

Case Study: *All of Us* Research Program

Background

Representation of diverse populations is important in clinical trials, in part to understand whether drug efficacy or effectiveness, dosage, and safety are equivalent across populations as well as for reasons of appropriate access to cutting edge therapies.

The *All of*

Us Research Program

(<https://allofus.nih.gov/>) is a large observational research study, part of the Precision

Medicine Initiative (PMI) and supported by National Institutes of Health (NIH).¹ The *All of Us* Research Program, launched nationally in May 2018, serves as a repository that is collecting data from a diverse and representative U.S. population and across a variety of health conditions. As of April 2020, the program has over 350,000 participants enrolled and plans to provide access to de-identified and encrypted data to researchers.²



The mission of the *All of Us* Research Program is to enable and accelerate health research and medical breakthroughs. One of its strategic priorities is to ensure that the program recruits a diverse group of participants – focusing on participants of every race, ethnicity, sex, gender, and sexual orientation who live in United States, and inclusive of individuals in rural and urban settings, with and without health insurance. A 2019 review of the *All of Us* Research Program indicated that more than 80% of participants in the *All of Us* Research Program are from groups that have been historically underrepresented in biomedical research and data repositories or clinical trial data to date.³

¹ Devaney S. All of Us Research Program. National Institutes of Health. National Advisory Child Health and Human Development Council. Jan. 31, 2017. Available online: https://www.nichd.nih.gov/sites/default/files/about/advisory/council/archive/201701/Documents/201701_devaney.pdf [Accessed Aug. 8, 2018].

² National Institutes of Health. Data Snapshots - All of Us Research Hub [Internet]. Available online: https://www.researchallofus.org/data-snapshots/?_ga=2.23730355.827964377.1586792768-646145407.1586544775 [Accessed April 13, 2020].

³ All of Us Research Program Investigators. The "All of Us" Research Program. *New England Journal of Medicine*. 2019 Aug 15;381(7):668-76.

Pre-launch stage: Considerations and steps taken

During the early planning process for the *All of US* Research Program, the NIH conducted public workshops on issues of design and vision for the cohort and issued two Requests for Information.^{4,5} One of the workshops concluded that continued engagement of a broad range of stakeholders would be needed to plan, execute, and sustain the PMI cohort program. As part of this larger public engagement effort, a survey of U.S. adults was conducted to measure support for such a study, acceptability of various design features, and to identify and prioritize concerns from the public.⁶

In addition to hosting public workshops, the NIH also conducted a preliminary pilot study,⁷ sponsored focus groups,⁸ sent out surveys,⁹ and held listening sessions with people about their hopes, ideas, and concerns regarding the collection of detailed and sensitive health information from a million or more people over their lifetimes.¹⁰ The listening sessions targeted LGBTQI groups,¹¹ vulnerable groups (sexual and gender minorities¹²) and others to understand their specific concerns and foster public engagement. In addition, online surveys were conducted to determine preferences of potential participants of the program. Seventy-nine percent of the U.S. adults who responded to the survey were supportive of a large national cohort study.¹³ Levels of support for the study as well as willingness to participate were consistent across most demographic groups.

⁴ National Institutes of Health. Summary of Responses from the Request for Information on Building the Precision Medicine Initiative National Research Participant Group [Internet]. Bethesda: National Institutes of Health; May 28, 2015. Available online: <https://www.nih.gov/sites/default/files/research-training/initiatives/pmi/pmi-workshop-20150528-rfi-summary.pdf> [Accessed Aug 21, 2018].

⁵ National Institutes of Health. Request for Information: NIH Precision Medicine Cohort—Strategies to Address Community Engagement and Health Disparities [Internet]. Bethesda: National Institutes of Health; June 22, 2015. Available online: <http://www.nih.gov/precisionmedicine/rfi-announcement-06022015.htm> [Accessed Aug. 21, 2018].

⁶ Kaufman DJ, Baker R, Milner LC, Devaney S, Hudson KL. A survey of US adults' opinions about conduct of a nationwide Precision Medicine Initiative® cohort study of genes and environment. *PLoS One*. 2016;11(8).

