

**Policy Perspectives from Members of the Scientific Community**  
*Sharon Kardia, Ph.D.*

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DR. WILLARD: With that, and thanking everyone for their patience with the nature of that connection, our next speaker is Dr. Sharon Kardia. She's an associate professor of epidemiology at the University of Michigan at Ann Arbor, director of the Public Health Genetics Program there, and co-director of the Michigan Center for Genomics and Public Health. She is particularly interested in gene/environment, gene/gene interactions, and in modeling complex relationships between genetic variation, environmental variation, and the risk of common and chronic diseases.

Dr. Kardia?

DR. KARDIA: Let me start by thanking the committee for inviting me and perhaps giving you a little bit more information on my background. I'm a human geneticist and statistician by training and study epidemiologically a number of diseases, including cardiovascular disease, hypertension, I've done some diabetes work, worked on the genetics of drug response, and nicotine dependence. I'm also currently a member of two National Academy of Science committees, one on toxicogenomics and the other on assessing social, behavioral and genetic interactions.

It's from these experiences that I have been accumulating a relatively broad understanding for a genetic epidemiologist about the social issues and the policy issues surrounding genetics research and its implications. From my point of view, a large population study of genetic and environmental factors has a lot of advantages and a lot of disadvantages. Although it's probably to my personal scientific benefit that such a study go on, right now I feel like the disadvantages outweigh the advantages.

Right now there are a number of critical social and regulatory policy issues that make the project, in my opinion, premature. For example, the current lack of genetic literacy in the public and health professional arenas make true informed consent for this type of research a major issue. If people don't understand the basic genetic consequences of this information, how are they supposed to properly consent for it? In addition, the lack of a federal genetic anti-discrimination law makes it a liability for the public to participate.

With such a big study involving hundreds of investigators and clinicians, the public is going to be concerned to the extent with which real privacy and confidentiality can be maintained. There is already a lot of fear on the part of the public as to what researchers, doctors, insurance companies, employers and government agencies will do with biobanks and genetic information. My current experiences reaching out to our Detroit Urban Research Center to do community-based participatory research have been, well, an eye-opener. I can hardly get my foot in the door. They don't really want to talk about doing genetics research because of what they perceive as information being out of their control, researchers playing God, and it's been an eye-opener.

There's also a lot of fear by the public health practice community that genetics research will increase health disparities and reduce access to care. For example, we already have instances where smokers are denied access to certain types of care. What if smoking is found to be genetic? What does that do to the way we think about current policies?

In addition, given the power of genetic information, there are serious concerns about having well justified and executed policies about the duty to warn research subjects and their families of the research results. I raise this point because much health education and health behavior research

has demonstrated that the public struggles with genetic risk communication and genetic concepts. They often don't retain genetic concepts after a session, and they misinterpret what has been very well crafted to be a precise genetic risk communication.

Many don't even know where their genes are located or why a genetic test might be predictive. For example, studies have shown that subjects receiving genetic information on early-onset colorectal cancer may ignore their negative results -- so these are people who do not carry their familial mutation -- and continue to get yearly screening, because the blood test is not relevant in their minds compared to the clinical examination of where the disease lies in their colons. So the disconnect, the basic public understanding is going to be a major barrier to any kind of communication.

This kind of misrepresentation does not just reside in the lay public but also with professionals, and that includes people at the policymaking level. In addition, given that most genetics research is still focused on identifying single causative factors and has not matured to complex models of genetic causation, this means that scientists themselves end up promoting a naive biological, deterministic interpretation of complex disorders. This is likely to lead to further misinterpretation and misuse of these genetic explanations in public policy, in courts, in health and life insurance policies, as well as medical practices.

The Burlington Northern Santa Fe Railroad decision to secretly test workers for a mutation associated with carpal tunnel syndrome is just one example of how this type of information could be misused. In this case, it appears that the company wanted to avoid financial responsibility for providing workmen's compensation for their workers' on-the-job injuries.

In general, I don't think we have the necessary experience, infrastructure or scientific culture in which to responsibly carry out a large and important study like this. Genetic science of common complex diseases is simply not mature enough. We're still using the single-gene paradigm of the last century, and we don't understand the real roots of why the genetic factors we are identifying as being significant in one study are not replicating in another.

