Gong et al., 2016). In terms of platonic relationships, one participant admitted that her friends

were unable to handle the fact that she would get Huntington's in the future, stating, "My closest friends turned their backs on me when I got the test results...so I never talk about Huntington..." (Hagberg et al., 2011, p. 74).

Adverse responses to test results emerged from both the carrier in regards to their family or directly from their family. For MacLeod et al., most participants anticipated the potential impact of their results on loved ones and sought out ways to avoid causing pain or distress (2014). Three participants in the study of Hagberg et al. described the harmful impact testing results had on their relationships with their families; several participants encountered emotional problems when informing their at-risk relatives, e.g. children and siblings (2011). All participants expressed difficulties concerning the issue of informing their children about their risk of getting HD and feelings of guilt about passing on the gene to their children. One participant described her adult son's upset and angry response when discussing her results with him. 10 years later, she still avoids talking about Huntington's Disease with him. These feelings of guilt towards one's children following a gene-positive test result may lead to additional distress (Hagberg et al., 2011). Conversely, one participant admitted to feeling angry with her father for giving her "bad genes" (Hagberg et al., 2011, p. 75).

Reproductive Choices: In the study by Gong et al., young participants experienced an overall decrease in their desire to have children after testing gene-positive. Their reasons were to avoid transmission of the mutation to future children, the "perceived moral obligation to stop HD", and to avoid putting children through taking care of an affected parent (2016, p. 1194).

Financial Investments: One female participant admitted to refraining from an expensive and long-term dental treatment, a gold crown, because she was not going to live as long as it would last (Hagberg et al., 2011).

### *Adverse Impacts on Well-Being*

The combination of one's gene-positive test result, a struggle to cope, uncertainty about onset, fear of discrimination, a lack of sufficient support, isolation, the restrictions of HD on aspects of adulthood, devastating symptoms, and the lack of cure culminates into adverse impacts on one's psychological state, ending in hopelessness. Some participants expressed that the knowledge of their mutation carrier status led to a negative effect on their psychological well-being. In contrast to the three participants in the study who described their test results as motivational, three other participants felt that they had no motivation. They no longer felt motivated to start a longer academic career, put money into healthcare, or continue their career (Hagberg et al., 2011).

### Decisional Regret

While many studies mentioned participants feeling no regret towards testing, decisional regret was a prominent reaction in the study of Hagberg et al. (2011). There is limited data on decisional regret and its factors in predictive testing for HD. This is possibly due to the fact it is a very difficult subject to discuss between participants and testing officials. Four of the 10 individuals described regret following test results. A common reason was that knowledge of their mutation carrier status was a "far heavier load" than expected. They strongly felt that "hope is gone" and that "life has ended." (Hagberg et al., 2011, p. 77). One participant commented, "...if one hadn't known then it would have been easier to put one's head in the sand...hope has disappeared" (Hagberg et al., 2011, p. 73).

## The Need for Genetic Counseling

### *Reactions to Genetic Counseling*

Participants in all studies had varying experiences with their genetic counseling services. Most participants who tested gene-positive in one study were pleased with the follow-up consultations conducted by healthcare providers and support services (Tillerås et al., 2020). In the study by MacLeod et al., predictive test counseling was viewed as useful in providing personalized information in comprehensive and accessible language (2014). Two participants in another study valued the opportunity to receive accurate information about Huntington's, discuss the pros and cons of testing, and receive support from other agencies, such as advice on end of life care from the Huntington's Association (Keenan et al., 2015).

Despite acknowledging the benefits of testing, many participants had issues with the process. Of the 11 young adults that received genetic counseling in the study by Gong et al., approximately half found it helpful, and the other half regarded it as a taxing process. The noted useful aspects of counseling included the assessment of emotional readiness, information, and resources about life and disability insurances. The downsides of counseling were that some found the process to be a "hurdle", "obstacle", or "unnecessarily lengthy"; these individuals were also those who tested at a center with prolonged counseling, felt they'd carefully considered testing prior to counseling, or "led a busy life" (2016, p. 1193). Similarly, young adults in another study who knew they wanted testing from the beginning felt that the counseling process was repetitive and inflexible (Keenan et al., 2015). Participants in MacLeod et al. were generally favorable towards the counseling process, but several had issues with the length of time between appointments and the lack of tailoring for the individual's specific situation (2014). For Keenan et al., one carrier who felt ambivalent about the testing process described genetic counseling as "information-rich" but lacking in emotional support and control over the testing process. Another participant felt similarly that while the information was helpful, "they never really looked into the emotional side of it, which is the side she struggled with mostly..." (Keenan et al., 2015, p. 565). Some young adults found the support person requirement prohibitive and unhelpful, preferring to attend alone (Keenan et al., 2015).

