Ned Culhane
All of Us
Oral History

The All of Us Research Program is an ambitious effort to gather health data from one million or more people living in the United States to accelerate research that may improve health. All of Us is working with participants across the country, collecting many types of information over time, and building a database that many researchers can use. This new model could shape how people do research in the future. All of Us will share lessons about what works well with other research programs around the world. The program is supported and overseen by the National Institutes of Health (NIH) and is the result of NIH's Precision Medicine Initiative Working Group of the Advisory Committee to the Director, which concluded its work in 2015.

Condon: I'm Aaron Condon, and it is Thursday, November 9, 2023. I am joined by Ned Culhane, who is the Director of Strategic Relationships and the Deputy Chief Financial and Management Officer for the All of Us Research Program. Today I'm going to conduct an interview to explore the origin of the All of Us and document it as part of an oral history series for the Office of NIH History and Stetten Museum.

How are you doing today, Ned?

Culhane: I'm doing great, Aaron. It's a pleasure to be with you. Thank you for the opportunity to connect this morning.

Condon: It's a pleasure to be with you as well. Thank you for joining me today. To begin, can you tell us a little bit about yourself and your background?

Culhane: Yeah, thank you, Aaron. My name is Ned Culhane, and I have been with NIH for more than 15 years now. I started my career as a summer student with the then National Center for Complementary and Alternative Medicine [NCCAM], which is now the National Center for Complementary and Integrative Health. I was fortunate to be selected for the NIH Management Intern Program where I was able to do rotations across the agency as well as one at HHS [Department of Health and Human Services], before converting into a position in the central NIH legislative office. I joined the All of Us Research Program in August of 2017, and really just have enjoyed my time here with this program and excited to share my recollections from that time here.

Condon: How did you learn about the precision medicine effort, and how did you become part of it?

Culhane: It's a great question. I was a legislative analyst in the main NIH legislative office from, I guess it was, 2012 through 2017. At that time, I did not have this specific precision medicine effort within my portfolio but was involved in various entities with the 21st Century Cures effort. That was an over two-year effort where Congress really started to identify what were opportunities within the 21st century to develop cures. The Precision Medicine Initiative was part of that discussion. In my role in the legislative office, I did have a chance to see all the different roundtables that members had hosted throughout the country in their districts and states and was fortunate enough to staff for Dr. Francis Collins, then the NIH Director, at an event in southwestern Michigan with the Energy and Commerce Committee Chair, Fred Upton [Representative for Michigan]. It was a really great opportunity to see firsthand the discussion in that district to understand: What are the opportunities? What are the cutting-edge efforts that could lead to more cures and discoveries in the future?

Condon: Okay, and from your perspective, how did the All of Us Research Program come to be?

Culhane: It really was an exciting chance. I think with the momentum on the Hill, there was an opportunity there. I think also, if you look back, Dr. Collins, back in 2004, had identified a paper and the title of it was "The Case for a U.S. Prospective Cohort Study of Genes and Environment." At the time, the human genome project had just finished, but at that particular time the science and the technology and the cost was prohibitive for such a cohort study to be developed. But fast forward to sort of 2014/2015/2016, [and] things had changed in a way that made such an opportunity more realistic. So, I think it just was the right time with the right support, both in the Administration and the Congress to launch such an ambitious effort.

Condon: Yes. Describe your role during those early years?

Culhane: Yeah, so I was within the [NIH's] central legislative office. Then in August of 2017, I joined the All of Us Research Program within the Office of the Director as the Strategic Relationships Team Lead. My team started off very small with just me and I was fortunate to hire a few individuals as well as develop opportunities for PMF — Presidential Management Fellows — to detail with us during that time. And in the initial months, that first year, all of our efforts were really focused on the national launch of enrollment that occurred in May of 2018. It was very focused; it was all hands on deck, a very small team that was working toward this with our award partners, and it was really a great effort to see that. For the national launch of enrollment, we had many events across the country. I was selected to go with our then Deputy Director, Stephanie Devaney, as well as NINDS [National Institute of Neurological Disorders and Stroke] Director Walter Koroshetz, to our launch event in Chicago, Illinois. It was a tremendous day to see the community come together to hear different speakers talk about their personal experiences with healthcare. Different leaders in the Chicagoland area, [such as] Senator [Dick] Durbin of Illinois, gave remarks, as well as Representative Bobby Rush, and just hearing them talk about the importance of this study, the importance of Chicago being represented, it really was a reminder of why I joined the program to have this positive change in research.

Condon: That sounds like a wonderful experience. President Obama highlighted the Precision Medicine Initiative or PMI, in his 2015, State of the Union address. How did the Obama administration and the U.S. Congress come to support precision medicine?

