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Genes, Eyeglasses, and Social Policy

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Someone reading empirical research relating human genetics to personal outcomes must be careful to distinguish two types of work. An old literature on *heritability* attempts to decompose cross-sectional variation in observed outcomes into unobservable genetic and environmental components. A new literature measures specific genes and uses them as observed covariates when predicting outcomes. I will discuss these two types of work in terms of how they may inform social policy. I will argue that research on heritability is fundamentally uninformative for policy analysis, but make a cautious argument that research using genes as covariates is potentially informative.

Heritability

The heritability of human traits has been a persistent topic of study and controversy since the latter third of the nineteenth century. The beginning of formal research in this area is usually attributed to the British scientist Francis Galton, who appears to have been the first to attempt to distinguish the roles of "nature" and "nurture." About 100 years after Galton started his studies, controversy about the heritability of IQ flared in the 1960s and 1970s. This subject has been particularly heated because some social scientists have sought to connect heritability of IQ with social policy, asserting that policy can do little to ameliorate inequality of achievement if IQ is largely heritable.

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Considering the state of thinking in the late 1970s, Goldberger (1979, p. 327) began his cogent critique of research on heritability this way:

> When we look across a national population, we see large differences in intelligence as measured by IQ tests. To what extent are those differences the result of differences in genetic make-up, and to what extent are they the result of differences in life experience? What proportion of the variance in IQ test scores is attributable to genetic variance, and what proportion to environmental variance? This question has fascinated mankind—or at least the Anglo-American academic sub-species—for several generations. The fascination, I suppose, arises from the notion that the answer has some relevance to social policy: if IQ variance is largely genetic, then it is natural, just and immutable; but if IQ variance is largely environmental, then it is unnatural, unjust and easily eradicated.

Goldberger concluded that heritability, whether it be of IQ or other traits, is irrelevant to social policy. I will explain why here. However, first I need to explain what the heritability statistic measures and how it has been interpreted.

Heritability as Analysis of Variance

Lay people often use the word "heritability" in the loose sense of the *Oxford English Dictionary*, which defines it as "the quality of being heritable, or capable of being inherited." However, formal research on heritability uses the word in a specific technical way. Stripped to its essentials, heritability research seeks to perform an analysis of variance.

Consider a population of persons. Researchers pose an equation of the form

$$\text{outcome} = \text{genetic factors} + \text{environmental factors}$$

or, more succinctly, $y = g + e$. Here, y is a scalar personal outcome (or phenotype) such as IQ, income, or height. The variable g symbolizes genetic factors, and e symbolizes environmental factors. It is commonly assumed that g and e are uncorrelated across the population. Then the ratio of the population variance of g to the variance of y is called the heritability of y. Researchers say that heritability gives the fraction of the variation in the outcome "explained by" or "due to" genetic factors.[1]

The equation studied in heritability research poses an extraordinarily simple idealization of the complex process by which modern scientists believe that a person's genome and environment actually produce outcomes. The scalar variables

[1] Formally, the population variance of y may be decomposed as follows:

$$\text{Var}(y) = \text{Var}(g) + 2\text{Cov}(g, e) + \text{Var}(e).$$

Researchers usually suppose that $\text{Cov}(g, e) = 0$, so the equation reduces to $\text{Var}(y) = \text{Var}(g) + \text{Var}(e)$. Then heritability is the ratio $\text{Var}(g)/\text{Var}(y)$.

g and *e* respectively summarize the entire genome and the spectrum of environmental factors that may combine to determine outcomes. The equation specifies a production function in which *g* and *e* contribute additively to outcomes, rather than interact with one another. The assumption that *g* and *e* are uncorrelated is at odds with the reasonable conjecture that persons who inherit relatively strong genetic endowments tend to grow up in families with more favorable environments for child development.

The simplicity of the equation studied in heritability research presumably stems from the fact that this body of research began long before the genome was known to exist, never mind measured, and also well before population surveys reporting individual-specific data on environmental factors became available. In this historical context, *g* and *e* could not be observable measures of a person's genome and environment. They were metaphors, symbolic representations of hypothesized latent forces. The somewhat mystifying technical intricacies of heritability research—its reliance on outcome data for biological relatives, usually twins or siblings, and on various strong statistical assumptions—derived from the desire of researchers to make heritability estimable despite the fact that *g* and *e* were metaphorical.

