COLUMBIA PRECISION MEDICINE INITIATIVE

PRECISION MEDICINE & SOCIETY

NEW PERSPECTIVES

THIRD ANNUAL CONFERENCE

MAY 7, 2021

COLUMBIA | PRECISION MEDICINE

Welcome Letter

Welcome to the virtual third annual Precision Medicine & Society Conference at Columbia University. This year's conference is entitled "Precision Medicine & Society: New Perspectives," and will present the work of emerging scholars in this fast-growing field.

The Precision Medicine & Society Program is an integral part of Columbia's Precision Medicine Initiative. This University-wide collaboration was created to jump-start academic discussion and research about the interplay between the biomedical advances of precision medicine and the social sciences, humanities, law, and business. It brings together biomedical and public health researchers, clinicians, and bioethicists working at our Medical Center with social scientists, legal scholars, and humanists in the Faculty of Arts and Sciences and the Law and Business Schools.

The first annual conference, held in 2019, focused on issues of particular relevance to the United States, while the second, held in 2020, brought together scholars from other countries to better understand the global impact of precision medicine and other important international issues.

Most of the presenters at our previous conferences have been seasoned scholars or practitioners. This year, the conference will showcase the next generation of scholars working on Precision Medicine & Society issues. For this purpose, we have organized two thematic sessions, each bringing together one senior scholar with three younger, emerging scholars working on a related set of problems. We hope that the ensuing discussion will bring broader recognition to the work of the younger participants, while also linking them to an inspiring model represented by the senior scholar.

The two themes were selected to capture exciting, cutting-edge research that is being conducted by emerging scholars and that is pertinent to the key concerns of Precision Medicine & Society. One set of issues relates to the promise of machine learning (ML) and artificial intelligence (AI) to provide more precise, predictive models capable of improving, individualizing, and perhaps even equalizing medical diagnosis, treatment, and care. Another set of issues relates to the ethical questions raised by genomics research—from the inclusion of underserved populations among research cohorts, to the problems encountered when extending precision medicine methods to the fields of psychiatry and sociogenomics.

We believe that Columbia University is ideally positioned to lead this conversation, not least because it was among the first academic institutions to create a program dedicated to Precision Medicine & Society. Our thanks to President Bollinger, the Columbia Precision Medicine Initiative, and its director, Tom Maniatis, for supporting the Precision Medicine & Society Program and making possible this third annual conference. We are also grateful to Roy Vagelos for his vision and support for precision medicine at Columbia.

Paul S. Appelbaum, MD, Elizabeth K. Dollard Professor of Psychiatry, Medicine and Law
Gil Eyal, PhD, Professor of Sociology
Co-Directors of the Columbia Precision Medicine & Society Program

Conference Schedule

PRECISION MEDICINE & SOCIETY: NEW PERSPECTIVES

Columbia University, New York

May 7, 2021

10:45 a.m.	Introduction by Gil Eyal, PhD, and Paul S. Appelbaum, MD
11:00 a.m.–12:45 p.m.	**The Contribution of Machine Learning and Predictive Analytics to Precision Medicine**
	Bhaven Sampat and Ashley Swanson (moderators)
11:00–11:25 a.m.	Ziad Obermeyer, MD
11:25–11:40 a.m.	Stephen Coussens, PhD
11:40–11:55 a.m.	Emma Pierson, PhD
11:55–12:10 p.m.	Dan Zeltzer, PhD
12:10–12:45 p.m.	**Q&A**
12:45–1:15 p.m.	Lunch break
1:15–3:00 p.m.	**Empirical Studies of Ethical Issues Raised by Genomics Research**
	Sandra Lee (moderator)
1:15–1:40 p.m.	Jenny Reardon, PhD, and Dennis Browe, PhD Student
1:40–1:55 p.m.	Krystal Tsosie, MPH, MA
1:55–2:10 p.m.	Daphne Martschenko, PhD
2:10–2:25 p.m.	Anna Jabloner, PhD
2:25–3:00 p.m.	**Q&A**

Ziad Obermeyer, MD

Blue Cross of California Distinguished Associate Professor of Health Policy and Management, School of Public Health, University of California, Berkeley

Ziad Obermeyer is the Blue Cross of California Distinguished Associate Professor of Health Policy and Management in the School of Public Health at UC Berkeley, where he does research at the intersection of machine learning, medicine, and public policy. He was named an Emerging Leader by the National Academy of Medicine and has received numerous awards including the Early Independence Award—the National Institutes of Health's most prestigious award for exceptional junior scientists—and the Young Investigator Award from the Society for Academic Emergency Medicine. Previously, he was an assistant professor at Harvard Medical School. He continues to practice emergency medicine in underserved communities.

