HHS Public Access

Author manuscript

Sci Technol Human Values. Author manuscript; available in PMC 2021 August 26.

Published in final edited form as:

Sci Technol Human Values. 2016 March 1; 41(2): 194–218. doi:10.1177/0162243915595462.

Accounting for Complexity: Gene–environment Interaction Research and the Moral Economy of Quantification

Sara L. Ackerman[1], **Katherine Weatherford Darling**[1], **Sandra Soo-Jin Lee**[2], **Robert A. Hiatt**[3], **Janet K. Shim**[1]

[1]Department of Social and Behavioral Sciences, University of California, San Francisco, San Francisco, CA, USA

[2]Stanford Center for Biomedical Ethics and Program in Science, Technology and Society, Stanford University, Stanford, CA, USA

[3]Department of Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA, USA

Abstract

Scientists now agree that common diseases arise through interactions of genetic and environmental factors, but there is less agreement about how scientific research should account for these interactions. This paper examines the politics of quantification in gene–environment interaction (GEI) research. Drawing on interviews and observations with GEI researchers who study common, complex diseases, we describe quantification as an unfolding moral economy of science, in which researchers collectively enact competing ‘‘virtues.’’ Dominant virtues include molecular precision, in which behavioral and social risk factors are moved into the body, and ‘‘harmonization,’’ in which scientists create large data sets and common interests in multisited consortia. We describe the negotiations and trade-offs scientists enact in order to produce credible knowledge and the forms of (self-)discipline that shape researchers, their practices, and objects of study. We describe how prevailing techniques of quantification are premised on the shrinking of the environment in the interest of producing harmonized data and harmonious scientists, leading some scientists to argue that social, economic, and political influences on disease patterns are sidelined in postgenomic research. We consider how a variety of GEI researchers navigate quantification’s productive and limiting effects on the science of etiological complexity.

Keywords

moral economies; quantification; standarization; genetics; epidemiology

Corresponding Author: Sara L. Ackerman, Department of Social and Behavioral Sciences, University of California, San Francisco, 3333 California St., Suite 455, San Francisco, CA 94118, USA. sara.ackerman@ucsf.edu.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Introduction

The twentieth century, in the words of Evelyn Fox Keller, was “the century of the gene,” in which DNA figured prominently in scientific and popular discourse as a distinct object assumed to have agency and causal power, and the genome was anticipated to provide a blueprint for life (Keller 2009). In the early twenty-first century, the gene continues to exert a persuasive hold on both popular and scientific imaginations witnessed by the persistent search for and belief in “genes for” diseases, behaviors, and even ideologies (see Reynolds 2014 for a recent example). Nevertheless, the lure of genetic determinism is loosening its grip as new understandings of developmental and etiological complexity undermine “the preordained genetic body” (Lock 2005, S49) and displace the gene as the prime mover of health and illness. Emerging knowledge about gene regulation, epigenetics, and gene–environment interactions (GEIs) contributes to a growing recognition among life scientists that disease arises through an interplay of genetic variations and social, political, economic, and environmental phenomena (Landecker and Panofsky 2012).

New scientific approaches to understanding disease causation as complex and emergent are embedded in the rapid expansion of genomic technologies and research in the wake of the Human Genome Project—a period often referred to as postgenomic.[1] Epidemiology is one area of scientific inquiry that has been strongly influenced by genomics. In the late twentieth century, epidemiologists focused predominantly on understanding behavioral and environmental “risk factors” for noncommunicable diseases, particularly those that could be influenced in order to change the risk or progression of disease. However, as disease causality is increasingly understood to arise through an entanglement of genetic and nongenetic variables, many epidemiologists now incorporate molecular concepts and technologies in their studies of common diseases. Population and molecular geneticists, for their part, are increasingly compelled to consider the roles of nongenetic influences on disease (Beaty and Khoury 2000).

This paper examines GEI research, an emerging domain of knowledge production about the causes and trajectories of common, complex diseases such as cancer, type 2 diabetes, and heart disease. GEI studies are premised on the idea that genetic differences mediate physiological responses to different environments, such as toxins, diet, stress, or socioeconomic inequality—and, reciprocally, that environmental exposures can regulate development or gene expression. Much hope is invested in GEIs’ potential to move the biosciences toward better explanations of complex diseases than are available through an examination of genetic or environmental factors alone (Davey Smith et al. 2005). Moreover, genomics advocates extend the promissory value of GEIs to public health by anticipating more effective disease prevention efforts based on knowledge about “genetic risk factors” (Khoury et al. 2005, 804).

However, recent investigations of how genomic information and infrastructures have influenced epidemiologic research on common diseases highlight heterogeneous practices,

[1]. The postgenomic era in the biomedical sciences started with the completion of a first map of the human genome and has encompassed research on gene expression, population-level genetic variation, and gene–environment interactions.

conflicting priorities, and multiple possible futures (Shostak 2003). On the one hand, the scientific gaze increasingly locates disease risk in genetic differences and renders behavioral and socioeconomic variables knowable through their molecular effects on human physiology (Niewohner 2011; Shostak 2013). This has led critics to argue that a "gene-centric" (Krieger 2013, 22) approach persists and that a move away from genetic determinism in the life sciences has nonetheless been accompanied by a "neoreductionism in which virtually everything external to the material body remains black-boxed" (Lock 2005, S48). On the other hand, a new emphasis on complex causality opens the possibility of moving beyond genetic reductionism and the body proper to assess how social, economic, political, and environmental forces entwine with genetic variations to produce patterns of disease. As genomic information and technologies transform "the societal agenda of public health science" (Bauer 2013, 511), many population scientists find themselves caught between a tendency to locate disease risk in genetic variants and molecular processes, and an understanding that common diseases arise through interactions of bodies and complex social and physical environments.

