

Ethical, anticipatory genomics research on human behavior means celebrating disagreement

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Summary

Despite the many social and ethical considerations in human genetics, researchers and communities remain largely siloed as for-profit, direct-to-consumer genetic testing and the application of polygenic scores to *in vitro* fertilization services become increasingly prevalent. The multifaceted challenges facing genomics, both empirical and ethical, require collaborations that foster critical dialogue and honest debate between communities inside and outside the research enterprise. This piece argues that in order to respond to the premature or inappropriate use of genomic data in industry, the scientific community needs to first embrace, understand, and be in dialogue about its disagreements. We introduce the research framework of adversarial collaboration as a way to celebrate disagreement and productively work toward policy-informed, ethical, and anticipatory genomics research.

Over the past decade, tens of millions of people in the United States alone have explored their genome using direct-to-consumer services like [Ancestry.com](https://www.ancestry.com) and [23andMe](https://www.23andme.com) (<https://www.technologyreview.com/2019/02/11/103446/more-than-26-million-people-have-taken-an-at-home-ancestry-test/>). For as little as \$10, consumers can turn to third-party, direct-to-consumer companies and receive their genetic risk profile for a host of behaviors and outcomes including intelligence, depression, and drug addiction (<https://www.genepalza.com/app-store>). For substantially more money, prospective parents undergoing *in vitro* fertilization can *optimize* the genes of their future children using polygenic scores (A polygenic score aggregates the many genetic variants statistically associated with a trait or outcome into a single measure to increase predictive power.) (<https://www.orchidhealth.com/>). Even dating apps have begun to use genomics to facilitate romantic matches (<https://www.dnaronance.com/about/>), and law enforcement agencies have ramped up efforts to use genetic databases to find criminal offenders (<https://www.gedmatch.com/>). In short, the genomic revolution has

made it increasingly possible for humans to begin interpreting, interacting with, and even manipulating their DNA.

The growing commercialization of genomics raises important social, ethical, and policy considerations. From a US policy perspective, however, little has been done to address the growing risks of genetic discrimination or the premature application of genomic research findings. One reason for this is that research into genetic influences on social and behavioral outcomes such as income or externalizing behavior elicits polarization about the risks and benefits of various applications and discoveries.^{1,2} This polarization is rooted in human genetics' ugly history^{3,4} and has grown such that researchers find themselves talking past rather than with each other, unable to articulate exactly what their disagreements are and why they exist. Disputes are too often relegated to drawn out critique-reply-rejoinders (e.g., GWAS on same-sex sexual behavior⁵ or combative Q&As sessions following lectures—neither of which do much to facilitate mutual understanding). As debates about the risks and possibilities of genomics stagnate and

policy efforts to regulate the use of genetic information languish in development, for-profit, direct-to-consumer genetic testing initiatives and prenatal genetic selection utilizing polygenic scores grow in prevalence, largely unchecked.

To achieve the necessary aims of ethical and anticipatory genomics research, human genetics must be able to outline, understand, and *celebrate* disagreements between individuals and groups. From developing new computational and statistical tools for analyzing large genomic datasets, to studying the ways in which genetic discoveries are context specific, to exploring how and why people react to genetic information, the possibilities and risks of human genomics are manifold. Despite the scientific, social, and ethical complexity of genomics, researchers find themselves in disparate groups: those who are partial to the quantitative insights of the biological sciences and those who favor the qualitative insights of the social sciences and humanities; those who are optimistic about the prospect of genomics to provide meaningful causal explanations and predictions of social outcomes and those who are pessimistic; and those

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who believe in the potential of such research to yield social benefits and those who worry about the emergence of new forms of eugenics. To limit the use of genetic discoveries for validating—or worse yet, biologically reifying—existing social inequalities, we must work to ensure that genomics benefit all and not just some. Doing so means recognizing that the social, ethical, and empirical challenges facing genomics are too expansive for any one group of researchers or thinkers to tackle in isolation.

