THE NATURE AND EXTENT OF GENETIC DISCRIMINATION AMONG PERSONS AT RISK FOR HUNTINGTON DISEASE

by

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Abstract

Huntington disease (HD), the "Dancing Mania" of the Middle Ages, has always been a particular target of social stigma and discrimination. With the discovery of a polymorphic DNA marker linked to HD in 1983, individuals at-risk for HD were able to learn whether or not they had inherited the causative HD mutation and possibly escape its stigma and discrimination. For those who had inherited the HD mutation increased discrimination became a real possibility.

Genetic discrimination (GD) refers to the differential treatment of asymptomatic individuals or their family based on genetic differences. It has been over twenty years since the introduction of predictive testing (PT) for HD, yet little is known about the nature and extent of GD and whether PT actually results in increased levels of GD. The objective of this dissertation was to use qualitative and quantitative methods to investigate the nature and extent of GD among persons at-risk for HD.

Qualitative findings provide insight into how individuals interpret, personalize and manage GD. Results from the national survey indicate that 40% of respondents reported at least one experience of GD. Reported experiences occurred most often in reference to life and disability insurance, and among family and friends. Surprisingly, there were few reports of GD in employment, health care and government settings. Experiences were not significantly associated with PT. However, the proportion of respondents who reported GD was 16% higher among persons who have the HD mutation than among those that do not and untested respondents. Interestingly, respondents' family history (FH), rather than their PT result, was the major reason given for their experiences as well as an important predictor of GD. Psychological distress was a health outcome of GD.

This is the first study to investigate the nature and extent of GD among an asymptomatic tested and untested population. This dissertation provides evidence that GD is a frequently reported experience and a source of distress for persons at-risk for HD. These findings provide insight for policy, identify areas where more education and support is needed, and provide direction to genetic professionals supporting their clients as they confront issues of GD.

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List of Abbreviations

CAG	cytosine-adenine-guanine nucleotide repeat
CI	confidence interval
DNA	deoxyribonucleic acid
ELSI	ethical, legal and social issues
FH	family history
GINA	genetic information non-discrimination act
GD	genetic discrimination
GTR	genetic test result
HD	Huntington disease
HD+	persons with CAG expansion
HD-	persons without CAG expansion
NT	not tested: persons that have chosen not to test for the CAG expansion
OR	odds ratio
PT	predictive testing
RNA	ribonucleic acid
SD	standard deviation
SDF	socio-demographic factors

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Co-authorship Statement

Chapter 3: The Nature of Genetic Discrimination

I conducted all of the interviews in this manuscript. I analyzed the data of all the interviews, developed the theory, generated the tables and figures and wrote the manuscript.

The initial concept for the study described in this and the following chapters was conceived by Michael Hayden and myself and was subsequently developed in collaboration with Elizabeth Penziner and Jane Paulsen. The interview guide was developed in collaboration with Elizabeth Penziner and Jane Paulsen. Oksana Suchowersky and Mark Guttman helped recruit the study sample. Joan Bottorff revised the interview guide. Michael Hayden and Joan Bottorff advised the data analysis and writing of this manuscript.

Chapter 4: The Strategies used to Manage Genetic Discrimination

The design of this chapter was conceived by me. I collected and analyzed all the data. I generated the tables and figures and wrote the manuscript.

The initial concept for the study described in this chapter was conceived by Michael Hayden and myself and was subsequently developed in collaboration with Elizabeth Penziner and Jane Paulsen. Joji Decolongon, Mary-Lou Klimek, Oksana Suchowersky and Mark Guttman helped recruit the study sample. Susan Creighton provided practical advice regarding the management of GD in the context of predictive testing for HD. Joan Bottorff revised the interview guide. Michael Hayden and Joan Bottorff advised the data analysis and writing of this manuscript.

Chapter 5: The Extent of Genetic Discrimination

I designed the study including the survey instruments and survey administration, described in this chapter with critical support of my supervisor, Michael Hayden. I adapted, pretest and piloted the survey instrument. I performed all of the data analysis, generated the tables and wrote the manuscript.

The initial concept for the study described in this chapter was conceived by Michael Hayden and myself and was subsequently developed in collaboration with Jane Paulsen. The members of the Canadian Respond-HD collaborative research group* include the seven clinical sites which helped collect the survey data. Lauren Currie coordinated the data collection and data entry and assisted with some of the analysis. Michael Hayden, Joan Bottorff, Gerry Veenstra, Jan

Friedman and Susan Creighton provided intellectual input on the survey instrument, provided methodological advice, and advised the writing of this manuscript.

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Chapter 1: Introduction

1.1. Statement of Problem

Although the inception of genetic testing for Huntington disease (HD) has led to much research and clinical care devoted to its risks and benefits, the ethical, legal, and social implications of knowing one's disease risk for HD are poorly understood. Genetic discrimination (GD), a potential risk of genetic testing, is the differential treatment of individuals or their family members based on genetic differences. It has been over 20 years since the global implementation of predictive testing for HD, yet considerable debate regarding the existence and prevalence of GD continues. Although anecdotal reports of GD exist, empirical data are needed to advance this debate and answer the fundamental ethical and social question: do persons at risk for HD experience genetic discrimination? If so, does having predictive testing lead to increased levels of discrimination against individuals found to have the HD mutation?

1.2. Background

1.2.1. Huntington Disease

1.2.1.1. Introduction

Huntington disease (HD) is a debilitating inherited neuropsychiatric disease which was first described in detail by George Huntington in his 1872 landmark paper entitled "On Chorea" (Huntington, 2003). The term chorea originates from *choros*, which means 'dance' in Greek, referring to its hallmark feature of rapid, involuntary dance-like movements. Huntington described individuals with HD as having "a dancing propensity." In fact this classic feature of HD subsequently led it to being branded as the "Dancing Mania" during the Middle Ages. In addition to chorea, individuals affected with HD suffer from mood and personality changes as well as cognitive impairment. HD symptoms usually become apparent between the ages of 35 and 45 and then gradually progress until death from pneumonia, malnutrition, and/or heart failure occur approximately 15 to 20 years after initial diagnosis (Harper, 1991; Hayden, 1981). Although clinical trials are now underway, no therapy is currently available to slow or prevent the disease.

1.2.1.2. Epidemiology

HD is a relatively rare disease with an overall prevalence of 1-10 per 100,000 (Hayden, 1981). Its prevalence varies across ethnic groups and regions largely because of founder effects. For example, immigrants carrying the mutant HD gene who settled over 100 years ago in Tasmania, Venezuela and Mauritius contributed to the high frequency of the disease presently seen in these areas (Hayden, 1981). Other countries such as Canada, Sweden, Scotland and England also have high frequencies of HD (Hayden, 1981). HD clusters mainly in

populations of European ancestry and is also noted to be relatively uncommon among Japanese, African and American black persons (Hayden, 1981; Squitieri et al., 1994).

1.2.1.3. CLINICAL FEATURES

The clinical features of HD include psychiatric, cognitive and movement disturbances. Its characteristics can be assessed using the Unified Huntington's Disease Rating Scale (UHDRS). The UHDRS assesses four features of HD: motor function, cognition, behaviour, and functional ability (Kieburtz et al., 1996). While persons affected with HD usually present with a combination of these features, the progression and severity vary from person to person and even, within the same family. Although the presence of specific motor signs is the current criterion for establishing a clinical diagnosis of HD, psychiatric and cognitive changes often precede the onset of motor dysfunction (Diamond et al., 1992; Duff et al., 2007; Foroud et al., 1995; Hahn-Barma et al., 1998; Jason et al., 1988; Johnson et al., 2007; Kirkwood et al., 1999; Langbehn and Paulsen, 2007; Marshall et al., 2007; Morris, 1991; Snowden et al., 2002; Solomon et al., 2007).

1.2.1.3.1. PSYCHIATRIC FEATURES

Psychiatric symptoms occur in 30-70% of persons with HD (Anderson and Marshall, 2005). Personality changes often occur early in the disease. Family members often describe these changes as seemingly exacerbating existing personality traits of the person or, at times, may even seem to reverse a person's character. For example, a previously irritable person may become more irritable or a previously even-tempered individual may become aggressive or hostile. Other psychiatric symptoms include irritability, aggression, depression, apathy, anxiety as well as obsessive thinking and compulsive behaviour (Anderson and Marshall, 2005; Burns et al., 1990; Paulsen et al., 2001). Delusions, paranoia, and psychosis have also been described (Mendez, 1994; Paulsen et al., 2001). There is no predictable time when these psychiatric changes begin (Anderson and Marshall, 2005; Morris, 1991), but they represent some of the most disturbing aspects of the disorder for caregivers, families and patients (Nordin et al., 1995).

1.2.1.3.2. COGNITIVE FEATURES

Psychiatric symptoms and cognitive decline are often linked as cognitive shortcomings evoking anxiety and irritability in preclinical patients. Because of the insidious nature of the disease, it is often difficult to distinguish early cognitive signs from everyday cognitive difficulties that people may exhibit as a result of being overworked, stressed or tired (e.g. forgetfulness, clumsiness or inability to concentrate). Visuo-spatial performance deficits may be some of the earliest cognitive changes in HD (Josiassen et al., 1983) and involve deficits in the ability to copy simple geometric or block designs and put together puzzles. The most prominent cognitive impairments involve executive functions, such as planning, organizing, sequencing, decision-

making and judgment (Paulsen and Conybeare, 2005). Learning and memory deficits are most frequently reported and include slowed rates of learning and impaired recall (Massman et al., 1990).

One of the most prominent features of latter stages of the disease is the motor speech impairment or dysarthia. Early speech impairments may include insufficient breath support and varying prosody which progress to reduced phrase length and increased pauses (Podoll et al., 1988). Unlike psychiatric symptoms, patients often are aware of their initial cognitive decline and become frustrated and depressed as they realize they are unable to perform at the level they were able to previously. This period is associated with increased withdrawal from clinical assessment (Paulsen and Conybeare, 2005) and suicide risk (Paulsen et al., 2005).

1.2.1.3.3. MOVEMENT FEATURES

The movement disorder of HD includes chorea, the classic involuntary jerky movements, changes in saccadic eye movements, inability to suppress reflexive glances to novel visual stimuli, impaired rapid alternating movements, balance problems and restlessness (Siemers et al., 1996). Some patients do not notice these movement symptoms, but family members often notice them and report that the patient is fidgety and unable to sit still or concentrate on tasks (Paulsen JS and Conybeare, 2005). Chorea typically worsens in the middle stages of the illness and then decreases as the person becomes more debilitated.

1.2.1.3.4. EARLY CHANGES PRECEDING HD ONSET

There is strong evidence for the ability to detect cognitive and behavioural changes before the formal diagnosis of HD in individuals with the CAG expansion (the mutation in the *HD* gene responsible for the disease – see the following section for an explanation) (Diamond et al., 1992; Duff et al., 2007; Foroud et al., 1995; Hahn-Barma et al., 1998; Jason et al., 1988; Johnson et al., 2007; Kirkwood et al., 1999; Langbehn and Paulsen, 2007; Marshall et al., 2007; Morris, 1991; Snowden et al., 2002; Solomon et al., 2007). Subtle motor signs, neurological deficits, psychiatric problems, neurophysiological alterations and brain changes often precede onset of motor symptoms.

Recent evidence has found motor timing variability increases in preclinical HD patients as estimated onset of motor symptoms approaches (Hinton et al., 2007). Further research indicates that verbal episodic memory declines in early pre-diagnostic HD patients and may decline as striatal volume decreases and individuals approach the motor diagnostic threshold (Solomon et al., 2007). Subtle, pre-clinical psychiatric symptoms, including depression, anxiety, or obsessive-compulsiveness, are also present in pre-diagnosed individuals carrying the CAG expansion (Duff et al., 2007).

With regards to neurophysiological changes, recognition of negative emotions, including anger, disgust, fear and sadness, have been found to decline among individuals with the CAG expansion early in the disease process, and poorer performance is associated with closer proximity to clinical diagnosis (Johnson et al., 2007). Moreover, altered morphology of cerebral cortex has been found in subjects with CAG expansion and no manifest disease. Specifically, enlarged gyral crowns and sulcal shapes suggest that abnormal neural development may be an additional component in the degenerative changes of HD (Nopoulos et al., 2007). Taken together, these findings suggest that pre-clinical motor signs and neuropsychological performance have prognostic importance in predicting diagnosis in HD and may assist with early therapeutic interventions.

1.2.1.4. GENETICS

1.2.1.4.1. INHERITANCE

HD is transmitted as an autosomal dominant trait (Hayden, 1981) affecting both sexes and conferring a 50% risk of transmission to every child of a person with HD. HD is caused by an abnormal expansion of trinucleotide repeats at the 5' of the *huntingtin* gene. The mutant expansion comprises an expansion of the cytosine-adenine-guanine (CAG) repeats in exon 1 of the *HD* gene (MacDonald et al., 1993).

Typical of autosomal dominant diseases, HD results in a gain of toxic function by the mutant protein produced by the HD gene. Mechanisms including excitotoxic effects of glutamatergic transmission, mitochondrial dysfunction, transcriptional dysregulation, enhanced apoptosis or cell death, deranged vesicular trafficking, disordered proteolysis, and inflammation have all been suggested as contributors underlying the neuronal dysfunction characteristic of HD (Hersch, 2003).

As an autosomal dominant disorder, HD was noted to conform to the classic definition of complete dominance (Wexler et al., 1987). That is, individuals with one (heterozygotes) or two (homozygotes) copies of the mutant allele present with similar severity of symptoms and should be phenotypically (i.e. physically) indistinguishable. However, more recent evidence indicates that homozygous individuals present with an increased rate of disease progression and a more severe clinical course (Squitieri et al., 2003). These findings point to a possible incomplete dominance mechanism, which suggests that the mechanisms underlying age at onset and progression in Huntington disease may differ.

1.2.1.4.2. CAG SIZE AND AGE OF ONSET

The *HD* gene is normally present in the human genome, since the gene is required for normal cell functioning. The difference, however, between a healthy person and one affected

with HD is the number of CAG repeats contained in the *HD* gene. Healthy individuals have between 9 and 26 CAG repeats, with most having 18 repeats on each allele. Individuals identified with the HD mutation have a CAG repeat length over 35 in one allele and are considered at 'increased risk' for developing HD in their lifetime, should they live long enough (Kremer et al., 1994). Some individuals with repeat lengths between 36-39 may never develop symptoms of HD in their lifetime, even if they live to an advanced age, as CAG expansions between 36-39 are in the affected range, but are not fully penetrant (Langbehn et al., 2004; Rubinsztein et al., 1996). CAG repeat lengths between 27-35 are referred to as intermediate alleles. Individuals with intermediate alleles are not at risk of developing symptoms of HD but may be at risk of having a child with an allele in the affected range. This occurs as a result of spontaneous expansions of the unstable CAG repeats of intermediate alleles during transmission to the next generation. The risk of CAG expansion of intermediate alleles has been observed in cases when the parent transmitting the allele is male (Goldberg et al., 1993).

There is a significant inverse relationship between CAG repeat length and age of onset of HD, with a larger CAG expansion associated with an earlier age of onset, given a person's current age and clinical presentation (Langbehn et al., 2004). For example, current parametric survival models predict that a 40 year-old individual with 41 CAG repeats has a 95% chance of disease onset by the age of 60, while a 40 year-old individual with 44 CAG repeats is almost certain to be affected by that age (Langbehn et al., 2004). However, caution must be exercised when predicting age of onset for a particular CAG repeat length, as the precision of the predictions is relatively low, with wide confidence limits. Predicting the age-range of disease onset in an individual based on CAG repeats is performed clinically. Furthermore, in addition to CAG length, other genetic and environmental factors are also likely to contribute to the variance in age of onset of HD (Rosenblatt et al., 2001).

Genetic anticipation, characteristic of autosomal dominant trinucleotide repeat disorders, occurs in HD. Due to faulty DNA replication and other unknown mechanisms, the CAG repeats can increase in number as the mutant allele is transmitted from generation to generation, particularly in the case of paternal inheritance. As a consequence, later generations tend to manifest the disease at a younger age.

1.2.2. Predictive Testing for Huntington disease

1.2.2.1. Introduction

The discovery of polymorphic DNA markers associated with HD (Gusella et al., 1983; Wasmuth et al., 1988) led to the first predictive test for an adult onset genetic disease in 1986,

allowing at-risk individuals to learn with near complete certainty whether or not they have inherited the HD expansion (Fox et al., 1989; Hayden et al., 1987; Hayden et al., 1988). Initially, predictive testing was offered by linkage analysis, where polymorphic markers known to be highly linked (or recombine infrequently) with HD were assessed using blood samples collected from family members from at least 3 generations (Hayden et al., 1988). This process required extensive participation among family members since consent and collection of blood samples from family members to establish segregation of genetic markers with the disease locus was necessary to perform the linkage analysis. This requirement often precluded some candidates from testing because not enough relatives were available or wished to cooperate, and some families were genetically uninformative (Simpson and Harding, 1993). In addition, there was also the remote possibility of error if the HD gene and markers recombined.

The discovery of a novel gene containing the CAG trinucleotide expansion that is expanded on HD chromosomes (MacDonald et al., 1993) heralded direct and highly accurate analysis of the CAG repeat, eliminating the necessity to request the participation and blood samples from relatives. While direct mutation analysis cleared the previous technical difficulties associated with linkage analysis, the psychosocial impact of learning this information remained largely unchanged.

Prior to the introduction of predictive testing, significant concerns were raised about whether it was ethical to offer predictive testing without the availability of a treatment to prevent or interrupt progression of the disease (Craufurd and Harris, 1986; Perry, 1981). There was apprehension that disclosure of results may precipitate depression, breakdown of family relationships or suicide (Farrer, 1986).

After substantial debate and consultation between scientists, families, and the lay groups that represent patients and families with HD worldwide, predictive testing guidelines for HD were established. These guidelines were developed in British Columbia (Benjamin et al., 1994) and subsequently implemented worldwide, and have served as a model for predictive testing for other genetic and non-genetic conditions (Evers-Kiebooms et al., 2000; Hayden, 2003).

1.2.2.2. Predictive Testing Programs for HD

The predictive testing protocols typically consists of a number of counseling sessions that deal with the risks and benefits of testing, psychosocial assessment of available support systems and the potential for genetic discrimination, particularly in the areas of insurance and employment (Broholm et al., 1994; Went, 1990). The guidelines ensure that test candidates are provided with up-to-date information regarding HD, the testing procedures and possible consequences, in order to make informed decisions and to ensure support of healthy adaptation to their changed status.

Predictive testing is provided in the context of a multidisciplinary health care team including, where possible, geneticists, genetic counselors, social workers, and psychologists. Eligibility criteria for predictive testing include: (1) a confirmed family history of HD and an *a priori* risk of 50% or 25%, (2) ability to provide informed consent, and (3) not having been given a clinical diagnosis of HD (Benjamin et al., 1994). Candidates are encouraged to bring support persons to provide ongoing emotional support during and after the testing process. The following outline provides a synopsis of the aims and topics covered during each of the sessions which was originally developed in British Columbia, Canada for linkage analysis (Bloch et al., 1989; Fox et al., 1989) and has been subsequently modified to reflect the provisions necessary for the direct test (Benjamin et al., 1994) (Figure 1.1). It should be also noted that this protocol continues to be used in Vancouver, Canada and may not necessarily reflect the protocol followed by other genetics clinics providing predictive testing for HD.

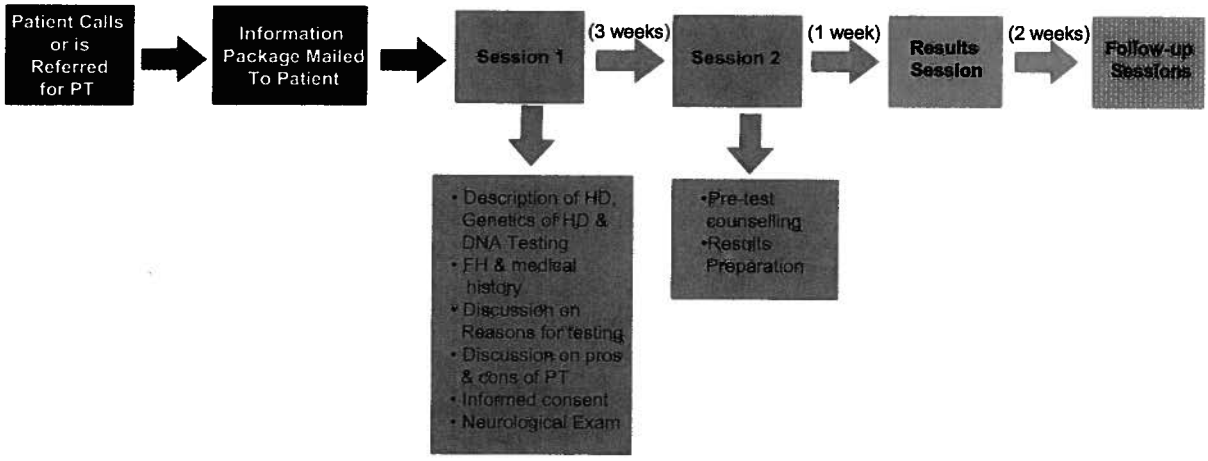

Figure 1.1 Summary of the predictive testing protocol for Huntington disease

(adapted, with permission, from Benjamin et al., 1994)

Session one provides candidates with information about the clinical description of HD, the genetics of HD, the direct analysis of CAG repeats and the benefits and possible harms of knowing one's mutation status (Benjamin et al., 1994). At this time, candidates' motives in pursuing testing and possible outcomes of the test are explored. Candidates are advised to secure desired levels of insurance before proceeding with testing and are made aware of possible implications of the results on future insurance assessments (Benjamin et al., 1994). The limitations of the test, available treatment options and current research are also discussed.

A medical and family history is taken documenting relevant affected relatives and known CAG sizes and current health statuses of siblings or other relatives. Particular emphasis is

placed on psychiatric episodes or history in the candidates, as adverse reactions to test results are more prevalent among persons with a psychiatric history (Almqvist et al., 1999). Candidates who raise concerns regarding psychological wellbeing before or after testing are referred for psychological counseling (Benjamin et al., 1994), and testing may be postponed (although this is a rare occurrence (Hayden, 2007)).

The candidates are told that they may withdraw from the testing process at any time. Once the candidates are fully informed of the predictive testing process, genetics of HD, and that risks and benefits of testing, the candidates are asked if they still wish to continue with testing and are asked to sign the consent form to have their blood drawn and proceed with the program.

A neurological exam, the final component of the first session, is performed to assess baseline levels of chorea and other early signs of HD. Prior to the exam the candidates are asked if they are aware or concerned about any signs or symptoms. Approximately 5-10% of people who enter predictive testing programs already manifest signs and symptoms of HD (Hayden and Bombard, 2005). The candidates are asked if they would like to learn the results of the exam before the results of the exam are disclosed. This aspect is an important element of the psychological process of adjusting to a possible HD status as some individuals are not prepared to learn if they are presently showing clinical signs of HD while for others disclosure of results is part of a gradual process of adjusting to receiving an eventual clinical diagnosis (Bloch et al., 1993). Careful assessment of these individuals and assessment of their psychological responses to this information have allowed the development of approaches suitable for the provision of the diagnosis of HD to affected persons. If early signs are present, the candidates are informed of them but it is stressed that soft signs may not necessarily be specific to HD, especially at an early stage. Before the session ends the candidates are asked if they would like a letter sent to their family physician so that they can be informed of the candidates' involvement in the predictive testing program. The decisions to learn of early neurological changes and inform family physicians further demonstrate the importance the predictive testing programs place on the personal autonomy of candidates.

For candidates who live significant distances from the genetics centre, a rural protocol is in place where the remainder of the sessions are conducted by the family physician or another health professional in the community (chosen by the candidate). The genetics clinic must send a letter along with adequate materials on providing counselling and support following disclosure of the results (Benjamin et al., 1994).

The candidates are notified that the results are not known to the genetics team until shortly before the results session in order to provide counselling in an unbiased way (Benjamin

et al., 1994) and so that the candidates do not attempt to infer the results from the counsellor's discussions during the next session(s). Moreover, previous experience indicates that 25% of individuals who enter the program choose not to learn the results (Quaid and Morris, 1993; Wiggins et al., 1992), thus the genetics team is not aware of the results until immediately before the candidates' results session.

The second session is intended to prepare candidates for the test results. Candidates' support persons or significant others are usually asked to attend these sessions in order to conduct the counselling jointly and assess levels of support. Discussions focus on what the candidates expect of the results and how they will be assimilated into their lives. Counselling also focuses on whom in the family and candidates' social circle is aware of their participation in the program and their plans for disclosure. Candidates are advised that it may be best not to specify the exact date they are receiving the results to these persons in order to circumvent any undesired/untimely involvement following the results. It is also recommended that candidates have a predetermined plan in place for the day they receive their results, regardless of the outcome of the test.

The candidates are asked again if they are still interested in proceeding with the test, given the lack of treatment to slow or stop progression of the disease (Benjamin et al., 1994). If the candidate is still interested in proceeding, a date is set up for the results session a short time later.

The third session is usually a brief meeting where the results are presented to the candidate in a clear, direct and unambiguous fashion (Benjamin et al., 1994). Despite efforts on behalf of the team and candidate, shock usually ensues, and the candidates may be given time alone with the support person to digest the information.

The fourth follow-up session occurs 2 weeks following the results for all persons and is designed to provide continuing support, contact or additional information (Benjamin et al., 1994). The timing of subsequent sessions is tailored to the results of the test as indicated by longitudinal psychological studies (Almqvist et al., 2003; Wiggins et al., 1992). Follow up for persons who were found to have the HD mutation occurs in person at intervals of 6 months to one year, while those who do not have the mutation are followed at similar intervals by phone or in person as needed. Ongoing contact at any time is always welcomed (Benjamin et al., 1994).

1.2.2.3. Uptake Rates of Predictive Testing

Although previous assessments of families at-risk for HD indicated that predictive testing was acceptable and should be made available (Craufurd et al., 1989; Decruyenaere et al., 1993; Evers-Kiebooms et al., 1987; Mastromauro et al., 1987; Meissen and Berchek, 1987), few individuals have requested this option as worldwide uptake currently ranges from 5% to 24%

(Creighton et al., 2003; Hayden, 1993). The geographical diversity of uptake rates both among and within countries is notable (Table 1.1). The lowest uptake rates are currently in Austria and Germany, where participation is approximately 3-4% (Laccone et al., 1999), while uptake in the Netherlands has been reported as high as 24% (Maat-Kievit et al., 2000). In Canada, uptake rates range from 12.5% in the Maritimes to 20.7% in British Columbia, with an overall average of 18% (Creighton et al., 2003). Issues of universal health care coverage, social programs and research activities may account for the differences in uptake among and within countries (Creighton et al., 2003).

Country	Testing Uptake	Reported Prevalence of HD	Reference
Canada	18%	8.4-23.3/100,000	(Shokeir, 1975)
United Kingdom	18%	7.5/100,000	(Harper et al., 2000)
the Netherlands	24%	6.5/100,000	(Maat-Kievit et al., 2000)
France	5%	5/100,000	(Goizet et al., 2002)
Worldwide study	5%	4/100,000	(The World Federation of Neurology Research Group on Huntington's Disease , 1993)
Germany, Austria, Switzerland	<3-4%	1-2.7/100,000	(Conneally, 1984; Laccone et al., 1999)

Table 1.1 Worldwide participation rates for predictive testing for HD

(adapted, with permission, from Creighton et al., 2003)

1.2.2.4. PSYCHOSOCIAL IMPACT OF PREDICTIVE TESTING FOR HD

Since the inception of the HD predictive testing program, much research and clinical care has been devoted to determining the risks and benefits as well as the psychosocial effects of predictive testing. The predominant reasons for requesting the predictive test have been to relieve uncertainty, inform reproductive decisions and plan for the future (Bloch et al., 1989). Reasons against testing often include the inability to cope with the results, lack of treatment, impact of the family and fear of genetic discrimination (Quaid and Morris, 1993). Studies indicate that persons with and without the HD mutation (HD+ & HD-, respectively) significantly differ in terms of short-term (7-10 days), but not long-term (6-12 months), psychological adjustment to test results (Almqvist et al., 2003; Decruyenaere et al., 2003; Timman et al., 2004; Wiggins et al., 1992).

Initially, it was expected that predictive testing promised most benefit to those found not to have inherited the HD mutation (Kessler et al., 1987; Mastromauro et al., 1987; Meissen and Berchek, 1987). Although, in general, the majority of people who have received an HD- result had improved psychological function, a significant proportion (10%) have also needed additional support due to significant difficulty coping with their results (Huggins et al., 1992). These individuals may be particularly vulnerable to adverse effects, which may be obvious if the test result contradicts the individual's consciously or unconsciously expected outcome or if s/he has made irreversible decisions based on the belief that s/he would develop HD in the future. These adverse reactions largely occur between 2-12 months after testing (Huggins et al., 1992).

Survivor's guilt and development of new self-identities have also been described among HD- persons following testing (Tibben et al., 1990; Williams et al., 2000a). As a consequence of these phenomena, HD- persons may exhibit over-caring behaviour toward their HD+ and affected relatives and may experience problems among their existing relationships. For some HD- persons, restructuring their life perspectives may prove to be difficult.

HD+ persons are considered to be at high risk for emotional difficulties in the short-term. The highest level of distress occurs immediately after receiving test results (Almqvist et al., 2003). Within the first year, however, this is followed in most instances by adjustment and return of distress and features of depression to baseline levels (Bloch et al., 1992). Numerous factors appear to facilitate adjustment to this information. The person's patterns of communication and mode of dealing with significant stress in the past are crucial variables in this process. A prior history of psychiatric disorder is also a risk factor for difficult adjustment to results of predictive testing (Bloch et al., 1992).

Overall, there have been few long-term psychological consequences for HD testing (Bundey, 1997). Psychological distress is significantly reduced for both HD+ and HD- persons following testing as compared to baseline levels prior to testing (Almqvist et al., 2003; Broadstock et al., 2000). Moreover, adverse events following testing are notably few. The frequency of clinically defined adverse events – namely clinical depression, psychiatric hospitalization, attempted suicide, a marked increase in alcohol consumption, planned suicide, or breakdown of a significant relationship with negative consequences - is 6.9% (14/202), and among these the most frequent adverse event is diagnosed clinical depression (Almqvist et al., 2003). Furthermore, few catastrophic events such as suicide, suicide attempt or psychiatric hospitalization occur following predictive testing for HD. The worldwide frequency of catastrophic events is 0.97% (44/4,527), a level similar to the general population (Almqvist et al., 1999). Lessons learned from long-term follow up studies point to the need to focus on test

candidates with low ego-strength and unspecified motivation for requesting testing, since these candidates exhibit most distress in the long-term (Decruyenaere et al., 2003).

Taken together, knowing the results of the predictive test reduces uncertainty and provides an opportunity for appropriate planning. The existence of few psychological consequences point to the success of the detailed pre-test counseling that clearly excludes many individuals with a greater likelihood of suffering an adverse event. Others argue that persons requesting predictive testing are a self-selected group, better equipped at handling 'bad' news and typically have high ego strength and have more resources (Bloch et al., 1989; Codori et al., 1994). It is also possible that pre-test expectations of receiving a positive test result may aid in mobilizing coping mechanisms such as denial (Tibben et al., 1993a). A person's social context often shapes that individual's perception of a test result. The perception of a test result as positive or negative is influenced by a person's family dynamics, as test results impact the family system as a whole (Kessler and Bloch, 1989; Williams et al., 2000b). A final explanation of why there have been few psychological consequences is that receiving predictive test results, although undoubtedly an emotional experience, eventually just becomes one of many other events that impact individuals during the course of their lives.

1.2.3. Genetic Discrimination

1.2.3.1. Introduction

Since the inception of predictive testing for HD, much research and clinical care has been devoted to its psychological consequences. The ethical, legal, and social implications of knowing one's disease risk for HD, however, are poorly understood. A particular risk identified from the inception of the program is genetic discrimination (GD).

GD refers to the differential treatment of individuals or their family members based on genetic differences, as opposed to different physical features. GD has the potential to generate economic and social consequences, often beyond the individual to include their family members.

While HD, the 'Dancing Mania of the Middle Ages' (Hayden, 1981), has always been a particular target of social stigma and discrimination, GD is not limited to HD. As history dictates, subtle influences of economic pressures along with health policies intended to improve the health of society can spiral quickly into eugenic practices across many diseases and populations. Today, with the increasing transparency of the human genome and reliance on employers and private insurance companies to access health care, threats of genetic abuse are ever more real. It stands to reason that third parties have a direct interest in genetic information

and there is potential for misuse of that information to discriminate against healthy individuals on the basis of genetic predisposition for a disease.

Indeed the fear of GD exists and is widespread (Apse et al., 2004; Hall et al., 2005). Fear of GD has prevented individuals from undergoing genetic testing (Apse et al., 2004; Peterson et al., 2002) and participating in genetic research (Hadley et al., 2003). These effects have significant public health implications, as GD directly hinders individuals' potentially beneficial engagement with genetic medicine and achievement of important scientific and medical advances. For example, many women at increased risk for breast cancer as well as persons at risk for HD do not undergo genetic testing in fear of its social implications for themselves and their families (Armstrong et al., 2003; Hall and Rich, 2000; Quaid and Morris, 1993). Furthermore, those who do volunteer for genetic research studies may be a self-selected group who may not represent the most generalizable findings.

1.2.3.2. Historical Perspectives

Concern about genetic discrimination has historical support. The dawn of the 20th century saw some of the most racist currents sweep through Western society. Against the backdrop of a perceived rise in social problems, such as unemployment, criminality, prostitution and alcoholism, anxiety developed among the North American middle class about an increasingly defective social system. With the rediscovery of Mendel's laws of inheritance and belief that such social issues are a consequence of defective genetic characteristics, came the birth of eugenics (Garver and Garver, 1991).

Eugenics, stemming from the Greek word, *eugenes*, literally meaning 'well-born', refers to the science intended to improve the human race by influencing hereditary factors (Garver and Garver, 1991). Negative eugenics and positive eugenics refer to the systematic efforts to minimize the transmission of deleterious genes and maximize the transmission of desirable genes, respectively (Garver and Garver, 1991).

The interest and promise of eugenics was supported by biologists and physicians who fuelled existent prejudicial views that immigrants from Southern and Eastern European, and of Asian or Jewish decent were responsible for the social problems as well as the eventual dilution of the 'Anglo-Saxon stock' (Garver and Garver, 1991). In Germany, the plight of racial hygiene in a post-World War I depression climate created the basis of their well-known negative eugenics programs. Systematically, this respective propaganda laid the groundwork for restrictive immigration laws as well as involuntary eugenic sterilization laws in the US, Canada and Germany. These laws mandated compulsory sterilization of institutionalized individuals who were 'feebleminded', criminals, orphans, 'mentally retarded', epileptic or generally 'diseased or degenerate' persons (Garver and Garver, 1991).

Germany took it one step further with euthanasia programs aimed, initially, at the annihilation of children born with birth defects, mental retardation and genetic disease. Soon after, these programs expanded to the mass murder of healthy children who were Jewish or of other undesirable races (Garver and Garver, 1991). By the 1940's their program developed into the widespread extermination of the Jews, Roma people, mental patients, and war prisoners.

HD did not escape these eugenic programs. In fact Charles Davenport, one of the early leaders of the eugenics movement and founder of the Eugenics Records Office in Cold Spring Harbor, New York, used HD as the prototype from which to justify restrictive immigration reforms. From surveys he conducted on the extent and origin of HD in New England, he concluded:

> All these evils in our study trace back to some half-dozen individuals including three brothers, who migrated to this country [from England] during the 17th century. Had these half-dozen individuals been kept out of this country much of misery might have been saved (Davenport and Muncey, 1916).

Given that the introduction of HD could not have been stopped, Davenport turned to the next best option: legislation to prevent its spread, as he indicated:

> It would be a work of far-seeing philanthropy to **sterilize all those in which chronic chorea** has already developed and to secure that such of their offspring as show prematurely its symptoms **shall not reproduce**. It is for the state to **investigate every case of Huntington's chorea** that appears and to concern itself with all the progeny of such. That is the least the state can do to fulfill its duty to the as yet unborn. **A state that knows who are its choreics and knows that half of the children of every one such will (on the average) become choreic and does not do the obvious thing to prevent the spread of this dire inheritable disease is impotent, stupid and blind and invites disaster.** We think of personal liberty and forget the rights and liberties of the unborn of whom that state is the sole protector. Unfortunate the nation when the state declines to fulfill this duty! (Davenport and Muncey, 1916).

Such ideas represented the undertones of the immigration policies of North America and were later echoed during the eugenic policies in Nazi Germany. With its psychiatric and hereditary nature, HD was an obvious candidate for inclusion in the compulsory sterilization laws in Germany (Harper, 1992).

Germany and North America were not the only countries where compulsory sterilizations took place, of HD at risk persons in particular. Spillane and Philips, U.K. scientists studying HD families in Wales, also supported the need for such legislation. As they indicated:

> Perhaps with the repeated advice and education, some would voluntarily abstain from marriage but the majority would no doubt be prepared to accept the even chance that nature offers them. We are thus left with the conclusion that only legislative measure will eventually succeed in eradicating the disease (Spillane and Phillips, 1937).

Approximately 3,000 affected HD patients were involuntarily sterilized beginning in 1933 (Harper, 1992). Genetic Health Courts were established in Germany and mandated to review and administer sterilizations and exterminations of psychiatric patients. These conditions were documented, along with the medical abuse used to justify these procedures, in the following account:

> The sterilization laws show how professional powers and state authority reinforced one another. Nine 'diseases' were selected: hereditary feeble-mindedness, Schizophrenia, manic-depression, hereditary epilepsy, **Huntington's chorea**, hereditary blindness, hereditary deafness, hereditary malformations, and (including the historical roots of the law) severe alcoholism. A system of hereditary courts was established; each tribunal was composed of a lawyer, a medical officer and a doctor with specialist training in racial hygiene. The medical officer could initiate proceedings as well as adjudicate, and doctors were in the majority. The state established primacy of reproduction, but left the operating of the controls to the medical profession (Weindling, 1989).

Details gleaned from extensive studies on HD and expert testimonies led to the identification (and quite possible extermination) of HD patients, asymptomatic relatives and children who were of reproductive age (Harper, 1992). For example, Panse, a neurologist who undertook a systematic survey and analysis of HD in Germany, acknowledged his role in identifying HD families to the Genetic Health Courts:

> We proceeded in a manner that we **reported all choreic cases**, and moreover all suspicious cases **and finally not yet choreic sibs and offspring as being at risk to the health authorities**.... 79 cases located and diagnosed by us were reported to the health administration. They have been passed on to the Genetic Health procedure, if they were of an age to procreate (Panse, 1942).

HD epitomized the prejudice towards a perceived existence of genetic perfection. Tensions ensue between the state and individuals when cost-effective or utilitarian health policies are used to trump individual rights and privacy. Lessons learned from the past, while illustrative of the potential abuses of genetics, may also be an important foreshadow. During Nazi Germany and the eugenic period of North America, presymptomatic persons could not be identified. Today they can. In today's climate of accurate, commercially-available genetic tests and the increasing dependence on private institutions for health care and access to social goods, the threat of eugenics and genetic discrimination may come in much more subtle forms of exclusion of social goods, such as insurance, employment and potentially also social rights such as education, adoption and health services. Without careful foresight and protections in place, individuals with HD and other disorders may again be subject to genetic abuse and discrimination. Lessons learned from the past must be kept in the foreground of discussions on the use of genetic information today, if only to remind us of the fine line between use and abuse.

1.2.3.3. Concept and Categories of Genetic Discrimination

One of the earliest expressions of concern about the potential for this type of discrimination was by Kenen and Schmidt who published a paper in 1978 warning of the dangers of stigmatisation of individuals genetically identified with the sickle cell trait. Subsequently, Paul Billings and colleagues in 1992 published some of the first case studies regarding negative treatment of people in the US allegedly because of their genetic characteristics. In this paper, Billings et al first used the now-familiar concept of "the asymptomatic ill" and warned of the potential emergence of a "genetic underclass" (Billings et al., 1992).

Genetic discrimination (GD) was first described by Billings et al (1992) as the differential treatment of individuals or their relatives due to actual or presumed genetic differences as opposed to discrimination based upon phenotype. Billings et al (1992) classified victims of GD under one of three categories. The asymptomatic ill is a category used to describe individuals who are healthy yet are found to have a hereditary disorder through genetic testing. Victims who fall under this category have early or adult onset disorders that have been properly managed, or are found to be heterozygote carriers or presymptomatic carriers (e.g. HD+ persons). Although they are clinically healthy, persons in this group are treated as if they are chronically ill by various societal institutions (Billings et al., 1992).

A second class comprises (a)symptomatic individuals who have a clinical diagnosis (e.g. Hemochromatosis) and are discriminated against because of an inaccurate or incomplete understanding of the clinical variability underlying many genetic disorders (i.e. penetrance, variable expressivity, and genetic heterogeneity). In these instances decisions were based primarily on a diagnostic label, assuming that the diagnosis equates to the most severe form of the disorder, without regard to the severity of the condition for each individual (Billings et al., 1992).

The final category is the at-risk group: individuals who are currently healthy but are at risk for a genetic disease and are undecided about whether to undergo testing. In this circumstance discrimination becomes a double edged sword: discrimination may ensue as a result of forgoing testing as well as testing and discovering they have the causative gene. Being at risk for HD was an example in this category, where Billings et al (1992) found that adoption agencies, for example, rejected families who were at 50% risk for HD. While these situations were the first to present this important ethical and social dilemma, a few highly publicized cases have since come to light.

1.2.3.4. EXAMPLES OF GENETIC DISCRIMINATION

Examples of genetic discrimination (GD) in the public domain are few. Cases that have been documented have been largely anecdotal or based on limited case reports. However, there have been a few high profile reports.

Some of the most prominent cases of GD arose in the early 1970s where many African Americans were denied insurance, jobs and educational opportunities because they were carriers of sickle cell anemia, even though they were quite healthy (Kenen and Schmidt, 1978; Rennie, 1994). Another well-publicized report involved the Burlington Northern Santa Fe Railway (BNSFR) which secretly tested its employees for a chromosomal deletion of a protein (peripheral myelin protein-22 on chromosome 17), which was thought to predispose to a syndrome similar to carpel tunnel syndrome (Schulte, 2004). The employees were never made aware of the purpose or motivation of the test and were concurrently seeking disability compensation as a result of carpal tunnel syndrome that occurred on the job. BNSFR intended to deny disability benefits to employees found to have the mutation associated with carpel tunnel syndrome, arguing that the mutation, not the job, was the cause (Gottlieb, 2001).