We find that among GEI researchers, the emerging "interactionist consensus" (Kitcher 2000, cited in Landecker and Panofsky 2012) coexists with significant uncertainty about how best to study etiologically complex diseases. Questions of proper measurement are a particular source of anxiety among scientists involved in GEI studies, and our findings suggest that measurement and other forms of quantification do not operate simply as value-neutral techniques of knowledge production. Rather, quantification is a field of social activity that is simultaneously moral and technical. As scientists collectively struggle to define what counts as "genes" and "environments" and how to count them, they debate which procedures and standards constitute the proper conduct of science, and who and what constitutes a "good" GEI scientist.

Invoking Lorraine Daston's historical analysis of the concept of moral economies of science, we focus on molecular measurement and the harmonization of phenotypic and environmental measures across ever-larger data sets as evidence of the prevailing values, or virtues, of an emerging and shifting moral economy of quantification among GEI researchers—and in the biomedical sciences more broadly (Daston 1995). The term virtue points to the collectively formed, value-laden aspects of scientific work, including how scientists strive to embody and enact methodological and moral principles through the conduct of scientific research.

Although quantification may entail widespread techniques and virtues, it is important to note that by referring to the politics of quantification as a moral economy we do not posit a uniform or rigid system independent of its constituents. Rather, we understand quantification to be a highly political, and ever-shifting, web of exchange. Any points of (temporary) stabilization in the enactment and value of quantification are derived from the actions and interactions of scientists, policy makers, and others. Indeed, our findings suggest that in order to make themselves, their cohort studies, and their data more virtuous according to prevailing techniques and norms of postgenomic quantification, GEI researchers are often compelled to make trade-offs or exchanges between competing priorities and commitments.

One of the exchanges that we highlight in this paper, and a significant source of consternation and conflict among our participants, is the relinquishing of environmental complexity that accompanies the fervent pursuit of statistical significance. Thus, even though GEI research enables scientists to consider both genetic and environmental contributions to disease risk, its techniques and collectively negotiated norms lead some scientists to move away from social, economic, political, and historical dimensions of disease risk as legitimate domains of inquiry—a compromise that is particularly fraught for researchers committed to understanding and intervening in these domains.[2]

Our emphasis on quantification as a collectively organized, but always unsettled, field of activity, characterized by the search for (often elusive) standards of measurement, aligns with two areas of recent scholarship. The first focuses on standardization as a dynamic, emergent, and political process of social and technical transformation (Timmermans and Epstein 2010). The second includes studies of how scientific networks, genomic technologies, and new regulatory frameworks are reconfiguring the biomedical sciences (e.g., Cambrosio et al. 2013).

Our paper is organized as follows. First, we offer a brief background on quantification, drawing together Daston's treatment of the concept of moral economy with historical accounts of the politics of measurement in early scientific communities and investigations of standards-in-the making among contemporary scientists. We then turn to our participants' accounts of adopting GEI research as a platform for scientific advancement, public health benefit, and professional development. These narratives highlight the growing dominance of molecular standards of measurement, whereas approaches to understanding and measuring nongenetic variables remain open and contested terrain. Next, we examine the politics of quantification within large, multisited research collaborations (called consortia) in the midst of a growing emphasis on molecular precision. These emerging platforms promise more credible scientific knowledge about disease etiology but also entail new social formations and modes of self-discipline among researchers. This work transforms diverse phenomena into variables that can be compared across large study populations and multiple research sites. Finally, we discuss how the resulting paradoxical loss of environmental complexity leads some scientists to question the real-world relevance of GEIs and to stake a renewed affiliation with "true" epidemiology and its hard-to-quantify social variables. In what ways, we ask, does the emerging politics of quantification engender and limit the potential of the scientific study of etiological complexity in an era of genomic promise?

Methods

Our analysis draws on in-depth interviews with thirty-two genetic epidemiologists and other scientists engaged in GEI research, and observations and informal interviews at nine scientific conferences at which GEI research was presented. We conducted a total of 200 hours of observations and fifty-three interviews between 2010 and 2014, including twenty-one follow-up interviews approximately one year after the first interview. All of our

[2]Our focus is on how approaches to the environment among GEI researchers are constrained by the norms and practices of quantification, but it is important to note that our participants' ways of thinking about and measuring the environment were hardly uniform. We address the myriad ways that scientists think about and work with the environment in a forthcoming paper.

participants are involved in GEI research on heart disease, type 2 diabetes, or cancer, which are all conditions thought to arise through complex interactions between environmental, behavioral, and molecular processes. We have removed or changed identifying information in order to maintain the anonymity of our participants.

Interview questions focused on participants' career paths, study practices, and assessments of GEI research more broadly. It is important to note that concerns about measurement as both a moral and methodological problem often arose unprompted during conversations about study design, analytic procedures, the uses of race, ethnicity, and ancestry in GEI studies, and conceptions of the environment. We noticed that many of our participants experienced conflicting demands as they attempted to adhere to prevailing norms of quantification and measurement and that these norms themselves seemed to be in flux.

