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Commentary

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Here we articulate a negative answer to Turkheimer and Greer's question: "Is it possible to envision a genetically informed program that ethically intervenes on campus drinking?" (Turkheimer & Greer, 2024). However, first, we note that the authors cover an immense amount of ground in their paper. They lend insight into how psychiatric genetics, at its very core, is conducted through their detailed examination of a large body of work in one specific area of this large field. A main result of this is to explain the gulf between results and conclusions, work that provides an invaluable service not just to various areas in philosophy and bioethics, but that are deserving of readership by a very wide audience. This gulf is explained via a careful accounting of the statistical measures used to assess the impact of genes on alcohol-related behavior in the college students sampled and comparisons between the strength of these measures and the strength and scope of conclusions drawn by the Spit for Science (S4S) researchers.

A brief mention of the statistical measures in question helps set up our main focus. As Turkheimer and Greer note, before advances in sequencing technology, human behavior geneticists generated heritability coefficients for traits of interest. These coefficients were standardly produced from twin study work, which historically was the best way of getting a sense of the relative contribution of genes to a trait of interest as we cannot, or rather should not, conduct breeding experiments on humans. Current descendants of heritability coefficients come from genome-wide association studies (GWAS), which can be conducted on large groups of unrelated people. One key measure of interest arising from GWAS is a polygenic score (PGS), which "can be thought of as an observed manifestation at the individual level of the abstract variance ratio estimated by a heritability" (Turkheimer & Greer, 2024). Turkheimer and Greer focus on R^2 values, which roughly "describe the magnitude of the relationship between the polygenic score and the phenotypes [of interest]"

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(Turkheimer & Greer, 2024). They point out that the largest R^2 reported in an S4S study is 6.5% (0.065). R^2 are taken to be small at 0.01, medium at 0.09, and large at 0.25 in many areas of social science research but there are fields, for example, drug assay work, where only much higher R^2 values are considered indication of a large effect. By this assessment, most of the R^2 values reported by the S4S researchers, or calculated by Turkheimer and Greer when not reported, are very, very small, sitting well below the level of small effect of 0.01.

Given these very low R^2 measures, we agree with Turkheimer and Greer that S4S researchers did not uncover genetic information that could be informative, let alone actionable, for administrators concerned with campus drinking. However, it is worth asking what it would have looked like if S4S had produced such information. Suppose that S4S had been wildly successful, producing the *Gattaca*-like genetic information of "polygenic scores making reliable predictions that individuals had a 35% chance of developing a psychiatric disorder [here, alcoholism]" (Turkheimer & Greer, 2024). If a student was given their PGS, how are they to interpret it and act on it? How would this information be put to use by an administrator to address the problem of campus drinking?

For the information to be leveraged at all, it would require consent from a significant number of students to have their PGS calculated and made available to themselves or administrators. Were scores to be calculated without active consent from the student (perhaps by using the sample provided to S4S), this would be a serious ethical violation. But even if a sufficient number of students did consent to having their PGS for alcoholism calculated, it is still not clear how this information could be used in an ethical manner to address the problem of campus drinking.

If this student was already aware of a family history of alcoholism, then the PGS might do little more than quantify information the student already had. Turkheimer and Greer acknowledge this. Charitably, one might imagine that a student with no known family history of alcoholism who is revealed to have a high PGS might be motivated to refrain from drinking, or take active steps to moderate their drinking in order to avoid the consequences of developing alcoholism down the road. But it seems equally likely that such a student would react by developing pessimism about their ability to control their alcohol use, which could actually make them more likely to develop problems with drinking. Empirically, when presented with information indicating a genetic predisposition to alcoholism, people have reacted in both ways (Dar-Nimrod et al., 2013). In the absence of evidence suggesting that acquiring this information is more likely to be helpful than not, providing access to it seems irresponsible at best and unethical at worst.

Perhaps, however, this information could be used to help an administrator determine how to distribute resources and attention in their attempt to combat campus drinking. But any way this could be done seems ethically suspicious. For instance, if the administrator were to use this information to direct resources and attention away from those with a high PGS—assuming that due to their PGS anti-alcoholism interventions are most likely to be wasted on them—this would seem to problematically divert resources away from those who are most at risk. And conversely, if the administrator were to direct resources toward those with a high PGS—assuming that this is the population which needs the most help—the consequences might be equally problematic.

If an administrator used this information to advertise a responsible drinking workshop to those students with a relatively high PGS for alcoholism, this would likely entail revealing to these students that they have a high PGS for alcoholism, leading to all the problems associated with this, as discussed. Such students might feel profiled and singled out from their peers, which might make them less likely to use the resources provided. In addition, this approach would risk denying resources to those who have a low PGS but are at high risk for problematic drinking due to other factors. Even if genetic information like a PGS were integrated into a broader risk assessment including environmental factors, it is unclear what good this added information would do either for an individual or an administrator crafting policy.

Any action related to the dissemination of this information (i.e., the envisaged high PGSs) will likely involve a complex interaction between the

individual involved, administrators, and genetic counselors. Genetic counselors are clinicians usually tasked with presenting genetic information to patients. Let's briefly consider this option. Although genetic counselors are often tasked with talking patients, or parents, through the results of genetic tests on individuals, they also counsel on the basis of family history information, which is probabilistic. For example, your child has an *X* probability of developing a disease. Turkheimer and Greer's imagined case of a 0.35 probability of developing one of the alcohol-related conditions is genetic information in this latter sense. Armed with just this information, however, a genetic counselor would not be in a much better position than they would be if they had accurate family history information on the individual in question. Further, the genetic information does not provide any useful additional information that would help individuals confront and deal with their alcohol-related behavior.

Contrast this with the case of phenylketonuria (PKU), a disease that is predicted via genetic tests, inferences from family history or tests for various enzymes present in an infant's (or fetus') bloodstream. With a positive test in hand for PKU, a genetic counselor can confidently pass on a patient to a dietician, as a medically supervised diet prevents infants from developing the debilitating symptoms of PKU. No clear and actionable interventions are indicated by even the high PGS scenario being considered here. The very small R^2 measures reported by Turkheimer and Greer put clinicians, genetic counselors, and others, in an even worse position, which we think amounts to having no genetic information whatsoever to act upon.

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