It's easy in an information age for our understanding of peoples’ health to be limited — in part, due to the lack of participant diversity in clinical research trials crucial to developing successful medicine and preventative care strategies. Focusing on efforts to include those who have been historically underrepresented, and with the help of advanced technology, a research program from the National Institutes of Health aims to improve how all of us are treated.
Trial-and-Error Treatment

In 2011, Ana Pavón noticed her five-year-old son walking differently. Soon after, he began to exhibit a set of troubling symptoms, such as uncontrollable jerking movements and itchiness across his body.

“He’s okay,” her son’s doctor told her during a scheduled office visit, unable to identify any harmful symptoms or alleviate any concerns.

So, Pavón took her son to an urgent care facility. He was prescribed medication and the jerking stopped, but he developed a vocal tic. Doctors believed her son had allergies, she said.

Frightened, Pavón turned to the internet and found that her son’s symptoms matched closely with those of Tourette’s syndrome. But due to the complexity of his symptoms, the search results were dismissed.

Later on, Pavón’s son was referred to psychiatric care by doctors and placed on new medication, but his abnormal symptoms continued to worsen. He started cursing, yelling blatant profanities, and acquired motor tics in his hands and shoulders. Over time, Pavón lost hope.

“At one point, the side effects from the meds made him so depressed, I thought, ‘Maybe, he’d be better off with the tics’,“ she said.

During childhood, Pavón, herself, had difficulty receiving medical care due to her mother’s limited access to basic health care information and support. “I never saw a pediatrician,” she admitted.

However, Pavón progressively became involved in health care services as an adult, learning its importance. After moving to South Carolina in 2001, she worked at a community health center as an interpreter and patient liaison for rural families, including many immigrant families — herself, a product of one.

One day, through a fortunate, chance encounter, Pavón’s son received the correct medical diagnosis they were searching for — Tourette's Syndrome.
“I wonder if precision medicine can one day lessen these burdens,” she said, recalling the stress spent testing ill-proposed, sweeping medical solutions.

Currently, there is not a single cure by itself or preventative treatment that exists for people diagnosed with Tourette syndrome. Treatment is targeted to help control tics that interfere with daily activities, but every medication available for the condition can cause even worse side effects. No specific test to diagnose the condition exists, either. Instead, it is diagnosed by reviewing the patient’s medical history after their tics have been persistent for at least a year.

The condition may also be associated with other disorders, such as ADHD and OCD, while certain tics such as eye blinking can be confused with allergies. Blood sampling and neuroimaging studies can be used to rule out other potential underlying diseases or causes, though these methods are usually for atypical cases.

**Advancing Precision Medicine with Diversity**

Today, Pavón works for the National Health Institute’s All of Us Research Program as a patient ambassador for those in rural, underrepresented communities to ensure the future of medicine is not as painful or tedious for families facing similar circumstances.

The program stems from President Obama’s 2015 Precision Medicine Initiative — a call to transform an innovative, emerging medical concept into a clinical reality. A year later, Congress passed the 21st Century Cures Act, which granted the NIH public funding for approximately $1.5 billion over the course of 10 years towards the cause.

Consequently, NIH opened participant enrollment for All of Us nationally in May 2018. Medicine would no longer follow a “one-size-fits-all” approach, but rather it would be tailored to the individual, as NIH director Dr. Francis Collins described at the program’s one-year anniversary symposium in May.
By evaluating multiple factors of health information from individuals — such as genetic, lifestyle, environmental, and metabolomic data — the process of diagnosing and treating a wide range of conditions ailing millions may significantly improve.

This advancement is at the heart of the program, the aim of which is to collect data from one million or more American volunteers over their lifespans to accelerate research and improve health outcomes. It hopes to meet this participant goal by 2023. Most importantly, it aims to serve those who have been historically left out in medical research.

“Almost 80% of the participants so far are from communities that have been typically underrepresented in research, and 50% are racial and ethnic minorities,” Dr. Collins said regarding the program’s progress, which exceeds the program's initial goal of at least 75% of participants from underrepresented groups. “Too often, such diverse communities have been left out during medical research and, therefore, left behind when cures are discovered.”

Biased information from medical research can negatively impact the kind of medications we use to treat people, as Chris Lunt, chief technology officer for the All of Us Research Program, explained.

He gave a brief example of a female, Asian American patient who was treated for coronary artery disease. Joshua Denny, one of the program’s principal investigators, saw the patient at a medical center, Lunt told GovernmentCIO Media & Research.

Initially, doctors prescribed the patient with a common blood thinner used to stop clots from forming in the heart, but she did not respond well to the medication as someone typically would. After genomic sequencing, she was found to be missing the particular gene that produces an enzyme that “unlocks” the medication for it to work.

Once the missing gene was discovered, doctors were able to prescribe a different medication that helped prevent additional clots from forming in the heart, saving her life.
Unfortunately, lacking a specific gene for this medication is fairly common among certain subpopulations of people, such as Asian Americans.

