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Perception, Experience, and Response to Genetic Discrimination in Huntington Disease: The International RESPOND-HD Study

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Abstract

Genetic discrimination—defined as the denial of rights, privileges, or opportunities or other adverse treatment based solely on genetic information (including family history)—is an important concern to patients, healthcare professionals, lawmakers, and family members at risk for carrying a deleterious gene. Data from the United States, Canada, and Australia were collected from 433 individuals at risk for Huntington disease (HD) who have tested either positive or negative for the gene that causes HD and family members of affected individuals who have a 50% risk for

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developing the disorder but remain untested. Across all three countries, a total of 46.2% of respondents report genetic discrimination or stigma based on either their family history of HD or genetic testing for the HD gene mutation. We report on the overall incidence of discrimination and stigma in the domains of insurance (25.9%), employment (6.5%), relationships (32.9%), and other transactions (4.6%) in the United States, Canada, and Australia combined. The incidence of self-reported discrimination is less than the overall worry about the risk of discrimination, which is more prevalent in each domain. Despite a relatively low rate of perceived genetic discrimination in the areas of health insurance and employment, compared to the perception of discrimination and stigma in personal relationships, the cumulative burden of genetic discrimination across all domains of experience represents a challenge to those at risk for HD. The effect of this cumulative burden on daily life decisions remains unknown.

Keywords

survey; employment; insurance; family history; genetic testing

INTRODUCTION

Discussion of the intended and unintended consequences of genetic testing began as early as the early linkage studies of Huntington disease (HD) [Morris et al., 1989]. In the early 1990s, the issue was explored in relation to the potential effects of the sequencing of the human genome [Billings et al., 1992]. Genetic discrimination may be experienced by individuals or their families based on actual or presumed genetic differences [Geller et al., 1996]. Early on, legal scholars and some in the health professions recognized concerns regarding the possibility of genetic discrimination in employment and insurance contexts as being of crucial importance to the effective use of new genetic technologies [Gostin, 1991]. These concerns prompted the National Human Genome Research Institute to call for investigations into how genetic risk information is conveyed in clinical settings, as well as how such information influences behaviors that may improve individual or public health [Collins et al., 2003].

We define genetic discrimination as the denial of rights, privileges, opportunities, or other adverse treatment based solely on genetic information, including family history or genetic test results [Gostin, 1991]. This definition is inclusive of a broad range of discriminatory activities that may arise in the interpersonal dealings of individuals in their daily lives and comports with the experience of familial discrimination [Treloar et al., 2004] or other social stigma and discrimination that is a feature of life experiences for some people who have family members with HD. While it is less narrowly tailored than some state laws that failed to include family history or clinically relevant medical data [Rothstein and Anderlik, 2001], it is concordant with the interviews done with individuals who live at risk for developing HD. The Genetic Information Non-Discrimination Act (GINA) of 2008 defines genetic discrimination in the context of both family history and genetic information, including medical information [United States Congress House Committee on Energy and Commerce, 2008]. Our definition, like that of others, includes individuals who experience the denial of rights, privileges, or opportunities based solely on genetic information, meaning those who have developed symptoms of the disease are not included in this definition. The definition is descriptive, not normative, and necessarily incorporates societal interpretations of whether it is fair or not to be denied such incidents of treatment. Such interpretations may be incorporated into the law when a society deems them important enough to receive specific legal protections.

In the United States, GINA does not address all instances where individuals may experience discrimination, or where they report they have perceived such events. However, with the passage of GINA, individuals in the United States are to be legally protected against genetic discrimination in health insurance and employment [Erwin, 2008]. Two areas of concern for genetic discrimination are health insurance and employment, where worries of discrimination have the potential to most directly impact the economic interests of these groups of individuals. Both insurers and employers may, for a variety of reasons, be interested in ascertaining an individual's genetic status especially in regard to a devastating adult onset disorder such as HD. Employers may also have legitimate reasons for desiring genetic information about employees, including the need to reduce the risk of exposure to hazardous materials or workplace environments among certain individuals. They may also wish to assess the fitness of certain individuals to perform necessary tasks or to reassign such individuals to jobs with a better fit [Rothstein, 1998]. In addition, employers are concerned about the increasing costs of healthcare coverage and may have economic reasons to use genetic information to make hiring and firing decisions based on these fears [Martindale, 2001]. In a 1997 survey of employers by the American Management Association, 78% of large and mid-sized employers disclosed that they conducted some type of medical testing, and 6% said they conducted some sort of genetic testing [Orthmann, 1997]. The perception of these risks by employees may influence some individuals to forego genetic testing for HD or to undergo testing anonymously to protect their privacy [Billings et al., 1992; King et al., 2006].

In an Australian study described by Taylor et al. [2004] the authors list several complicating factors that make securing an adequate response directly from employers problematic. To this list we add the possibility that insurers may wish to keep information about how decisions concerning eligibility or premium rating as a trade secret, or simply wish to decline requests to disclose this information.

For these reasons, among others, little data exist on the actual extent of insurance and employer use of genetic information. We know from legal literature that such cases exist, and that some types of genetic testing without employee knowledge and consent are illegal [Norman-Bloodsaw v Lawrence Berkeley Laboratory, 1998], and that other types of employee testing are legally risky [EEOC, 2002] to the employer. Thus, corporate entities may be understandably reluctant to admit to uses of genetic information that may stretch the boundaries of legality. For these reasons we rely on self-reports of employee perceptions that discrimination has occurred, for any purposes the employee discerns and to which they are likely to respond.

