

REVIEW ARTICLE

GENOMIC MEDICINE

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## Ethical, Legal, and Social Implications of Genomic Medicine

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AS DETAILED IN OTHER ARTICLES IN THE GENOMIC MEDICINE SERIES, genomics has contributed greatly to our understanding of the molecular basis of disease and, to a lesser but growing extent, to the development of effective interventions. Clinicians and society at large, however, are concerned about the effect genetic knowledge will have on the well-being of individual persons and groups. Much effort is being devoted to trying to anticipate, understand, and address the ethical, legal, social, and political implications of genetics and genomics.

The inquiry is complex. Understanding the social effects of genomics requires an analysis of the ways in which genetic information and a genetic approach to disease affect people individually, within their families and communities, and in their social and working lives. Genomics presents particular challenges with respect to clinicians' ethical and professional responsibilities, including the appropriate use of genomic information in the health care setting. In this article, I examine public concerns about genetic information and discuss a few recent cases in some depth to highlight a few of the dilemmas presented by genomics and emerging solutions.

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### WHAT GENETIC INFORMATION IS AND WHAT PEOPLE ARE WORRIED ABOUT

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Genes affect virtually all human characteristics and diseases. These influences can be ascertained in individual patients through a review of the family history, physical examination, and the use of medical diagnostics. In some conditions, such as cystic fibrosis and sickle cell disease, the specific molecular mechanisms are largely understood, but in many, including such common chronic diseases as diabetes mellitus and hypertension, the relevant genes — and there are often many — are only beginning to be identified. Given the variety of these effects and the limits of our knowledge, it is not surprising that the term “genetic information” is used in different ways at different times. Sometimes it is used to mean the influence of the entire genome, but more often it is used to refer to recognized, single-gene disorders or, even more narrowly, the results of DNA-based tests. These various meanings may make sense in context, but confusion can occur unless the speaker and listener are defining the term in the same way.

The most commonly expressed fear is that genetic information will be used in ways that could harm people — for example, to deny them access to health insurance, employment, education, and even loans. Part of that concern is fueled by the growing recognition that health information is not entirely private, despite people's expectations and desires to the contrary. In fact, both federal and state governments have been actively engaged in discussions about who ought to have access to health information and under what conditions.<sup>1,2</sup> This debate is informed appropriately by the recognition that limit-

ing access to the medical record to the patient and the treating clinician is neither possible nor unequivocally desirable.<sup>3</sup>

People tend to see genetic information as more definitive and predictive than other types of data, in the sense that “you cannot change your genes” and that “genes tell all about your future.” This notion of genetic determinism, however, includes an unwarranted sense of inevitability, because it reflects a fundamental failure to understand the nature of biologic systems. The DNA sequence is not the Book of Life. Human characteristics are the product of complex interactions over time between genes — both a person’s own and those of other organisms — and the environment. Both germ-line and somatic cells undergo mutations, the latter being a primary way in which cancer develops. Moreover, a pathogenic mutation does not doom one to ill health; many diseases can be treated. As is true for so many conditions in medicine, clinicians have a variable but usually limited ability to predict when, how severely, and even whether a person with a genetic predisposition to a certain illness is going to become ill.

One might be tempted to conclude that the way to allay people’s fears about genetics is simply to give them a more realistic understanding of the informative power of these tools. Given the optimistic predictions about genetics that pervade the media and public opinion today, that path is unlikely to succeed in the short term. A more promising approach to addressing the social implications of genetics requires us to consider both how genes are perceived in the real world and what is actually known about their function.

