Screening for Hereditary Hemochromatosis in Siblings and Children of Affected Patients

A Cost-Effectiveness Analysis

Hashem B. El-Serag, MD, MPH; John M. Inadomi, MD; and Kris V. Kowdley, MD

**Background:** Screening for hereditary hemochromatosis is traditionally done by using serum iron studies. However, mutation analysis of the hemochromatosis-associated HFE gene has recently become available.

**Objective:** To compare the cost-effectiveness of no screening with four screening strategies that incorporate HFE gene testing or serum iron studies.

**Design:** Cost-effectiveness analysis.

**Data Sources:** Published literature.

**Target Population:** Siblings and children of an affected proband.

**Time Horizon:** Lifetime from 10 years of age (children) or 45 years of age (siblings).

**Perspective:** Societal.

**Intervention:** 1) Serum iron studies. 2) Gene testing of the proband. If the proband is homozygous (C282Y/1), the spouse undergoes gene testing; if he or she is heterozygous (C282Y/0), the children undergo gene testing. 3) Gene testing of the proband; if he or she is homozygous, relatives undergo gene testing. 4) Direct gene testing of relatives.

**Outcome Measures:** Cost per life-year saved and incremental cost-effectiveness ratio.

**Results of Base-Case Analysis:** In children, HFE gene testing of the proband was the most cost-effective strategy for screening one child (incremental cost-effectiveness ratio, $508 per life-year saved). HFE gene testing of the proband followed by testing of the spouse was the most cost-effective strategy for screening two or more children (incremental cost-effectiveness ratio, $3665 per life-year saved). In siblings, all screening strategies were dominant compared with no screening. Strategies using HFE gene testing were less costly than serum iron studies.

**Results of Sensitivity Analysis:** Despite varying the prevalence of mutations and regardless of the cost of the genetic test in one- and two-way sensitivity analyses, HFE gene testing remained cost-effective.

**Conclusions:** HFE gene testing for the C282Y mutation is a cost-effective method of screening relatives of patients with hereditary hemochromatosis.

**Hereditary hemochromatosis** is an inherited disease characterized by progressive abnormal deposition of iron in the liver, heart, pancreas, and other vital organs. It is the most common genetic disease among persons of northern European descent, with a prevalence of 1:200 to 1:250 for homozygosity and a carrier rate of 1:8 to 1:12 (1–3). Because hereditary hemochromatosis is an autosomal recessive condition, children and especially siblings are at increased risk for the disease (4–6). Family screening for hereditary hemochromatosis is therefore recommended (7). Screening is traditionally done by measuring serum transferrin saturation and ferritin levels (8). Transferrin saturation may be elevated by 10 years of age, and almost all homozygous patients will have an elevated transferrin saturation by 40 years of age (8, 9). Hereditary hemochromatosis is traditionally confirmed by liver biopsy and measurement of hepatic iron concentration and hepatic iron index (6, 7). Early diagnosis and treatment before cirrhosis develops can ensure a normal life expectancy; in contrast, patients with cirrhosis have a reduced life expectancy despite iron depletion therapy (10–14).

A recently identified novel MHC class I gene called HFE appears to be mutated in most cases of hereditary hemochromatosis. Two missense mutations have been identified in this gene. The so-called major mutation is characterized by a cysteine–tyrosine substitution (C282Y). Eighty-five percent to 100% of persons of northern European descent with phenotypic evidence of hereditary hemochromatosis are homozygous for this mutation. A second mutation in the HFE gene, called H63D, has also been identified, but its significance is unclear (1, 7, 15–17). The prevalence of homozygosity for the C282Y mutation in patients with hereditary hemochromatosis varies among populations and ranges from 60% in Italy to approximately 100% in Australia (7, 18–20). Studies from the United States have revealed an 80% to 90% prevalence of C282Y/0 among patients with phenotypic evidence of hereditary hemochromatosis (15, 21). Tests for both genetic mutations are now commercially available. However, the role of HFE gene testing in screening for hereditary hemochromatosis is still undetermined.
We performed a cost-effectiveness analysis to compare a strategy of no screening among siblings and children of a proband with screening using serum iron studies or screening strategies that incorporate \textit{HFE} gene testing. In the base-case scenario, only testing for C282Y\textsuperscript{1}/\textsuperscript{1} was considered; testing for H63D was added in the sensitivity analysis.