Algorithmic Bias

ABSTRACT

Algorithms can reproduce and even scale up racial biases. Using examples from my own work, I'll show that a major mechanism by which bias gets into algorithms is via label choice: training the algorithm to predict a biased target variable. For example, a widely used family of algorithms in healthcare predicts healthcare costs rather than illness. But because of unequal access to care, Black patients cost less than White patients, inducing large racial bias in predictions and leading to deprioritization of Black patients. Crucially, label choice bias is fixable: I will also show that retraining algorithms to predict less-biased proxies can reduce disparities rather than perpetuate them, turning algorithms into a force for social good.

Stephen Coussens, PhD

Assistant Professor of Health Policy and Management, Columbia University Mailman School of Public Health

Dr. Coussens is an assistant professor of health policy and management at the Columbia University Mailman School of Public Health. He is a health economist who uses large-scale electronic health records and insurance claims databases to study clinician decision-making and its effects on patient treatment and outcomes. His research in this space employs quasi-experimental study designs paired with econometric and machine learning approaches to estimate causal treatment effects from observational data. His experience working with real-world data in this space has led him to pursue the development of new statistical methods to address practical causal inference problems frequently faced by social science and health service researchers. In particular, he has focused on improving the precision of instrumental variables (IV) treatment effect estimates in experimental and quasi-experimental studies, and their implications for the design of randomized controlled trials. Prior to joining the Columbia University faculty, he received his PhD from Harvard University after working as a research associate in the Urban Labs at the University of Chicago.

Improving the Precision of Treatment Effect Estimates through Compliance Prediction

ABSTRACT

A primary goal of clinical research is to determine the causal effect of treatments on patient outcomes in order to appropriately inform healthcare decisions made by clinicians and their patients. When conducting a randomized controlled trial (RCT) is not a viable option, quasi-experimental research designs using observational data and instrumental variables (IV) estimation techniques are frequently employed to obtain unbiased estimates of these causal treatment effects. IV is also commonly used even within the context of RCTs to address nonrandom deviations from assignment protocol. For a number of reasons, including the clinical judgment of healthcare providers as well as patient preferences, it is often the case that some patients randomly assigned to the "treatment" arm of a trial do not ultimately receive the treatment, and some randomly assigned to the "control" arm nonetheless obtain the treatment. In this setting, even when such deviations are correlated with patients' potential outcomes, IV produces unbiased estimates of the average treatment effect on the "compliers," the subset of patients for whom random assignment actually determines treatment receipt.

Although IV can eliminate the bias that would otherwise arise from the presence of noncompliers in a study, it does so at the cost of estimate precision. The increase in statistical noise that is generated by imperfect compliance can lead to substantial degradation of a study's statistical power, leading to imprecise "null" findings even when the underlying treatment effects may in fact be clinically meaningful. This loss of statistical power can be particularly problematic

for evaluating the treatment of precision medicine (PM) interventions. Since PM seeks to tailor treatments to relatively small subpopulations, improving the statistical power of a study by substantially increasing the number of participants is typically not feasible, so improvements in precision must be achieved through other means. In ongoing work, we are developing a framework that leverages machine learning methods to predict study participants' likelihood of compliance and applies these predictions in ways that can substantially increase the precision of treatment effect estimates, thereby improving the quality of information available to clinicians and their patients about the effectiveness of available treatments.

