Dr. Sheri Schully
Behind the Mask
September 17, 2021

Barr: Good afternoon. Today is September 17, 2021. My name is Gabrielle Barr. I am the archivist at the office of NIH History Museum. And today I have the pleasure of speaking with Dr. Sheri Schully. Dr. Schully is the Deputy Chief Medical and Scientific Officer of the *All of Us* Research Program, which is part of the Office of Director. Today she's going to speak about some of the ways in which the *All of Us* Research Program has contributed to NIH COVID-19 efforts. Thank you very much for being with me.

Schully: Thanks for having me. I appreciate it.

Barr: Briefly, can you please introduce what the *All of Us* Research Program is and its mission?

Schully: The *All of Us* Research Program is a really innovative research effort to recruit a million or more participants that reflect the broad diversity of the United States and to collect several data types on them, including surveys that the participants complete, whole genome sequencing, genotyping, as well as electronic health records and other data sources. It's pretty ambitious, one of the biggest studies ever funded to date and one of the most data diverse studies as well.

Barr: When did the *All of Us* Program begin brainstorming ways it could contribute to understanding COVID-19?

Schully: The *All of Us* Program was in a very fortuitous place, and as soon as the March 2020 timeframe came around, and we started to see that this was a worldwide pandemic, we started to think through how can we leverage the infrastructure that we already have in place to answer important questions that might be relevant to COVID-19. Which is how we developed the serology study as well as a series of surveys for our participants, evaluation of EHR [electronic health records] for early signs and diagnoses of COVID-19.

Barr: How's the *All of Us* Program engaged in education and community outreach because I know that's also something you all have been doing during the pandemic?

Schully: We developed resources on our webpage, as well as reached out through several of our community partners, to try to get out information about the pandemic as well as vaccination, and different treatment modalities, etc., so that our participants can be well informed about what's out there for them.

Barr: I think we're going to start with some of the ways that the *All of Us* has taken charge and looking at the COVID-19 pandemic. You were talking about the survey that you all put out. How did you and others decide on the types of questions you are going to ask on the COPE survey, which is the survey that you all put together for COVID-19, and what did you and your team hope to learn? It was interesting to see the sections on mental health, substance abuse, and discrimination that maybe you ordinarily would not see in a health survey.

Schully: The team that was responsible for the survey development worked very closely with other NIH groups to ask questions about symptomology of COVID so that we can combine data with other studies, but the *All of Us* Program is quite different in that we focus on our participants' lived experiences. We really wanted to explore the mental health impact as well as the economic impact of this pandemic. The current survey not only focuses on symptoms and what we might see in a typical COVID-19 survey, but specifically asks about the effect of COVID-19 in other aspects of there lives. For example: Has social isolation left you feeling more depressed or down?; Have you lost your insurance or your job or anything like that, because of COVID-19? So really getting into the causes affecting your life in general, not just about symptoms. Many of these things could be huge stressors that lead to longer-term chronic diseases, and we wanted to ensure we captured these experiences as well.

Barr: When did you add the discrimination portion, or did you already foresee that this could be an issue for people?

Schully: We added questions about discrimination early on because we started to see that there were some differences in people who were contracting COVID-19 and others that don't, and we wanted to ask that question to see if there was some feeling of discrimination that some of our participants may have been feeling during this time.

Barr: Yeah. That's discrimination in terms of being part of studies and treatment. Did anyone report in that section feeling discriminated against in other ways, like the Asian-American community has been so discriminated against at this time, which could affect their mental health?

Schully: The innovative thing about the *All of Us* Program as a whole is that we are creating an infrastructure for people to do research on, we aren't doing that research ourselves in-house. So, I don't know what the answer to that is, but we are really hoping that people will leverage the resource to ask those questions.

Barr: There are several iterations of the COPE survey, I should say that before asking my next question. Can you talk about the different iterations, and how you modified the questions to reflect different stages of the pandemic?

Schully: The first few, specifically, were a little bit longer and asked about symptomology, as well as the other effects of COVID-19, and then as vaccines became available, we saw this as an opportunity to ask about vaccine uptake. If they were not planning on getting the vaccine, why that is. As we've seen, a lot of changes happened throughout the pandemic; we tried to be flexible and really adjusted surveys so that we can address the questions that were relevant at the time.

Barr: A very high percentage of people have responded. I saw over 60,000 responses, which is really exciting, but people could respond to the survey more than once to the different iterations. What percentage of those who responded answered the survey at least twice, because that would be interesting to follow?

Schully: Actually over 124,000 participants have responded to the COPE minute surveys.

Barr: That’s great.

Schully: Then we have over 60,000 that have responded to at least two of our COPE surveys. That's pretty good as far as being able to track things over time. There is a small percentage of people who have done all six COPE surveys.

Barr: What networks did you use, or [how did you] put your surveys out there for people to respond to?