**Methods**

A decision-tree model was created by using Microsoft Excel (Microsoft Corp., Redmond, Washington). We assumed that a proband had been confirmed to have hereditary hemochromatosis on the basis of standard phenotypic criteria, as described elsewhere (8, 22). The model was used to determine the most cost-effective screening strategy for hereditary hemochromatosis among the children or siblings of the proband under base-case assumptions.

The perspective of the analysis is societal. The Appendix Table enumerates the different tests recorded by their code number in the Current Procedural Terminology and their costs as given by the United Physicians Association at the University of New Mexico Health Sciences Center (23). The charge for gene testing is listed according to a quote given by SmithKline Beecham Laboratories. The base-case rates and costs were varied over a range of probabilities and values in a sensitivity analysis. The cost of serum iron studies as given by the Health Care Financing Administration was considered in the sensitivity analysis.

Because morbidity and mortality in hereditary hemochromatosis are related to iron overload rather than to \textit{HFE} mutations per se, our strategies incorporated serum iron studies among persons identified to be C282Y\textsuperscript{1}/\textsuperscript{1}. A no-screening strategy was compared with four screening strategies for hereditary hemochromatosis (Figure 1). All strategies were developed to screen both children and siblings of a proband, with the exception of the strategy in which the spouse was gene tested; this strategy applied only to screening of children. It was estimated that 5\% of the children would be homozygous, assuming that the proband was homozygous and that the prevalence of heterozygotes is 10\% among white persons. Nonconsanguinity was presumed. Twenty-five percent of siblings were projected to be homozygous, assuming that both of the proband’s parents were heterozygous carriers of the affected gene. Equal sex distribution was assumed in the screened pedigree.

**No-Screening Strategy**

We assumed that 80\% of persons with hereditary hemochromatosis would have elevated transferrin.
saturation or ferritin levels, of whom 50% would develop organ damage in the form of cirrhosis with or without hepatocellular carcinoma, diabetes mellitus, or congestive heart failure (6, 24). Assumptions about the incidence of and mortality associated with these complications have been published elsewhere (6, 24–29) (Appendix Table).

Serum Iron Studies Strategy

This strategy entailed measuring serum transferrin iron saturation and ferritin levels in relatives of the proband. Screening of children was assumed to start at 10 years of age and continue until 40 years of age or until an abnormal test result is found. Previous studies illustrated that transferrin saturation may be elevated by 10 years of age in homozygotes, and most will have an elevated serum transferrin saturation by 40 years of age (6, 9, 22). The model assumed that C282Y homozygotes with normal serum ferritin and transferrin saturation values did not undergo liver biopsy (6). A Markov process was used to model this strategy. Three states were included: the initial screening, from which patients either tested positive (abnormal results on iron tests) or negative. In subsequent intervals, patients who tested negative underwent repeated testing. The cycle length (that is, the interval between testing) was modeled to be 5 years in the base case and 10 years in the sensitivity analysis (22). The probability of testing positive in each cycle was varied over time as an exponential function, with an upper limit of 5% of the screened population eventually testing positive.

Siblings were screened by one-time serum iron measurement at the time of the proband’s identification, with repeated testing in patients with elevated values. It was assumed that siblings of a proband with hereditary hemochromatosis in whom disease was diagnosed outside of screening programs would be of sufficient age (>40 years) to manifest biochemical evidence of iron overload.

Gene Testing the Proband Followed by Testing the Spouse

In this strategy a proband was gene tested first, and if he or she was found to be homozygous, the spouse was tested for the same mutation. Children who were gene tested only if the spouse was heterozygous; the probability of any child being homozygous for the C282Y mutation was 50%. If children had the C282Y+/+ mutation, they underwent repeated iron studies (that is, they entered the Markov process explained under the first strategy). If a child was found not to be homozygous, no further screening was performed. If the proband did not have the C282Y+/+ mutation, further gene testing of children would not be useful and serum iron studies would be needed for screening.

Gene Testing the Proband Followed by Testing Relatives

Children

This strategy also started by HFE gene testing the proband, followed by gene testing the children if the proband was homozygous (C282Y+/+). However, the spouse was not gene tested. Children who were found to be homozygous underwent repeated iron studies; those who tested negative for the C282Y+/+ mutation were not at risk for disease and did not require further evaluation. In a pedigree in which the proband was found not to be homozygous, each child would be tested further with periodic iron studies.

Siblings

The proband would be tested for HFE gene mutation and if he or she had the C282Y+/+ mutation, siblings would be gene tested. Siblings who tested positive for the C282Y+/+ mutation would require iron studies; those who tested negative would not require further investigation. If the proband was not homozygous, siblings would be tested once with serum iron studies.