This is going to be especially relevant for a large population study, because there will be a desire to use all that power of that sample size to highlight definitive findings and statements that, by and large, might be overall a result for the population but do not reflect the local heterogeneity of the genetic/environmental factors where the actual clinical utility will matter in its applications.

Another major issue for me as a scientist is that most geneticists are not well versed enough in the social, behavioral and environmental causes of disease. True interdisciplinary research that integrates knowledge across the levels, from the influence of the genome to the influence of our human ecology, are just now getting started, and currently the two ends of the spectrums, the geneticists and the social behaviorists, are pitted against each other at the funding tables and in institutions. My own experience being a part of our school's Robert Wood Johnson Health and Society Scholars Program has shown me the genuine lack of respect that genetics commands compared to health effects of poverty, racism and unfair social practices. Through a lot of hard work, we are just now sitting down at the table and trying to work from the bottom up and the top down to learn each other's languages and methodologies.

It is clear that we need new models, systems models as an example, and models that incorporate a person's lifetime of exposure to adequately understand genetic influences on health and disease. In this arena, geneticists are appropriately criticized for our simplistic genocentric analyses, our lack of key social behavioral measurements, the lack of replicable results, and the lack of clear

causative mechanisms. It's incredibly difficult in many cases to move from a statistical genetic association to an understanding of the mechanism of action that would suggest new therapies, prevention, and that would withstand evidence-based regulatory decisionmaking.

The last point troubles me the most because it means that genetic findings in complex disorders, especially gene/environment interactions, are not likely to pass the muster that would allow regulatory bodies to create policies to protect people. Although there has been some progress lately in the field of gene/environment interactions, namely people are starting to look at them, such as in toxicogenomic and pharmacogenomic research, the results themselves have exposed immense complexity in integrating this type of knowledge into existing policy standards and methods.

Traditionally, public health policy has focused on the population-level solutions, the one size fits all model, for example, the ubiquitous anti-smoking campaigns. Nobody would disagree with that as a population public health effort. In contrast, genetic information is individual based, family based, ethnic group based, and will require intense research on the implications of specialized policies and regulations for the protection of vulnerable populations.

What if we found that some people are sensitive to their environments and others are not? Is it the responsibility of the individual to take themselves out of harm's way when the rest of society can ignore their vulnerability?

Barbara Koenig's group's paper on looking at smoking through the neurogenetic prism highlights many of the unintended stigmatization, discrimination and ethical issues that come with a difference in sensitivity to environmental factors.

The current risk assessment paradigm in the EPA and the FDA are other examples of issues that are going to arise as we get more genetic information. How are they going to set standards and guidelines for businesses and products based on complex susceptible genetic subgroups? One of the other key issues merging the science, then, with the policy is that for every disease, there's likely to be a different combination of genetic factors. So even defining a vulnerable subgroup or a susceptible subgroup could end up being a nightmare in and of itself, especially when we overlay those genetic definitions with already existing definitions of vulnerable populations based on age, race and disability.

In addition, to my knowledge, the regulatory agencies such as the FDA, the EPC and the Federal Trade Commission, do not have the resources to tackle an upheaval in their systems, and they often do not have enough staff that really understand genetics and genomics. This is slowly changing, but again, it's slowly, and I worry that moving the science along in our particular culture, looking at genetic associations when our regulatory bodies aren't ready for it, would be a mistake.

An example of that that is already playing out is the current lack of oversight on genetic information, genetic testing, and the lack of public education, which leaves the public vulnerable. Genetic testing companies can market directly to consumers, they can market directly to doctors without any regulations at this point. There's no need for them to disclose the real utility or the makeup of their products. We haven't pushed any truth in advertising for genetic testing companies at this point, and guess what's happening? The American market system is working, and Best Buy has recently released a nutrigenomics DNA testing kit. To the best of my scientific knowledge, there's not enough real evidence that would warrant such a direct-to-the-public testing kit.

But the alternative is people are excited by knowing genetics information. The Human Genome Project has done a great job for moving genetics into the public eye, and daily newspaper articles that are trying to show the public what genetic findings are out there are, in a sense, a mixed blessing. Because of their basic paradigm of reporting the news you can use, they tend to overstate the research findings, and this leads to a whole cycle within our society of aggrandizing simple genetic solutions to complex problems.