HD offers an exemplary setting for exploring the issues of genetic discrimination because HD is a devastating neurological disorder with up to 100% penetrance in those who carry the unstable expanded HD allele. The identification of the unstable expanded HD allele in 1993 [Huntington's Disease Collaborative Research Group, 1993] enabled the development of genetic testing that allows individuals to determine the presence of the gene mutation years before disease symptoms appear [Gusella and MacDonald, 1993]. This information could also be used by third parties, including employers and insurers, to deny those same individuals opportunities they may have otherwise be entitled to receive. The International Examination of Responses to Potential Discrimination From Individuals At-Risk for HD (I-RESPOND-HD) research study includes individuals who have tested either positive or negative for the HD mutation, as well as untested persons at risk for developing HD due to family history.

Genetic discrimination and stigma are coexisting concerns of individuals who are at risk for genetic illness [Sankar et al., 2006]. Stigma is the co-occurrence of components that include

labeling, stereotyping, separation, and status loss [Link and Phelan, 2001], and its central feature is the perception of an attribute of the stigmatized person that conveys a devalued social identity within a particular social context [Crocker et al., 1998]. Stigma and discrimination are the outwardly demonstrated aspects of a socially devalued identity that lies beyond the ability of the affected individual to determine. Both family history and genetic testing may be the basis for stigma and discrimination [Biser, 2004]. While particularly salient to the individuals affected, the more subtle aspects of genetic discrimination that result in a devaluation or stigma have received less attention than the loss of specific opportunities or associated costs.

Understandably, the major concerns about genetic discrimination in the United States focus on employment and health insurance contexts [Kass et al., 2007]. These concerns were reflected in the pilot study, as well as in and initial interviews conducted as a part of the current research [Bombard et al., 2008; Penziner et al., 2008]. Studies report genetic discrimination in Australia, where universal health coverage is provided by the state on principles of community rather than ratings of risk [Taylor et al., 2004] and in Canada, despite some prior legal protections [Bombard et al., 2009]. For instance, Canadians are protected against general discrimination by the Canadian Charter of Rights and Freedoms and the Canadian Human Rights Act [Lemmens, 2000], but there remains no legislation specifically defending against genetic discrimination [Harper et al., 2004]. Although not everyone in Canada is of the same opinion, the broad need for a Canadian response to the challenges posed by genetic technologies has been echoed elsewhere in that country's legal commentary [Orr, 2004]. The I-RESPOND-HD study examines differences in the perception and experience of genetic discrimination across the United States, Canada, and Australia.

In the United States, previous surveys of genetic discrimination identified a range of reported experiences, with most surveys focusing on one or two issues in the range of potential discriminations. Beginning in 1996, researchers queried consumers and healthcare professionals to ascertain the prevalence of genetic discrimination, finding rates from 22% of consumer respondents reporting genetic discrimination in health insurance in 1996 [Lapham et al., 1996] to 11% of genetic counselors reporting knowledge of incidents of genetic discrimination in health insurance in 2000 [Hall et al., 2005]. Some surveys included individuals with symptoms of genetic illness, however, making direct comparisons to asymptomatic populations somewhat difficult. These prior studies provide a window into the different aspects of genetic discrimination, including discrimination in health insurance, life insurance, employment, social stigma, and knowledge of legal remedies for such behaviors. The reported rates of genetic discrimination vary according to the age of participants, with studies that include participants under 18 years of age reporting the lowest rates [Apse et al., 2004]. Table I summarizes the results of several surveys across a range of genetic conditions and respondents.

The I-RESPOND-HD survey was designed to incorporate multiple elements of genetic discrimination as well as potential benefits of knowing one's genetic risk status into a survey that will inform policy and personal understanding of the discrimination experiences of persons at risk for the devastating genetic illness of HD. The perceptions, experiences, and responses of these individuals may be helpful in understanding how we may inform public policy in a society where genetic information will be more accessible, and how individuals can preserve the privacy of decisions for purposes of health care, life planning, or other personal interests.

Our approach was to develop a comprehensive picture of the prevalence of genetic discrimination with inquiry into both instances of adverse treatment and instances where

knowing one's genetic risk status may have some benefit in the employment or insurance contexts. Although genetic discrimination has been reported in the literature since the early 1990s [Billings et al., 1992; Lapham et al., 1996; Wingrove et al., 1996], the potential for benefit is less well researched. We asked participants to report any incidents of benefit from either family history or a genetic test. The benefits derived from knowing one's family history or genetic test results are reported in the companion article by Williams et al. [2010].

MATERIALS AND METHODS

Recruitment and Data Collection

The participants in the I-RESPOND-HD study were recruited from the PREDICT-HD or PHAROS studies, or individuals attending an Annual Huntington's Disease Society of America (HDSA) meeting who met the inclusion criteria for one of the aforementioned studies. As a condition of inclusion, participants must have been an adult who had not previously been clinically diagnosed with HD. The PREDICT-HD study is an ongoing multinational observational research study that includes at-risk individuals who have previously undergone elective DNA analyses for the CAG expansion in the HD gene and who were not clinically diagnosed with HD at the time of their enrollment. The goal of PREDICT-HD is to identify the primary emerging clinical and biological precursors of HD, quantify when such precursors begin to emerge, determine the most accurate markers in detecting HD onset and progression, and establish what factors influence the age of symptomatic HD onset. The PHAROS study was a multinational observational research study of at-risk individuals who had previously not undergone elective DNA analyses for the CAG expansion in the HD gene, who were not clinically diagnosed with HD at the time of their enrollment, and who did not wish to know their genetic test results. The goal of PHAROS was to identify the emerging clinical precursors of early symptomatic HD onset in a manner blinded to genetic data [Huntington Study Group, 2006].