All interviews were transcribed verbatim, and interview transcripts and field notes were uploaded to the qualitative data analysis software ATLAS.ti. We conducted data analysis using a collaborative process that included an initial reading of the first few interviews, iterative development of a code book, and assignment of codes to the data. We then extracted data assigned to codes relevant to our analysis for this paper (including "issues or problems in measurement," "public health, societal, social implication," "career trajectory," "ethics," and "patterns/trends in genetics, epidemiology, or GEI") and then circulated analytic memos related to the extracted data. The first author also read all primary interviews in order to identify and extract discussions relevant to the concept of moral economy.

The Moral Economy of Quantification: Making Measurement a Virtue

Although measurement is commonly understood simply as description, historians of science remind us that it is a strategy of quantification, which, along with other scientific values such as empiricism and objectivity, has a contingent and altogether social history. In *A Social History of Truth: Civility and Science in Seventeenth Century England*, Steven Shapin (1994) turns to early scientific practices in Europe to examine how decisions about scientific precision and accuracy emerged through efforts to maintain trust and credibility among colleagues in the form of proper social conduct. Evaluations of scientific reports, he explains, always contain normative judgments about the "skill and probity of the practitioners who produce these reports, and, accordingly, they embed norms about the degree of exactness and certainty *it is right* to expect … " (Shapin 1994, 310-11). This means that the expectation of impartiality and fairness achieved by way of quantification is simultaneously a practical *and* moral demand.

Although quantification is a term that has taken many forms, only some of which assume a connection with measurement, the definition that we draw on here is broad, encompassing the use of mathematical models, measurement, statistics, and methods of data representation and analysis. Lorraine Daston describes quantification as a kind of "moral economy" of science, and she parses the historical emergence of specific "mathematical virtues" in this field of exchange (Daston 1995, 8). Virtues are value-laden characteristics, or ideals, that are attributed not only to the quality of measurements but also to the character of those doing the measuring. They are established and enacted collectively, as scientists learn, think, and practice their craft in "communities of practice" (Lave and Wenger 1991) whose boundaries

are often fluid but who share a "common *reverence* for an ideal—the ideal of objective truth, clarity, and accuracy" (Fleck [1935] 1979, 142). Thus, virtues are always embedded in, and constituted by, locally and historically contingent scientific practices. Likewise, tensions between competing virtues are enacted in routine, context-dependent procedures for data collection and analysis.

In our close look at GEI research practices, we refer to both the politics and moral economy of quantification—the former because quantification is a site of uncertainty and negotiation among GEI researchers, and the latter because technical decisions, values, and new and existing forms of relatedness among scientists are intertwined in attempts to establish norms of quantification.

Objectivity is the hallmark ideal or virtue of science, and emerging understandings of objectivity—particularly aperspectival objectivity, or "the view from nowhere" (Daston and Galison 2010,5)—became embedded in practices of quantification as early as the seventeenth century. The alignment of quantification and objectivity was made possible because numbers and other modes of quantification serve as "immutable and combinable mobiles" (Latour 1987, 227), or objects that move without changing their meaning or form. This mobility links objectivity with the related virtue of communicability, which emphasizes the importance of translating scientific knowledge "across barriers of distance and distrust" (Daston 1992, 609). In other words, scientific knowledge is considered objective and value free when it can be mobilized among practitioners, not because it necessarily offers a more accurate representation of reality (Porter 1995). By the mid-nineteenth century, quantification enabled "the contraction of nature to the communicable" to become standard practice among scientists (Daston 1992, 609).

Quantification's other virtues include accuracy, precision, and impartiality. Accuracy concerns the fit of numbers to some aspect of the world, whereas precision aims for clarity and intelligibility, and "by itself, stipulates nothing about whether and how those concepts match the world" (Daston 1995, 8). Impartiality, in turn, is not a property that is inherent in numbers themselves but is achieved through the exercise of social discipline and self-restraint among scientists, since individual idiosyncrasies are anathema to standardization. Each of these virtues strives for a distinct goal, and devotion to them has varied across time and between scientific collectives. Moreover, a moral economy is a "contingent, malleable thing" under constant negotiation and revision (Daston 1995, 4), as we will demonstrate in our discussion of GEI researchers' struggles for credibility and relevance through measurement.

We explore GEI researchers' striving for molecular precision and attempts to "harmonize" themselves, and their data, as both an enactment of the virtues of quantification and a politics of standardization. Science studies scholars have examined the sociotechnical negotiations through which standards are made and made to work, calling into question assumptions that standards are value neutral and highlighting the local contingencies and unintended consequences of the use of standards (Berg 1997; Latour and Woolgar 1979; Timmermans and Berg 2003). A related concept, commensuration, emphasizes standards development as a form of quantification and points to the simultaneously social and

technical work—and erasures of specificity—required to transform disparate qualities into a common quantity (Espeland and Stevens 1998). In our findings sections, we draw on these concepts to examine standards-in-the-making as "a sort of crafting of treaties" (Bowker and Star 2000, 7), whose exchanges and negotiations reconfigure the possibilities and limits of scientific knowledge production. We turn first to an account of the various paths by which scientists enter GEI research, and a consideration of how GEI research is invested with the promise of better etiological knowledge.

