Dr. Akinlolu Ojo
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. It is Tuesday, November 21, 2023, and I am joined by Dr. Akinlolu Ojo, who is actually a longtime All of Us awardee and consortium Principal Investigator, as well as the Executive Dean of the School of Medicine at Kansas University Medical Center. 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. Dr. Ojo, how are you today?

Ojo: Very well, Aaron, thank you.

Condon: Excellent. To begin with, can you give us a little bit about your background, and how you became involved with the All of Us Research Program?

Ojo: My medical training specialty is in the field of internal medicine and nephrology. Over the last three decades, I have worked as a clinician, a researcher, and a medical educator. Most of my research work has been in clinical research with a particular focus on chronic kidney disease in people of recent African ancestry. I came to know of All of Us when it was the federal Precision Medicine Initiative (PMI), when it was announced by the President, the 44th president [Barack Obama] in 2015.

Condon: Okay, great. And that's when I first heard about it as well. When did you become aware of the Precision Medicine Initiative in the field?

Ojo: In the middle of the early 2000s: 2005-2006. There were many advances in the area of oncology primarily, and it was about that time, I am not an oncologist, but it was about that time that I started to learn more about precision medicine, in the context of oncology therapeutics. At about the same time, there were efforts in the

FDA to have a mechanism in place to help accelerate the application for approval process for those medications. There was a precision medicine effort in the FDA as well. So, I will say, my initial knowledge of precision medicine was in the context of precision oncology, in about 2005-2006. Of course, the concept had existed well before that. All those were accelerated, of course, by the completion of the whole genome sequencing, as well as the rapid advances in information technology.

Condon: And I know that they leveraged the Cancer Genome Atlas project as well to help come to those results in the early 2000s, so that's wonderful. Can you tell me how you became involved with the All of Us Research Program?

Ojo: I was moving to Arizona at about the time that the NIH Office of the Director issued the first notice of funding opportunities to assemble a precision medicine cohort of a million or more individuals. In Arizona, we worked with several people and several colleges within the university and with Banner Health, which is our primary clinical partner in Arizona, to develop a proposal for the first set of applications that were received, that were submitted to what we now call regional medical centers. We received one of the first five awards in June 2016, I will say.

Condon: Okay, and can you help me understand a little bit more about your role during those inaugural years?

Ojo: I was the Principal Investigator of the Banner University Medicine of Arizona Consortium. And during those initial years we, together with the other members of the Steering Committee and the NIH leadership, were responsible for working on the initial protocol for the first program developing an IRB application in collaboration with Sage. We spent about a year and a half in preparation to launch enrollment. Many of the partners in terms of regional medical centers, the laboratory of Mayo Clinic, that are part of the All of Us today, as well as the federally qualified health centers, were there in the beginning. Over that initial one and a half years, many more partners joined, including community organizations to help with engagement, and additional regional academic medical centers were brought in during 2017, for a total of 11. During those planning stages, when we were talking about the protocol, what initial procedures would be in the protocol, one institution withdrew, that was the Geisinger Health System, because they were dissatisfied with some of the way the protocol was evolving in that it was not consistent with what was in the funding opportunity announcement. And there are some contentious issues that we had to work through.

Condon: It's understandable why. You're working in a new field, almost. And there's a lot of sensitivity around the subjects that we're tackling. Let me back up for just a moment. You did mention Barack Obama's mentioning the Precision Medicine Initiative at his 2015 State of the Union address. From your perspective, how did his presidential administration, him, as well as Congress, begin to support the Precision Medicine Initiative in the United States?