The I-RESPOND-HD survey was conducted from January 2007 to December 2008 in compliance with the Code of Ethics of the World Medical Association (Declaration of Helsinki), and Institutional Review Board (or equivalent) approval was obtained at each site. Table II lists the clinical sites where the I-RESPOND-HD survey was distributed.

Exclusion Criteria

The PREDICT-HD and PHAROS studies both excluded symptomatic individuals from enrollment. All I-RESPOND-HD participants had not received a clinical diagnosis of HD [The Huntington Study Group, 1996] at the time of their participation in this study. However, since both contributing studies are/were longitudinal and observational in nature, participants may range with regard to proximity to disease manifestations. Individuals were not eligible for either study if they self-reported any unstable medical or psychiatric illness (including substance abuse), had a history of a severe learning disability, mental retardation, other central nervous system disease or event (e.g., seizures, head trauma), or were undergoing treatment with antipsychotic medications.

Instruments

The I-RESPOND-HD instrument was developed with the following objectives: (1) to examine the perceptions of stigmatization and discrimination experiences and the behavioral responses to those perceptions; (2) to design a measure that could be administered to citizens of various countries regardless of the specifics of their healthcare system and insurance laws; and (3) to design a questionnaire that could be administered to persons who had or had not undergone genetic testing. The major topics of concern to individuals at risk were derived from the literature [Taylor et al., 2004], and common topics were further elucidated

by interviews with at-risk individuals in the United States [Penziner et al., 2008] and Canada [Bombard et al., 2007, 2008]. These included concerns and experiences about genetic discrimination related to insurance, employment, family and social issues, and legal protections.

The I-RESPOND-HD booklet contained standardized measures of stress, personality, coping, and quality of life, as well as a questionnaire designed specifically for this study, which inquired about experiences of genetic discrimination. The I-RESPOND-HD survey consisted of five sections for participant perceptions and experiences with genetic discrimination: family history, genetic test results (if applicable), employment, insurance, and legal issues. There were additional sections for demographic information. The survey included both closed-and open-ended questions and concluded with several blank pages that allowed respondents additional space to elaborate on their experiences and/or to clarify closed-ended responses.

Content Validation

Validation of content was accomplished through expert validation as well as cognitive interviewing [Drennan, 2003] with participants at risk for—but undiagnosed with—HD. Four U.S. and Canadian experts in genetic counseling, predictive HD genetic testing, management of presymptomatic HD, and genetic discrimination reviewed the clarity and comprehensiveness of the survey and were asked to provide feedback regarding the survey's content validity prior to booklet printing and distribution. The reviewers were solicited to evaluate the specific questions deemed relevant to this topic and to provide their expert knowledge to help tailor all questions to appropriate concerns about genetic discrimination and stigma.

Six individuals at risk for HD who had completed predictive gene testing were contacted through the Iowa Huntington Disease Registry and asked to pilot test the I-RESPOND-HD survey and provide feedback through cognitive interviewing [Drennan, 2003]. Content was revised for comprehension, resonance, clarity, appropriateness, domain specificity, and representativeness using results from these expert and cognitive validations. Following the pilot test, the survey and the questions were organized into the categories of perceptions and experiences attributable to family history and experiences attributable solely to genetic testing. Special attention was paid to question order, wording effects, and the design of response options [Rugg and Cantril, 1942; Moser and Kalton, 1972; Bishop et al., 1980].

Subscales and Clinical Rating

Supplementary assessment measures were chosen for the entire IRESPOND-HD packet to evaluate personal attributes (i.e., behavioral style, response to stress, coping strategies) and quality of life that might influence the experience and perception of any adverse effects resulting from genetic testing, thus allowing characterization and comparison of all study cohorts.

All I-RESPOND-HD participants were asked to complete the *Medical Outcomes Study Short Form* [Ware and Sherbourne, 1992; McHorney et al., 1993], the *Rydell-Rosen Ambiguity Tolerance Scale* [Macdonald, 1970], the *Miller Behavioral Style Scale* [Miller, 1979, 1980], *Spiritual Well-Being Scale* [Paloutzian and Ellison, 1982; Ellison, 1983], and the *Life Orientation Test-Revised* [Scheier et al., 1994]. In addition, I-RESPOND-HD participants originating from the PREDICT-HD study cohort were asked to answer the *Impact of Event Scale-Revised* [Horowitz et al., 1993; Miller et al., 1998] to help document perceived stress responses resulting from undergoing genetic testing. Subscale data will be examined in future reports.

Available Preexisting PREDICT-HD and PHAROS Data

A significant strength of the I-RESPOND-HD study was its ability to augment collected survey data with cognitive and motor data collected during associated PREDICT-HD and PHAROS research visits. I-RESPOND-HD participants consented to have previously collected data from other NIH-funded studies released to the IRESPOND-HD investigators, including (but not limited to) the following demographic and clinical variables collected on an annual basis: age, gender, education, employment status, medical history, psychiatric history, transmission of HD (maternal vs. paternal), parental age of symptom onset, subjective reports of participant symptom onset, the motor exam and functional capacity ratings from the Unified Huntington's Disease Rating Scale (UHDRS) [The Huntington Study Group, 1996], brief cognitive assessments of Stroop [Stroop, 1935; Golden, 1978], symbol digit [Golden, 1978], and verbal fluency [Benton and Hamsher, 1978], Beck Depression Inventory (BDI-II) [Beck et al., 1996], Beck Hopelessness Scale (BDH) [Beck, 1993], and CAG repeat length via either PHAROS or PREDICT-HD confirmed DNA testing. CAG repeat length was used to calculate estimated age of disease onset, based upon current age, for each participant [Langbehn et al., 2009]. Clinical correlate results will be examined in future reports.

