

The Ethics of Genetic Testing: Is More Always Better?

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The recent explosion of interest in prognostic genetic testing raises a host of ethical issues for patients, research subjects, physicians, investigators, policymakers, and the public. None of these issues is really new, but all of them have gained new significance as the science of gene finding accelerates and new genetic tests become more widely available.

Public expectations are high regarding the potential value of genetic information. This confidence extends to the information obtained from new genetic tests, especially those identifying genes associated with common complex disorders. After all, nearly everyone knows someone with diabetes, heart disease, depression, asthma, attention deficit hyperactivity disorder, osteoarthritis, cancer, or any of the other common multifactorial disorders that mark the human condition, and the promise of the Human Genome Project^a has always been both to explain the human condition and to ameliorate it.

Today, science is increasingly able to assign precise percentages to at least some of the genetic contribution to an individual's chance of developing a common complex condition. This quantification of risk is a seductive enterprise. Simply knowing that many people develop emphysema later in life does not seem to mean as much as knowing that individuals with a particular genetic test result are a specified percentage more likely to develop emphysema than those whose test is negative. But are we

right to think this? Does more precision mean more accuracy, or more truth? Is it meaningful to base clinical recommendations, health behavior change, or public policy on predictive genetic testing?

Ethical questions arise in the process of research, development, and marketing of predictive genetic tests; in their use and interpretation by physicians and patients; and in the utilization of predictive genetic test results in public health and other policy contexts. The issues to consider include understanding probabilistic and uncertain information, informed decision making, the medicalization of nondisease states, stigmatization of individuals and groups, genetic essentialism and fatalism, and the potential for genetic discrimination.

Logically, first among issues are those surrounding gene finding. To identify genetic associations of interest requires large-sample gene discovery research and biospecimen collection, "biobanking," and specimen sharing. Long-standing questions exist about the scope of consent to biospecimen research and sharing, how biobanks should be established and overseen, and how research results should be reported and interpreted.^{1,2} It is far from clear, for example, that everyone who provides a biospecimen for genetic research into one disorder (eg, Tourette syndrome) would agree to share that specimen with investigators seeking genes associated with a different disorder (eg, colon cancer or

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a The US Human Genome Project was begun in 1990 by the US Department of Energy and the National Institutes of Health to identify all the genes in human DNA, determine the sequences of the base pairs that make up human DNA, store this information in databases, improve tools for data analysis, transfer related technologies to the private sector, and address the ethical, legal, and social issues that may arise from the project. (US Department of Energy Office of Science. Human Genome Project Information. Available at: http://www.ornl.gov/sci/techresources/Human_Genome/home.shtml. Accessed March 21, 2007.)

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cystic acne). Should they be asked? Or should consent forms simply inform specimen providers that their DNA could be shared and studied for any scientific purpose? And is such a broad consent really consent at all?

Once research is underway, questions arise about its results. There is considerable uncertainty about the significance of genetic associations in common complex disorders and gene-environment interactions. Even though knowledge is expanding rapidly in genetics, it is simply not yet known how the interplay of multiple genetic and environmental factors affects the likelihood of developing a disorder or its probable severity.³ Thus, associating a gene with a disorder is only a small piece of a rather large puzzle. How, then, should researchers and clinicians describe that single piece? Moreover, as is already well recognized, population-based research results are difficult to translate into individual application. Although the espoused goal of genetic research is “personalized medicine” (ie, prediction at the individual level), at present, genetic associations are usually reported in broad general categories of questionable meaning. Most notably, genetic research results are grouped by race and ethnicity (eg, “X gene, associated with Y disease, is three times as common in African-Americans as in whites.”). Although genetic research has definitively shown that racial categories have no biological meaning, such racialized characterizations remain all too common.^{4,5} Ironically, these categories help to wrongly reify race as genetically significant. Not incidentally, reporting about research in this way is often highly stigmatizing to members of the racial and ethnic groups thus identified (eg, “Another ‘Jewish gene’ has been identified by researchers.”).⁶