Ojo: When the Precision Medicine Initiative was announced by President Obama at the State of the Union, it resonated with many people in the country because it conveyed the sense that we are on the cusp of making the practice of medicine individualized, that every person with the help of this initiative will have access to care at the right time, in the right place, and that care will be tailored for that individual. That resonated throughout the country. Shortly after that, as they were preparing to issue the defense for the opportunity announcement, there was, to my knowledge, at least one important effort that was overseen at the White House and that was developing the security and the confidentiality regime of the data that will be collected, and how that was going to be a major and serious effort. There was also effort to emphasize from the beginning that the individuals who participate in the Precision Medicine Initiative as it was called then, were not going to be research subjects, they were going to be partners in research and so [there would be] a strong emphasis on confidentiality, a strong emphasis on the benefit of the of the Precision Medicine Initiative as a step towards broad availability of individualized care, as well as the elevation of participation into a partnership rather than a research subject that is having things done to them by scientists and investigators. I think these were the salient features of the Precision Medicine Initiative that resonated with all segments of the population, especially racial ethnic minority populations. Also, as the program was being launched, emphasis was placed in the original white paper that was first developed that if we're going to get to a state in the country where we reduce significantly or even eliminate health disparities and [achieve] health equity, the All of Us program or the Precision Medicine Initiative was going to help us to do that because of that concept of individualizing care, tailoring care to the need of an individual, [and] taking into context all the attributes that make each one of us a unique person.

Condon: In your answer, you hit a lot of the phrases that we say around here regarding precision medicine. I'd like you to if you can expand on that a little bit. I mean, what does precision medicine mean to you?

Ojo: Precision Medicine means to me that the treatment or prevention of disease will occur in the context of multi-dimensional information about an individual from their genetics, to their behavior, to their environment, and all other aspects of the life of individuals where they live, where they work; all that information from all those domains will be taken into account in customizing the treatment of disease, the prevention of disease, for every individual. The analogy that came in very early into the process that I use, because it resonates with me, is the idea of prescription glasses or prescription contact lenses. Every person who gets corrective lenses has a prescription that is customized for that individual. And that is analogous to the concept of precision medicine, in that your glasses are made for you and not for anybody else. And it fits you perfectly, well, as perfect as we could given the information that we have about the characteristics of your eyesight.

Condon: That’s a good analogy. I don't think I've heard that before. I think that's a perfect fit for the definition of precision medicine. So, thank you for that. The precision medicine cohort, the Precision Medicine Initiative Cohort Program or PMICP was a term used for the program between 2015 and the summer 2016. Then the name changed to the All of Us Research Program. Can you tell us if you notice any effects of the changing of the name or the rebranding, and what you think about the rebranding personally?

Ojo: My own sense and experience are that it is a lot easier to connect with participants, as well as the medical community as a whole with the All of Us Research Program as the name rather than Precision Medicine Initiative. Precision medicine is a technical jargon. It is accurate, it's an accurate jargon. But it doesn't explain the concept of the program in a catchy phrase. I think All of Us emphasizes a spirit of collectiveness. And yet, in that collectiveness we are going to derive benefits that is unique to the individual. I think the All of Us name captures that very well. It rolls off the tongue easily. It is a terminology, or a phrase, that people use in day-to-day life in order to describe all of us in our daily activities. And so, it's a readily accessible phrase to me and is readily accessible to everyone, regardless of the level of their education, their social economic status, and whatever language they are fluent, or conversant, with.

Condon: Great, thank you. The current enrollment goal of one million participants in 10 years is ambitious. The Working Group determined that they would reach that goal within four years of the program enrollment start date. Why did that change from the initial four years to now 10 years, and what's being done to reach the goal of enrolling one million participants?

Ojo: The number by itself is ambitious because it's not been done before in our country, and it is also larger than what other countries have done. Most importantly, it is more comprehensive than any similar initiative anywhere in the world. Prior to the US program, there was the UK—the United Kingdom Biobank, UK Biobank of 500,000 [participants] initially. And, as you know, that program was nowhere near as comprehensive as the All of Us program. And it's been done in the context of the national healthcare system that you have in the United Kingdom. So, it was less of an ambitious effort to undertake in the UK. To set out to enroll more than a million or more people was ambitious, regardless of the timeframe that you set. I believe the timeframe for enrolling one million or more in five years was ambitious but achievable. I don't know what went into the initial decision to set a target of one million people in five years, but, it was clear that we, if you look at the academic medical centers, the original academic medical centers that were the initial cohort of institutions that started enrolling people, the first five and then the second five, we all presented information that we have access to such large populations, that we have patient bases with electronic medical records that we are currently seeing across consortia, that will make it possible for us to be able to achieve those enrollment goals.

