Policy Implications of Genetic Testing: Not Just for Geneticists Anymore

Gail H. Javitt

Genetic testing is expanding rapidly to become part of mainstream medicine. While genetic tests bring with them the promise of improved diagnosis and treatment for patients, they also raise several policy challenges. These challenges include the lack of a coherent oversight system to ensure the quality of tests and testing laboratories, the rise of direct-to-consumer genetic testing, the dearth of professional guidelines to assist the transition of genetic tests from research to medical practice, and the absence of federal legislation to protect the privacy of genetic information and prevent genetic discrimination.

Index Words: Genetic testing; Direct-to-consumer; Genetic privacy; Genetic discrimination; Professional guidelines; Provider education; Government regulation

Genetic testing is becoming an increasingly important part of medical care. Once the province of a few testing laboratories and limited to rare diseases or conditions, genetic tests are now being offered by a growing number of clinical laboratories for an increasing number and variety of conditions or health risks. For some individuals with a genetic condition, having a genetic test performed may be the first step in understanding the cause of the particular problem and initiating needed therapy. For others, the lack of a diagnostic test can leave them with continuing uncertainties. From the health-care provider's perspective, genetic testing has the potential to become a potent addition to the existing diagnostic and therapeutic arsenal, as well as an additional means to provide medical advice prospectively to improve a patient's health. Yet, the current policy landscape for genetic testing leaves many reasons to be concerned.

Genetic testing can be performed at all stages of the human life cycle, from adults, to fetuses, to preimplantation human embryos.[1] Today, genetic tests for more than 900 diseases are clinically available, and tests for several hundred more diseases are at the research stage of development.[2] Genetic tests can be used to diagnose existing disease, to predict future risk of disease, to identify carriers of mutations that might cause disease in one's offspring, or to identify particular traits in a fetus or embryo such as gender or HLA type.[1] Recently, interest has turned to the development of tests to guide therapeutic decision making by identification of genetic variants associated with drug metabolism or drug efficacy. Although pharmacogenetics—as it is called—is in its infancy, proponents hope it will be an important means to better target those likely to benefit from a particular therapy.[3]

Current Oversight of Genetic Tests

Although the number of genetic tests that are now or will soon be clinically available is exploding, no concomitant reconfiguration of the regulatory regime for these tests has been done. As a consequence, laboratories that provide genetic testing are subject to only limited oversight, and most genetic tests receive no government review before they are marketed. Although concerns have repeatedly been raised about the vulnerabilities of the current regulatory system, little concrete change has occurred. Specifically, although clinical laboratories offering genetic tests are subject to regulation under the Clinical Laboratory Improvement Amendments of 1988 (CLIA),[4] no specialty area has been developed for genetic testing laboratories with specifically tailored requirements for the now burgeoning genetic-

From the Genetics and Public Policy Center, Berman Bioethics Institute, Johns Hopkins University, Washington, DC.

Address Correspondence to Gail H. Javitt, JD, MPH, Bioethics Institute, Washington Campus, Johns Hopkins University, 1717 Massachusetts Avenue, NW 530, Washington, DC 20036. E-mail: gjavitt1@jhv.edu

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testing industry, which hampers the government's ability to oversee the quality of genetic testing and to adequately ensure its safety. Furthermore, the clinical validity of genetic tests is subject to premarket review by the Food and Drug Administration (FDA) only when the test is sold as an *in vitro* diagnostic device, or "test kit." Of the more than 900 diseases for which genetic tests are used clinically, test kits are available for only about a dozen; the rest are developed as in-house or "home brew" tests by clinical laboratories and are not currently reviewed by the FDA before they are offered clinically. This situation stands in stark contrast to pharmaceuticals and medical devices, which must undergo premarket review by the FDA to demonstrate their safety and effectiveness.

More than a decade ago, federal officials began to take note of the growing use of genetic tests in clinical practice and to raise concerns about the adequacy of oversight for both genetic tests and the laboratories that develop and perform them. Two separate government advisory committees have issued reports that recommend genetic tests not be offered clinically until clinical validity is established and that a genetic testing specialty and proficiency testing be established for genetic-testing laboratories.[5,6] In 2000, the government announced that it would create a genetic-testing specialty under CLIA,[7] but no further action has been taken to create the specialty.