Gene Testing Relatives before the Proband

If HFE gene mutation testing detects most cases of hereditary hemochromatosis, one can theoretically forgo testing the proband and test only relatives for the mutation. This is the rationale for including a strategy that used initial gene testing of relatives. Serum iron studies were performed only in relatives who tested positive for the C282Y+/+ mutation, thus saving the cost of gene testing the proband. However, if all relatives lacked the C282Y mutation, the proband would need to be gene tested; if the proband was positive for the C282Y+/+ mutation, hereditary hemochromatosis would be excluded in the relatives. The probabilities for each of these transitions were calculated by applying Bayes theorem and the laws of conditional probability (30). All of the screening strategies had a final common pathway in which evidence of iron overload was sought by obtaining serum iron studies. Patients with iron overload and hereditary hemochromatosis (a true-positive iron study) would undergo phlebotomy; children would require only maintenance phlebotomy (three times annually), and siblings would require an initial set of 40 phlebotomies before maintenance therapy. Patients with iron overload but without hereditary hemochromatosis (a false-positive iron study) would undergo 5 phlebotomies before the hematocrit value significantly decreased.
Persons with no iron overload and no hemochromatosis (a true-negative iron study) would require no further treatment. All patients in the above three groups were assumed to have normal life expectancy. Patients with hereditary hemochromatosis but no iron overload on serum iron studies (a false-negative iron study) would follow a course similar to that in those who did not undergo screening.

The total cost and life-years remaining at the end of each strategy were calculated. Incremental cost-effectiveness ratios were calculated for each screening strategy as compared with no screening (31). All costs and outcomes (life-years) were discounted at a rate of 3%.

Combination of Children and Siblings

Because most pedigrees contain a variable combination of children and siblings, the costs resulting from screening all possible combinations of up to three children and three siblings were algebraically summed and presented in a three-dimensional bar graph. The algorithm for genetic screening of a combination of relatives is summarized in Figure 2.

Sensitivity Analysis

The stability of the model was tested by subjecting key variables to one-way and two-way sensitivity analyses. First, the cost of the gene test was varied between $191 (the current cost at SmithKline Beecham Laboratories when the test for H63D mutation was added) and $85. Second, the cost of measuring serum iron transferrin saturation and serum ferritin was varied from $85 to a minimum of $40, which corresponds to the amount reimbursed by the Health Care Financing Administration in 1998. Third, the relative proportions of patients with hemochromatosis in whom HFE gene testing is positive for the C282Y+/+ mutation was varied between 60% and 100% on the basis of previous studies of the prevalence of C282Y+/+ among patients with phenotypic evidence of hemochromatosis. Adding the H63D mutation to the HFE gene test was also assessed. Fourth, the sensitivity and specificity of iron studies in detecting hereditary hemochromatosis were varied between 90% and 100%. Fifth, the frequency of serum iron studies in children was reduced to examine the effect of screening once every decade between 10 and 30 years of age. We also tested a serum iron studies strategy in which only transferrin iron saturation ($20) was measured initially and was followed by measurement of both transferrin saturation and ferritin if the transferrin iron saturation was elevated. Finally, the prevalence of the C282Y+/− mutation in the population was varied between 1 per 1000 persons to 20 per 1000 persons.

None of the authors have any conflict of interest in terms of the design, conduct, and reporting of the study.

Results

Screening Children

Figure 3 shows, under base-case assumptions, the cost of four screening strategies for hereditary hemochromatosis in a pedigree that consists of up to three children. A strategy of no screening (not shown) was associated with a cost of $230 per child and a life expectancy of 39 years; both values were discounted at an annual rate of 3%. HFE gene testing of the proband followed by testing of a child
was the least expensive and most cost-effective strategy to screen one child (incremental cost-effectiveness ratio, $508 per life-year saved). However, for screening two or more children, the strategy of gene testing the spouse if the proband was found to be homozygous for the mutation was the most cost-effective strategy. For example, screening two children was associated with an incremental cost-effectiveness ratio of $3665 per additional life-year saved, whereas screening using serum iron studies was a more expensive strategy (incremental cost-effectiveness ratio, $7934), and the strategy in which children were gene tested before the proband was the most expensive (incremental cost-effectiveness ratio, $12 277). As shown by the divergent lines in Figure 3, the savings associated with the strategy of spouse testing increased as the number of screened children increased.