“You can say, ‘You can’t really justify [sequencing a patient’s genome] to find out if they produce this or not,’” Lunt said, referring to arguments against individual gene sequencing based on time or financial restraints. Though, “the reality is that it is very, very rare for Caucasians [to be missing the gene]. But for Asian Americans, it’s not that rare.”

That is a significant reason why the All of Us program exists — to not only improve how we provide diagnostics and treatment to be more equitable for people but also to just work better, Lunt said. With more information about groups traditionally excluded from biomedical research, medications can become more attuned to particular groups of people who react differently to them, and as a result, be more effective.

He compared the pool of research to a swimming pool, with the depth being the amount of data collected and length being the timeframe.

“The key is to think about breadth in terms of where our priorities are,” Lunt said, “breadth to bring as diverse of an audience as we can to understand how people interact differently with interventions.”

Data Collection Technologies

Different technologies and platforms are also being used to collect information, including gathering data from participants’ electronic health records, bio-wearable devices, and certain mobile applications.

“There’s a tremendous amount of dark matter in our health,” Lunt said, and the “only way to figure that out is to collect those patterns.”

All of Us partnered with Fitbit through its “bring-your-own-device” program that allows researchers to connect to participants’ Fitbit devices to pull personally tracked health data. The team is exploring other technologies from other companies who have their own bio-wearables, such as Apple and Samsung, and intend to distribute devices to measure activity.
The program also has its own mobile application that allows participants to complete surveys and access program information on their smartphones. In addition to using a cardiorespiratory fitness app to track heart and lung health, the program is looking into next-generation development of mood apps to collect participants’ emotional states.

“As we develop more instruments to measure and understand all the factors that contribute to someone’s individual health, we can prescribe to them a set of behaviors or intakes that can help improve or maintain their health,” Lunt said.

Lunt is also excited about the prospects of artificial intelligence for data collection and analysis but said there is still a lot to consider when it comes to the current limitations with machine learning. The hardest part is coming to terms with “hyper disillusionment,” as he put it.

“At this point, people don’t realize that for machine learning to really work well, you need incredibly fine-tuned control over your data,” he said. “When they do studies to say, ‘Run a bunch of cells through visual processing and then try to learn from that,’ the first thing the system learns is which machine [the data] has run on, which site was this run in and which tech was run in the machine at the time. It’s like the noise that we create inadvertently. The way that we create the data swamps the underlying data.”

For example, sorting through the information in someone's personal electronic health record is difficult, mainly because of decentralized standards for data collection among physicians and hospitals. Moreover, defining and interpreting what good health means for a patient may be subject to multiple discrepancies.

This brings back an important, overarching ethical question, Lunt said, “Is that data collected with enough acuity to reveal the underlying truth of what’s going on with people’s health?”

**Data Tools and Patient Privacy**
According to Lunt, health researchers “couldn’t bring data together” to “see the bigger patterns that were there.” The health data was also largely inaccessible because of pre-existing information silos, which hinder new discoveries, treatment advancements, and meaningful outcomes.

That’s why All of Us is creating a national health database — a collection of data points from blood and saliva assays, electronic health records, personal surveys and more from its participants — that is accessible to researchers to study previously hidden trends.

The national database plans to be split into three tiers of data security (public, registered, and controlled) that offer different levels of access to participant data based on viewer credentials.

In May, All of Us director Eric Dishman announced the release of a beta version of the public Data Browser. The interactive tool is available online and provides summary statistics from aggregate participant data, stripped of personally identifiable information, gathered from electronic health records and participant surveys.

The Researcher Workbench, accessible to registered researchers who have completed a required ethics training and data use agreement, will be available this winter for in-depth data analyses. Afterward, a controlled tier with access to genomic information will be released to those approved researchers.

In regard to protecting participant privacy, the program wrote in a news statement, “All of Us stores all data on a secure, encrypted platform that receives routine updates. The program strips data of personal identifiers, such as names and addresses, and displays information only in aggregated groups. Users cannot view individual records. As an added safeguard, the public Data Browser limits cross tabulation, or analyses of data using two or more variables such as age and sex.”

The program will also ensure every research participant has information about their health data and genomic sequencing results given back to them, enabling people to have control of their data and health.

“That’s one of our commitments,” Lunt said. “We want to really embrace the community of participants, and then in the hope, we can bring in a broader, more
A diverse set of people than has been traditionally a part of these programs in the past.”

More than 230,000 participants have enrolled in the program so far, with a majority of those having completed the full protocol that includes sharing biospecimen. U.S. citizens over the age of 18 can voluntarily enroll through the program’s website or through participating health care provider organizations.

“This program, ultimately, will bring out the best in us,” expressed Dr. Robert Winn, one of the principal investigators for All of Us, during the program's symposium, “because when history looks at us, what I’m hoping someone will say is that we may not have gotten everything right in the beginning, but we kept it on the tracks. We kept it moving for the future.”

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