What Does "More Important" Mean?

Suppose that a researcher obtains data on the outcomes experienced by twins or other relatives, makes enough assumptions, and reports an estimate of the heritability of the outcome. What does this number reveal that may be of economic interest? Researchers often say that heritability measures the relative "importance" of genetic and environmental factors. For example, in a recent article on the heritability of behavior among monozygotic (identical) and dizygotic (fraternal) twins playing a trust game, Cesarini, Dawes, Fowler, Johannesson, Lichtenstein, and Wallace (2008) write:

> [A] result that may surprise some social scientists is that genetic differences appear to be a more important source of phenotypic variation than differences in common environment. This finding is in line with a broad consensus in the behavior genetics literature. Indeed, the second "law of behavior genetics" proposed by Turkheimer (30) [2000] is that the effect of being raised in the same family is generally smaller than the effect of genes.

When these authors state that genetic differences are a "more important" source of outcome variation than differences in common environment, they apparently mean this comment in the tautological sense that the procedure used to decompose the observed variance in behavior attributes more of this variance to variation in the genetic factor *g* than to variation in a common (that is, family-specific) component of the environmental factor *e*.

Loose use of the term "more important" is unfortunately common in empirical social science research. A notoriously prominent example is *The Bell Curve*, where Herrnstein and Murray (1994, p. 135) proclaimed: "Cognitive ability is more important

than parental SES [socioeconomic status] in determining poverty." *The Bell Curve* differed from traditional heritability research in some ways. In particular, Herrnstein and Murray observed their g and e using statistically standardized measures of cognitive ability to capture g and parental socioeconomic status obtained in a population survey to capture e. However, Herrnstein and Murray shared with traditional heritability research the objective of assessing the relative importance of genetic and environmental factors in explaining the observed variation of population outcomes such as poverty.

In our 1995 *Journal of Economic Literatur*e critique of *The Bell Curve*, Arthur Goldberger and I called attention to a clearheaded appraisal of social science efforts to assess "importance" made 25 years earlier by Cain and Watts (1970), writing then on the Coleman Report (Coleman, Campbell, Hobson, McPartland, and Mood, 1966). Rather than paraphrase, I will quote our passage directly (Goldberger and Manski, 1995, p. 769–70):

> We find no substantively meaningful way to interpret the empirical analysis in Part II of *The Bell Curve* as showing that IQ is "more important" than SES [socioeconomic status] as a determinant of social behaviors. How might the phrase "more important" be given policy-relevant content? The answer was given years ago by Glen Cain and Harold Watts (1970) in their critique of the Coleman Report on equality of educational opportunity . . .
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> The Coleman Report sought to measure the "strength" of the relationship between various school factors and pupil achievement through the percent of variance explained by each factor, an approach similar to that of HM [Herrnstein and Murray]. Cain and Watts write (p. 231): "this measure of strength is totally inappropriate for the purpose of informing policy choice, and cannot provide relevant information for the policy maker." They go on to offer an alternative approach:
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> > [I]t would seem evident that our interest lies in purposive manipulation of the x's in order to effect an improved performance in terms of y. We can, and should, ask for the expected change in y induced by spending some specific amount of money (or political capital, man hours, etc.) on working a change in x_2, say, as compared with the alternative of spending the same sum on x_3. Budgetary cost is not necessarily the only basis of comparability. But unless *some* such basis is defined and its relevance to policy explained, the question of "strength" has no meaning.
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> To apply this approach in the context of *The Bell Curve*, one could contemplate allocating some fixed sum to improve IQ or to improve SES. It would be meaningful to say that IQ is more important than SES if spending the sum on IQ improvement rather than SES improvement were to yield a larger expected change in some outcome of interest.

Heritability and Social Policy

What has made research on heritability particularly controversial has been the inclination of some researchers to interpret the magnitude of heritability estimates as indicators of the potential responsiveness of individual achievement to social policy. In particular, large estimates of heritability have been interpreted as implying small potential policy effectiveness.