Survey Distribution

The surveys were distributed, either by mail or in person, to participants via site coordinators at 3 Australian, 2 Canadian, and 10 U.S. PREDICT-HD or PHAROS research sites, as well as the 2007 HDSA annual convention. Applicable components of Dillman's [1978] method for mailed surveys were used in cases where participants were sent booklets via mail. These included an announcement with a reply form and postage paid envelope from the research team, as well as reminder letters and additional surveys 2 weeks after initial mailings. Participants were asked to complete and mail back surveys within 30 days of initial receipt. Participants took between 20 and 40 min to complete the entire booklet in both research and home settings. Participants were compensated for returned survey booklets according to the guidance provided by each site. Enrollments took place from January 2007 until December 2008.

Data Coordination and Analysis

Completed I-RESPOND-HD surveys were initially sent to the Huntington Study Group (HSG) Coordination Center located at the University of Rochester for quantitative data management, where they were logged, date-stamped, visually inspected for completion and legibility, and double-keyed into a database. After data entry, the HSG Coordination Center released I-RESPOND-HD data sets to the University of Iowa, where the qualitative data were entered into a companion database and analyzed. Individual survey items or scales containing missing data were multiply imputed if the missing data were plausibly missing at random, with separate imputation modeling and averaging where appropriate [Little and Rubin, 2002]. Where a missing-at-random approach was not plausible for important missing data, sensitivity analyses were performed regarding the range of plausible non-response biases [Cochran, 1977]. Finally, the data sets were compared and indexed by subject with available preexisting demographic and clinical data from the PREDICT-HD and PHAROS studies. Answers to both checkbox and fill in the blank questions were tabulated to arrive at the overall number of individuals who answered each question in the affirmative. Where the write-in answers merely duplicated or gave further detail to support the checkbox answers the individual respondent was not double counted in arriving at the final tally of unique individuals reporting a perceived experience. All responses were reviewed by three or more trained members of the team for accuracy throughout the process.

RESULTS

Full or partial surveys were completed and returned by 433 of 480 consenting participants for a response rate of 90.2% overall. Throughout the survey, questions were asked about feelings, experiences, or actions a person has relative to two distinct contexts: (1) knowing they have a family history of HD or (2) in the context of the person knowing their genetic test result. Because some participants had chosen not to be tested, only a subset of the study sample had knowledge of both its family history and its genetic test results. Using this subset, the consistency of answers for the subset that had knowledge of family history and genetic test results was examined.

When PHAROS and PREDICT-HD subgroup data were compared, the percentage of perfect agreement between the two studies for the Insurance section was similar to that found between the two studies for both Feelings and Experiences sections. This provides evidence that separating the context into two sections versus asking about the contexts at the same time did not result in widely varying rates of agreement.

Demographic Information

A summary of survey respondent demographics is given in Table III. 71.8% of respondents were female and 80.2% had completed some collegiate level education. A total of 67.8% of the data was received from U.S. participants, with 21.5% and 10.7% coming from Australian and Canadian respondents, respectively.

Cumulative Rates of Genetic Discrimination

The cumulative results of all persons reporting one or more instances of genetic discrimination reveal that 46.2% of individuals at risk for HD experienced some form of unfair treatment. The cumulative reports of all persons who experienced genetic discrimination, overt or covert, legal or illegal, are given in Table IV. These reports are broken into more detailed descriptions of particular experiences below.

Differences between the underlying studies—Table V presents a summary of the responses received to the survey, including *only* respondents who self-reported instances of discrimination. Overall, 200 participants reported discrimination. Of these, a total of 157 participants from the PREDICT study (71.5%) and 43 participants from the PHAROS study (28.5%) reported the perception or experience of genetic discrimination on the I-RESPOND-HD survey.

Specific Incidents of Benefit

A total of 97 individuals, or 22.4% of participants reported benefits from knowing their family history or their positive test result. We specifically asked participants to report benefits that went beyond those which may accrue to their medical care. A full analysis of these benefit data is planned for future report.

Specific Instances of Discrimination and Stigma

As presented in Table IV, a total of 200 out of 433 individuals reported at least one instance of discrimination, for an overall rate of 40% (46.2%) of at-risk respondents. A majority (56.5%) of individuals indicated more than one discrimination event. The largest category of occurrence of discriminatory event involved relationships with other individuals rather than with institutions or organizations such as insurance, employment, or courts. The incidents of discrimination that the participants encountered fell into four domains: (1) discrimination or

stigma within relation ships, (2) insurance discrimination, (3) employment discrimination or stigma, and (4) discrimination or stigma in transactions of daily living.