Schully: We have various mechanisms to implement our surveys. They live on the participant’s digital portal and participants that they can always go to and answer any surveys that are outstanding. But those who prefer can get a SMS text as well as an email. Those are two different ways they can be alerted that there's a survey in the portal. Then we also have a computer-assisted telephonic interviewing survey modality, where they can call a site and an interviewer will walk them through the questions, and we're able to capture their responses that way. So that's been effective, especially in underrepresented populations.

Barr: What arrangements have been made for people that may have other disabilities who can maybe not see the text or the computer?

Schully: One is the telephonic interviewing that I mentioned, and we are working on various modalities of how we might reach various groups.

Barr: That's exciting. What were some of the difficulties in crafting, disseminating, and analyzing or putting together the data from the server?

Schully: Trying to find the balance between how we can match what other studies are doing so that our data can be combined as well as meeting our participants where they are, which is really around how this pandemic is affecting people holistically, not just if they were infected with COVID-19, but how did it affect their ability to get a job or have insurance, etc. It's always difficult coming up with a survey, especially whenever you're trying to come up with one in short order, so that you can really answer a question that's emerging and needs to be answered right away like with COVID-19. It was a huge effort by a large number of people within our consortium as well as NIH staff who put it together and implemented in a very timely fashion. We were so excited that we had these data available for researchers to analyze especially since it was launched six times. It allows researchers to look at people over time, which is great.

Barr: I know you said that your program doesn't look at the findings, but have these findings started to be looked at by others, and if so, have there been notable observations?

Schully: We do have people who are using some of the early COVID data. On our website, which is researchallofus.org we have a research project directory where you can see what different researchers are doing with our data. You can see the researchers that are using the survey data from our COPE survey or combining it with electronic health record data as well as survey completions of other types.

Barr: When did the *All of Us* Research Program launch the minute surveys, and what types of information did they gather?

Schully: The minute surveys are an extension of our COPE surveys, and specifically, we changed the name because we want it to make clear that participants could take the survey in minute or less. Those came about specifically when we started to think about people getting vaccinations and wanting to know what type of vaccination they got, as well as if they had any breakthrough infection. The other thing is trying to understand why people may be hesitant to get the vaccine.

Barr: Do you hope to put out another survey given the Delta variant and all the questions surrounding the boosters?

Schully: We were not specifically going to ask about the Delta variant, but we are interested in breakthrough cases, which we've seen a lot more during the Delta variant during this pandemic. We are hoping to put out a minute survey this fall that asks about plans to get boosters for folks who have gotten the first two, or one if they had Johnson and Johnson shots, and their plans for getting boosters. We're waiting on the FDA actually to make a decision. I think it's going to be today; that's exciting, but we are hoping to ask about that question because it's something that a lot of our participants are asking about.

Barr: Are there other questions that you're hoping to ask that have come about?

Schully: If you've gotten the vaccine, and if you've already answered yes, you will not see more questions. But for those who've answered, no, it's asked again, “Do you plan on getting it, and why or why not?” Some of those questions will still appear for those who have not gotten vaccinated, but for the most part, the newest questions are about boosters and things like that.

Barr: Another aspect of *All of Us* has been working on electronic health records. Can you speak about how the All of Us program has contributed to the electronic health records being analyzed to better understand COVID-19 origins and its different manifestations?

Schully: With electronic health records, we’ve partnered a lot with the National Center for Advancing Translational Sciences [NCATS] and the N3C [National COVID Cohort Collaborative] to really look at what are the symptoms of COVID 19? How can we diagnose or evaluate people that may have actually been COVID-19 positive but didn't have a positive PCR test or don't have one within the EHR record? And then also specifically looking at the long-COVID phenotype. Here, we are looking at people who have had a positive COVID test and then looking at the symptoms that they may have lingering for months after and trying to define what the long COVID phenotype looks like because it's very complex.

Barr: A third way that you have been very involved with looking at COVID is serology, which is something personally you have done a lot with. How has the All of Us program supported antibody testing on samples from

enrolled participants to understand COVID-19 origins and spread? In what way did the serology test differ from other COVID serosurveys? There have been a lot of COVID serology surveys by a number of groups.

Schully: When COVID-19 really first broke out in March of 2020—when you see a pandemic or epidemic very early on, there is transmission throughout person-to-person contact, but the prevalence was very low at first. So, you may not see it on a national level. We really wanted to understand for participants that a blood specimen collected between January and March of 2020, in how many of those we see a signature for having COVID-19. We undertook a very rigorous testing modality, where testing was performed on the Abbott platform, as well as the EuroImmun platform. When an individual tested positive for antibodies on both tests- meaning that they had both the nucleoprotein as well as the spike protein, we labeled them as positive for COVID-19 antibodies. Had we just done any one test, we had easily 250 or more cases show up during that time. But since we did this rigorous, very conservative screening, we found nine individuals who had COVID-19 antibodies during this very early period. Seven of those were before the state's first reported case. We found cases in Illinois, Massachusetts, Wisconsin, Pennsylvania, and Mississippi. And we're now going to be following up with those individuals to find out if this was a community-spread type of thing, or if these individuals had traveled in December of 2019, all the way to March of 2020.