⁷ Beasley, D. Verily, Vanderbilt to test enrollment in U.S. Precision Medicine Pilot. *Health News*. Feb 25, 2016. Available online: <https://www.reuters.com/article/us-health-us-precisionmedicine-idUSKCN0VY1BL> [Accessed Aug 20, 2018].

⁸ Kaufman D, Murphy J, Scott J, Hudson K. Subjects matter: a survey of public opinions about a large genetic cohort study. *Genet Med*. 2008;10(11):831-839.

⁹ Murphy-Bollinger J, Bridges JF, Mohamed A, Kaufman D. Public preferences for the return of research results in genetic research: a conjoint analysis. *Genet Med*. 2014;16(12):932-939.

¹⁰ Dishman, E. "I handed over my genetic data to the NIH. Here's why you should, too." *Stat News*. June 13, 2018. Available online: <https://www.statnews.com/2018/06/13/entrusted-my-genetic-data-nih/> [Accessed Aug. 20, 2018].

¹¹ The Montrose Center. The LGBTQI Health Community Listening Sessions – All of Us Research Survey. Huston. Available online: <http://www.montrosecenter.org/all-of-us-research-survey/> [Accessed Aug 20, 2018].

¹² Baker, M. UCSF to Develop National Network for Health. Data of Sexual, Gender Minorities. University California San Francisco. Aug 22, 2017. Available online: <https://www.ucsf.edu/news/2017/08/408116/ucsf-develop-national-network-health-data-sexual-gender-minorities> [Accessed Aug. 20, 2018].

¹³ Kaufman D, Murphy J, Scott J, Hudson K. Subjects matter: a survey of public opinions about a large genetic cohort study. *Genet Med*. 2008;10(11):831-839.

The opportunity to learn about one's own health information from the study appeared to be a strong motivation to participate.¹⁴

The *All of Us* Research Program continues to successfully engage people and provide them with information about participation.¹⁵ From the outset, the program embodied the following recruitment and enrollment ideas and marketing strategies to encourage diverse inclusion in clinical research:

Recruitment and enrollment ideas	
<p>Eligibility criteria: The <i>All of Us</i> Research Program considered how to address barriers for certain groups. Minorities are more likely to be un- or under-insured, to seek care at under-resourced hospitals, and to have concerns about the cost of participating in a clinical trial.¹⁶ Lack of or inadequate health insurance can act as a barrier to enrollment in clinical trials for several under-represented populations, including racial and ethnic minorities.¹⁶ Language complexity and translation are also considered to be barriers for certain populations.¹⁶ Enrollment as a participant in <i>All of Us</i> Research Program encourages inclusion of diverse participation by stipulating that:¹⁷</p> <ul style="list-style-type: none"> - No health insurance is required. - Joining the program and any appointments or activities that are part of the study are free of costs. - Participation is irrespective of one's nationality or health status. - Spanish speaking advisors are provided. Plans are underway to add additional languages. - No computer, tablet or smartphone devices are required to join. 	

¹⁴ National Institutes of Health. Request for Information: NIH Precision Medicine Cohort—Strategies to Address Community Engagement and Health Disparities [Internet]. Bethesda: National Institutes of Health; June 22, 2015. Available online: <http://www.nih.gov/precisionmedicine/rfi-announcement-06022015.htm> [Accessed Aug. 21, 2018].

¹⁵ Ross, B. Precision Communication for Precision Medicine: How NIH's All of Us Is Tackling Patient Recruitment [Internet]. Clinical. Research News Online. Aug 2, 2018. Available online: <https://www.clinicalresearchnews.com/news/2018/08/02/precision-communication-for-precision-medicine-how-nih-s-all-of-us-is-tackling-patient-recruitment.aspx> [Accessed Sept. 11, 2018].

¹⁶ Ford JG, Howerton MW, Lai GY, Gary TL, Bolen S, Gibbons MC, Tilburt J, Baffi C, Tanpitukpongse TP, Wilson RF, Powe NR. Barriers to recruiting underrepresented populations to cancer clinical trials: a systematic review. *Cancer: Interdisciplinary International Journal of the American Cancer Society*. 2008 Jan 15;112(2):228-42.

