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Genetic screening for iron overload: No evidence of discrimination at 1 year

Few patients had insurance or employment problems after being screened for hemochromatosis and iron overload

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Abstract

Purpose This study measured the extent of insurance and employment problems associated with population screening for hereditary hemochromatosis and iron overload.

Methods 101,168 primary care patients from the US and Canada were screened for iron phenotypes and *HFE* genotypes associated with hemochromatosis. Those identified to be at risk (2253) were offered a clinical examination, which 1677 (74%) accepted, and the 1154 of these who responded to an initial questionnaire about psychosocial issues were surveyed 1 year later about whether they had experienced problems with insurance or employment that they attributed to hereditary hemochromatosis and iron overload.

Results 832 (72.1%) of the 1154 participants surveyed after 1 year responded to the second survey. Three (0.4%) had verified problems with insurance or employment that they believed were related to hereditary hemochromatosis and iron overload. Two had problems with life insurance, and one with long-term care insurance. All 3 had elevated iron levels but not a relevant *HFE* genotype. One of the life insurance problems was resolved; the second one was not serious. The participant who was denied long-term care insurance had other health conditions unrelated to hereditary hemochromatosis and iron overload that could have contributed to the denial. No problems were verified for health insurance or employment, or from any of the comparison group participants (controls and those with inconclusive screening results).

Conclusions The risk of insurance or employment problems 1 year after phenotype and genotype screening for hereditary hemochromatosis and iron overload is very low.

Social risks from genetic testing are a major public policy concern in medical genetics and genetics research.[1–3] These concerns are focused mainly on health insurance, as insurers have an incentive to avoid those clients it will be costly for them to insure. This concern also applies to employers, who pay for most private health care in the US.

Since the beginnings of the Human Genome Project in 1990, legislation has been proposed to head off possible genetic discrimination. The Health Insurance Portability and Accountability

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TABLE 1

Characteristics of all who responded to follow-up

	CLINICAL EXAM	COMPARISON GROUPS
Number of follow-up surveys	1154	1742
Number (%) of respondents	832 (72.1)	1130 (64.9)
Age: mean (SD)	56.5 years (13.4)	53.2 years (13.6)
Gender: N (%)*		
Male	439 (52.8)	357 (31.7)
Female	393 (47.2)	768 (68.3)
Race: N (%)		
White	461 (55.4)	788 (69.7)
Other	371 (44.6)	342 (30.3)
Language: N (%)*		
English	728 (87.5)	1027 (91.4)
Other	104 (12.5)	97 (8.6)
Insurance coverage: N (%)*		
Disability insurance	240 (31.1)	391 (37.1)
Life insurance	494 (62.2)	736 (67.8)
Health insurance	678 (83.4)	980 (88.7)
Employed: N (%)*	394 (55.7)	646 (65.5)

* Not all survey respondents answered these questions. Percent is based on those who answered.

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Healthy people have experienced discrimination in insurance or employment based on their phenotype or genotype

Act of 1996 (HIPAA) prohibited most insurers from considering genetic risks as preexisting conditions. Since the 1990s, all but 2 states have passed laws that limit genetic discrimination in health insurance; 34 states ban or limit genetic discrimination by employers.[4] In addition, a piece of federal legislation is pending. The Genetic Information Nondiscrimination Act, intended to prohibit health insurance and employment discrimination on the basis of genetic information, passed the House in April 2007 but, at press time, had not been voted on by the Senate.

Because state laws usually do not apply to life or disability insurance, and their applicability to employment is inconsistent, the potential for discrimination problems is still of concern to patients with costly conditions that may be uncovered by genetic screening.

Hereditary hemochromatosis—early detection is key

Members of the health care community have expressed concern that genetic discrimination will hamper efforts to detect and mitigate hereditary hemochromatosis, a relatively common condition marked by iron overload, which can lead to irreversible organ damage and related health problems.[5–9] Hereditary hemochromatosis is an autosomal recessive condition that typically is associated with 2 copies of the C282Y mutation in the *HFE* gene on chromosome 6, although the H63D *HFE* mutation is also associated with hereditary hemochromatosis in some cases.[10,11] If detected early, health problems from iron overload can be prevented by periodic phlebotomy. Not surprisingly, then, there is public health interest in the screening and detection of hemochromatosis or iron overload before symptoms arise.[9,12–14]

There are documented instances, however, of healthy people who experienced discrimination in insurance or employment based on having a phenotype or genotype associated with hereditary hemochromatosis.[8,15,16] Alper and colleagues noted that "[i]n a general screening program of 100 million people . . . even if only 5% of these people [who screen positive for hereditary hemochromatosis] encounter discrimination, this amounts to approximately 28,000 people."[8] Alper's speculation has not been tested because no large-scale studies of discrimination resulting from screening the general population have been conducted.