Seeking the Center: Scientists' Points of Entry to GEI Research

In recounting their career trajectories, many of our participants explained that they had come to GEI research by way of a prior (or ongoing) commitment to either genetic or environmental influences on the risk or course of a particular complex disease. Although disciplinary affiliation is certainly not unrelated to this persistent binary division of effort, we found that individual careers were shaped more by a broader organization of the biomedical sciences around a long-standing assumption that genes and environment, that is, nature and nurture, are "two domains, each separate from the other, waiting to be conjoined" (Keller 2010, 11). For this reason, we identify our participants primarily by their research interests, mentioning disciplinary affiliation only when it is relevant to our participants' navigation of the politics of quantification. Coalescing around GEIs as a research problem, or "gravitating toward the center," as one researcher puts it, was narratively situated in a broader shift toward etiological complexity, and multidisciplinary collaboration, that has characterized postgenomic biomedical research in recent decades.

Many of our participants described arriving at GEI research via their previous work on genome-wide association studies (GWAS). Propelled by significant public investment in the early twenty-first century, GWAS involve searching across the genomes of many individuals for commonly occurring variants and estimating their association with the risk of common diseases. After several years of large-scale GWAS, the "genetic component" of disease risk estimated by these studies has turned out to be much smaller than anticipated (Goldstein 2009, 1696), and scientists agree that genomic studies have explained little of the variation in risk at the population level when it comes to understanding common complex diseases. "I haven't seen anything that adds more than a couple of percentage of explaining what's going on in a person," said a researcher about genetic explanations of common diseases, suggesting a tacit understanding of how much risk is "good enough" to serve as credible and actionable etiological knowledge.

For scientists focused primarily on genetics, GEI research offers a means of repurposing GWAS findings while considering the role of nongenetic influences on disease risk. Here, a researcher studying the causes of type 2 diabetes recounts his conversion from a technologically mediated faith in the explanatory power of genomics to an understanding that his disease of interest also has an "environmental component":

> I think we got really excited about the fact that we can look at millions of SNPs [single nucleotide polymorphisms] overnight … I think people thought … "I can really be the one that can deliver the silver bullet." … But I think we are taking a step back now and reflecting and saying … you can't solve everything with a

> gene chip … We can explain only 10 percent of the inheritability of that particular disease and so … you really need to understand the social, behavioral, kind of the environmental component as well.

In this telling, GWAS fell short of expectations, whereas "adding in" the environment promises to bolster risk estimates without forfeiting the advantages of molecular measures.

An example of researchers' recurrent attempts to incorporate the environment to enhance explanatory power is genetic studies of lung cancer, which often show much stronger associations between genes and disease when smoking is taken into consideration. However, this requires that exposure to the chemicals in smoke be measured with precision across large numbers of research participants. A lung cancer researcher narrated her approach, "We got smoking history on all of them, how much did they smoke, how long, when did they start, when did they stop, all that kind of stuff. … They were collecting environmental exposures … It was a huge data collection effort."

Conversely, researchers whose prior research focused almost exclusively on nongenetic risk factors—such as environmental stressors and diet—offered accounts of the benefits of incorporating genetic analysis into their research. Incorporating genetic and other molecular measures was narrated as "building for the future" by enabling insight into the biological mechanisms of disease and was described as an obligatory passage point for epidemiologic research: "In getting epidemiologic studies funded these days … it usually helps if you have a molecular component, and more specifically a genetic component."

Other scientists described genetic analysis as a platform from which to build support for a model of complex causation and to work against the persistent lure of genetic explanations —to return etiological inquiry to what some of our participants referred to as "traditional" epidemiology: "We can leverage some of this interest, money, excitement about genetics to help us have a more holistic or epidemiologic perspective on health and disease … we don't have to be dazzled. We don't have to say it's all genetic." In other words, measuring genes is assumed to be an essential aspect of proving that they are not the primary cause of disease.

Valuing Harmonization and Molecular Precision

Transforming human activities into measurable scientific objects has never been a simple endeavor for epidemiologists who continually grapple with methodological and moral quandaries that emerge in the quantification and management of scientific data. However, the rapid expansion of genomics has prompted a particularly intense, reflexive critique of traditional epidemiologic methods of creating and caring for data—with concern that mainstay approaches are troubled by bias, error, and insufficient statistical "power" under these new criteria. For example, in scientific publications on GEI research, epidemiology is often depicted as a discipline "beleaguered" by the demands of quantification and offered "fresh hope" by the use of genetic technologies, which are assumed to be less prone to bias and thereby more objective (Davey Smith et al. 2005, 1498; see also Ioannidis et al. 2008). Similarly, many of our participants drew a distinction between epidemiology and genomics and explained with a confessional tone that epidemiology is "soft," that it "has a very dull razor to try to understand something" and that "one of the lessons learned

from genome-wide association studies is that likely a lot of our studies are just grossly underpowered." We found this preoccupation to be particularly acute among researchers focused primarily on nongenetic risk factors for common diseases.

This "disciplining" of epidemiology arises in part from recent advancements in genomic and other molecular technologies, which have coupled increasing speed of analysis with shrinking costs. Researchers can now measure millions of genetic variants in the bodies of thousands of study participants for a fraction of the cost and time than is required to define, measure, and interpret variables related to complicated human behaviors, social patterns, and environmental exposures. Thus, the analysis of genetic variation, on the one hand, was equated with the "harder science part" of GEI research—setting molecular measures against "messy and slippery epidemiological or social factors" such as socioeconomic status, diet, or exercise (Conrad 1999, 238), on the other.