Insurance discrimination—Discrimination in the context of insurance was deemed the "most significant" discrimination experience by the participants. We do not intend this to indicate statistical significance, but rather an attribution of how meaningful a particular event was to an individual within the context of their life. A combined total of 25.9% of respondents reported at least one incident of genetic discrimination while seeking insurance coverage. Discrimination in the context of life insurance was the most common incident reported with 14.5% of respondents reporting genetic discrimination. Health insurance discrimination was experienced by 6.9% of respondents. When those in Canada and Australia are excluded, the reported discrimination drops to 4.5% of participants from the United States who report they were denied health insurance. For Australians and Canadians, discrimination events refer to private health insurance coverage as these countries have universal public health insurance coverage. Participants (excluding Australians) reported being denied long-term care insurance (9.4%), and disability insurance (6.8%). For all countries reports were made of disability claims (3.1%) and automobile insurance (0.8%). A total of 83 (23.6%) individuals reported their genetic information was either accessed by insurance companies without their consent or was requested by an insurance company.

Employment discrimination—Employment provided the third most common domain for genetic discrimination. A total of 26 (6.5%) participants report genetic discrimination while at work or while seeking work. Experiences ranged from being denied a job (10 or 2.6%), to being fired (10 or 2.6%), being covertly watched (11 or 3.1%), or denied a promotion (10 or 2.6%). The data reported exclude the discrimination and adverse treatment by coworkers, which did not result in a formal employment action, such as the loss of a job or promotion.

Relationships—Within personal relationships, our definition of genetic discrimination includes the notion of "adverse treatment." Some participants report the *only* discrimination event they have experienced thus far is in the realm of personal relationships. Overall 138 (32.9%) respondents reported some type of discriminatory behavior in the domain of relationships, whereas 101 (24.4%) said people changed the way they talked to them. Ninety-five (22.9%) respondents experienced negative comments, and 26 (6.9%) reported they were discouraged from continuing their education due to their genetic risk for HD.

Discrimination in daily transactions—A small number (4.6%) of individuals reported discrimination in their transactions with the legal system, healthcare providers, housing, or other areas of life. Six individuals (1.8%) in the survey report having their genetic status raised as an issue in a legal proceeding, including being denied custody of their children based on their family history of HD or genetic test results. Two individuals (0.6%) reported being denied the opportunity to adopt a child based on their family history or genetic test result. Two participants reported that healthcare providers disclosed the participant's genetic risk without their consent (0.6%), and three participants reported that healthcare providers disclosed genetic information without their consent (0.9%). Two participants reported being denied housing due to at-risk status for HD, either as a mortgage denial (0.3%) or other denial of housing (0.3%). One person reported being denied the opportunity to give blood at a blood bank (0.3%). None of the I-RESPOND-HD participants reported discrimination from the armed services.

Table VI details the variety of discriminatory events about which we queried participants.

Worry about discrimination—Individuals at risk for HD reported worry about potential discrimination at higher rates than those actually reported incidents. Those at risk for HD report a 32.9% overall occurrence of discrimination or stigma within their personal relationships. Overall 51.2% of respondents report worrying about the possibility of discrimination or stigma within relationships, including worry about entering into a new relationship and the possibility of being treated differently on account of their family history or genetic test results. Participants also report a higher rate of worry about discrimination in the contexts of insurance (70.0% worry vs. 25.9% experience), employment (44.0% worry vs. 6.5% experience), and transactions (33.3% worry Table VII reflects the relative lack of knowledge of legal options vs. 4.6% experience).

Knowledge of Legal Protections

We found 11.5% of participants at risk for HD were able to affirm their knowledge of legal protections and how they might make a complaint about genetic discrimination. While some respondents had actual experience making a complaint, these tended to be within organizations such as complaining an insurance agency manager and not through the legal system. Others noted that they might wish to consult a lawyer to pursue legal issues in addition to pursuing complaints, but the lack of monetary resources sufficient to hire an attorney was an issue for at least two respondents. Table VII reflects the relative lack of knowledge of legal options among individuals at risk for HD relative to the cumulative burden of genetic discrimination or stigmatization.

DISCUSSION

Studies that validate that genetic discrimination is not an infrequent phenomenon have been emerging over the past few years, but few have included new knowledge about the particular burdens of individuals at risk for HD. The I-RESPOND-HD study has demonstrated that 46.2% of individuals at risk for HD in three countries report the perception or experience genetic discrimination. Those residing in Canada and Australia report more experiences of genetic discrimination than those in the United States (50.0% and 60.2% vs. 41.2%). The self-reports of genetic discrimination in this study indicate the experience of being treated unfairly and suffering other adverse consequences as a result of institutional and individual responses to knowledge of individual genetic risk is perceived as real, harmful, and possibly deserving of legal redress through complaints, advocacy, and education. It is worth noting recent studies have indicated that individuals in the premanifest stage of HD may have difficulty cognitively assessing situations [Paulsen et al., 2008]; however, this does not detract from their perceptions of their own experiences.

This instrument goes beyond prior surveys to examine a comprehensive range of discrimination behaviors that we have classified as falling into the domains of relationships (including stigma), insurance (including health insurance), employment (including worry and knowledge of legal protections), and transactions (including legal cases and housing rights). The perception and experience of genetic discrimination appears to be a cumulative effect of several possible incidents of being treated differently based solely on one’s genetic information. Most individuals who experience genetic discrimination report more than one incident that may occur in areas of their life that include family, friends, co-workers, employers, insurance companies, healthcare providers, housing, and the courts. This cumulative burden of stigma and risk of adverse treatment has led to widespread worry about the possibility of such events. While the anxiety produced by this worry is not unfounded, a specific event in a given category is less likely to occur than the experience of worry. While specific incidents within any domain of relationships, insurance, employment, or transactions carries a low probability of occurrence, the cumulative burden of the possible

occurrence of any one of these events may explain the high incidence of worry about genetic discrimination and stigma across domains.