Focusing on young adults, there was much confusion and stress regarding unclear information on the amount and time span between testing appointments. Young adults were also confused as they expected the clinic to contact them about the appointments, when clinic practice was for the young adults to reach out. Most felt that the pre-test period was too long, but those who had clear and engaging information about the testing protocol coped better. Data reports that prolonging or shortening the recommended testing protocol can make young adults feel that it is a "battle to get tested", adding distress and detrimental impact (Keenan et al., 2015, p. 568). One participant in the study by Tillerås et al. shared that no options for follow-up consultations were offered to the participants' partners or immediate family (2020).

### *Improvements on Genetic Counseling*

The paper reviews the literature of the dichotomous psychological states following predictive testing for Huntington's Disease with the goal of improving the lives of the HD population. While a cure is currently not available, improvement in genetic counseling for those afflicted and at-risk is feasible. Noting the favorable reactions to genetic counseling and utilizing the criticisms in unfavorable reactions creates a stance on the benefits of genetic counseling and what needs to be improved on. Ensuring long-term, informative, supportive, and tailored counseling can deeply influence one's life following a gene-positive test result.

Many of the afflicted, presymptomatic participants varied in their coping, with some adjusting well to their mutation carrier status many years following results and some deeply struggling as the symptoms approached. The extensive time period from a presymptomatic individual testing to suffering from symptomatic onset calls for long-term genetic counseling. As stated by Tillerås et al., individuals who test positive may need comprehensive follow-up to adapt to their test results (2020). Four young adults in the study of Gong et al. expressed an appreciation or desire

for long-term follow-up after test results. One participant, 29-year-old Megan, who didn't receive follow-up, commented, "I wish somebody would have followed up with me after I tested positive" (2016, p. 1193). Long-term follow-ups are a great means for individuals to update on their health, discuss concerns, and ask for help. Following-up also detects the first subtle, non-motor symptoms of the disease, such as adverse behaviors and reactions (Gargiulo et al., 2009). Three of the four participants who deeply regretted testing in Hagberg et al. felt this way several years after their results (2011). Adverse responses, such as regret, occurring years after the test proves the necessity of long-term counseling in order to ensure that afflicted individuals receive the help they need when issues arise. There is evidence in HD literature that individuals who drop out of follow-up may be the patients with the greatest need as they begin to develop symptoms (MacLeod et al., 2014). Thus, long-term genetic counseling is needed for HD afflicted individuals.

Genetic counseling that provides clear, comprehensive, and unhurried information can be valued as an ongoing, helpful resource for many individuals (Bernhardt et al., 2000). Many participants in the studies expressed great appreciation for genetic counselors' information on multiple topics related to Huntington's given in an accessible language (Keenan et al., 2015; MacLeod et al., 2014). However, there were areas in which participants felt genetic counseling failed to address. As previously mentioned, those in the study of Keenan et al. struggled without clear information on the amount, time, and standards of communication for genetic counseling appointments (2015). Providing technical information on the counseling process itself is important for young adults in maintaining good relations with their counselor and counseling itself. While genetic counseling can provide a great amount of information and guidance on Huntington's, there were some areas that lacked such. Four participants in Gong et al. reported a lack of practical information in significant categories: alternative reproductive options and advice on obtaining life and disability insurance (2016). The particular note of younger adults being more likely to experience discrimination in insurance, possibly due to a lack of professional experience, calls for guidance on an unmentioned category. Thus, genetic counselors should emphasize information on these undiscussed issues, even so far as recommending external professionals and organizations (Gong et al., 2016).

Society's lack of general knowledge on the rare condition that is Huntington's may exacerbate feelings of loneliness for individuals (Tillerås et al., 2020). Participants in the studies felt a lack of peer support or chose not to share results with a wider support network (Gong et al., 2016; Keenan et al., 2015; MacLeod et al., 2014). Therefore, genetic counselors should stress the importance of a good support system. Genetic counselors should also prepare individuals for the possibility of misunderstanding and stigmatization, which some participants faced from friends and family (Hagberg et al., 2011; Tillerås et al., 2020). One mutation carrier shared that no follow-up consultations were offered to the participants' partner or immediate family, which would be a great means of helping the afflicted individual's support system become informed and cope with any difficulties the test result may bring (Tillerås et al., 2020). The generally isolating nature of Huntington's can be improved by genetic counselors through the aforementioned suggestions, but counselors should also provide additional resources, HD support groups, and advocacy organizations, such as the Huntington's Disease Youth Organization (HDYO) (MacLeod et al., 2014).