Culhane: Thank you for the question. Going back to my old days, we had done some research and as a senator, then Senator Obama had introduced legislation both back in 2006, and 2008. The act was the Genomics and Personalized Medicine Act. There was this history that the President had while he was a senator with an interest in genomics and personalized medicine. Going back to sort of the summary of those two acts, it's really interesting, and I'm happy to share links to this for your research. But it talked about developing a plan for a national biobank and research initiative. And expanding efforts to increase knowledge about the interaction between genetics and the environment and about ways in which molecular genetic screening diagnoses and treatments may be used to improve health and health care of racial and ethnic minority populations, increased recruitment and retention of trainees in genetics and genomics. It really had this nexus and personal interest of the president. And as I mentioned earlier, the cost of genomic sequencing had been decreasing. And it just seemed right scientifically to launch such a bold, ambitious effort to really enroll one million or more individuals that reflect the diversity of the U.S. and drive precision medicine discoveries.

Condon: That term, precision medicine, what does it mean to you?

Culhane: It really is a chance to look at strategies for medical advances, both prevention, treatment and diagnosis that are tailored to individual differences. As you look at the history of how medicine, medical research, has been conducted, so often, it's been done on research on a very small subset of our population that may not reflect the broader population as a whole. So yes, tests and research have identified these things, but sometimes your genetic makeup may not react to medicine as it had done in the broader population, so you may not have the right reaction or desired outcome compared to others. I think it really is important to understand these differences and how that can help enhance our efforts to drive prevention and diagnosis, and treatment strategies.

Condon: In late 2016, I believe the name of the group changed from the Precision Medicine Initiative, the PMI changed to the All of Us Research Program. Do you remember how or why it evolved to this name?

Culhane: Yeah, no, it's a great question…and, yes, so initially, in the State of the Union, President Obama announced launching the Precision Medicine Initiative. As that was developed and launched, it contained two parts. One focus was on oncology led by the National Cancer Institute and other key entities across the government. Then the other part of it was originally described as the Precision Medicine Initiative Cohort Program. As you can imagine, PMI, or the Precision Medicine Initiative Cohort Program, or PMICP, it just doesn't quite have the ring to it as something that really gets at what the core values of the program are and where we

aim to go. I wasn't involved directly with the name change. I do think there were some efforts to understand how the program could have a name that really reflects what it hopes to do, and in something that potential participants or participants could resonate with. I think that's where we ended up with the All of Us Research Program, because this program really is intended to include all of us so that these discoveries may be applicable to all of us and not just a subset.

Condon: From your perspective, did you notice any effect of the name change? Was there any, you know, difference in the environment or in the way that you're perceived by the public?

Culhane: I don't have a line of sight into that in terms of perceptions by the public.

Condon: Okay, a couple of questions ago, you actually referred to the Cures Act. Can you describe the Cures Act and the relevance that it has to the origin of the All of Us Research Program?

Culhane: Yeah, happy to, Aaron. The Cures Act was a very large piece of legislation that got signed into law in December of 2016. It really culminated from efforts, both in the House and the Senate, to engage key constituency groups across the country. As part of that, one of the things the [PMI] program benefited from was [that] the Cures Act formally established, and in statute, the PMI effort. The Cures Act really set the stage for the Secretary of HHS as well as NIH leadership to guide this program, and it had the congressional intent and what factors should be included. It really is the legislation that formally established the program. Prior to that being enacted, the program did receive funding to get set up. But the Cures Act really did meet the moment in terms of having that sort of explicit statute within the Public Health Service Act to drive what we're doing.

Condon: Great, thank you. You may have a unique perspective as you manage the Government Relations staff. Can you talk about how the atmosphere the program was when you first joined the organization and how that's changed over the years?

Culhane: Yeah, Aaron. It's a great question. When the program was established, there were many different champions in both chambers of the Congress, as well as others within the community, I think, having several of these individuals speak in our national launch events. One thing that has changed, right, and it's, it's just a matter of time, and I think this would happen in any period. But when you look at several of the champions that really helped stand up this program, and were supportive in the early years, many of them have retired: Fred Upton of Michigan, Bobby Rush of Illinois, who I had mentioned, Senator Roy Blunt of Missouri, Senator Lamar Alexander of Tennessee, they all are no longer serving in the Congress. I think that's one thing that has happened in terms of just the ecosystem of the Hill; some of the champions, they have since moved on. The program has worked to identify new champions on the Hill to support the program into the future.

Condon: Right. One of the most heralded goals of the All of Us Research Programs to is to recruit one million active members or participants. Another goal that doesn't get quite as much attention as that is the sharing of data to research institutions. I love this goal. I try to highlight it when talking with colleagues across the agency or describing what we do outside of the office. Essentially, the availability of data that the All of Us collects enables researchers to skip participant recruitments for their own studies. How did the data sharing elements begin? What models, commitments or concerns lead to including it in the *All of Us* design?