As researchers adopt the techniques and standards of genomics in order to produce GEIs, they are compelled to seek credibility through the pursuit of greater statistical power, or the probability that a statistical test finds a difference when such a difference "actually" exists. With a somewhat chastened tone, an epidemiologist told us that "people who measure genes at this point measure them so accurately. I mean, the error is really, really small … when you have p values that are like 10 to the minus 18 and what not, it's like a completely different ball game." A p value represents an estimate of the probability that the results of a statistical analysis were arrived at by chance. A lower p value increases the trustworthiness of a study's results within—and potentially beyond—scientific collectives. The p values common in genomics are nearly impossible to achieve in conventional epidemiologic studies, both because sample sizes are usually smaller and because "risk factors," such as socioeconomic status and diet, are prone to what epidemiologists call "error" and "bias" (i.e., they are variously conceived and measured and do not as readily translate into discrete, standardized variables).

As we discuss below, new research platforms set up to maximize sample size and statistical significance require researchers to adjust how they think about and measure the environment, how they collaborate with other scientists, and the kinds of scientific knowledge they produce. In the following sections, we discuss three virtues of quantification —accuracy, harmonization (akin to Daston's "communicability"), and precision and examine how GEI researchers make trade-offs between these three virtues as they produce knowledge about complex etiology.

The virtue of accuracy: Knowing and measuring the environment.—The received definition of accuracy emphasizes the extent to which a measurement reflects the "true value" of the phenomenon being studied. In talking with our participants, however, we learned that accuracy in practice is far less straightforward than it is in definition. Understandings of accuracy were particularly troubled when they concerned the inclusion of environmental variables in GEI research. Many of our participants pondered how the true value of what one respondent described as a "fantastically multidimensional and rich" environment can be known. Here we describe how GEI researchers, in striving for statistical and professional significance in the moral economy of quantification, often exchange a good

approximation of a complex environment (accuracy) for a more consistently measurable environment (precision).

Achieving meaningful approximations of environmental factors, including behavioral, social, economic, and other nongenetic contributors to disease risk, was described as particularly difficult in GEI research because the “E [environment] side,” as several of our participants put it, is continually evaluated in comparison with the molecular-level measures of the “G [genetic] side.” For example, a researcher found standard measures of diet lacking when compared to measures of DNA and suggested that some researchers avoid studying diet because it is less amenable to measurement:

> People don’t like diet, even though it’s probably really important, because it’s measured with a lot of error, whereas you take someone’s DNA sample, you run it on this chip, you get these million different SNP sort of data points, and you take another DNA sample from the same person a week later and you run it on the same assay, you’ll get the same results. They’re highly repeatable, so people like that.

Another researcher suggested that the solution for a messy variable like diet is to create an experimental environment in which eating is no longer subject to the vagaries of participants’ choices and self-reporting. She recommended an “in-hospital feeding study … where everyone is fixed to the same environment” by providing them with controlled amounts of specific foods, without which “it would be just about impossible to conceptualize with much precision a diet–gene interaction.” In this scenario, a scientific approach to diet emphasizes precision measurement and the elimination—rather than investigation—of the economic, social, and cultural variability of actual dietary practices. In other words, stabilizing the environment-as-diet under experimental conditions requires a trade-off: enhanced measurability and precision is exchanged for investigating the actual, lived dietary environment.

Seeking measurable environments, researchers also encountered the high statistical bar set by molecular measures, such that environmental measures were often blamed for jeopardizing the statistical significance of their companion genomic data. One of our participants described the struggle to attain adequate statistical power when genetic and environmental measures were analyzed together:

> We typically are doing studies with GWAS data or some other huge data set where there’s barely enough power to observe a main effect of the genotype, and if you’re going to try and introduce an environmental exposure in there and then interaction terms, there’s just no power there. The whole analysis just kind of explodes; it’s out of control.

An “out-of-control” analysis refers to a vastly decreased likelihood of achieving statistical significance. However, the consequences of an out-of-control analysis are professional as well as statistical, since the failure to produce credible findings can jeopardize a researcher’s access to funding and status. Narrating her career trajectory, a researcher somewhat wistfully described relinquishing an interest in the wide array of carcinogens that are suspected of contributing to the development of breast cancer but that are difficult to measure:

> Even though in animal models there are many mammary carcinogens that are out there, it's something that we really can't nail down through epidemiology very well … Quantifying and measuring those types of exposures is pretty difficult … and so [in] some of my first research … I ended up just looking at smoking.

Thus, both the environment and those who study it must be disciplined in the interest of quantification and measurement at the molecular level. Acknowledging the important links between disease risk and socioeconomic problems, such as poverty and racial discrimination, many of our participants nonetheless included more narrowly defined environmental variables and measures in order to improve measurability across large study populations and scientific collectives. A participant's account of including measures of "stress" in a multisited study demonstrates this process of simplification:

> … we added a set of questions for stress, for example … they're things that are very standardized that anyone can get ahold of. They're not necessarily the best measures for what it is we might want to study. But they're something that anybody can do and a lot of people are sort of familiar with already, so again, least common denominator kind of approach.