The process of translating such imperfect data into a genetic test used predictively in individuals is similarly fraught with ethical challenges. Standards for the development and marketing of genetic tests are at present nearly nonexistent. Whether and how to regulate these tests is the subject of major policy debate.^{7,8} What counts as a valid and reliable test? How are commercial genetic tests advertised to practitioners and consumers? Even when these questions have been answered satisfactorily, others loom regarding the best uses of such tests. Should children be tested for genetic predispositions to adult-onset disorders?^{9,10} Does it matter whether the test results are used to monitor the child’s health, to initiate a prophylactic regimen, or to help the child’s parents make decisions about future reproduction?

How should doctors decide whether to base recommendations to their patients on genetic test results? It has long been known that health care providers may themselves have difficulty understanding and explaining probabilities to patients. Making use of probabilistic information in the context of risk reduction, which is how predictive genetic test results will be used, is even more complex than applying probabilities to treatment choices. This difficulty is compounded in genetic testing by the temptation to view genes as deterministic and, thus, to overestimate their importance—especially in common complex disorders.¹¹ Since the beginning of the Human Genome Project, much attention has been given to providing genetic education to primary care providers and the general public. However, the available information changes so quickly that it’s necessary to run very fast to keep up—and

it’s all too easy to fall behind. As a result, much decision making about genetic testing is likely to be based on poor information and poor understanding. Not surprisingly, poor information and poor understanding make for imperfect decisions about whether to test, how to interpret the results, and what to do with them.

What should be done with the information that predictive genetic testing provides? It is essential to acknowledge that even with perfect information, there is a substantial gap between gene identification and effective prophylaxis (let alone treatment).¹² Just consider the decision making challenges faced by women who learn they have a breast cancer (BRCA) gene: intensive monitoring? prophylactic drug regimens? radical surgery? or only standard exams and mammography, since having a BRCA gene is far from a guarantee of developing breast or ovarian cancer?¹³ Now multiply that range of options by every new genetic association identified by prognostic testing, such as other cancers, type II diabetes, cardiac disease, obesity, psychiatric and behavioral disorders, asthma and allergies, and lots more we probably haven’t even thought of as disorders—yet.¹⁴

One issue of principal concern has not materialized as a significant reality, but profoundly affects public perceptions about genetic testing information. The risk of genetic discrimination can deter testing, even when test results are well characterized and prophylaxis can make a difference. There is little evidence to date of discrimination in the cost or availability of health insurance, or in employment, on the basis of genetic predisposition information, although discrimination on the basis of existing disease is common, and troubling.^{15,16} However, many states—North Carolina included¹⁷—have legislation in place prohibiting genetic discrimination, and federal legislation (the Genetic Information Nondiscrimination Act, “GINA”¹⁸) stands an increasingly good chance in Congress.

Another kind of discrimination by health insurers, in the name of health promotion, is actually somewhat more likely. Many health insurers are beginning to offer incentives to their insured members to change their behavior in an effort to reduce health care costs. Could an insurer require members to undergo predictive genetic testing and use the results to adjust premium rates? Could an insurer base those adjustments not solely on the test results, but on whether members with certain test results make use of certain preventive or health maintenance services (eg, stop smoking, successfully lower cholesterol or blood pressure levels, or maintain a certain weight) because their genetic profiles make them more likely to develop associated disorders? This may make good fiscal sense, or even good public health sense, but it can be quite intrusive on personal privacy. In most cases it makes little sense to distinguish between those with and without incriminating genetic profiles for disorders that are common in the general population.

