

## NEURODEGENERATIVE DISEASE

# Genetic discrimination in Huntington disease

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**A survey conducted in Canada examined the prevalence of perceived genetic discrimination against patients with Huntington disease. The respondents reported discrimination not only by insurance or mortgage companies, but also in family and social contexts. Discrimination was more frequently attributed to family history than to genetic test results.**

Presymptomatic testing for Huntington disease (HD) has been available for much longer than testing for most other human genetic diseases. A cross-sectional survey addressing perceived genetic discrimination in individuals who are at risk of HD is, therefore, an important and timely addition to the literature.

Bombard and colleagues surveyed 233 individuals drawn from seven rural and urban genetic and movement disorders clinics in Canada.<sup>1</sup> 167 individuals had been tested for the HD mutation (83 tested positive and 84 tested negative), and 66 had chosen not to have the genetic test. The main outcome measure was self-reported experience of genetic discrimination on the basis of either family history or genetic test results, accompanied by psychological distress. Around 30% of the respondents had experienced discrimination with regard to life insurance or long-term disability insurance, or from mortgage companies. Discrimination was perceived as insurance rejection, premium increases, or requests to take a predictive test. Around 15% reported

discrimination by family members, particularly when making reproductive choices, and 12% reported discrimination in social settings; for example, by friends or in establishing a relationship. Discriminatory attitudes among doctors and other health-care professionals were also reported, and, somewhat surprisingly, five individuals reported discrimination by the genetic counseling service. Interestingly, the main reason cited for discrimination was family history, as opposed to the results of genetic testing.

The authors took alleged discrimination *prima facie* without a strict legal definition or further follow-up of the veracity of the claims. For an initial survey, this approach seems not only practical, but also valid, as subjective experiences are considered to be important and necessary in understanding health-related issues.<sup>2</sup> The definition of discrimination was broad, and was based on “being unfairly prevented from doing something or being treated unfairly”. The authors used a survey instrument based on both their own HD work and other surveys of racial and genetic discrimination. The sample was somewhat older and better educated than comparative HD clinic samples, and women were overrepresented (ratio of women to men ~2:1). As an individual’s gender can play a major part in the decision leading to presymptomatic testing in HD,<sup>3</sup> a separate data analysis for men and women with regard to perceived discrimination would have been of interest.

Nearly 40% of all respondents in the study were affected by perceived discrimination. Comparing the prevalence of genetic discrimination reported by Bombard and colleagues<sup>1</sup> with that reported in other studies is difficult, owing to differing methodologies and samples. In the Australian Genetic Discrimination Project, 56 of 332

respondents in the neurodegenerative subgroup reported discrimination.<sup>4</sup> A large-scale study of life insurance discrimination in the UK showed that in the subset of respondents with HD or at-risk of HD, nearly half who had applied for insurance experienced problems.<sup>5</sup>

The authors of the present study were not in a position to verify any claims of discrimination. Discrimination could, therefore, have been overreported or underreported. An Australian study that verified perceived discrimination was able to confirm and clarify several instances of discrimination.<sup>6</sup> Although that particular study was not exclusive to HD, it supports the notion that perception of discrimination is, in many instances, associated with manifest discrimination.

The Bombard *et al.* study comes at a time of major changes in US law. On 21 May 2008, US President Bush signed the Genetic Information Nondiscrimination Act of 2008 (GINA) into federal law. GINA protects Americans from being treated unfairly because of differences in their DNA that could affect their health, and prevents discrimination by health insurers and employers. The parts of the law relating to health insurers took effect in May 2009, and those relating to employers will take effect by November 2009. Unfortunately, the main sources of discrimination cited in the Canadian study—life insurance and long-term-care insurance companies, as well as mortgage companies and their agents—are not covered by GINA.

In addition to documenting the extent of discrimination, the Bombard *et al.* study was remarkable for the finding that discrimination on the basis of family history was even more prevalent than discrimination on the basis of genetic testing. Of 71 respondents who had undergone a genetic test



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and reported genetic discrimination, 41 attributed their experiences to their family history, whereas only 13 believed that their genetic test results were the main reason for their negative experiences. In what might be termed actuarial discrimination, one-quarter of the respondents who tested negative for the HD mutation reported insurance discrimination, although the data presented do not indicate whether the negative test result was known by or made available to the insurance carrier.

