

Towards Precision Medicine, March 2020

Spero Manson (Pembina Chippewa), PhD, Distinguished Professor, Public Health and Psychiatry. Director, Centers for American Indian and Alaska Native Health. University of Colorado Denver's Anschutz Medical Center, Colorado School of Public Health. *Native Peoples and the All of Us Research Program: Inclusion, Collaboration, Governance, and Benefit.*

By Franklin Faust

Dr. Spero Manson presented on the landscape of genetic research in Native American communities and the barriers to outreach, recruitment, and engagement of Native Americans and Alaskan Natives in research. He also discussed the unique scientific challenges that arise from working with tribal communities, he and used the All of Us genetics research program as an example of the journey towards agreeable and effective research that can bring tribal communities into the fold of precision medicine.

Dr. Manson discussed how the history of tribal participation in research is a source of concern in Native communities. Two studies are particularly well known. The Barrow Alcohol Study and a study initially intended to investigate diabetes among members of the Havasupai tribe, disseminated research findings in insensitive and irresponsible ways that bred cultural stigma and economic fallout for Native communities. These studies still affect Native American perceptions of collaboration in genetic research, and they represent a fundamental disconnect between the promises made to Native communities in U.S. history and the actual outcomes of governmental interactions.

Throughout U.S. history, Native Americans have been increasingly characterized as members of Domestic Dependent Sovereignities, nations within the nation. The Federal Government developed its relationship with Native Tribes by organizing procedures for a tribal consultation processes, but tensions still exist between Tribal governance structures and institutional review boards at universities and in the Federal Government.

Dr. Manson summarized the tensions which arise from organizational, political, and cultural disconnects in the world view of Americans compared to Tribal cultures, producing systemic differences in leadership, group identity, decision making, authority, and values that make finding common ground an arduous task. Taking the time to properly sort through these differences is necessary for conducting effective research and creating longstanding relationships where both scientists and tribe members stand to benefit. To do this, Dr. Manson recommends aligning research goals and agendas to local priorities through frequent discussion and consensus.

Dr. Manson underscores that respect for tribal views and a willingness to compromise with tribal voices are paramount for a successful research collaboration. Dr. Manson suggests designing the retrieval of informed consent without excessive legal language and with consideration for tribal consent vs. individual consent. He also says researchers should ensure that tribes have a seat at the table for decisions of accountability and the control of production, publication, and dissemination, because disagreements and lack of transparency in these topics has resulted in

negative tribal outcomes and burned bridges. Knowledge of such history demonstrates dedication to forging long-term research partnerships that are successful for both parties.

According to Dr. Manson, “The Human Genome Project ran afoul of virtually every underrepresented racial and ethnic group in the country.” In American Indian Alaska, there was no consultation or true attempt in developing a partnership, and its interactions with the Navajo nation played a part in their ban on all genetic research.

To their credit, the NIH has made strides in advocacy to right the wrongs of previous failures in Native research collaborations. The NIH addressed and apologized for the failures of the Human Genome Project, and central authority figures worked to improve the government-to-government consultation process. They established organizations, committees, and initiatives to better communicate sponsorship, funding, and distribution of research supported by NIH across the country. “The advocacy within the National Institutes of Health for advancing this particular agenda has been remarkable,” Dr. Manson said.

With lessons learned, in 2015, the Precision Medicine Initiative was sent to the federal government. The All of Us research project became a funded part of the 21st Century Cures Act.

All of Us aimed to establish a cohort of one million or more volunteers that would grow over time, with each participant supplying environmental, genetic, and lifestyle information. Proven, documented practices were to ensure optimal outreach, recruitment, and engagement, and data were to be gathered through innovative methods, with proper communication regarding access and control. Policy recommendations were put in place to navigate genetic research policy and emphasize security, privacy, and usability of various Electronic Health Records (EHRs), a primary source for data on lifestyle and environment. While the All of Us project followed better staffing procedures and designed new outreach and engagement methods for Native communities, the implementation echoed the past failures of the Human Genome Project.

The All of Us program began dealing with these ORE issues, in part, by establishing a tribal collaboration group. The group drafted a framework to serve as a jumping off point towards more formal tribal collaboration. Native communities received notice that the All of Us project would soon begin and were promised that Project stakeholders were committed to a comprehensive consultation process, which included organizing listening sessions and producing online resources. So far, there have been nine federal government-to-tribal-government consultation programs that have brought together tribal leaders and representatives to All of Us research program presentations and question and answer sessions. Researchers matched this effort by attending listening sessions at tribal conferences and sessions tailored towards lay members of these communities. Together, this work hopes to address the cautionary mantra: “Nothing About Us Without Us.”

Even after teams satisfy recruitment goals, they still need to consider important practical measures for a study’s structure and goals. In the three-legged stool of precision medicine—genes, lifestyle, and environment—genes often receive disproportionate attention. Genes may play a different role in Native populations than in others. A challenge is harmonizing a study’s methods between heterogeneous tribes with different standards for membership that value

genetic inheritance to different extents. Many federally localized tribes are small and dispersed, which has important implications for studies of precision health. Since precision medicine has been most successful with rare disorders, a smaller population affects the questions that a study can realistically answer – and demands statistical methods that can work with small sample sizes.

There is little data to tell us what problems exist in these communities, and Native health data are often out-of-date, limited, and not well standardized across different studies, according to Dr. Manson.

“The answer lies in the journey,” says Dr. Manson, “I am impressed with our younger colleagues that see the importance of these issues and have stepped forward to seek out answers to these problems.” He has a vested interest in promoting the careers of young people that will provide future guidance to Native communities, forging the compromises necessary to expand precision medicine to Native communities.