Emma Pierson, PhD

Senior Researcher, Microsoft New England; Incoming Assistant Professor of Computer Science, Cornell Tech

Emma Pierson is a senior researcher at Microsoft Research and an incoming assistant professor of computer science at Cornell Tech. She develops data science and machine learning methods to study inequality and healthcare. Her work has been recognized by a Rhodes Scholarship, Hertz Fellowship, Rising Star in EECS, and *Forbes* 30 Under 30 in Science. She has written for the *New York Times, FiveThirtyEight,* the *Atlantic,* the *Washington Post, Wired*, and various other publications.

Using Machine Learning to Increase Equality in Healthcare and Public Health

ABSTRACT

Our society remains profoundly unequal. Worse, there is abundant evidence that algorithms can, improperly applied, exacerbate inequality in healthcare and other domains. This talk pursues a more optimistic counterpoint—that data science and machine learning can also be used to illuminate and reduce inequality in healthcare and public health—by presenting vignettes about women's health, COVID-19, and pain.

Dan Zeltzer, PhD

Assistant Professor, Tel Aviv University School of Economics

Dan Zeltzer is an assistant professor of economics at Tel Aviv University. He received his PhD from Princeton University in 2016. An applied health economist, his research spans various contemporary aspects of healthcare delivery, including physician referral networks, medical technology adoption, the use of machine learning for predictive modeling in healthcare, and telemedicine.

Why Is End-of-Life Spending So High? Evidence from Cancer Patients

ABSTRACT

TThe concentration of healthcare spending at the end of life is widely documented but poorly understood. To gain insight, we focus on patients newly diagnosed with cancer. They display the familiar pattern: even among cancer patients with similar initial prognoses, monthly spending in the year postdiagnosis is over twice as high for those who die within the year as for those who survive. This elevated spending on decedents is almost entirely driven by higher inpatient spending, particularly low-intensity admissions, which rise as the prognosis deteriorates. However, even for patients with very poor prognoses at the time of admission, most low-intensity admissions do not result in death, making it difficult to target spending reductions. We also find that among patients with the same cancer type and initial prognosis, end-of-life spending is substantially more elevated for younger patients compared to older patients, suggesting that treatment decisions are not exclusively present-focused. Taken together, these results provide a richer understanding of the sources of high end-of-life spending, without revealing any natural "remedies."

The preprint is available here: https://www.nber.org/papers/w28162.

Jenny Reardon, PhD

Professor; Director, Science and Justice Research Center, University of California, Santa Cruz

Jenny Reardon is a professor of sociology and the founding director of the Science and Justice Research Center at the University of California, Santa Cruz. Her research draws into focus questions about identity, justice, and democracy that are often silently embedded in scientific ideas and practices, particularly in modern genomic research. Her training spans molecular biology; the history of biology; science studies; feminist and critical race studies; and the sociology of science, technology, and medicine.

Dr. Reardon is the author of *Race to the Finish: Identity and Governance in an Age of Genomics* (Princeton University Press, 2005) and *The Postgenomic Condition: Ethics, Justice, and Knowledge after the Genome* (Chicago University Press, 2017).

She has been the recipient of fellowships and awards from, among other entities, the National Science Foundation, the Max Planck Institute, the Humboldt Foundation, the London School of Economics, the Westinghouse Science Talent Search, and the United States Congressional Committee on Science, Space, and Technology. Recently, she started a project to bike over one thousand miles through her home state of Kansas to learn from farmers, ranchers, and other denizens of the high plains about how best to know and care for the prairie.

Dennis Browe

PhD Student, Sociology, University of California, Santa Cruz

Dennis Browe is a PhD student in the Department of Sociology at the University of California, Santa Cruz, and a graduate student fellow with the Science and Justice Research Center. His work lies at the intersections of medical sociology, science & technology studies (STS), public health, gender and sexuality studies, and feminist theory. Before coming to Santa Cruz, he worked in public health on a large-scale HIV/AIDS community engagement project, whose goal was to connect organizations working with HIV+ clients in both San Francisco and Oakland, and ultimately link clients into sustained medical care. He is interested in understanding how community-based healthcare models and other forms of public health do, and do not, fit into imaginaries of health and healthy living being fostered through biomedicine. He is developing a dissertation project studying the growing field of biogerontology (which investigates the biomolecular processes of aging), looking particularly into these scientists' visions of how manipulating the aging process(es) in humans can and will be translated into clinical and public health interventions.