Another alleged report involved treatment of a symptomatic individual. Upon learning of her Alpha-1-antitrypsin deficiency, a woman underwent preventative replacement therapy, which was covered by her employer's health insurance. Shortly after beginning her treatment, she was fired from her work despite the fact that she was healthy and received excellent performance reviews (Miller, 1998).

In relation to HD there was the recent report of a healthy German teacher was denied a job because she had a family history of HD (Burgermeister, 2003). During routine medical examination that all applicants to the German civil service, including teachers, have to undergo, this teacher was refused a permanent position because of the perceived future risk of absenteeism and medical costs (Burgermeister, 2003). Under German law medical authorities can reject applications for civil service jobs on the basis of ill health. This teacher subsequently went to court to win the right to refuse to take predictive testing (Burgermeister, 2003).

These cases, although somewhat anecdotal, exposed an important ethical and social issue. However, the prevalence of genetic discrimination is unknown.

1.2.3.5. PREVALENCE OF GENETIC DISCRIMINATION

Attempts to document the extent of GD have been limited to cohorts of symptomatic individuals or third hand reports (Apse et al., 2004; Kass et al., 2007; Lapham et al., 1996; Low et al., 1998).

The first empirical study on GD from the perspectives of genetic support group members was reported by Lapham et al (1996) in which 332 members from a representative 101 disease groups were surveyed by telephone. They found that as a result of a genetic disorder (i.e. symptoms), 25% of respondents or affected family members believed they were refused life insurance; 22% believed they were refused health insurance; and 13% believed that they were denied or let go from a job (Lapham et al., 1996). While this was the first study to examine the extent of GD, the sample consisted of symptomatic individuals, third hand reports and was limited to insurance and employment settings.

Low et al (1998) compared experiences of GD between a sample of individuals with a genetic condition (genetic sample) and a representative sample of the general population and found that the genetic sample experienced significantly more GD (33.4% vs 5%, p=0.01) (Low et al., 1998). They also found that 13% of respondents who represent no adverse actuarial and genetic risk (non-carriers, carriers of autosomal recessive diseases) experienced problems with insurance that respondents believed to be a result of their family history. These results are significant since they show that those with genetic diseases in their families are at significantly higher risk for GD. Finally, their results point to the tendency of insurers to misinterpret and misuse genetic information in their actuarial assessments. Although Low et al (1998) assembled a representative sample, it consisted of symptomatic respondents. In fact they purposefully excluded surveys of unaffected carriers from their analysis. The question as to whether they were assessing GD as opposed to disability discrimination is an important limitation.

The work of Apse et al (2004) was the first study to report perceptions of GD among an asymptomatic sample. Among their sample of individuals at risk for colorectal cancer (CRC), 7% reported GD experiences in the way of premium increases, denial of life and health insurance, difficulty in obtaining coverage, and perceived inability to change jobs (Apse et al., 2004). However, upon further analysis, the reported experiences of GD were not related to CRC but to other genetic and non-genetic conditions. Important limitations of this study were that their findings included third hand reports which were ultimately unrelated to their risk for CRC and were restricted to the insurance setting.

Kass et al (2007) published the first study to compare GD experiences among genetic and non-genetic conditions, namely, cystic fibrosis, sickle cell disease, breast/ovarian cancer, colon cancer, diabetes and HIV/AIDS. A total of 27% of their sample reported 'being denied insurance or offered it at a prohibitive rate' (Kass et al., 2007). They also found that those with genetic conditions are 2-3 times more likely to report GD when obtaining insurance. It is unknown how representative their sample was because a response rate was not provided.

Furthermore, their sample consisted of "persons with chronic medical conditions", used third-hand reports and was also limited to the insurance setting.

In the context of HD specifically, a US case study analysis documented experiences of GD in 44% of a subset of HD respondents (Geller et al., 1996). In their survey of 27,790 individuals and children at risk for genetic disorders discovered 276 reports of GD among the 623 HD respondents (Geller et al., 1996). Of the 206 follow-up verification interviews conducted five cases concerned discrimination against individuals at-risk for HD. These reports included: life insurance rejection, coercion by a physician to undergo prenatal genetic testing and abort an affected fetus, two cases of adoption denials and a job refusal for the US Air Force (Geller et al., 1996).

Related discussion on GD in the HD literature involves GD being cited as an important reason for declining predictive testing despite the fact that test-related expenses were covered by some states for Americans (Quaid and Morris, 1993). Many persons at-risk for HD believed that the financial risk of potentially losing health insurance was too high to outweigh the benefits of learning of one's genetic status (Quaid and Morris, 1993). Moreover, health care professionals' concerns focused on the possibility that individuals would feel a fiduciary responsibility to disclose results to their employers. Professionals were concerned that individuals would also feel pressure to terminate affected pregnancies. Further they believed a potential exists for the misuse of genetic information to stigmatize those found to have the HD mutation (Craufurd and Harris, 1986; Harper, 1993).

1.2.3.6. Fear of Genetic Discrimination

There is substantial public apprehension concerning the uses of genetic information. A 2003 public opinion telephone survey found that a large majority of Canadians (1092/1200; 91%) reject the right of insurance companies to ask for genetic information, even if applicants are aware of a genetic condition (Government of Canada, 2003). This survey also revealed that 90% (1080/1200) of individuals opposed the notion that employers should have access to the GI of workers or job applicants (Government of Canada, 2003). In fact another survey found that 18% of surveyed Americans (18/100) did not reveal genetic information to insurers and another 17% (17/100) did not reveal any information to their employers (Lapham et al 1996) in fear of GD. These results imply a high level of distrust among Canadians and Americans with regard to their genetic privacy and use of their genetic information.

A large scale study of insurance concerns among a US and Canadian hemochromatosis population found that 40% of individuals in their 86,859 sample were concerned that genetic testing may lead to difficulty in obtaining or keeping 'insurance' (it was not stated which type of insurance) (Hall et al., 2005).

Health insurance discrimination is a major threat for women in seeking breast cancer risk assessment. Over half (48/78, 61.5%) of eligible U.S. women decline testing for the BRCA1/2 susceptibility gene for fear of health insurance discrimination (Peterson et al., 2002). Moreover, concern about health insurance discrimination was found to be inversely associated with the decision to undergo testing. Statistically speaking, approximately half of those who declined would be positive (Peterson et al., 2002) and, therefore, deny themselves possible psychological relief, preventative management and/or treatment opportunities due to fear of GD.

In the context of HD specifically, the threat of health insurance discrimination has impelled some at-risk Americans to seek predictive testing in Canada (Hayden, 2007). Still others, Canadian and American, have sought predictive testing under the auspices of anonymity in fear of insurance discrimination for themselves and their families (Burgess et al., 1997). These types of situation creates difficulties for clinicians and candidates seeking anonymous testing as the quality of patient care, such as appropriate counseling and follow up, is compromised in an anonymous provision.

A comparative case study analysis of U.S. genetic counselors and geneticists also revealed interesting insights into their perceptions of GD. Almost all (27/29, 92%) genetic counselors have found that adult patients seeking predictive testing approach genetic testing with some awareness and concern for health insurance discrimination (Hall and Rich, 2000). Although the majority of genetic counselors noted that they believed the actual incidence of discrimination to be very low, a significant majority (20/29, 67%) found patients to be very concerned about GD. According to these counselors, 38% (11/29) of adults requesting predictive testing eventually decline due to health insurance discrimination concerns (Hall and Rich, 2000). Interestingly, according to these counselors, individuals seeking predictive testing for HD demonstrate an acute knowledge and concern for genetic discrimination (Hall and Rich, 2000). In fact, it has been suggested that concern among these patients may come from their own experiences with affected family members.

1.2.3.7. THIRD PARTY PERSPECTIVES

1.2.3.7.1. INSURANCE

Insurance is a business contract which transfers the risk of a loss from an individual to a group of individuals who are sharing the loss on some equitable basis (Ostrer et al., 1993). Since insurance institutions provide a commercial product, not a social good, the question becomes one of access which can be understood only through a comprehensive analysis of the insurance system.

There are many types of insurance, all of which protect against a specific form of loss. Life insurance, for example, provides income security to beneficiaries in the event of the

insured's death (Knoppers and Joly, 2004). Disability insurance offers financial security when an accident or illness causes a disability, no longer allowing the insured to work. Critical illness insurance, on the other hand, provides a lump-sum payment in the event the insured becomes seriously ill with a specified illness. Finally, mortgage insurance protects a lender or investor against loss if the borrower is unable to repay the mortgage. Similarly, mortgage life insurance pays off the mortgage if the borrower dies.

Unlike Canada, where health insurance is covered by its universal health care system, private health care insurers are the major sponsors of health care services in the U.S. There are various types of health insurance carriers where the cost of insurance and eligibility depends on categories of insurance carriers. Commercial, generally for-profit companies provide benefits to individuals and groups and reimburse the insured directly for medical expenses (Jecker, 1993). Health care service contractors (HCSCs), such as Blue Cross- Blue Shield, hold exclusive contracts with a network of health care providers and reimburse a provider or hospital. Health Management Organizations (HMOs) typically undertake a contractual agreement which provides health services directly to the insured, with hospitals and physicians incorporated in the HMO.

By its very nature, insurance is discriminating. The process of medical underwriting, classifying risk, discriminates between applicants by pooling them into at-risk groups (Knoppers and Joly, 2004). Premiums, for life insurance as an example, are based upon the risk of dying in the near future and they are calculated using information such as sex, age, health status, lifestyle and medical history of the applicant and her family. If the insurer accepts the applicant's risks, the insured is then assigned to a group of insured people with similar risk factors and charged the appropriate premiums. In this way the 'discrimination' is as actuarially sound as possible – that is, based on rational, scientifically sound and empirically supported assessments (Anderlik and Rothstein, 2001).

Based on the principle of "utmost good faith," applicants have a legal obligation to disclose any relevant information at the time of application so that a contract can be entered into on an "equal information" basis (Canadian Life and Health Insurance Association, 2000). Thus, applicants are required to disclose family history and relevant test results. Companies often require a physician's statement of the applicant's current physical condition as well as all test results. Further, when individuals carrying a disease associated gene attempt to renew or upgrade policies, insurers may impose additional restrictions. Likewise, tests that predict the risk of having children with genetic diseases also could provide a basis for denying coverage for future dependents.

Within the insurance system there are various types of insurance. Individual insurance determines an individual's eligibility using medical underwriting, with each insurer prescribing its own range of acceptable risk factors. In contrast, group plans do not require individual applicants to complete a medical form. Group plans involve a contract between an employer and the insurer. Many group plans are based on the costs of previous claims from the group (Jecker 1993). Therefore, individuals with medical liabilities increase group costs and raise costs to their employers.

In essence, the premise of insurance is that the lucky subsidize the cost of loss for the unlucky. By reducing the uncertainty about individuals' future health status, genetic testing may weaken the principle of risk-spreading and mutuality of information upon which insurance is founded. Individuals who discover a decreased risk for a disease may be able to target their few areas of risk and purchase insurance accordingly, or they may drop out of the insurance market altogether. Conversely, individuals aware they are at a higher risk of early death from a genetic test purchase more life insurance at bargain prices. This is the basis underlying adverse selection, a phenomenon that the insurance industry has used to rationalize the use of genetic information for insurance underwriting.

Adverse selection refers to the asymmetrical process by which people make decisions based on information known to them but not revealed to the insurer. Over time, insurers will experience a higher overall rate of death, which will raise premiums for all buyers to cover the higher costs, which may then lead individuals at low risk to buy less life insurance and may even drive some with the lowest risk entirely out of the market and further increase the price of life insurance (Armstrong et al 2003) (Figure 1.2). This, insurers argue, will eventually lead to the collapse of the insurance market, since the original risk sharing model will shift to a risk pool made up of primarily those with high risk.

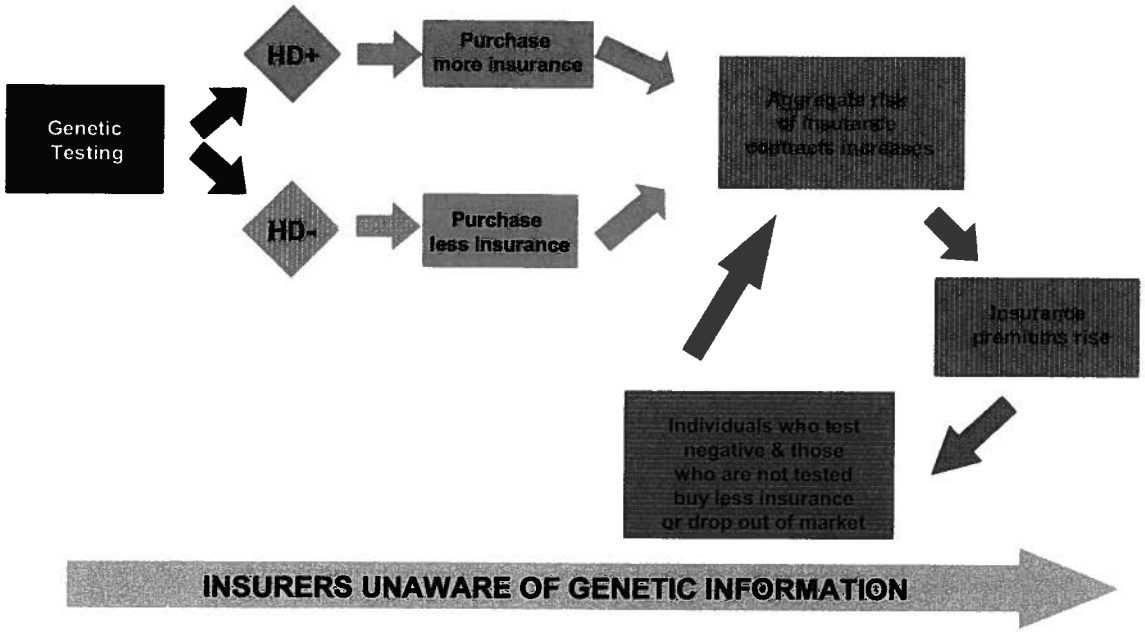

Figure 1.2 Schema representing the concept of adverse selection using HD as an example

(adapted, with permission, from Armstrong et al., 2003, of Wiley-Liss, Inc. a subsidiary of John Wiley & Sons, Inc)

The risk of adverse selection may be exaggerated since only a relatively small number of diseases are caused by single genes and ultimately large claims will affect adverse selections. Evidently women testing positive for the BRCA1 mutation do not capitalize on the information asymmetry by buying disproportionately large amounts of insurance (Zick et al., 2000). Furthermore, the predictive value of most genetic tests is currently limited, even in the case of HD with regards to low penetrant alleles (CAG range: 36-39). Still, a positive test result does not necessarily mean that a person will develop a disease. Likewise, there are many factors, environmental or social, that affect the susceptibility of disease manifestation. Further, a positive test result may motivate a person to take specific steps to significantly alter the likelihood of developing the disease. Then again, a negative test result may instill a false sense of security that may reduce precautionary measures that may lead to another disease or premature death. Moreover, as treatments become available for genetic diseases, the risk of being affected by a genetic disease will decline and fears of adverse selection should fade.

Ultimately the heart of the debate centres on the role of insurance in our society. If insurance remains considered a commercial contract, and not a social good that is of significant social importance and that should therefore be shared and accessible to all members of a given society, then current practice using GI to set premiums might be permissible as long as the information is scientifically and actuarially valid and confidentiality is respected. But, if insurance

is deemed essential and necessary (especially given the current climate requiring life insurance to access other social goods and thus full participation in social life) then insurance moves to the status of a societal right, based on concepts of social solidarity, and is subject to laws and conventions governing equal access and discrimination (Lemmens, 2000).

Insurance and employment are inherently linked, as the vast majority of individuals obtain their life or (extended) health insurance policies through their employers' (or spouses' employers') group plans. While concerns of GD relate to both insurance and employment, as illustrated below, the use of genetic information in employment presents its own issues.

1.2.3.7.2. EMPLOYMENT

In the employment landscape, workers fear that employers will use their confidential genetic information to their disadvantage. Presumably, employers may be able to lower their insurance and sick leave costs by weeding out individuals at increased risk for a medical condition.

Indeed a small proportion of employers admitted to pursuing this option. A 1989 survey of 400 employers affiliated with Northwest Life Insurance found that 15% of employers plan to check the genetic status of prospective employees and their dependents before making job offers (Geller et al., 1996). In fact 15% of 332 individuals at risk for a genetic condition had been asked questions about genetic diseases on a job application (Lapham et al., 1996). Unsurprisingly, the vast majority (87%) of those respondents declared that they would not want their employers to know if they were tested and found to be at high risk for a genetic disorder (Lapham et al., 1996). These feelings are echoed in the general population, as surveys found that 92% of 1,211 Americans sampled oppose allowing employers access to their genetic information (Hudson et al., 2004). Importantly, concern about employers' access to genetic information, is growing, since this figure is up from 85% in 2002 (Hudson et al., 2004).

Indeed individuals with medical liabilities increase group insurance costs and therefore raise costs to their employers. Thus, the costs of including high risk or ill individuals may prove prohibitive. Employers wishing to limit health care costs may exclude high risk individuals by refusing to hire them or promote them, by firing them, or by eliminating or reducing their insurance benefits. Further, when individuals carrying a disease associated gene attempt to renew or upgrade policies, employers may impose additional restrictions.

While employers are legally restricted from making pre-employment medical inquiries, there are limited legal restrictions (in the US and Canada) prohibiting employers from requesting medical information, including genetic information, after a conditional offer of employment by way of pre-placement medical exams, which may include physical exams and blood tests as well as a general medical release of an individual's medical records (Rothenberg et al., 1997).

Further, an employer may request annual medical exams from which recent genetic test information may be gleaned.

It is important, however, to distinguish between the use of genetic information to screen potential or current employees for the purposes of reducing human resource costs and maximizing profits from genetic monitoring. Genetic monitoring involves periodic testing of employees to identify potential effects of long-term exposure to workplace toxins (Office of Technology Assessment, 1990). Thus employers would use such information to protect or accommodate occupational health and safety of their employees with known conditions or risks affected by particular work environments. It is also possible that employers could use this information to their employees' detriment to deny jobs or worker's compensation claims, or to shirk their responsibility to adhere to safe and healthy workplace standards by selecting employees free of genetic susceptibilities to environmental hazards (Schulte, 2004).

The use of genetic information in the workplace presents societal risks that may have significant impact on employment possibilities, health insurance, health management and privacy. Being intertwined as they are, employment and insurance settings are the biggest threats for GD. Thus, policy-makers need to develop legislation or regulatory policy to address these concerns.

1.2.3.8. Ethical, Legal and Policy Considerations

1.2.3.8.1. Ethical Issues

Beauchamp and Childress's (2001) classic principles of bioethics - autonomy, justice and beneficence – may be used to demonstrate that genetic discrimination is morally unacceptable and unethical (Beauchamp and Childress, 2001).

Respect for autonomy entitles people to be fully informed and free agents, and to be respected in and of themselves. More generally, it refers to the right to independence or self-determination and privacy (Beauchamp and Childress, 2001). Privacy encompasses many different rights, including the right to limit access to a person, the right to be left alone and the right to confidentiality (Rothstein and Anderlik, 2001). GD infringes on autonomy, privacy and in turn confidentiality when a third party requests an individual to take a genetic test as a condition to receive goods such as a job or insurance. If that person would have otherwise chosen not to know that information, they lose the freedom to remain ignorant of their genetic risk, and they lose control over access to their bodies as well as their genetic information, which in turn may be disseminated beyond their control (Rothstein and Anderlik, 2001). Hence, when knowledge is forced upon a person, choice and the ability to be an autonomous agent are removed.

It may be argued that harm is inflicted to that person if they did not want to learn of the information or were otherwise not prepared for it, potentially producing psychological, emotional

or familial harms. Furthermore, it can not be assumed that it is always better to know a genetic risk, given the variability in treatment or management options and, especially, when little may be done where an incurable genetic disease is concerned. Moreover, knowing about one's genetic makeup can cause an uneven playing field for other members in the family, which may lead to altered family dynamics. A related dilemma occurs when the informed individual discloses genetic information to an uninformed relative that results in the infringement of a family member's personal autonomy. By learning of one's genetic information and disclosing this information to other family members, the informed person impinges on his or her family members' ability to be autonomous agents, should they have preferred to remain in ignorance.

The principle of justice requires that 'like cases be treated alike' (Beauchamp and Childress, 2001). This principle is the core ethical principle enshrined in the United Nations Educational, Scientific and Cultural Organization's (UNESCO) 1997 Universal Declaration on the Human Genome and Human Rights which states in Article 6:

> no one shall be subjected to discrimination based on genetic characteristics that is intended to infringe or has the effect of infringing on human rights, fundamental freedoms and human dignity (UNESCO, 1997).

Many other national constitutions and declarations of human rights worldwide have similarly acknowledged that "each individual is entitled to lead a life in which genetic characteristics are not the basis for unjust discrimination" (Council of Europe, 1997; Human Genetics Commission, 2002).

A related principle, genetic equity, posits that since humans are born equal, they are entitled to freedom from discrimination and equality of opportunity to flourish, and genetic information, like race, gender or otherwise, should not be used to limit that equality (Harris and Sulston, 2004).

The principle of justice may be directly applied to actuarial fairness in insurance assessments. It is important, however, to distinguish between rational and irrational discrimination. In insurance, irrational discrimination results from decision making on the basis of faulty or incomplete data, or from misunderstandings of genetic science or of the implications of genetic test results for morbidity and mortality (Anderlik and Rothstein 2001). Unfortunately, there is no way to monitor irrational discriminatory acts, even though there are laws that prohibit the unjustified use of unsound actuarial data for risk calculations in many countries, including Canada (Canadian Life and Health Insurance Association, 2000).

Rational insurance discrimination refers to scientifically sound and empirically supported use of genetic information for assessments. Thus it is permitted to base risk calculations on such characteristics as age, individual and family history, health status, occupation, serum

cholesterol, and alcohol and tobacco use (Rothstein and Anderlik, 2001). Ironically, more information available to insurers is better since the more precise the discriminations, the greater the actuarial fairness of the system. Essentially, discrimination on the basis of genetic characteristics is rational unless it can be demonstrated that it is not unfair. Thus the burden of proof is on those who discriminate to prove the fairness in doing so (Harris and Sulston, 2004).

GD in reference to the principle of beneficence, the duty to do good (i.e. charity, kind acts or otherwise virtuous behaviours), requires consideration of the consequences of general social practices. The consequences of allowing insurers and employers to use genetic information in their assessments propagates the existent climate of fear which has impelled individuals to avoid testing (Apse et al., 2004; Hall et al., 2005) and not take advantage of possible interventions which could lead lower morbidity and mortality associated with genetic conditions (Rothstein and Anderlik, 2001). From the Utilitarian perspective, which promotes the greatest good for the greatest number, fear of GD limits individuals' participation in research (Hadley et al., 2003) which may have significant impact on the achievements of medical advancements, impacting society as a whole.

GD expresses an underlying notion of genetic determinism, in which genes fully determine our fate (Hellman, 2003). Moreover, the practices of making employment and insurance decisions on the basis of genetic traits, therefore, convey the notion that some individuals are intrinsically flawed and by extension, are less suitable (Hellman, 2003). Both of these notions are morally troubling as this view implies a limited contribution of person identity, individuality, free will, equality, and the ability to control one's destiny.

Genetic discrimination, albeit in the subtlest forms, seems highly reminiscent of the eugenic crusade towards genetic perfection. Although these genetic determinist ideals are becoming increasingly untenable now that research is revealing complex interactions among genes and environment in the development of human traits (even in the pathology of HD (Rosenblatt et al., 2001; van Dellen et al., 2005)), promoting legislation against genetic discrimination would express change in our current practices as well as what is morally permissible.

1.2.3.8.2. LEGAL CONTEXT

A specific federal law does not exist in Canada which prohibits GD. The *Canadian Charter of Rights and Freedoms* and *Human Rights Act* prohibit discrimination on the basis of race, national or ethnic origin, colour, religion, sex, age or mental or physical disability (Government of Canada: Canadian Heritage, 2007). Provincial human rights codes also exist that protect against discrimination in employment on the grounds of sex, race, color, ethnicity,

marital status and disability (Ontario human rights commission, 1999). Clearly, genetic information (GI) is not included.

More recently, the Supreme Court of Canada has found that the term "handicap" in the Quebec *Charter of Human Rights and Freedoms* includes the perception of a handicap and the actual or perceived possibility that an individual may develop a handicap in the future (Quebec v.Boisbriand, 2000). In fact this interpretation now applies to the definition of "disability" in most provincial human rights codes. Ontario, for example, adopts a 'socio-political dimension' of disability where "disability must be interpreted to include its subjective component, since discrimination may be based as much on perceptions, myths and stereotypes, as on the existence of actual functional limitations" (Ontario human rights commission, 1999). This allows some measure of protection for genetic predisposition as well as the perceived predisposition in the employment environment (although one would likely be subject to increased scrutiny) but the protection offered by human rights codes in the insurance context is far more difficult to discern.

Insurers are bound by privacy laws which protect the personal information of individuals but differ in scope. The Privacy Act protects federal government employees' personal information. In the private sector, the Personal Information Protection and Electronic Documents Act (PIPEDA) regulates how private organizations may collect, use or disclose personal information of customers or employees during federal and provincial commercial transactions (Privacy Commissioner of Canada, 2003). It is important to note that neither acts' definitions of personal information make specific mention of genetic information, genetic testing or genetic service.

Most provinces have established laws that overlap substantially with PIPEDA. Currently Quebec is the only province that has privacy legislation for both private and public institutions, which includes genetic information; however, insurance companies are not prohibited from collecting and using medical information with the appropriate informed consent.

In summary, the Privacy Act regulates the collection, use and disclosure of personal information held only by *federal* government agencies. PIPEDA extends protection to personal information used in *commercial activity* related to *federal works, undertakings or businesses.* Moreover, while the definition of personal health information likely includes genetic information and the current interpretation of what constitutes disability has been expanded, it remains to be seen if current protection and case law is sufficient or whether specific protection for GI is warranted.

The legal landscape surrounding GD in the U.S. is quite different. Americans are covered by three federal discrimination laws. First, the Rehabilitation Act prohibits employment

discrimination on the basis of handicap by federal agencies. Aside from being restricted to federal agencies, this Act does not apply to persons with a genetic predisposition.

Second, the Americans with Disabilities Act (ADA) prohibits an employer from discriminating against an individual because of a protected disability. Although the ADA extends to both private and public agencies, the ADA applies only to persons who are symptomatic and does not cover insurance underwriting policies (Natowicz et al., 1992).

Finally, the Health Insurance Portability and Accountability Act of 1996 (HIPAA) provides some protection against GD in the U.S., such as prohibiting the use of genetic information in denying or limiting health insurance coverage for members of a group plan (Rothenberg et al., 1997). It also maintains that genetic information should not be regarded as a preexisting condition in the absence of a formal diagnosis (Rothenberg et al., 1997). Further, it bans group health plans from disclosing health information to employers, and requires consent for any other disclosures. However, the law does not provide protection for persons seeking insurance in the individual market, nor does it provide privacy protection. HIPAA also does not prohibit rating based on genetic information or prevent health insurers from disclosing or demanding access to genetic information. Moreover, it does not prohibit employers who may request that employees take genetic tests and disclose that information (Shinaman et al., 2003).

There are 36 states in the U.S. that have enacted laws regulating use and access of genetic information in health insurance and 32 states that prohibit employment discrimination based on genetic information (National Conference of State Legislatures, 2007). State laws are not uniform and only afford individuals limited rights against discrimination. Therefore, the major problem with the majority of the individual state legislation is that the state laws are narrow in scope and have limited penalties for violation. This leaves many loopholes and a patchwork of safeguards.

Recent U.S. initiatives have seen the introduction of the federal Bill entitled Genetic Information Nondiscrimination Act (GINA) to address the spotty nature of the current state laws. GINA aims to prohibit the use of GI in health insurance and employment decisions at a national level. Specifically, GINA will prohibit group and individual health insurers from using a person's GI in determining eligibility and setting premiums as well as requesting or requiring potential applicants undergo genetic testing. Furthermore GINA would bar employers from using genetic test results in their hiring, firing, job placement, or promotion decisions (Hudson, 2007). The bill defines GI as information about the genetic tests of an individual or family member, or the occurrence of a disease or disorder in family members of an individual. A genetic test refers to the analysis of human DNA, RNA, chromosomes, proteins, or metabolites that detects genotypes, mutations, or chromosomal changes (Bettinger, 2007). While the bill outlines that

civil action may be pursued in response to a violation of the prohibitions outlined, the exact penalties are not stated.

On January 16, 2007 the Genetic Information Nondiscrimination Act of 2007 was introduced by Hon. Louise M. Slaughter as House resolution H.R. 493. Following a series of referrals and reports, GINA has passed in the U.S. House of Representatives, by a vote of 420-3 on April 25, 2007 (National Human Genome Research Institute, 2007). As of the writing of this dissertation, GINA is currently awaiting the Senate's review.

Given the uncertainties and gaps in state and federal protection in the US and the complete lack of legal safeguards in Canada, comprehensive federal legislation to establish minimum protections is needed to ensure that advances in genetic technology and research may be realized with minimal social discrimination.

1.2.3.8.3. POLICY CONSIDERATIONS

Many bills have been developed in the US, yet few have been successful. The reason underlying this obstacle in the development of comprehensive legislation is that a clear distinction between genetic and non-genetic information is difficult to achieve. Various laws have defined genetic information differently. Genetic information can be restricted to information about the actual genetic material itself, such as DNA or RNA, or proteins. In some laws the definition of genetic information extends to include family history. To complicate matters further, some have argued that most medical tests are ordered in an effort to detect conditions or potential conditions that have an underlying genetic contribution (Lemmens, 2000).

Another ambiguity underlies multifactorial diseases where genetic and non-genetic tests may be performed to detect a susceptibility to disease. Consider a situation where an asymptomatic individual is identified with a genetic susceptibility to colon cancer via a genetic test. That individual would be theoretically protected by a genetic anti-discrimination law. However, another individual may have a non-genetic test that identifies a precancerous condition that may at some point in time lead to cancer. Both these individuals may be at risk for developing the same disease, yet the second individual would not be protected by the same law by virtue of the fact that her test was non-genetic (Beckwith and Alper, 1998). Thus, current laws are flawed because they are either too broad or too narrow in their definition of GI (Lemmens, 2000).

Another problem that afflicts policy making is the inherent overlap between genetic and other health information, thus making it not feasible to separate genetic information from other health information in a person's medical file. Given that family history information and other related information is often combined in a person's medical file, attempts at separating genetic from other medical information in patient records would be burdensome, impractical and may in

fact compromise the quality of patient care (Rothstein and Anderlik, 2001). Ultimately it may be difficult to classify diseases and risk factors into genetic and non-genetic categories as many diseases comprise both categories or will not neatly fit into one category or the other (Murray, 1997).

The final complication considers the consequences of bestowing genetic information special safeguards. Is genetic information inherently special, or deserving of special treatment? Some argue that special treatment increases the perceived stigma attached to genetic diseases, since singling out genetic information may indicate that genetic diseases may indeed be particularly shameful (Rothstein and Anderlik, 2001). Information held in a person's medical file, such as demographics, financial, social and behavioural data may provide many personal details. However, proponents of bestowing genetic information special treatment argue that genetic information is more sensitive than other medical information. Genetic information is also regarded as unique because of its predictive nature and social, psychological and economic implications. Moreover, there is a greater chance of misinterpretation given the advanced technology and variability in the validity of genetic tests. Finally, and most importantly, genetic information is highly identifiable and reveals information about family members, and thus has wide impact beyond just the individual (Hodge, Jr., 2004).

Legislative prohibition is often regarded as the most radical and inflexible approach. A popular alternative is the adoption of a wait and see approach or moratorium. A moratorium is a temporary and voluntary agreement on behalf of the insurers (frequently achieved with the support of the government) to abstain from asking and using genetic tests in their premium assessments. Moratoria are attractive to insurers since they are flexible, temporary arrangements which may be tailored as appropriate. Moratoria are an ideal measure in response to public pressure to technological developments where governments or regulators are unsure about a suitable regulatory structure (Lemmens et al., 2004) and allow time for research to take place or allow the insurance industry to formulate an alternative policy strategy. A limitation of such an approach is the voluntary nature of the arrangement which relies on the goodwill of those involved (Lemmens et al., 2004).

Moratoria range in scope from partial to unlimited. Under partial moratoria, insurers would not request that an applicant undergo testing, but may request the results of previous tests (Lemmens et al., 2004). Under limited amount moratoria, insurers would not ask an applicant to undergo genetic testing or request previous test results for policies under a certain dollar amount. Beyond this 'threshold or ceiling', insurers would be permitted to request and use the genetic testing in their premium assessments. Such a system exists in the U.K. where insurers do not request or use genetic information for life insurance policies below £500,000 and

disability insurance or critical illness insurance policies below £300,000 (Secretary of State for Health, 2003). Companies are permitted to use the results of genetic tests that have been approved by the Human Genetics Committee in the U.K., an advisory body designed to review the actuarial and scientific validity of genetic test information. To date, the genetic test for HD is the only test currently approved (Secretary of State for Health, 2003). On the other end of the spectrum, an unlimited amount moratorium would envisage a situation where insurers would never ask potential applications to undergo testing or use results from previous tests (Lemmens et al., 2004). Limited or partial moratoria are currently in effect in the U.K., Canada, Greece, New Zealand, South Africa, Switzerland and Turkey. Moratoria have recently expired in the following countries: Australia, Finland, France, Germany, Ireland and Sweden (Lemmens et al., 2004). (Table 1.2)

Country	Existence/ Type of Moratorium	Legislation
Austria	X	√
Australia	Partial	X
Belgium	X	√
Bulgaria	X	X
Canada	Partial	X
Chile	X	X
Cyprus	X	X
Czech Republic	X	X
Croatia	X	X
Denmark	X	√
Estonia	X	√
Finland	X	√
France	√	√
Germany	√	X
Georgia	X	√
Greece	Partial	X
Hungary	X	X
Iceland	X	X
India	X	X
Ireland	Limited	X
Israel	X	√
Italy	X	X
Japan	X	X
Lithuania	X	X
Luxemberg	X	√
Moldova	X	X
Netherlands	X	√
New Zealand	Partial	X
Norway	X	√
Portugal	X	X
Romania	X	X
San Marino	X	X
Singapore	X	X
Slovakia	X	√
Slovenia	X	X
South Africa	Partial	X
South Korea	X	X
Spain	X	X
Sweden	Limited	√
Switzerland	√	√
Taiwan	X	X
Turkey	√	X
United Kingdom	Limited	x
United States	x	x

Table 1.2 Regulatory structures concerning GD across developed countries

(Adapted, with permission, from Lemmens et al., 2004) (Legend: √: existent and X: non-existent regulatory structures)

Some countries have established a system of regulatory review of the use of genetic tests. In such a system the government appoints an expert panel which reviews the actuarial reliability, validity and social impact of using certain genetic tests proposed by insurers to set premiums (Lemmens et al., 2004). Such is the case in the U.K. in concordance with their recently extended moratoria, where the only test approved for use is the HD predictive test (Secretary of State for Health, 2003). Ontario has supported such a system in their recent recommendations (Lemmens et al., 2004).

1.2.3.9. Conclusion

Clearly, developing policies to address the concerns and experiences of GD is complex. The definition of genetic information, what constitutes GD and what the public perceptions and fears all need to be understood in order to inform policy development and address this issue comprehensively. While HD has served as a model for the development of predictive testing guidelines and a leader on research and clinical care of the psychological consequences of testing, the social consequences, however, have received little attention. Given the lack of empirical research on GD in general, and with respect to HD in particular, this dissertation studied the nature and extent of GD in order to answer these fundamental ethical and social questions towards the ultimate goal of protecting individuals from unfair discrimination over things of which they have no control.

1.2.4. Gaps in Existing Research

While extant literature is replete with theoretical discourse and anecdotal evidence regarding GD, the perspectives of those at-risk or who have experienced GD – the targets of discrimination - have been excluded. A description of the concerns and experiences of those facing these issues has surprisingly been overlooked. Moreover, the insurance and employment settings have received a disproportionate amount of attention with regards to GD. Understandably these settings are the focus of existing discourse on GD since they may be more tangible to determine. Yet the relationships among family members and friends following testing or knowledge of genetic risk are of equal, if not of more importance, especially in the field of genetics, and have been neglected thus far. In addition to the narrow lens previously applied to explore the nature of GD, there is also a paucity of evidence on the extent of the problem; it is not yet known what the prevalence of GD is among an asymptomatic (tested and untested)

genetic population. Furthermore, from a clinical perspective, an understanding of the predictors and health outcomes of GD have also been ignored. Only with a full appreciation of the issue from its precursors, nature, extent to outcomes can we begin to address ways of protecting our genetic inheritance from unjust discrimination.

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Chapter 2: Overview of Research Project

[1]A version of this chapter will be submitted for publication as:

Yvonne Bombard, Gerry Veenstra, Joan L. Bottorff and Michael R. Hayden. On stigma: new insights from an empirical study on genetic discrimination among persons at risk for Huntington disease.

2.1 Theoretical Perspective

The theoretical framework informing this research study is based upon Goffman's Stigma Theory (1963). Scholars define stigma as a distinguishing attribute that discredits or devalues a stigmatized person's identity within a particular context (Crocker et al., 1998; Goffman, 1963; Jones et al., 1987). Stigma results in labeling, negative stereotyping, exclusion, discrimination and low status in the context of a power situation (Link and Phelan, 2001). Stigma is a broad concept under which prejudice and discrimination are inextricably linked: stigma permeates many stereotypes, which are collectively held beliefs about members of a social group. Prejudice is the endorsement of negative stereotypes, and discrimination is the behavioural response based on prejudice (Arboleda-Florez, 2003).

Goffman distinguishes three types: tribal identities, abominations of the body, and blemishes of individual character (Goffman, 1963). Tribal identities refer to the social situation into which one is born. This may include: religious, ethnic, racial or national groups. Abominations of the body represent physical ailments, such as: deformities, illnesses, and paralysis. Goffman uses blemishes of individual character, such as drug addictions, to describe moral transgressions of weakness of will. Furthermore, Goffman characterizes various dimensions in his definition of stigma. Such dimensions include: concealibility, stability, disruptiveness and the extent to which a stigma is physically unappealing to others (Goffman, 1963).

Stigmatizing 'marks' or diseases are further distinguished by their visibility and obtrusiveness. Goffman describes those with disorders that are stigmatizing and that can not be hidden or disguised as discredited, while describing those with the conditions that allow people to "pass as normal" as discreditable. Whereas the discredited may deal with problems of "impression management", the discreditable may face difficulties of "information management" (Goffman, 1963).

An interesting distinction is drawn by Scambler and Hopkins in their Hidden-Distress model, which distinguishes between enacted and felt stigma. Enacted stigma refers to actual discrimination, whereas felt stigma refers to the fear of such discrimination (Scambler and Hopkins, 1986). Their model, as applied to epileptic adults, asserts that on diagnosis, adults experience felt stigma before exposure to enacted stigma. Furthermore, as a result of felt stigma, people adopt strategies of non-disclosure and concealment of their symptoms (i.e. seizures) and their diagnostic label. Their model claims that cases of enacted stigma are relatively few, and as a function of successful

concealment, felt stigma typically proves more disruptive than enacted stigma (Scambler and Hopkins, 1986).

Stigma is a powerful social phenomenon with widespread effects on its targets. Stigma leads to potential prejudice and discrimination across a broad range of social contexts. Stigmatized individuals are discriminated against in the housing market, workplace, educational settings, health care, and the criminal justice system (Major and O'Brien, 2005; Sidanius J and Pratto F, 1999). Discrimination directly affects the social status, psychological well-being, and physical health of the stigmatized (Allison K.W., 1998). Stigma can be a source of stress for stigmatized individuals that poses some unique demands on the individual (Miller and Major, 2000). To cope with these stressors individuals rely on physiological, cognitive, emotional and behavioural resources.

In applying this conceptual framework to the proposed study, persons at risk for HD can be considered to possess a form of tribal identity, as the nature of their genetic status is a matter of inheritance. They are also discreditable because they are not displaying overt symptoms of HD and, therefore, face issues of information management and likely use various cognitive, emotional and behaviour strategies to manage GD. It is the intent of this study to ascertain whether and to what extent these individuals suffer from felt or enacted stigma and to determine how they cope with or manage GD.

2.2 Hypothesis and Objectives

The availability of predictive testing for HD by linkage analysis in 1986 heralded the first predictive test for an adult-onset disorder. Subsequent to this a direct test predicting onset of HD was made available in 1993. By determining the number of CAG repeats in the HD gene, this test can "predict" whether an individual will develop HD in her lifetime. Genetic testing has allowed at-risk individuals to relieve their uncertainties and plan for the future; however, there are many unexplored issues surrounding the implications of this process.

A longstanding question since the inception of HD predictive testing is: does participating in predictive testing lead to increased levels of discrimination against persons who are found to have the HD mutation? Moreover, on a fundamental level, does GD exist in persons at risk for HD and, if so, to what extent and in which situations? A full characterization of the prevalence of GD and the situations in which people encounter discrimination are required to obtain full appreciation of the social impact of learning of one's genetic status for HD.

Given the anecdotal evidence of the existence of GD in other populations and countries, it is hypothesized that:

1. GD is experienced by persons at risk for HD in Canada.
2. Persons at-risk for HD who participate in predictive testing report more discriminatory experiences compared to those who choose not to participate in predictive testing.
3. HD mutation carriers encounter more discrimination compared to HD non-carriers or individuals who chose not to undergo testing.

Accordingly, the overall purpose of this study is to investigate the nature and extent of GD. The specific research objectives were:

1. To describe the nature of experiences, concerns and strategies for GD from the perspective of the HD community.
2. To examine whether genetic testing is associated with increased levels of GD.
3. To examine whether mutation carriers (HD+) are more likely to experience GD vs. non-carriers (HD-) or those who did not test (NT).
4. To identify the prevalence of experiences of GD in insurance, employment, government, health care, family, and social settings.
5. To define and differentiate between the relationships of GD based on family history and genetic testing.
6. To examine the socio-demographic predictors and health outcomes of GD.