One of the questions that the committee asked me to address was how much consultation was needed within the broader scientific community to inform a decision about undertaking a U.S. population study. I have to admit some skepticism here on my part as a researcher. I think asking for the scientific community to comment will lead to a biased sample of very outspoken antagonists from the social epidemiology field who are worried about the geneticization of disease and the excessive use of resources by geneticists. It will also lead to the outspoken proponents who want to be a part of such a large funding -- i.e., revenue -- source for their own operations. When the National Childhood Study started to create working groups to formulate plans for their large population study, I was asked to be on the Gene/Environment Working Group and participated for about a year before getting fed up with the obvious and, I would say, natural self-serving interests of the committee members.

Another key question that you asked is is there general awareness among scientists of the potential of a U.S. large population study. In my experience, the answer is a definite yes, and again it is with some skepticism. Many of the genetic epidemiologists I know think that there is merit to the idea but that this mega-science model will fund a few insiders very, very well and not leave much for the rest of the scientific community. It also won't build on the years and years of experience of doing epidemiological studies, and especially utilizing what genetic epidemiologists have already accrued in terms of cohort studies such as the ERIC Study, the Cardia Study, the Framingham Study, and those experiences, which have taken a huge amount of work to collect information on people and collect it well, makes many of us think that the 500,000 or 1 million person goal is an unrealistically large and broad target to accomplish in a high-quality manner.

I've been fortunate to be a part of NHLBI's Family Blood Pressure Program over the last 10 years that's collected 13,000 individuals and five racial and ethnic groups through over a dozen field centers. It takes a tremendous amount of effort to agree on what should be measured, and how, and then how to package the results. Science is not value-free and neutral. We have a long way to go in terms of learning how to collaborate together and to use existing resources at hand, and this goes not just for the genetics to social epidemiology bridge but among geneticists. We are often competitive, and we also have very strong opinions about what is right and what is not right.

I think you can see from my comments that I just don't think we've had enough time and resources to build the necessary experience or infrastructure to support this kind of ambitious project right now. Maybe in five or ten years it would be an appropriate thing. I think there are a lot of intermediate steps that can be taken along the way. Just getting genetics researchers to work together so that they can use already existing cohorts that can be used to confirm and reject claims of genetic associations would be a major step. Getting genetic researchers to work with social and behavioral epidemiologists and researchers would be a major step.

Another thing which we have not typically done in genetics research is engage the resources of departments of health. There are cancer registries, early death registries, environmental health

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registries that could be used as a first wave of research. We're trying to do that right now in Michigan, and there are big gaps that expose even more issues.

As the state holders of these registries and the knowledge about the key environmental factors influencing the public's health, it's amazing to me that we have not involved them in this kind of effort. They have important roles not only as resources but from a policy perspective. Departments of health need to be more prepared for dealing with the genetic information on common disorders and to have working staff investigating the implications of state-level policies on things like informed consent, and setting up mechanisms to handle the public's need for genetic services, like counseling.

In Michigan, we recently had a case where a doctor did a diagnostic genetic test prompted by what we think is a direct-to-doctor advertising campaign by a company, and he did not tell the individual that he was doing the genetic test. He then called up the individual, gave the person the results over the phone, and said there was nothing he could do, this person had a genetic disorder that was basically going to ruin his life, and hung up. This family then contacted the department of health, who tried to figure out whether or not there was anything on the books in terms of what the doctor had done wrong.

The family was left very devastated, and according to Michigan's laws right now, the doctor was under no duty to provide an informed consent or counseling. So this provides an example of things that can happen. We're lucky in Michigan that we have one of the most genetically progressive departments of health in the nation, and still they were left scrambling trying to figure out what to do for this family, who now faced the real possibility of employment discrimination, as well as health and life insurance discrimination.

To end, I think that one of the things that really needs to be done if we're going to use genetics in this country is to invest in the infrastructure, and that means the EPA has got to be ready, the FDA has got to be ready, the FTC has got to be ready, state departments of health have got to be ready, and the public has got to be ready. The last thing we want to do is repeat the sickle cell screening debacle in the '70s, where well intentioned legislatures passed marriage laws to protect people.

Given the right social investment and the investment in new policy systems, I would be greatly enthusiastic about this project. This is my field. I would love to have access to 500,000 people and their genetic information. I just don't think the timing is right, not right now. Thank you.