The authors did not identify which factors promote or reduce perceived discrimination. For example, it would have been interesting to know whether gender, overall pedigree size, number of affected individuals in a pedigree, socioeconomic status, age of disease onset or rate of institutionalization had an effect on discrimination. Some of these variables might affect the behavior of the 'asymptotically ill' as well as the 'discriminator'. Similarly, the reasons why certain insurance carriers denied coverage whereas others apparently provided coverage are unknown. The details provided do not indicate whether respondents who had not experienced insurance discrimination had actually applied for insurance. Conversely, some individuals who were denied insurance might not have perceived their experience as discrimination. Knowledge of these factors could be essential when designing educational efforts to reduce discrimination. As the authors rightfully point out, discrimination by family members or friends is not amenable to legislative remedies, and might be best approached by general educational efforts and specific efforts by support groups.

HD has always been at the forefront of neurogenetics, from chromosomal localization to gene discovery and the availability of genetic testing, and has served as a model for monogenic diseases. Despite some limitations, the Bombard *et al.* survey will stand as a landmark study of genetic discrimination in a late-onset neurological disease. Of particular note are its coverage of familial and social as well as insurance settings, and the attribution of discrimination to family history rather than genetic testing. This approach now needs to be extended to other countries and health-care systems, as well as other disease communities. The ataxia community, for example, has traditionally shown limited interest in pre-symptomatic or prenatal testing, and little

is known about perceived genetic discrimination within that community. Further work is also needed to assess the potential for discrimination in Mendelian diseases with strongly reduced penetrance, such as *LRRK2*-mediated Parkinson disease,<sup>8</sup> and in carriers of major-effect risk alleles such as the apolipoprotein E  $\epsilon 4$  allele.

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#### Competing interests

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1. Bombard, Y. *et al.* Perceptions of genetic discrimination among people at risk for Huntington's disease: a cross-sectional survey. *BMJ* **338**, b2175 (2009).

2. Sullivan, M. The new subjective medicine: taking the patient's point of view of health care and health. *Soc. Sci. Med.* **56**, 1595–1604 (2003).
3. Taylor, S. Gender differences in attitudes among those at risk for Huntington's disease. *Genet. Test.* **9**, 152–157 (2005).
4. Low, L., King, S. & Wilkie, T. Genetic discrimination in life insurance: empirical evidence from a cross-sectional survey of genetic support groups in the UK. *BMJ* **317**, 1632–1635 (1998).
5. Taylor, S., Treloar, S., Barlow-Stewart, K., Stranger, M. & Otlowski, M. Investigating genetic discrimination in Australia: a large-scale survey of clinical genetics clients. *Clin. Genet.* **74**, 20–30 (2008).
6. Barlow-Stewart, K., Taylor, S. D., Treloar, S. A., Stranger, M. & Otlowski, M. Verification of consumers' experiences and perceptions of genetic discrimination and its impact on utilization of genetic testing. *Genet. Med.* **11**, 193–201 (2009).
7. Billings, P. R. *et al.* Discrimination as a consequence of genetic testing. *Am. J. Hum. Genet.* **50**, 476–482 (1992).
8. Latourelle, J. C. *et al.* The Gly2019Ser mutation in *LRRK2* is not fully penetrant in familial Parkinson's disease: the GenePD study. *BMC Med.* **6**, 32 (2008).

## STROKE

# 'Spotting' patients at the highest risk of hematoma growth

Kyra Becker and David Tirschwell

**Clinical trials aimed at preventing hematoma expansion in patients with intraparenchymal hemorrhage have failed to show benefit from experimental intervention. Novel methods for identifying those patients at the highest risk of hemorrhage growth might enable better patient selection and, hence, increase the chance of demonstrating an improvement in clinical outcome.**

Intraparenchymal hemorrhage (IPH) is the most deadly type of stroke, killing up to half of the patients who develop the condition.<sup>1</sup> The mortality risk is increased in patients who experience hematoma enlargement over the early hours after symptom onset.<sup>2</sup> Preventing hematoma expansion is thus an attractive therapeutic target for IPH.<sup>2</sup> Clinical studies have examined whether hematoma expansion can be limited through administration of the hemostatic drug recombinant factor VIIa or by aggressive blood pressure lowering. Despite the fact that both intervention strategies limited IPH growth, neither led to improvement in patient outcomes.<sup>3,4</sup> A study by Delgado Almandoz

*et al.* highlights the potential importance of patient selection in administration of such strategies.<sup>5</sup>

The failure of interventions that limit IPH growth to translate into clinical benefit might have several plausible explanations. Hematoma enlargement could merely be a marker of poor outcome rather than the cause of the poor outcome, and would not, therefore, be a valid therapeutic target. The effects of the intervention strategies on IPH growth could have been too small to 'salvage' enough brain tissue to be clinically meaningful. Another possibility is that the clinical trials might not have been sufficiently powered to demonstrate the benefit of therapy. Indeed, given that hematoma