2.3 Methodological Challenges

Current evidence of GD has been considerably hampered by various methodological constraints ranging from definitional issues, sampling issues, to response issues (Treloar et al., 2004). The definition of GD has varied from narrow to broad definitions referring, for example, to the misuse of genetic information by insurers or, more broadly, to the use of genetic information for the psychosocial disadvantage of individuals as a result of prejudice or stigma (Treloar et al., 2004). Given its legal nature,

GD can also be conceptualized as the unjust distinctions, which may be prohibited to varying degrees depending on the legislation available in a particular jurisdiction. From a human rights perspective, GD may also refer to socially unacceptable distinctions, whereas an actuarial view would classify GD as irrational distinctions (Rothstein and Anderlik, 2001).

Ultimately the generally recognized concept of GD refers to differential treatment of asymptomatic individuals or their family members based on real or perceived genetic characteristics, which involve elements of social unacceptability as well as irrationality. Given the subjective nature of this social phenomenon, it is best to allow those at risk or those who have experienced GD to define and identify the conceptual dimensions and characteristics of GD themselves.

It is important to acknowledge that the process of making distinctions or providing differential treatment may not necessarily only involve disadvantage. Individuals may be treated differentially but in a positive way. This may be especially true in the case of HD since genetic information is inextricably linked to family, and outcomes such as increased understanding and support may also occur after disclosure of genetic information.

Targeting the appropriate subpopulations in which to investigate GD also presents unique challenges. Although GD includes individuals and family members, family members who may be at risk but who have not been genetically tested may not necessarily see the relevance of GD to them. Stigma or prejudicial attitudes may occur towards an HD family, for example, but since GD is commonly regarded as the denial of opportunities such as insurance or employment, the issue of GD may not be considered as relevant for members who either have not had a particular experience of GD or who have not been genetically tested or for those who have tested 'negative' (Treloar et al., 2004). Thus, identifying the study population is particularly challenging since individuals who would represent the target population of GD may not necessarily view themselves as targets of GD.

Furthermore, the distinction between an asymptomatic individual from a presymptomatic or once-symptomatic but now asymptomatic person is equally difficult to define and will likely continue to evolve as the clinical validity of genetic testing and understanding of the natural histories of diseases develop. In the context of HD specifically, for example, the classification of asymptomatic persons continues to evolve

as new insights reveal very early cognitive and psychiatric changes occurring in HD mutation carriers which even precede the unequivocal clinical diagnosis of HD (Duff et al., 2007; Hinton et al., 2007; Johnson et al., 2007; Snowden et al., 2002; Solomon et al., 2007). Likewise, the previous category of 'asymptomatic' has evolved to include states such as: "prediagnosed", "preclinical", or "premanifest" recognizing the continuum of sub-clinical changes that occur in persons carrying the HD mutation ranging up to 39 years from estimated onset of HD (Hinton et al., 2007).

The need to sample populations at risk for genetic conditions also presents issues since sampling frames such as support groups, clinical patients or disease registries may be skewed towards individuals who may be more resourceful and willing to identify themselves. Thus, perhaps, those most vulnerable to GD or those who fear GD most may not be captured by such sampling frames and the extent of the concern or experience of GD may not be fully ascertained. Moreover targeting socially identifiable subpopulations at risk for GD entails the risk of stigmatizing them (Foster et al., 1998).

Investigating the extent of GD is further challenged by the requirement to base prevalence estimates on large, community datasets. Thus, high participation of a defined (as opposed to a self-defined, self-selected) population and comparisons of responders to non-responders is required to appropriately generalize prevalence estimates (Treloar et al., 2004). Ideally such estimates are compared to another population, genetic as well as non-genetic or general, to achieve a better appreciation of the extent of the issue.

2.4 Research Design

A sequential mix method design was selected as a means to meet the challenge of conceptualizing GD, describing the concerns, experiences and strategies of GD as well as measuring its extent across the population. The philosophical assumption which underlies this mixed method study is pragmatism. The focus of the pragmatic paradigm is on a particular research problem. Pragmatist knowledge claims are not committed to one system of approach: they draw on many methods since they are concerned with their application and real-world practice (Creswell, 2003).

Mixed methods are also warranted as each method addresses a particular aspect of the research question. That is, the nature of GD is explored qualitatively while its extent is investigated quantitatively. Furthermore, quantitative approaches allow statistical generalizability and establish relationships between variables, while qualitative approaches add rich description and facilitate interpretation of the quantitative findings.

By mixing methods, a triangulation of the data may be achieved to deepen the understanding of the nature and extent of GD.

Phase 1: Qualitative Study of the Nature of Concerns, Experiences and Strategies for Genetic Discrimination

Although the definition of GD has been recognized and subjected to considerable debate by scholars, the concept of GD has not been developed so as to delineate its conceptual features. Only when a concept's characteristics, boundaries, preconditions and outcomes have been defined can the concept be measured (Morse et al., 1996). Existing literature lacks a mature conceptualization of genetic discrimination as well as an understanding of genetic discrimination, from the perspective of persons at risk for a genetic disorder. Furthermore, the strategies used to manage GD are unknown.

Qualitative research approaches facilitate the conceptual exploration of otherwise unexplored phenomena and can generate insights for further development or testing on representative samples (Morse and Field, 1995). Qualitative research approaches are also appropriate when the intent of the study is to gain insights into the meaning of experiences from individuals (Rubin and Rubin, 1995).

Grounded theory was used as the qualitative method for this study. The choice of grounded theory is appropriate as it is typically used to explore basic social processes (Strauss and Corbin, 1998) based on the theoretical assumptions of symbolic interactionism (Blumer, 1969). It is also consistent with the assumption that GD is situated in the social interactions and consequences that occur following disclosure of one's risk or genetic status. Thus, grounded theory aided the conceptual development of GD, aided the description of the concerns and experiences of GD and informed the survey questions and response options of a genetic discrimination survey specific to HD.

Phase 2: Questionnaire Development, Pretest and Pilot

Primary topics of discrimination specific to the HD population identified during the initial qualitative approach were used to modify an existing version of a GD survey. The original survey was used to examine the extent of GD across Australia for a range of genetic disorders. It lacked specificity and sensitivity to capture the scope of factors influencing GD in this at risk Canadian HD population. A survey instrument was thus developed to assess the perceptions and experiences of discrimination in the proposed population. The developed survey underwent expert critique, oral debriefing and pilot

testing. Details related to the development and content of the questionnaire are addressed in Chapter 5.

PHASE 3: SURVEY ON THE EXTENT OF GENETIC DISCRIMINATION AMONG PERSONS AT RISK FOR HD:

A large-scale survey of the at-risk HD Canadian population was undertaken to identify the prevalence and scope of GD. Details related to the sampling decisions, data collection and analyses for the survey are presented in Chapter 4.

Details relating to sampling decisions, data collection and analyses for each study phase are not addressed in the present chapter. Chapter 3 and 4 address the qualitative methods details and Chapter 5 outlines the quantitative method details relevant for the present study. Accompanying the details of the study procedures in Chapters 3, 4, and 5 are 4 appendices: Appendix A (consent forms), Appendix B (semi-structured interview guide), Appendix C (cognitive interview guide), and Appendix D (survey instrument).

2.5 ETHICAL CONSIDERATIONS

Ethical issues are inherent to all research. Such issues may be addressed at the outset of the study while others can not be anticipated. The following considerations represent the ethical issues which were considered during the planning stages as well as those that surfaced unexpectedly.

Although there is no potential for causing physical harm to participants in this particular study, there is a possibility of causing undue stress or psychological harm. The possibility of harm exists by virtue of questioning individuals about their perceptions and experiences of discrimination, an undoubtedly unpleasant experience. Persons are asked to recall, or re-live, experiences that may have otherwise been buried or avoided. If emotional reactions occurred during the data collection the interview was stopped and, if permitted, continued at another time. At the conclusion of each interview the well-being and need for further support was assessed. A follow up phone call occurred by the researcher and/or by a clinician if the participant consented to disclose his/her contact information. Additional support was offered for any study participant who was interested in consulting with a health care professional.

Another ethical consideration of the utmost importance is the protection of participants' sensitive information, especially when dealing with genetic information. Confidentiality issues that concern sensitive data were considered at the outset of the study. Several steps were taken to ensure that the information provided by participants will not compromise their current status of employment, level of insurance and current or future level of care. First, all invitations to join the study were prefaced by a statement ensuring the individual that their level of care would not be compromised by their decision to participate in the study. The interviews were conducted in a secure environment (i.e. in private, away from third parties and family members) to allow the participants to speak freely. The participants were also ensured that it will not be possible to identify participants since any identifying information was replaced with a number on any of the survey instruments or transcribed interviews. Furthermore participants were notified that all data was stored in a secure, locked storage cabinet. Any information collected in the study was only to be seen by the research team and in the event of publication pseudonyms would be used to protect the identity of participants.

Finally, qualitative research methods pose challenges in predicting how and what data will be collected. Likewise, there were some ethical issues that were simply unanticipated. For example, inherent to most participants' narratives about being at-risk for HD, included their stories and strategies of how they came to grips with their risk status. Although most participants spoke of cognitive strategies and new life plans, one participant described her intent to commit suicide should she become symptomatic in the future. Indeed confidentiality could not be upheld in this situation since I had the moral obligation to report her suicide ideation to her physician. After notifying her physician, follow up occurred by the clinic staff to assess the suicide risk and wellbeing of the participant. Ongoing support is being provided for this participant in the context of a multi-disciplinary health care team.

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Chapter 3: The Nature of Genetic Discrimination

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3.1 Introduction

Huntington disease (HD) is a degenerative neuropsychiatric disorder that usually presents in mid-life as a triad of cognitive, psychiatric and movement disturbances. It is inherited in an autosomal dominant manner and is caused by a mutation comprising a CAG trinucleotide expansion in the *HD* gene (MacDonald et al., 1993). Individuals affected with HD suffer from mood and personality changes, progressive cognitive decline and worsening of the movement disorder, which ends in death approximately 15 to 20 years from diagnosis (Hayden, 1981). No therapy is currently available to alter the course of the disease.

The discovery of a polymorphic DNA marker tightly linked to HD (Gusella et al., 1983) led to the first predictive test for an adult onset genetic disease in 1986, allowing at-risk individuals to learn with near complete certainty whether or not they have inherited the HD mutation (Hayden et al., 1988). Although early surveys indicated that predictive testing would be requested by 66-79% of individuals at-risk for HD (Kessler et al., 1987; Mastromauro et al., 1987), worldwide uptake currently ranges between 3% and 24% among at-risk individuals (Creighton et al., 2003). The most frequently cited reasons for declining predictive testing have been the absence of a cure, concerns about coping and the fear of genetic discrimination (Quaid and Morris, 1993).

Genetic discrimination (GD) refers to the perceived differential treatment of individuals or their family members based on presumed or actual genetic differences rather than physical characteristics (Billings et al., 1992). Although considerable debate surrounds the existence of GD in the context of HD (Harper et al., 2004), there is a paucity of research on the nature and experiences of GD among this community. Reports of GD have been documented among a variety of genetic disease communities (Alper et al., 1994; Apse et al., 2004; Armstrong et al., 2003; Billings et al., 1992; Geller et al., 1996; Hall et al., 2005; Lapham et al., 1996; Low et al., 1998). The anecdotal report of a teacher in Germany who was deemed unfit to teach only because she was at high risk for HD focused international attention on this issue (Burgermeister, 2003; Harper et al., 2004). Strategies to manage the risk and experiences of GD have been described (Bombard et al., 2007b). They included "keeping low" (i.e., attempts to pass or carry on and keeping results private) as well as preempting, minimizing and confronting

GD. These strategies varied depending on the form of the GD experience and the degree to which individuals engage with (or internalize) GD.

The consequences of GD, both for individuals and society, are far-reaching as they have the potential to create significant social, health and economic burdens by limiting opportunities for individuals at genetic risk in a range of contexts (Otlowski et al., 2003). Given the likelihood that similar tests will become increasingly available for predicting risks for other diseases, exploring the nature of GD in the context of HD will be generally instructive for other disorders. As individuals' strategies for managing GD appeared to vary in terms of how they constructed their experiences, it would be helpful to have a better understanding of their initial reactions to GD (or the risk of GD) and how they make sense of these experiences. The aim of this study was to explore concerns and experiences of GD among asymptomatic individuals from HD families.

3.2 Methods

Qualitative research approaches facilitate the conceptual exploration of otherwise unexplored phenomena (Morse et al., 1996) and are also appropriate when the intent of the study is to gain insights into the meaning of experiences from individuals. As such, this study aimed to explore the concept of GD as well as the concerns and experiences of GD. This inquiry was informed by grounded theory, a qualitative research approach typically used to explore basic social processes (Strauss and Corbin, 1998) based on the theoretical assumptions of symbolic interactionism (Blumer, 1969). The choice of grounded theory is consistent with the assumption that GD is situated in the social interactions that occur when presumptions or information about genetic status come into play.

Study Sample and Recruitment

The approval of the relevant research ethics boards was received to recruit individuals from three genetic and movement disorder clinics in Vancouver, Calgary and Toronto, Canada. To facilitate the exploration of discrimination based on genetic information as opposed to symptoms or disability, only individuals who were not diagnosed with HD were eligible to participate. Symptom status was confirmed with recent neurological assessments at these clinics. Written and verbally recorded informed consent was obtained from all participants.

Thirty-seven individuals who were found to have the HD mutation (HD+; 'positive test result') were sampled according to purposive sampling procedures where variation

across participant demographic variables was sought (e.g., age, gender, education and time since genetic testing) and formed the primary sample for this study. Ten people with a family history of HD but who chose not to undergo testing (NT; 'not tested'), as well as eight people who were found not to have the HD mutation (HD-; 'negative test result'), were recruited for the purpose of making theoretical comparisons. Theoretical comparisons are a vital part of discovering the properties and dimensions in the data and enable identification of variations in the developed theory (Strauss and Corbin, 1998). Inclusion of these comparison cases provides the opportunity to assess how family history and 'negative' test results influenced concerns and experiences of GD and tested the limits of the proposed theory. Participant recruitment continued until no new themes developed from subsequent interviews (Strauss and Corbin, 1998).

Data Collection

Data were collected through individual, semi-structured, open-ended interviews conducted by telephone (N=16) and in person (N=39). All the interviews were conducted by the first author and lasted 65 minutes on average (range: 50 - 90 minutes). The interviews were digitally recorded, transcribed *verbatim* and checked for accuracy. Field notes were maintained to document important contextual and behavioural information.

During the interviews, participants were encouraged to reflect on the following issues: their interpretations of GD, their experiences and concerns for GD, their thoughts on genetic privacy, as well as personal, social and other factors involved in their concerns and experiences of GD. In view of the sensitivity and potential bias introduced with the term discrimination, interviews were conducted using its definition, 'differential treatment,' which enabled participants to reflect on both the positive and negative aspects of learning about their predictive test results or family history of HD.

Data Analysis

Constant comparison analysis was used to explore the concerns and experiences of GD. Interview transcripts were entered into a software program (NVivo 2, QSR International) to facilitate coding and data retrieval. The way in which the grounded theory analysis was used is described in detail elsewhere (Bombard et al., 2007).

3.3 Results

Sample Characteristics

The characteristics of the participants in our study are presented in Table 3.1. The characteristics of our tested sample appear similar to previous reports of Canadian

adults who receive predictive testing results for HD (Bloch et al., 1989; Creighton et al., 2003). The characteristics of our untested sample appear similar to individuals who choose not to test, although our untested sample are more educated (Quaid and Morris, 1993).

CONCERNS AND EXPERIENCES OF GENETIC DISCRIMINATION

In the course of discussions about GD, participants spoke about their concerns and experiences in a pensive manner, yet with a tone of conviction. At times, non-verbal cues such as hand-gesturing and shifting in their seats were evident among some individuals, suggesting some discomfort with this potentially sensitive topic. Although most discussions of their concerns and experiences were fairly detailed, some participants limited their narratives to matter-of-fact statements (e.g., as in the case of insurance GD), not providing much in the way of feelings or details. In addition to the word '*discrimination,*' participants frequently used other terms such as "*issues,*" "*ramifications*" and "*adverse consequences*" when referring to GD.

Individuals reported concerns about and experiences of GD in various forms including increased symptom monitoring, communication changes, a perceived lack of closeness or support, as well as pressure regarding reproductive, educational and marriage decisions from relatives. Loss of financial benefits was also linked with GD in the form of insurance rejection and increased premiums, imposed limits to opportunities in the workplace, promotional denials and forced retirement. Perceived differential treatment related to HD familial history and genetic test results were also associated with increased surveillance by employers, experiences of social avoidance and pity as well as perceptions of altered medical advice by health care professionals. Individuals also reported feelings of being "*tainted*" by their family history of HD in social and employment situations. A summary of these concerns and experiences is presented in table 3.2.

For all of the participants, GD was not an issue they thought about on a regular basis but one that they considered *"occasionally"* when an event sensitized them to the issue. Renee (HD-; pseudonyms have been used to protect the identity of participants.) explained: "*you're not constantly thinking about it every moment and you just kind of get on with life and every now and then, you know, something hits you.*" Awareness of GD was precipitated by events that suggested to the participants that having a genetic difference may have consequences.

AWARENESS EVENTS

Participants became aware of GD through observations of affected relatives' experiences of stigma and discrimination, through information provided by genetic counselors and through their own experiences of GD. Growing up with a symptomatic family member sensitized participants early to HD-related stigma and discrimination. Kate (HD+) recalled the "*ignorance*" she experienced when members of the public would react to her affected mother by asking: "*what's wrong with her; she's drunk?*" Similar experiences were reported among the other groups. Tanya (HD-) described her frustration with how her symptomatic mother was treated as though she were "*dumb*" and a "*homeless person*" by those around her, despite efforts to educate others about the disease. Frances (NT) also recalled how her father's neighborhood ostracized him when he began exhibiting the illness, owing to a lack of understanding.

Receiving information about GD constituted the second type of awareness event. Genetic counselors were the primary source of this information for participants who received genetic counseling. For example, being advised by genetic counselors to "*look into*" life insurance before proceeding with predictive testing and to be careful about disclosing test results directly highlighted the potential for GD. Participants from all groups also became aware of the potential for GD from questions on insurance applications, reports from social support groups, the HD newsletter and television programs which highlighted particular cases of GD in the United States.

Personal experiences of differential treatment constituted the third type of awareness event. These experiences were most clearly represented among our primary sample (HD+ group) and occurred in five domains: insurance, family, social, health care and employment. Of the 25 individuals who experienced GD, nine described experiences of being treated differently in insurance underwriting, being denied insurance policies and upgrades. Subtle forms of differential treatment in family situations also arose that participants related to their real or assumed genetic status. Thirteen individuals described experiences that included altered patterns of interaction, symptom monitoring and events where they felt their test results were used against them by family members. For example, some participants spoke of their discomfort with the fact that their spouses began watching them "*like a hawk*" for symptoms of HD after learning their test results. In one instance, a single mother recalled an unexpected

encounter with GD during legal proceedings where her test results were "*used against*" her by her ex-partner as a threat to pursue custody of their daughter.

With respect to their social domain, six participants linked experiences of romantic relationship rejection, social "*shunning*" and being treated as having a "*contagious disease*" to their new HD genetic status. In the health care domain, two individuals described altered medical advice following disclosure of their HD genetic status. One believed that the advice she received that her daughter should not have children if genetic tests were positive for HD was insulting. The other was frustrated when her physician attributed her current, unrelated medical issues to her genetic test result for HD and did not manage her symptoms with the attention she felt they deserved.

The most blatant forms of discrimination were reported to have occurred in the workplace by five participants. The participants believed that the information about their genetic status was directly related to unsuccessful bids to get a promotion, imposition of an unwanted early retirement and increased surveillance by their employers. For example, Michelle, a healthcare professional, felt singled out because of her genetic test results when her supervisor requested access to her medical files so that her employers could *"monitor"* her for symptoms "*faster, easier than taking* [her] *word for it"*. Awareness events like these prompted individuals to begin a cognitive and emotional process of engagement with GD as a preliminary step toward attending to their feelings of frustration or concern and determining their risk and consequences of GD.

The Concept of Engagement with Genetic Discrimination (GD)

Engagement with GD describes a cognitive and emotional process individuals used to interpret the meaning of GD and personalize its risk and consequences in their lives. The process of engagement is precipitated by awareness events and results in personal formulations of the risk and effects of GD. Engagement with GD provides a framework to understand individuals' perceptions and experiences of GD as well as their reactions to and strategies for GD. Each phase of engagement with GD and factors that influenced this process is described in more detail in the following sections. Examples reflecting differences in the engagement process between the groups are highlighted where appropriate.

States of Engagement with Genetic Discrimination (GD)

On the basis of differences observed among participants, three broad states with respect to engagement with GD were identified: engaged, disengaged and resisting engagement. The state of engagement with GD was directly influenced by one's genetic status and risk perception for HD. Although all the participants in our study were at risk for HD at some point in their lives (i.e., they were "*all in the same boat*"), the way in which they engaged with GD either with respect to their family histories or their genetic test results varied with their genetic status and risk perception for HD. Individuals who chose not to undergo genetic testing (NT) usually thought about their risk for developing HD with a certain degree of optimism or pessimism. Untested participants who spoke as though they had the HD mutation (pessimistic bias) engaged with GD in similar ways to HD+ participants. In contrast, participants who held an optimistic bias (low perceived risk for HD) normalized their genetic risk for HD arguing that they are no different than colleagues or members of their social circles who have family members suffering from other common disorders. Anna (NT) alluded to this: "*I'm thinking well, yeah, I'm a potential risk* [but] *so is the guy next door; he could die of a heart attack tomorrow, you know.*" They did not believe that their family history of HD necessarily set them apart from others. They also maintained a position that they were just as likely not to have the HD mutation as to have it. Hillary (NT) explained: "*I choose to look at it that there's a fifty percent chance that I'm not going to get it and there is no more chance that I will.*" Thus they perceived that their risk for GD is no different than the general public and deflected the need to engage with GD. Hannah asserted: *"I don't go there, I don't think about it... I acknowledge the existence of it and that's about it.*" Thus some untested participants who held an optimistic bias were able to deflect the need to engage with GD, and ultimately, resisted engagement.

Individuals who underwent genetic testing were required to engage with GD as part of the informed consent process. However, those who learned that they did not have the HD mutation were able to disengage themselves from GD as they were no longer at risk for HD. They discussed their ability to "*un-attach*" themselves from *"the baggage of HD*" or "*remove the stigma of the disease"* by "*reinforcing*" their "*negative*" test results to others. After learning of their results, these individuals simply disengaged

themselves from GD because they felt that GD was a "*non-issue*", as they considered themselves "*normal.*"

Ultimately, four groups can be discerned from the categorization of engagement along the dimensions of their risk perception and genetic status for HD: tested individuals who had the HD mutation (HD+), tested individuals who did not to have the HD mutation (HD-), untested individuals who held a pessimistic bias about their HD risk (NT-P) and untested individuals who held an optimistic bias about their HD risk (NT-O). Essentially, all groups except for the latter engaged with GD (Figure 3.1). It is important to note, however, that individuals' genetic status for HD and risk perception is not a static state. HD- participants, for example, spoke about past experiences of stigma and discrimination based on their family history despite the fact that they were in a position to disengage with GD. Likewise, one's risk perception for HD can presumably fluctuate over time. Categorizing participants along these dimensions, nonetheless, was helpful in illustrating how one's genetic status and risk perception at the time of their particular awareness event influenced the way in which they engaged with GD.

THE PROCESS OF ENGAGEMENT WITH GD

Engagement with GD involved two phases. Initially, individuals formed meaningful interpretations of GD by making sense of GD, defining its various forms and validating the threat of GD. In the second phase, individuals personalized GD to determine its risk or consequences for themselves or their families. They did this by conducting a mental survey - taking into account their social, financial, employment or familial circumstances as a way of assessing their potential for GD or of understanding the consequence of a particular GD experience. Emotional reactions often ensued in the course of engagement, which included feelings of concern, irritation, anger, frustration or indifference.

FORMING MEANINGFUL INTERPRETATIONS OF GD

The phase of forming meaningful interpretations of GD occurred when individuals began to reflect on what they learned or experienced that raised the issue of GD. Three themes in the data describe the cognitive strategies used: assigning meaning, defining forms of GD and validating the threat of GD.

Assigning Meaning: As most participants attempted to make sense of awareness events, they did not immediately label them as 'genetic discrimination.' Rather they associated GD with notions of "*exclusion*," "*restricting access*," "*disallowing*,"

"*being prevented from doing something*," "*isolation*" and "*unfair treatment*." For the participants who engaged with GD, differential treatment consisted of both positive and negative forms, but discrimination was regarded as a negative, "*stronger*" form of differential treatment.

Participants invoked human rights issues and shared strong reactions as they attempted to makes sense of negative forms of differential treatment. Scott (HD+) deemed employment GD as "*totally unfair, illegal, and inappropriate, a travesty which we as a society shouldn't accept*." Kerry (HD-) interpreted insurance and social GD as "*horrible negative treatment, having something taken away based on a birth defect*." Participants likened differential treatment related to genetic status to other types of discrimination based on ethnicity or religion which were similarly "*unethical*." Patrick (HD+), for example, explained why his GD experiences were a "*definite Charter* [of Rights and Freedoms] *issue*:"

> From a legislative point of view, discrimination based on genetic testing...is no different than discriminating against somebody who's a visible minority or [has] a handicap, you know, because right now you can't, under the Charter [of Rights and Freedoms], you can't discriminate against people because of a disability, right? So do I have a disability? Right now, today, no, but I'm being discriminated against.

Prejudice and stigma were elements highly intertwined in participants' interpretations of GD. Hillary (NT-P) explained the moral underpinnings of GD when she asserted, "*They're disallowing people for things that have not affected them yet. Yeah, I think that's absolutely prejudicial*." Kerry (HD-) recounted her thoughts about GD before receiving her test results and described these consequences as "*stigmatizing*:"

> I get energy from people. So to take that away from me, you're draining me and by stigmatizing me, isolating me, singling me out, you are taking that away from me. So for me that would be, that would be a very horrible thing, I would hate that.

Defining Forms of GD: Participants' interpretations of GD also included defining the various forms of differential treatment related to genetic status: actual or perceived and interpersonal or institutional forms. Actual GD was characterized by participants as having "*proof*" of a GD event whereas perceived GD was associated with the absence of objective evidence. Patrick (HD+) used this distinction to conceptualize his GD

experiences of being required to pay increased life insurance premiums and having been denied a promotion.

> It's actual [discrimination] because the insurance company is asking have you been tested for Huntington's disease or has any family member been tested for Huntington's. That's not perceived. That's actual because it's written on... the [insurance] forms. So perceived discrimination is ... where I think it impacted in a significant way the decision of me not getting that position, [but] I could be completely wrong.

Some individuals also drew a distinction between institutional and interpersonal GD. Interpersonal forms of GD, underpinned by "*personal interaction*" and "*emotions,*" occurred in family and social environments. This contrasted with institutional forms of GD such as in the workplace, courts, adoption, health care or insurance industry, which lacked an emotional basis.

Validating the threat of GD: Concepts of rights, fairness and rationality were used by participants to validate GD. Participants' interpretations of GD were founded upon a perception that genetic information is inherently special. Individuals regarded this information as "*personal*" and therefore it did not need to be shared. Accordingly, participants believed that insurance companies and other third parties had *"no right"* to their genetic information and questioned the fairness of denying or terminating insurance coverage on the basis of predictive test results.

Others who focused on the "*unfairness*" of being treated differently by insurers thought that they should not be penalized for things over which they have no control. As one participant explained, *"It's the luck of the draw and unfortunately I've got the defective gene so it's not my fault that I got it* [HD mutation] *but you* [insurer] *should cover me.*" Paul (HD-) believed that using genetic information in hiring practices would be "*unfair*" and have widespread consequences:

> There's so many tests for genetics these days and would an employer... have the right then not to hire you based upon that? ...I think probably because testing has got so specific and accurate now to identify these things, it's [GD] probably unfair because ...it could affect thousands of people too, you know, look at the number of identified genetic diseases, that could affect an awful lot of people.

PERSONALIZING THE RISK FOR AND CONSEQUENCES OF GD

The second phase of engagement with GD included participants' efforts to determine how GD may affect them or their families as well as their emotional responses to GD. Participants conducted a mental survey of their personal circumstances to predict or imagine the consequences of having a genetic difference. Although some participants engaged with GD to attend to their feelings of concern or anxiety, others described concern or indifference as a result of personalizing the risks and consequences of GD.

Conducting a mental survey: Participants used a 'factoring in' process in which they systematically reviewed their current and future circumstances to make the best possible assessment of their potential for GD. They placed emphasis on those contexts potentially affected by their genetic status, such as insurance policies, workplace environment and interpersonal relationships. Patricia (HD+) recalled explicitly surveying her current circumstances: "*I took my time to stop and think about this whole thing .... The people you work for and your family, you know your associates... especially insurance.*" She explained how her 'factoring in' process took a few months, "*I wanted to cover all my bases and do research and find out what coverage I had, what benefits I had, what I would lose if I told anybody.*" However, uncertainties about possible reactions by others often complicated this mental survey. In thinking about his potential for GD at work, Wesley (HD+), a married father and corporate executive, characterized his efforts to determine his personal risk for GD as a '*struggle*.' He said:

> I struggled a lot... I thought about ... taking on a new job which I've just recently done... should I tell somebody that I have this condition that in five years time might affect me and all of that and I said, you know what: "no."

Similarly, Kerry (HD-) explained her 'factoring in' process before predictive testing and described the consequences of GD as "*horrible*"':

> I'd thought about insurance and I knew... that I would be at risk, that my job would be at risk that my ability to get insurance would be at risk which would, in my view, would put my family at risk if I couldn't be insured and that was a horrible, horrible feeling just knowing that, because you're treated, you're treated differently if you have this [HD mutation]."

In conducting this mental survey, participants relied upon their experience. Individuals sometimes 'factored in' their experiences of public reaction to other diseases

in personalizing their risk for GD. Brendan (HD+) considered how lack of public understanding about HIV/AIDS affected the way people with the disease were treated to support his concerns about GD. He recalled:

> Ignorance breeds fear as people do not understand something, then they fear it and if they fear it, then, yes, they're going to treat you differently. I mean a perfect example of that is, is people with AIDS and how that was handled when we didn't understand how that disease was transmitted from person to person.

Individuals reflected on both positive and negative experiences in their assessment of their potential for GD. Although increased support, empathy and acceptance were recognized as positive experiences following predictive testing, participants dwelt on the impact of negative experiences.

Reacting to the risk and consequences of GD: Personalizing GD involved a range of emotional reactions that informed the way individuals internalized the consequences of GD. These included feelings of concern, irritation, anger, frustration and indifference. Concern, however, was the predominant emotion expressed by participants for themselves and, particularly, for their children. Ethan's (HD+) concern about the possible implications of his genetic test result for his children are reflected in the following quote: *"I suppose the possibility of people who do understand the genetics of it are going to look at my three kids and say, "There's one in half of them right there, wonder which ones?"*

The nature of concern for GD was wide-ranging but centered on a feeling of vulnerability. Rachel's (HD+) sentiments of employment insecurity were typical:

> Any mistakes that I make or anything might be blamed on that or you know might be "Oh well, you know, it's because she's got that gene"....I think it could be used as a you know as a reason or an excuse to not promote me further if an opportunity like that were to arise, you know, and worrying, you know well, "Is it safe to give that job to her because you know, you know she might not be all there?"

Similarly, Paul (HD-) recalled feeling vulnerable because of his HD family history:

> There was never any chance then [before testing] of changing [jobs] because I felt if I went to another employer that to give them that information [family history of HD], there's a lot of issues over ... [and] I wasn't willing to take a chance at a secure job.

In the social context, individuals were concerned about: being "*looked at differently*," being judged or socially rejected and bearing the brunt of "*adverse reactions*." Brendan's (HD+) cautious approach in social settings reflects his concern for being stigmatized:

> Huntington's is something that I would be concerned to just blurt out in a social setting because it would change the way people think....I mean that would change things immensely.... that would absolutely change how people deal with me.

Individuals also indicated concern for future isolation and decline of current levels of family support and altered medical care. Rachel, for example, was apprehensive about how knowledge of her HD status could bias her physician's clinical assessments:

> But even in my doctor's....I'd rather that, you know, that if he at some point needs to determine that I'm symptomatic or not, that he's making that from a purely clinical point of view.

Indifference usually ensued when individuals determined that they were protected in some way from the effects of GD. Zara (HD+) explained why she was indifferent:

> Afterwards I felt well, I really don't give a damn because I'm covered. You know, where I worked, the people are good. I'm not going to lose any pay. I'm not going to lose any of my benefits. My Blue Cross or hospitalization coverage is maintained throughout...so I don't have to worry.

FACTORS INFLUENCING THE DEGREE OF ENGAGEMENT WITH GD

Individuals engaged with GD to different degrees depending on various factors which served to facilitate or impede the process. Individuals who engaged with GD to a greater extent acknowledged the relevance of GD and directly attended to its potential or experience in an active manner. Frequently individuals highly engaged with GD

described strong emotional reactions. In contrast, participants who engaged with GD to a lesser extent did not actively reflect upon the experience or its potential, and neither did they make strong connections between their experiences and GD. Two factors had a major influence on the degree of engagement with GD: stage of life and the nature of the awareness events.

Stage of life: Individuals' engagement with GD fluctuated over time as their lives and family circumstances evolved. Participants in the earlier stages of building their lives, with young families, entering new careers and still building relationships, for example, engaged actively with GD. In contrast, those for whom most life building events occurred before learning of their genetic status or risk for HD perceived GD as less relevant, as reproductive, financial and career decisions were already set in place.

Nature of the awareness events: Participants who became aware of GD in a direct manner engaged with GD to a greater extent. During genetic counseling sessions, for example, patients are routinely prompted to consider the psychosocial impact of predictive test results. Warnings received from genetic counselors during predictive testing sessions raised alarms for Zara (HD+):

> You get so many warnings when you're in counseling. They tell you don't disclose this to outside members of the family, don't disclose this to your insurance, don't disclose this to your employer, don't disclose it to so many areas, you know, and that's why I was concerned because I thought ooh what am I going to do?

In contrast, those who became aware of GD through an indirect or emotionally-neutral event such as through information obtained in a newsletter or support group engaged to a lesser degree with GD.

3.4 Discussion

Our findings demonstrate that a majority of genetically tested and untested individuals in this HD sample are concerned about and experience GD across a wide variety of contexts. This study introduces the psychosocial process of engagement with GD and provides insight into at-risk persons' perceptions of what constitutes GD.

While our results support previous surveys that explored the existence of GD in the domains of insurance and employment (Apse et al., 2004; Armstrong et al., 2003;

Geller et al., 1996; Lapham et al., 1996; Low et al., 1998), our study is the first to provide a detailed description of the concerns and experiences of GD in the HD population, and at the same time to extend the context of GD to include family, social, government and health care settings. Although changes in family relationships have previously been noted to occur after predictive testing for HD (Sobel and Cowan, 2000) this report highlights the fact that individuals link disrupted interactions and patterns of behaviour within the family with discrimination. Although discriminatory experiences have not been typically linked to family interactions, this form of GD needs to be considered along with more obvious forms of GD related to insurance and employment.

Most importantly, the study offers an insight into the cognitive and emotional process of engagement with GD aimed at interpreting the meaning of GD and personalizing its risk and consequences. Although other studies indicate that patients learn about GD from news media (Apse et al., 2004; Hall et al., 2005) as well as through their own experiences (Hall and Rich, 2000), the majority of participants in our study became aware of GD through interactions with genetic counselors. Indeed, in a study of 25 US genetic counselors, 96% routinely discuss GD in cancer genetics (Pfeffer et al., 2003). An inherent tension exists, however, where, in the process of informing their clients of the potential risks and benefits of genetic testing, genetic professionals may be instilling an unconfirmed perception that GD exists or is widespread. Coupling the provision of information about GD with opportunities for clients to discuss concerns about and past experiences with GD is likely to be helpful in supporting the process of personalizing the factual information presented about GD and identifying strategies to minimize or manage the consequences of GD (Bombard et al., 2007b). The framework of engagement with GD provides clinicians with a helpful tool to understand and contextualize clients' experiences and may help identify areas where more education and support are needed.

Our findings suggest that individuals regard GD in relation to HD as a basic human rights issue grounded in concepts of privacy, stigma and prejudice. Included in individuals' interpretations of GD were taxonomies and validations that resonate closely with others' conceptualizations based on rationality and social acceptability (Otlowski, 2005; Rothstein and Anderlik, 2001). Many of our participants reasoned that increasing life insurance premiums is a form of rational and legal discrimination, yet it remains socially unacceptable. This particular discord lies in the balance of whether one

considers life insurance a commercial or social good (Lemmens, 2000). In a cultural context where universal health care is considered a social right, one may question the existence of equality when access to commercial goods such as mortgage insurance and small business loans rely increasingly on life insurance eligibility. Given our findings of life insurance and promotional denials, social avoidance and altered medical advice, it appears that opportunities are indeed being limited for these individuals. Thus, former warnings of a looming 'genetic underclass' (Billings et al., 1992) may become a real risk.

Engagement as the overarching concept in explaining how individuals interpreted and personalized GD in this study is supported by recent studies developed in relation to genetic risk for HD and hereditary nonpolyposis colon cancer (HNPCC) (McAllister, 2002; Taylor, 2005b). Although research by McAllister (2002, 2003) and Taylor (2005) contribute important conceptual understanding about the process of engagement in the context of genetics, their conclusions did not serve as theoretical frameworks for the present study. Taylor's (2005) use of the concept of engagement to describe varying degrees of openness and involvement in HD genetic test decision making observed among at-risk individuals is not directly related to this study. In her insightful contribution, McAllister's (2002) theory of engagement in relation to genetic risk for HNPCC is based on findings that the degree of cognitive and emotional involvement with individuals' risk for cancer varied from partial to intense over time with the unfolding of critical events in family life (McAllister, 2002). McAllister's theory of engagement and the engagement with GD theory proposed in this study both involve cognitive and emotional processes which are precipitated by critical events (life events in relation to engagement with genetic risk and awareness events in relation to engagement with GD). Likewise, the degree of engagement with cancer risk and GD influences approaches and reactions (McAllister, 2002) as well as strategies (Bombard et al., 2007b) regarding one's risk for genetic risk or GD, respectively. The relationship between engagement with GD and risk perception is also similar to that described by McAllister (2003) with individuals' beliefs about carrier status linked to their engagement with genetic risk (McAllister, 2003). Although McAllister's theory did not suggest a direction of the causal link between engagement status and beliefs about carrier status, the results of the present study suggest that pessimistic biases toward being an HD carrier promoted engagement while optimistic biases toward not carrying the HD mutation hindered engagement, at least within the context of GD.

There are also important distinctions in the contexts and concepts of these theories. McAllister's (2002) theory of engagement related to *genetic risk* was developed in the context of studying individuals at 50% risk of carrying the HNPCC mutation before and after undergoing predictive testing. However, the theory of engagement with GD is based on data provided by genetically tested as well as untested individuals from HD families and refers to engagement with *genetic discrimination*. The contexts of HD and HNPCC are notably different in the degree of validity of the test results as well as the nature, penetrance and management of the diseases.

There are also important differences between the concepts of genetic risk and genetic discrimination. Genetic risk for a future disease presents individuals with information about their personal susceptibility and the challenge of understanding and assimilating this information into their self-image. Although this experience is influenced by emotions (Klein and Stefanek, 2007) and family contexts (Cox and McKellin, 1999; McAllister, 2002), the focus is on the way that risk information shapes individual lives. Genetic discrimination, on the contrary, is grounded in social interactions and relationships and requires individuals to make sense of others' reactions and their own responses to them. Ultimately one may view engagement with genetic risk as a necessary step toward engagement with GD: individuals may engage with disease risk without ever engaging with GD. Our findings provide further support for McAllister's (2002) theory of engagement and extend the theory to the context of HD and GD. Clearly engagement appears to be an important concept which requires further exploration and development in other contexts.

There were several limitations in this study that should be considered in the interpretation of our findings. First and foremost, participants who take part in research studies are a self-selected group (Codori et al., 1994) that differs from individuals who decline to participate in terms of their perspectives and experiences of GD. Given that GD is one of the reasons individuals at-risk for HD do not participate in predictive testing (Quaid and Morris, 1993), it is possible that we have not fully captured at-risk persons' experiences and concerns for discrimination. As a consequence of our sampling and timeframe for recruitment only one untested man was available and volunteered to participate in our study. This artifact may support previous suggestions that men can have difficulty in accepting implications of being at risk and cope by using denial (Maat-Kievit et al., 2000). In addition, because the sample consisted of individuals from the HD

community, the study findings may not necessarily apply to other genetic and non-genetic populations. However, with GD cited as one of the main reasons against pursuing predictive testing for HD, individuals from the HD community may be a well-suited population in which to explore these issues. These data are based on self-reports, which rely on individuals' perception of the events that occurred and how they felt they were treated on the basis of their genetic status. In counseling, however, it is the clients' perceptions that are important, and thus these findings provide counselors a framework to understand and contextualize the experiences and concerns that clients share with them. It is also acknowledged that the data were based on experiences from a Canadian sample whose concerns and experiences may not apply to other populations where health-care funding is privatized.

In conclusion, this qualitative study focused on the concerns and experiences of GD which were grounded in the experience of HD families and may provide a useful framework for understanding individuals' concerns, experiences and management of GD in other contexts. These results help identify areas where more education and support is needed and provide direction to counselors supporting their clients as they struggle with issues of GD and genetic testing.

	PRIMARY SAMPLE		COMPARISON CASES				TOTAL	
	Participants with HD Mutation (N=37)		Participants without HD Mutation (N=8)		Participants who have Not Tested (N=10)		(N=55)	
	N	%	N	%	N	%	N	%
Gender								
Female	23	62%	5	63%	9	90%	37	67%
Male	14	38%	3	38%	1	10%	18	33%
Marital Status								
Married/common-law	23	62%	6	75%	8	80%	37	67%
Single/separated/divorced/widow	14	38%	2	25%	2	20%	18	33%
Education								
Some college & above	31	84%	8	100%	9	90%	48	87%
Highschool & below	6	16%	0	0%	1	10%	7	13%
Employment								
Employed	26	70%	6	75%	10	100%	42	76%
Unemployed	11	30%	2	25%	0	0%	13	24%
Children								
Have children	27	73%	6	75%	7	70%	40	73%
Have no children	10	27%	2	25%	3	30%	15	27%
Time since Testing								
0-4 years	9	24%	2	25%	-	-	11*	41%*
5-9 years	16	43%	1	13%	-	-	17*	63%*
10-14 years	10	27%	3	38%	-	-	13*	48%*
15-20 years	2	5%	2	25%	-	-	4*	15%*

* Based on Tested Sample (N=27)

Table 3.1 Sample demographics

	PRIMARY SAMPLE		COMPARISON CASES					
	HD+ (N=37)		HD- (N=8)		NT (N=10)		TOTAL (N=55)	
	Concerns N	Experiences N	Concerns N	Experiences N	Concerns N	Experiences N	Concerns N	Experiences N
Overall	28	25	4	5	5	5	37	32
Family	4	13	0	4	0	1	4	19
Insurance	16	9	2	1	3	4	21	14
Employment	19	5	3	3	3	0	25	8
Social	11	6	1	0	1	1	13	7
Health Care	3	2	0	0	0	0	3	2
Government (i.e. adoption, blood bank)	0	0	0	0	0	2	0	2

Table 3.2 Proportion of concern and experiences of genetic discrimination

(Categories are not mutually exclusive; participants may have spoken about experiences/concerns under various domains.)