Krystal Tsosie, MPH, MA

PhD Candidate in Genomics and Health Disparities, Vanderbilt University

Krystal Tsosie (Diné/Navajo), MPH, MA, is currently completing an interdisciplinary PhD in genomics and health disparities at Vanderbilt University. As an advocate for Indigenous genomic and data sovereignty, she co-founded the first US Indigenous-led biobank, a 501(c)(3) nonprofit research institution called the Native BioData Consortium. Much of her current research centers on ethical engagement with Indigenous communities in precision health. She also incorporates biostatistics, genetic epidemiology, public health, and computational approaches to cancer health disparities, particularly in women's health. At the laboratory bench, she developed and patented a combined targeted ultrasound imaging and chemotherapeutic drug delivery device for treating early metastases in cancer. Krystal's research and educational endeavors have received international media attention in such outlets as the *Washington Post*, NPR, *PBS NOVA*, the *New York Times*, the *Atlantic*, *Forbes*, and the *Boston Globe*, among others.

Mere Inclusion Is Not Enough: Reframing Indigenous Representation in Precision Health Research toward Empowerment

ABSTRACT

Indigenous people constitute the lowest-represented minority and ethnic group in most genomic and precision health research studies. However, most efforts to increase engagement of Indigenous people have been problematized in terms of increasing recruitment, but without correcting past research practices deemed extractive by Indigenous communities. For instance, recent efforts to increase engagement of Indigenous people in research are tied to increasing "inclusion of diverse populations" but with vague promises of someday leading to future innovations in genomic and precision health. Yet, structural barriers and lack of preventative healthcare contribute more proximally to gaps in health disparities and are unlikely to be addressed by indeterminate advances of precision medicine in Indigenous communities. Furthermore, Indigenous people have always expressed concern over broad informed consent models that they felt granted too much decision-making authority to researchers acting outside of a tribal research regulatory framework—a concern that has renewed significance in the current Big Data Era that collectivizes Indigenous genomes in databases controlled by nontribal entities.

Merely increasing inclusion of Indigenous people in precision health research without also expanding decision-making agency and equity is effectively misusing "inclusivity" as a guise for continued extractive work. Empowering Indigenous-led biorepositories enables participation and tribal oversight, but still facilitates research under tribal oversight that is more culturally consistent with Indigenous models of consent. Change is needed to build trust and encourage tribal participation in precision health research. Empowering Indigenous genomic and data sovereignty is the path forward for truly increasing health equity.

Daphne Martschenko, PhD

Postdoctoral Fellow, Stanford University Center for Biomedical Ethics; BioFutures Fellow, Stanford Department of Bioengineering

Daphne Martschenko, PhD, is a postdoctoral research fellow at the Stanford Center for Biomedical Ethics, a BioFutures Fellow in the Stanford Department of Bioengineering, and co-organizer of the international Race, Empire, and Education Research Collective (REE). Dr. Martschenko holds an MPhil from the University of Cambridge in politics, development, and democratic education and a PhD in education, also from the University of Cambridge. Her doctoral work investigated teacher perspectives on the role and relevance of genetic data for education, focusing on how behavioral genetics research on educational attainment and intelligence intersected with educators' conceptualizations of racial and socioeconomic disparities in the American education system. She has appeared in numerous podcasts including Freakonomics Radio and has had her work published in publicly accessible media outlets such as the Independent, the Conversation, BOLD Blog, and the Hastings Center Bioethics Forum. Currently, Dr. Martschenko's work advocates for and facilitates research efforts that promote socially and ethically responsible research, research communication, and community engagement with social and behavioral genomics.

"The Elephant in the Room": Social Responsibility in the Production of Sociogenomics Research

ABSTRACT

Social genomics, or sociogenomics, is an emerging field interested in understanding the relationship between genetic differences among individuals and differences in behaviors and socioeconomic outcomes. The field is interdisciplinary, drawing in sociologists, economists, psychologists, and education researchers, among others. Researchers are interested in everything from educational attainment and household deprivation, to same-sex sexual behavior, to physical and mental health. Sociogenomics evokes mixed reactions. For some, the field runs the risk of normalizing eugenic attitudes and legitimizing social inequalities. For others, it brings the promise of more robust and nuanced understandings of human behavior, and better-evidenced and more personalized approaches to clinical care, education, and social and public policy.