Secondly, the history of the UK Biobank will suggest that it is feasible to enroll such a large number, because in the UK Biobank the uptake was very, very fast. We didn't need to, I don't think, take into consideration the fact that it was a somewhat different, if less comprehensive effort, at least in the base cohort without the special studies that UK Biobank started doing in a subset of those individuals. It was reasonable, given access to the population and strong support from Congress and the president [and the] line item budget that were laid out for a long period of time. We were all enthusiastic and felt that it was possible to enroll that one million people within a within the initial five years. Once we started the enrollment process, it became clear that the logistics of enrolling people and retaining them in the program requires a lot more time, a lot more effort, and we were not prepared to embark on a program that was all digital. At a time when, maybe even up to now, 30 percent of the

country is not versatile or have no sufficiently functional access to digital technologies in a way that will enable them to be able to participate in a paperless program, which was what All of Us was from the beginning. That coupled with the logistics of getting biosamples to Mayo Clinic. We realized that very quickly, so the initial group of regional medical centers, our goal was 20,000 participants a year. That means that you had to enroll more than 100 people every day. To enroll one person takes an average of three hours. On top of all that states may require an additional two to three hour per person. After the first year, it was clear that those goals were not achievable. They were modified, using the rate of enrollment at that time, as a gauge to say okay, maybe we should modify the targets to a 7-year enrollment period instead of a five-year duration of enrollment.

As that was taking place, then there was the COVID-19 pandemic, which further setback the enrollment and retention activities. I believe that the goal of reaching one million people in the next four years is attainable. I believe that it will require additional resources to the current partners, especially to the Regional Medical Centers, to be able to furnish themselves with more personnel to sustain engagement and attract more people to the All of Us program. When the first set of requests for applications that was issued in late 2015, early 2016, we were expected to plan for follow-up visits. In fact, the application that we submitted, we said that we're going to be seeing every participant once a year. And the way people get into a study and stay in study is when they have contact with the investigators. In this case, we are making the participants partners and we didn't have in place a strategy that will include in-person visits for a subsequent period of time. And, for a variety of reasons for which no one is to blame, we did not have in place a set of expectations for people who joined All of Us what to expect for the next 5-10 years. Typically, as you know when somebody joins a research study, you will say this research study is going to require you to have blood tests X number of times, every year. You will come in and attend a visit X number of times, every year, every other year, or whatever the frequency is, this is what you will get back from the studies at this interval. We didn't have that; we still don't have that laid out. We had a series of follow up surveys that we added into the pile of surveys that people needed to complete and notify them electronically when they are supposed to do those surveys.

I may be wrong; I'm going to use my experience in studies over the last two decades: If we had included an annual in-person visit in the All of Us program, we could have doubled enrollment rate and doubled our retention rate. Because the original goal was that people are going to bring their family members, they're going to bring their friends. Well, if we're not seeing people in person at all, after enrollment, how are they going to bring people? How are they going to tell friends they are going? [How] are they going to excite people enough to say you need to join All of Us? If somebody is excited about the All of Us program and they enroll, an average person is going to have difficulty in asking a friend or group of friends or family members to enroll if it requires that they go online to sign up, to go register to do this. But if I say, “Hey, I'm going to my office visit next week. I would like you to come with me to meet a team that I'm working with, join this program.” It has much more benefit to enrollees. Our participants can be the greatest recruiters for the All of Us program. I think that we shortchange ourselves by not including in-person follow-up visits, and I know that in-person follow-up visits double the resources that are needed, but I believe that that is where the focus of resources should be. I think enrollees are better ambassadors. They will engage their communities more than many of the community engagement partners that we have because of the nature of people in family and community organizations, and I have an award from the All of Us to engage the community and direct them to go enroll.