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#### THE PROBLEM OF DISCRIMINATION

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The question of whether genetic information should ever be used to affect one’s access to health and other forms of insurance has been a dominant issue of public concern in the past decade. People cite fear of losing insurance as a major reason to avoid genetic testing.<sup>4</sup> Others argue that discrimination by insurance companies is not a problem, often pointing out that few of these cases, which are difficult for employees to win, have been filed.<sup>5</sup> Insurers assert that they do not perform tests to obtain genetic information but argue that they should be free to use such information if it is available, citing the need to avoid “moral hazard” — the risk that people who know they will become ill or die soon will try to obtain in-

surance at regular rates.<sup>6</sup> In response to consumer pressure, many states have passed laws in this area (Table 1).<sup>7,8</sup> In passing the Health Insurance Portability and Accountability Act (HIPAA),<sup>9</sup> Congress specifically banned certain uses of genetic information in determining insurance eligibility, but it placed no limits on rate setting.<sup>10</sup> Vigorous debate about optimal solutions is ongoing,<sup>11</sup> and bills have been introduced in every recent session of Congress.<sup>12</sup>

The complexity of the issues surrounding discrimination can be illustrated more generally by examining a case involving Burlington Northern Santa Fe Railroad (BNSF). Allegedly relying on the advice of its company physician, who in turn had apparently relied on the representations of a diagnostic company, BNSF began obtaining blood for DNA testing from employees who were seeking disability compensation as a result of carpal tunnel syndrome that occurred on the job. The employees were reportedly not told the purpose of the tests, which was to detect a mutation associated with hereditary neuropathy with liability to pressure palsies.<sup>13</sup> The company’s motive for pursuing testing was never made clear, but it seems reasonable to suspect that BNSF would have tried to deny disability benefits to any employee who had such a mutation, arguing that the mutation, and not the job, caused the carpal tunnel syndrome. When the company’s practice came to light, it was almost immediately stopped by the federal Equal Employment Opportunity Commission,<sup>14</sup> and shortly thereafter, the company settled claims brought by its employees for an undisclosed amount of money.<sup>15</sup>

What lessons can be learned here? One is that the company’s effort to find mutations for hereditary neuropathy with liability to pressure palsies made little sense. This disorder is very rare, affecting about 3 to 10 persons per 100,000, and more important, although carpal tunnel syndrome can be a part of hereditary neuropathy with liability to pressure palsies, it has not been reported as the sole symptom. The injuries these employees sustained were not the result of an epidemic of hereditary neuropathy with liability to pressure palsies. Getting the biologic process correct is a critical step in making decisions about genetic testing.

Another important lesson is that identifying a genetic predisposition to carpal tunnel syndrome would not have been the end of the discussion in the eyes of the law. The company got in trouble because its practice violated numerous laws forbid-

**Table 1. Summary of Statutes Regarding Discrimination on the Basis of Genetic Information and the Privacy of Such Information.\***

State or District	Health Insurance	Life Insurance	Employment	Confidentiality
Alabama	Yes, for cancer only†			
Alaska	Yes‡			
Arizona	Yes	Yes	Yes	Yes
Arkansas	Yes†‡		Yes	Yes
California	Yes§	Yes§	Yes	Yes
Colorado	Yes	Yes		Yes
Connecticut	Yes‡		Yes§	Yes
Delaware	Yes		Yes§	Yes
District of Columbia	Yes‡			
Florida	Yes‡			Yes
Georgia	Yes			Yes¶
Hawaii	Yes†‡§			
Idaho	Yes‡			
Illinois	Yes‡			Yes
Indiana	Yes†§			Yes
Iowa	Yes†‡		Yes†	
Kansas	Yes†§		Yes†	
Kentucky	Yes†‡			
Louisiana	Yes†		Yes	Yes
Maine	Yes‡	Yes	Yes†	
Maryland	Yes†	Yes	Yes†	
Massachusetts	Yes†	Yes	Yes	Yes
Michigan	Yes†		Yes†	
Minnesota	Yes†§		Yes†	
Mississippi				
Missouri	Yes†		Yes	Yes
Montana	Yes†‡¶	Yes		
Nebraska	Yes‡		Yes†	
Nevada	Yes†‡§		Yes†	Yes

ding discrimination in the workplace. In particular, the Americans with Disabilities Act permits employers to require a medical evaluation only under clearly specified circumstances.<sup>16</sup> Testing employees after they were disabled without their informed consent clearly fell outside the bounds of this and other antidiscrimination laws.