Throughout the varied responses to genetic counseling, a key theme persisted: the need for tailored and personalized counseling. While the test result of Huntington's is short and simple, the reactions and impacts are complex. A standard counseling protocol is vital, but the experiences of individuals in testing should be taken heavily into account. For many young adults, the preferences for length, depth, and content of counseling varied greatly and depended on each individual's lifestyle, mindset prior to testing, expectations, eagerness, etc. The importance of flexible, tailored genetic counseling for young adults was recognized by the studies of Gong et al. and MacLeod et al. (2016; 2014). Duncan et al. highlighted the need to understand young adults within a broader context, prior and following testing, in order to create better counseling strategies (2007). Counselors were also recommended to keep updated with information on peer support groups and clinics specifically targeted to young adults, as well as staying aware of factors that may disengage young people from discussions surrounding HD testing (Gong et al., 2016; MacLeod et al., 2014). Other recommendations for counselors were: not underestimating the extent of single, childless young

adults' thoughts about future children; exploring diverse models of delivering support following testing; and not excluding emotional support (Keenan et al., 2015; MacLeod et al., 2014).

As previously mentioned, there is evidence that individuals who drop out of follow-up may be in greatest need of it (MacLeod et al., 2014). Another study had a similar observation, stating it is possible that those who are more psychologically vulnerable do not follow through the rigorous testing and counseling process (Meiser & Dunn, 2000). These afflicted individuals resort to denial-avoidance coping, rejecting support from physicians, counselors, and the HD community. In order to provide aid to the most vulnerable of the HD population, counseling must be tailored to their needs. This means altering the counseling process to be less "rigorous," creating gentler and more accessible ways to aid adjustment to test results and acceptance of help.

## Conclusion

This literature review encompasses the complex variety of impacts and experiences of a gene-positive test result for Huntington's Disease on at-risk, presymptomatic participants, especially gene-positive young adults. By utilizing the participants' reported psychological well-being, social relationships, and outlook on the future, the responses to test results were categorized into the dichotomous psychological states of motivation vs. hopelessness. These motivated or hopeless responses included adjustments to results, newfound relationships with uncertainty and regret, appreciation of life and limited health, arising struggles of discrimination and loneliness, and effects of results on the key milestones of adulthood. Ultimately, predictive testing results for HD were observed as having both beneficial and detrimental influence on the mutation carriers' lives, serving as a positive motivator or negative hindrance. The review also acknowledges limitations and gaps in literature, recommending further study on the impacts, broad experiences, and decisional regret of testing for HD. Although there is no cure for Huntington's Disease, studying the participants' psychological states can contribute to long-term, informative, supportive, and tailored genetic counseling, subsequently enhancing a quality of life for the at-risk and afflicted HD community. By recognizing the favorable aspects and utilizing the critiques, this review argues for the benefits and needed improvements of genetic counseling.

## Limitations

A majority of the studies used qualitative data and self-reports on retrospective experiences, which are vulnerable to recall bias (Duncan et al., 2007; Gong et al., 2016; MacLeod et al., 2014). Many of the studies had primarily female samples, as well as many highly educated individuals (Gargiulo et al., 2009; Gong et al., 2016; Hagberg et al., 2011; Keenan et al., 2015; MacLeod et al., 2014; Tillerås et al., 2020). It's been observed that participants who choose to take part in such in-depth research following predictive testing for HD tend to be those coping best or struggling most. Thus, these more extreme experiences may not be representative of the general population of HD mutation carriers (Duncan et al., 2007; Gong et al., 2016; MacLeod et al., 2014). The sample sizes for many of the studies were also quite small in comparison to psychological evaluations of the normal population, limiting the studies' generalizations (Duncan et al., 2007; Gong et al., 2016). However, these studies are equipped to accurately represent the smallness of the HD population.

## Acknowledgments

I would like to thank my advisor for the valuable insight provided to me on this topic.