Will the future bring us to more precise information and the truly personalized genome? Perhaps, in awhile; but what we do until we get there matters a great deal. If we can encourage both health care providers and patients to learn more about the meaning of genetic information, ask lots of questions about genetic information, and examine each use of genetic information

carefully and comprehensively, then it may be possible to make both scientific and moral progress.¹⁹

There are, unfortunately, no easy answers. The best way to address these ethical issues is the hard way: taking great care in how we think about, talk about, understand, and use genetic information. We are not just our genes. For every genetic test that informs us of a susceptibility to a common complex disorder, there are many ways to alter the environmental influences that we know are also implicated, both at the individual level and as matters of public health and social policy. We already have

ample reason to change habits of diet and exercise, improve the availability of healthy food choices in shops and schools, reduce environmental pollutants and hazards in the workplace, and make safe physical activity possible in all communities. The discovery of genetic associations adds scant momentum, if any, to these efforts and could be detrimental if poorly understood.²⁰

More information isn't always better; only good information is better. It may be time to say no to the genetic testing explosion—at least until we know what is hype and what is not. **NCMJ**

REFERENCES

- 1 Rothstein M. Expanding the ethical analysis of biobanks. *J Law Med Ethics*. 2004;33:89-101.
- 2 National Institutes of Health. First generation guidelines for NCI-supported biorepositories. Federal Register. 71:25184-25203 (April 28, 2006).
- 3 Welch HG, Burke W. Uncertainties in genetic testing for chronic disease. *JAMA*. 1998;280:1525-1527.
- 4 Wolf S, ed. Symposium. The responsible use of racial and ethnic categories in biomedical research: Where do we go from here? *J Law Med Ethics*. 2006;34:483-558.
- 5 Collins FS. What we do and don't know about 'race', 'ethnicity', genetics and health at the dawn of the genome era. *Nature Genetics*. 2004;36:S13-16.
- 6 Weiss R. Discovery of 'Jewish' cancer gene raises fears of more than disease. Washington Post. September 3, 1997:A03.
- 7 Pollack A. The wide, wild world of genetic testing. New York Times. Available at: <http://www.nytimes.com>. September 12, 2006.
- 8 Caruso D. Genetic tests offer promise, but raise questions, too. New York Times. Available at: <http://www.nytimes.com>. February 18, 2007.
- 9 American Academy of Pediatrics Committee on Bioethics. Position statement: Ethical issues with genetic testing in pediatrics. *Pediatrics*. 2001;107:1451-1455.
- 10 Rhodes R. Why test children for adult-onset genetic diseases? *Mt Sinai J Med*. 2006;73:609-616.
- 11 Giardiello FM, Brensinger JD, Petersen GM, et al. The use and interpretation of commercial APC gene testing for familial adenomatous polyposis. *NEJM*. 1997;336:823-827.
- 12 Geller G, Botkin JR, Green MJ, et al. Genetic testing for susceptibility to adult-onset cancer: the process and content of informed consent. *JAMA*. 1997;277:1467-1474.
- 13 Klitzman R. Genetic testing creates new versions of ancient dilemmas. New York Times. Available at: <http://www.nytimes.com>. January 17, 2006.
- 14 National Office of Public Health Genomics. Obesity and genetics: What we know, what we don't know, and what it means. June 2006. Available at: <http://www.cdc.gov/genomics/training/perspectives/files/obeseknow.htm>. Accessed March 12, 2007.
- 15 Hall MA. Genetic Discrimination. Paper commissioned by the North Carolina Genomics and Bioinformatics Consortium, LLC. Nov. 2001. Available online at: http://www.ncbiotech.org/services_and_programs/genomics_consortium/consortium_projects_and_events/geneticdiscrimination.pdf. Accessed March 12, 2007.
- 16 Greely HT. Banning genetic discrimination. *NEJM*. 2005;353:865-867.
- 17 General Assembly of North Carolina, 1997 Session, SL 1997-350, SB 254. An act to prohibit discrimination in health insurance and employment based on genetic information.
- 18 H.R.493, 110th Congress 1st session.
- 19 North Carolina Task Force on Genomics and Public Health, North Carolina Public Health Genomics Plan (2004). Available online at: http://statgen.ncsu.edu/ggibson/nc_gph/nc_public_health.html. Accessed March 12, 2007.
- 20 Grady D. Genetic test for diabetes may gauge risk, but is the risk worth knowing? New York Times. Available at: <http://www.nytimes.com>. August 8, 2006.



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