The actions of BNSF led to widespread criticism

and, not surprisingly, to calls to ban genetic discrimination in the workplace.<sup>17</sup> Although some states have enacted laws (Table 1), the need for federal action has grown as the Supreme Court has progressively narrowed the protection provided under the Americans with Disabilities Act.<sup>18,19</sup> The answer, however, is not simply to forbid employers to use genetic information or to require genetic testing.

**Table 1. (Continued.)**

State or District	Health Insurance	Life Insurance	Employment	Confidentiality
New Hampshire	Yes†	Yes	Yes	Yes
New Jersey	Yes‡	Yes	Yes	Yes
New Mexico	Yes‡			Yes¶
New York	Yes		Yes	Yes
North Carolina	Yes		Yes	
North Dakota	Yes‡			Yes
Ohio	Yes†‡			
Oklahoma	Yes†‡		Yes†	Yes†
Oregon	Yes		Yes†	Yes
Pennsylvania				
Rhode Island	Yes		Yes	
South Carolina	Yes§			Yes
South Dakota	Yes†‡		Yes	Yes
Tennessee	Yes‡			
Texas	Yes**		Yes	Yes¶
Utah	Yes		Yes	Yes
Vermont	Yes†	Yes	Yes†	Yes
Virginia	Yes§		Yes	
Washington				
West Virginia	Yes‡			
Wisconsin	Yes†	Yes	Yes†	
Wyoming	Yes‡			

\* Yes indicates that the state has enacted legislation concerning the use of genetic information in the indicated circumstance. This table was compiled in June 2003. Because these are areas of intense legislative activity, the laws change frequently. In addition, the laws vary far more widely from state to state than can be reflected in a table such as this. This table is not intended to be a legal opinion about the coverage of these laws. Readers are encouraged to consult the laws in their own states.

† Testing cannot be required.

‡ According to the statute, genetic information cannot be considered to indicate a preexisting condition in the absence of symptoms.

§ The statute specifically addresses illnesses in family members.

¶ The statute contains exemptions about the use of information for certain research and other purposes.

|| Testing can be required for certain purposes, such as evaluating workers' compensation claims or surveillance.

\*\* The statute permits testing to be required under certain circumstances.

The first step in developing an appropriate response is to determine how the use of genetic information fits within the broader framework of anti-discrimination laws, which were passed to create a certain kind of society, one in which people must be included regardless of race, sex, or disability, even at some cost to employers. Biology alone does not determine the social outcome. To use an analogy,

an employer cannot exclude women from the workplace, even if he or she believes, with some justification, that women are more likely than men to take time off to care for family members. At the same time, employers are not required to bear unlimited costs to promote these social goals—the employee, male or female, who misses months of work at a time to care for sick relatives can still be fired.

A similar debate about social goals and the limits of our pursuit of them must occur with regard to genetic discrimination. The Equal Employment Opportunity Commission recently awarded damages to Terri Sergeant, who was fired from her job as an office manager for an insurance broker because she required extremely expensive medication to treat her at-worst mildly symptomatic alpha<sub>1</sub>-antitrypsin deficiency.<sup>20</sup> A person's need for expensive health care is not sufficient reason to fire that person or to refuse to hire him or her in the first place. The fact that the costs may cause the employer to go under or to decide not to provide health insurance simply underlines the inherent weakness of employment-based health insurance.

At the same time, one can imagine a genetic condition that might affect a person's ability to perform a job in ways that could not be accommodated with reasonable efforts. Suppose a person with a recurrent and untreatable cardiac arrhythmia that leads to loss of consciousness, owing to an inherited ion-channel defect, is seeking employment as a long-distance truck driver. Because of the risk to third parties, such a person would not even be able to get

a driver's license in many jurisdictions. The more difficult question — and the one posed particularly with respect to genetics — would arise if an asymptomatic person had a predisposing, but incompletely penetrant, mutation for the same disorder. Deciding what to do about such predispositions will require close attention both to the true, as opposed to the feared, likelihood that symptoms will develop and to the complex weighing of the interests of the individual, the employer, and society.