The I-RESPOND-HD instrument reports on the broader range of behaviors within genetic discrimination and reports a broad overlap of these experiences with those more typically associated with stigma in the social science literature. This is troublesome insofar as it makes it difficult to distinguish the effects of stigma from the effects of discrimination. Stigma is felt in the devalued status accorded by others and may become a sort of “master status” over time due to these framing effects that are expressed in subtle forms of discriminatory or negative comments or discouragement [Goffman, 1963]. The I-RESPOND-HD instrument sought to capture these phenomena as particular incidents of individual experience through inquiry into specific types of potential discrimination, such as the loss of a job, combined with more general questions about worry over losing a job due to discrimination. The participants in this study report that they experience stigma and discrimination in many forms. The social stigma of being devalued due to one’s genetic risk for serious illness is reported by individuals who have not yet borne the loss of an opportunity such as a job or insurance. Yet, even those who have suffered more overt discrimination find social stigma to be the second most significant (or meaningful) experience of unfair treatment. Because of the blurring of these concepts in the lived reality of HD, it is not possible to distinguish where being treated differently ends in relationships and being terminated from a job begins. The responses demonstrate that these experiences are all experienced as a whole in daily life. It is important to note that nearly half of participants reported some experience of genetic discrimination. This rate is higher than some prior surveys report and reflects the broad range of discriminatory effects and the inclusive definition of genetic discrimination that was adopted for this study.

Genetic discrimination in the domain of insurance is reported by participants as the single most significant (meaningful), although not most prevalent, form of genetic discrimination experienced. Life insurance is extremely important to these individuals who are balancing their own risk of HD with a desire to provide for their family and loved ones. While many respondents report genetic discrimination in life insurance, it is important to note that notions of actuarial fairness compete with conceptions of social fairness in the insurance industry, and life insurance is often viewed as less of a moral good than a financial good [Hall and Rich, 2000]. Health insurance has a stronger claim as a moral good, yet it remains an area where only 6.9% of respondents encountered genetic discrimination. Further inquiry after the full enactment of GINA will be needed to determine the evolving conditions of access to health insurance in the United States in coming years.

There was a relatively low incidence of genetic discrimination by employers, but those in the US who had this experience found it damaging not only to their income but also to their ability to keep their health insurance. Although there are not a large numbers of individuals affected by genetic discrimination in employment, those who reported employment-based discrimination sometimes wrote narrative descriptions of these events that evoked the sense of betrayal felt when their loyalty to a company was repaid with dismissal, denial of a promotion, or loss of an opportunity to apply for a better job [Williams et al., 2010]. The impact of the actions of co-workers was treated as a separate issue and provides a second layer of discriminatory impact.

Individual relationships proved to be the largest area of genetic discrimination. The domain of social relationships was also the second most significant (meaningful) area of concern for these individuals. Although respondents did not worry as much about their relationships as about insurance concerns, it was in the area of relationships where they most frequently experienced discrimination. While this article addresses the statistical incidence of these

events, the companion article contains narrative descriptions of the types of discriminatory events encountered and participant reactions to these events [Williams et al., 2010].

Genetic discrimination in the domain of other institutions and the transactions of daily life were reported by participants who had encountered difficulties in health care, legal system, and housing. These findings are often difficult to reconcile with an emerging conception of genetic justice. Although it is legally acceptable to introduce evidence of a soon to be ex-spouse's genetic risk status in a custody battle, it is morally problematic to deny parental custody based on genetic risk. The use of genetic information in specific legal cases, in housing, and certain other transactional domains has not been widely reported by previous medical studies. Although small in number, this is an area that is worthy of further inquiry and research.

Legal restrictions on genetic discrimination are varied across the countries where the I-RESPOND-HD study was conducted. In the United States, although genetic discrimination had been the subject of 22 state legislative schemes by 2005, a firm legal definition remained elusive [Greely, 2001; Rothstein and Anderlik, 2001]. The various states that had enacted legislation prohibiting genetic discrimination by turns failed to include family history in the definition, failed to provide sanctions for violation of the statutes, or failed to include both access to genetic information and use of genetic information for discriminatory purposes. With GINA, this has changed with regard to health insurance and employment, but for the timeframe of this study the aforementioned legal conditions prevailed. In Canada, core healthcare services are unaffected by the lack of specific statutes addressing genetic discrimination, but additional insurance schemes may require legal protection against genetic discrimination [Lemmens, 2003]. Australian researchers have noted the complexity of making complaints or seeking redress within the Australian legal system [Otlowski et al., 2007]. In the United States, previous studies have estimated 42% of genetic counselors are aware of legal protections [Hall and Rich, 2000] but only 4% of consumers are aware of the legal prohibitions of genetic discrimination [Apse et al., 2004]. The complexity of the laws and the low level of consumer knowledge of the laws present a distressing picture.

Legal protections on the books are not useful in preventing genetic discrimination if the individuals affected by the experience are not aware of their legal rights. While the law of genetic discrimination in the United States was greatly simplified with the enactment of GINA in 2008 [United States Congress House Committee on Energy and Commerce SoH, 2008], the I-RESPOND-HD survey was conducted between 2005 and 2008, just prior to the signing of the law and prior to its full enactment in 2009. Citizens of Canada and Australia confronted their own legal complexities, as indicated above. The finding that 11.48% of individuals at risk for HD consider themselves aware of legal protections indicates a need for consumer education about these issues as well as further study to determine the impact of GINA upon these issues in the United States.