A notable example was given by Goldberger (1979). Discussing a *London Times* report of research relating genetics to earnings and drawing implications for social policy, he wrote (p. 337):

> For a more recent source we turn to the front page of *The Times* (13 May 1977), where under the heading "Twins show heredity link with earnings" the social policy correspondent Neville Hodgkinson reported:
>
> > A study of more than two thousand pairs of twins indicates that genetic factors play a huge role in determining an individual's earning capacity . . . According to some British researchers, the study provides the best evidence to date in the protracted debate over the respective contributions of genetics and environment to an individual's fate . . . The findings are significant for matters of social policy because of the implication that attempts to make society more equal by breaking "cycles of disadvantage" . . . are likely to have much less effect than has commonly been supposed.
>
> Professor Hans Eysenck was so moved by the twin study that he immediately announced to Hodgkinson that it "really tells the [Royal] Commission [on the Distribution of Income and Wealth] that they might as well pack up."

Commenting on Eysenck, Goldberger continued (p. 337):

> (A powerful intellect was at work. In the same vein, if it were shown that a large proportion of the variance in eyesight were due to genetic causes, then the Royal Commission on the Distribution of Eyeglasses might as well pack up. And if it were shown that most of the variation in rainfall is due to natural causes, then the Royal Commission on the Distribution of Umbrellas could pack up too.)

This parenthetical passage, displaying Goldberger's characteristic combination of utter seriousness and devastating wit, shows the absurdity of considering heritability estimates to be policy relevant. At the end of a beautifully written article that deserves to be read in full, Goldberger concluded (p. 346): "On this assessment, heritability estimates serve no worthwhile purpose."

It is important to understand that Goldberger's conclusion did not rest on the metaphorical nature of g and e in heritability research. It was based, more

fundamentally, on the fact that variance decompositions do not yield estimands of policy relevance.

To place heritability research on the best imaginable footing, suppose that g and e are not metaphors but rather are observable summary statistics for a person's genome and environment, as they were in *The Bell Curve*. Suppose that the equation $y = g + e$ is a physical law showing how the genome and environment combine to determine outcomes. Also suppose that g and e are uncorrelated in the population, as is typically assumed in heritability research. Then a researcher who observes the population may directly compute the heritability of y, without the need for special data on twins or obscure assumptions.

At one extreme, suppose that the population is composed entirely of clones who face diverse environments. Then the variance of g is zero, implying that heritability is zero. At the other extreme, suppose that the population is composed of genetically diverse persons who share the same environment. Then the variance of e is zero, implying that heritability is one.

What does this have to do with policy analysis? Nothing. Policy analysis asks what would happen to outcomes if a conjectured intervention were to change persons' environments in some manner. Heritability is uninformative about this.

Some symbols help to sharpen the point. Let t denote a treatment that might potentially be assigned to a person, let $e(t)$ denote the environment that this person would face under this treatment, and suppose that the resulting potential outcome is $y(t) = g + e(t)$. A policy analysis evaluating the intervention would seek to predict these potential outcomes. Heritability is determined within the environments that persons actually face, not the environments that they would face if the intervention were to occur. Hence, heritability reveals nothing about outcomes under the intervention.

Illustration

Consider Goldberger's use of distribution of eyeglasses as the intervention. For simplicity, suppose that nearsightedness derives entirely from the presence of a particular allele of a specific gene. Suppose that this gene is observable, taking the value $g = 0$ if a person has the allele for nearsightedness and $g = 1$ if he has the one that yields normal sight.

Let the outcome of interest be effective quality of sight, where "effective" means sight when augmented by eyeglasses, should they be available. A person has effective normal sight either if he has the allele for normal sight or if eyeglasses are available. A person is effectively nearsighted if that person has the allele for nearsightedness and eyeglasses are unavailable.

Now suppose that the entire population lacks eyeglasses. Then the heritability of effective quality of sight is one. What does this imply about the usefulness of distributing eyeglasses as a treatment for nearsightedness? Nothing, of course. The policy question of interest concerns effective quality of sight in a conjectured environment where eyeglasses are available. However, the available data only reveal what happens when eyeglasses are unavailable.

Why Does Heritability Research Persist?