**Screening Siblings**

For a sibling, no screening was associated with a discounted cost of $2773 and a discounted life expectancy of 65.5 years. Compared with no screening, all screening strategies were dominant: that is, they cost less and yielded greater benefit than no screening (31). The cost of screening a pedigree that consists of up to three siblings is shown in Figure 4. Screening with serum iron studies was the most expensive screening strategy throughout. Of the two strategies that used HFE gene testing, gene testing of the siblings first resulted in lower costs when only one sibling was screened. For two or more siblings, performing HFE gene testing of the proband first was less costly.

Figure 5 compares the costs associated with screening using either serum iron studies or the suggested HFE gene testing strategy outlined in Figure 2. In screening any combination of relatives, HFE gene testing of the proband followed by HFE gene testing of the spouse was the least expensive strategy. For example, the cost of screening two children and two siblings with iron studies was $4110 ($1180 + $2930), whereas using a gene testing strategy to screen the same combination was $3309.

**Sensitivity Analysis**

The Table shows the results of one-way sensitivity analysis applied to screening one child or two children.

**Proportion of Probands with the C282Y+/+ Mutation**

When the relative proportion of patients with phenotypic hemochromatosis in whom the HFE gene test is positive for the C282Y+/+ mutation was increased to 100%, gene testing of relatives before the proband became a less expensive strategy for screening siblings. In addition, it became the least expensive strategy for screening one child. When this proportion was varied between 60% and 100%, gene testing of the proband followed by the spouse remained the least expensive strategy for screening two or more children.

**Cost of Gene Testing and Serum Iron Studies**

If the cost of genetic testing decreased to less than $95, the suggested strategy in Figure 2 became less expensive than iron studies to screen any number of siblings or children. In a two-way sensitivity analysis, a threshold value of $101 for the gene test was found, and gene testing of the proband followed by testing the spouse was the least expensive strategy even when the lowest value of $40 for

![Figure 3. Screening of children for hereditary hemochromatosis.](image3.png)

![Figure 4. Screening of siblings for hereditary hemochromatosis.](image4.png)
serum iron studies was considered. When the cost of the H63D screening test was added to the gene test (total cost, $191), testing for HFE gene mutations increased the detection of significant mutations (C282Y+/+ or C282Y/H63D) to 92%. Therefore, the incremental cost-effectiveness ratios did not significantly differ from the base-case results.

Frequency of Screening Children with Serum Iron Studies

When the tested pedigree contained two or more children, HFE gene testing of the proband followed by the spouse remained the least expensive strategy even when the frequency of serum iron studies was reduced to three times between the ages of 10 and 30 years. When only measurement of serum transferrin saturation ($20) was used for initial screening, the gene test had to cost less than $131 to remain less expensive than iron studies for screening two or more children. A two-way sensitivity analysis indicated that in siblings, genetic screening was a dominant strategy at $173 for the gene test, even if the cost of serum iron studies decreased to $0. Varying the sensitivity and specificity of serum iron studies between 90% and 100% did not significantly change the results.

Prevalence of C282Y Carriers (C282Y+/−) in the General Population

The lower the prevalence of C282Y carriers, the higher the savings achieved by gene testing the spouse before screening children compared with other strategies. Gene testing of the spouse remained the least expensive strategy for screening two or more children, even when a high prevalence of C282Y carriers (13 per 1000 persons) was assumed.

Discussion

Our analysis shows that screening to detect homozygosity for the C282Y mutation of the HFE gene in first-degree relatives of a patient with hereditary hemochromatosis is a cost-effective practice. HFE gene testing is also associated with cost savings compared with traditional screening with serum iron studies. On the basis of these results, our recommended strategy to screen pedigrees comprising both children and siblings is as follows. First, HFE gene testing of the patient should be performed. If the patient tests positive, the spouse should undergo HFE gene testing. If the spouse is found to be heterozygous for C282Y, children should be gene tested. Siblings would undergo HFE gene testing if the proband was homozygous for C282Y. HFE gene testing in this model served to identify persons with the C282Y+/+ mutation, who then underwent screening with serum iron studies for early biochemical evidence of iron overload. It is important to note that we conducted this cost-effectiveness analysis from a societal perspective using direct costs only. Although multiple-way (n-way) sensitivity analysis was not performed, we identified key variables that produced the greatest impact on outcome in one-way and two-way analyses.