## References

- Bailey, R., & Pico, J. (2023). Defense Mechanisms. In *StatPearls*. StatPearls Publishing.  
<https://pubmed.ncbi.nlm.nih.gov/32644532/>
- Bernhardt, B. A., Biesecker, B. B., & Mastromarino, C. L. (2000). Goals, benefits, and outcomes of genetic counseling: client and genetic counselor assessment. *American journal of medical genetics*, 94(3), 189–197.  
<https://pubmed.ncbi.nlm.nih.gov/10995504/>
- Bonham, V. L., Jr.. (2023). Genetic Discrimination. *National Human Genome Research Institute*.  
<https://www.genome.gov/genetics-glossary/Genetic-Discrimination>
- Cofer, C. N., & Petri, H. L. (2023, April 27). Motivation. *Encyclopedia Britannica*.  
<https://www.britannica.com/topic/motivation>
- Drinkwater, K., Denovan, A., Dagnall, N., & Williams, C. (2023). The General Hopelessness Scale: Development of a measure of hopelessness for non-clinical samples. *PloS one*, 18(6), e0287016.  
<https://doi.org/10.1371/journal.pone.0287016>
- DufRASne, S., Roy, M., Galvez, M., & Rosenblatt, D. S. (2011). Experience over fifteen years with a protocol for predictive testing for Huntington disease. *Molecular genetics and metabolism*, 102(4), 494–504.  
<https://doi.org/10.1016/j.ymgme.2010.12.001>
- Duncan, R. E., Gillam, L., Savulescu, J., Williamson, R., Rogers, J. G., & Delatycki, M. B. (2007). "Holding your breath": interviews with young people who have undergone predictive genetic testing for Huntington disease. *American journal of medical genetics. Part A*, 143A(17), 1984–1989. <https://doi.org/10.1002/ajmg.a.31720>
- Evans, J. P., Skrzynia, C., & Burke, W. (2001). The complexities of predictive genetic testing. *BMJ (Clinical research ed.)*, 322(7293), 1052–1056. <https://doi.org/10.1136/bmj.322.7293.1052>
- Gargiulo, M., Lejeune, S., Tanguy, M. L., Lahlou-Laforêt, K., Faudet, A., Cohen, D., Feingold, J., & Durr, A. (2009). Long-term outcome of presymptomatic testing in Huntington disease. *European journal of human genetics : EJHG*, 17(2), 165–171. <https://doi.org/10.1038/ejhg.2008.146>
- Gong, P., Fanos, J. H., Korty, L., Siskind, C. E., & Hanson-Kahn, A. K. (2016). Impact of Huntington Disease Gene-Positive Status on Pre-Symptomatic Young Adults and Recommendations for Genetic Counselors. *Journal of genetic counseling*, 25(6), 1188–1197. <https://doi.org/10.1007/s10897-016-9951-z>
- Hagberg, A., Bui, T. H., & Winnberg, E. (2011). More appreciation of life or regretting the test? Experiences of living as a mutation carrier of Huntington's disease. *Journal of genetic counseling*, 20(1), 70–79.  
<https://doi.org/10.1007/s10897-010-9329-6>
- Huntington's Disease Society of America. (2016). Genetic Testing Protocol For Huntington's Disease. *HDSA*, 1-20.  
<http://hdsa.org/wp-content/uploads/2015/02/HDSA-Gen-Testing-Protocol-for-HD.pdf>
- Huntington's Disease Society of America. (2020, November 6). Overview of Huntington's Disease. *HDSA*,  
<https://hdsa.org/what-is-hd/overview-of-huntingtons-disease/>



Keenan, F. K., McKee, L., & Miedzybrodzka, Z. (2015). Help or hindrance: young people's experiences of predictive testing for Huntington's disease. *Clinical genetics*, 87(6), 563–569. <https://doi.org/10.1111/cge.12439>

Lewis, R. G., & Simpson, B. (2023). Genetics, Autosomal Dominant. In *StatPearls*. StatPearls Publishing. <https://pubmed.ncbi.nlm.nih.gov/32491444/>

MacLeod, R., Beach, A., Henriques, S., Knopp, J., Nelson, K., & Kerzin-Storarr, L. (2014). Experiences of predictive testing in young people at risk of Huntington's disease, familial cardiomyopathy or hereditary breast and ovarian cancer. *European journal of human genetics : EJHG*, 22(3), 396–401. <https://doi.org/10.1038/ejhg.2013.143>

Mandal, Ananya. (2019, February 26). Huntington's Disease History. News-Medical, <https://www.news-medical.net/health/Huntingtons-Disease-History.aspx>

Marchetti, I., Alloy, L.B. & Koster, E.H.W. (2023). Breaking the Vise of Hopelessness: Targeting its Components, Antecedents, and Context. *J Cogn Ther*. <https://doi.org/10.1007/s41811-023-00165-1>