A path forward

Grappling with the scientific nuances of the genomic analysis of social traits, while navigating genetics' powerful and contested grip on the popular imagination, calls for collaborations that facilitate open, critical dialogue and honest debate across a diversity of communities both inside and outside the academy. Unfortunately, collaboration can be difficult; researchers may feel that collaborations across disciplines and epistemologies require that participants compromise their positions and views, especially when consensus is an end goal.⁶ We believe that an overemphasis on consensus serves to reinforce existing intellectual silos and reduce the already limited incentives for interdisciplinary collaborations and community engagement. The pressure to come to agreement constrains who is in conversation with whom and leads us to miss avenues for improving the understanding, communication, and application of research findings.

What if collaboration was about more than achieving consensus? Instead, what if collaboration was viewed as a precious chance to precisely articulate where disagreements lie and why they come to arise? The framework of adversarial collaboration provides an opportunity to reimagine collaborative research and “make controversies more productive and constructive.”⁷ Adversarial collaboration is a research partnership between individuals of different and,

at times, opposing viewpoints that leverages disagreement into a constructive dialogue to inform a broader audience.⁸ This framework originally emerged in behavioral economics and psychology as an alternative to “the format of critique–reply–rejoinder in which debates are currently conducted in the social sciences.”⁷ Early applications of adversarial collaboration brought together researchers using similar methodological techniques who held different theoretical views on an empirical issue.⁹ Collaborators began with a statement outlining where they agreed followed by short debates on the issues on which they disagreed before identifying and conducting empirical studies to test their opposing hypotheses and potentially resolve their dispute.¹⁰ When necessary, collaborators recruited a neutral arbiter to help with refereeing disagreements.¹⁰ The publications resulting from these adversarial collaborations give each participant an equal amount of space within the manuscript to articulate their positions and explain from their perspective which disagreements remained after the collaboration and why.¹⁰ Such research efforts have been found to generate more impactful insights through direct dialogue.^{11,12}

Adversarial collaboration is evolving to navigate ethical and moral disagreements—disagreements that typically cannot be resolved through empirical study alone. In the starkly polarized field of genomics, adversarial collaboration's celebration of disagreement has the potential to bring together parties who may have otherwise been hesitant to collaborate.^{8,13} Genetics' fraught history and the emerging uses of polygenic scores in clinical settings have heightened the need for socially responsible research and communication. Given the ways in which this science is being quickly translated into products for consumers, public discussion and understanding of these issues is of paramount importance. By facilitating dialogue and debate, adversarial collaboration offers a constructive

way for disparate groups to build understanding and mutual respect, map the edges of disagreement, and over time, often narrow differences of opinion.^{7,14}

As participants in adversarial collaborations, we have witnessed first-hand the benefits of engaging in dialogue and debate without the pressures of consensus. For instance, our first adversarial collaboration brought together social genomics researchers and a bioethicist trained in critical theory to explore the threats and possibilities of integrating genomics into education.⁸ The members of this adversarial collaboration later teamed up with a philosopher to build a public repository of pre-existing explanatory documents on genomic studies in social and behavioral genomics (<https://www.thehastingscenter.org/genomics-research-index/>), hoping to ignite a larger dialogue on how to socially and ethically responsibly communicate genomic findings.¹³ In these examples, collaborators learned how to outline and articulate their disagreements on the utility and applicability of genomics to those operating with different baseline assumptions, priorities, and values. They began to understand the different conceptualizations of the societal risks of using genomic data to study social behaviors and outcomes and considered the trade-offs they each make in their approaches to science. In comparison with other interdisciplinary collaborations that require parties to come to a level of consensus (e.g., consensus conferences, embedded ethics), adversarial collaborations better enable those who disagree to engage with each other while maintaining their positions. In a field where disagreement engenders polarization, often at the expense of meaningful policy reform, adversarial collaboration provides a way to insert a switch-line between different communities.