Genetic screening of first-degree relatives could also detect persons with heterozygous mutations. Compound heterozygotes (C282Y+/− and H63D+/−) are at increased risk for iron overload and should therefore probably undergo periodic screening with iron studies (32). However, regular screening with iron studies need not be done in simple heterozygotes. In the absence of confounding conditions, such as hepatitis C virus infection, alco-
holic hepatitis, or nonalcoholic steatohepatitis, clinically significant iron overload remains a rare event among this group (32, 33).

Whether or not the spouse of a proband is a carrier of the hereditary hemochromatosis gene determines the children’s likelihood of being homozygous. If the spouse lacks the C282Y mutation, children can be at most heterozygous for C282Y, and screening for iron overload can therefore be forgone. In a retrospective study by Adams (34), genotyping the spouse had the potential to reduce the number of children tested by 92% and costs of screening by 39%. Our analysis qualifies the conditions under which this strategy reduces costs. Gene testing of the spouse should be done only if the proband is homozygous for the C282Y mutation. HFE gene testing of the spouse is the most cost-effective strategy if two or more children are involved or the prevalence of C282Y carriers in the population is low (less than 13 per 1000 persons).

Our model assumed a high prevalence of HFE mutations among first-degree relatives of patients with hereditary hemochromatosis. Extrapolating our results to screening in the general population may therefore not be appropriate. The high prevalence of disease among first-degree relatives increases the predictive value of gene testing and therefore boosts its cost-effectiveness as a screening tool. Our results complement those of previous studies demonstrating the appropriateness of screening for hereditary hemochromatosis among first-degree relatives of affected patients (5, 6). If patients with hereditary hemochromatosis are identified and treated early, they can have a normal life expectancy (10–14). Standard treatment of hemochromatosis, phlebotomy, is widely available and inexpensive (35).

One concern about the use of gene testing in screening for hereditary hemochromatosis is the variable phenotypic expression of the disease. A recent study found that 50% of persons who are homozygous for the C282 mutation may not have clinically significant iron overload; however, follow-up was short (32, 36). Nonetheless, all patients had elevated transferrin saturation, suggesting that some degree of phenotypic expression is universal. Studies with long-term follow-up are needed to determine the proportion of patients with the characteristic genotype who will not develop iron overload with organ damage. The degree of phenotypic expression seems to be greater among family members of patients with hereditary hemochromatosis than among sporadic cases. For instance, the prevalence of the mutation has been described in 93% to 100% of persons in pedigrees with evidence of iron overload (19, 20, 37).

Other concerns about genetic screening include the cost of the test and its potential for causing unnecessary discomfort, anxiety, or stigmatization among those tested. Inexpensive tests, such as transferrin saturation or unconjugated iron–binding capacity, are promising as one-time screening tests for hereditary hemochromatosis in the general adult population. The routine use of such tests for screening is not currently practical, however, due to the cost and lack of evidence indicating their utility in identifying persons at risk for iron overload.

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**Table. One-Way Sensitivity Analysis for Hemochromatosis Screening**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cost Per Patient (Incremental Cost-Effectiveness Ratio*)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>One Child</td>
</tr>
<tr>
<td></td>
<td>Proband First</td>
</tr>
<tr>
<td>Proportion of probands with HFE gene mutation 100% 60%</td>
<td>590 (553)</td>
</tr>
<tr>
<td>Cost of genetic test $191 $85</td>
<td>590 (553)</td>
</tr>
<tr>
<td>Cost of iron studies $85 $40</td>
<td>382 (345)</td>
</tr>
<tr>
<td>Screening frequency in children§ Start at 10 years of age, every 5 years until 40 years of age</td>
<td>590 (553)</td>
</tr>
<tr>
<td>Start at 10 years of age, every 10 years until 30 years of age</td>
<td>393 (356)</td>
</tr>
</tbody>
</table>

* Compared with no screening.
† Serum iron level, transferrin saturation, and ferritin level.
§ Screening by using iron studies either as a primary screening strategy or in persons found by genetic screening to have the C282Y+/+ mutation.
Appendix Table. Model Assumptions