Finally, we report the incidence of benefit from knowing one's genetic status is more frequent than the use of genetic information in a discriminatory manner in health insurance or employment. The benefits reported by participants are not as frequent as either the reported risk of subtle discrimination, or stigmatization within personal relationships, or the cumulative burden of all types of discrimination or stigmatization, yet it appears to be a salient aspect of living at risk for HD. The experience of benefit is a highly individualized phenomenon and will be reported in detail in future reports.

Limitations to this survey include the lack of third-party validation of claims of discriminatory behavior. It would help to have third-party input concerning the decisions that were made during the events reported by our participants. However, while validation

from other parties might confirm perceptions, these may be unlikely to be accurately depicted by the perpetrator of discrimination. Additionally, individuals respond to their own perception of events even if such framing is inaccurate. Thus, those at risk for genetic illness will have the subjective experience of discrimination if they perceive discrimination, whether or third parties intended not such perception. A potential limitation to this survey includes the over-representation of women (71.8%) and individuals with at least some college education (80.2%) in the sample. The opportunity to participate in this research was extended to men and women equally, but educated women tended to participate more in this research. The possible difference in the experience of discrimination between genders is beyond the scope of this article. The recruitment of participants at the Annual Huntington Disease Society of America Meeting may create the appearance of a bias. The opportunity to participate in this research was made available through a number of ways including regular clinical visits, and those attending the HDSA meeting did not represent a different sample except for their financial ability to travel.

The scope of this study is limited to HD but contributes an understanding of genetic discrimination in one of the most devastating neurological disorders. Participants report a 46% rate of genetic discrimination and stigmatization overall. Those living in the United States experienced less discrimination and stigma (41.3%) than those in Canada (50%) and Australia (60.2%). We report self-reported occurrences of genetic discrimination, including the subtle discrimination or stigmatization of being treated differently, across three countries. We have confirmed that genetic discrimination occurs as a result of family history as well as genetic testing. The rate of experienced genetic discrimination from this population is similar to the frequency of discrimination in health insurance found by studies of other asymptomatic genetic conditions. However, it is difficult to compare the results of different surveys for several reasons. First, different surveys may define genetic discrimination differently, or open the survey to symptomatic individuals. Second, others may measure discriminatory events differently or use language that could lead to different interpretations of the incidence of worry and the incidence of actual discrimination events. Finally, societal changes may make it more likely that these topics are being conceived differently than they were in early surveys, with a more nuanced understanding of covert discrimination and subtle stigmatization emerging and differentiated from overt discrimination in employment or insurance. As the U.S. Discussion of the Genetic Information Non-Discrimination Act emerges over the next years, it is possible that new understandings and new awareness of genetic discrimination will shape our consciousness of and sensitivity to these events.

The I-RESPOND-HD study provides a broad look at the perceptions and experiences of genetic discrimination among persons at risk for HD. The survey was developed to give insight into the ways in which persons at risk for genetic disease manage and respond to the multiple social, ethical, and legal challenges they confront. The findings may have clinical application in better informing individuals considering predictive testing and the challenges posed by genetic discrimination. They may also illustrate the need to limit one’s worry commensurate with a level indicated by the actual experiences reported here. Individuals at risk for HD may find these experiences give validity to their own subjective impressions, or this information may help them to anticipate potential issues and take action to prevent unnecessary disclosures of their status by knowing the possible outcomes. The issues faced by this group of individuals at risk for genetic illness include discrimination on many fronts, including insurance, relationships, employment experiences, and daily transactions that make up many of life’s interactions with individuals and institutions.

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TABLE I

Prior/Concurrent Studies Estimating Frequency of Genetic Discrimination

References	Method	Reported rate of genetic discrimination				Proportion knowledgeable (%); Legal protections against genetic discrimination	Medical condition	Location
		Health insurance	Life insurance	Employment	Family or social stigma			
Lapham et al. [1996]	Consumer	22%	25%	13%			Various genetic conditions, N = 332	United States
Wingrove et al. [1996]	Consumer	15.4% declined coverage based on family history; 33.3% classified as “preexisting condition” after testing					Fragile X syndrome, N =39	United States
Shaheen et al. [2003]	Consumer	8/126 = 6%	14/126 = 11%	1/126 = 1%			Hereditary hemochromatosis, N = 126	United States
Hall and Rich [2000]	Third-party professional	11% overall, 9–36% HD				42	Various genetic conditions, N = 106	United States
Nedelcu et al. [2004]	Healthcare professionals					45.8	Various genetic conditions, N =271	California, United States
Apse et al. [2004]	Consumer and youth	10/470 = 0.02%	7/470 = 0.01%	1/470 = 0.002%		4	Colorectal cancer, N = 470	United States
Kass et al. [2007]	Consumer	37%		30%	18%		CF, SCD, DM, HIV, diabetes, family history of breast cancer, N = 541	United States
Lowstuter et al. [2008]	Healthcare professionals					31	Not reported, N =1181	California, United States
Taylor et al. [2008]	Consumer		45/951	5/951	22% family; 11% social; 20% health	15	Various genetic conditions, N = 951	Australia
Bombard et al. [2009]	Consumer		63/233 (27%)	16/233 (6.9%)	36/233 (15.5%)		HD	Canada