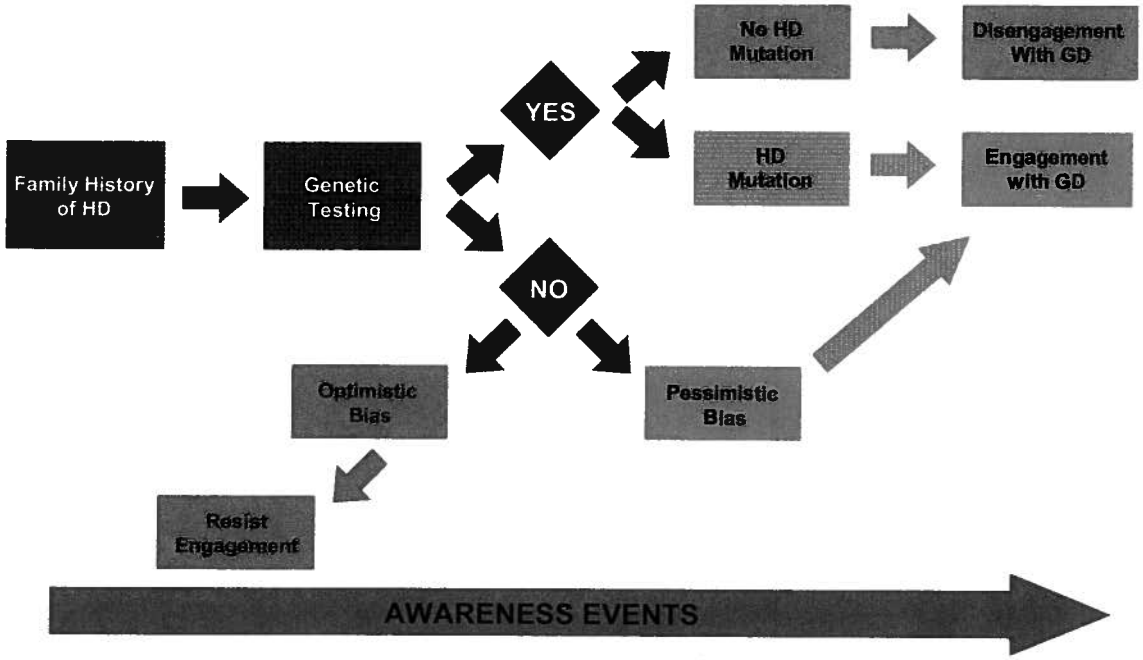

Figure 3.1 States of engagement with genetic discrimination in relation to genetic status and risk perception for Huntington disease

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Chapter 4: The Strategies used to Manage Genetic Discrimination

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4.1 Introduction

Huntington disease (HD) is an autosomal-dominant neurodegenerative disorder that usually presents in adult life with cognitive, psychiatric and motor disturbances. HD has a prevalence of approximately 5-10 per 100,000 and is inexorably progressive ending in death approximately 15 to 20 years from onset (Harper, 1981; Hayden, 1981). New approaches to treatment are being explored; however a cure or therapy does not currently exist to alter the course of the illness.

The discovery of an expanded CAG trinucleotide repeat as the underlying mutation that causes HD led to the availability of direct predictive testing (MacDonald et al., 1993). The introduction of predictive testing for HD has led to a new group of individuals found to have the HD expansion who are currently asymptomatic yet destined in all likelihood to become affected at some point in the future (Langbehn et al., 2004). Individuals identified with the HD expansion have a CAG repeat length over 35 and are considered at 'increased risk' for developing HD in their lifetime, should they live long enough (Kremer et al., 1994). In fact, there is a significant inverse relationship between CAG repeat lengths and age of onset of HD with a larger CAG expansion associated with an earlier age of onset (Langbehn et al., 2004). Some individuals with repeat lengths between 36-39 may never develop symptoms of HD in their lifetime, even if they live to an advanced age as CAG expansions between 36-39 are in the affected range but are not fully penetrant (Langbehn et al., 2004; Rubinsztein et al., 1996). While CAG length is the major determinant of the age of onset, other genetic and environmental factors are also likely to contribute to the variance in age of onset of HD (Rosenblatt et al., 2001).

The advent of predictive testing for HD introduced many opportunities as well as potential challenges for individuals at risk for HD. One potential consequence of predictive testing is genetic discrimination. Genetic discrimination (GD) refers to the differential treatment of individuals or their family members based on presumed or actual genotypic difference rather than phenotype (Billings et al., 1992).

There have been four reports of genetic discrimination in the context of HD (Burgermeister, 2003; Geller et al., 1996; Kenen and Schmidt, 1978). Kenen and Schmidt (1978) warned of the dangers of stigmatization of individuals found to have the HD expansion. Although testing was not available at that time, they speculated that at-risk individuals live their lives in a "suspect state", neither fully stigmatized nor "considered fully normal as the label of defective individual lurks in the background"

(Kenen and Schmidt, 1978). Predictive testing, they presumed, would replace this uncertainty with social stigma and limit opportunities of these individuals as a result of their future illness. A survey of 27,790 individuals and children at risk for genetic disorders discovered 276 reports of GD among the 623 HD respondents (Geller et al., 1996). Of the 206 follow-up verification interviews conducted 5 cases concerned discrimination against individuals at-risk for HD. These reports included: life insurance rejection, coercion by a physician to undergo prenatal genetic testing and abort an affected fetus, 2 cases of adoption denials and a job refusal for the US Air Force (Geller et al., 1996).

An informal poll in Canada found frequent unreported instances of genetic discrimination because of a family history of HD or based on predictive testing (Harper et al., 2004). Furthermore, three individuals reported employment difficulties following disclosure of their genetic test results to their employers (Harper et al., 2004). The recent case of a teacher in Germany who was refused a job because of being at risk for HD (Burgermeister, 2003) lends credence to the potential for such discrimination in the HD community worldwide.

Fears of genetic discrimination have precipitated altered behaviour around predictive testing for HD including the request for anonymous predictive testing. Several individuals have sought predictive testing under anonymity in fear of genetic discrimination for themselves and their families in Canada, the United States and Europe (Burgess et al., 1997; Harper et al., 2000; Maat-Kievit et al., 2000; Visintainer et al., 2001). The selective disclosure of genetic risk information for fear of discrimination has also been reported as another strategy to avoid potential loss of opportunities in the employment context (Australian Law Reform Commission & Australian Health Ethics Committee, 2006). Finally, withholding information about seeking HD predictive testing from health care providers has been previously shown as another method of limiting insurance or employment discrimination (Williams et al., 1999).

While limited evidence for genetic discrimination in the context of HD exists (Burgermeister, 2003; Geller et al., 1996; Harper et al., 2004), little is known about how individuals found to have the HD expansion manage the potential for or experiences of genetic discrimination. Insight into the coping strategies used to deal with genetic discrimination can offer approaches for other persons at risk for late onset disorders. We have conducted this qualitative study to explore how individuals found to have the HD expansion manage the risk and experience of genetic discrimination.

4.2 Methods

This study aimed to explore the strategies individuals use to manage the risk and experience of genetic discrimination. As such, the grounded theory method was appropriate as it is typically used to develop a theory of a process or interaction in response to a phenomenon, 'grounded' in the views of participants (Creswell, 2003). This qualitative research approach is characterized by simultaneous data collection and analysis. The developed theory is based on constant comparison of data with emerging themes from subsequent interviews. Further data collection and sampling are based on the emerging analysis, aimed at maximizing the similarities and differences among the developing patterns. Thus, it is an iterative process of moving between data collection, theorizing/conceptualizing and sampling based on emergent patterns (Strauss and Corbin, 1998).

Recruitment and Participants

Asymptomatic individuals found to have the HD expansion were recruited by mailed invitation from three HD clinics across Canada. Asymptomatic status was confirmed with recent neurological assessments at these clinics. No other exclusion criteria were used for study eligibility. Variation across time since testing, age, gender, marital status and education level was sought, which is in accordance with purposive sampling for grounded theory research. Recruitment continued until data emerging from subsequent interviews achieved adequate saturation of the themes (Strauss and Corbin, 1998) which was determined when no new information emerged during the analysis. This study received the approval of relevant research ethics boards. Written and verbally recorded informed consent was obtained from all participants.

Data Collection

Thirty-seven individual semi-structured interviews were conducted by telephone (N=14) and face-to-face (N=23), digitally recorded and transcribed verbatim. Interviews conducted by telephone and face-to-face did not vary in overall length or quality, consistent with other qualitative research (Janofsky, 1971; Sturges and Hanrahan, 2004). All interview transcripts were reviewed and checked for accuracy.

An interview guide was developed to reflect the research questions. It was based upon literature on genetic discrimination and prior research on the concerns of persons who are at increased-risk for HD. Acknowledging the sensitivity and potential bias introduced with the term 'discrimination', the interview guide did not use the word

discrimination rather its definition, differential treatment. This term allowed the participants to reflect on their responses to the potential or experience(s) of GD in an open and non-directive way. Participants frequently alluded to GD using terms such as "*issue*", "*ramifications*" and "*adverse consequences.*"

The interview topics included: experiences with and concern for differential treatment in the family, social, insurance and employment domains, as well as factors influencing the use of particular strategies to manage GD. Some of the questions included: what are your experiences in obtaining or keeping life insurance since learning of your test results? Can you tell me what you decided about telling people at work about your test results and how this went? What do you believe would happen if your employer knew of your test results? How has having predictive testing changed things in your family? Follow up probes were used to encourage fuller descriptions and emotion regarding participants' strategies for their concerns and experiences. (The interview guide was continually revised as data collection and analysis continued and the researchers' understanding of the theoretical concepts developed.)

Interviews lasted 65 minutes on average (range: 50-90 minutes). At the conclusion of each interview the well-being and need for further support was assessed. Fieldnotes were maintained following each interview to document what the participants spoke about, their behaviour, intonation, emotional responses, the interviewer's (YB) initial impressions on the results and directions for follow-up.

Data Analysis

A grounded theory approach with constant comparison analysis was used to explore how participants managed the potential for or experience of genetic discrimination. The analysis process included 3 sequential steps: (a) open coding, (b) axial coding, and (c) selective coding. The analysis began by examining the text and identifying descriptive labels for the data. This process fractures the data into the major ideas brought up by the participants. These first-level codes were condensed and conceptual labels (categories) were generated (e.g. take action in advance to avoid GD, ignoring a GD experience). A coding framework was developed to enable identification of recurrent categories discussed by the participants. Following the initial process of taking the data apart, relationships were explored between the categories in the form of causes, consequences and interactions to generate a theoretical model (referred to as axial coding). During this stage, questions and comparisons were made among concepts and new data to facilitate the discovery of patterns and variations among the data

(referred to as 'constant comparison'). The final analytic step of selective coding involved integrating all the categories under a core abstract category or central phenomenon (e.g. managing GD) which connects all categories together to build a theory.

A computer-assisted qualitative data analysis program (NVivo 2) was used to facilitate coding and management of the interview data. Rigor was established by the use of member-checking where developing themes and theory were presented to participants for verification throughout the analysis. The coding framework and developing theory was also presented to experts in the field for further validation. Finally, recursive questioning during interviews also contributed to data validation.

4.3 Results

Participant Demographics

The demographic characteristics of the 37 participants are illustrated in Table 1. These characteristics are similar to previous reports of Canadian adults seeking predictive testing and were found to have the HD expansion (Almqvist et al., 2003). In fact, previous studies have reported an excess of females seeking predictive testing for HD (Almqvist et al., 2003; Creighton et al., 2003; Harper et al., 2000; Maat-Kievit et al., 2000; Mastromauro et al., 1987). Thus, this sample appears representative of individuals among the HD population who receive increased risk predictive testing results in Canada. Furthermore, this sample is highly similar to the general population in most demographic variables, although it is less ethnically diverse (97% vs 87% European decent) and slightly more educated (89% vs 77% high school graduates) (Statistics Canada Housing, 2002; Statistics Canada Housing, 2003).

Dimensions of the GD Strategies Model

In the course of discussions on GD it became evident that participants attempted to manage both the effect of a GD experience as well as the potential of its occurrence in the future. Participants used these behavioural responses to protect themselves and family from GD and, to preserve financial and social opportunities. Although differential treatment may present as positive (advantageous, e.g., increased support) or negative (disadvantageous) treatment (Treloar et al., 2004), strategies were used to manage the effects or potential of a negative GD experience. We noted that participants' behavioural responses or 'strategies' varied along two dimensions: the level of engagement with GD and the nature of the GD experience (actual experience or concern for its potential).

Participants' level of engagement with GD was reflected in the way they dealt with the potential for or experience of GD and varied from high to low levels. Individuals

who were highly engaged with GD formed an understanding of it and factored it into their own as well as their families' lives. Engaged participants acknowledged the relevance of GD and directly attended to its potential or experience in an active fashion. In contrast, participants who engaged with GD to a lesser extent did not directly attend to GD and managed its potential or experience in a reserved or limited way. For example, participants did not reflect upon the experience, nor made strong connections between their experiences and GD (Bombard et al., 2007a).

The nature of the GD experience, that is, whether individuals were managing actual experiences of GD or concerns related to the potential for GD, also influenced the type of strategies used. Those who were concerned about the potential of GD included participants who never experienced GD as well as those who had a GD experience and wanted to manage the future occurrence of another GD event. Participants were concerned about the potential of GD in various contexts including their workplace, insurance, health care, family and social relationships. There were varying degrees of concern for themselves and their family members. In contrast, participants that had an actual experience of GD responded in ways to manage the effect of that experience. (It is important to note, however, that references to the participants' experiences of GD are based on their perception of the event that occurred. Thus, no distinctions have been drawn between their perceptions and actual experiences of GD.)

Depending on participants' level of engagement with and experience of GD, four discernable strategies to manage GD were reflected in their accounts: "*keeping low*", minimizing GD, preempting GD and confronting GD (See Figure 1). Although a certain strategy was dominant for each individual in a particular context, strategies varied across time and context and depended on the number of concerns or GD experiences.

"KEEPING LOW"

"*Keeping low*" was the strategy used to manage GD by individuals who displayed a low level of engagement with GD and were concerned about its potential. This behavioural strategy involved attempts to pass or carry on as though they did not have a stigmatizing identity due to their genetic test results. Overall, 23 participants (62%) described using this strategy.

Keeping private about one's family history or genetic test results was a predominant feature of this strategy. Participants kept private about their risk to varying degrees. Some participants spoke about not "*sharing the information*" at all or only with a "*very limited*" group of people. This group typically included family and close friends,

described as the "*inner circle*." Others approached their predictive test results in a protective or "*cautious*" fashion, concealing their genetic test results more than their family history. Ben (pseudonyms have been used to protect the identity of participants), a participant in his thirties, explained:

> I'm a bit more careful now I think, just I don't really tell many people I've tested positive. Whereas I might have told them that there was this family history of Huntington's, I probably did tell a few friends about that. But I think now that the result was positive I haven't told many people.

Many participants who "kept low" by deliberately keeping their test results private reasoned that such information was "*unnecessary*" or "*none of their* [others/employers'] *business.*" The distinction between "*having a gene and diagnosis*" was a particularly important point for some participants. Prior to diagnosis, they are healthy and did not feel that this information was relevant. Moreover, participants explained that since the disease is the "*way it is*" with an undefined time of symptom onset they may perceived as 'crying wolf' by disclosing their predictive test results. Wesley, a corporate executive, described his decision to keep private as a "*struggle*" as he explained,

> I struggled a lot....I thought about if, you know, taking on a new role, taking on a new job which I've just recently done, is not something I should do, it's not something I should tell somebody about, you know, should I tell somebody that I have this condition that in five years time might affect me and all of that and I said, you know what: "no."

Those who worried about the possibility that disclosure of their genetic test result may lead to "*judgment*" did not want to have people wondering about their job performance. Rachel, involved in middle management, did not want to give her co-workers or employers "*a chance*" to treat her negatively, a sentiment shared by others. Another participant perceived the notion of disclosure as "*ludicrous*" conveying the strong endorsement for this strategy which was shared by other participants. In contrast, others spoke of this strategy as a "*preference*." Some participants employed this strategy in a default fashion, rather than a predetermined plan. These participants suggested that their genetic test results simply "*never came up*" or "*never been an issue*."

"*Keeping low*" was also reflected in actions related to avoiding changes in employment or insurance arrangements. Individuals explained that they stayed in their job in order to avoid the potential loss of insurance benefits, while others did not bother applying for insurance because they were convinced that they would not qualify and thus avoided the probable rejection. Participants also found it important to "*keep low*"

because of the inherent connection between employment and insurance contexts; where disclosure in one area may lead to disclosure in the other. Also, laying low was perceived to be necessary when some participants were concerned about GD in unknown contexts. Hugh, a father of three, explained the nature of his concerns for his children in a variety of contexts,

> I mean... [GD can occur in] any context that they [children] operate in, I suppose, might be potentially one that they could be treated differently in. As I say they go to school and they go to work and they have their friends and social settings and you know potentially even family settings, I suppose...

Some participants also kept low because they perceived their HD risk status as something potentially stigmatizing. A few participants spoke of their HD risk status as "*in the closet*", a notion typically associated with stigma and shame. Charles, a married father of two, perceived his HD status as potentially stigmatizing for his children when he asserted: "*There's enough bias out there based on* [one's] *religion and race, they* [his children] *don't need anything else to jump into the picture*." Thus he kept "*it tight*" because of the perceived sensitivity of the information.

Some individuals conceivably used this strategy as a general coping or avoidance mechanism. Upon reflecting on disclosing her HD status to others, Kate, a participant in her twenties, exclaimed: "*Oh god…. I would have to explain the whole situation over and over again….it was tough going through it and tough dealing with the answer when I got it.*" Keeping low may be considered as a strategy to cope with the test results in general.

The level of familiarity and trust with another person or contact was an important factor in determining how individuals kept low. For example, Rachel recognized that she disclosed her HD status to her old boss because he "*was a friend*" whereas her current boss was not and could not be trusted to refrain from using the information in the "*wrong way.*" Level of familiarity and trust were perceived to be important factors in how participants kept low.

MINIMIZING GD

Minimizing GD characterized the behavioural strategy of participants that had experienced GD and had low levels of engagement with GD. Typically, participants using this strategy did not reflect upon the experience, nor made strong connections between their experiences and GD. Moreover, some participants were ambivalent about whether particular experiences constituted GD. In these circumstances, individuals

screened out the incident (s), in effect minimized the GD experience. This strategy of minimizing GD included: backing off, avoiding confrontation and disregarding a GD encounter. Overall, 11 participants (30%) discussed using this strategy.

Many participants discussed backing off from a GD situation, essentially not pursing the incident further. Individuals "*backed off*" from legal proceedings where their test results were used against them, others "*backed down*" when early retirement was imposed on them due to their test results. Patricia, involved in administration, explained her reaction to her employer's demand for her early retirement to minimize their long term disability policy costs: "*I have to retire at my earliest retirement date so that's the only, you know, thing that has been imposed to me is that so, you know, I think that I have backed down.*"

Although backing off may be considered as shying away from a situation and avoiding confrontation, some participants perceived the use of this strategy as important in maintaining relationships. For example, Rachel discussed her preference of not expressing her discomfort with her mother's change in communication patterns with her following notification of her genetic test results. She explained, "*I don't want to address it with her* [mother]*....I didn't want to bring it up.... I don't want to make her feel like she's getting any kind of pressure from me.*" Backing off included resignation and an acceptance of GD. Kate shrugged off the suggestion of re-applying for insurance after being denied when she retorted: "*Why go through that if you're going to get denied again.*" She reconciled the experience by concluding she did not need insurance.

Participants reasoned that minimizing GD allowed them to move on with their lives. Patricia explained this approach: "*It will have to, you know, be like water on the duck's back, you just ignore it* [GD] *and do the best you can with it.*" Participants also discussed how they "*blow off*" discriminatory incidents claiming: "*It doesn't matter.*" Beth, a participant in her forties, expressed this sentiment after considering challenging her insurance denial: "*Then I thought what's the point, it would just be long, drawn out ...it* [confronting GD] *would be a waste of my time and my effort.*"

Minimizing GD was also a strategy used by individuals who thought they understood the reason behind the discrimination. Upon reflecting on her experience of a retirement date being imposed on her, Patricia said:

> I understand that because... I don't think that I should be able to use the long term disability benefits until I'm sixty-five. I think that would be wasting the long term benefits. I can get my pension next year although it's going to be less than what I

> would normally get but I can understand why they [employers] wouldn't want me to be on long term disability for a long period of time.

In other instances, participants covered or minimized the significance of their GD experience by constructing GD as "*logical*" or "*just business*". Elle, a mother of two, maintained that being charged an additional premium for her insurance "*wasn't huge.*" Participants appeared to minimize the consequences of GD in order to reduce the tension or emotional reaction caused by the experience of GD.

Sometimes participants chose to disregard or defer dealing with their GD experiences in order to focus their attention elsewhere. Danielle, a single mother, discussed going through a difficult period in her life when her boyfriend "*dumped*" her after she tested positive for HD. Her response to this experience was "*whatever*" because at the time of this incident she was helping her best friend through a cancer diagnosis and also chose to minimize the importance of their relationship. Thus, individuals may minimize GD when they are distracted or required to manage other, more pressing issues. Similar to '*keeping low*', minimizing GD may also be considered an avoidant coping response to a difficult or potentially damaging GD event.

Participants also minimized the experience of GD when they found other means to get what they were after. For example, Beth thought "*what's the point*" of confronting the insurance discrimination since she managed to secure life insurance through a group policy, but admitted, "*It would have been maybe different if I hadn't been able to get life insurance, period.*" Kate, who was denied life insurance, also felt "*it's not the biggest deal in the world*" since she was covered by her work benefits. In addition, when participants anticipated discriminatory outcome they readily minimized its occurrence. Kate minimized her insurance rejection but also spoke of expecting her insurance denial beforehand. She said, "*Well I was expecting it, you know…At the same token it doesn't feel too good but I had the notion that they would, that it was more of a 95% no than the 5% possibility that it would be a yes.*"

PREEMPTING GD

Preempting GD was a behavioural strategy used by participants who were highly engaged with GD and concerned about the potential for GD for themselves and their family. Preempting GD involved taking action to evade or "*protect*" themselves from GD. Individuals cited concern for the lack of legal safeguards for GD in Canada as a reason for this approach. Zara, a participant in her forties, explained: "*In Canada there's no real*

laws yet developed about it [GD]... [so] *there's some concern .... Until some laws are in place or something ...why take a chance.*"

An important feature of preempting GD was taking initiative in an open and direct fashion to reduce the potential for GD. The following measures characterized this strategy: purchasing life insurance prior to predictive testing, educating the public about HD, and ensuring one's predictive test results were not listed in their GP's medical files.

A predominant example of preempting GD was purchasing insurance before undergoing predictive testing or prior to a family member's official HD diagnosis, a strategy frequently encouraged by genetic professionals. In this way individuals may qualify for insurance based on their family histories so that the principle of *good faith* may be upheld, since applicants have an obligation to disclose any relevant information at the time of application otherwise they risk having their contract annulled. This strategy was described as "*slipping through*" the insurance system in order to have a "*safety net.*" Similarly, participants spoke of extending this "*safety net*" to their children. Wesley, a married father of three, proposed purchasing insurance for his children to "*protect*" them from GD.

> One of the things I can do for them [children] before they have any [genetic] testing done or anything like that is to perhaps buy them some insurance policies... because once you have the insurance it's easier to keep it.... Just have them [children] do the medicals and so then at least they have something with base protection.

Some participants instructed their children to obtain insurance benefits through their workplace and avoid predictive testing until they've secured insurance.

Educating the public about HD was another method of preempting GD. Participants described talking to others about HD in an effort to reverse their perceptions of a general lack of awareness of HD in the public, referred to as the "*ignorance factor*". They took it upon themselves to provide factual information on HD whenever possible. Usually this interaction was less personal because the participants did not explicitly mention details about themselves. In this respect, preempting GD was a general educational campaign about HD and at times included an explanation of the availability and implications of predictive testing. In more intimate environments, educating individual contacts with whom participants shared their test results was a subjective and personal educational process, with the intention of avoiding a specific, personal encounter with GD. Rachel described her form of educating others as "*giving*" her friends a "*little lecture on it* [HD]" so as to avoid being "*treated differently.*" In a related approach

Wendy, a single woman in her fifties, discussed disclosing her test results "*fairly early*" in romantic relationships to avoid the potential for "*adverse reaction*" later.

Participants also took measures to ensure that their predictive test results were not listed in their medical files by instructing their geneticists not to send medical letters to their GPs. Some participants did this to minimize the chance that insurance companies discover their predictive test results if they applied for insurance in the future. Rachel said,

> What concerns me if an insurance company says that they want to look through the medical records and they find this [genetic test result], are they now going to say: "No, we're not going to cover you"?...I don't want anything on my medical file that says that's a positive result because I believe that insurance companies would treat me differently knowing that even though I'm not symptomatic.

Others were concerned that they could be treated differently by physicians when they are diagnosed with HD in the future. Participants also encouraged others to preempt GD. Zara told her nephew, "*Go back to your doctor and tell him to take it [test results] out of the [medical] file, keep it out of there.*"

Financial circumstances were also taken into account. Those in higher socio-economic positions were less concerned about preempting insurance and employment discrimination. Wesley alluded to this after he discussed his plan to purchase life insurance for his children,

> But again financially I'm not too worried because unless we have a huge stock market wreck or a big crash or something, I can help them [children], you know, if they get into a situation where, you know, this affects their ability to get insurance or whatever, you know, I can help them.

CONFRONTING GD

Unlike highly engaged participants who were concerned about the potential for GD, those who were highly engaged with GD and had an encounter with GD confronted it head on, resisting or challenging the GD experience. Confronting GD was characterized by a spectrum of approaches including: challenging the perpetrator, seeking advice, and refuting the basis for discrimination.

In responding to differential treatment such as judgmental comments participants discussed confronting their perpetrators by "*making others listen*" and telling others that they "*don't want to be treated that way.*" An experience with GD seemed to empower some to confront further discriminatory experiences. Whistle blowing became a strategy of choice for those with multiple GD experiences. Michelle, a healthcare professional,

considered her HD test result as an "*ace card*" for exposing GD. Her boss requested access to her medical files for surveillance purposes after discovering her genetic test results. Although Michelle refused this request, she believed she retained the upper hand:

> I hold the ace card basically because, if they, if I feel I am being shafted in anyway I can pull out the ace card and say prejudice....If I apply for a position and I feel that, you know, they've declined me because of Huntington's...if I feel that in any way I would have no qualms about going to the Times columnist and going hey you know...this is what's happened.

Participants also sought the advice of legal experts, protection of unions, and support of friends and trusted health care providers in confronting GD. Oliver, a participant involved in public transit who had been recently fired at the time of the interview, sought assistance from his union in dealing with conspiracy he perceived occurred among his physicians and a driving instructor which culminated in his dismissal. Others, who wanted to confront uncomfortable behavioural and communication changes in their family related to GD, sought the support of health care professionals, such as psychologists. After learning of his test results, Wesley recalled: "*She* [wife] *began to evaluate me through a different lens and she was seeing changes in me that I wasn't seeing.*" He worried that this treatment impacted their relationship. He encouraged his partner to attend joint counseling sessions "*for the sake of the relationship*."

Some participants complained of being "*shunned*" or were treated as though they had a "*contagious disease.*" When they faced a discriminatory situation some individuals attempted to refute the basis for the differential treatment. They would attempt to explain the distinction between having a gene mutation and having a disease while others would explain to others that they are not currently sick. Beth described her friends' treatment of her after she told them of her genetic test results:

> At first they treated me like I was made of glass, like I was going to break and that lasted for about a month.... [They were] just very-very careful in what they said and how they said it. I mean you could tell the effort was there but they were being very-very careful and everything they said and everything they did so it wouldn't upset me. And that just drove me nuts. And I just looked at them and I said, "I'm not sick" "I'm not dying" I said, "Sure I have this thing but I'm fine".

Individuals' tolerance for ambiguous or awkward situations determined how they confronted GD. Beth discussed her lack of tolerance for the "*shunning*" and thus

frequently confronted individuals that "*have a problem*" with her. These personality traits in addition to being generally "*strong and stubborn*" individuals were perceived to be important factors in how participants confronted GD experiences.

4.4 Discussion

The results of this study suggest four broad strategies are used to deal with genetic discrimination: "keeping low", minimizing, preempting and confronting genetic discrimination. This typology is presumed to be specific for asymptomatic individuals coping with a potentially discreditable identity as a consequence of being at increased risk for a late onset genetic disease. Given the recent attention surrounding genetic discrimination (Apse et al., 2004; Lapham et al., 1996; Peters et al., 2005), learning how individuals deal with real or potential genetic discrimination is of importance to genetics professionals in assisting individuals effectively mange these issues. Thus, these strategies may provide a framework for understanding how other individuals manage genetic discrimination for other genetic diseases for which predictive testing is available. These include breast and colons cancers, and other neurological and cardiovascular conditions such as spinocerebelar ataxias, myotonic and muscular dystrophies, Alzheimer's disease, thrombophilia, hypertrophic cardiomyopathy and Marfan Syndrome. These findings may prove particularly relevant for cancer genetics settings where calls for new approaches to address genetic discrimination during genetic counseling have been recommended (Kausmeyer et al., 2006).

Research attention has recently focused on the stigmatization and discrimination against asymptomatic individuals at risk for various genetic diseases (Apse et al., 2004; Geller et al., 1996; Lapham et al., 1996; Peters et al., 2005). The stigma-related coping literature provides a basis for understanding the results of this study. Stigma can be a source of stress for stigmatized individuals (Miller and Major, 2000), and to cope with it, individuals employ strategies that are aimed at controlling and modifying the situation by using psychological, social, behavioural, economic or educational approaches (Compas et al., 2001). Similarly, individuals found to have the HD expansion use predominantly behavioural strategies to manage the experience of GD and to control its potential. Although our typology attempts to group responses into clearly defined categories, there can be overlap between categories, especially in different contexts and situations. Consequently, different strategies may be employed by any one person at different times and across various contexts. Individuals' use of different strategies depended on their

level of engagement with GD and on the type of discrimination experience (actual or concern for the potential of GD).

The conceptualization of engagement as an underlying dimension in explaining how individuals manage the risk and experience of GD is supported by recent studies in relation to coping with stigma-related stress and genetic risk for HD (Crocker et al., 1998; Lazarus and Folkman, 1984; Taylor, 2005a). Responding to stigma always involves cognitive appraisals about the seriousness and relevance of the threat (Lazarus and Folkman, 1984). Moreover, the perception of threat is likely to occur only among stigmatized people who self-identify with the stigma (Crocker et al., 1998). Our findings support these models since a GD strategy is employed as a consequence of the individual's perception that the threat of GD is relevant to them and that they have something personal at stake. In other words, one must be engaged with GD in order to perceive GD as a threat and consequently respond to it. Moreover, the nature of one's response to GD will depend on their level of engagement with GD. Although engagement with GD is likely represented as a continuum, dichotomizing engagement was nonetheless helpful to illustrate the different strategies individuals used to manage GD.

Our results indicate that individuals who engaged with GD to a lesser extent adopted strategies of non-disclosure of their genetic test results in potentially stigmatizing situations and stayed in unsatisfying jobs because of concerns related to having the HD expansion, which is consistent with previous research (Angermeyer et al., 1987; Kittikorn et al., 2006; Peters et al., 2005; Scambler and Hopkins, 1986). The participants in our study divided their world into a large group to whom they tell nothing ("keeping low") and a small group ("*the inner circle*") who were informed of their genetic status. Medical practitioners often recommend this type of information management by instructing patients to take caution when and with whom to discuss their test results. The effectiveness of such a strategy may be called into question because some stigma theorists speculate that felt stigma (fear of discrimination) typically proves more disruptive than enacted stigma (actual discrimination) (Scambler and Hopkins, 1986). In fact, the use of secrecy to manage social stigma has been linked to emotional distress among caregivers of people living with AIDS (Kittikorn et al., 2006) and thus it is plausible that individuals who 'keep low' may experience distress. The pre-test counseling process and informed consent includes consideration of the potential implications and negative effects of having predictive testing which could be considered

an attempt to encourage greater engagement with GD. However, given the potential distress and risk of exacerbating felt stigma inherent in this process attempts should be made to temper these discussions. Given the emphasis of "keeping low" as a choice strategy for those at risk of GD, further research is warranted in exploring the effectiveness of using this strategy as well as its long term impacts on emotional well-being.

Low levels of engagement with GD coupled with an actual experience of GD resulted in the use of strategies focused on minimizing GD among participants in our study. This approach has been previously described as a disengaged response to discrimination in which participants' choose not to reflect upon or discuss the incident (Crocker et al., 1998; Lubkin, 1986). Some participants were ambivalent about whether a particular reaction constituted discrimination. Avoidance, acceptance and minimization, elements of this strategy, have also been previously reported to be associated with disengaged coping responses to discrimination (Ruggiero et al., 1997; Swim et al., 1998). Avoidance, characterized as withdrawal, resonates with the participants' desire to avoid confrontation following a GD encounter. Moreover, those who used this approach minimally engaged with GD. In fact, some research has suggested that minimal engagement is a choice strategy to cope with discrimination since individuals are able to successfully reduce psychological distress and thus maintain emotional equilibrium without taxing their coping resources (Mogg et al., 1994; Ruggiero et al., 1997). Conversely, other evidence suggests that disengaged coping responses to stigma are less adaptive strategies to cope with stigma-related stress and may lead to adverse consequences. For example, previous discrimination research has demonstrated that African Americans who accepted unfair treatment were more hypertensive than those who took some action (Krieger and Sidney, 1996). Moreover, African Americans who asserted that they did not experience racial discrimination were more likely to be hypertensive (Krieger and Sidney, 1996). As emerging evidence suggests, individuals who chose low engagement strategies may experience less distress yet perhaps at the expense of their physical well-being. Further research would be required to establish correlates between low engagement strategies and psychological or physical outcomes.

In contrast, those who engaged with genetic discrimination to a greater degree responded to its potential by preempting it. Adapting one's social interaction strategies included behaving in a socially skillful manner in the face of prejudice. Participants' measures of purchasing insurance policies before genetic testing and keeping test

results off their GP's medical files may be considered as dimensions of preempting the risk of genetic discrimination and attempting to achieve their goals despite their genetic difference. Educating the public, an important measure of preempting genetic discrimination, was evident as participants embraced opportunities to inform others about HD and in doing so attempted to change other's negative perceptions of HD. Similar approaches have been adopted by others. For example, 51% of respondents on a survey on coping with Marfan's disease endorsed the use of education as a strategy to cope with disease-related stigma (Peters et al., 2005). The use of preemptive strategies may be likened to "passing," an important response described by Goffman (1963) in which individuals act as if they have a less stigmatic identity or even a normal one (Goffman, 1963). Although the relative effectiveness of preempting GD is unknown, our results suggest that this strategy may be employed in a range of contexts and circumstances.

Resistance has been a described as a response to stigma in which participants speak out or challenge rules or the stigma (Dudley J, 1983). Similar to our results, some individuals experiencing GD confronted the incident by challenging the person or institution responsible, seeking professional advice and refuting the basis for GD. These engaged strategies are characterized by a "fight" motivation (Compas et al., 2001) and an attempt to change these circumstances. Our findings suggest that participants who confronted GD did so in certain contexts (e.g. social and family settings) and were largely individuals with a low tolerance for ambiguity.

There are several caveats in the interpretation of this study. First, participants were recruited from a larger observational study of individuals who underwent predictive testing for HD. This recruitment strategy may have biased the findings because the participants may be considered a self-selected group (Codori et al., 1994). In addition, our study primarily explored behavioural responses to the potential or experience of GD. The array of responses to stigma is vast, including emotional, cognitive, and physiological responses which can occur both voluntarily and involuntarily. Consideration of the diversity of coping responses may be necessary to gain a complete understanding of the consequences of GD. The interpretations and typology is thus tentative and we are unable to immediately generalize to a larger population. Additional research is warranted to explore the predictors and outcomes of using these strategies in a more broadly representative sample. These insights would be helpful to predict the

variation in approaches and reactions to GD among individuals found to have the HD expansion.

The results of this study have implications for the care of asymptomatic individuals living with a positive test result for HD. Genetic discrimination can be detrimental to one's well-being. Genetics professionals can assist their patients to anticipate struggles and encourage the use of engaged strategies to help them manage GD. Thus in the context of genetic counseling for HD predictive testing, it is imperative to explore patients' experiences with stigma or GD and assess individuals' resources to cope with GD. Furthermore, clinicians should mobilize effective engaged strategies and refer individuals who are struggling with issues of discrimination for additional support or legal counsel. It is through insights from stigmatized individuals that we may learn how to help others cope with potentially discreditable identities as a consequence of testing positive for a late onset genetic disease.

		Participants with HD expansion (n=37)	
		N	%
Gender	Female	23	62.2%
	Male	14	37.8%
Marital Status	Married/common-law	23	62.2%
	Single/separated/divorced/widow	14	37.8%
Education	Some college & above	31	83.8%
	Highschool & below	6	16.2%
Employment	Employed	26	70.3%
	Unemployed/homemaker	11	29.7%
Children	Have children	27	73.0%
	Have no children	10	27.0%
Time since Testing	0-4 years	9	24.3%
	5-9 years	16	43.2%
	10-14 years	10	27.0%
	15-20 years	2	5.4%

Table 4.1 Participants' demographic information

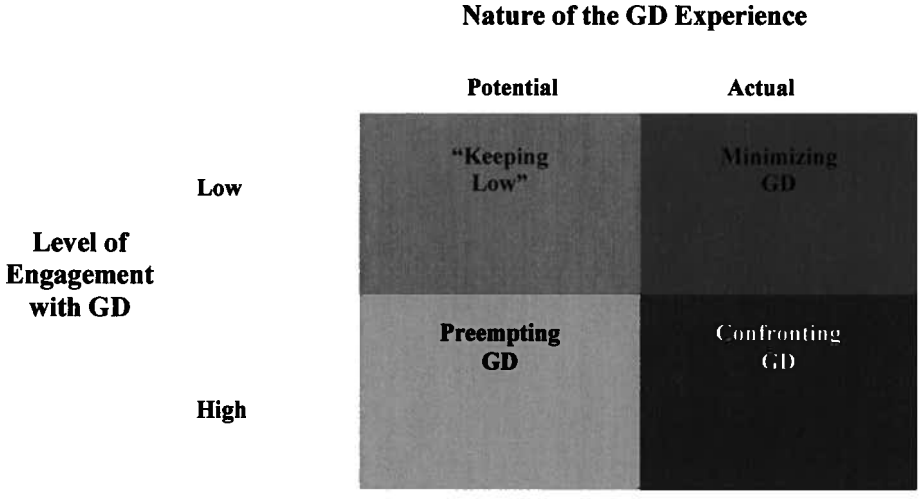

Figure 4.1 Strategies to manage genetic discrimination (GD)

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Chapter 5: The Extent of Genetic Discrimination

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Yvonne Bombard, Lauren Curry, Gerry Veenstra, Susan Creighton, Jan Friedman, Jane S. Paulsen, Joan L. Bottorff and Michael R. Hayden on behalf of the Canadian Respond-HD collaborative research group*. Family history, rather than genetic test results, is the major reason for experiences of genetic discrimination among persons at risk for Huntington disease.

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5.1 Introduction

The completion of the Human Genome and HapMap Projects along with accelerating advances in genomics has heralded a revolution in genetic medicine. Genetic medicine offers many diagnostic, treatment and reproductive options that can inform decision-making and relieve uncertainty. However, these powerful new technologies have also produced significant fear for the potential misuse of genetic information to discriminate against healthy individuals on the basis of genetic predisposition for a disease (Apse et al., 2004; Hall et al., 2005).

Indeed fear of genetic discrimination (GD) is widespread and has prevented individuals from undergoing genetic testing (Apse et al., 2004; Peterson et al., 2002) and participating in genetic research (Hadley et al., 2003), thereby hindering potentially beneficial engagement with genetic medicine and possible treatment opportunities. In the context of breast cancer, for example, many women at increased risk decline testing for the BRCA1/2 susceptibility gene for fear of health insurance discrimination (Peterson et al., 2002). Statistically half of those who decline would be positive (Peterson et al., 2002) and thus deny themselves possible psychological relief, preventative management and/or treatment opportunities due to fear of GD.

Policy makers in the United States have responded with a bill to prohibit the use of genetic information in health insurance and employment decisions. The Genetic Information Nondiscrimination Act (GINA) proposes to prohibit group and individual health insurers from using a person's genetic information in determining eligibility and setting premiums as well as requesting or requiring potential applicants to undergo genetic testing. GINA would also bar employers from using genetic test results in their hiring, firing, job placement, or promotion decisions (Hudson, 2007). GINA has now passed in the House of Representatives and is currently awaiting review in the Senate.

Despite significant efforts aimed at protecting individuals from the potential of GD, it is still unclear as to the frequency and severity of GD. In fact, evidence to support the promulgation of this law is hampered by a paucity of evidence indicating whether GD exists and in which settings. Reports of GD have been largely anecdotal to date. Early reports were often third-hand, and allegations of discrimination were usually based on disease as opposed to genetic predisposition (Apse et al., 2004; Kass et al., 2007; Lapham et al., 1996; Low et al., 1998). To date, no large-scale empirical studies have

investigated the nature and prevalence of GD in a population that is currently healthy but is predicted by genetic testing to have a very high likelihood of developing a genetic disease.