While Goldberger's eyeglasses example got to the heart of the logical problem with heritability research in a particularly succinct and effective way, he was not alone in grasping the irrelevance of heritability to policy. Writing contemporaneously, the statistician Oscar Kempthorne (1978, p. 1) summarized his view of the matter this way: "The conclusion is that the heredity–IQ controversy has been a 'tale full of sound and fury, signifying nothing.' To suppose that one can establish effects of an intervention process when it does not occur in the data is plainly ludicrous."

Given that it was widely recognized more than 30 years ago that heritability research is irrelevant to policy, I find it both remarkable and disheartening that some have continued to assert its relevance subsequently. For example, Herrnstein and Murray did so in *The Bell Curve*, referring to (p. 109) "the limits that heritability puts on the ability to manipulate intelligence." Research on the heritability of all sorts of outcomes continues to appear regularly today. Recent studies such as the one by Cesarini et al. cited earlier tend not to explicitly refer to policy, but neither do they provide any other articulate interpretation of the heritability statistics they report. The work goes on, but I do not know why.

Genes as Covariates

Technological progress in gene measurement has increasingly enabled collection of data on the expression of specific genes in large samples of individuals. It is becoming routine to ask the respondents to major household surveys to provide saliva from which DNA may be extracted. For example, the nationwide Health and Retirement Study has done this.[2]

Gene measurement replaces the metaphorical *g* of heritability research and the indicators of *The Bell Curve* with direct observation of pieces of the genome that may be used in all of the ways that researchers ordinarily use data on personal covariates. It transforms research relating human genetics to personal outcomes from a mystical exercise into ordinary social science. I will first discuss the use of genes as covariates in conditional prediction and then their use in analysis of treatment response.

Conditional Prediction

A staple concern of empirical research is prediction of realized outcomes conditional on observed covariates—that is, regression. It has long been routine to predict outcomes conditional on personal attributes that are themselves partially determined by genetics, such as gender, health, and race. One may now similarly predict outcomes conditional on gene measurements. Regressions describe statistical association rather than causation. Nevertheless, it is often useful to be able to

[2] See the Health and Retirement Study's "2006 Biomarker Data" (2007) at ⟨http://hrsonline.isr.umich.edu/modules/meta/bio2006/desc/biomkr06dd.pdf⟩.

predict realized outcomes conditional on observed covariates, whatever the causal mechanism may be.

For example, Caspi et al. (2003) used longitudinal data from a representative birth cohort to study prediction of depression conditional on the expression of a specific gene and aspects of a person's environment. The authors found predictive power in interactions of the gene with stressful life events, rather than in the gene per se. A subsequent meta-analysis of multiple studies by Risch et al. (2009) found that the findings reported by Caspi et al. were not systematically replicated, and Caspi, Hariri, Holmes, Uher, and Moffitt (2010) then responded to this criticism. The controversy about the replicability of the Caspi et al. findings does not tarnish the idea of prediction of health outcomes conditional on gene measurement. It just shows the familiar dynamic processes of science at work in a frontier area. While this and other studies to date have largely focused on prediction of health outcomes, researchers could similarly study prediction of socioeconomic outcomes conditional on genes and other covariates.

The use of specific measured genes to predict personal outcomes is entirely out of the scope of heritability research, where g is a latent construct rather than an observed covariate. Moreover, heritability research traditionally assumes that gene–environment interactions such as those found by Caspi et al. do not exist. The equation $y = g + e$ that typically forms the starting point for analysis of heritability assumes that g and e contribute additively to outcomes.

Analysis of Treatment Response

A more ambitious objective than conditional prediction of realized outcomes is prediction of the potential outcomes of conjectured interventions—that is, analysis of treatment response. For example, medical researchers have long sought to understand how treatment response varies with observed risk factors, the aim being to tailor treatment to the person as well as possible. Similarly, educational researchers may seek to learn how well various interventions work for students with different attributes, the aim again being to choose the most effective interventions. Making treatment choice conditional on observed covariates is referred to as *targeting* or *profiling*.

Gene measurements may be informative about treatment response. If it were found that the outcomes of medical treatments or educational interventions vary systematically across persons with different observed genes, then physicians or school counselors may want to condition treatment decisions on these covariates. Other social planners making treatment decisions might similarly benefit from gene measurement. Thus, whereas heritability research has erroneously claimed relevance to social policy, using measured genes as covariates can be policy relevant.