The community engagement partners, they are valuable, and it is true that they are disseminating information about the All of Us program into the community, but they are as effective ambassadors as individual participants who are continuously interacting with the program. People sign up for a research study with a full understanding that it is going to require time and effort on their part, and when that time and effort requires driving to a place to meet and interact with people, the investigators who are their partners. I think by the time you make a decision to sign up for this study, you will have become incorporated into that decision, the time and effort commitment that is going to come down the road. We have not had that in the All of Us program. I enroll; I don't know where my information is in terms of being able to go back in and do my survey. I can see that [happens] for a lot of people that I know. To make it a paperless digital program from the beginning I think was not the optimum approach. To make it digital or paperless and not have touch points like in-person visits, year after year, I think is very suboptimal. That is why I nearly jumped out of my seat at the last steering committee meeting when Josh said [that] we are planning towards a reassessment strategy that will include reassessment for everyone and the subset will have more detailed reassessment. I think that is the greatest thing that can happen to the program.

Condon: I think it's important, what you mentioned about those within the community, bringing in their families and other people in the community. I think that's especially important when we're talking about historically underrepresented communities and healthcare research. It's clear to me from my work within the program, as well as my review of the historic material, that inclusivity has always been paramount to both the enrollment of participants and the workforce composition of the All of Us Research Program. Why is it important, from your perspective, to have a diverse set of program participants?

Ojo: Medical advances in the United States inadvertently left many segments of our population behind. When we do clinical trials, we are looking for people who [can] easily be compliant with the protocol. We're looking for people [for whom it's] easy to get access to lots of resources to enable their participation. We are looking for people that we're familiar with as study team members in the context of the history, and all the things that are going on in our country, that have not readily invited the involvement of underrepresented populations. Precision medicine, more than anything ever, requires that we have information on all segments of our population to be able to come up with the best prevention and treatment approaches. If we have a large chunk of the population that we don't know how well the medicine is going to work in them, that we don't know how they're going to respond or how we're going to be able to diagnose conditions with new tools, we just extrapolate. My own field of kidney transplantation, the care of people who have kidney failure, is a good example where when a new drug is being tested for transplantation, the investigators are looking for low risk patients [because] by definition in kidney transplantation [they] have better allograft. African Americans are high risk patients. So, you do a clinical trial for a new drug, and this has been going on for more than 50 years, you have very few African Americans or Native Americans, and non-White Hispanics. Very few of those populations [are] in your clinical trial, then you end up with a set of results. Since you have patients from those communities, you simply extrapolate out to treat those individuals. There are at least four or five medications that we use in transplantation that were not tested in an adequate number of African Americans in the registration clinical trials because African Americans are considered high risk for poor allograft outcome. When

the drug is approved, we just increase the dose given to African Americans empirically. That is a very crude approach.

To the extent that health disparities, health inequities, are drawing out a trillion dollars every year in losses in our economy on top of the incalculable human suffering, of not having access to good care, I believe that a big part of the answer to the solution is to be able to capture information from all segments of the population, so that researchers can learn as much about their genes, about the physiologic and behavioral characteristics or how their disease behaves biologically, to be able to assemble the necessary information and make the discovery that will benefit those individuals. Nothing is more individualized than precision medicine. If you don't have information about who people are, can you give them individualized care? I think the crux of our solution to health disparities is the All of Us program. I believe the program is doing a fantastic job in bringing into the program the faces of individuals from all segments of the society, because that is a powerful signal. That sends a message, removes doubt, and I know from the beginning, that there were a lot of focus group and listening sessions that were conducted before the All of Us program ever went into the field, to understand different communities, African American, Hispanic, non-White Hispanics, Native Americans, and I think that part of the program is one of the best aspects of the All of Us program that it has done a great deal to bring into the All of Us as participants and as researchers, underrepresented—racial, ethnic underrepresented minorities. I take off my hat to the to the All of Us program for spending resources and making that a commitment.