Huntington disease (HD) was the first adult-onset genetic disease for which a predictive test was developed that allows at-risk individuals to know with near certainty whether they inherited the causative CAG trinucleotide expansion in the *HD* gene (Langbehn et al., 2004; MacDonald et al., 1993). The introduction of the HD predictive testing program has led to the advent of a new group of individuals - individuals who have the CAG expansion and are currently healthy yet are destined to develop the disease should they live long enough. GD was identified as a potential risk of predictive testing (Craufurd and Harris, 1986; Perry, 1981), yet little is known about whether predictive testing for HD actually results in discrimination. While discrimination on the basis of family history has been known to occur in the insurance context (Harper et al., 2004), the question of whether predictive testing for HD confers heightened risk of discrimination has yet to be answered. We assessed the nature and prevalence of GD in a cohort of asymptomatic genetically tested and untested individuals at risk for HD. We also examined whether genetic testing is associated with increased levels of GD.

5.2 Methods

Study Population

A cross sectional survey of asymptomatic persons at risk for HD was undertaken. Seven genetics and movement disorders clinics, servicing rural and urban communities and representing ten of Canada's provinces, were invited to participate. Approval of the relevant research ethics boards was received.

A total of 300 asymptomatic individuals at risk for HD were targeted in the following three categories: individuals who underwent genetic testing and were found to have the HD mutation (HD+), individuals at 50% risk who were found not to have the HD mutation (HD-), and individuals who chose not to undergo genetic testing for HD (Not Tested; NT). We chose to focus on experiences of GD based on genetic information rather than discrimination experiences based on symptoms of HD or disability concerns. Asymptomatic individuals were identified from clinical charts using the Unified Huntington Disease Rating Scale (UHDRS) and recent neurological assessments. The population of interest included all individuals age $\geq$ 18 years from HD families who had

UHDRS scores $\leq$ 2 and had not been diagnosed with signs or symptoms of HD within the past year.

Development of the Survey Instrument and Testing

The study instrument was developed based on an initial qualitative study of the experiences and concerns of GD among persons at risk for HD (Bombard et al., 2007a; Bombard et al., 2007b) and included questions adapted (with permission) from the validated and frequently used instruments developed by Taylor et al (Taylor et al., 2004) and Krieger et al (Krieger et al., 2005). The study instrument was validated by an expert reference group who individually critiqued the questionnaire to ensure that the items were relevant and consistent with GD issues experienced by persons at risk for HD. Cognitive interviews were used to test for uniformity in comprehension and comfort with question wording and response formats. The pretest questionnaire was mailed to 19 individuals in order to test the comprehension of questions, instructions and skip patterns and pilot the data collection procedures and to ensure variability in the data.

The final questionnaire included 122 questions and skip patterns suitable for the 3 subgroups of our study. The sections focused on: (1) genetic status and family history (FH) of HD, (2) perceptions of genetic testing, (3) concerns and experiences of knowing about FH, (4) concerns and experiences of knowing genetic test results (GTR), (5) specific incidents of disadvantage or unfair treatment, (6) thoughts and experiences related to insurance, (7) knowledge and attitudes towards genetic issues and (8) socio-demographic information.

Assessment of Family History & Genetic Status

Respondents were asked the following question with regard to their family history: "In approximately what year did you first become aware that HD was in your family?" The genetic status of the respondents was assessed using the following question: "have you had a genetic test for Huntington disease?" The follow-up questions were: "in what year did you have the genetic test?" and "did you get a positive test result (i.e. you have inherited the HD gene expansion)?" Responses to these questions formed the basis for classifying individuals as tested, not tested, HD+ and HD-.

Assessment of experiences of genetic discrimination

We asked respondents whether they have ever experienced discrimination in various situations because of their FH. To differentiate between experiences of GD

based on GTR as opposed to experiences of GD based on FH, we also asked tested respondents whether they have ever experienced discrimination in similar situations based on their GTR. We operationalized discrimination as 'being unfairly prevented from doing something or being treated differently' which was the dominant interpretation provided by participants in the qualitative study. A total of twenty-three possible contexts for discrimination were provided to the respondents, as listed in Table 5.2. Response categories were yes, no and not applicable. Respondents who checked yes to any category were considered to have had an experience with GD. In order to identify the prevalence of GD in major settings, the 23 items were collapsed into the following sub-categories: insurance, employment, social, family, government and health care, as indicated in Table 5.2.

The questionnaire also included the following open-ended question to allow respondents to describe or further elaborate on their experience(s): "Are the any clear incidents of disadvantage or unfair treatment related to your family history of HD or genetic test results?" Quotes were selected that represented the most frequent type of GD experience in a particular setting or that provided details of the event that occurred.

ASSESSMENT OF PSYCHOLOGICAL DISTRESS

Psychological distress was chosen *a priori* to be a primary psychological outcome measure since it has been previously associated with racial, gender, sexual and ethnic discrimination (Amaro et al., 1987; Landrine et al., 1995; Meyer, 1995; Williams, 1997). Respondents nominating at least one experience of GD were asked to rank the resulting level of distress they experienced on a scale of 1-5 (where 1 indicated 'not distressing' and 5 indicated 'very distressing').

DEMOGRAPHIC INFORMATION

Respondents were asked to report their age, marital status, employment status, whether they had children, the highest grade or level of education attained, cultural background, income level, the type(s) of insurance purchased and which of their parents had HD and their age of onset.

ADMINISTRATION OF THE SURVEY

The questionnaires were administered during individuals' annual scheduled clinic appointments or by mail between June and December 2006. Using the Dillman tailored design survey method (Dillman, 2000), postal respondents were mailed the

questionnaire, a personalized introductory letter, a postage-paid return envelope and a $25 honorarium by health professionals at each clinic. Approximately one week after the initial mailing all postal respondents were sent a reminder/thank you postcard. A second set of survey materials was sent to non-respondents four weeks after the initial mailing. Additional telephone contact was made with non-respondents after five weeks. Written consent was obtained from all respondents.

STATISTICAL ANALYSIS

Descriptive statistics are reported for the experiences and prevalence of GD. The prevalence of GD is reported in three dimensions: GD based on FH, GD based on GTR and overall (i.e. we made no distinction between FH and GTR; those who reported an experience of GD based on either or both FH and GD were counted once). The Fisher's exact test and Pearson's chi-squared tests of significance were used to investigate baseline demographic differences between the study groups (tested (HD+ & HD-), not-tested (NT), HD+, HD- & NT) as well as differences between the study groups and settings among respondents reporting experiences of GD. Comparisons of means were conducted using Mann-Whitney U and Kruskal Wallis tests[1]. Logistic regression analysis was used to develop a model to predict the likelihood of experiencing GD. Three regression models were developed: (1) unadjusted: where all variables were entered in the model individually, (2) adjusted for age, and (3) adjusted for all demographic factors. All analyses were conducted using the statistical software package SPSS version 11.5.

Significance tests were two-tailed and alpha was set to 0.05. The false discovery rate (FDR) procedure was used for multiple comparisons in our exploratory analyses (sub-analyses of differences in GD between groups within the various settings, given that there are over 42 comparisons). Since fewer comparisons were being made in our hypothesis-driven analyses (overall differences in GD between tested versus untested respondents, HD+, HD- & NT, i.e., 4 comparisons), no procedure to correct for multiple comparisons was deemed necessary.

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[1] Non-parametric tests were used since the sample size was relatively small and the parameters of the variables of interest were unknown.

5.3 Results

CHARACTERISTICS OF THE RESPONDENTS

Of the 299 individuals invited to participate in the survey, 239 individuals returned a completed questionnaire, representing an overall response rate of 80%. Six surveys were excluded from analyses since these individuals were found to have UHDRS scores >2 at some point after consenting to join the study but before completing the survey questionnaire, rendering an adjusted response rate of 79.5% (233/293). Characteristics of the remaining 233 asymptomatic respondents are presented in Table 5.1. No significant differences in baseline characteristics were detected between the study groups. Furthermore, there were no significant differences between the responders and non-responders with respect to gender (P =0.206), age (P =0.077), test status (P =0.334) and gene status (P =0.365). Socio-demographic characteristics of our sample appear similar to those of other HD populations in North America (Almqvist et al., 2003; Babul et al., 1993; Codori and Brandt, 1994; Quaid and Morris, 1993; Wiggins et al., 1992) and the Netherlands (van, I et al., 1994) as well as several other genetic populations (Apse et al., 2004; Armstrong et al., 2003; Hall et al., 2005; Kass et al., 2007) with the general exception that our sample is older and more educated.

NATURE AND EXTENT OF GENETIC DISCRIMINATION

Table 2 shows that genetic discrimination was reported by 39.9% (n=93) of the sample. Discrimination experiences were most prevalent in insurance (n=68, 29.3%), family (n=36, 15.5%) and social (n=29; 12.6%) settings, with discrimination in employment, health care and government settings reported less frequently as shown in Table 3.

In the insurance setting, discrimination occurred most often in relation to life insurance (n=63, 27%) and long-term disability insurance (n=49, 21%). Seventy respondents (30.0%) completed the open-ended area of the questionnaire, elaborating

on their experiences[2]. Some respondents offered the following descriptions of their insurance-related experiences: "*I was so angry because I was told I was denied* [life insurance] *because of my gene*", "[I was] *refused coverage for life insurance due to* [my] *family history. They wanted me to take the test and find out the results to determine if they would give me coverage*", "*insurer agreed to provide insurance but at a rate over 10 times higher then the normal because of the family history of HD...at the time* [I] *did not receive genetic testing*".

In the family domain discrimination occurred most often in reference to making reproductive decisions (n=27, 11.6%) and experiences with family members (n=15, 6.4%). Respondents explained: "[My] *mother and brother* [were] *insisting* [that] *I get tested when I was pregnant* [saying] *it was my responsibility*", "[A] *family relative voiced her opinion that I might not want to complete a master's degree given I had tested positive for HD.*"

Within their social circles, some respondents believed they were sometimes treated unfairly by their friends (n=18, 7.7%) and when establishing relationships (n=14, 6.0%). A respondent mentioned "*basically* [boyfriend] *dumped me* [after testing positive]." In health care, most discrimination was reported to occur when getting medical care (n=11, 4.7%), by doctors (n=8, 3.4%) and by other health care professionals (n=7, 3.0%). One respondent shared that "[my] *doctor recommended not having children when Father's diagnosis was disclosed that he had HD.*"

There were few reports of GD within employment settings (6.9% overall). When reported, GD occurred most often at work (n=15, 6.4%) as opposed to gaining access to jobs n=7, 3.0%). One man explained: "*I disclosed my positive result to my employer.* [I] *was denied a promotion, in large part, because of the perceived future liability to the company.*" Another tested woman described her experience prior to her genetic testing: "*I was denied an opportunity to interview for a more senior position in my present place*

[2] Respondents offered descriptions of GD experiences related to most settings; however, the majority of descriptions involved insurance (n=36), family (n=11) and employment (n=9). Experiences related to health-care (n=8), social (n=3) and government (n=2) were offered less frequently. One respondent's description was not clear and thus was not categorized.

of employment, despite that I had the necessary skills, knowledge, and experience. The manager responsible for hiring for the position told me they thought that I was not interested in upward professional mobility and that my greater focus was on having a more well rounded life, that the job was a more demanding one than I wanted - despite the fact that I applied for the job and thought that to be a clear indicator of my interest in it."

In government settings, discrimination was reported infrequently (3.9%) but when reported it occurred most often in reference to getting access to or custody of children (n=5, 2.1%), in the law courts (n=4, 1.7%) and during adoption (n=3, 1.3%). The following tested respondent offered her experience prior to undergoing genetic testing: "*We had already been approved and were waiting to adopt when my mother was diagnosed with HD. All of a sudden,* [we were] *no longer considered a viable couple.* [We were] *told* [we] *could adopt a special needs child but not a healthy baby.*"

GENETIC STATUS AND GENETIC DISCRIMINATION

As table 5.3 shows the proportion of respondents who experienced GD was at least 16% higher in the HD+ group than in the HD- ($\chi^2 P$=0.042) and NT ($\chi^2 P$ =0.045) groups. This suggests that respondents who test positive for HD are the most likely to report experiences of GD. Interestingly, there were no significant differences in the proportions of GD experiences between HD- and NT respondents (n=29/84; 34.5% vs. n=22/66; 33.3%, χ^2 *P* =1.00), suggesting that testing negative for HD may not necessarily decrease the likelihood of experiencing GD (a possible explanation is offered below).

Trends across most of the settings and groups suggest that reports of GD by HD+ respondents were up to 11.2% higher than in the HD- group and up to 15.3% higher than in the NT group (Table 3). In fact, compared to NT respondents, reports of GD by HD+ respondents were 15.3% higher in the family setting (χ^2 *P*=0.013), 14.4% higher in social settings (χ^2 *P*=0.016) and 12.9% higher in employment settings (χ^2 *P*=0.007) (*P*-values did not reach the required FDR-adjusted significance levels of *P*≤0.007, 0.011 and 0.005, respectively). Moreover, within the employment setting, HD+ respondents also reported 10.9% more experiences of GD than HD- respondents (χ^2 *P*=0.016 – above the required level of significance of *P*≤0.010).

When comparing discrimination experiences between the tested (i.e. HD+ & HD-) and NT groups, the proportion of respondents who experienced GD was 9.2% higher in

the tested group (n=71 vs. 22, χ^2 P =0.236; Table 3). Although this difference is not significant at the group level, trends across most of the settings indicate that tested respondents experienced 5 -11% more GD than did NT respondents. Specifically, in the family and employment settings, tested respondents reported 7.5 and 11% more GD than those who did not test (family: n=31 vs 5 [χ^2 P =0.044] and employment: n=15 vs. 1 [χ^2 P = 0.045]. However, after adjusting for multiple comparisons, these differences were not statistically significant (the required levels of significance were $P \leq 0.014$ and $P \leq 0.015$, respectively).

In summary, while participating in genetic testing itself is not significantly associated with discrimination, testing positive for HD is associated with an increased likelihood of reporting discriminatory experiences that tend to occur mostly in family, social and employment settings.

REPORTED REASONS FOR GENETIC DISCRIMINATION

Respondents' family histories (FH) rather than their genetic test results (GTR) were reported as the major reason for GD. Among the 71 tested respondents who reported at least one experience of GD, 41 individuals attributed their experience(s) to their FH while 13 of the respondents believed that their GTR was the major reason for their discriminatory experiences. Seventeen tested respondents (17/71; 24%) attributed their experiences to both FH and GTR[3].

Attribution differences varied between the HD+ and HD- groups. Among 29 HD- respondents, two respondents attributed their GD experiences to both their FH and GTR, 26 respondents attributed their discriminatory experiences to their FH alone while one individual ascribed the experience to her test results only. This woman reported GD among her siblings, noting that *"they were envious"*.

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[3] Statistically significant differences in proportions between experiences of GD based on FH versus GTR were not assessed since non-parametric tests on paired samples, such as the McNemar's test of marginal homogeneity, do not take into account the respondents who chose both FH & GTR which represent an important category of responses.

Attribution differences were less evident among the 42 HD+ respondents. Fifteen HD+ respondents attributed their GD experiences to both their FH and GTR. Among the 27 respondents who distinguished between the bases of their experience(s), 15 individuals believed they were discriminated against because of their FH and 12 others considered their GTR to be the primary reason for their GD experience(s). It is notable that a large proportion of the HD+ respondents (n=15) attributed their GD experiences to their GTR and FH.

PREDICTORS OF GENETIC DISCRIMINATION

The results of the regression models predicting GD are reported in Table 4. The models have an overall R squared of 0.064, 0.083 and 0.204, respectively. Individuals who reported first-hand experience with HD, were aware of their FH at a younger age and knew about their FH for over 15 years were at greater risk of experiencing GD (Table 4). Individuals who had known people with HD symptoms or who have died from HD were more likely to report GD (OR = 3.36, P=0.01). Respondents who have known about their FH for 15 years or more also were more likely to report GD (OR = 2.63, P=0.005). Older individuals were less likely to experience GD (OR = 0.95, P=0.004). While a significant association existed between having a college/university degree and experiencing GD (OR = 2.03, P=0.038), this relationship was not significant after adjusting for socio-demographic factors.

The odds of experiencing GD were 3.39-3.55 times as high for respondents who became aware of their FH before age 34 compared with those who learned about it when they were over 35 years old (P=0.016). The majority of GD among those who learned about their FH at a young age occurred in reference to insurance (χ^2, P=0.005), in the family (χ^2, P=0.033) and in the health care setting (χ^2, P=0.006).

PSYCHOLOGICAL DISTRESS AND GENETIC DISCRIMINATION

Psychological distress was found to be associated with the experience of GD (χ^2: relationship between distress and GD based on FH: $P \leq 0.0001$ and GD based on GTR:

P=0.011[4]). Experiencing GD in more situations based on FH and GTR was associated with increased levels of distress (Pearson R = 0.384 and 0.526, $P \leq 0.0001$, respectively).

Among those who attributed their experiences of GD to FH only, the mean level of distress was 3.57 (n=63 [tested n=41, NT n=22], SD=1.28). Levels of distress related to GD based on FH did not differ between the tested and NT groups (tested mean=3.51 vs. NT mean=3.68, Mann-Whitney U P=0.480) nor between all three groups (HD+=3.00, HD-=3.81, NT=3.68, Kruskal Wallis P=0.121).

Among those who attributed their experiences of GD to GTR only, the mean level of distress related to GD based on GTR was 2.85 (n=13, SD=1.56). Distress levels did not significantly differ between HD+ and HD- respondents (HD+=2.92 vs. HD-=2.00, Mann-Whitney U P=0.769).

Among those who attributed their experiences of GD to both FH and GTR, the mean level of distress was 3.65 (n=17, SD=1.32). Interestingly, levels of distress did not differ significantly between perceived causes of GD (FH vs GTR vs both, Mann-Whitney U P>0.05) or genetic status (Mann-Whitney U P=0.721).

5.4 Discussion

This is the first study to report the nature and prevalence of GD among asymptomatic individuals who have participated in genetic testing in comparison to individuals who chose not to be tested. Discrimination was reported by 40% of the sample and occurred most often in reference to life and disability insurance, making reproductive decisions, friends and establishing relationships. Testing positive for HD was associated with increased experiences of GD. FH appears to be a major reason for and predictor of experiences of GD. Those who discover their FH at a younger age and know of their FH for longer are also at greater risk for GD. Our results demonstrate that GD is a significant social issue and source of distress for persons at-risk for HD.

These results raise important ethical, legal and social issues regarding genetic information and the consequences of genetic testing. Clearly, reports of discrimination

[4] Due to the small sample sizes, ranks 1-3 and 4-5 were collapsed to represent low-moderate and high levels of distress

experiences were relatively common among persons at-risk for HD with forty percent of the respondents reporting at least one experience of GD. Nearly one in three respondents experienced insurance discrimination, largely by life and disability insurance companies in the forms of insurance rejection, premium increases or requests to take a predictive test. Discrimination by insurance is a significant concern among various at-risk populations (Apse et al., 2004; Hall et al., 2005; Peterson et al., 2002) and studies have shown that genetic populations are at greater risk for insurance GD compared to both the general population (Low et al., 1998) and those with common disorders (Kass et al., 2007). However, our results do not support such trends as genetic status was not associated with increased levels of GD in the insurance settings. It has been documented that individuals at-risk for HD employ various strategies to manage GD (Bombard et al., 2007b), thus it is plausible that these findings support the notion that individuals may be preempting GD by purchasing insurance prior to undergoing genetic testing.

Surprisingly, family and social circles were the next major sources of discriminatory experiences. Twelve - fifteen percent of the respondents reported GD in these settings, mostly with regards to reproductive decision making, by relatives and friends and when establishing relationships. No survey to date has explored discrimination in areas other than insurance and employment; and our results are the first to report experiences of discrimination in the family context. However, discrimination in the family must be viewed through a wider lens that captures the profound impact the presence of HD has on the family system. Often when HD is known to be present in a family it becomes part of that family's identity and patterns of behaviour. Genetic testing has also been shown to have profound impact on family functioning (Sobel and Cowan, 2000). As others have aptly recognized, the decision to test itself can become a "litmus test by which relatives perceive and judge each other's loyalty to the family" (Sobel and Cowan, 2000) and predictive testing often produces a "ripple effect" across the family system (Kessler, 1994). Our findings that tested respondents experienced more GD than those who chose not to participate in testing are consistent with previous reports of relationship and communication changes within the family system following testing (Sobel and Cowan, 2000) and respondents' perception of these changes as discriminatory (Bombard et al., 2007a).

Contrary to expectations, discrimination in the health care, employment or government settings was only cited by 4-8% of respondents, largely in reference to

getting medical care, work, doctors, other health professionals or when getting custody and access to children. Despite significant concern for GD in the employment context (Harper et al., 2004), very little GD seems to be occurring in this setting. Furthermore, the low levels of GD in the health-care domain support the assumption that health care professionals have a better understanding of genetic risk, family history and test results, and likely use such information appropriately.

Interestingly, tested respondents attributed their experiences of GD to their FH more often than to their genetic test result. These results lend further support to the similar levels of discrimination seen between the tested and untested study groups: regardless of testing status, most individuals believed that FH was the predominant reason for their discriminatory experiences. These findings suggest that disease-related stigma is an important underlying issue and that more education and awareness of genetic disease is needed in our society. Respondents who tested positive, however, attributed their discriminatory experiences more often to both their FH and GTR. While it may have been more difficult for these participants to differentiate between the causes of discrimination, it seemed that these two aspects are inextricably linked: only after inquiring about one's FH do third parties inquire further about genetic testing. The interactive effects of one's FH and GTR may not be easy to discern retrospectively for individuals after they have completed genetic testing. A prospective, longitudinal study including (future) test participants and non-participants should be conducted to address differences in experiences of GD before and after genetic testing. Nonetheless, the finding that both GTR and FH are perceived to play an important role in discriminatory experiences points to the fundamental nature of the FH in people's social interactions regardless of testing status. Clearly, there is a need to shift the current focus of GD as a genetic testing issue to one which equally highlights the significant impact FH plays in people's lives.

Family history of HD was also found to be the major predictor of GD experiences. The effects of knowing one's FH for a long period of time, becoming aware of the FH at a younger age and knowing individuals with HD symptoms or who have died contributed substantially to the likelihood of experiencing GD. These results further support the significant influence that the FH plays in individuals' discriminatory experiences. Learning of one's FH early in life likely impacts future insurance eligibility assessments and general life plans. Indeed, FH and experience with HD are important frameworks underpinning individuals' marital, reproductive, career and predictive testing decisions

(Cox and McKellin, 1999; Taylor, 2004). Moreover, age at perceived parental onset and knowledge of FH are significant factors in psychological functioning before and after predictive testing for HD (Decruyenaere et al., 1999; McAllister, 2002).

These results point to the delicate balance involved in choosing the appropriate time to inform children of their FH of HD and personal genetic risk. While studies suggest that adult children prefer early disclosure of genetic risk and that growing up knowing about HD at an early age allows youth to cope better when relatives are symptomatic (Forrest, 2007; Forrest et al., 2007; Holt, 2006), our results suggest that discovering the FH at a young age increases their risk for GD. The question thus remains as to whether it is better to live a life as long as possible without the knowledge of a potential impending disease or whether it is better to learn about one's genetic risk early and plan one's life and manage the possible psychosocial consequences accordingly. Further research around these critical issues is warranted.

It is important to note that psychological distress was found to be a significant outcome of GD. The psychological consequences of GD to date have not been explored and our results indicating associations between distress and GD are consistent with documented associations of distress with racial, gender, sexual and ethnic discrimination (Amaro et al., 1987; Landrine et al., 1995; Meyer, 1995; Williams, 1997). Moreover, psychological distress was not found to differ on the basis of perceived cause or group, this suggests that psychological distress is a fairly universal outcome of GD. These results point to the need to view GD as a mental health and social issue that requires appropriate counselling and support.

The prevalence of insurance GD among persons at risk for HD was generally consistent with previous surveys of GD among other genetic and non-genetic populations, which indicate that 25-33% of individuals were denied life insurance or offered it at a prohibitive rate (Kass et al., 2007; Lapham et al., 1996; Low et al., 1998). However, there are a few exceptions of note. An Australian study investigating the use of GTR in life insurance underwriting decisions found only one case of a HD+ applicant disclosing his GTR who received coverage at standard rates but the policy was limited to 50 years of age (Otlowski et al., 2007). Moreover, persons with an HD+ GTR in the U.K. are not declined life insurance even though insurers are permitted to use the HD GTR for underwriting purposes of policies in excess of £500,000 (Otlowski et al., 2007; Secretary of State for Health, 2003). Furthermore, applicants with a FH of HD are not imposed higher premiums or 'loadings' (Otlowski et al., 2007). Thus, in practice, reported

experiences of GD in Canada may be more frequent than the U.K. because regulations restricting the use of genetic information by insurers are not in place and those with FH of HD are commonly required to pay higher premiums. Our results highlight the need for legislative protection against GD in insurance as well as a need to pay special attention to family and social domains during pre- and post test counselling.

These findings are particularly important in light of the US federal genetic nondiscrimination bill (GINA) under consideration by the Senate. Given the availability of a universal health care in Canada, similar legislation would allay GD in employment and extended health insurance plans. Such protections may ameliorate the increased premium rates for health insurance plans for those with a FH of HD. Although GD in employment was not a frequent occurrence in this Canadian HD sample, GINA may alleviate persons' concerns for GD in this setting. However, GINA does not address the commonly occurring life and disability insurance discrimination, the disrupted social and family relationships nor unfair treatment in health care and government domains.

Other avenues are thus needed to assist persons at risk for HD and other genetic disorders to mitigate GD. Discrimination affects all aspects of people's lives; it impacts self-esteem (Link and Phelan, 2001) and, as the findings of the present research indicate, limits their participation in our society. Clearly, comprehensive education and support programs are needed to inform and engage society about genetics to reduce ignorance and the resultant level of stigma and discrimination. Support groups are common for many hereditary disorders and may be used to strengthen social support networks and provide information and support for persons to lodge formal complaints in relevant jurisdictions. Ultimately, structural interventions are necessary to change the social climate around genetic diseases. Given the vacuum of legal protection from GD in many countries, current human rights legislation ought to include genetic information or future disability under the rubric of anti-discrimination laws.

The current findings should, however, be interpreted in light of the study's methodological limitations. Our findings are based on data from ten Canadian provinces and may not be generalizable to other jurisdictions. The cross-sectional design did not allow us to make definitive conclusions about causal effects of genetic status or FH on experiences of GD. Longitudinal studies of the experiences of GD are needed. In addition, GD experiences were self-reported and could not be validated. Although discriminatory experiences are inherently subjective experiences, self-reports of discrimination are commonly used. Previous studies have shown consistent

associations between self-reports of discrimination and health consequences ranging from mental health, substance abuse to physiological outcomes (Amaro et al., 1987; Landrine et al., 1995; Meyer, 1995; Williams, 1997).

Our sampling strategy relied on reports of discrimination among persons attending clinics and participating in research. Individuals who actively participate in research and predictive testing may be more resourceful and better able to cope with the psychosocial consequences of testing and/or research. The motivation and emotional well-being of people who are connected with clinics and participate in research or predictive testing may therefore be unrepresentative of the general at risk HD population. It is thus possible that our results represent an overly optimistic view of the nature and extent of genetic discrimination. Alternatively, study participants may be more cognizant of the issue of GD and thus be better able to recognize its occurrence. Finally, our measure of psychological distress was not a diagnostic instrument and can only be interpreted as a sign of negative effect or emotional difficulty not as psychological distress per se.

This is the first study to report the nature and prevalence of GD among asymptomatic individuals who have participated in genetic testing in comparison to individuals who chose not to be tested. This is also the first study to distinguish between discrimination based on FH and GTR, explore the breadth of GD across a wide variety of settings and examine the psychological impact of GD. Our findings demonstrate that GD is common in this sample, and that FH appears to be a major reason for and predictor of experiences of GD. Those who discover their FH at a younger age and know of their FH for longer are also at greater risk for GD. Testing positive for HD is associated with increased experiences of GD. Moreover, GD is a significant social issue and source of distress for persons at-risk for HD.

	Total (n=233)		HD+ (n=83)		HD- (n=84)		Not Tested (n=66)		p-value[a]
	n	%	n	%	n	%	n	%	
Gender									
Female	153	65.7%	53	63.9%	52	61.9%	48	72.7%	0.35[c]
Male	80	34.3%	30	36.1%	32	38.1%	18	27.3%	
Average Age	45.5 (11.7)[b]		47.0 (11.0)[b]		46.0 (13.7)[b]		42.9 (9.5)[b]		0.09[d]
Marital Status (n= 231)									
Married/common law	176	76.2%	64	79.0%	59	70.2%	53	80.3%	0.27[c]
Single/separated/divorced/widowed	55	23.8%	17	21.0%	25	29.8%	13	19.7%	
Education (n=226)									
Some college & above	206	91.2%	77	95.1%	72	88.9%	57	89.1%	0.30[c]
High school & below	20	8.8%	4	4.9%	9	11.1%	7	10.8%	
Employment (n=228)									
Employed	165	72.4%	56	68.3%	55	67.1%	54	84.4%	
Unemployed and seeking work	11	4.8%	4	4.9%	3	3.7%	4	6.3%	–[c,e]
Unemployed and not seeking work	52	22.8%	22	26.8%	24	29.3%	6	9.4%	
Children (n=232)									
One or more children	169	72.8%	61	74.4%	64	76.2%	44	66.7%	0.40[c]
Have no children	63	27.2%	21	25.6%	20	23.8%	22	33.3%	
Community/Setting[f] (n=233)									
Urban	192	82.8%	65	78.3%	73	86.9%	54	81.8%	0.34[c]
Rural	41	17.7%	18	21.7%	11	13.1%	12	18.2%	
Time since testing (n=150)									
4 years or less	77	51.3%	37	50.0%	40	52.6%	n/a		
5-9 years	35	23.3%	19	25.7%	16	21.1%	n/a		0.80[c]
10 years or greater	38	25.3%	18	24.3%	20	26.3%	n/a		
Time since learning of FH (n=211)									
9 years or less	61	28.9%	23	29.9%	18	24.3%	20	33.3%	
10-19 years	56	26.5%	25	32.5%	15	20.3%	16	26.7%	
20-29 years	48	22.7%	15	19.5%	19	25.7%	14	23.3%	0.38[c]
30-31 years	33	15.6%	11	14.3%	14	18.9%	8	13.3%	
40 years or greater	13	6.2%	3	3.9%	8	10.8%	2	3.3%	

a Missing values are excluded, values are two-sided
b Values are mean (SD)
c 2x3 Pearson chi-square
d One-way anova
e Does not meet assumptions of chi-square test
f Based on Statistics Canada's rural postal code definition whereby individuals with a "0" as the second character in their postal code live in areas where there are no letter carriers and are considered to live in rural or small towns (ref: Statistics Canada. Rural and small town Canada anlaysis bulletin, 3(3). November 2001).
FH: Family History

Table 5.1 Demographic characteristics of respondents

Setting/Item	TOTAL n	TOTAL %
Overall	93	39.9%
Insurance		
by life insurance company or agent	63	27.0%
by long term disability company or agent	49	21.0%
by mortgage company or agent	13	5.6%
Family		
when making choices about having children	27	11.6%
by family member	15	6.4%
by spouse	13	5.6%
Social		
by friend	18	7.7%
when establishing a relationship	14	6.0%
by boy/girlfriend	9	3.9%
by community	7	3.0%
at school	5	2.1%
by religious organization	2	0.9%
Employment		
at work	15	6.4%
when getting a job	7	3.0%
Health Care		
when getting medical care	11	4.7%
by doctor	8	3.4%
by other health care professional(s)	7	3.0%
by genetic counseling service	5	2.1%
Government		
when getting access to or custody of children	5	2.1%
in the law courts	4	1.7%
by adoption agency	3	1.3%
by blood bank	2	0.9%
by Canadian Forces	2	0.9%

Respondents selected all that applied.

Table 5.2 Experiences of genetic discrimination

(Respondents reporting 'yes', they did experience discrimination as a result of either or both their family history and genetic test result)

	TOTAL		Tested (n=167)		Not Tested (n=66)			HD+ (n=83)		HD- (n=84)		NT (n=66)		
	n	%	n	%	n	%	P-Value[a]	n	%	n	%	n	%	P-Value[b]
Across all settings	93	39.9%	71	42.5%	22	33.3%	0.236	42	50.6%	29	34.5%	22	33.3%	0.046
Insurance*	68	29.2%	53	31.7%	15	22.7%	0.202	31	37.3%	22	26.2%	15	22.7%	0.112
Family*	36	15.5%	31	18.6%	5	7.6%	0.044[c]	19	22.9%	12	14.3%	5	7.6%	0.034[c]
Social*	29	12.4%	25	15.0%	4	6.1%	0.078	17	20.5%	8	9.5%	4	6.1%	0.018[c]
Employment*	16	6.9%	15	9.0%	1	1.5%	--[c,d]	12	14.5%	3	3.6%	1	1.5%	0.003[c]
Health Care*	20	8.6%	14	8.4%	6	9.1%	0.802	11	13.3%	3	3.6%	6	9.1%	0.081
Government*	9	3.9%	9	5.4%	0	0.0%	--[d]	5	6.0%	4	4.8%	0	0.0%	--[d]

* Categories are not mutually exclusive

[a] Fisher's exact test. Values are two-sided

[b] Pearson chi-squared test. Values are two sided

[c] Did not reach significance after adjusting for multiple comparisons

[d] Does not meet assumptions of test

Table 5.3 Prevalence of genetic discrimination

(Respondents reporting 'yes', they did experience discrimination as a result of either or both their family history and genetic test result)

Table 5.4 Predictors of genetic discrimination

	Experience of Genetic Discrimination (n=181)					
	Model 1 - Unadjusted		Model 2 - Adjusted for Age[a]		Model 3 - Adjusted for SDF[b]	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (years)	0.96 (0.93-0.98)	**0.001**	-	-	0.95 (0.92-0.98)	**0.004**
Female	0.87 (0.46-1.64)	0.669	0.77 (0.40-1.48)	0.431	0.88 (0.44-1.78)	0.728
College or University Degree	2.03 (1.04-3.97)	**0.038**	1.75 (0.88-3.48)	0.113	1.74 (0.84-3.57)	0.134
Income ≥$40,000	1.39 (0.77-2.51)	0.281	1.33 (0.72-2.45)	0.363	1.23 (0.60-2.51)	0.568
Have at least one child	0.95 (0.48-1.87)	0.882	1.32 (0.64-2.73)	0.448	1.35 (0.59-3.07)	0.477
Married or common law	1.27 (0.63-2.58)	0.507	1.51 (0.72-3.17)	0.277	1.32 (0.58-3.01)	0.509
Employed	1.68 (0.83-3.39)	0.152	0.99 (.44-2.21)	0.972	0.89 (0.37-2.12)	0.804
Have life insurance	1.11 (0.53-2.31)	0.783	1.21 (0.52-2.40)	0.770	0.96 (0.42-2.21)	0.917
Had genetic testing	1.33 (0.68-2.62)	0.411	1.65 (0.81-3.34)	0.166	1.60 (0.76-3.34)	0.214
Known people with HD or who have died from HD	3.51 (1.44-8.56)	**0.006**	3.28 (1.32-8.14)	**0.011**	3.36 (1.33-8.50)	**0.010**
Learned about Family History ≥15 yrs ago	2.05 (1.10-3.79)	**0.023**	2.50 (1.30-4.82)	**0.006**	2.63 (1.33-5.18)	**0.005**
Age when FH was discovered[c]	-	**0.001**	-	**0.024**	-	**0.016**
Discovered FH under 18 yrs old	4.28 (1.89-9.68)	**<0.0001**	3.10 (1.25-.7.68)	**0.015**	3.39 (1.33-8.63)	**0.010**
Discovered FH between 19-34 yrs old	4.18 (1.82-9.62)	**0.001**	3.23 (1.32-7.89)	**0.010**	3.55 (1.42-8.86)	**0.007**

Respondents were considered to have an experience of genetic discrimination if they responded yes to either or both of the following questions:
"Have you ever experienced genetic discrimination in any of the following situations because of your *family history of HD*?"
"Have you ever experienced genetic discrimination in any of the following situations because of your *genetic test results*?"

Legend:

[a] Odds ratios were adjusted for age

[b] Odds ratios were adjusted for the following socio-demographic factors (SDF): age, gender, education, marital status, children, employment & income.

[c] The reference category is 35 yrs and older.

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Chapter 6: Discussion

6.1 Introduction

The findings of this study provide a contribution to the ethical, legal and social implications (ELSI) produced by genetic testing and genetic discrimination (GD) in particular. Since the beginning of the Human Genome Project and HapMap Project the investigation of ELSI issues has been recognized as an integral process of the development, testing and implementation of genomic advances (Collins et al., 2003; Foster, 2004).

In this respect, the predictive testing program for HD serves as a model for genetic testing programs. From its very inception considerable efforts have been directed at understanding its benefits and psychological impacts. However, the risks of predictive testing, particularly GD, have not been adequately addressed. Although GD was a longstanding concern even before the introduction of the predictive testing program (Craufurd and Harris, 1986; Perry, 1981), little has been achieved in understanding or addressing this issue other than incorporating a discussion of the possibility of GD in pre-counselling sessions (Broholm et al., 1994; Went, 1990).

Unfortunately, HD is only a microcosm of the global realities of GD since the issue extends to other genetic disease groups as well as to the general population, both of which have expressed significant fear of participating in genetic testing (Apse et al., 2004; Armstrong et al., 2003; Genetics and Public Policy Center, 2007; Government of Canada, 2003) and genetic research (Hadley et al., 2003). The participation of large, diverse populations is required to ensure that genetic research studies are as valid and generalizable as possible. Many medical and social scientists alike have called on governments to respond to the public's significant apprehension towards genetics research, suggesting that the public's reluctance to enter the genomics era will prevent them from "fully reaping the rewards of the investment already made in human genome research" (Collins and Watson, 2003).

These calls for action have begun to be heard and are currently being addressed through the implementation of various policy strategies, ranging from moratoria to legislation proposals. The United States, for example, has proposed a federal bill dedicated to the prohibition of the use of genetic information in health insurance and employment decisions. While the bill, the Genetic Information Non-Discrimination Act

(GINA), has received wide support among scientists, disease advocates, health care professionals, and lawmakers, it remains stalled in the Senate, presumably because, among those definitional issues, opponents of the bills maintain that evidence of GD is scant. A comprehensive review of the literature supports their claim. Evidence of GD remains significantly hampered by anecdotal reports and methodological challenges.

If the pace of scientific discovery is to continue and if society is to benefit from the potential diagnostic and treatment advances from genomics and genetics research, then the realities of GD must be investigated so as to advance these crucial policies. The findings of this study address these gaps and provide substantial evidence of GD. A qualitative study offered an understanding of the issue from the perspective of persons at-risk for HD, the target of GD (Chapter 3), and contributed to the description of strategies used to manage the risk and experience of GD (Chapter 4). The development and administration of a national survey resulted in the description of the nature and extent of experiences of GD among persons at-risk for HD (Chapter 5). Perhaps equally important is the elucidation of predictors of GD experiences as well as the possible outcomes of its effects on its target (Chapter 5). Integrating these findings into practice and policy changes will likely contribute towards the ultimate goal of mitigating unfair discrimination on the basis of our most fundamental feature: our genes. Everyone should have the right to benefit from the scientific advances of genomic medicine without discrimination.

6.2 Summary of Findings

The objective of this dissertation was to conduct qualitative and quantitative studies to investigate the nature and extent of GD in a population at risk for HD.

The first specific objective was to describe the concerns, experiences and strategies regarding GD from the perspective of the HD community. To do this, semi-structured interviews were conducted with 45 genetically-tested and 10 untested individuals and analyzed using grounded theory methods. The findings demonstrate that a majority of individuals were concerned about (37/55) and reported that they had experienced GD (32/55) across a variety of contexts which extend beyond the traditionally examined contexts of insurance and employment to include family, social, government and health care domains. A process of engagement with GD is described in which individuals formed meaningful interpretations of GD and personalized its risk and consequences in their lives. Furthermore, depending on individuals' level of

engagement with GD and the nature of the experience (actual experience of GD or concern for its potential), four main strategies: "keeping low", minimizing, preempting and confronting GD were identified as mechanisms to manage GD.

The second, third and fourth specific objectives related to identifying the nature and prevalence of experiences of GD and comparing these levels between persons who have been tested and untested as well as by mutation status. The self-report, cross sectional survey results indicate that 93 respondents (40%) reported at least one experience of GD. GD occurred most often in reference to life insurance (n=63), disability insurance (n=49), making reproductive decisions (n=27), friends (n=18) and establishing relationships (n=14). Surprisingly, there were few reports of GD in employment, health care and government settings (4-7%). GD did not differ in overall prevalence between the tested and not-tested respondents (n=71 vs. 22, P=0.236). However, by mutation status, the proportion of respondents who experienced GD was at least 16% higher in HD+ group than in the HD- (χ^2P=0.042) and NT (χ^2P =0.045) groups (HD+: n=42 (50.6%), HD-: n=29 (34.5%), NT: n=22 (33.3%)). This suggests that respondents who test positive for HD are the most likely to report experiences of GD. Interestingly, there were also no significant differences in the proportions of GD experiences between HD- and NT respondents (n=29 vs. 22, χ^2 P =1.00), suggesting that testing negative for HD may not necessarily decrease the likelihood of experiencing GD.

The fifth and sixth specific objectives were to identify the socio-demographic predictors and health outcomes of GD experiences. The results demonstrate that family history (FH), rather than genetic test result (GTR), was the major reason given for reported experiences of GD (GD based on FH: n=41 vs GTR: n=13 vs both: n=17). In addition to being an important reason for GD, the FH was also an important predictor of GD experiences. The present study showed that those who become aware of their FH at a younger age (OR: 3.4-3.6, P=0.016), have first-hand experience with HD (OR: 3.4, P=0.01) and know of their FH for a longer time (OR: 2.6, P=0.005) are at greater risk for GD. Finally, psychological distress was a health outcome associated with the experience of GD (χ^2: relationship between distress and GD based on FH: $P\leq$0.0001 and GD based on GTR: P=0.011). In fact, experiencing GD in more situations based on FH and GTR was associated with increased levels of distress (Pearson R = 0.384 and 0.526, $P\leq$0.0001, respectively). Moreover, levels of distress did not differ significantly between

perceived causes of GD (FH vs GTR vs both, Mann-Whitney U $P>0.05$) and genetic status (Mann-Whitney U $P=0.721$), suggesting that psychological distress is commonly associated with experiences of GD.

6.3 Integrating the Findings

To appreciate the contribution of the findings of this dissertation they must be placed in context of the current literature in the field. This discussion will begin by reflecting on the conceptualization of GD, paying particular attention to its dimensions and inherent subjectivity. Next, the findings related to the nature and extent of GD are considered in reference to each of the settings examined. Insight is also provided on the profound effects growing up in a family affected by HD has on the individual as well as social dynamics to understand the importance of the FH in shaping GD experiences. Finally, the health outcome of GD is discussed in reference to other findings linking discrimination and health.