<table>
<thead>
<tr>
<th>Assumption</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genetic test</td>
<td></td>
</tr>
<tr>
<td>Parents of proband are heterozygous for hereditary hemochromatosis gene</td>
<td></td>
</tr>
<tr>
<td>The spouse of the proband is not homozygous for hereditary hemochromatosis</td>
<td></td>
</tr>
<tr>
<td>age</td>
<td></td>
</tr>
<tr>
<td>Frequency of screening with a genetic test</td>
<td>Once</td>
</tr>
<tr>
<td>Prevalence of genetic mutation among patients with hereditary hemochromatosis</td>
<td>90</td>
</tr>
<tr>
<td>Prevalence of hereditary hemochromatosis, % gene carriers in the population</td>
<td>10</td>
</tr>
<tr>
<td>Iron studies</td>
<td></td>
</tr>
<tr>
<td>Frequency and duration of screening using iron studies</td>
<td></td>
</tr>
<tr>
<td>For children (starts at 10 years of age, repeated every 5 years for 30 years)</td>
<td>7 times</td>
</tr>
<tr>
<td>For siblings</td>
<td>Once, if result is abnormal</td>
</tr>
<tr>
<td>Sensitivity of serum iron studies for diagnosing hereditary hemochromatosis</td>
<td>98</td>
</tr>
<tr>
<td>Specificity of serum iron studies for diagnosing hereditary hemochromatosis</td>
<td>96</td>
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<tr>
<td>Probability of developing complications</td>
<td></td>
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<tr>
<td>Cirrhosis</td>
<td>0.30</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
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</tr>
<tr>
<td>Heart failure</td>
<td>0.05</td>
</tr>
<tr>
<td>All of the above</td>
<td>0.12</td>
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<tr>
<td>Heart failure and cirrhosis</td>
<td>0.09</td>
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<td>Cirrhosis and diabetes</td>
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<td>Hepatocellular carcinoma among cirrhotic patients</td>
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<td>Age at first symptoms, y</td>
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<td>Age at death, y</td>
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<td>Normal persons (without hereditary hemochromatosis)</td>
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<tr>
<td>Persons with cirrhosis</td>
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<td>Persons with hepatocellular carcinoma</td>
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<tr>
<td>Persons with diabetes mellitus</td>
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<tr>
<td>Persons with heart failure</td>
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<tr>
<td>Medical care costs, $</td>
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<td>Cost of iron studies</td>
<td>85</td>
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<tr>
<td>Cost of genetic test</td>
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<tr>
<td>Annual cost of cirrhosis care</td>
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<tr>
<td>Annual cost of diabetes care</td>
<td>1500</td>
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<tr>
<td>Hepatocellular carcinoma</td>
<td>50,000 one time</td>
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<tr>
<td>Heart failure</td>
<td>45,000 in the year preceding death†</td>
</tr>
<tr>
<td>Phlebotomy</td>
<td>50 per session</td>
</tr>
</tbody>
</table>

* Figures are averaged for men and women.
† Serum iron level, transferrin saturation, and ferritin level.
‡ Ambulatory care and management of diuretic-sensitive ascites. Based on data from reference 29.
§ Based on data from references 6, 24, 26, and 28.
¶ Based on data from references 26 and 28.
‖ Based on data from reference 24.

population (38). However, without HFE gene testing, all first-degree relatives of an affected proband would probably have to undergo repeated screening with serum iron studies until 40 years of age. By contrast, with gene testing, 95% of children and 75% of siblings who are negative for C282Y homozygosity are spared further investigation, which translates into significant monetary savings (as shown in our analysis).

The cost of the HFE genetic test was shown in our analysis to be an important determinant of overall costs. Currently, most laboratories charge more than $100 for gene testing; if the gene test cost decreases to less than $95, gene testing the proband with subsequent testing of the spouse becomes by far the most economical strategy for screening any number of children or siblings. We assume that screening affects the number of patients who develop cirrhosis but does not alter the course of cirrhosis once it occurs. Varying the costs of medical care for clinical sequelae, such as cirrhosis and diabetes, may change the magnitude of difference but not the relative difference between screening strategies. The exception to this is the “no screening” strategy that dominates if one unrealistically assumes that no medical care costs are associated with cirrhosis. We have purposely chosen costs that bias against screening; in reality, cost savings are likely to be greater than those found in our analysis.

The results of our analysis show that genetic screening is a cost-effective option for screening relatives of a proband with hereditary hemochromatosis. Further study is required to examine the ethical, legal, and social implications of genetic testing among asymptomatic persons.

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Acknowledgment: The authors thank Professor Denis M. McCarthy for his overall support and Amnon Sonnenberg, MD, MSc, for advice on mathematical issues.

Grant Support: In part by a Glaxo Wellcome Foundation for Digestive Health Award for Outcomes Research (Dr. El-Serag) and by the Veterans Affairs HSR&D Houston Center of Excellence.

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References