TABLE II

I-RESPOND-HD Participating Sites

United States (also running PREDICT-HD and PHAROS)
University of Rochester (NY)
Columbia Presbyterian Medical Center (NY)
University of Iowa (IA)
Johns Hopkins University (MD)
Emory University (GA)
Indiana University (IN)
University of California, Los Angeles (CA)
University of California, Davis (CA)
University of California, San Francisco (CA)
University of Washington (WA)
Canada (also running PREDICT-HD and PHAROS)
University of Toronto (ON)
University of British Columbia (BC)
Australia (also running PREDICT-HD)
University of Melbourne, St. Vincent's (VIC)
Perth Selby-Lemnos & SHCS (WA)
University of Melbourne, RMH (VIC)
Westmead Hospital (NSW)

TABLE III

Participants Demographics

	P-value	PREDICT-HD	PHAROS	Total
		310	123	433
Gender, N (%)				
Female	0.0002	207 (66.8%)	104 (84.6%)	311 (71.8%)
Male		103 (33.2%)	19 (15.5%)	122 (28.2%)
Country, N (%)				
Australia	—	93 (30.0%)	0 (0.0%)	93 (21.5%)
Canada		27 (8.7%)	19 (15.6%)	46 (10.7%)
United States		191 (61.3%)	103 (84.4%)	294 (67.8%)
Education, N(%)				
High school or less	0.0707	64 (22.5%)	15 (12.9%)	79 (19.8%)
Some college or university		60 (21.1%)	21 (18.1%)	81 (20.3%)
2-year degree		32 (11.3%)	18 (15.5%)	50 (12.5%)
4-year degree		61 (21.5%)	23 (19.8%)	84 (21.0%)
Postgraduate education or degree		67 (23.65)	39 (33.6%)	106 (26.5%)
Age, mean (SD)	0.0002	44.47 (11.24)	48.27 (8.39)	45.54 (10.65)

TABLE IV

Self-Reported Genetic Discrimination[*] by Country ($P = 0.0049$)

Genetic discrimination[*]	Australia	Canada	United States	Total
No	37 (39.8%)	23 (50.0%)	173 (58.8%)	233 (53.8%)
Yes	56 (60.2%)	23 (50.0%)	121 (41.2%)	200 (46.2%)
Total	93	46	294	433

[a]Genetic discrimination is defined as the denial of rights, privileges, or opportunities or other adverse treatment based solely on genetic information, including family history of HD.

TABLE V

Reports of Genetic Discrimination by Underlying Study Population

	P-value	PREDICT-HD	PHAROS	Total
		157	43	200
Gender, N (%)				
Female	0.2146	109 (69.4)	34 (79.1)	136 (71.5)
Male		48 (30.6)	9 (20.9)	55 (28.5)
Country, N (%)				
Australia	—	56 (35.7)	0 (0.0)	56 (28.0)
Canada		14 (8.9)	9 (20.9)	23 (11.5)
United States		87 (55.4)	34 (79.1)	121 (60.5)
Education, N (%)				
High school or less	0.1383	30 (21.6)	3 (7.7)	33 (18.5)
Some college or university		30 (21.6)	6 (15.4)	36 (20.2)
2-year degree		13 (10.7)	6 (15.4)	19 (10.7)
4-year degree		32 (23.0)	9 (23.1)	41 (23.0)
Postgraduate education or degree		34 (24.5)	15 (38.5)	49 (27.5)
Age, mean (SD)	0.0012	42.62 (11.27)	47.86 (8.37)	43.75 (10.91)

TABLE VI

Variety of Discriminatory Occurrences: Survey of Perceptions and Experiences Due To Family History or Gene Test Results

Type of reported experience	Experienced discrimination	Worry about discrimination
Relationships (all categories)	32.9% (138)	51.2% (215)
People changed how they talk to me	24.4% (101)	
Have had negative comments	22.9% (95)	
Discouraged continuing education	6.9% (26)	
Insurance (combined)	25.9% (110)	70.2% (283)
Denied life insurance	14.5% (54)	
Denied long-term care insurance[a]	9.4% (31)	
Denied health insurance[a]	6.9% (26)	
Denied disability insurance	6.8% (23)	
Denied disability claim	3.1% (10)	
Denied auto insurance	0.8% (3)	
Unconsented access or request to access genetic information	23.6% (83)	
Employment (combined)	6.5% (26)	44.0% (169)
Placed under surveillance at work	3.1% (11)	
Fired from job	2.6% (10)	
Denied job	2.6% (10)	
Denied promotion	2.6% (10)	
Transactional (combined)	4.6% (18)	33.3% (130)
Health provider/inappropriate comments	0.6% (2)	
Health provider disclosed without consent	0.9% (3)	
Health provider discriminatory practices	0.6% (2)	
Blood bank refused donation	0.3% (1)	
Legal issues/denied custody of children	1.8% (6)	
Denied opportunity to adopt	0.6% (2)	
Denied housing rental	0.3% (1)	
Denied mortgage	0.3% (1)	

[a]Includes individuals who report they were offered insurance cover at prohibitively high rates.

TABLE VII

Cumulative Burden of Genetic Discrimination and Stigma in the I RESPOND HD Study

International reported rate of genetic discrimination					Proportion knowledgeable		
Health insurance	**Life insurance**	**Employment**	**Relations or social stigma**	**Transactions or legal issues**	**Cumulative burden, any discrimination reported, all domains**	**Legal protections against genetic discrimination**	**N**
6.9%	14.5%	6.5%	32.9%	4.6%	46.2%	11.5%	433