6.3.1 Genetic Discrimination: A multidimensional concept

The qualitative findings of this dissertation contribute novel insight into the conceptualization of GD by those at-risk for or who have experienced GD. Engagement with GD is a process which describes how individuals participants attempted to interpret the meaning of GD and personalized its consequences into the context of their lives. Both these processes – interpretation and personalization - provide important understanding of the multidimensional nature of GD, its dimensions and inherent subjectivity.

Genetic distinctions or genetic discrimination?

Discrimination is defined as the process of making a distinction between things with the mind, or in action (The Oxford English Dictionary, 2007). The definition and dimensions of *genetic discrimination*, to date, have depended upon academic conceptualizations (Anderlik and Rothstein, 2001; Otlowski, 2005) and quantitative instruments (Apse et al., 2004; Kass et al., 2007; Lapham et al., 1996; Low et al., 1998), but what has been excluded is the perspectives of those at-risk or who have experienced GD themselves – the targets of stigma or discrimination.

Genetic discrimination was conceptualized by those at-risk for or who have experienced GD as being unfairly prevented from doing something or being treated differently. Inherent in participants' conceptualizations of GD were elements of legal and

social ideals. Human rights and privacy underpinned the unjust aspects of GD for participants since it was similar to other forms of discrimination. Genetic discrimination, according to these persons, manifests from stigma and prejudice, elements highly intertwined and fundamental to GD. These conceptualizations resonate with broader definitions of GD that pay due attention to the crucial elements of stigma, prejudice and human rights.

The terms used to elicit perceptions of GD influence the nature of responses. The qualitative investigation used the neutral term 'differential treatment', which produced both positive and negative outcomes following disclosures of FH or GTR. Individuals' descriptions included advantageous as well as disadvantageous interactions. Moreover, an important element for most participants interviewed was the need to include positive forms of genetic distinctions with the study of negative distinctions. The term 'differential treatment', however, is not inherently neutral because some abnormal treatment must occur (or be perceived) in order to distinguish it from normal, day-to-day interactions. Thus, genetic distinction is an all-encompassing concept to describe the differential treatment, either negative or positive, related to genetic status. Moreover, it may be necessary to understand the positive forms of genetic distinctions in order to appreciate why the converse was perceived as disadvantageous. Future work would thus be missing a vital component of the complete picture unless all forms of genetic distinctions were included.

SUBJECTIVITY: AN INHERENT COMPONENT

The nature of making distinctions is dependent on the perceptions belonging to the target. What is considered 'unfair', 'unacceptable', 'irrational' or 'different' is ultimately a matter of debate, and depends on the target's world view, cultural context, as well as what society deems appropriate or acceptable. Moreover, GD being grounded in social interactions requires individuals to make sense of others' reactions and their own responses to them. The target's perceptions may not necessarily include or be consistent with the intentions of the perpetrator. This process is thus inherently subjective in nature and is dependent upon many factors.

There may be some individuals who accept and internalize the negative views or discrimination as "deserved" and hence view it as non discriminatory (Krieger, 1999). As alluded to above, there may be differing views of what constitutes positive and negative treatment. For example, monitoring the HD+ person for symptoms may be perceived by

some individuals as caring behaviour while for others it may be considered unwanted and inappropriate. Self-representation biases, in which people may be (un)consciously shaping their responses to be "socially acceptable", may be at play and participants may also vary their responses according to whether they find it helpful or distressing to discuss such issues (Ross, 1989). Finally, people may exaggerate discrimination in order to attribute blame to others instead of themselves (Neighbors et al., 1996).

The effects of such biases in the interpretation of discriminatory insults may impact prevalence estimates as well as their effect on health (Krieger, 1999). The existence of such limitations, however, does not render studies on discrimination based on self-report infalsifiable. Similar to the inherent subjectivity of reports of other perceived health outcomes, these studies provide suggestive links between health and discrimination.

Given the subjectivity inherent to discrimination, previous calls to 'verify' accounts of GD with the relevant third parties or via independent review (Treloar et al., 2004) seem inappropriate if not impossible. Instead, validation should focus on qualitative approaches to understand these perceptions to ensure they are reflected in quantitative tools intended to measure their prevalence and impact on health. Ultimately, the subjective perception of the target is, and ought to be, sufficient to claim genetic distinctions as discriminatory or otherwise.

6.3.2 Experiences of Genetic Discrimination: The Nature and Extent

Insurance Discrimination

Insurance discrimination was the most common form of GD among individuals at-risk for HD. Nearly one in three respondents experienced insurance discrimination, largely by life and disability insurance companies, in the forms of insurance rejection, premium increases and requests to take a predictive test. Moreover, levels of insurance discrimination were similar among all the respondents and were attributed mostly to having a family history of HD. These findings suggest that it is being part of an HD family, regardless of genetic status, that predisposes individuals to rejection, premium increases and requests to take a predictive test.

These findings are generally consistent with previous surveys of GD among other genetic and non-genetic populations, which indicate that 25-33% of individuals were

denied life insurance or offered it at a prohibitive rate (Kass et al., 2007; Lapham et al., 1996; Low et al., 1998).

These results do differ substantially from two studies concerning HNPCC and Fragile X families. Among relatives of HNPCC patients, the prevalence of GD was found to be 7% (Apse et al., 2004). Upon further investigation, these experiences were not related to their cancer risk but to other genetic and non-genetic conditions. Although Apse's (2004) sample consisted of significantly more females, gender differences are not known to affect experiences of GD. However, Apse's definition of GD provided to respondents was: "when people or organizations make unfair decisions about someone who is currently healthy based on genetic information". The definition of GD provided in the present study was: "being unfairly prevented from doing something, or being treated unfairly" which was the interpretation of GD provided by the interviewees (Chapter 3 – forming meaningful interpretations). While Apse's definition of GD is fairly comparable to the one in the present survey since both definitions used 'unfair' to define discrimination, their definition involves decision making while ours necessitates treatment. This difference would likely elicit different interpretations of GD and thus different responses.

Moreover, the response format for the experience of GD question used by Apse et al. (2004) was left open-ended, while the present study required respondents to review a list of 22 possible GD situations and check all that applied. The difference in response formats was also likely to contribute to prevalence differences, as respondents of the present study were prompted to consider a wide range of scenarios, while Apse's format relied on the spontaneous recall of their respondents.

A survey of insurance discrimination among 39 families diagnosed with Fragile X Syndrome reported no insurance cancellations, nor were carriers given increased premiums for any coverage purchased (Wingrove et al., 1996). Three families (7.7%) did report that contract riders had been placed on their policies to exclude all Fragile X-related expenses. It is important to note, however, that in that study discrimination was strictly defined as the misuse of GI in insurance writing, which included cancellation of insurance for a child with Fragile X after genetic testing or refusal to insure carriers. This actuarial definition contrasts significantly with the broader definition used in this study, which likely accounts for the difference in prevalence of GD between the study of Wingrove et al (1996) and the study reported here.

The issue of definition is an important one, as most studies of GD to date have defined the term differently; this is an issue that would have substantial effects on the

prevalence of GD, notwithstanding the inclusion of symptomatic respondents or third-hand reports. Thus it is necessary to view these comparisons as informative but not conclusive.

The comparison of the insurance landscape in Australia and the United Kingdom paints a different picture than experiences of GD in Canada. An Australian study investigating the use of GTR in life insurance underwriting decisions found only one case of a HD+ applicant disclosing his GTR. This person received coverage at standard rates but the policy was limited to 50 years of age (Otlowski et al., 2007). In comparison, in the current study, there were 20 cases where HD- results were disclosed, suggesting that most individuals apply for life insurance prior to testing and those with HD+ GTR are self-selecting and deciding not to apply for life insurance all-together (Otlowski et al., 2007). In contrast, persons with an HD+ GTR in the U.K. are not declined life insurance even though insurers are permitted to use the HD GTR for underwriting purposes of policies in excess of £500,000 (Secretary of State for Health, 2003). Furthermore, applicants with a FH of HD are not given higher premiums or 'loadings' (Otlowski et al., 2007). Thus, reported experiences of GD in Canada may be more frequent than the U.K. because regulations restricting the use of genetic information are not in place and those with a FH of HD are commonly required to pay higher premiums.

Discrimination in the Family

Discrimination in the family must be viewed through a wider lens that captures the profound impact the presence of HD has on the family system. The following quote from Alice Wexler, a member of a prominent HD family, illustrates the initial discovery and pervasive impact of HD on the family:

> First there is the grandfather who has died of "nervous trouble" on the back ward of a state hospital, the uncle who attracts whispers and stares from the neighbours as he staggers down the street, the doctor who says, "Women do not get it." ... Divorce, arrests, abandonment, suicide punctuate the action. There is always a moment of discovery, when the protagonists finally learn the truth, usually after having several children. In the end, the characters all come to resemble one another, and the actions winds down to a predictably gruesome close, with no resolution or release and always the promise of more performances to come ((Wexler, 1995) page xi).

Often when HD is known to be present in a family it becomes part of that family's identity – part of its beliefs, norms, and values. Family myths surrounding the

transmission and expression of HD can be particular to a family. Pre-selection may even occur where one relative or child is singled out as likely to be carrying the HD mutation since 'he looks and acts just like dad' (Kessler, 1988). Resource allocation, often in the form of attention and educational decisions, may also be influenced by the possibility of future disease; thus, opportunities for those believed to be carrying the HD mutation may be limited as resources are considered to be better directed elsewhere. Altered expectation and role assignment for the pre-selected person are typical outcomes such as situations in which pre-selected individuals are given the task of caring for their affected parents since these individuals are expected to fail in school or their careers. While pre-selection is an unconscious process intended to control the uncertainty and anxiety inherent to HD, the process has profound psychosocial effects on the person assigned the "sick" role. While these occurrences are subtle in nature, they involve definite forms of differential treatment.

It thus follows that the existence of genetic testing exerts added pressures on the family as a whole. It does not come as a surprise that the second most frequent setting for GD is the family. It is also consistent that tested respondents reported more experiences of GD than those who chose not to participate in testing (n=31 vs. 5, P=0.044). Moreover, those who tested positive reported the highest levels of GD in the family (HD+ n=19 (22.9%), HD- n=12 (14.3%), NT n=5 (5.9%) P=0.034). As others have aptly recognized, the decision to test itself can become a "litmus test by which relatives perceive and judge each other's loyalty to the family" (Sobel and Cowan, 2000) and predictive testing often produces a "ripple effect" across the family system (Kessler, 1994).

Genetic testing has been shown to have a significant impact on family functioning. Specifically, membership changes have been noted to occur as a result of testing, positive or negative, causing rifts as well as re-connections among relatives. For example following negative test results family members have experienced distancing since they have become free of the impeding disease and thereby lost previous communality of being "at-risk" with the family (Sobel and Cowan, 2000). Consistent with the present findings, HD+ and HD- respondents reported GD among family members whereas those who did not test did not (HD+ n=8 (9.6%), HD- n=7 (8.3%), NT n=0 χ^2 P=0.04). Alternatively, testing negative has given others the entitlement to disconnect from their family of origin for reasons that may include a desire to have a family in which

HD is not the basis for membership (Sobel and Cowan, 2000). The proportion of membership changes following testing was reported by over 80% of an unrepresentative, interview sample of 18 families (55 participants) (Sobel and Cowan, 2000).

The second area of family functioning reported to be affected by genetic testing is communication. Similar to membership changes, communication changes vary. Predictive testing could act to intensify previous patterns of communication or alter the patterns altogether. Sobel and Cowan (2000) describe communication patterns in which HD was considered a family secret and knowledge of HD was just part of the many "whisperings". The interview and survey results support these trends as they indicate that significant changes in communication patterns occur following testing, especially for those who test positive. Overall, 16 (10%) respondents reported communication pattern changes. These were more pronounced in the HD+ group compared to those who test negative (HD+ n=12 (15.6%), HD- n=4 (5.3%) χ^2 P=0.062). In comparison, communication pattern changes have been described by 50% of families interviewed (Sobel and Cowan, 2000). Open styles of communication have also been described in which searching for symptoms in the mutation carrier was considered one family's "favourite indoor sport" (Sobel and Cowan, 2000). In the present study, symptom monitoring has been reported by 26 (15.6%) of respondents following testing, and, as expected was cited mostly by HD+ respondents: (HD+ n=20 (26.3%), HD- n=6 (8.0%), χ^2 P=0.004)

Recent work examining the impact of genetic testing on couples' relationships provides an additional basis for understanding these results. For the majority of couples predictive testing appeared to have no overall adverse effect on their relationship, which is consistent with the present findings indicating GD by a spouse was the least frequent source of GD in the family setting overall (respondents reported GD in reference to: reproductive choices n=27 (11.6%), by family member n=15 (6.4%) and by spouse n=13 (5.6%)).

However, for a small number of cases there is breakdown of the relationship that occurs more frequently among tested-partner couples than untested-partner couples in the short-term (Richards and Williams, 2004). This supports the findings in the present study indicating that tested respondents, specifically HD+ persons, reported more GD by spouses than the HD- and NT groups (HD+ n=9 (10.8%), HD- n=3 (3.6%), NT n=1

(1.5%) $\chi^2 P$=0.029). It seems that these issues stem from the differences in the quality of relationships perceived by tested persons and their partners following testing. Partners report more adverse effects following testing compared to carriers (Tibben et al., 1993b; Tibben et al., 1993a). Carriers rated the quality of the relationship higher than did their partners, and they perceived more positive changes (Decruyenaere et al., 2004). Our findings are further supported by various studies indicating relationship breakdown has been noted to occur more frequently in carrier than non-carrier relationships: 10% vs. 3% (Codori and Brandt, 1994), 24% vs. 10% (Tibben et al., 1993a) and 20% vs. 10% (Sobel and Cowan, 2000).

Contradictory findings have been reported where marital adjustment issues are more pronounced among non-carrier couples than among relationships that involve a carrier (Richards and Williams, 2004). Factors found to be associated with these perceptions were the (premature) changing roles that induced post-test marital distress, which may explain this discrepancy (Decruyenaere et al., 2004; Sobel and Cowan, 2000).

Cleary there are profound impacts of genetic testing on the family system. The frequency of family GD and its nature, exemplified by symptom-monitoring, communication changes, a perceived lack of closeness or support, and pressure from relatives regarding reproductive, educational and marriage decisions are consistent with previously described disturbed interactions in the family following testing. Moreover, the association between the likelihood of experiencing GD and the length of time and type of exposure to the FH of HD is consistent with studies indicating altered behaviour and functioning in families with long-standing histories of HD (Kessler and Bloch, 1989; Sobel and Cowan, 2000). Evidence of pressure during reproductive decision making is also consistent with previous work indicating that the opinions and choices of relatives regarding reproduction (Downing, 2005) are a source of competing interests and priorities to contend with during reproductive decision-making.

Taken together, the availability of predictive testing produces pressures and reactions towards those who test as well as those who choose not to test. While these issues are reflected in the current findings, a broader exploration of GD in the context of the family unit as a whole may provide a better appreciation from a holistic, family systems perspective.

DISCRIMINATION IN SOCIAL CIRCLES

Social circles were the third most frequent settings in which GD was reported. Overall 12.4% of respondents believed that they were discriminated against, mostly by friends and when establishing relationships. These findings were more prevalent among tested respondents than untested respondents. Specifically, the HD+ respondents reported more than twice the level of discrimination as the other groups. This is consistent with findings from work on the impact of genetic testing on couples' relationships (Codori and Brandt, 1994; Sobel and Cowan, 2000; Tibben et al., 1993a). Although these studies focus on established relationships and not *establishing* relationships, they elucidate trends that may be expected when HD+ persons develop new relationships. Extrapolating from the finding that tested couples, particularly carrier couples, experience adjustment difficulties, it is hypothesized that the same would occur within newly formed relationships, and the present findings are consistent with this hypothesis.

Overall, the findings that experiences of GD occur most often reported in insurance, family and social settings are consistent with the study's overall theoretical assumption that GD is situated in the social interactions and consequences that occur following disclosure of one's risk or genetic status. Indeed insurance, family and social contexts are the most likely contexts in which disclosure (or discussion) of one's FH or GTR would take place, and thus it is not surprising that these were the settings in which GD occurred most often.

EMPLOYMENT DISCRIMINATION

Contrary to expectations, GD in employment settings was reported by only 6.9% of respondents and was largely in reference to current working conditions as opposed to during the hiring process. These findings are consistent with individuals' qualitative descriptions of limits to opportunities in the workplace, denials of promotions and forced retirement, all of which involve current working conditions. The qualitative findings also highlighted individuals' tendency to avoid seeking new employment out of fear of GD, which may explain the surprisingly low levels of GD in this setting. Furthermore, it may also be possible that individuals consciously seek work where GD is unlikely. These hypotheses may explain the findings that experiences of employment GD significantly differed between tested and NT groups (n=15 vs. 1, P=0.045), where significantly more HD+ respondents reported employment difficulties than both HD- and NT respondents

(HD+ n=12 (14.5%), HD- n=3 (3.6%), NT n=1 (1.5%) χ^2 P=0.003 – did not reach significance after adjusting for multiple comparisons).

Employment GD reported in the present study was considerably lower than in previous reports. Among 332 members of genetic support groups, 13% reported being denied or let go from a job (Lapham et al., 1996). Another study of adults or parents of children with cystic fibrosis, sickle cell disease, diabetes and AIDS found that 19% of all respondents were not hired due to their medical conditions and those with genetic conditions experienced significantly more GD than those with non-genetic conditions (Kass et al., 2004). It is important to note that both these samples consisted of symptomatic respondents. Among the respondents who were at-risk for cancer in Kass' sample (2004), reports of employment GD were 0-4.17%. Thus, it is possible that these differences in the prevalence of employment GD may be largely due to the presence of symptoms and do not entirely represent GD based on genetic information (GI) alone.

GOVERNMENT & HEALTH CARE DISCRIMINATION

There was little evidence for GD in health care and government settings. The most compelling findings were discriminatory issues in reference to getting medical care and by doctors, which were cited most frequently (respondents reported GD in reference to: getting medical care n=11 (4.7%), by doctor n=8 (3.4%), other health care professionals n=7 (3.0%) and by a genetic counseling service n=5 (2.1%)). As respondents' reports indicate, directive counselling regarding reproduction was a prominent issue. Related surveys on the attitudes of medical professionals reveal disconcerting insights. Elger and Harding (2003) found that Swiss medical students are directive in some counselling situations and exhibit eugenic pressures on and discrimination against persons at-risk for HD (Elger and Harding, 2003). Specifically, they reported that 39.4% of medical students agreed that society should do everything possible to diminish the frequency of HD, including non-governmental pressure on carriers to undergo systematic genetic testing and recommendation of sterilization (Elger and Harding, 2003).

Chinese geneticists' eugenic views are even more striking: 86% of geneticists surveyed believe that governments should require premarital carrier tests and that carriers of the same gene mutation should not mate with each other (91%). In the case of HD, 85% supported the notion that children should be tested for the gene mutation

(Elger and Harding, 2003). It must be acknowledged, however, that these views are deeply embedded in a culture that promulgates "improving the quality of the newborn" as mandated through their Maternal and Infant Health Care Law (1994). This law requires couples planning marriage to undergo genetic screening for genetic and infectious diseases and mental disorders. Any couples carrying disease-related mutations are permitted to marry only if they agree to sterilization or long-term contraception (United Nations Economic and Social Commission for Asia and the Pacific, 2007).

Societal attitudes towards individuals with a perceived future disability or disease predisposition reflect social and cultural values and foster beliefs that influence attitudes and behaviour. Thus, unsolicited pressure on reproductive choices and directive counselling are but two elements of health care influences that devalue individuals' personal control and free informed decision making. Efforts to address GD need to extend to health-care and government settings.

6.3.3 FAMILY HISTORY: THE FUNDAMENTAL ISSUE

Family history (FH) was found to be the major cause and predictor of reported GD experiences. A large majority of respondents attributed their GD experiences to their FH (GD based on FH: n=41 vs GTR: n=13 vs both: n=17). In fact, all aspects related to the FH of HD, including length of time one is aware of their FH (OR: 2.6, P=0.005), age when one becomes aware of HD (OR: 3.4-3.6, P=0.016), and the type of exposure to HD one has had (OR: 3.4, P=0.010), significantly impacted on the likelihood of experiencing GD. These findings highlight and confirm the profound effects growing up in a family affected by HD have not only on individual and family dynamics but, as the present findings indicate, on social relationships and interactions.

HD is a family disorder (Brouwer-Dudokdewit et al., 2002; Sobel and Cowan, 2000; Vamos et al., 2007). Indeed growing up in a family with a long-standing history of HD introduces specific stressors that may influence the relationship between parents and children (Brouwer-Dudokdewit et al., 2002; Vamos et al., 2007). With the onset of disease come disturbing personality changes such as a depression and aggression, which may be frightening for children and strain the parent-child bond. Onset of disease often results in changes to the structure of the family, in which the unaffected parent takes on greater responsibilities, shifting the general household structure and attention to children even further (Vamos et al., 2007; Van der Meer et al., 2006). At times, these

changes and responsibilities may become too large burden to bear for unaffected parents and may cause them to leave the household. Children may then take up the role of caregiver, which can have far-reaching emotional, psychological and behavioural impact (Forrest et al., 2007).

Even prior to the onset of disease, the existence of HD in the family has been shown to have severe impact on family functioning in terms of low cohesion and expressiveness and high levels of conflict (Vamos et al., 2007). In fact 80% of adult children in HD families reported that "it's difficult being part of a family with HD", and another 40% admitted that "HD split us apart" (Vamos et al., 2007). In fact research and clinical experience suggest that young people growing up in families affected by HD may experience social and emotional difficulties and may experience adverse effects on other developmental phases of adolescence such as establishing peer relations, independence and the initiation of intimate relationships (Forrest et al., 2007).

Some of these difficulties stem from a lack of secure attachment representations between parent and child, in which the instinctual need to form close affectionate bonds is not met (Van der Meer et al., 2006). These alterations lead to lack of emotional security and have been associated in difficulty maintaining social relationships (Van der Meer et al., 2006). Moreover, childhood experiences of HD and growing up in a disordered household are known to contribute to conduct disorder in adolescents and antisocial personality disorder in adults (Folstein et al., 1983). Regression analyses among persons requesting predictive testing has shown that the younger persons were at the parental onset of HD, the more likely it was that they would have lower ego strength, greater anxiety, and a higher level of depression in the period before testing (Decruyenaere et al., 1999). Beyond the intra-personal level, when HD is known to segregate in a family, shame, stigma or social isolation of the family often may ensue. Growing up in a family affected by HD has far-reaching impacts and, as suggested by the present study's findings, has influence on individuals' experiences and attributions of GD. Not only does HD affect the life-cycle of a family as well as the social functioning of its members but also their perceptions of how people treat and interact with them.

In regards to insurance, having a FH and knowing of this risk for a longer time have direct impact on insurance underwriting. Concealing this information is illegal, and the earlier one is aware of a FH, the greater the impact the FH information has on all future eligibility and premium assessments. This situation is analogous to the hereditary

cancer context, in which risk for breast and colorectal cancer has been shown to lead to premium loadings on life insurance as well as denial of critical care and disability insurance (Norum and Tranebjaerg, 2000; Otlowski et al., 2007).

Ultimately, because of the psychiatric, cognitive and motor disturbances in HD patients, family dynamics in families affected by HD differ significantly from those in non-HD families (Folstein, 1991; Kessler and Bloch, 1989). These dynamics form crucial frameworks for personal decision-making regarding reproductive, marital, career and predictive testing choices (Cox and McKellin, 1999; Taylor, 2004). Furthermore, as suggested by the findings of the present study, these dynamics also influence social interactions and experiences of differential treatment: the greater the exposure one has to HD in the family, the greater the influence exposure to HD has on perceptions and experiences of GD.

6.3.4 Psychosocial Impact of Genetic Discrimination: Distress

From a century of epidemiological research, it is now established that discrimination harms health (Krieger, 1999). Inequality of various kinds has been shown to be associated with health consequences ranging from mental health, substance abuse to physiological outcomes. Examples include: sexual discrimination resulting in elevated rates of smoking, suicide and substance abuse (Council of Scientific Affairs, 1996), disability discrimination associated with denial of health insurance thus resulting in inadequate medical care (Gill, 1996), age discrimination associated with poorer survival of the elderly due to less aggressive treatment (Minkler and Estes, 1991), social class discrimination associated with excess morbidity and mortality (Williams and Collins, 1995), racial discrimination associated with higher mortality rates (National Center for Health Statistics, 1997), and gender discrimination associated with sexual abuse and fewer years of disability-free life (adjusted for life expectancy) (Bachman and Saltzman, 1995; Cosentino and Collins, 1996; National Center for Health Statistics, 1997). It stands to reason that GD would also result in adverse health consequences.

Results from the present study suggest that this is indeed the case. High levels of psychological distress were significantly associated with reported experiences of GD. Given the well-documented associations between other forms of discrimination and health, these findings are not surprising and support previous associations between distress and racial, gender, sexual and ethnic discrimination (Amaro et al., 1987; Brown

et al., 2001; Jackson et al., 1996; Landrine et al., 1995; McNeilly et al., 1996; Meyer, 1995; Williams, 1997; Williams et al., 2003). Still, the health impact of GD has not been described before, raising the effects of GD to a level that suggests it ought to be recognized as a significant mental health concern in addition to an economic or policy issue. With the recent establishment of a Canadian Mental Health Commission, mental health discrimination has become a policy priority in Canada. It is hoped that these findings may contribute to similar measures related to GD.

6.4 Practice Recommendations

Introduction

GD is one of the major ethical and professional challenges for genetic professionals, including genetic counselors, physicians and nurses (McCarthy Veach et al., 2001). Genetic counsellors encounter reports of discrimination among clients at a frequency of 29% (Bower et al., 2002). Thus, the results of the present study may be helpful for genetic professionals supporting clients confronting issues of GD.

Genetic counselors practicing in the U.S. routinely discuss GD in cancer genetics (Pfeffer et al., 2003). Their discussions typically include a definition of GD, description and limitations of federal and state legislation, types of insurance (e.g., health, life and disability), prevention strategies and examples of discrimination (Pfeffer et al., 2003). However, over 40% of genetic counselors indicate they do not discuss particular topics consistently with all their cancer clients (Pfeffer et al., 2003). In fact, anecdotal evidence from the qualitative component of the present study suggests that discussions on GD are not uniform or consistent across Canadian HD testing centres.

Engaging clients in discussions of GD is essential. The National Society of Genetic Counselors (NSGC) Code of Ethics states that genetic counselors should "*enable their clients to make informed independent decisions...by providing or illuminating necessary facts*" (National Society of Genetic Counselors, 1992). The challenge appears to lie in determining what constitutes an appropriate balance between informed consent and perpetuating the perception that GD exists or is widespread. Indeed an inherent tension exists in the process of discussing GD.

Discussing GD in an abstract fashion where the risk of GD is not put into context does indeed instill a perception that GD exists or is widespread (see 'nature of the awareness events' in Chapter 3). However, coupling the provision of information about GD with opportunities for clients to discuss concerns about and past experiences with GD is likely to be helpful in supporting the process of personalizing the factual information presented about GD and identifying strategies to minimize or manage the consequences of GD. Thus, the framework of engagement with GD and survey findings may provide clinicians with helpful tools to direct such discussions and suggest ways to mitigate GD.

Predictors of Genetic Discrimination

Given the present findings, it would be helpful for genetic professionals to stress that having a FH of HD was the major reason given for individuals' GD experiences. Moreover, participating in genetic testing itself was not significantly associated with experiences of GD. While it is true that HD+ persons reported significantly higher levels of GD than HD- and NT groups, the HD- and NT groups also reported GD, and at similar levels as a consequence of having a FH of HD. In other words, while testing positive adds an extra layer of burden to bear, those who do not undergo testing and those who did and tested negative, both report similar levels of GD because of their FH.

While the FH is the major cause given for GD, the nature of the FH was also an important predictor of who was most likely to experience GD. Individuals who had first-hand experience with HD symptoms or death, discovered their FH at a younger age or knew about their FH for over 15 years were 2.6-3.5 times more likely to experience GD. Thus, it may be helpful for genetic professionals to pay particular attention to clients who have first hand exposure to HD, learned about their FH earlier in life and have known about their FH for longer, since these clients are at greatest risk for GD.

These findings are consistent with counselling experience indicating that members of new mutation families have distinct counseling needs compared to individuals who grew up in HD families (Maat-Kievit et al., 2001) A new mutation family refers to a situation in which a family member is clinically diagnosed with HD without a prior family history (Semaka et al., 2006). Relatives, namely siblings, of new mutation patients become eligible for predictive testing given their new genetic risk for HD. Candidates for testing who are unexpectedly confronted with the risk for themselves,

their offspring, and relatives find this uncertainty difficult to deal with. In order to restore control over their lives, new mutation testing candidates are generally known to seek testing as soon as possible, potentially at the expense of becoming aware of the full ramifications of testing (Maat-Kievit et al., 2001) and understanding HD. One may further speculate that since new mutation candidates generally learn of their risk later in life, after insurance arrangements, career and reproductive decisions are set in place, they are less likely to be at-risk for GD. In fact this relationship is consistent with the study's findings, which indicate that those who learned of their FH after the age of 35 are significantly less likely to experience GD. An alternative explanation is that individuals that became aware of their FH earlier simply had more time to encounter GD. (It should also be noted that in the Canadian context, new mutation families do not seek testing as frequently (Hayden, 2007)).

MANAGEMENT OF GENETIC DISCRIMINATION

In light of the current vacuum of legal protection from GD in Canada and a many other countries, genetic professionals may be in a unique position to help testing candidates mitigate fears and experiences of discrimination.

Non-directiveness has been a central tenet of genetic counseling since its formal inception and is a principle of the NSGC Code of Ethics (National Society of Genetic Counselors, 1992). The NSGC Code of Ethics further states that genetic counselors should be "*illuminating anticipated consequences...and prevent discrimination on the basis of genetic status*" (National Society of Genetic Counselors, 1992). Although genetic counselors have traditionally ascribed to value-neutral non-directive counseling, some authors have called on genetic counselors to adopt a more directive approach in their counseling (Bowles Biesecker, 2000; Kessler, 1992). This recommendation is echoed for the purposes of managing GD.

Genetic professionals should continue to urge candidates to secure desired levels of insurance before proceeding with testing and make the possible implications of the test results on future insurance assessments explicit. In fact, some authors recommend that the informed consent process for cancer testing include an "individualized assessment of insurance and employment discrimination risks" (Stopfer, 2000). The results of the present study support this recommendation and suggest extending these discussions into the familial and social contexts. A pre-test discussion of

the possible impact of the test result on relationships, including marital, sibling, parental, romantic and platonic, should result in a better preparation for and more understanding of the reactions after testing.

A cursory discussion of GD limited to the informed consent process is not sufficient. Rather an independent, explicit part of pre-test counselling is preferred in which plans for disclosure of GTR or lack thereof should continue to be discussed, paying particular attention to employment, family and social contexts. During such discussions clients' past experiences and concern for GD can illuminate previous approaches used to manage GD. Professionals should be aware that unengaged stigma-related coping strategies have been associated with adverse physical consequences such as hypertension (Krieger and Sidney, 1996).

Further strategies to mitigate GD may include withholding information from insurers and employers, as well as from candidates' medical records. It is not unusual for genetics clinics to maintain shadow charts (Bower et al., 2002). These can be used for the purposes of predictive testing for those candidates who are particularly concerned about possible GD for themselves or families and may otherwise deny themselves the possible benefits of testing such as possible psychological relief and/or planning opportunities. Similarly, it may be recommended (as opposed to simply being offered as it currently is in some clinics (Benjamin et al., 1994)) that a letter not be sent to family physicians so that they, along with insurers and employers, would be unaware of the candidates' involvement in the predictive testing program.

A final strategy involves anonymous predictive testing. Several Americans at-risk for HD have sought predictive testing in Canada under the auspices of anonymity, in fear of health insurance discrimination for themselves and their families (Burgess et al., 1997).

Indeed these strategies raise salient issues. Clinicians cooperate in excluding insurance companies and employers from risk information when a public policy response would be preferable. Candid discussion with candidates about the implications of these strategies is strongly recommended. This will ensure that candidates are aware of the risks: insurance contracts may be subject to annulment and, more importantly, optimal care, such as appropriate counseling and follow up, may be compromised because of the discontinuity of information in an individual's medical files and between health care professionals.

AVENUES FOR RECOURSE

Discussion of the relevant laws and avenue for recourse is likely to be helpful, not only to inform patients that differential treatment based on perceived future disability is discriminatory, but to empower patients with the means to address future discriminatory issues. Professionals may wish to discuss the availability and purposes of provincial human rights commissions as well as labour unions for employment disputes. Ongoing contact with genetic professionals would also be helpful, as this allows the genetic professional to be the point person for any future GD issues, if any. Moreover, this would ensure that individuals may be referred for additional counselling or legal counsel specializing in human rights issues where appropriate.

6.5 POLICY RECOMMENDATIONS

INTRODUCTION

Genetic testing is becoming a vital tool in the standard armoury of clinical medicine, which makes it increasingly difficult to distinguish genetic information from health information. There are over 1000 genetic tests that utilize DNA-based, cytogenetic and biochemical methods to determine underlying causes of both genetic and non-genetic diseases in persons who may be symptomatic or asymptomatic. This is the nature of clinical medicine, which is likely to become more complex as advances in pharmacogenomics and preventative medicine continue to push the boundaries of health care.

A less genetic-centric approach is clearly required, which considers the adaptation of current protections as well as the creation of novel ones. These may include public and professional awareness and, ultimately, an anti-GD law.

PUBLIC & PROFESSIONAL AWARENESS

Contrary to the U.S. where GD is a 'somewhat of a household word' (Barash, 2000), the issue has received little attention in the Canadian media or general discourse. The lack of legislative debate, along with the presence of a universal health care system, creates the impression that GD may not be a relevant issue in Canada. However, the present study's findings suggest the contrary: experiences of GD are common and GD is

a real concern for those at-risk for HD. Other studies suggest it is a significant problem among other genetic populations (Apse et al., 2004; Armstrong et al., 2003; Hall et al., 2005). It would thus be helpful to initiate public discussion and educational campaigns about genetics and genetic disease. Increasing public awareness about genetics, genetic research and ELSI may have the added benefits of reducing fears of GD and stigma related to genetic disease as well as encouraging engagement with genetic medicine and participation in genetic research. Public awareness campaigns for genetics have been successful in Australia and the U.K., where genetics education centres have been established to promote public engagement and professional education on genetics and public health campaigns have been established to encourage greater discussion with families and GPs about FH of genetic disease (Centre for Genetics Education, 2007; North West Genetics Knowledge Parks, 2007). Such centres are lacking in Canada and are needed to fill this apparent gap in public engagement and education in the areas of genetics, public health and social issues.

In conjunction with these public awareness efforts, education of health care professionals, especially genetic professionals, should include an overview of GD and related legal protections. In this way discussions on the current climate of legal protections against GD may become an integral component of pre-test counseling for all adult-onset hereditary conditions for which presymptomatic testing is available in Canada.

On a fundamental level, it may be also be helpful to make insurance and employment decisions more transparent, to ensure that GI is not being used to the detriment of individuals or their families and communities. Public awareness of these decision-making processes may help dispel erroneous beliefs as well as reduce fears of GD.

Anti-Genetic Discrimination Legislation

The results of the present study provide knowledge for direct use by policy-makers. First, the present findings suggest that the concerns and experiences of GD are very real and, most importantly, common among persons at-risk for HD. Previous claims that GD is a "rare" occurrence (National Society of Genetic Counselors and FORCE: Facing our risk of cancer empowered, 2004; Walker, 2007) are untrue. Second, the perception among those at-risk for GD is that treating people who do not have symptoms of disability unfairly is a human rights issue that should be forbidden by law similar to

discrimination against disabled people. Thus the policy imperative to address the fears of GD and experiences is justly supported.

Third, the findings clearly suggest that any definition of GI should include family history, since it was perceived by most respondents as the major reason for experiences of GD, despite testing status or results. Finally, any policy discussion will need to include protection from GD in life, disability and long term care/disability insurance policies, since these areas were found to be areas of significant concern for and experiences of GD.

6.6 Future research directions

The data presented in this dissertation suggest numerous avenues for future investigation. This includes qualitative and quantitative approaches aimed at understanding the full extent of GD and respective health outcomes.

Mechanisms of response to genetic discrimination

While it is now established that psychological distress is associated with GD; it is unknown whether other psychological and possible physiological responses occur as a consequence of GD. Moreover, it is unclear whether or how psychological, and possible physiological responses, are mediated by GD, if at all.

This may be achieved by many means, but an individual-level approach using cross-sectional and longitudinal data may be best. An individual-level approach would examine whether self-reported experiences of GD are associated with specified health outcomes, using instruments aimed at measuring the relevant outcomes such as physiologic responses (cardiovascular, endocrine, neurologic, immune, etc.) and/or more general health outcomes (psychological distress, self-rated ill health, psychological well-being, stress, depression, quality of life, etc.). Ultimately, however, longitudinal studies are needed to fully appreciate the impact of GD on health on time and may provide further insight on the mechanisms of response to GD.

Concern for genetic discrimination: a major factor?

While findings from the present study provide a rich description of individuals' concerns for GD, it is unknown how these concerns influence behaviour and management strategies among persons at-risk for HD. For example, do these concerns

influence at-risks persons' participation in genetic testing or genetic research? Such trends indeed exist among other populations, and until they are examined they can not be addressed to ensure that the concern for GD does not hinder the potentially beneficial engagement with genetic testing and research.

Furthermore, given the integral role concern plays in responses to GD, investigating the extent and influence of concern for GD in the HD population will provide a more holistic appreciation of GD. For example, does concern precede or mediate resultant distress? Do particular types of GD lead to greater amounts of concern (and thus distress)? Is concern for GD associated with physiological responses, and if so how?

THE MULTIPLE TARGETS OF GENETIC DISCRIMINATION: WHAT ABOUT THE FAMILY MEMBERS?

HD and GD affect families. Given that a large motivator for undergoing predictive testing among individuals at-risk for HD is to inform (and thus benefit) their children, it is seem likely that individuals have concerns about how their GTR, including GD, may impact their children. Findings from the present study suggest that individuals have significant concerns for GD for their children. Thus the extent of GD may be under-represented if experiences of and concern for GD for family members is not taken into account. Clearly, understanding how and if GD impacts other family members is necessary to achieve a complete appreciation of how GD, like HD, affects people's and families' lives.

NEW MUTATION FAMILIES: AN IDEAL COMPARISON GROUP

Given the fundamental influence the FH has on GD experiences, it would be helpful to compare GD experiences among individuals who are at-risk for HD but who have not been aware of their FH for a significant period of time. This would ultimately be the 'litmus-test' for the significant influence the FH has on GD experiences. Arguably, this hypothesis has been tested in the regression models that demonstrated that respondents who became aware of their FH when they were 35 years or older are significantly less likely to experience GD than to those who discovered their FH earlier. However, it is not certain that these respondents are in fact new mutation families or whether the FH was not known to these particular respondents due various circumstances surrounding the family communication of HD.

New mutation families, in which no FH existed prior to a relatively recent diagnosis of a family member (Semaka et al., 2006), generally learn of their risk later in

life, after insurance arrangements, career and reproductive decisions are set in place, are less likely to be at-risk for GD. Thus, these individuals would be an ideal comparison group in which to test the hypothesis that those who do not have (as opposed to not aware of) a FH of HD do not encounter GD, or at least at lower levels than those that do not test. This approach may further establish the fact that it is knowingly being part of an HD family, regardless of genetic status, that predisposes individuals to GD.

THE FULL EXTENT OF GENETIC DISCRIMINATION: CONSIDERING FREQUENCY, DURATION & TIMING

The present study is the first to report on the nature and prevalence of GD among persons at-risk for HD, explore the breadth of GD across a wide variety of settings and examine the predictors and outcomes of GD. However, what has not been achieved is an understanding of how often particular types of GD occur, for how long and at which point in time. While insurance GD was reported most often, this form of GD may have occurred relatively infrequently, given the fact that individuals typically apply for insurance a small number of times, and at particular stages in their lives. On the contrary, family and social GD may actually occur more frequently and for longer durations. Given the fundamental impact of the FH on GD, it is conceivable that GD in social and familial contexts is more pervasive and perhaps more distressing than GD in other contexts. Likewise, employment GD was cited by few individuals, but in terms of day-to-day functioning or job-related tasks, the frequency at which this form of GD occurs or pervades peoples' fears and decisions is unknown. Survey instruments designed to address frequency, duration and timing of particular forms of GD are warranted to appreciate the full extent of the issue as well as its definite impact on health outcomes better.

6.7 CONCLUSION

"*We know that if one man's rights are denied, the rights of all are endangered*" (Robert F. Kennedy, 1966). The findings of this dissertation have implications beyond Huntington disease. Indeed as a classic monogenic disease fundamental principles of the HD predictive testing program have served as a model for presymptomatic testing programs for genetic and non-genetic diseases (Hayden, 2003). Likewise, the findings of this dissertation provide additional insight for genetic screening programs for diseases with small effect genes as well as other late onset and neurological conditions. Even with its relatively high test validity and penetrance, this study highlights the importance of the

HD family history in persons' experiences of GD. Irrespective of the predictive validity of a genetic test or the penetrance of a genetic mutation for a disease, having a family history of disease plays a fundamental role in the perceived experiences of GD.

As the first study to investigate the nature and extent of GD among an asymptomatic tested and untested population, this dissertation provides evidence that GD is a frequently reported experience and a source of distress for persons at-risk for HD. It is hoped that these findings will provide insight for policy, identify areas where more education and support is needed, and provide direction to genetic professionals supporting their clients as they confront issues of GD.

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Appendix

A1. BEHAVIOURAL RESEARCH ETHICS APPROVAL

The University of British Columbia
Office of Research Services and Administration
Behavioural Research Ethics Board

Certificate of Approval

PRINCIPAL INVESTIGATOR	DEPARTMENT	NUMBER
Hayden, M.R.	Medical Genetics	**B03-0845**

INSTITUTION(S) WHERE RESEARCH WILL BE CARRIED OUT

Children's & Women's Health Centre ,

CO-INVESTIGATORS

Bombard, Yvonne, Medical Genetics; Bottorff, Joan, Nursing; Erwin, Cheryl, Medicine; Ludman, Mark, ; Paulsen, Jane, Medicine; Penziner, Elizabeth, Medicine

SPONSORING AGENCIES

Canadian Institutes of Health Research

TITLE:

Genetic Discrimnation in Mutation Carriers Identified Through Predictive Genetic Testing for Huntington Disease (HD)

APPROVAL DATE (yr/mo/day)	TERM (YEARS)	AMENDMENT	AMENDMENT APPROVED
06-03-28	1	June 5, 2006, Co-PI	JUN - 6 2006

CERTIFICATION

The request for continuing review of an amendment to the above-named project has been reviewed and the procedures were found to be acceptable on ethical grounds for research involving human subjects.