Policy implications

Designing and implementing policies requires dialogue. Although improved

dialogue within academia is not guaranteed to result in meaningful changes to public policy, clarifying key trade-offs is an important initial step in the policy-making process. Yet, debates over the uncertain future of genomics continue to stall. While they do, the policies and regulations necessary for facilitating ethical applications of genetic information related to social and behavioral outcomes lag behind current uses of genomic data. For instance, despite the limited clinical validity and utility of polygenic scores, companies are beginning to offer families the promise of “healthy babies” (<https://www.orchidhealth.com/>). Polygenic scores are limited in their utility and validity for several reasons, including 1) large amounts of measurement error due to finite genome-wide association study samples, 2) the fact that they capture only the effects of common genetic variants, 3) confounding from non-genetic factors, such as indirect genetic effects and population stratification, and 4) their comparatively poor performance in non-European and admixed genetic ancestral populations.^{15,16} To implement impactful policies on the use of polygenic scores, genomics must first remove the pressures of trying to achieve consensus. Doing so will enable a more integrated examination of research questions that have typically been reserved for a particular discipline or community. For example, questions surrounding (1) which genes are associated with what outcomes, (2) how contextual factors mediate and moderate genetics effects, and (3) the ways in which information about genetic risk impacts how individuals see themselves and others ought to be considered alongside one another. Each category of question is typically asked by groups who utilize different research methods, draw upon different epistemologies, and may come from different disciplines. Yet, identifying appropriate strategies for answering them would greatly benefit from bringing together diverse insights, including those outside academia.

Let us consider one particular service offered by industry: prenatal genetic embryo selection on schizophrenia risk, as indexed by a polygenic score.¹⁶ In deciding whether and how to regulate such uses of genetic information, policymakers will want to conduct a societal cost-benefit analysis. A key piece of the cost-benefit analysis concerns phenomena studied by researchers who ask questions such as (1) have GWAS identified the regions of the genome that index genetic effects (rather than environmental confounding), and have these effects been identified precisely enough to be meaningfully useful in genetic screening? However, to understand the implications of the widespread application of genetic selection on these traits and gain clarity on the role polygenic scores play in schizophrenia risk prediction and prevention, we must also bring to bear gene-environment interaction insights from researchers who ask questions such as (2) what mechanisms do the identified genetic effects on schizophrenia operate through and are these effects robust across contexts? Even if the polygenic score for schizophrenia is strongly predictive, if the genetic effects are deeply socially mediated, then which genes connate risk in one environment will likely differ from which genes connate risk in another. Finally, to think about the psychosocial effects of incorporating genetic screening for schizophrenia into our institutions, we must turn to insights from members of the public. Those who can help scholars answer questions such as (3) how do people feel about the use of genetic data for embryo selection and interpret or even stigmatize their risk and the risk of others around them? The methodological limitations and contextual nature of polygenic scores, coupled with the psychosocial impacts of providing and receiving a polygenic score,¹⁷ may outweigh potential clinical benefits, establishing a need for regulatory policies on their application that may have otherwise been missed. In addition, if the result of prenatal screening

is to create new lines of social division, allowing selection may be net harmful to society even if we see a reduction in schizophrenia risk among the next generation. Thus, a full accounting of whether and under what circumstances prenatal schizophrenia screening using genotype would help the world (and therefore should be allowed) requires knowledge from all three domains, which seldom communicate with each other.

Challenges and opportunities

As participants in and proponents of adversarial collaborations ourselves, we believe they provide much needed avenues for proactively expanding the conversation about the social and ethical implications of molecular genetic discoveries. More importantly, we argue that it enables more intentional and expansive consideration of the kinds of research questions and perspectives that are necessary to mitigate the use of genomics to detrimental ends (e.g., justifying and exacerbating social inequality). For instance, adversarial collaborations might facilitate conversations about questions such as which traits (e.g., intelligence) should or should not be the subject of genomic research? For which traits should polygenic embryo selection be permissible? Are clinical applications of polygenic scores more appropriate than social policy applications? And, what trade-offs emerge as we try to answer these questions? In order to enact policies about, for example, evidentiary thresholds for utilizing polygenic scores in clinical or nonclinical settings, we must first have a conversation about whether it is even appropriate to use genomic data in clinical and/or social policy settings, and under what conditions. Being able to identify the breadth of perspectives and the contours of disagreement on the implications and applications of genomics will enable us to make progress in improving clinical practice guidelines, guiding the prioritization of public funding in related basic and

translational research, and determining whether and how to regulate research practices. It opens the door for more inclusive, ethical, and anticipatory genomics research, and offers a foundation upon which to begin devising policies.

As our world learns ever more about how genes contribute to the complex processes that shape behavioral and social outcomes, mining the diversity of perspectives on the uncertain future of genomics will be difficult but necessary. Celebrating disagreement is an important step toward helping genomics identify knowledge gaps, loopholes, and blind spots in existing research programs and public regulations and programs.

Data and code availability

This study did not generate nor analyze datasets or code.

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