This study looks to identify possible social risks from genetic screening by surveying a large and diverse racial/ethnic primary care population participating in a study of iron overload and hereditary hemochromatosis in the US and Canada. We have sought to determine the number and types of problems associated with insurance and employment 1 year after screening and clinical examination for relevant hereditary hemochromatosis phenotypes and genotypes.

Methods

The data for this analysis come from the Hemochromatosis and Iron Over-

load Screening (HEIRS) Study. A full description of the study's rationale, design, and methods has been published elsewhere.[17]

Identifying the subjects

The research team screened a multiracial/ethnic sample of 101,168 primary care patients, 25 years of age and older, over a 2-year period beginning in March 2001. We recruited participants in approximately equal numbers at 5 field centers, 4 in the US and 1 in Canada. We chose study sites and recruitment goals to produce a sample with about 50% non-Caucasians. A central laboratory assayed blood samples for transferrin saturation, serum ferritin, and *HFE* C282Y and H63D mutations. A comprehensive clinical evaluation was offered to all C282Y homozygotes and to all non-C282Y homozygotes who met study thresholds for elevated transferrin saturation and serum ferritin iron measures.[17]

We identified a total of 2253 such participants. Of these, 1677 (74%) participated in the clinical exam, which assessed body iron stores and attempted to distinguish between primary and secondary causes of iron overload. Clinical exam results were provided to the participants—and, if they consented, to their primary care providers. We then mailed an extended survey to all 1677 participants assessing various psychological and behavioral issues related to genetic screening and testing; 1154 responded (68.8%).

Follow-up 1 year later

One year after the clinical exam, we resurveyed these 1154 respondents and asked additional questions about any problems with employment or insurance (health, life, or disability) in the past year "related to hemochromatosis or iron overload." Participants who had problems were contacted by telephone for follow-up questions about the nature and circumstances of the problem.

For comparison with clinical exam participants, we surveyed a stratified random sample of 939 screening participants in a similar fashion 1 year following screening. These participants were not eligible for a clinical exam but they had inconclusive screening results, indicating possible elevated risk of hereditary hemochromatosis/iron overload, such as *HFE* genotypes other than C282Y homozygosity, or lesser elevations of transferrin saturation or serum ferritin.[18] Also surveyed at 1 year were 803 controls (469 of whom had a clinical exam and 334 who did not), who were randomly selected following the age distribution of the other participants. All controls had no known *HFE* genotypes associated with iron overload and had transferrin saturation and serum ferritin values below study-defined thresholds for risk of iron overload.

Results

Overall, 832 clinical exam participants (72.1%) responded among the 1154 who were surveyed 1 year after their exam. Sample characteristics are shown in **TABLE 1**.

Few discrimination problems were found

Twenty-four (2.8%) reported they had 1 or more problems with employment or insurance that they believed were related to hereditary hemochromatosis/iron overload. Researchers made follow-up phone contact with 17 of these (70.8%), but 7 were lost to follow-up. Only 3 of these 17 participants verified problems that were possibly related to the participation in the HEIRS Study. Among the comparison group respondents (controls and inconclusive screening results), 6 (0.5%) reported a problem with employment or insurance. However, after we made contact with 5 of the 6 respondents, we were unable to verify any of the 5 cases.