As with the researcher quoted above, the implications of reducing behaviors, social contexts, and disease definitions to the "least common denominator" were not lost on our participants. Many expressed concern that the results of GEI research offer a crude approximation of actual etiological complexity, at best. However, hard-to-quantify social factors are often judged as "soft," that is, less scientific, mentioned one researcher, resulting in a reluctance among scientists to talk about—let alone study—the social and political forces that are known to influence health:

> It's the environment that is the major challenge … the social factors get ignored in many ways, because [they are] soft science … and how do we even measure the impact of race and racism, the impact of economic deprivation? … and for many people, the thinking is, we can't measure them, so we don't include them, or we don't even talk about them.

Of course, many researchers *do* talk about racism and poverty. However, most GEI researchers approach nongenetic variables first and foremost in terms of their amenability to measurement and their ability to approach the de facto standard of quantification set by molecular measures. This is not to say that genomic tests are always uniform across study sites, or that they do not contain contested assumptions about human difference, such as when DNA is classified using received categories of race and ethnicity (Montoya 2007). Nonetheless, GEI researchers engage in compromises as they attempt to adapt environmental variables to the "gold standard" of molecular measures, and the nature of these compromises are shaped in part by a politics of quantification.

The virtue of harmonization: Measuring up with consortia and big data.—One of the strategies used by scientists to increase statistical power in GEI research is to build research studies with more participants, or combine data from multiple, similar studies. The demand for larger sample sizes, alongside recent declines in US federal funding for basic and biomedical research, has propelled the formation of research consortia and their

constituent assemblages of geographically dispersed scientists, research staff, and study participants. As simultaneously scientific and social formations, consortia have transformed how scientists interact with one another as well as the kinds of scientific knowledge they produce. Thus, we understand harmonization—a term used by scientists to refer to the process of rendering different data, phenotypes, and disease definitions comparable—as a virtue of both data and scientists themselves, since both are subject to a common standard in order to do good science. In this section, we describe how GEI researchers negotiate the strong emphasis on standardization and mobilization of environmental and genomic information in consortia and the long-held scientific virtues (and rewards) of independence, inventiveness, and accuracy.

These imperatives to harmonize both data and researchers were imbricated in our participants' narratives of consortium work, which often contained moral injunctions alongside descriptions of data reconciliation: consortia members should "collaborate," be "open minded" and "play nice together." A researcher discussed trying to harmonize both researchers and measures of diet across multiple studies:

> Then we would send them a list saying, "Please send us these variables in this format." We'd get that back. Of course, it wouldn't be exactly in that format. And some people wouldn't have it. The data wouldn't quite fit in that format, so they'd send us whatever they could. We would come up with some way of harmonizing them and report that back to the group, at which point either people say, "Yes, that seems reasonable to us." Or they'd say, "No. Wait. This particular variable—can't we tweak it this way?"

Thus, when scientists attempt to harmonize variables and procedures across multiple studies, playing nice may mean relinquishing one's potentially unique or more locally relevant approach to conceiving and measuring a study variable so that data can be compared and analyzed across studies. Or it may mean submitting to the alteration of one's data so that it can be made comparable to data from other studies. As the above example illustrates, however, standardization of measures among GEI consortia is rarely a top-down, unidirectional process.

Another example of the "complex negotiations" (Timmermans and Epstein 2010, 73) required in standards creation comes from a researcher working with a consortium studying the associations between walking speed, genetic variation, and longevity: "The problem we're having in our analysis is that we probably got 15 cohorts that have measured gait speed, but they've all measured it differently … different investigators champion different phenotypes." With so many champions invested in their own approaches to measurement, trying to come to a common understanding in order to render cross-study data comparable was both necessary and frustratingly like "herding cats." This is in part because common measures, or standards, contain assumptions about the best way to understand and approach a given phenomenon, such as walking, and these assumptions run up against the context-dependent approaches that different researchers use to think about and measure the phenomenon (Timmermans and Berg 2003).

The goals of data harmonization also conflict with what researchers identified as "the culture of epidemiology" and institutional norms of professional advancement, in which "you're rewarded for developing new approaches and once you develop it, you don't want to give something up that you've worked hard to develop," in the words of one scientist. This reward structure made researchers hesitant to share measures, scales, or assays. Many of our participants also complained that consortia require "extra work," that is, not paid for by a grant, while yielding little academic credit in the form of additional grants and first-authored publications. For example, a researcher studying aging and longevity described the importance of analyzing data across a ten-site consortium, and the burden: " … that is not a trivial amount of time, and we're not funded to do that specific thing. But yet, if you don't do it, then you're not in the game."

Scientists' narratives about consortium work also illustrate exchanges made between what our participants described as "real-world" environments and harmonizable variables, particularly in large consortia in which data are collected across a broad geographical and cultural landscape. For example, one of our participants described the conundrum of merging data on socioeconomic status from different countries: "I really think we need to collaborate with other consortia and my worry is that … all these countries—how are you going to do these gene–environment interactions when they're coming from completely different environments?" A researcher working with a transnational cancer consortium echoed this concern, listing genetic differences, diet and environmental exposures as examples of the "dramatically different" contexts across which they are trying to pool data. The concern here is not just about the loss of local specificity demanded by harmonization, but that "environments" themselves may actually be incommensurable and therefore resistant to standard measures.