Massey, M., Orem, T., & Sung, V. (2021). Cost of Predictive Genetic Testing for Huntington's Disease at Centers of Excellence in the US. *MDS Abstracts*, <https://www.mdsabstracts.org/abstract/cost-of-predictive-genetic-testing-for-huntingtons-disease-at-centers-of-excellence-in-the-us/>

Matz, O. C., & Spocter, M. (2022). The Effect of Huntington's Disease on the Basal Nuclei: A Review. *Cureus*, 14(4), e24473. <https://doi.org/10.7759/cureus.24473>

McColgan, P., & Tabrizi, S. J. (2018). Huntington's disease: a clinical review. *European journal of neurology*, 25(1), 24–34. <https://doi.org/10.1111/ene.13413>

MedlinePlus. (2021, July 28). What is genetic discrimination? *MedlinePlus*, National Library of Medicine. <https://medlineplus.gov/genetics/understanding/testing/discrimination/#:~:text=Genetic%20discrimination%20occurs%20when%20people,among%20people%20considering%20genetic%20testing>

MedlinePlus. (2021, July 28). What is genetic testing? *MedlinePlus*, National Library of Medicine. <https://medlineplus.gov/genetics/understanding/testing/geneticstesting/>

Meiser, B., & Dunn, S. (2000). Psychological impact of genetic testing for Huntington's disease: an update of the literature. *Journal of neurology, neurosurgery, and psychiatry*, 69(5), 574–578. <https://doi.org/10.1136/jnnp.69.5.574>

National Institute of Neurological Disorders and Stroke. (2023). Huntington's Disease. *U.S. Department of Health and Human Services*, <https://www.ninds.nih.gov/health-information/disorders/huntingtons-disease>

Novak, M. J. U., & Tabrizi, S. J. (2010). Huntington's disease. *BMJ: British Medical Journal*, 341(7762), 34–40. <http://www.jstor.org/stable/20734704>

O'Connor, A. M. (1996). User Manual - Decision Regret Scale. *Ottawa: Ottawa Hospital Research Institute*, 3 p. [https://decisionaid.ohri.ca/docs/develop/User\\_Manuals/UM\\_Regret\\_Scale.pdf](https://decisionaid.ohri.ca/docs/develop/User_Manuals/UM_Regret_Scale.pdf)

- Pulst S. M. (1999). Genetic linkage analysis. *Archives of neurology*, 56(6), 667–672. <https://doi.org/10.1001/archneur.56.6.667>
- Reiner, A., Dragatsis, I., & Dietrich, P. (2011). Genetics and neuropathology of Huntington's disease. *International review of neurobiology*, 98, 325–372. <https://doi.org/10.1016/B978-0-12-381328-2.00014-6>
- Roos R. A. (2010). Huntington's disease: a clinical review. *Orphanet journal of rare diseases*, 5, 40. <https://doi.org/10.1186/1750-1172-5-40>
- Simpson, E. H., & Balsam, P. D. (2016). The Behavioral Neuroscience of Motivation: An Overview of Concepts, Measures, and Translational Applications. *Current topics in behavioral neurosciences*, 27, 1–12. [https://doi.org/10.1007/7854\\_2015\\_402](https://doi.org/10.1007/7854_2015_402)
- Tillerås, K. H., Kjoelaas, S. H., Dramstad, E., Feragen, K. B., & von der Lippe, C. (2020). Psychological reactions to predictive genetic testing for Huntington's disease: A qualitative study. *Journal of genetic counseling*, 29(6), 1093–1105. <https://doi.org/10.1002/jgc4.1245>
- Torrico, T. J., & Munakomi, S. (2022). Neuroanatomy, Thalamus. In *StatPearls*. StatPearls Publishing. <https://pubmed.ncbi.nlm.nih.gov/31194341/>
- Vale, T. C., & Cardoso, F. (2015). Chorea: A Journey through History. *Tremor and other hyperkinetic movements (New York, N.Y.)*, 5, tre-5-296. <https://doi.org/10.7916/D8WM1C98>
- Wexler, A., Wild, E. J., & Tabrizi, S. J. (2016). George Huntington: a legacy of inquiry, empathy and hope. *Brain: a journal of neurology*, 139(Pt 8), 2326–2333. <https://doi.org/10.1093/brain/aww165>
- Xu, R. H., Zhou, L. M., & Wang, D. (2021). The Relationship Between Decisional Regret and Well-Being in Patients With and Without Depressive Disorders: Mediating Role of Shared Decision-Making. *Frontiers in psychiatry*, 12, 657224. <https://doi.org/10.3389/fpsy.2021.657224>