Culhane: Aaron, thank you for the question. It's a great point. One thing that our team has really focused on as we engage with stakeholders is to think about our program, really, as a scientific infrastructure endeavor. We're building this longitudinal cohort of one million or more individuals that reflect the rich diversity [of the US] and making that data broadly accessible. That was one of the core values and something that came out also, and I should have mentioned this earlier, right, but as part of the effort to establish the program. After the State of the Union address in 2015, NIH Director, Dr. Collins charged his Advisory Committee to the Director, through a Working Group focused on the Precision Medicine Initiative, to come up with a report, and that was released in September. That really helped outline the importance of what is needed. And I think that broadly accessible data is so critical. We are building this platform engaging with participants, both to empower them about their health decisions with their healthcare providers, but then also allowing the research community to have access to this in a secure and protected environment. Our program specifically is disease agnostic, we are not focused on a particular disease or condition. As you know, much of the rest of the NIH is very focused on particular diseases, conditions, or types of science, I think, as you look at our program now in November of 2023.

Just let me take a second to step back and walk you through some of the timeline because I think oftentimes science is very: Let's do the experiment, let's collect the data, let's analyze it, and then release it. But with our program, we have taken a forward leaning look to identify ways as to how can we expedite and actually get data out there as quickly as possible, so that researchers may start to leverage the great contributions our participants have provided for this scientific study to drive precision medicine discoveries. Back in May of 2019, just one year after launching national enrollment, the program launched a data browser which had information online at the aggregate level, to help the research community start to understand the types of data collected, etc., so that they could start thinking about the scientific questions they may wish to pursue. Back in May of 2020, just two years after national launch, the program began beta testing of the data platform, the researcher workbench, and in March of 2022, the program released its first data set that included genomic information, and that included nearly 100,000 whole genome sequences as well as 165,000 genotyping arrays.

One important thing too is the program has had a commitment to including those that have been historically underrepresented in biomedical research. Nearly 50 percent of the data in that first genetic or genomic data released was provided by participants who self-identify with a racial or ethnic minority group. If you just go back to this past April, the program released additional whole genome sequences which brought the total to nearly 250,000 whole genomes sequences available in the researcher workbench. And this makes the genomic data set the world's largest, most diverse of its kind integrated with other robust data. It really is an effort. We are about

five and a half years after launching national enrollment. We're making tremendous progress both on our goal to enroll 1 million or more individuals, as well as ensuring that this data is broadly accessible in a safe environment so that researchers may start doing an analysis. It's really a great effort to be part of.

Condon: Great, thanks for that. I'm glad that you mentioned diversity in your answer. Because my next question is about diversity. It is clear from my work within the program, as well as my review of historical material, that inclusivity has always been paramount in both the enrollment of participants and in the workforce composition of the All of Us Research Program. Why is it important that participants be from diverse ethnic histories or socio-economic origins?

Culhane: Yeah, no, it's a very important question. As you look at the history of science and genomic studies, more than 90 percent of them to date have been done on individuals of European ancestry. Those insights are really missing critical information that is lacking because it's been really focused on these individuals of a certain ancestry. By focusing on diversity, it really is an opportunity to understand if there are other genetic variants or information that helps shape and drive interactions with biology and environment to understand how different populations may be at a greater risk for certain conditions, may have different types of progressions of diseases, etc., that because of the way that research has been conducted to date and the populations they focused on, we just haven't had that line of sight yet.

Condon: From your perspective, are you aware of any of the steps that have been taken to ensure that traditionally underrepresented communities are involved in the program as participants?

Culhane: Our program really has had a very intentional effort to meet participants where they are, and under the leadership of Dr. Karriem Watson, who's our chief engagement officer, he and his team have led efforts to engage numerous community partners that have connections with important communities across this country, and really engage in a bi-directional relationship to understand their perspectives about participating in research, any concerns that they may have. I mean, unfortunately, Aaron, there have been many historical transgressions that have happened to specific communities over time in the medical research environment. It's a shame that that has happened. These communities have an understanding of that and a reluctancy to engage. Our program has really started efforts to recognize that and help stress how it is important for these communities to be reflected in this study so that insights [and] knowledge gained from this can actually be truly representative of all of us, because without their participation, we're not going to be able to gain that insight.

Condon: Great, thank you. Really, I think that speaks to the historic mistrust of government and also medical institutions. As part of that, privacy is always a concern — being that, you know, some populations are scared that their information might make it to the wrong hands for the wrong reasons. While privacy is always a

concern when gathering [and] storing study participant health data, from your specific perspective, what are the main ethical challenges you see with collecting, storing, and reporting data to participants?