Approved on behalf of the Behavioural Research Ethics Board
by one of the following:
Dr. Peter Suedfeld, Chair,
Dr. Susan Rowley, Associate Chair
Dr. Jim Rupert, Associate Chair
Dr. Arminee Kazanjian, Associate Chair

This Certificate of Approval is valid for the above term provided there is no change in the experimental procedures

THE UNIVERSITY OF BRITISH COLUMBIA

CONSENT FORM

(Re: Interview & Survey. For: gene-tested subjects)

Project Title: **RESPOND-HD**
Research Team: **Michael R. Hayden, MB ChB PhD FRCP(C) FRSC., Joan L. Bottorff, Ph.D., RN., Yvonne Bombard BSc., Susan Creighton MSc, Joji Decolongon, MSC., Cheryl J.Erwin, JD, Ph.D., Michael Hayden, MD, Ph.D., Lori Jarmon, MA, Elizabeth A. Penziner, M.A., C.H.E.S., Anne Wallis, Ph.D. , Janet K. Williams, Ph.D., RN, Jane S. Paulsen, Ph.D.**

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We are inviting you to participate in this research study because you ***have completed predictive testing*** for a genetic disease.

The purpose of this research study is to help us better understand the experiences and perceptions regarding differential treatment among persons who have undergone presymptomatic testing for Huntington's disease. You are being invited to participate in an interview and survey about your experiences and perceptions regarding being treated differently. With this research, we hope to better understand the experiences and practices of persons who have received genetic testing.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 75 people will take part in this study from the United States and Canada.

HOW LONG WILL I BE IN THIS STUDY?

This study will be completed in one year. If you agree to take part in this study, your involvement will include the completion of a one-hour long interview, and you may be asked to respond to a telephone survey that should take approximately 30 minutes to complete. Some individuals may be asked to participate in a second interview to provide feedback on preliminary findings and additional information about their experiences. It

may take up to one month from the time you agree to participate to schedule a convenient time for you to be interviewed.

WHAT WILL HAPPEN DURING THIS STUDY?

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WHAT ARE THE RISKS OF THIS STUDY?

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WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You will not have any costs for being in this research study. There will no charge to your telephone bill, and no charge for any part of your participation.

WILL I BE PAID FOR PARTICIPATING?

You will be paid for being in this research study. You will be compensated $25 for the time you provide to complete the interview. If you are asked to participate in the survey portion of the study and you choose to complete the survey, you will be compensated an additional $25. You maintain the right to withdraw your consent to participate at any time. Payment will be mailed to your home address after the interview and again after completion of the survey *(if applicable)*. If you would NOT like your payment mailed to your home, please inform the study coordinator.

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IS BEING IN THIS STUDY VOLUNTARY?

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WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: XXXX at XXXXX; or Yvonne Bombard at XXXX.

If you have questions about the rights of research subjects or research related injury, please contact the Office of Research Services at the University of British Columbia, at 604-827-5114.

Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a copy of this form.

Subject's Name (printed):

_____

_____ _____

(Signature of Subject) (Date)

Statement of Person Who Obtained Consent

I have discussed the above points with the subject or, where appropriate, with the subject's legally authorized representative. It is my opinion that the subject understands the risks, benefits, and procedures involved with participation in this research study.

_____ _____

(Signature of Person who Obtained Consent) (Date)

THE UNIVERSITY OF BRITISH COLUMBIA

CONSENT FORM

(Re: Interview & Survey. For: untested subjects)

Project Title: **RESPOND-HD**
Research Team: **Michael R. Hayden, MB ChB PhD FRCP(C) FRSC., Joan L. Bottorff, Ph.D., RN., Yvonne Bombard BSc., Susan Creighton MSc, Joji Decolongon, MSC., Cheryl J.Erwin, JD, Ph.D., Michael Hayden, MD, Ph.D., Lori Jarmon, MA, Elizabeth A. Penziner, M.A., C.H.E.S., Anne Wallis, Ph.D. , Janet K. Williams, Ph.D., RN, Jane S. Paulsen, Ph.D.**

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We are inviting you to participate in this research study because you ***have NOT completed predictive testing*** for a genetic disease.

The purpose of this research study is to help us better understand the experiences and perceptions regarding differential treatment among persons who have undergone presymptomatic testing for Huntington's disease. You are being invited to participate in an interview and survey about your experiences and perceptions regarding being treated differently. With this research, we hope to better understand the experiences and practices of persons who have received genetic testing.

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(Signature of Subject) (Date)

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_____ _____

(Signature of Person who Obtained Consent) (Date)

THE UNIVERSITY OF BRITISH COLUMBIA

CONSENT FORM

(Re: Survey Only. For: gene-tested subjects)

Project Title: **RESPOND-HD**
Research Team: **Michael R. Hayden, MB ChB PhD FRCP(C) FRSC., Joan L. Bottorff, Ph.D., RN., Yvonne Bombard BSc., Susan Creighton MSc, Joji Decolongon, MSC., Cheryl J.Erwin, JD, Ph.D., Michael Hayden, MD, Ph.D., Lori Jarmon, MA, Elizabeth A. Penziner, M.A., C.H.E.S., Anne Wallis, Ph.D. , Janet K. Williams, Ph.D., RN, Jane S. Paulsen, Ph.D., Wendy Meschino M.D., Oksana Suchowersky M.D., and Mark Guttman M.D.**

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HOW MANY PEOPLE WILL PARTICIPATE?

Approximately ***300 people*** will take part in this study from Canada.

HOW LONG WILL I BE IN THIS STUDY?

This study will be completed in one year. If you agree to take part in this study, your involvement will include the ***completion of a survey*** that should take approximately 30 minutes to complete.

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WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: Yvonne Bombard toll-free at XXXXX.

If you have questions about the rights of research subjects or research related injury, please contact the Office of Research Services at the University of British Columbia, at 604-822-8598.

CONSENT

I acknowledge that the research procedures described on the attached study information sheet and of which I have a copy, have been explained to me. Any questions that I have asked have been answered to my satisfaction. I have been informed of the alternatives to participation in this study. The possible risk and discomforts have been explained to me. I know that I may ask now, or in the future, any question I have about the study of the research procedures. I have been assured that records relating to my care will be kept confidential and that no information will be released or printed that would disclose my personal identity without my permission.

I understand that I am free to withdraw from the study at any time. I further understand that if the study is not completed, or if there is withdrawal from it at any time, the quality of medical care for me will not be affected.

I herby consent to participate.

_____ _____

(Signature) (Name)

_____ _____

(Witness) (Date)

The person who may be contacted about this research is: Yvonne Bombard who can be reached toll-free at XXXX.

THE UNIVERSITY OF BRITISH COLUMBIA

CONSENT FORM

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We encourage you to ask questions. If you have any questions about the research study itself, please contact: Yvonne Bombard toll-free at XXXXXX.

If you have questions about the rights of research subjects or research related injury, please contact the Office of Research Services at the University of British Columbia, at 604-822-8598.

CONSENT

I acknowledge that the research procedures described on the attached study information sheet and of which I have a copy, have been explained to me. Any questions that I have asked have been answered to my satisfaction. I have been informed of the alternatives to participation in this study. The possible risk and discomforts have been explained to me. I know that I may ask now, or in the future, any question I have about the study of the research procedures. I have been assured that records relating to my care will be kept confidential and that no information will be released or printed that would disclose my personal identity without my permission.

I understand that I am free to withdraw from the study at any time. I further understand that if the study is not completed, or if there is withdrawal from it at any time, the quality of medical care for me will not be affected.

I herby consent to participate.

_____ _____

(Signature) (Name)

_____ _____

(Witness) (Date)

The person who may be contacted about this research is: Yvonne Bombard who can be reached toll-free at XXXX.

A3. SEMI STRUCTURED INTERVIEW GUIDE

Interview Guide –Tested Group

Thank you for agreeing to participate in this interview with me. Is now an all right time for you to speak with me about your experiences? I will tape record our conversation. Your personal identifying information will be removed from the transcribed records of our conversation. If for any reason you wish to stop the interview, please tell me and then if you want, we can find another time to complete the interview. Please also feel free to tell me if you prefer not to answer a question that I ask.

Self:

1. To get us started, can you tell me how you have been since your predictive testing?
2. How has learning of your test results changed things for you? We are interested in hearing about what, if anything has changed for you personally because of your [in/decreased] risk for HD.
3. Has your risk for HD changed any of your future plans?
    a. Life planning?
    b. Career planning?
    c. Family planning?
    d. Financial planning?
4. Can you tell me if your test results have influenced the way you view yourself [probe: before and after DT, if any]?

Interactions within Families:

5. How has your genetic test influenced your family relationships?
6. Please tell me about any times when you felt treated differently by your family since you learned of your test results?
7. How did you feel? [Probe for: familial pre-selection]
8. What has it been like to be part of a HD family in your community? How were you and your family treated by others?
9. When people learn of their family history for HD they may share this information. Can you tell me about how you decided who to share this information with and who not to share the information with?
10. What kinds of things influenced your decisions?
11. What exactly did you tell them?
12. *Can you tell me how is this decision process may be different from sharing other types of information, say a vacation?*
13. *What prompts this decision process?*
14. *How long does this decision process take?*

a. *How do you choose to disclose such information? [probe: large/small company, children older than 18, contact has experience with illness?]*

15. We are interested in hearing about your experiences in telling others about your test results. Can you tell me about how this went with one of the people you decided to share this information with? [Probe for: who, when, how, and expected and actual reaction to risk status].
    b. Can you give me another example of telling someone in where the way you shared this information or their reaction was different?

Insurance:

16. People have different needs for life insurance. How important is life insurance to you at this time in your life? Has this changed since you learned about your genetic test results?
17. What are your experiences in obtaining or keeping life insurance after you learned of your test results?
18. <u>If disclosure is not required (e.g., group plan at work)</u>: What concerns, if any, do you have about life insurance if you had to leave your job or retire and were no longer eligible for the group insurance you are on now?
19. <u>If no disclosure to insurance company:</u> What do you believe would happen if your insurance company knew of your test results?
    a. If concerns are indicated: What kinds of concerns have led you to avoid sharing health information with your insurer?
        i. Paid out of pocket, asked for anonymity, or not revealed requested information? *(Asked if the participant does not already mention).*
    b. If concerns are indicated: What kinds of concerns have led you to avoid sharing health information with your health care provider?
20. <u>If disclosure to insurance company:</u> What was the result of your insurer discovering your genetic test results?

Employment:

21. Are you employed right now?
    a. If yes: Can you tell me about the job you currently have? [probe for position in organization, length of service, unionized, educational background, etc]
22. We are interested in learning about your experiences at work with regard to your test results.
    b. Can you tell me what you decided about telling people at work about your test results and how this went? [Probes: Who was told, what influenced the decision to disclose, how explanation was given, and what response was; Who was not told and the reasons for this]

c. If individuals were told at work: How has telling individuals about your test results changed things at work for you (e.g., how you were treated after this)? Did you have any of these experiences before you knew of your at risk status for HD? Do you have any concerns about how you may be treated at work in the future?

23. If individual did not disclose to employer: What do you believe would happen if your employer knew of your risk for HD?
    a. If concerns are indicated: In what way have these concerns affected your financial or employment decisions or employment conditions?
24. If you were deciding to look for a new employer, would your test results impact this decision?
    d. If concern is indicated: What concerns would you have about being hired, receiving insurance, or receiving other benefits?

Social

25. What has it been like to share your genetic test results with friends or neighbours? How have you made decisions about whom, when to tell? What factors influenced these decisions? What were their reactions?

26. If neighbours(s) were told: How has telling your neighbours(s) about your genetic test results changed things for you? Can you give me an example of a time when you felt you were treated differently by your neighbors because of your risk for Huntington disease?
    a. What about your children? Can you tell me about any times you felt your children were treated differently by neighbours(s)?
27. Do you have any concerns that your children may be treated differently?

28. If friend(s) were told: How has telling your friend(s) about your test results changed things for you? What about times where you felt you were treated differently by your friend(s) because of your test results?
    a. Please describe any occasions where you felt your children were treated differently by friend(s).

29. Have you ever felt you were treated differently by others not yet mentioned because of your test results? Can you tell me about this?

Final Questions

30. We have been speaking about issues around being treated differently, others have called this discrimination.

    a. What do you think about this word?
        i. What does it mean to you?
        ii. Does it mean differential treatment to you?

b. What does genetic discrimination mean to you?
c. Would you use this word to describe the experiences or concerns that you have mentioned? Why or why not?
d. Are you comfortable describing the experiences or concerns as discrimination? Why or why not?
e. What is different about your experience/concern of discrimination and another of differential treatment?

31. Have you altered your life in any way to avoid being treated differently? Can you tell me about this?
    a. Would you describe this as an active or passive strategy? Why or why not
    b. What would cause someone to use an active or passive strategy?

32. How have you responded to DT or discrimination?
    a. What caused you to react in this way?
    b. Would you refer to this as passive or active?

33. In what situations or at what times do you think people have to worry most about being treated differently because they are at risk for HD?

34. Have you altered your life in any way to avoid being treated differently? Can you tell me about this?

35. Have you altered your view of yourself if you have been treated differently? Can you tell me about this?

36. Is there any additional information that you would like to share with me that I haven't asked about?

Interview Guide – Not Tested Group

Thank you for agreeing to participate in this interview with me. Is now an all right time for you to speak with me about your experiences? I will tape record our conversation. Your personal identifying information will be removed from the transcribed records of our conversation. If for any reason you wish to stop the interview, please tell me and then if you want, we can find another time to complete the interview. Please also feel free to tell me if you prefer not to answer a question that I ask.

Self:

1. To get us started, can you tell me how you first learned of your HD family history? [Probe: when, by whom, what was said, reaction (s)]
2. How has learning of your family history for HD changed things for you? We are interested in hearing about what, if anything has changed for you personally because of your risk for HD.
3. Has your risk for HD changed any of your future plans?
    a. Life planning?
    b. Career planning?
    c. Family planning?
    d. Financial planning?
4. Can you tell me if your family history for HD has influenced the way you view yourself [probe: before and after DT, if any]?

Interactions within Families:

5. How has your family history for HD influenced your family relationships?
6. Please tell me about any times when you felt treated differently by your family since you learned of your family history for HD?
7. How did you feel? [Probe for: familial preselection]
8. What has it been like to be part of a HD family in your community? How were you and your family treated by others?
9. Sometimes, family members raise concerns about how caring for people with HD may influence them. We are interested in learning about occasions where this may have happened to you.
10. How do members of your family feel about the potential passing the gene mutation on to your children? How has this influenced your relationships with them or how you are treated?
11. When people learn of their family history for HD they may share this information. Can you tell me about how you decided who to share this information with and who not to share the information with?
    a. What kinds of things influenced your decisions?
    b. What exactly did you tell them?

c. *Can you tell me how is this decision process may be different from sharing other types of information, say a vacation?*
d. *What prompts this decision process?*
e. *How long does this decision process take?*
f. *How do you choose to disclose such information? [probe: large/small company, children older than 18, contact has experience with illness?]*

12. We are interested in hearing about your experiences in telling others about being part of an HD family. Can you tell me about how this went with one of the people you decided to share this information with? [Probe for: who, when, how, and expected and actual reaction to risk status].
    a. Can you give me another example of telling someone in where the way you shared this information or their reaction was different?

Insurance:

13. People have different needs for life insurance. How important is life insurance to you at this time in your life? Has this changed since you learned about your family history for HD?
14. What are your experiences in obtaining or keeping life insurance after you learned of your risk for HD?
15. <u>If disclosure is not required (e.g., group plan at work)</u>: What concerns, if any, do you have about life insurance if you had to leave your job or retire and were no longer eligible for the group insurance you are on now?
16. <u>If no disclosure to insurance company:</u> What do you believe would happen if your insurance company knew of your family history for HD?
    a. If concerns are indicated: What kinds of concerns have led you to avoid sharing health information with your insurer?
        i. Paid out of pocket, asked for anonymity, or not revealed requested information? *(Asked if the participant does not already mention).*
    b. If concerns are indicated: What kinds of concerns have led you to avoid sharing health information with your health care provider?
17. <u>If disclosure to insurance company:</u> What was the result of your insurer discovering your family history for HD?

Employment:

18. Are you employed right now?
    a. If yes: Can you tell me about the job you currently have? [probe for position in organization, length of service, unionized, educational background, etc]
19. We are interested in learning about your experiences at work with regard to your family history for HD.
    a. Can you tell me what you decided about telling people at work about your risk for HD and how this went? [Probes: Who was told,

what influenced the decision to disclose, how explanation was given, and what response was; Who was not told and the reasons for this]

b. If individuals were told at work: How has telling individuals about your risk for HD changed things at work for you (e.g., how you were treated after this)? Did you have any of these experiences before you knew of your at risk status for HD? Do you have any concerns about how you may be treated at work in the future?

20. If individual did not disclose to employer: What do you believe would happen if your employer knew of your risk for HD?
    b. If concerns are indicated: In what way have these concerns affected your financial or employment decisions or employment conditions?
21. If you were deciding to look for a new employer, would your risk for HD impact this decision?
    a. If concern is indicated: What concerns would you have about being hired, receiving insurance, or receiving other benefits?

Social

22. What has it been like to share your family history for HD with friends or neighbours? How have you made decisions about whom, when to tell? What factors influenced these decisions? What were their reactions?

23. If neighbours(s) were told: How has telling your neighbours(s) about your family history for HD changed things for you? Can you give me an example of a time when you felt you were treated differently by your neighbors because of your risk for Huntington disease?
    a. What about your children? Can you tell me about any times you felt your children were treated differently by neighbours(s)?

24. If friend(s) were told: How has telling your friend(s) about your risk for HD changed things for you? What about times where you felt you were treated differently by your friend(s) because of your risk for Huntington disease?
    a. Please describe any occasions where you felt your children were treated differently by friend(s).

25. Have you ever felt you were treated differently by others not yet mentioned because of your risk for Huntington disease? Can you tell me about this?

Final Questions

26. Have you considered predictive testing? What have you decided about this? Can you tell me about the advantages or disadvantages of predictive testing for you?

27. In what situations or at what times do you think people have to worry most about being treated differently because they are at risk for HD?

28. Have you altered your life in any way to avoid being treated differently? Can you tell me about this?

29. Have you altered your view of yourself if you have been treated differently? Can you tell me about this?

30. Is there any additional information that you would like to share with me that I haven't asked about?

COGNITIVE INTERVIEW FIELDNOTES

General Information

Participant Code: Interview Date:

Start Time: End Time:

Pre – Interview Notes

Pre - interview Goals:

Location of Interview:

Instructions to be read to Subject:

Thanks for coming in/ helping with our study. Let me tell you a little more about what we'll be doing today.

1. We're testing a new questionnaire with the help of people such as yourself.
2. You'll read through these questions and answer them, just like a regular survey.
3. However, our goal here is to get a better idea of how the questions are working. So I'd like you to write notes, circle things to remind yourself about things you or others would not understand/are not clear.
4. After you're finished, I will come back to get your reaction to this questionnaire. Please keep in mind that I really want to hear all of your opinions and reactions. Don't hesitate to let me know about anything that seems unclear, is hard to answer, or doesn't seem to apply to you. I'll also take notes.
5. After this I will ask you more questions about the terms and phrases in the questions and what you think the question is asking about.
6. We will do this for about an hour.
7. Do you have any questions before we start?
8. Please let me know when you have finished the survey.

Survey Start Time: _____ **Survey End Time:** _____

Subject's General Comments:

Verbal Probes:

A4 a-ii (pg 2): "What was the number of CAG repeats in your gene?"

1. Tell me what you were thinking when I asked you about your '*CAG repeats.*'
2. What does the term "*CAG repeats*" mean to you?
3. How did you arrive at this answer?

Interviewer's Notes:

A5-b (pg 2): *"As far as you are aware, how many people in your immediate family"*

1. Tell me what you were thinking when I asked you about your 'immediate family.'
2. What does the term "immediate family" mean to you?
3. How did you arrive at this answer?
4. Was it difficult for you, what about for others?

5. How sure are you about this estimate?

Interviewer's Notes:

C1 (pg 5): *"How much benefit or advantage, if any, have you felt from knowing about your family history of HD?"*

1. Tell me what you were thinking when I asked you about BENEFIT.
    - Do you like advantages better?
2. Tell me what you were thinking when I asked you about FAMILY HISTORY FOR HD.

Interviewer's Notes:

C2 (pg 5): *"Do you think knowing about your family history of HD has brought benefit because knowing….*

1. In general, how do you feel about this question?

Interviewer's Notes:

C3-4 (pg 5-6): *When you were a child or teenager (up to age 18), how much did you worry about [you] [members of your family] being treated unfairly because of your family history of HD?*

1. In general, how do you feel about this question?
2. Can you tell me in your own words what these questions are asking?
3. Can you tell me how C3 is different than C4?
4. What does the term BEING TREATED UNFAIRLY mean to you?
5. Does being treated unfairly sound OK to you, or would you choose something different?
6. How do you remember how much you worried about being treated unfairly?

Interviewer's Notes:

C8-b (pg 7): What else do you feel other than distress?

1. Can you tell me in your own words what this question is asking?
2. How easy was it to see and answer this question?

Interviewer's Notes:

C11 (pg 8): *In general, when you become aware of the POSSIBILITY of being treated unfairly because of your family history of HD, do you usually:*

1. Can you tell me in your own words what this question is asking?
2. What does the terms *POSSIBILITY of being treated unfairly* mean to you?

Interviewer's Notes:

C12 (pg 8): *In general, how satisfied or dissatisfied are you with your response(s) in preventing the possibility of being treated unfairly because of your family history of HD?*

1. Can you tell me in your own words what this question is asking?
2. What does the term *satisfied* mean to you?
3. What does response mean to you?
4. How do you come to decide how satisfied you are?
5. How do you remember what your response was?

Interviewer's Notes:

C14 (pg 9): *Have you ever experienced discrimination, been prevented from doing something, or been treated unfairly in the following situations or by any of these people because of your FAMILY HISTORY OF HD?*

1. In general, how do you feel about this question?
2. Can you tell me in your own words what this question is asking
3. Is discrimination OK to talk about in a survey, or is it uncomfortable?
4. Does *discrimination, been prevented from doing something, or been treated unfairly* sound OK to you, or would you chose something different?
5. How do you remember whether you have experienced discrimination?
6. How sure are you about this?

Interviewer's Notes:

C17 (pg 11): In general, how do you respond to being treated unfairly?

1. What does respond mean to you?
2. Does this refer to before or after the incident of unfair treatment?

Interviewer's Notes:

Section D (pg 12):

1. In general, how do you feel about this section?
2. Can you tell me how this section is different from the previous one?

Interviewer's Notes:

E1 (pg 19): *Are there any clear incidents of disadvantage or negative treatment related to your family history of HD or genetic test results?*

1. Can you tell me in your own words what this question is asking?
2. Can you tell me how this question is different from the previous one?

Interviewer's Notes:

E2-6 (pg 19): *Please estimate how many incidents of disadvantage…*

1. How do you remember how many incidents of being disadvantaged have occurred?
2. How sure are you about this estimate?

Interviewer's Notes:

_____
_____
_____
_____
_____
_____
_____

E9-b (pg 21): *Did you question or challenge the incident of disadvantage?*

1. What does the term *challenge* mean to you?

Interviewer's Notes:

_____
_____
_____

 **(pg 22):** *Did you or others place a complaint about the disadvantage?*

1. What does the term *complaint* mean to you?

Interviewer's Notes:

_____
_____
_____
_____

E19 (pg 23): *Are there any clear incidents where you have been made to feel different because of your family history of HD or genetic test results?*

1. Can you tell me in your own words what this question is asking?
2. What does the term INCIDENTS mean to you?

Interviewer's Notes:

F3 (pg 24): *Do/did you feel concerned about the possibility of being charged higher insurance premiums because of your:*

1. What does the term *premium* mean to you?

Interviewer's Notes:

F4 (pg 24): *Do/did you feel concerned about the possibility of insurance rejection because of your:*

1. What does the term *insurance rejection* mean to you?

Interviewer's Notes:

F17 (pg 27): *Were you offered Standard Coverage for all applications?*

1. What does the term *Standard Coverage* mean to you?

Interviewer's Notes:

F27 (pg 29): Have you ever asked for genetic testing for HD anonymously so that your genetic test results would not be made available to an insurance agent or company?

1. What does the term anonymously mean to you?

Interviewer's Notes:

Follow Up Probes

1. How is the format? (Suggestions for format, administration (booklet)
2. How is the length of the survey?
3. How are the instructions?
4. Are there things that you wanted to write but didn't have space or option?
5. Anything that they would change?
    a. Are there any questions that should be removed?
    b. Are there any questions that should be added?
6. What would make it easier to fill out?

Interviewer's Notes:

Post – Interview Information

- **Nonverbal Behaviour** (e.g. tone of voice, posture, facial expressions, eye movements/contact, forcefulness of speech, body movements, and hand gestures):

- **Content of Interview** (e.g. use key words, topics, focus, exact words, or phrases that stand out):

- **Researcher's impressions** (e.g. discomfort of participant with certain topics, emotional responses to people, events or objects)

- **Analysis** (e.g. researcher's questions, tentative hunches, trends in data, and emerging patterns):

- **Technological Problems** (e.g. lost 5 minutes of IV):

A5. SURVEY INSTRUMENT

RESPOND–HD SURVEY 2006

We invite you to participate in this study which investigates the way an individual's genetic information is used in certain decision-making processes in Canada. RESPOND–HD is a national research project funded by the Canadian Institutes of Health Research (CIHR). Your participation is voluntary and your answers are strictly confidential.

HOW TO FILL OUT THIS QUESTIONNAIRE

- This questionnaire should take approximately 30 minutes to complete.
- Most of the questions require that you simply TICK (☑) the box indicating the appropriate answer(s).
- There are no right or wrong answers; we are interested in your personal opinions and experiences.
- Some questions may appear repetitive, please note that there are subtle and important differences.
- If you need more space when answering a question, please use the additional pages at the back of the booklet.
- If you have any questions or would like to talk to us about any of your experiences, please call us **toll-free at 1-877-811-0116.**

All questions in this questionnaire apply to the person to whom this package was addressed

I would prefer not to complete this questionnaire. ☐ (☑)

My reasons are (optional): .....

.....

Please return the questionnaire in the enclosed Postage-Paid envelope. Thank you.

* *Modified from a similar survey with permission from the University of Queensland and the University of Tasmania.*
* *Modified from a similar survey, described in N Krieger Soc Sci Med 1990, N Krieger et al Am J Public Health 1996 & N Krieger et al Soc Sci Med 2005.*
* *In collaboration with the NINDS-funded study, PREDICT-HD (PI: Jane S. Paulsen).*

SECTION A: ABOUT YOU

*This section asks about **your family history of Huntington disease (HD) and genetic testing**, if applicable. (Genetic testing determines if one has inherited the gene mutation which causes HD. The HD gene mutation is what is analyzed during genetic testing.)*

A1 Are you …? Male ☐ 1 Female ☐ 2

A2 In what year were you born? 1 9 __ __

A3 What are the first 3 digits of your postal code? __ __ __

	YES	NO	Don't Know (DK)
A4 Have you had a genetic test for Huntington disease?	☐ Y	☐ N	☐ DK
i In what year did you have the genetic test?	Year: _ _ _ _		☐ DK
ii Did you get a positive test result (i.e. you **HAVE** inherited the HD gene expansion)?	☐ Y	☐ N	☐ DK

A5 Do you **have symptoms** of Huntington disease?	☐ Y	☐ N	☐ DK
i Has a doctor diagnosed your symptoms?	☐ Y	☐ N	
ii In what year was this diagnosis made?	Year: __ __ __ __		

A6 Please answer each of the following questions pertaining to your family history of Huntington disease (HD):

a In approximately what year did you first become aware that HD was in your family? (e.g. 1998) — Year _____ ☐ DK

b *Note: the following question asks for information about your blood relatives (i.e. parents, siblings, aunts, grandparents).* As far as you are aware, **how many people in your immediate family:**

	Number (0,1,2…)	Which Family Members (i.e. mom)?	Don't Know
i Carry the HD gene mutation but have **no** symptoms	____	_____	☐ DK
ii Carry the HD gene mutation and **have** symptoms	____	_____	☐ DK
iii Know that they do **not** carry the HD gene mutation	____	_____	☐ DK
iv Do **not** know whether they carry the HD gene mutation	____	_____	☐ DK

SECTION B: GENETIC TESTING

*This section asks about your **thoughts and opinions related to genetic testing** for HD.*

B1 **How would you rate your knowledge of the possible advantages and disadvantages of genetic testing for HD?** *Please choose a number between 1 and 5 where 1 = Not very knowledgeable and 5 = Very knowledgeable* (☑).

Not Very Knowledgeable				Very Knowledgeable
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Have you had a genetic test for HD? ☐ **Yes** → Go to **question B3, page 4**
☐ **No** → Go to **question B2 on this page.**

B2 **What are the reasons that you have chosen NOT to be tested for HD?** *Please rate how strongly you agree or disagree with EACH of the following statements by placing a tick* (☑) *in the appropriate box*

		STRONGLY DISAGREE	SOMEWHAT DISAGREE	NEUTRAL	SOMEWHAT AGREE	STRONGLY AGREE
a	It is not an important issue for me.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b	I don't want to know.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c	I would prefer to be tested at a later date.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d	I have concerns about coping with the results.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
e	I have concerns about family members coping with the results.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
f	I have concerns about the implications of the test results for family members.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
g	I have concerns about privacy and confidentiality.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
h	I have concerns about insurance.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
i	I have concerns about the cost of testing.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
j	I have concerns about employment/employers.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
k	I have concerns about how others will treat me if they know I have the gene mutation.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
l	There is no cure for Huntington disease.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
m	I have already had all the children I planned to have.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
n	Other *(please specify)*:.....					

B3 **Have any of the following persons/organizations ever suggested that you take a genetic test for HD?** *Please answer EACH of the following by TICKING (☑) Yes, No or Don't Know:*

		YES	NO	Don't Know
a	Family member (*please specify*):	☐ Y	☐ N	☐ DK
b	Doctor	☐ Y	☐ N	☐ DK
c	Geneticist or genetic counselor	☐ Y	☐ N	☐ DK
d	Insurance company	☐ Y	☐ N	☐ DK
e	Employer	☐ Y	☐ N	☐ DK
f	Bank/financial organization	☐ Y	☐ N	☐ DK
g	Researcher	☐ Y	☐ N	☐ DK
h	Other (*please specify*):			

B4 **Upon reflection, how much pressure have you felt from the following persons/organizations to take a genetic test for HD?** *Please answer EACH of the following by TICKING (☑) None, Some or A lot:*

		None	Some	A lot
a	Family member (*please specify*):	☐ 0	☐ 1	☐ 2
b	Doctor	☐ 0	☐ 1	☐ 2
c	Geneticist or genetic counselor	☐ 0	☐ 1	☐ 2
d	Insurance company	☐ 0	☐ 1	☐ 2
e	Employer	☐ 0	☐ 1	☐ 2
f	Bank/financial organization	☐ 0	☐ 1	☐ 2
g	Researcher	☐ 0	☐ 1	☐ 2
h	Other (*please specify*):			

B5 **To what degree, if any, did this pressure cause you distress?** *Please choose a number between 0 and 5 where 0 = I have not experienced any pressure and 5 = A lot of Distress* (☑).

		Very Little Distress				A lot of Distress
I have not experienced any pressure	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

SECTION C: FEELINGS AND EXPERIENCES BASED ON FAMILY HISTORY

The first part of this section** asks about any possible **benefits or advantages** in knowing about your **family history of HD**; the **next part** asks about any possible **disadvantages or unfair treatment.

We are trying to examine the perceptions and experiences of genetic discrimination, defined as the denial of rights, privileges or opportunities or other adverse treatment based solely on genetic information including family history of HD or genetic testing for HD. This can be experienced as being treated unfairly. In the questions that follow the term "treated unfairly" refers to the experience of genetic discrimination.

C1 How much benefit or advantage, if any, have you felt from knowing about your family history of HD?
Please choose a number between 1 and 5 where 1 = Very little benefit and 5 = Great benefit (☑).

Very little benefit				Great benefit
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

C2 Do you think knowing about your family history of HD has brought benefit because ...: *Please rate how strongly you agree or disagree with EACH of the following statements by placing a tick* (☑) *in the appropriate box.*

		STRONGLY DISAGREE	SOMEWHAT DISAGREE	NEUTRAL	SOMEWHAT AGREE	STRONGLY AGREE
a	Knowing is better than not knowing, even if it can be stressful	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b	Knowing has helped you understand the role of genetics in your or your family's lives	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c	Knowing has given you a greater sense of personal control and certainty	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d	Knowing has helped you plan your future	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
e	Knowing has helped you with choices about having children	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
f	Knowing has helped in your communication and relationships with family	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
g	Knowing has helped in your communication and relationships with others	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
h	Knowing has helped you to share the family history with others at risk in your family	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
i	Knowing has given you the opportunity to take preventive actions to control or monitor the development of symptoms	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
j	Knowing has given you a reliable scientific basis to use in explaining your or your family's situation to others	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
k	Knowing has allowed you to support and/or be supported by others	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
l	other (*please specify*):					
	.....					

		Not Applicable	Rarely or Never	Some of the Time	Most of the Time
C3	When you were a child or teenager (up to age 18), how much did you worry about **you** being treated unfairly because of **your** family history of HD?	☐ NA	☐ N	☐ S	☐ M
C4	When you were a child or teenager (up to age 18), how much did you worry about **members of your family** being treated unfairly because of **their** family history of HD?	☐ NA	☐ N	☐ S	☐ M
C5	In the last year, how much did you worry about **you** being treated unfairly because of **your** family history of HD?		☐ N	☐ S	☐ M
C6	In the last year, how much did you worry about **members of your family** being treated unfairly because of **their** family history of HD?	☐ NA	☐ N	☐ S	☐ M
C7	How often do you feel that **people with a family history of HD** are treated unfairly?		☐ N	☐ S	☐ M

C8 Have you ever worried about being treated unfairly because of your family history of HD? *Please answer EACH of the following*

		Yes	No	Not Appli-cable
a	At school	☐ Y	☐ N	☐ NA
b	At work	☐ Y	☐ N	☐ NA
c	In the law courts	☐ Y	☐ N	☐ NA
d	When getting hired or getting a job	☐ Y	☐ N	☐ NA
e	When establishing a relationship	☐ Y	☐ N	☐ NA
f	When making choices about having children	☐ Y	☐ N	☐ NA
g	When getting medical care	☐ Y	☐ N	☐ NA
h	When getting custody or access to your children	☐ Y	☐ N	☐ NA
i	By a life insurance company or agent	☐ Y	☐ N	☐ NA
j	By a long term disability insurance company or agent	☐ Y	☐ N	☐ NA
k	By a mortgage company or agent	☐ Y	☐ N	☐ NA
l	By a member of your family (*please specify*):	☐ Y	☐ N	☐ NA
m	By a friend	☐ Y	☐ N	☐ NA
n	By your spouse	☐ Y	☐ N	☐ NA
o	By a boy/girl friend	☐ Y	☐ N	☐ NA
p	By your community	☐ Y	☐ N	☐ NA
q	By your religious organization	☐ Y	☐ N	☐ NA
r	By your doctor	☐ Y	☐ N	☐ NA
s	By other health care professional(s)	☐ Y	☐ N	☐ NA
t	By a genetic counselling service	☐ Y	☐ N	☐ NA
u	By a blood bank	☐ Y	☐ N	☐ NA
v	By the Canadian Forces	☐ Y	☐ N	☐ NA
w	By an adoption agency	☐ Y	☐ N	☐ NA
x	Other (*please specify*):			

Did you select *"YES"* for any part of question C8? ☐ **Yes** → **Please continue to C9, page 7** ☐ **No** → Go to **question C11, page 7**

C9 **In general, to what degree are you worried about being treated unfairly because of your family history of HD?** *Please choose a number between 1 and 5 where 1 = Not very worried and 5 =Very worried* (☑).

Not very worried				Very worried
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

C10 **To what degree, if any, is it distressing to worry about being treated unfairly because of your family history of HD?** *Please choose a number between 1 and 5 where 1 = Not very distressing and 5= Very distressing* (☑).

	Not very distressing				Very distressing
a	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

b **What else do you feel other than distress?** *(please specify)*: .....
.....

C11 **Have you ever worried about members of your family being treated unfairly because of their family history of HD?** *Please answer EACH of the following*

		Yes	No	Not Appli -cable
a	At school	☐ Y	☐ N	☐ NA
b	At work	☐ Y	☐ N	☐ NA
c	In the law courts	☐ Y	☐ N	☐ NA
d	When getting hired or getting a job	☐ Y	☐ N	☐ NA
e	When establishing a relationship	☐ Y	☐ N	☐ NA
f	When making choices about having children	☐ Y	☐ N	☐ NA
g	When getting medical care	☐ Y	☐ N	☐ NA
h	When getting custody or access to their children	☐ Y	☐ N	☐ NA
i	By a life insurance company or agent	☐ Y	☐ N	☐ NA
j	By a long term disability insurance company or agent	☐ Y	☐ N	☐ NA
k	By a mortgage company or agent	☐ Y	☐ N	☐ NA
l	By a member of your family *(please specify)*:	☐ Y	☐ N	☐ NA

		Yes	No	Not Appli -cable
m	By a friend	☐ Y	☐ N	☐ NA
n	By your spouse	☐ Y	☐ N	☐ NA
o	By a boy/girl friend	☐ Y	☐ N	☐ NA
p	By your community	☐ Y	☐ N	☐ NA
q	By your religious organization	☐ Y	☐ N	☐ NA
r	By your doctor	☐ Y	☐ N	☐ NA
s	By other health care professional(s)	☐ Y	☐ N	☐ NA
t	By a genetic counselling service	☐ Y	☐ N	☐ NA
u	By a blood bank	☐ Y	☐ N	☐ NA
v	By the Canadian Forces	☐ Y	☐ N	☐ NA
w	By an adoption agency	☐ Y	☐ N	☐ NA
x	Other *(please specify)*:			

Did you select *"YES"* for any part of question C11? ☐ **Yes** → **Please continue to C12, page 8** ☐ **No** → **Go to question C14, page 8**

C12 **In general, to what degree are you worried about members of your family being treated unfairly because of their family history of HD?** *Please choose a number between 1 and 5 where 1 = Not very worried and 5 =Very worried* (☑).

Not very worried				Very worried
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

C13 **To what degree, if any, is it distressing to worry about members of your family being treated unfairly because of their family history of HD?** *Please choose a number between 1 and 5 where 1 = Not very distressing and 5 = Very distressing* (☑).

	Not very distressing				Very distressing
a	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

b **What else do you feel other than distress?** *(please specify)*: .....

.....

C14 **In general, when you become aware of the possibility of being treated unfairly because of your family history of HD, do you usually**: *Please answer EACH of the following*

		Yes	No	Not Applicable
a	Try to take action in advance to avoid the possible situation?	☐ Y	☐ N	
b	Keep quiet about your family history of HD?	☐ Y	☐ N	
c	Stay in the same job?	☐ Y	☐ N	☐ NA
d	Choose a job primarily on the basis of employee benefits offered?	☐ Y	☐ N	☐ NA
e	Refrain from applying for a promotion?	☐ Y	☐ N	☐ NA
f	Talk to others about Huntington disease in order to educate the public?	☐ Y	☐ N	
g	Disclose your family history of HD so others can be aware that you may develop symptoms in the future?	☐ Y	☐ N	
h	Disclose your family history of HD so others can watch you for symptoms?	☐ Y	☐ N	
i	Other (*please specify):*			

C15 **To what degree are you satisfied with your response(s) in preventing the possibility of being treated unfairly because of your family history of HD?** *Please choose a number between 1 and 5 where 1 = Not very satisfied and 5 =Very satisfied* (☑).

Not very satisfied				Very satisfied
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

C16 **How much disadvantage, if any, have you felt from knowing about your family history of HD?** *Please choose a number between 1 and 5 where 1 = No Disadvantage and 5 = Great Disadvantage* (☑).

No Disadvantage				Great Disadvantage
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

C17 We are interested in learning about experiences with discrimination, by this we mean being unfairly prevented from doing something, or being treated unfairly. Have you ever experienced discrimination in any of the following situations because of your family history of HD? *Please answer EACH of the following*

	Yes	No	Not Appli -cable
a At school	☐ Y	☐ N	☐ NA
b At work	☐ Y	☐ N	☐ NA
c In the law courts	☐ Y	☐ N	☐ NA
d When getting hired or getting a job	☐ Y	☐ N	☐ NA
e When establishing a relationship	☐ Y	☐ N	☐ NA
f When making choices about having children	☐ Y	☐ N	☐ NA
g When getting medical care	☐ Y	☐ N	☐ NA
h When getting custody or access to your children	☐ Y	☐ N	☐ NA
i By a life insurance company or agent	☐ Y	☐ N	☐ NA
j By a long term disability insurance company or agent	☐ Y	☐ N	☐ NA
k By a mortgage company or agent	☐ Y	☐ N	☐ NA
l By a member of your family (*please specify*):	☐ Y	☐ N	☐ NA
m By a friend	☐ Y	☐ N	☐ NA
n By your spouse	☐ Y	☐ N	☐ NA
o By a boy/girl friend	☐ Y	☐ N	☐ NA
p By your community	☐ Y	☐ N	☐ NA
q By your religious organization	☐ Y	☐ N	☐ NA
r By your doctor	☐ Y	☐ N	☐ NA
s By other health care professional(s)	☐ Y	☐ N	☐ NA
t By a genetic counselling service	☐ Y	☐ N	☐ NA
u By a blood bank	☐ Y	☐ N	☐ NA
v By the Canadian Forces	☐ Y	☐ N	☐ NA
w By an adoption agency	☐ Y	☐ N	☐ NA
x Other (*please specify*):			

Did you select *"YES"* for any part of question C17? ☐ **Yes** → **Please continue to C18, below** ☐ **No** → **Go to question C19, page 10**

C18 To what degree, if any, is it distressing to be treated unfairly because of your family history of HD? *Please choose a number between 1 and 5 where 1 = Not very distressing and 5 = Very distressing* (☑).

a

Not very distressing				Very distressing
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

b What else do you feel other than distress? *(please specify)*: .....
.....