Condon: Excellent, great. Privacy is always concerned when gathering and storing participant health data. From your perspective, what one of the main ethical challenges you see when collecting, storing and reporting data to program participants?

Ojo: I was concerned about the privacy and confidentiality and a very high possibility that people will say, I'm not giving my DNA to the federal government. I'm not giving my electronic health record to the government. I think one of the most brilliant aspects of this program was that there was a White House privacy policy or committee or something that was set up at the beginning to specifically address the issue of data security and privacy in the All of Us program. When I meet participants, or when I give presentations about All of Us, I usually tell people, the audiences and individual participants when I have the opportunity to meet them, that the privacy principles and the infrastructure to ensure the privacy was a major part of this program that started in the White House before the program was launched. I don't know where I learned it from, but it was early in the beginning program to tell people that your All of Us data is as secure as your bank information. We're not going to say that there will not be any breach, but if you think about your bank information and your bank account, which is highly secure—there is hacking, of course, and banks lose people's information. Well, that is a level of security that people understand. Your data is as secure as your bank information. It allows people to say, okay, my bank information is pretty secure. Occasionally there are bad actors and steps are taken to address it. But if you told me that I don't have anything to worry about privacy, because it has the same level of security and protection, I am willing to accept that. I have been pleasantly surprised, especially in Arizona, on how it was not an issue for people. They were not concerned. People were excited to have the opportunity to participate. We

promise them their genomic information; that drives people, and to be able to contribute to these advances. I'm sure you have seen those anthems that were made by Wondros. I show that at every presentation.

Condon: I'm glad you said that. Actually, I don't think that we're leveraging those enough, so I'm gonna get access to all of them and I'm going to start forcing them on people because they are they're wonderful and we paid a lot of money for them, and they're just wonderful media you know, clips of what this could be. From your perspective, what is the biggest challenge All of Us has or will have in reaching its goals?

Ojo: The biggest challenge that we have in reaching our goal is not enough boots on the ground at the regional medical centers which are the healthcare provider organizations, and lack of a structured set of expectations for every participant. We can excite people about joining the All of Us program, but we cannot tell them other than you're going to get survey online at some periodic interval, and as we develop additional surveys, you will get them. We want you to do something every six months. Number one, that is not asking enough of people. When people sign up, they're willing to put in the time and the effort to do it well. You should be able to say in six months you will get a phone call or an email. If you don't respond to an email, you get a phone call. In 12 months, we're going to see you back here. And when that 12 months is close, when we reach more than 10 months, we will give you a window of four months now you can come in for that visit. And [at] that visit you're going to spend 45 minutes doing X, Y and Z. They're going to collect two tubes of blood; we're going to collect blood. We're going to contact you in six months to participate in a special study. And if you are interested you will have to sign up separately for that. But we don't have that and so there is no, there is no hook into our participants, and we face as much challenge in enrollment as well as retention because there is no hook. There is a soft hook. It is a digital hook. And people may respond to a text message of a deal for Black Friday or shop on Amazon, or any of those things. I don't think text messages, deals, and Instagram flags are strong hooks or a strong motivator for people to engage. I think the regional medical centers and the HPOs [healthcare provider organizations], FQHCs [Federally Qualified Healthcare Centers], we all have to do more to connect with participants who are already in the program and also bringing more people into the program.

Condon: Okay, that makes sense. That also concludes my list of questions for you today. Do you have anything else you'd like to mention to get it on the record?

Ojo: I would like to have it on record that coming back to the All of Us meeting [All of Us Face to Face Meeting in Bethesda, MD held October 19-20, 2023] this time, I was enormously impressed by the level of organization, the structure, the format of the meeting, and the approach to setting goals. Josh stood up there and described the goal for All of Us for next year. All those things were not there five years ago. It was a struggle. I think All of Us has matured due to the effort of a lot of people and attending that standing committee meeting in October gave me a strong, a high level of confidence that the goals will be achieved.