Barr: How did you choose those particular tests to look at their antibody? There's a number of different testing platforms out there.

Schully: There sure are, and that was the challenge that we had at first. One of the things that the *All of Us* research program really has is a set of core values that we have with our participants- one of those is returning information as much as possible. It was decided very early on that we'd like to have a test where we could actually do it in a clinical setting so that we can return the results to our participants. In order to return results, they have to be done in this sort of what's called CLIA or clinical type setting. We partnered with the National Cancer Institute at Frederick and contracted with Quest Diagnostics to have that done in a clinical setting and have been returning results to those who were positive and those who were negative during that time period with the caveat, this was a year ago, you may have contracted the virus since then, but at the time when you gave blood sample, you did not have antibodies for this.

Barr: Did you see anybody in your testing that showed that there is possible infection with COVID-19 earlier than January, like in 2019?

Schully: The interesting thing is that we were testing specifically for antibodies. The antibody we were testing for is IgG, immunoglobulin G, and that typically takes about two weeks to appear in a person's system. The fact that we saw seropositive samples on January 7 tells us that that person likely contracted the disease in December 2019. That timeframe can vary from 10 to 15 days, but for the most part, it's two weeks average, when you start to see detectable levels in the blood.

Barr: What are some things that you're going to look at specifically? Are you going to see if they have long COVID effects? What are some of the other questions they're going to look at?

Schully: We can certainly look at the EHRs and see if they are having signals for long COVID.

Barr: That's very interesting. You have been involved in a number of ways with all of these endeavors. Can you speak about what your role has been managing these different aspects of the *All of U*s response?

Schully: I have given scientific input on all three of these efforts that we've done. I specifically led a lot of the serology in conjunction with a great team who helped me execute and get this done and return results to participants. We're excited that we were able to do that. Another team led the survey efforts.

Barr: Do you all have plans to launch another large serology study?

Schully: We don't currently have plans to do a large serology study; I think that was that specifically was designed so that we can look at the early stages of the pandemic. Now it would be complicated now that folks have gotten vaccines, they will have antibodies that are in response to vaccine, specifically to the spike protein. We don't have plans to go back out and do another serology study although we have been asked by participants who've gotten the results if we were willing to do that.

Barr: Can you talk about some other ways that you think that the *All of Us* program probes the pandemic? I know that these three things were done, but you have also other plans.

Schully: We're really trying to get our overall cohort, and the COVID 19 pandemic really had us pivot. We were still doing our normal everyday work and making sure we were engaging with our participants and making sure that they felt heard and that they were part of a program that's going to help affect the health status as a whole. We're really trying to get back to getting that cohort up and running with the realization that several of our sites are still shut down because of various Delta variants and things like that and pandemics being in hotspots. We're trying to make sure that our frontline staff as well as our participants are safe, but we want to get back to the overall cohort and answer some of the important questions that we have there.

Barr: Can you talk about what it was like to balance your COVID-19 work with your mission and what you do? I'm sure it was very difficult. Can you talk about how you went about doing that?

Schully: That definitely was not an easy, straightforward call because we have a lot on our plate every day just to get one million people engaged, performing whole genome sequencing and genotypes, and answering surveys. I think scientists felt a need to, if they have the resources and the right study to answer questions about how this pandemic started and how we might stop something like this earlier next time it happens, the need to be able to do something.

Barr: It's great that you all had so many samples from before March.

Schully: Prior to the pandemic, we were approaching 3,000 people enrolling per week, which was amazing. It was really great to have very diverse and very numerous samples from across all 50 states. Not many resources have that type of infrastructure in place.

Barr: As a person, what have been some personal challenges and opportunities for you throughout this year?

Schully: I think some of the challenges are ones that a lot of other people are facing, including having to telework during this whole time and oversee a very complex project while moving to totally virtual wasn't easy, but we made it work. And certainly, [the pandemic] added the other piece: just how do we keep our overall mission as a cohort to recruit a million diverse participants successful, while balancing this additional work? I think that a lot of people had to deal with sort of new and unexpected things popping up. We weren't alone in that, but it was not easy.

Barr: Well, is there anything else that you would like to share either about your COVID work with the *All of Us* Program or just in general?

Schully: Just for readers to know that they can join the *All of Us* Research Program (joinallofus.org) or sign up to have access to the amazing data that we have available for researchers (researchallofus.org).

Barr: Sounds great. Well, thank you very much for all your work that you have done, and I wish you and everyone who works with you continued safety and success.

Schully: Thank you so much. It was so great talking with you.

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