Culhane: Yeah, and I know from my time with the program, really privacy and security is a very large concern both to the participants as well as various stakeholders that we interact with about the program. I think, if I may share, I am a participant myself within this program, and there is a lot of information that you are able to contribute. I think as the program has set up its interactions and how it collects information and communicates [that] it's very transparent with participants. It goes through great lengths to describe through our informed consent process about the information gathered, why it is needed. Also what are some of the risks of participating with a study. The program is very mindful as it provides information in aggregate as well. There's a code of conduct that we've developed that all researchers accessing our data must go through. There's trainings and other efforts in place to really ensure that researchers are using this information correctly to advance science and not for other nefarious purposes.

Condon: Thank you, what is the greatest challenge that All of Us has or will have in reaching its goals?

Culhane: As a program, one of the challenges is really first getting to one million participants. I think as we launched in 2018, no one could have envisioned the COVID pandemic that we went through, and I think, as a program, we were able to pivot. We had to stop in person enrollment, because that was the safest thing to do both for potential participants as well as our frontline staff. We did have a decrease in our enrollment numbers and, as with the larger biomedical research community, had to adapt to how we conduct research. I think there was also a scientific opportunity to better understand how our participants were interacting with the pandemic and faring, so we actually had a survey to look at that and gain information from our participants in real time about their experience during the pandemic. Because we had bio samples being collected in the month leading up to the pandemic, we did a serology analysis to [see if] the SARS-CoV-2 virus [was] present in any of our participants ahead of the first declared cases within several states. It's really interesting to see that as a nonscientist and to understand, hey, this is a program that we're involved in and some of the interesting questions we can ask and get insight into.

I think the other challenge is, we really want to build relationships with participants for decades. Since I completed high school in Massachusetts, I was aware of the Framingham Heart Study that started many years ago, and, I think, probably recently celebrated its 75th anniversary [the study began in 1948 and celebrated its 75th anniversary in 2023]. I'd have to double check that, but that is a very small study that happened in the town of Framingham, Massachusetts, that has transformed the way that we understand cardiovascular risk factors and other pieces of information that we just take for granted now, but back in the 1950s, and 1960s, we just didn't have the information or insight. I remember our founding director, Eric Dishman, he really sees this [All of Us] as a relationship with participants for decades to come. I think that's something. How do we build those relationships and engage with participants and continue to gain insight and whether it's through surveys, other

ways that they may provide information back to the program for researchers to gain further insight? How do we continue to foster and nurture that moving into the future?

Condon: All right, excellent. Thank you very much, then that actually concludes my list of questions. Is there anything else do you want to share about your experience with All of Us?

Culhane: I think one thing that has hit home is that really this has been the most driven organization that I've been involved with in my 15 plus year career, and it really is something that we all care so passionately about—I know you do—as to how can we enable this program to be successful. I think it is important to drive scientific discovery and I think a part of our mission really is to make the program an indispensable part of medical research, and a positive catalyst for change. I think I've been able to see bits and pieces of that through my time here and am just really excited about the future.

Condon: All right, excellent. Thank you very much. I appreciate your time today.

Culhane: Aaron, can I jump in with one other thing too, I'm sorry. One effort is, as we think about researchers and ensuring that this resource really is that indispensable part, [that] one of our partners convenes a research summit with high school teachers. I think they've done it for probably two or three years now, and it was held this summer. I was talking to my colleague, and one thing that I'm incredibly proud of is, [that] with that information, I was like, "Hey, like, is it okay, if I share this with some folks in one of the high schools that I went to?" And I was able to reach out to the science chair and, obviously I had gone to high school many years ago so it wasn't someone that I was familiar with back in my time there, but it's actually the institution that President Obama went to for his high school education as well. So Punahou School of Honolulu, Hawaii was able to send a teacher to this, and this teacher is actually using All of Us as a way to help teach current students about precision medicine and information and research. I'm incredibly proud to see something like that come full circle, both in terms of our platform being this resource that can be used in classrooms across this country and [that] I kind of regret that I didn't have such experiences, because maybe I would have pursued an actual degree in the research realm, rather than on the administrative side.

Condon: That's wonderful to hear, and it's quite an interesting anecdote. I would think that, you know, we're going to make huge changes with this program. That's what I see from my perspective, but I think what we're unable to measure at this point is the impact we could be having on those future researchers. While this is the beginning—I guess the beginning was in 2004, almost with Dr. Collins' first paper similar to the subject, really, but this is still the beginning—I imagine what it could be in 50 years when our kids will be building on this. That's just wonderful. It's a great discussion today, and I do thank you for it.

Culhane: No, thank you again, for taking the time.