A similar calculus must be applied to every question regarding who can obtain and use genetic information to distinguish, or discriminate, among people in ways that affect their ability to obtain social goods, such as health insurance and education (Table 2).<sup>21</sup> If, as is likely, some uses are deemed to be appropriate, the challenge for clinicians will be to discuss with their patients the potential adverse social consequences of testing so that the patients can make informed choices about whether or not to proceed with testing.

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THE CHALLENGE OF GENOMIC  
MEDICINE WITH RESPECT TO THE  
PHYSICIAN–PATIENT RELATIONSHIP

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**Table 2. Elements to Be Considered in Decisions about the Use of Genetic Information.**

<p>What are some potential implications of genetic information?</p> <ul style="list-style-type: none"> <li>The patient may be more likely to require expensive therapy</li> <li>The patient may be more likely to be injured by certain types of exposure</li> <li>The patient may present a danger to others in the future</li> </ul> <p>What principles need to be taken into account, recognizing that none are absolute?</p> <ul style="list-style-type: none"> <li>Protection of autonomy</li> <li>The public health</li> <li>The importance of inclusiveness</li> <li>Allocation of costs</li> </ul> <p>Who decides whether the test will be done?</p> <ul style="list-style-type: none"> <li>The patient</li> <li>The patient's employer or another private third party</li> <li>The government</li> </ul> <p>Who decides what to do with the results?</p> <ul style="list-style-type: none"> <li>The patient</li> <li>A private third party</li> <li>The government</li> </ul>
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Consider the case of a man who died of colon cancer in the 1960s. When the same disease developed in his daughter approximately 25 years later, she obtained her father's pathology slides, discovered that he had had diffuse adenomatous polyposis coli, and sued the estate of her father's surgeon, alleging that the physician should have warned her about her 50 percent risk of having the disorder. An intermediate appellate court in New Jersey ruled that the physician had a duty to warn the daughter directly (she would have been a child at the time of her father's death), perhaps even over her father's objections.<sup>22</sup>

This is only one court's view in one case, but given how much attention it received, it is important to ask whether this was a good result. Two central tenets of Western medicine are that physicians should focus on the interests of their patients and that they should protect the confidentiality of their patients' medical information. Yet the tools of genomic medicine often reveal information about health risks faced not only by patients but also by their relatives. What should clinicians do? It seems clear that they should tell their patients about the risks faced by family members. The harder questions are whether physicians are ethically permitted to contact the relatives themselves, in contravention of traditional

patient-centered norms, and whether they should be legally required to do so.

This issue must be viewed in the light of the fact that the duty to protect confidentiality is not absolute. Physicians are required to report numerous infectious diseases,<sup>23</sup> and they have been held liable for failing to warn people whom their patients have specifically threatened with violence.<sup>24</sup> The question then becomes more complex: are genetic risks sufficiently similar to these existing exceptions to the requirement of confidentiality that they warrant an exception as well? Over the years, numerous prominent advisory bodies have said no, opining that physicians should be permitted to breach confidentiality in order to warn third parties of genetic risks only as a last resort to avert serious harm.<sup>25-27</sup>

These learned opinions, however, are not the end of the matter, in part because they lack the force of law. In fact, as the case above illustrates, relatives have sued the primary patients' physicians for failing to warn them of their own genetic risks — and won limited victories, although none have been awarded monetary damages. The decisions in the colon-cancer case and a similar one in Florida<sup>28</sup> have been criticized for both their legal reasoning and their deviation from ethical guidelines, but they have not been overturned and, in the tradition of the common law, may be persuasive to other courts. Physicians who breach their patients' confidentiality and warn family members are not likely to incur substantial liability, even under HIPAA.<sup>29</sup> As a result, physicians might understandably conclude that warning relatives is the least risky option.