To conclude, we find that consortia are becoming an indispensable platform for producing credible etiological knowledge in GEI research, but that participating researchers must work to articulate competing obligations and currencies. On the one hand, their careers hinge on their productivity as independent researchers and their commitment to accurate measures. On the other hand, amassing and integrating large data sets require that they subsume their hard-won strategies, know-how, and independence to the demands of precision and standardization made by a larger, dispersed collective. In the face of these trade-offs made in order to "fit" environmental variables with the imperatives of ever-larger data sets and communities of practice, there has been a push to reconceive social and behavioral risk factors in terms of discrete substances or molecular processes inside the body. We now consider molecular precision as an emerging and contested virtue in the moral economy of quantification.

The virtue of precision: Better measurement through molecularization.—As we have described, GEI researchers often strive to produce credible scientific knowledge through the creation of variables that can be mobilized across studies and through the enactment of specific forms of sociability, collaboration, and self-discipline among practitioners. As they work to accrue credit in the moral economy of quantification, researchers variously subscribe to, and make trade-offs between, its constituent virtues. An increasingly popular strategy for producing and amassing large quantities of comparable

and replicable data, and faithfully enacting the virtue of precision, is the use of molecular technologies and forms of measurement. Promising a greater degree of precision than traditional surveys and questionnaires, molecular measures detect substances or processes in participants' bodies through extracted blood or other tissues.

Molecular measures reconceive "modifiable" risk factors such as diet, exercise, and smoking, as discrete markers or substances. Moving risk factors into the body transforms them from behaviors or social practices prone to varied interpretations among researchers and study participants, to biological substances or "markers" that can be measured the same way in any number of research participants and across multiple studies. As one researcher reported, "the ways of measuring the environment have gotten better, so you can do proteomic kinds of measurements, that are [blood] serum biomarkers … those are getting less expensive and more reliable."

Our participants explained that molecular measures of hard-to-quantify risk factors such as diet are increasingly associated with scientific progress and rigor, and as such they are replacing questionnaires and other procedures for gathering data based on study participants' recollections or reports. This shift is guided both by technological developments and by members of scientific collectives who influence funding and publication decisions, as in the case of a scientist who studies links between nutrition and prostate cancer and equated learning molecular techniques and methods with "stay[ing] current and with the times." She situated this narrative of progress in technological advancements and changing assumptions about what constitutes good diet data:

> There was a perception in the field that some of the senior scientists, you know, don't like self-reported data. […] they just thought that type of data was so poor […] And they think you need to go into the body. You need to measure the nutrient level in the body. And so I think it was a convergence of that school of thought held by some senior investigators, and also a laboratory technology innovation that allowed these things to be done more cheaply.

In other words, scientists who use self-reported measures of diet are subject to both collective and self-discipline, resulting in a realignment of study procedures with new standards and values of quantification. Self-reported information about diet—long a standard epidemiologic measure—no longer constitutes "good science," whereas the high value of molecular precision can be realized in readily available technologies and their numerical outputs. The stakes in this struggle for precision were visually represented at a "nutrigenomics" panel that we observed during a scientific conference, when a speaker discussing GEIs and type 2 diabetes showed a slide depicting the scales of justice, with a DNA strand on one side and a food pyramid on the other. The DNA was weighted more heavily, in part, explained the speaker, because of the "really, really high random error in diet." Although many of our participants acknowledged that the genetic contributions to type 2 diabetes are miniscule compared to environmental factors such as diet and physical activity, this presenter was keen to illustrate that molecular measures are less prone to variations in interpretation and measurement ("error") and are therefore more precise and more faithful contributors to statistical significance.

A shift from self-report to molecular measurement can also be seen in studies that attempt to account for differences in disease prevalence across populations—including those classified by race or ethnicity. While self-identified race and ethnicity (SIRE) continues to be widely used to stratify study populations in epidemiologic research, ancestry informative markers (AIMs)—genetic variants that purportedly estimate the geographic origins of an individual's ancestors—are increasingly considered to be a more precise method for measuring human difference (see Shim et al. 2014 for an extended discussion of SIRE and AIMS in GEI research). Not all of our participants agreed that AIMs were a superior method for understanding human difference and health disparities, but they were disciplined by their peers toward the virtue of greater precision:

> Now I think that if you're proposing to do any study that's related to race, if you don't talk about ancestry-informative markers, you're not going to get funded. Whether they really make a difference or not …

One reason that precision is so fervently sought by GEI researchers is that molecular measures render environmental variables more readily comparable to the data produced by tests of genetic variance and thereby more amenable to GEI analytic procedures. In other words, a good GEI is one in which environmental variables are made to more closely resemble genetic markers—both in how they are thought about and in how they are transformed into units of measurement. In the epidemiologic literature, however, commentators have expressed concern that reconceiving risk factors as substances and processes inside the body (re)focuses the study of causality to the molecular level and shifts scientific attention away from the more traditional focus of epidemiology that is inclusive of social, economic, political, and historical influences on disease risk (Susser and Susser 1996; McMichael 1999). Our findings suggest the crucial role played by the politics of quantification in the move to molecularize the environment in the context of GEI research.