It is important to understand that, when performing analysis of treatment response, it does not matter whether observed covariates "cause" treatment response to differ across persons or are only statistically associated with treatment response. A planner considering making treatment a function of genes or other covariates need not prove that these covariates cause treatment response to differ across persons. He

need only find it credible to assume that the statistical association observed in the past will persist into the future. With this important caveat, observation of covariates that are statistically associated with treatment response can improve treatment decisions whatever the causal mechanism may be (Manski, 2007, Sec. 11.4). For example, a finding that a certain gene is strongly associated with nearsightedness would be a useful diagnostic tool for pediatricians evaluating infant vision, whatever the causal mechanism may be.

Ethical issues sometimes arise when conditioning treatment on covariates. Writers have called attention to potential ethical issues associated with *genetic profiling* (for example, Almond, 2006). These issues require attention, and may limit applications. However, society already faces ethical issues when contemplating use of gender, race, and other personal attributes to choose treatments. It seems to me that using genes as covariates does not raise unique ethical concerns.

Another issue is the difficulty of determining how treatment response actually varies with genetic covariates. Many economists are sensitive to the fact that analysis of treatment response commonly confronts severe identification problems; see Manski (2007, chaps. 7–10) for an extended exposition. However, conditioning on observed covariates does not qualitatively affect the severity of these problems. Hence, using genes as covariates is not particularly troublesome.

An Embarrassment of Data Riches

As gene measurement advances, researchers will have to learn how to cope with an unusual problem—an embarrassment of data riches. The human genome is composed of about three billion base pairs, organized into over 30,000 genes. In the past, many researchers have focused on a single gene or a very small number as covariates, but they are beginning to use a richer set of genes as the data become available. Moreover, they will want to interact genetic covariates with a host of environmental factors. Indeed, the number of observable genetic and environmental variables available for use as covariates will no doubt exceed the size of humanity before too long.

Econometricians and statisticians have long sought to prescribe effective approaches to conditional prediction and analysis of treatment response when the number of observed covariates is large relative to the size of the available sample of persons. Perhaps the simplest and most common practice is to a priori choose a reasonably small subset of the observed covariates and use this subset as the conditioning variables, ignoring the other covariates. This practice is legitimate. As I emphasized earlier, use of covariates in conditional prediction and analysis of treatment response requires no causal interpretation of the covariates. Statistical association between the covariates and the outcomes of interest suffices, provided that one finds it credible to assume that the past association will persist into the future.

While restricting attention to a small subset of the observed covariates has merit, econometricians and statisticians have sought to devise approaches that improve on this elementary idea. Early research on linear regression proposed such

ideas as principal component analysis and stepwise regression. Recent research on nonparametric regression refers to the inferential problem as the *curse of dimensionality* and studies various *dimension-reducing* approaches. These seek to make the analysis tractable by placing various assumptions on the shape of regression functions. Moreover, they seek to prevent researchers from over-fitting the data; that is, finding statistical patterns in a sample that do not actually exist in the population from which the sample is drawn.

While dimension-reducing methods may be useful, I doubt that statistical theory per se will generate effective means of exploiting the coming wealth of genetic information. To discipline the use of genes as covariates, I think that biologists, medical researchers, and social scientists should work in concert to develop a structural understanding of the way genes and the environment determine health and socioeconomic outcomes. This work may suggest what genetic information and environmental factors have predictive power, enabling researchers to focus attention on these covariates. And it may suggest how the relevant genetic and environmental covariates interact to determine outcomes. Thus, structural analysis can potentially provide a credible foundation for dimension reduction.

Conclusion

For over 100 years, research relating genetics to human outcomes was crippled by two problems, one conceptual and the other technological. The conceptual problem was the focus of research attention on estimating heritability, producing percentages or claims of "more important" or "less important" that served no worthwhile purpose. The technological problem was the absence of means to measure genes. The latter problem may have contributed to the former by stimulating researchers to invent the metaphorical *g* in the absence of gene measurements.

The conceptual problem has been understood since the 1970s and the technological one has been overcome in the past decade. There is therefore no rationale for further research on heritability. However, while a variety of practical problems remain to be overcome, I see a potentially productive future for use of observed genes as covariates.

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