All 3 verified reports of problems came from participants who received a clinical exam based on elevated transfer-

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Of 832 patients who responded to a follow-up survey a year later, only 3 had verified discrimination problems

TABLE 2

Characteristics of the 3 participants reporting insurance problems

Race	Caucasian, Asian, Pacific Islander (one each)		
Gender	Two males and one female		
	PARTICIPANT 1	**PARTICIPANT 2**	**PARTICIPANT 3**
Age	over 64	45–64	45–64
Genotype	normal (wild-type) *HFE*	normal (wild-type) *HFE*	normal (wild-type) *HFE*
Phenotype	Elevated transferrin saturation (51%) and serum ferritin (917 mcg/L)	Elevated transferrin saturation (53%) and serum ferritin (740 mcg/L)	Elevated transferrin saturation (76%) and serum ferritin (2871 mcg/L)
Other health problems	Obese; spherocytosis; reported history of arrhythmia	Reported history of thalassemia trait	Reports 5 alcohol servings per day; evidence of liver abnormality
Study classification	Primary iron overload	Cause of iron overload indeterminate	Cause of iron overload indeterminate
Reported problem	Denied long-term-care insurance by 2 large companies	Obtained life insurance but at an increased rate	Initially denied life insurance, but successfully appealed with a physician's letter stating no iron overload
Notes	Self-rated health status of 2 ("fair") out of 5 ("excellent")	Participant believes this was not due to participation in HEIRS Study, but was due to iron elevations that were identified by the study and reconfirmed by independent testing done for the insurance company	Reports that iron level returned to normal after ceasing to drink red wine

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Discrimination problems found in this study were not related to genetic testing but were instead due to elevated blood iron measures

rin saturation and serum ferritin levels, rather than based on their *HFE* genotypes. There were no verified reports from any of the 153 newly identified C282Y homozygotes who responded (out of a total of 252 such participants in the HEIRS Study). Details of the 3 verified problems are shown in **TABLE 2**.

One person with primary iron overload was denied long-term care insurance. Two people with elevated transferrin saturation and serum ferritin levels of undetermined cause reported having problems with life insurance. One was charged an increased rate, and the second one was initially refused insurance but was later covered after a physician explained that serum iron measures had returned to normal. There were no verified reports of problems with health insurance or employment. (None of the 7 participants who reported problems but who were lost to further follow-up were newly identified C282Y homozygotes, nor did any have C282Y or H63D *HFE* mutations.)

Discussion

Legal definitions and jurisdictions: Their role in discrimination

In the present study, all 3 participants who reported problems received a clinical examination based on elevated blood iron measures (transferrin saturation and serum ferritin). We verified no problems among participants with any C282Y or H63D *HFE* genotypes (including both homozygotes or heterozygotes). Therefore, under prevailing definitions, the reported problems do not appear to constitute "genetic discrimination."[15] Furthermore, we received no verified reports of problems with employment or health insurance, for which legal protections are much stronger than for other types of potential discrimination.[19]

Of note, though: None of our study jurisdictions had legal protections against genetic discrimination by life insurers or long-term-care insurers, and these are the 2 areas where our participants encountered problems. This suggests that existing legal protections may be somewhat

effective, although it is also consistent with the argument that such protections address potential problems that are rare or nonexistent.[1]

Examining the individual case reports (**TABLE 2**), insurance was denied outright in just one case, involving long-term care insurance, and that participant had health problems unrelated to iron overload that could have contributed to the denial. In the 2 life insurance cases, one person was insured with the help of a physician's letter, and the other person obtained insurance with an increased premium.

Limitations of this study

Because this study had only a 1-year follow-up period, it provides no basis for determining the long-term prevalence of insurance or employment problems. However, it appears that after 1 year, the extent of these problems is very small. No verified problems were reported by newly identified C282Y homozygotes or by participants with any other C282Y or H63D *HFE* genotypes.

Our findings contrast with the 20% prevalence of discrimination among hemochromatosis patients reported by Shaheen et al.[16] Their study, however, evaluated subjects who had been diagnosed in routine medical care to have hemochromatosis an average of 4.5 years before discrimination evaluation, and who were under treatment for iron overload.

Verification contacts in our study were made with those reporting a problem, which may have resulted in some underreporting among respondents. Also, we did not determine which participants sought or changed insurance during the study period, so we do not know the exposure rate to potential discrimination. Nevertheless, these findings provide some empirical basis for informing clinicians, researchers, patients, and Institution Review Boards that the risk of insurance or employment problems following genetic screening for hemochromatosis appears to be quite small. ■

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All authors had full access to all of the data in the study and they take responsibility for the integrity of the data and the accuracy of the data analysis.

The HEIRS Study investigators are listed at www.heirs-study.org/PP_Policy.htm.

Disclosure
No potential conflict of interest relevant to this article was reported.

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None of the 3 reported problems involved health insurance or employment—areas with strong legal protections against discrimination

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