Despite the many hours that have been spent in thoughtful contemplation of genetic-testing quality by some of the leading scientists, lawyers, and regulators in the United States, little in the way of concrete policy change has occurred, and most genetic tests still fall between the regulatory "cracks." Meanwhile, the number of genetic tests has expanded dramatically and tests are being offered for increasingly complex indications and, often, without clear predictive value and in the absence of therapeutic interventions.

Particularly challenging, from a regulatory perspective, are those tests for which some, but incomplete, data have been published to support clinical validity (ie, that the mutation correlates with current or future health status of a patient). Because no government agency reviews most tests before they are marketed, no accepted standard exists for determination of clinical validity, and each laboratory director makes an independent judgment. In contrast, for drugs and medical devices, the FDA requires the submission of both nonclinical and clinical data that are sufficient to demonstrate that the product provides reasonable assurance of safety and effectiveness.

Similarly challenging are tests that may be clinically valid in only a small subset of individuals but for which a laboratory makes far-reaching claims of benefit. Because no government agency reviews most tests before they are marketed, no oversight is exercised with respect to the indications for which a test is marketed. In contrast, the FDA's authority to review and approve the safety and effectiveness of drugs before they are marketed includes the authority to regulate the labeled indications for use that are permitted with respect to the drug, while leaving to the health-care provider the discretion to prescribe the drug as he or she considers appropriate.

The Rise of "DTC" Testing

Another policy challenge that results from the explosion of genetic tests and the limited oversight is the rise of direct-to-consumer (DTC) genetic testing. DTC genetic testing refers to two related phenomena: advertising to consumers regarding the availability of genetic tests that they may obtain only through health-care providers, and direct ordering of genetic tests and receipt of test results without a health-care provider intermediary.[8] The predominant method of advertising and sale of DTC genetic tests has been via the Internet. Although significant turnover occurs in the DTC-testing marketplace, overall the phenomenon has persisted over the past several years, an indication that it may prove to be a successful business model for the delivery of genetic-testing services. The types of tests offered range from those that are currently used by physicians in clinical practice to those for which no published data support clinical validity.

Numerous concerns have been raised regarding DTC genetic testing. These concerns

generally start with the premise that genetic information is complicated and results are not straightforward, and that consumers cannot understand the information without a provider or counselor's assistance.[9–12] Thus, some worry that consumers are vulnerable to exaggerated claims and fear tactics. They are also concerned that consumers may choose to get tested without adequately considering the consequences to themselves and family members. Critics of DTC marketing further worry that in the absence of counseling by a health-care provider to explain the appropriate context, consumers may make bad choices, such as have an abortion or forego standard treatment in favor of unproven regimens.

Because of the myriad concerns raised by DTC genetic testing, in 2004, the American College of Medical Genetics issued a policy statement that concluded with the recommendation that self-ordering of genetic tests by consumers is potentially harmful and that genetic tests should be provided to the public only through the services of an appropriately qualified health-care professional.[13]

The current regulatory environment impedes the government's ability to protect consumers from the potential harms from DTC testing. Even where the government's authority to act is clear, this authority has not been exercised, for reasons that are not evident.

With respect to those genetic tests marketed DTC for which no scientific basis exists to support the claimed benefits, the government currently has the legal authority to ban such tests from the marketplace. At the federal level, the Federal Trade Commission (FTC) has the power to prohibit unfair, deceptive or fraudulent trade practices, including false or misleading advertising claims.[14] Advertisements violate the law if they make false statements about a product or service, fail to disclose material information, or lack adequate substantiation.[15] The FTC has enforced the law against manufacturers of a variety of purported health products. Although the FTC has asserted its authority to take action against fraudulent genetic tests,[16] and has announced a joint effort with the FDA and the National Institutes of Health (NIH) to identify appropriate targets for legal action,[17] the FTC has not taken any regulatory action with respect to fraudulent claims for genetic tests. With respect to tests that are not clearly fraudulent, the lack of oversight of clinical validity or indications for use, described above, hampers the ability to regulate DTC tests as well.

State law is a potential but limited avenue for restricting direct access to genetic testing. Some states prohibit laboratories from accepting orders for laboratory tests without a health-care provider's requisition and from giving results of tests to anyone other than the health-care provider. However, most states either expressly permit DTC laboratory testing or are silent on the issue.[18] Moreover, some laboratories comply with this requirement by employing health-care providers directly who can authorize the testing, and individual states may have difficulty enforcing their laws with respect to transactions conducted via the Internet.