Conclusion

We have drawn on the wide-ranging perspectives of scientists who straddle the nature–nurture divide by studying etiology as the interactions between genes and environments. A close look at our participants' perspectives and research practices has illuminated a host of exchanges and trade-offs involved in the production of GEIs, including the articulation of scientists and study variables with the needs of large research consortia and technologies of molecular measurement. In analyzing an emergent moral economy of quantification, we argue that measurement is not simply a set of strategies for producing more credible scientific knowledge or more accurate descriptions of the world. Rather, quantification operates through intersecting, collectively negotiated virtues—virtues that are ascribed to research objects, procedures, and scientists themselves. These negotiations reveal a politics that shapes how knowledge about complex causality can be produced. As scientists navigate this field, they collectively reproduce and transform what constitutes good science and what qualities a good scientist should possess.

Of particular concern among many of our participants was the exchange of real-world complexity for statistical significance through precise measurement and harmonizable data. This has resulted in scientific practices in which social, economic, political, and historical

influences on health are rendered less knowable because they are deemed less amenable to precise, standardized measurement. Indeed, the narrowing of the environment to molecular substances and processes, and to easily measurable behaviors, has become embedded in the very procedures and technologies of genomic science, even as it engenders an unprecedented examination of etiological complexity and disease mechanisms. This shift toward “very big epidemiology” has led some epidemiologists to warn against “lowest-common-denominator science,” in which complexity is relinquished in favor of larger sample sizes and simpler measures (Kaplan 2007, 18-19).

Many of our participants, however, argued that oversimplified representations of the environment are not inevitable or fixed in GEI research, nor are they merely a product of the privileging of molecular precision and large-scale population studies that is emblematic of postgenomic science. Rather, they insisted, a shrinking of the environment is the result of an imbalance in scientific attention and commitment, and a too-easy reliance on “simple models to understand life.” A more symmetrical approach, they claimed, would involve a significant financial and scientific investment in creating better—not necessarily molecular—measures of socioeconomic and political processes that influence disease patterns across populations. In this imagined epidemiology, cross-disciplinary collaborations would result in environmental measures that adhere to prevailing norms of quantification *and* better represent the complex contexts that shape human health.

It is impossible to predict whether GEI research will embrace complex, less measurable environments while continuing down the path of molecularization. At present, however, GEI research presents an irony that does not go unnoticed among its practitioners. Many researchers become involved in GEI studies after conducting GWAS and concluding that genes do not tell us enough about disease. However, demands for greater precision and measurability in postgenomic epidemiology have led many GEI researchers to focus on the “G” at the expense of the “E” and thereby reproduce the very privileging of genetics that prompted the search for GEIs.

By pointing out this irony, however, we do not mean to suggest fixity. Our findings demonstrate how postgenomic science and its practitioners are shaped by techniques and virtues of quantification that are under constant reconstruction and reconsideration. By examining the trade-offs and compromises researchers are willing to make in pursuit of these virtues, we underscore the politics that shape what can be known about the causes of complex diseases. And by defining this politics as a moral economy, we point to the importance of new forms of sociality among scientists, as they work to create larger cohorts and data sets, and to the value systems that inflect scientists’ truth claims in relation to measurement.

Thus, the modes and meanings of quantification are not as settled or foundational as they are often assumed to be. The paradox of the current politics of quantification is that it engenders a multitude of interactions among researchers, genes, and environments, while simultaneously constraining what actually counts as a knowable environment. If an environment is not knowable, how can it be acted on? It remains to be seen, then, how knowledge produced by GEI research will be taken up, and how it will influence public

health approaches to disease prevention. Will risk be further consolidated as an individual attribute and responsibility, or will knowledge about GEIs contribute to the creation of more equitable and health-promoting environments? Either way, how genes and environments are imagined and credibly quantified will have a great bearing on these—and other—possible futures.

Acknowledgments

We would like to thank our study participants for generously answering our many questions about gene–environment interaction research. We also thank the editorial staff and two anonymous reviewers for their thoughtful and constructive comments.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Research reported in this publication was supported by the National Human Genome Research Institute's Ethical, Legal, and Social Implications Research Program of the National Institutes of Health under award number R01HG005848. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Biography

Sara L. Ackerman is a medical anthropologist and assistant professor of social and behavioral sciences at the University of California, San Francisco. Her research interests include the sociocultural aspects of genomic science and technology and their translation into the clinic.

Katherine Weatherford Darling is a doctoral candidate in sociology and Rosenberg-Hill Graduate Research Fellow at University of California, San Francisco. Her dissertation is an ethnography tracing the uses of health information technologies within clinical and policy strategies for managing human immunodeficiency virus (HIV) as a chronic illness in U.S. health care.

Sandra Soo-Jin Lee is a medical anthropologist and senior research scholar at the Stanford Center for Biomedical Ethics, and faculty in the Program in Science, Technology and Society at Stanford University. Dr. Lee's research interests are in the sociocultural and ethical dimensions of emerging genomic technologies and their translation into biomedical practice.

Robert A. Hiatt is professor and chair of the Department of Epidemiology and Biostatistics, University of California, San Francisco, and associate director for Population Science of the UCSF Helen Diller Family Comprehensive Cancer Center. His research interests include cancer epidemiology, health services and outcomes research, and the social determinants of cancer.

Janet K. Shim is associate professor of sociology in the Department of Social and Behavioral Sciences, University of California, San Francisco. Her current research focuses on analyzing the science of health disparities and the production of health care inequalities. She is the author of *Heart-Sick: The Politics of Risk, Inequality, and Heart Disease* (2014, NYU Press).

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