The existing directives are thus in conflict: “expert consensus,” ethical analysis, and the HIPAA regulations argue for honoring confidentiality, whereas at least one legal opinion holds that physicians fail to warn a patient's relatives at their peril. Given the press of other business, legislators are not likely to resolve this conflict soon. In this setting, clinicians should inform their patients about the risks their relatives face, discuss the appropriateness of sharing this information and offer assistance, trust — usually realistically — that patients will in turn tell their relatives who are at risk, and hope that the courts will get it right in the future.

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GENOMIC MEDICINE  
AND PUBLIC HEALTH

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When Sierra Creason underwent state-mandated newborn screening, she had abnormally low levels

of both thyroxine and thyrotropin, findings consistent with the presence of congenital hypothyroidism. Her physician was not notified of these results, however, because the state had chosen not to divulge the actual values and, instead, to report as abnormal only results in which thyroxine levels were low and thyrotropin levels were high.<sup>30</sup> As a result, the diagnosis of congenital hypothyroidism and subsequent treatment were seriously delayed, resulting in permanent harm. When the child's family sued the state, however, the California Supreme Court ruled that the state program could not be held liable, in part to avoid diverting funds that would have been used for other state purposes. By contrast, had a private diagnostic laboratory given the same report, especially without providing the actual results, which would have enabled the child's physician to make an independent assessment, it almost certainly would have been held responsible.

Complex questions arise when the government requires testing and interventions. State-mandated screening of newborns for metabolic and genetic disorders was described by Khoury et al. in an earlier article in this series.<sup>31</sup> Governments undertake many activities to promote health — universal screening of newborns for phenylketonuria, for example, is generally considered a resounding success — but it is worth asking in each case whether there is sufficient justification to pursue mandatory as opposed to voluntary action or to place such activities in the public rather than the private sector. Requiring public health agencies to assume such responsibilities has advantages, such as more transparent accountability to the public and greater uniformity in access and results. Relying on public health entities in matters that directly affect the health of individual persons, however, entails certain risks as well. Physicians and patients count on receiving accurate and informative results regardless of whether a private or a public entity is doing the testing. Permitting state agencies to avoid financial responsibility when their actions harm patients like Sierra Creason is unjust and should raise questions about the wisdom of proposals that would dramatically expand newborn screening.

A public health analysis of genomics, of course, involves more than state-run testing. The broadest question is whether the public's health is actually improved by the knowledge derived. A major determinant is access to testing and to the medical interventions that may be warranted as a result. In our current multipayer system of health care, people will



have widely differing levels of access to these forms of technology. One cannot assume that everyone will reap the benefits of this knowledge.

From a public health perspective, it might do to go one step further and ask whether people will actually use the test results to alter their behavior in ways that improve health. Some people whom testing identifies as predisposed to cancer subsequently decline to undergo surveillance or other interventions for psychological reasons or because of other demands on their time. Some preventive or therapeutic measures are more likely to be pursued than others; most people find it difficult to take medications for a lifetime or to maintain major lifestyle changes, no matter how important such approaches are for their health.

Public health agencies exist not only to identify barriers to health but also to improve health and health care. Efforts to determine when genetic tests are reliable enough for routine clinical use are quintessential public health activities.<sup>32,33</sup> The Secretary's Advisory Committee on Genetic Testing and its successor, the Secretary's Advisory Committee on Genetics, Health, and Society, were formed to

provide such guidance.<sup>34</sup> The development of strategies to educate health care providers and patients about genomic medicine, a long-standing goal of the Human Genome Project, and to decrease obstacles to health-promoting behavior also falls comfortably within this rubric.

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## CONCLUSIONS

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This brief discussion illustrates public expectations and fears about the effect of genomics, challenges to the goals of antidiscrimination laws and to the nature of the physician-patient relationship, and the contrasting perspectives and legal rules that apply to personal medical care and public health. Acknowledgment and examination of these complex issues are critical for identifying the appropriate ethical principles that should be applied and for creating the necessary legislative and regulatory responses.

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