Limited Provider Education and Professional Guidelines

Another policy challenge relates to limitations in provider education regarding genetics and the absence of professional guidelines to assist in the transition of genetic tests from research to clinical practice. Studies have documented that providers are inadequately trained to use genetic tests appropriately in clinical practice.[19,20] At the same time, only a handful of practice guidelines about genetic testing have been developed. As new discoveries move from research to clinical practice, that gap will only widen. Practice guidelines can help guide medical professionals in making judgments about how, when, to whom, and under what circumstances tests should be offered. Professional societies play an important role in developing guidelines. However, professional societies are largely volunteer organizations, with limited resources. Additionally, the desire of professional societies to have a strong evidence base before developing guidelines may be incompatible with the rapid entry and low evidence threshold needed to market genetic tests.

Privacy and Discrimination

Finally, a longstanding concern with regard to genetic testing relates to privacy and discrimination, that is, who is authorized to access a

patient's genetic test results and what actions they may lawfully take on the basis of that information. Whereas Americans generally approve of genetic-testing procedures to benefit health, an overwhelming majority of Americans oppose employers and health-insurance companies having access to genetic information. In a 2004 survey conducted by the Genetics and Public Policy Center of 4,834 Americans, 92% of respondents answered no when asked, "If a genetic test shows that a person has an increased risk for disease, does the employer have the right to know?" Similarly, 80% opposed health-insurance companies having access to this information. In contrast, most respondents were comfortable with their spouse or partner knowing their genetic-test results.[21]

In a few documented cases, employers or health-insurers have used genetic testing in an adverse manner against employees or insured individuals. For example, in 2001, the federal Equal Employment Opportunity Commission (EEOC) settled a lawsuit against the Burlington Northern Santa Fe Railroad.[22] The company had engaged in surreptitious genetic testing of employees to determine if they had a supposed genetic basis for work-related carpal tunnel syndrome, which many observers believed was for the purpose of limiting workers' compensation claims by these employees. Other anecdotal examples of genetic discrimination have been collected by nonprofit organizations.[23] Studies have also documented that fear about genetic discrimination is a deterrent to patient utilization of genetic tests.[24]

The current legal environment provides incomplete protection against discrimination based on genetic information.[25,26] The Americans with Disabilities Act (ADA) of 1990 [27] has been interpreted by the federal government as prohibiting genetic discrimination by employers,[28] but this interpretation has yet to be subject to review by a court and, therefore, may provide only limited and uncertain protection.[25,26] The Health Insurance Portability and Accountability Act of 1996[29] prohibits health insurers from considering genetic information in making decisions regarding insurability, but the law applies only to the group health-insurance market.[30]

Congress has considered enacting federal genetic nondiscrimination legislation for many years. Most recently, the Genetic Information Nondiscrimination Act of 2005 passed the Senate on February 17, 2005 by a vote of 98 to 0.[31] It faces a less certain future in the House. At the state level, 41 states have enacted legislation related to genetic discrimination in health insurance, and 31 states have adopted laws regarding genetic discrimination in the workplace,[30] but the scope of the protections provided by these laws is variable and limited.

What does this uncertain policy landscape mean for the health-care provider? The lack of oversight for most genetic tests, coupled with the dearth of professional guidelines and lack of provider education, means that providers may be ill-equipped to handle the onslaught of new tests being marketed to them and to their patients. Because of the limited oversight of testing laboratories, providers may have inadequate assurance regarding the quality of the test results they receive. Additionally, the absence of expert review of or clear standards for the clinical validity of tests, specified indications for use, or uniform methods for reporting test results may cause difficulty for the provider in deciding whether a genetic test is indicated for a patient or in interpreting the clinical meaning or relevance of the test results after the test is ordered. Furthermore, the growing availability of DTC testing may increase the number of patients who arrive at the provider's office with test results of uncertain validity in hand. The lack of therapeutic interventions in response to many tests may result in situations in which providers know much but can do little if anything in response, a frustrating situation for both provider and patient. The limited protection against discrimination based on genetic-test results may deter patients from seeking genetic tests even if the tests have a clear health benefit.

Conclusion

Genetic medicine holds great promise for improving human health. However, the current policy landscape poses many barriers to achieving that promise. What is needed is a system of oversight in which the validity of

tests is supported by the science before they are offered to patients and uses of outcomes of tests are evaluated over time; all laboratories demonstrate their ability to get the right answer reliably; health-care providers are educated about these tests and able to provide them to patients with adequate context and counseling; and patients have confidence in the claims and results of genetic tests and security that the results of those tests cannot be used to their detriment by employers or insurers.

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