Regardless, a history of misuse and misapplication of genetics in and out of clinical settings raises important questions about researchers' social responsibilities. This presentation draws on semistructured interviews with sociogenomics researchers who investigate the genetic etiologies of intelligence and educational attainment. It does so to understand how researchers' motivations for engaging in a socially fraught field connect to their views on social responsibility and the challenges that come with it. In interviews, researchers highlighted the trade-off between engaging in socially contested research and the potential benefits their work pose to the social sciences and clinical research. They also highlighted the dilemmas of engaging with the public, including the existence of multiple publics. Finally, researchers elucidated uncertainties over what social responsibility is in practice and whether protecting against the misuse and

misinterpretation of their research is wholly possible. I conclude this presentation by offering ways to address some of the challenges of social responsibility in the production of knowledge. For example, I introduce an ongoing interdisciplinary project to collect and house "Frequently Asked Questions" on individual genome-wide association studies in social and behavioral genomics.

Anna Jabloner, PhD

College Fellow, Department of Anthropology, Harvard University

Anna Jabloner is an anthropologist and feminist science studies scholar and currently a visiting faculty member in the Department of Anthropology at Harvard University. She previously held postdoctoral positions at the Stanford Center for Biomedical Ethics and at Columbia University's Center for Research on Ethical, Legal & Social Implications of Psychiatric, Neurologic & Behavioral Genetics. Jabloner's research focuses on uses of genetic technologies across the societal realms of clinical practice, industry, law, and criminology in the United States. Her current book project, Future Pending: Genomics, California, and the American Technological Imagination, is an ethnography of California through the lens of future-oriented technology development. The book tracks genomics as an emerging data infrastructure that implicates Californians in a range of social engineering projects. Her new research examines ethical dimensions of precision psychiatry and this emerging field's trajectory of investigating and intervening in disordered human behavior. Jabloner teaches courses in anthropology, gender studies, and science and technology studies. Her scholarship has been published by Passagen Verlag Wien and by the journals *Science as Culture, Nature Biotechnology, Catalyst: Feminism, Theory, Technoscience,* and *Anthropology Now.* Jabloner holds a MagPhil from the University of Vienna (2004) and PhD from the University of Chicago (2015).

Mental Health Environments, or Bringing the Social into Precision Psychiatry

ABSTRACT

Echoing the global advent of precision and translational medicine, the emerging precision psychiatry field embraces uses of genomic, clinical, and environmental data to identify the causes of mental disorders and innovate pathways for prevention and treatment. While in theory aiming to consider the range of factors causing mental disorders, the field builds on advances in psychiatric genetics and neurobiology and has homed in on the biologic processes that underlie these disorders in individual human bodies, to the exclusion of environmental factors such as the social and structural interaction effects (housing, food, employment, etc.) that dynamically shape mental health. The promise of precision, in some versions, indeed entails using sociological, anthropological and historical data to generate tailored accounts of a person's health. In practice, precision psychiatry has yet been uninformed by findings from disciplines that empirically characterize contributors to mental illness at scales other than the human body and its measurement. Laying out an agenda for a research project on, and productive intervention into, the ethics of precision psychiatry, this paper will make two points and ask a question. First, empirical research on precision psychiatry ethics should have a vested interest in pushing the inclusion of mental health environments forward, so that this new version of medicine can live up to its promise of better healthcare for the public. Second, precision psychiatry can arguably become ethical only when it understands itself as hinging on the provision of care, not just the exchange of information, and, thus, as an intrinsically social endeavor. Generally, how can we build bridges

between the social, human, natural, and medical sciences such that (a) cross-fertilization in shaping precision medicine becomes institutionally anchored and (b) precision itself opens up as one possible avenue toward better health(care) rather than being posited as a foregone conclusion?