C19 **In the following questions, we are interested in the way other people have treated you. Can you tell us if ANY of the following has ever happened to you <u>because of your family history of HD</u>:** *Please answer EACH of the following.*

		Yes	No	Not Applicable
a	Have you ever been fired at any time in your life **because of your family history of HD?**	☐ Y	☐ N	☐ NA
b	Have you ever been denied a promotion **because of your family history of HD?**	☐ Y	☐ N	☐ NA
c	Have you ever been denied a job **because of your family history of HD?**	☐ Y	☐ N	☐ NA
d	Have you ever been discouraged by a teacher or advisor from continuing your education **because of your family history of HD?**	☐ Y	☐ N	☐ NA
e	Have you ever been discouraged by a family member from continuing your education **because of your family history of HD?**	☐ Y	☐ N	☐ NA
f	Have you ever been prevented from moving into a neighborhood because the landlord or a realtor refused to rent or sell you a house or apartment **because of your family history of HD?**	☐ Y	☐ N	☐ NA
g	Have you ever been denied a bank loan **because of your family history of HD?**	☐ Y	☐ N	☐ NA
h	Have you ever been denied life insurance **because of your family history of HD?**	☐ Y	☐ N	☐ NA
i	Have you ever been denied long term disability benefits **because of your family history of HD?**	☐ Y	☐ N	☐ NA
j	Have you ever been denied critical care insurance **because of your family history of HD?**	☐ Y	☐ N	☐ NA
k	Have you ever been denied custody or access to your children **because of your family history of HD?**	☐ Y	☐ N	☐ NA
l	Have you ever been watched for symptoms by a family member(s) **because of your family history of HD?**	☐ Y	☐ N	☐ NA
m	Have you received negative comments **because of your family history of HD?**	☐ Y	☐ N	☐ NA
n	Have you seen people change their communication patterns with you **because of your family history of HD?**	☐ Y	☐ N	☐ NA
o	Have you been denied when claiming disability benefits **because of your family history of HD?**	☐ Y	☐ N	☐ NA
p	Have you been placed under surveillance at work **because of your family history of HD?**	☐ Y	☐ N	☐ NA
q	Other (*please specify*):			

Did you select *"YES"* for any part of question C19?	☐ **Yes** ➔ **Please continue to C20, below** ☐ **No** ➔ Go to the ***box with a hand sign*** (✋) **below**

C20 **In general, how did you <u>respond</u> to being treated unfairly because of your <u>family history of HD</u>?** *Please answer EACH of the following*

		Yes	No
a	Tried to do something about the situation	☐ Y	☐ N
b	Accepted it as a fact of life	☐ Y	☐ N
c	Worked harder to prove them wrong	☐ Y	☐ N
d	Realized that I brought it on myself	☐ Y	☐ N
e	Talked to someone about how I was feeling	☐ Y	☐ N
f	Expressed anger or get mad	☐ Y	☐ N
g	Prayed about the situation	☐ Y	☐ N
h	Ignored the situation	☐ Y	☐ N
i	Sought advice about the situation	☐ Y	☐ N
j	Placed a complaint	☐ Y	☐ N
k	Kept how I felt or what happened to myself	☐ Y	☐ N
l	Tried to educate others	☐ Y	☐ N
m	Other (*please specify*):		

C21 **To what degree are you <u>satisfied</u> with your response(s) to being treated unfairly?** *Please choose a number between 1 and 5 where 1 = Not very satisfied and 5 =Very satisfied* (☑).

Not very satisfied				Very satisfied
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Have you had a genetic test for HD?	☐ **Yes** ➔ **Please continue to Section D, page 12** ☐ **No** ➔ Go to **Section E, page 19**

SECTION D: FEELINGS AND EXPERIENCES BASED ON GENETIC TESTING

The first part of this section** asks about any possible **benefits or advantages** in knowing about your **genetic test result**; the **next part** asks about any possible **disadvantages or unfair treatment.

We are trying to examine the perceptions and experiences of genetic discrimination, defined as the denial of rights, privileges or opportunities or other adverse treatment based solely on genetic information including family history of HD or genetic testing for HD. This can be experienced as being treated unfairly. In the questions that follow the term "treated unfairly" refers to the experience of genetic discrimination.

D1 **How much benefit or advantage, if any, have you felt from knowing about your genetic test result?**
Please choose a number between 1 and 5 where 1 =Very little benefit and 5 = Great benefit (☑).

Very little benefit				Great benefit
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

D2 **Do you think knowing about your genetic test result has brought benefit because ...:** *Please rate how strongly you agree or disagree with EACH of the following statements by placing a tick* (☑) *in the appropriate box.*

		STRONGLY DISAGREE	SOMEWHAT DISAGREE	NEUTRAL	SOMEWHAT AGREE	STRONGLY AGREE
a	Knowing is better than not knowing, even if it can be stressful	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b	Knowing has helped you understand the role of genetics in your or your family's lives	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c	Knowing has given you a greater sense of personal control and certainty	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d	Knowing has helped you plan your future	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
e	Knowing has helped you with choices about having children	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
f	Knowing has helped in your communication and relationships with family	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
g	Knowing has helped in your communication and relationships with others	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
h	Knowing has helped you to share the family history with others at risk in your family	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
i	Knowing has given you the opportunity to take preventive actions to control or monitor the development of symptoms	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
j	Knowing has given you a reliable scientific basis to use in explaining your or your family's situation to others	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
k	Knowing has allowed you to support and/or be supported by others	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
l	other (*please specify*):					

.....

		Not Applicable	Rarely or Never	Some of the Time	Most of the Time
D3	When you were a child or teenager (up to age 18), how much did you worry about **members of your family** being treated unfairly because of **their** genetic test result?	☐ NA	☐ N	☐ S	☐ M
D4	In the last year, how much did you worry about **you** being treated unfairly because of **your** genetic test result?		☐ N	☐ S	☐ M
D5	In the last year, how much did you worry about **members of your family** being treated unfairly because of **their** genetic test result?	☐ NA	☐ N	☐ S	☐ M
D6	How often do you feel that **people with a positive genetic test result** are treated unfairly?		☐ N	☐ S	☐ M

D7 **Have <u>you</u> ever worried about being treated unfairly because of <u>your genetic test result</u>?** *Please answer EACH of the following*

		Yes	No	Not Appli -cable
a	At school	☐ Y	☐ N	☐ NA
b	At work	☐ Y	☐ N	☐ NA
c	In the law courts	☐ Y	☐ N	☐ NA
d	When getting hired or getting a job	☐ Y	☐ N	☐ NA
e	When establishing a relationship	☐ Y	☐ N	☐ NA
f	When making choices about having children	☐ Y	☐ N	☐ NA
g	When getting medical care	☐ Y	☐ N	☐ NA
h	When getting custody or access to your children	☐ Y	☐ N	☐ NA
i	By a life insurance company or agent	☐ Y	☐ N	☐ NA
j	By a long term disability insurance company or agent	☐ Y	☐ N	☐ NA
k	By a mortgage company or agent	☐ Y	☐ N	☐ NA
l	By a member of your family (*please specify*):	☐ Y	☐ N	☐ NA
m	By a friend	☐ Y	☐ N	☐ NA
n	By your spouse	☐ Y	☐ N	☐ NA
o	By a boy/girl friend	☐ Y	☐ N	☐ NA
p	By your community	☐ Y	☐ N	☐ NA
q	By your religious organization	☐ Y	☐ N	☐ NA
r	By your doctor	☐ Y	☐ N	☐ NA
s	By other health care professional(s)	☐ Y	☐ N	☐ NA
t	By a genetic counselling service	☐ Y	☐ N	☐ NA
u	By a blood bank	☐ Y	☐ N	☐ NA
v	By the Canadian Forces	☐ Y	☐ N	☐ NA
w	By an adoption agency	☐ Y	☐ N	☐ NA
x	Other (*please specify*):			

Did you select *"YES"* for any part of question D7? ☐ **Yes** → **Please continue to D8, page 14**
☐ **No** → Go to **question D10, page 14**

D8 **In general, to what degree are you worried about being treated unfairly because of your genetic test result?** *Please choose a number between 1 and 5 where 1 = Not very worried and 5 =Very worried* (☑).

Not very worried				Very worried
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

D9 **To what degree, if any, is it distressing to worry about being treated unfairly because of your genetic test result?** *Please choose a number between 1 and 5 where 1 = Not very distressing and 5 = Very distressing* (☑).

	Not very distressing				Very distressing
A	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

B **What else do you feel other than distress?** *(please specify)*: .....

.....

D10 **Have you ever worried about members of your family being treated unfairly because of your genetic test result?** *Please answer EACH of the following*

		Yes	No	Not Appli-cable
a	At school	☐ Y	☐ N	☐ NA
b	At work	☐ Y	☐ N	☐ NA
c	In the law courts	☐ Y	☐ N	☐ NA
d	When getting hired or getting a job	☐ Y	☐ N	☐ NA
e	When establishing a relationship	☐ Y	☐ N	☐ NA
f	When making choices about having children	☐ Y	☐ N	☐ NA
g	When getting medical care	☐ Y	☐ N	☐ NA
h	When getting custody or access to their children	☐ Y	☐ N	☐ NA
i	By a life insurance company or agent	☐ Y	☐ N	☐ NA
j	By a long term disability insurance company or agent	☐ Y	☐ N	☐ NA
k	By a mortgage company or agent	☐ Y	☐ N	☐ NA
l	By a member of your family *(please specify)*:	☐ Y	☐ N	☐ NA
m	By a friend	☐ Y	☐ N	☐ NA
n	By your spouse	☐ Y	☐ N	☐ NA
o	By a boy/girl friend	☐ Y	☐ N	☐ NA
p	By your community	☐ Y	☐ N	☐ NA
q	By your religious organization	☐ Y	☐ N	☐ NA
r	By your doctor	☐ Y	☐ N	☐ NA
s	By other health care professional(s)	☐ Y	☐ N	☐ NA
t	By a genetic counselling service	☐ Y	☐ N	☐ NA
u	By a blood bank	☐ Y	☐ N	☐ NA
v	By the Canadian Forces	☐ Y	☐ N	☐ NA
w	By an adoption agency	☐ Y	☐ N	☐ NA
x	Other *(please specify)*:			

Did you select *"YES"* for any part of question D10? ☐ **Yes** → **Please continue to D11, page 15** ☐ **No** → **Go to question D13, page 15**

D11 **In general, to what degree are you worried about members of your family being treated unfairly because of your genetic test result?** *Please choose a number between 1 and 5 where 1 = Not very worried and 5 =Very worried* (☑).

Not very worried				Very worried
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

D12 **To what degree, if any, is it distressing to worry about members of your family being treated unfairly because of your genetic test result?** *Please choose a number between 1 and 5 where 1 = Not very distressing and 5 = Very distressing* (☑).

	Not very distressing				Very distressing
a	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

b **What else do you feel other than distress?** *(please specify)*: .....

.....

D13 **In general, when you become aware of the possibility of being treated unfairly because of your genetic test result, do you usually**: *Please answer EACH of the following*

		Yes	No	Not Applicable
a	Try to take action in advance to avoid the possibility of being treated unfairly?	☐ Y	☐ N	
b	Keep quiet about your family history of HD?	☐ Y	☐ N	
c	Keep quiet about your genetic test results?	☐ Y	☐ N	
d	Stay in the same job?	☐ Y	☐ N	☐ NA
e	Choose a job primarily on the basis of employee benefits offered?	☐ Y	☐ N	☐ NA
f	Refrain from applying for a promotion?	☐ Y	☐ N	☐ NA
g	Talk to others about Huntington disease in order to educate the public?	☐ Y	☐ N	
h	Disclose your family history of HD so others can be aware that you may develop symptoms in the future?	☐ Y	☐ N	
i	Disclose your family history of HD so others can watch you for symptoms?	☐ Y	☐ N	
j	Disclose your genetic test result so others can be aware that you may develop symptoms in the future?	☐ Y	☐ N	
k	Disclose your genetic test result so others can watch you for symptoms?	☐ Y	☐ N	

l Other (*please specify*): .....

.....

.....

D14 **To what degree are you satisfied with your response(s) in preventing the possibility of being treated unfairly because of your genetic test result?** *Please choose a number between 1 and 5 where 1 = Not very satisfied and 5 =Very satisfied* (☑).

Not very satisfied				Very satisfied
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

D15 **How much <u>disadvantage</u>, if any, have you felt from knowing about your <u>genetic test result</u>?** *Please choose a number between 1 and 5 where 1 = No Disadvantage and 5 = Great Disadvantage* (☑).

No Disadvantage				Great Disadvantage
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

D16 **We are interested in learning about experiences with discrimination, by this we mean being <u>unfairly prevented</u> from doing something, or being <u>treated unfairly</u>. Have you ever experienced discrimination in any of the following situations because of your <u>genetic test result</u>?** *Please answer EACH of the following*

		Yes	No	Not Appli-cable
a	At school	☐ Y	☐ N	☐ NA
b	At work	☐ Y	☐ N	☐ NA
c	In the law courts	☐ Y	☐ N	☐ NA
d	When getting hired or getting a job	☐ Y	☐ N	☐ NA
e	When establishing a relationship	☐ Y	☐ N	☐ NA
f	When making choices about having children	☐ Y	☐ N	☐ NA
g	When getting medical care	☐ Y	☐ N	☐ NA
h	When getting custody or access to your children	☐ Y	☐ N	☐ NA
i	By a life insurance company or agent	☐ Y	☐ N	☐ NA
j	By a long term disability insurance company or agent	☐ Y	☐ N	☐ NA
k	By a mortgage company or agent	☐ Y	☐ N	☐ NA
l	By a member of your family (*please specify*):	☐ Y	☐ N	☐ NA
m	By a friend	☐ Y	☐ N	☐ NA
n	By your spouse	☐ Y	☐ N	☐ NA
o	By a boy/girl friend	☐ Y	☐ N	☐ NA
p	By your community	☐ Y	☐ N	☐ NA
q	By your religious organization	☐ Y	☐ N	☐ NA
r	By your doctor	☐ Y	☐ N	☐ NA
s	By other health care professional(s)	☐ Y	☐ N	☐ NA
t	By a genetic counselling service	☐ Y	☐ N	☐ NA
u	By a blood bank	☐ Y	☐ N	☐ NA
v	By the Canadian Forces	☐ Y	☐ N	☐ NA
w	By an adoption agency	☐ Y	☐ N	☐ NA
x	Other (*please specify*):			

Did you select *"YES"* for any part of question D16? ☐ **Yes** → **Please continue to D17, page 17** ☐ **No** → **Go to question D18, page 17**

D17 **To what degree, if any, is it distressing to be treated unfairly because of <u>your genetic test result</u>?**
Please choose a number between 1 and 5 where 1 = Not very distressing and 5 = Very distressing (☑).

	Not very distressing				Very distressing
a	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

b **What else do you feel other than distress?** *(please specify)*: .....

.....

D18 **In the following questions, we are interested in the way other people have treated you. Can you tell us if any of the following has ever happened to you <u>because of your genetic test result</u>:** *Please answer EACH of the following*

		Yes	No	Not Applicable
a	Have you ever been fired at any time in your life **because of your genetic test result?**	☐ Y	☐ N	☐ NA
b	Have you ever been denied a promotion **because of your genetic test result?**	☐ Y	☐ N	☐ NA
c	Have you ever been denied for a job **because of your genetic test result?**	☐ Y	☐ N	☐ NA
d	Have you ever been discouraged by a teacher from continuing your education **because of your genetic test result?**	☐ Y	☐ N	☐ NA
e	Have you ever been discouraged by a family member from continuing your education **because of your genetic test result?**	☐ Y	☐ N	☐ NA
f	Have you ever been watched for symptoms by a family member(s) **because of your genetic test result?**	☐ Y	☐ N	☐ NA
g	Have you ever been denied a bank loan **because of your genetic test result?**	☐ Y	☐ N	☐ NA
h	Have you ever been denied life insurance **because of your genetic test result?**	☐ Y	☐ N	☐ NA
i	Have you ever been denied long term disability benefits **because of your genetic test result?**	☐ Y	☐ N	☐ NA
j	Have you ever been denied critical care insurance **because of your genetic test result?**	☐ Y	☐ N	☐ NA
k	Have you ever been denied custody or access to your children **because of your genetic test result?**	☐ Y	☐ N	☐ NA
l	Have you received negative comments **because of your genetic test result?**	☐ Y	☐ N	☐ NA
m	Have you had your **genetic test results used against you?**	☐ Y	☐ N	☐ NA
n	Have people changed their communication patterns with you **because of your genetic test result?**	☐ Y	☐ N	☐ NA
o	Have you been denied when claiming disability benefits **because of your genetic test result?**	☐ Y	☐ N	☐ NA
p	Have you been placed under surveillance at work **because of your genetic test result?**	☐ Y	☐ N	☐ NA
	Other (*please specify*):			

Did you select *"YES"* for any part of question D18?	☐ **Yes** ➔ **Please continue to D19, below** ☐ **No** ➔ **Please go to Section E, page 19**

D19 **In general, how did you respond to being treated unfairly because of your genetic test result?**
Please answer EACH of the following

		Yes	No
a	Tried to do something about the situation	☐ Y	☐ N
b	Accepted it as a fact of life	☐ Y	☐ N
c	Worked harder to prove them wrong	☐ Y	☐ N
d	Realized that I brought it on myself	☐ Y	☐ N
e	Talked to someone about how I was feeling	☐ Y	☐ N
f	Expressed anger or got mad	☐ Y	☐ N
g	Prayed about the situation	☐ Y	☐ N
h	Ignored the situation	☐ Y	☐ N
i	Sought advice about the situation	☐ Y	☐ N
j	Placed a complaint	☐ Y	☐ N
k	Kept it to myself	☐ Y	☐ N
l	Tried to educate others	☐ Y	☐ N
m	Other (*please specify):*		

D20 **To what degree are you satisfied with your response(s) to being treated unfairly?** *Please choose a number between 1 and 5 where 1 = Not very satisfied and 5 =Very satisfied* (☑).

Not very satisfied				Very satisfied
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

SECTION E: SPECIFIC INCIDENTS

This section addresses ***specific incidents of disadvantage or unfair treatment*** *that you believe have occurred as a result of your family history or your genetic test result pertaining to HD.*

We are trying to examine the perceptions and experiences of genetic discrimination, defined as the denial of rights, privileges or opportunities or other adverse treatment based solely on genetic information including family history of HD or genetic testing for HD. This can be experienced as being treated unfairly. In the questions that follow the term "treated unfairly" refers to the experience of genetic discrimination.

If you require more space *when answering a question,* ***please use the additional pages at the end of this booklet.***

E1 **Are there any *clear incidents* of disadvantage or unfair treatment related to your family history of HD or genetic test results?**

☐ **Yes**	**Please continue to E2**
☐ **No**	Go to **E19**, page 23
☐ **Don't know**	Go to **E19**, page 23

E2 **Please estimate how many incidents of disadvantage or unfair treatment related to your HD family history or genetic test results you have experienced.** *Please tick the number (☑)*

☐ **1** ☐ **2** ☐ **3** ☐ **4** ☐ **5** ☐ **6** ☐ **7** ☐ **8** ☐ **9** ☐ **10 or more**

E3 **In what year did the <u>most significant</u> incident occur?** ___ ___ ___ ___

E4 **Please describe the <u>most significant incident</u>:** .....

.....

.....

.....

.....

.....

.....

.....

.....

E5 **What explanation, if any, was given by the person/organization responsible for the unfair treatment?**

.....

.....

.....

.....

.....

.....

E6 At the time of this particular incident ... : *Please answer EACH of the following*

		Yes	No	Don't Know
a	I knew I had a family history of Huntington disease (HD)	☐ Y	☐ N	☐ DK
b	A family member had received a genetic test result for HD	☐ Y	☐ N	☐ DK
c	A family member was showing symptoms of HD	☐ Y	☐ N	☐ DK
d	I had received a genetic test result for HD	☐ Y	☐ N	☐ DK
e	I had **no** symptoms of HD	☐ Y	☐ N	☐ DK
f	I had **early** symptoms of HD	☐ Y	☐ N	☐ DK
g	I had been diagnosed with HD by a doctor	☐ Y	☐ N	☐ DK
h	Other (*please specify*):			
	.....			
	.....			

E7 How did the person(s)/organization connected with your unfair treatment obtain information about your risk for HD?

a	I provided this information **without** being asked	☐ Y	☐ N	
b	I provided this information when asked	☐ Y	☐ N	
c	Someone else provided this information to them	☐ Y	☐ N	☐ DK
	i. Who was this person? (e.g. doctor, family member)			
	ii. Did they provide this information WITH your permission?	☐ Y	☐ N	
d	My family history and/or a family member was already known to them	☐ Y	☐ N	☐ DK
e	I do not know how they obtained the information	☐ Y	☐ N	☐ DK
f	Other (*please specify*)			
g	What information was obtained by the person/organization? *Please answer EACH of the following.* Your...			
	i. Family history of HD	☐ Y	☐ N	
	ii. Genetic test result	☐ Y	☐ N	☐ NA

E8 **Did the unfair treatment involve any of the following?** *Please answer EACH of the following*

		Yes	No	Don't Know
a	Conversations/discussions with the relevant person(s) or organization(s)	☐ Y	☐ N	☐ DK
	i. Were the conversations directly with you?	☐ Y	☐ N	
	ii. Were the conversations with a broker or agent?	☐ Y	☐ N	
	iii. Did the conversations involve a lawyer acting for you?	☐ Y	☐ N	
	iv. Other (*please specify*):			
b	Written correspondence (letters, faxes or emails)	☐ Y	☐ N	☐ DK

c Please describe briefly the conversation(s) or correspondence (if any):

.....

.....

.....

E9 **As a result of the unfair treatment:** *Please answer EACH of the following*

a Did you seek support or advice from anyone? ☐ Y ☐ N ☐ DK

i. From whom? (*Describe the person by their relationship to you or their position (e.g. family member or coworker)*.....

.....

b Did you question or challenge the unfair treatment? ☐ Y ☐ N ☐ DK

i. Whom did you challenge? (*Describe the person by their relationship to you or their position e.g. family member or coworker*).....

.....

c Did you make any complaint or take any action? ☐ Y ☐ N ☐ DK

i. Please give details.

.....

.....

E10 **To what extent did the unfair treatment cause <u>you</u> distress?** *Please choose a number between 0 and 5 where 0 = I have not experienced any distress and 5 =A lot of distress* (☑).

		Very Little Distress				A lot of Distress
I have not experienced any distress	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

E11 **To what extent did the unfair treatment cause <u>your family</u> distress?** *Please choose a number between 0 and 5 where 0 = My family has not experienced any distress and 5 =A lot of distress* (☑).

		Very Little Distress				A lot of Distress
My family has not experienced any distress	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

E12 **How important were the following barriers in deciding whether to make a complaint or take action?** *Please answer EACH of the following*

		Not Very Important	Of Little Importance	Moderately Important	Important	Very Important
a	Emotional or psychological barriers	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b	Cost of pursuing a complaint	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c	Bureaucratic problems ("red tape")	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d	Lack of information on where to complain	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
e	Concerns about consequences	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

f Other (*please specify*): .....

.....

.....

Did you or others place a complaint about the unfair treatment? ☐ **Yes** ➔ Please continue to **E13**, below ☐ **No** ➔ Go to **E19**, on page 23

E13 **Who handled the complaint?** *Please answer EACH of the following* (☑)

		Yes	No	Don't Know
a	Self	☐ Y	☐ N	☐ DK
b	Advocate	☐ Y	☐ N	☐ DK
c	Lawyer	☐ Y	☐ N	☐ DK

d Other (*please specify*): .....

		Yes	No	Don't Know
E14	**Was your case reconsidered because of the complaint?**	☐ Y	☐ N	☐ DK

E15 **Was the final outcome ...?** *Please tick ☑ ONE of the following*

in your favour	☐ 1
in the favour of other person(s)/organizations	☐ 2
a compromise between both parties	☐ 3
pending, i.e. still in process	☐ 4
other (*please specify*):	☐ 5

E16 **Do you have any written documents pertaining to the complaint?** ☐ Y ☐ N ☐ DK

E17 **To what extent did the complaint process cause <u>you</u> distress?** *Please choose a number between 0 and 5 where 0 = I have not experienced any distress and 5 =A lot of distress* (☑).

I have not experienced any distress ☐ 0	Very Little Distress ☐ 1	☐ 2	☐ 3	☐ 4	A lot of Distress ☐ 5

E18 **To what extent did the complaint process cause <u>your family</u> distress?** *Please choose a number between 0 and 5 where 0 = My family has not experienced any distress and 5 =A lot of distress* (☑).

My family has not experienced any distress ☐ 0	Very Little Distress ☐ 1	☐ 2	☐ 3	☐ 4	A lot of Distress ☐ 5

E19 **Are there any *clear incidents* where you were <u>made to feel different</u> because of your family history of HD or genetic test results?**

☐ **Yes**	**Please continue to E20**
☐ **No**	Go to **Section F**, page 24
☐ **Don't know**	Go to **Section F**, page 24

E20 **Please describe the incident(s):** .....

.....

.....

.....

.....

If you need more space for any answer, please use the additional pages at the end of this booklet.

SECTION F INSURANCE

*This section asks about your **thoughts and experiences related to insurance** and your family history or your genetic test result pertaining to HD.*

F1 Please specify which of these insurance policies, if any, you received **through an individual policy** or **through a group plan** (i.e., employer benefits)? *Please answer EACH of the following:*

		Individual	Group Plan	Both	Neither
a	Life Insurance	☐ I	☐ G	☐ B	☐ N
b	Disability/Income protection	☐ I	☐ G	☐ B	☐ N
c	Mortgage Insurance	☐ I	☐ G	☐ B	☐ N
d	Accidental death Insurance	☐ I	☐ G	☐ B	☐ N
e	Travel Insurance	☐ I	☐ G	☐ B	☐ N
f	Crisis/Trauma Insurance	☐ I	☐ G	☐ B	☐ N
g	Private health insurance	☐ I	☐ G	☐ B	☐ N
h	Other (*please specify*)	☐ I	☐ G	☐ B	☐ N

.....

F2 **In general terms, how important is insurance to you?** *Please choose a number between 1 and 5 where 1 = Not very important and 5 = Very Important* (☑).

Not Very Important				Very Important
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Please answer EACH of the following:	Yes	No	Not Applicable
F3 Do/did you feel **concerned** about the possibility of being charged **higher insurance premiums because of your:**			
i. Family history of HD	☐ Y	☐ N	
ii. Genetic test result	☐ Y	☐ N	☐ NA
F4 Do/did you feel **concerned** about the possibility of **insurance rejection because of your:**			
i. Family history of HD	☐ Y	☐ N	
ii. Genetic test result	☐ Y	☐ N	☐ NA
F5 Do/did you feel **concerned** about the possibility of **receiving special conditions** for your insurance (i.e. limited term coverage) **because of your:**			
i. Family history of HD	☐ Y	☐ N	
ii. Genetic test result	☐ Y	☐ N	☐ NA

	Please answer EACH of the following:	Yes	No	Not Applicable
F6	Have you **avoided applying** for insurance **because of your fear of disclosing your**:			
	i. Family history of HD	☐ Y	☐ N	
	ii. Genetic test result	☐ Y	☐ N	☐ NA
F7	Have you ever "**given up**" before applying for insurance believing you would not be covered **because of your:**			
	i. Family history of HD	☐ Y	☐ N	
	ii. Genetic test result	☐ Y	☐ N	☐ NA
F8	Have you ever been **advised not to bother applying** for insurance **because of your**:			
	i. Family history of HD	☐ Y	☐ N	
	ii. Genetic test result	☐ Y	☐ N	☐ NA
	a. Who was it that advised you? (*Describe a person by relationship or position e.g. family member, broker/agent)*.....			
F9	Do you think that **relatives** may have **kept any of the following information from you** because of insurance concerns?			
	i. Family history of HD	☐ Y	☐ N	
	ii. Genetic test result	☐ Y	☐ N	☐ NA
F10	Have **you** ever **concealed any of the following information from relatives** because of insurance concerns for others?			
	i. Family history of HD	☐ Y	☐ N	
	ii. Genetic test result	☐ Y	☐ N	☐ NA
F11	Have you ever **thought about concealing any of the following information** from your **insurance company**?			
	i. Family history of HD	☐ Y	☐ N	
	ii. Genetic test result	☐ Y	☐ N	☐ NA
F12	Have you ever **kept** any of the information below **out of your medical files** because you believed you **would not get insurance** coverage?			
	i. Family history of HD	☐ Y	☐ N	
	ii. Genetic test result	☐ Y	☐ N	☐ NA

F13 Has **knowing** about any of the following information made you **feel that your insurance needs have changed**?

	Yes	No	Not Applicable
i. Family history of HD	☐ Y	☐ N	
ii. Genetic test result	☐ Y	☐ N	☐ NA

a. Do you feel you **need more, less or the same** of the following types of insurance **than you would otherwise?**

	More	Less	Same
1. Health Insurance	☐ M	☐ L	☐ S
2. Life Insurance	☐ M	☐ L	☐ S
3. Disability Insurance	☐ M	☐ L	☐ S

F14 Have you ever **postponed having a genetic test** for HD so that you could put desired insurance in place first? ☐ Y ☐ N ☐ NA

i Were you advised to do this by someone else? ☐ Y ☐ N

ii Who advised you? (*Describe the person by relationship or position e.g. family member, genetic counselor)* .....

Have you ever applied for any type of insurance? ☐ **Yes** → Please **continue to F15,** below
☐ **No** → Go to **Section G,** on page 30

F15 Have you ever **bought more insurance** than you would have otherwise **because of your**:

i. Family history of HD	☐ Y	☐ N	
ii. Genetic test result	☐ Y	☐ N	☐ NA

F16 Have you ever felt the need to make **multiple applications** for insurance at the same time in case of refusal **because of your:**

i. Family history of HD	☐ Y	☐ N	
ii. Genetic test result	☐ Y	☐ N	☐ NA

F17 Do/did you feel **concerned** about the possibility of having your **current insurance cancelled because of your**:

i. Family history of HD	☐ Y	☐ N	
ii. Genetic test result	☐ Y	☐ N	☐ NA

F18 **Were you offered Standard Coverage for all insurance applications?**

- ☐ **Yes for all** → Go to **question F22, page 28**
- ☐ **Yes for some** → Go to **question F19, below**
- ☐ **No** → Go to **question F19, below**
- ☐ **Don't know** → Go to **question F19, below**

F19	***Please answer EACH of the following***	**Yes**	**Type(s) of insurance?**	**No**	**Don't know**
a	**Were you refused insurance coverage?**	☐ Y	.....	☐ N	☐ DK
b	Were you offered coverage, but at a **higher premium**?	☐ Y	.....	☐ N	☐ DK
c	**Were you offered limited coverage?**	☐ Y	.....	☐ N	☐ DK
d	Were you offered a **limited term** for the coverage?	☐ Y	.....	☐ N	☐ DK
e	**Was your coverage cancelled?**	☐ Y	.....	☐ N	☐ DK
f	Was your family history information for HD given as the reason for any non-standard coverage?	☐ Y		☐ N	☐ DK
g	**Was your genetic test result for HD given as the reason for any non-standard coverage?**	☐ Y		☐ N	☐ DK
h	Were you given a verbal reason for any non-standard coverage?	☐ Y		☐ N	☐ DK
i	**Were you given a reason in writing for any non-standard coverage?**	☐ Y		☐ N	☐ DK
j	Did the communication come from the company directly?	☐ Y		☐ N	☐ DK
k	**Did the communication come from an agent / broker?**	☐ Y		☐ N	☐ DK
l	Please provide any details of what you recall being told:				
	.....				

Did you select *"YES"* for any part of question F19?

- ☐ **Yes** → **Please continue to F20, below**
- ☐ **No / Don't know** → Go to **question F22, page 28**

F20 **How did you respond to this experience?**

		Yes	**No**	**Don't Know**
i	**Disregarded the experience**	☐ Y	☐ N	☐ DK
ii	Sought advice about the experience	☐ Y	☐ N	☐ DK
iii	**Placed a complaint about the experience**	☐ Y	☐ N	☐ DK
iv	Other (*please specify*):			
	.....			

F21 **To what degree, if any, did this experience cause you distress?** *Please choose a number between 1 and 5 where 0 = I have not experienced any distress and 5 = A lot of distress* (☑).

		Very Little Distress			A lot of Distress
I have not experienced any distress ☐ **0**	☐ **1**	☐ **2**	☐ **3**	☐ **4**	☐ **5**

		Yes	No	Not Applicable
F22	Have you ever been **denied life insurance** because of your :			
	i **Family history of HD**	☐ Y	☐ N	
	ii Genetic test result	☐ Y	☐ N	☐ NA
	iii **Please describe:**			
F23	Have you ever been **denied long-term care insurance** because of your :			
	i **Family history of HD**	☐ Y	☐ N	
	ii Genetic test result	☐ Y	☐ N	☐ NA
	iii **Please describe:**			
F24	Have you ever been **denied health insurance** because of your :			
	i **Family history of HD**	☐ Y	☐ N	
	ii Genetic test result	☐ Y	☐ N	☐ NA
	iii **Please describe:**			
F25	Have you ever been **denied long-term disability insurance** because of your :			
	i **Family history of HD**	☐ Y	☐ N	
	ii Genetic test result	☐ Y	☐ N	☐ NA
	iii **Please describe:**			
F26	Have you ever been **denied** an insurance **claim** because of your:			
	i **Family history of HD**	☐ Y	☐ N	
	ii Genetic test result	☐ Y	☐ N	☐ NA
	iii **Please describe:**			

		Yes	No	Don't Know
F27 a	Have you ever been **asked to take a genetic test for HD** by an insurance broker, agent, body or company?	☐ Y	☐ N	☐ DK
			Please go to the ☞ below	
b	**At what stage was this?**			
	i When **applying** for insurance	☐ Y	☐ N	☐ DK
	ii **During the processing** of your application	☐ Y	☐ N	☐ DK
	iii When **making a claim** on the insurance	☐ Y	☐ N	☐ DK
	iv Please give details of who, when, etc.:			

Have you had a genetic test for HD?

☐ **Yes** ➔ **Please continue to F28, page 29**

☐ **No** ➔ Go to **Section G on page 30**

F28 a Have you ever been asked by an insurance broker, agent, body or company to **disclose genetic test results**? ☐ Y ☐ N ☐ DK

b **At what stage was this ...?**

i When **applying** for insurance ☐ Y ☐ N ☐ DK

ii **During the processing** of your application ☐ Y ☐ N ☐ DK

iii When **making a claim** on the insurance ☐ Y ☐ N ☐ DK

iv **Please give details of who, when, etc**.....

F29 a Have you ever **paid** for health care services **out of pocket** so that your genetic test results would not be made available to an insurance agent or company? ☐ Y ☐ N ☐ DK

b **Please specify the service (s):**

i Genetic testing consultation ☐ Y ☐ N ☐ DK

ii Genetic test ☐ Y ☐ N ☐ DK

F30 Have you ever asked for genetic testing for HD **anonymously** so that your genetic test results would not be made available to an insurance agent or company? ☐ Y ☐ N ☐ DK

F31 Have you ever asked for genetic testing for HD **in another country** so that your genetic test results would not be made available to an insurance agent or company? ☐ Y ☐ N ☐ DK

SECTION G: GENETICS ISSUES

Have you ever learned about the possibility of being treated unfairly before today? ☐ **Yes** ➔ **Please continue to G1, below** ☐ **No** ➔ **Please go to G3 on page 31**

G1 **How did you first learn about the possibility of being treated unfairly because of your family history or your genetic test result?** ***From...*** *(please answer EACH of the following)*

		Yes	No
a	Family member	☐ Y	☐ N
b	Family Doctor	☐ Y	☐ N
c	Genetic Counselor	☐ Y	☐ N
d	Friend	☐ Y	☐ N
e	Support Group	☐ Y	☐ N
f	Researcher	☐ Y	☐ N
g	Magazine or Newsletter (e.g. Horizon)	☐ Y	☐ N
h	Television	☐ Y	☐ N
i	Newspaper	☐ Y	☐ N
j	Radio	☐ Y	☐ N
k	From this survey	☐ Y	☐ N
l	Other *(please specify)*:.....		
	.....		

G2 **After learning about the possibility of being treated unfairly because of your family history or genetic test result, did you...** *(please answer EACH of the following)*:

a	Disregard this possibility	☐ Y	☐ N
b	Seek advice regarding this possibility	☐ Y	☐ N
c	Take action to prevent this possibility	☐ Y	☐ N
d	Keep quiet about your genetic test results	☐ Y	☐ N
e	Become anxious about this possibility	☐ Y	☐ N

i. **To what degree were you anxious?** *Please choose a number between 1 and 5 where 1 = Not very anxious and 5 = Very Anxious* (☑).

Not Very Anxious				Very Anxious
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

G3 a Do you know of any official places where people can complain if they feel they are being treated unfairly because of genetic issues? ☐ Y ☐ N ☐ DK

b Please specify: .....

.....

G4 a Do you know of any laws to prevent discrimination based on genetic information? ☐ Y ☐ N ☐ DK

b Please specify: .....

.....

G5 Have you ever said "No" to being in a genetic research study because of concerns about your own or your children's future eligibility for insurance? ☐ Y ☐ N ☐ DK

G6 Do any concerns that you may have about the use of genetic information by others relate more to … ?
Please tick ☑ ONE response

a Employment ☐ 1

b Insurance ☐ 2

c Employment and insurance equally ☐ 3

d Neither employment or insurance ☐ 4

e other *(please specify)*: ..... ☐ 5

.....

Just one more section remaining; you are almost finished…

We need to ask a few more questions in order to describe the people that have participated in this study.

SECTION H: ABOUT YOU

H1 **What is your marital status?** *Please tick ☑ ONE*

- Never married (single) ☐ 1
- Married and living with spouse ☐ 2
- Separated ☐ 3
- Divorced ☐ 4
- Widowed ☐ 5
- Common law/ live-in partner ☐ 6
- Other (*please specify*): ..... ☐ 7

i. **Please indicate the number of times you have been married:** .....

H2 **Do you have children?** ☐ Y ☐ N

i. **Please indicate the number of children you have:** .....

ii. Please indicate the number of biological children: .....

iii. **Please indicate the ages and gender of all your children in the chart below:**

	Age (yrs)	Gender (M/F)
1st Child:		
2nd Child:		
3rd Child:		
4th Child:		
5th Child:		
6th Child:		

H3 **People living in Canada come from many different cultural and racial backgrounds. To which ethnic or cultural group do you belong?** *Please tick ☑ ONE*

White or European descent	☐ 1
Aboriginal (North American Indian, Métis, or Inuit)	☐ 2
Black or African American	☐ 3
Latin American	☐ 4
Chinese	☐ 5
Japanese	☐ 6
Korean	☐ 7
South Asian (i.e. East Indian, Pakistani, Sri Lankan)	☐ 8
South East Asian (i.e. Cambodian, Indonesian, Laotian, Vietnamese)	☐ 9
West Asian (i.e. Afghan, Iranian)	☐ 10
Filipino	☐ 11
Arab	☐ 12
Don't know	☐ 98
Other (*please specify*):	☐ 99

H4 **What is the highest grade or level of education you have attained?** *Please tick ☑ ONE*

No schooling	☐ 1
Some elementary	☐ 2
Completed elementary	☐ 3
Some Secondary	☐ 4
Completed Secondary	☐ 5
Some community college, technical college, CEGEP or Nursing training	☐ 6
Completed community college, technical college, CEGEP or Nursing training	☐ 7
Some university or teacher's college	☐ 8
Completed university or teacher's college	☐ 9
Other (*please specify*):	☐ 99

H5 **What is your current employment status?** *Please tick ☑ ONE*

Full-time	☐ 1
Part-time	☐ 2
Unemployed and seeking work	☐ 3
Unemployed or retired and not seeking work	☐ 4

Go to question H10

H6 **Please describe your occupation:** .....

H7 **Please indicate the length of time that you have been employed in your current position:** ..... (years) .....(months)

H8 **Do you have a unionized position?** ☐ Y ☐ N

H9 **What type of position do you hold?** *Please tick ☑ ONE*

Permanent/continuing position	☐ 1
Temporary	☐ 2
Contract	☐ 3
Seasonal	☐ 4
Self-employed (i.e. contractor, entrepreneur, consultant, in-home business)	☐ 5
Other (*please specify*):	☐ 99

H10 **What is your best estimate of your total personal income in the last 12 months before taxes and deductions?** *Please tick ☑ ONE*

Less than $10,000	☐ 1
10,000 - 19,999	☐ 2
20,000 – 29,999	☐ 3
30,000 - 39,999	☐ 4
40,000 - 49,999	☐ 5
50,000 – 59,999	☐ 6
60,000 - 69,999	☐ 7
70,000 – 79,999	☐ 8
80,000 – 89,999	☐ 9
90,000 – 99,999	☐ 10
$100,000 or more	☐ 11
Don't know	☐ 98
Other (*please specify*):	☐ 99

H11 **Which of the following best describes your mother?** *Please tick ☑ ONE*

My mother is/was NOT affected by HD	☐ 1
My mother was ____ years old at symptom onset	☐ 2
My mother was affected with HD, but I do not know her age at symptom onset	☐ 3
I don't know if my mother is/was affected with HD	☐ 4

H12 **Which of the following best describes your father?** *Please tick ☑ ONE*

My father is/was NOT affected by HD	☐ 1
My father was ____ years old at symptom onset	☐ 2
My father was affected with HD, but I do not know his age at symptom onset	☐ 3
I don't know if my father is/was affected with HD	☐ 4

H13 **Which of the following best describes your experience with HD?** *Please tick ☑ ONE*

I have had no prior experience with people who had HD	☐ 1
I have known people who have had early symptoms of HD	☐ 2
I have known people who have had severe disease or have died	☐ 3

Do you have any comments, questions or concerns?

THANK YOU VERY MUCH!
Your time and efforts are greatly appreciated.

The following information is OPTIONAL.

May we contact you to discuss or clarify any of the information you have provided in this survey? If so, please provide your contact information. **When all responses have been coded, this page will be removed from your questionnaire before it is stored in a locked cabinet.**

Your name:.....

Address:.....

.....Zip/Postal code:.....State/Prov:.....Country:.....

Telephone: (home) (.....)..... (business) (.....).....

(mobile) ..... (fax) (.....).....

Email:.....

Do you have any comments, questions or concerns?

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Please put the questionnaire in the addressed, postage-paid envelope and mail it to:

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