¹⁷ National Institutes of Health. Who can join, All of Us Research Program [Internet]. 2020. Available online: <https://www.joinallofus.org/en/who-can-join> [Accessed Sept. 11, 2018]

- **Benefits to encourage participation:** Participants are offered a one-time payment of \$25 in the form of cash, gift card, or electronic voucher if they agree to provide blood, urine, saliva samples and to have physical measurements such as height, weight, blood pressure and heart rate recorded.
- **Building trust:** Building trust across the diverse population and understanding concerns/feedback through community partnerships is critically important.¹⁸ The *All of Us* Research Program utilizes community advocacy groups and participant advisory boards at participating health care organizations provide reports on participant feedback to better understand what was successful and what continues to be a challenge. Privacy and security of the information collected are considered important issues.
- **Privacy Safeguards:** The data that participants give to the *All of Us* Research Program are personal, and the program is designed to follow strict security protocols and processes to ensure protection.¹⁹ All the data that are received by the *All of Us* Research Program are encrypted and de-identified before they are deposited on the secure platform. In anticipating of opening access to the data for research, the *All of Us* Research Program plans to require requesting researchers to undergo ethics training and to abide by a code of conduct for data use. In addition to this, the platform tracks researcher activity and no data can be downloaded from the platform.
- **Legal Protections:** Participant data in the *All of Us* Research Program are afforded special legal protections and the program has U.S.-issued Certificates of Confidentiality to protect the privacy of research participants.

Marketing strategies

- **Community Resources:** The *All of Us* Research Program produced brochures and documents as resources to potential participants. These resources are available on the *All of Us* Research Program website (<https://allofus.nih.gov>) as free, downloadable material to assist community members explain and disseminate information about the program. These brochures are customized based on communities, and include:
 - National Brochure - General Community
 - National Brochure - African American Community
 - National Brochure - Asian American Community
 - National Brochure - Hispanic American Community
 - Program FAQ (Document with 60 answers to common questions) and National Program FAQ (7 most frequently asked questions)

¹⁸Sankar PL, Parker LS. The Precision Medicine Initiative's All of Us Research Program: an agenda for research on its ethical, legal, and social issues. *Genetics in Medicine*. 2017 Jul;19(7):743-50.

¹⁹National Institutes of Health. Privacy Safeguards – Join All of Us [Internet]. Available online: <https://www.joinallofus.org/privacy-safeguards> [Accessed Aug. 8, 2018].

- **Multi-media educational resources:** In addition to available brochures, the message about the *All of Us* Research Program is disseminated through short videos that include information about the program, its benefits, and the importance of diverse participation. The videos are posted online (<https://allofus.nih.gov/news-and-events/all-us-sharable-resources>) and also on a designated YouTube channel (<https://www.youtube.com/channel/UCQId1TfpwPaYiDIGlxEhlkA>) accessible to the public. Videos are also available in Spanish.
- **Additional informational resources:** Workshops, webinars, and a 37-week national tour were held to invite community members to join the cohort. The events were free and open to the public, assisted by volunteers that, additionally, offered other interactive sessions: CPR trainings, face painting and balloon art for the children, photo booth, live music, and art, all to promote the *All of Us* Research Program.²⁰
- **Representative Considerations:** Marketing strategies, documents, and pictures consciously represent diverse populations and promote inclusion. All resources are freely accessible, translated and customized based on the targeted community.

What will success look like?

The *All of Us* Research Program invested considerable time and resources from its vision in 2015 to national launch in spring 2018 to understand and ensure diverse recruitment. To be successful, the *All of Us* Research Program will need to add value to its stakeholders: participants, health care providers, researchers and communities. Recruitment into the study is estimated to continue into 2024 with new sites adding to the weekly recruitment rate of 3,000+ participants.²¹ As participants are longitudinally followed over decades to come, the *All of Us* Research Program should help researchers better understand health and disease of underrepresented populations, and as a result, improve accuracy of diagnoses, disease- prevention strategies, treatment selections and targeted therapies. We will all continue to learn from analyses of the *All of Us* Research Program's successful strategies.



²⁰National Institutes of Health. Journey and Events - Join All of Us [Internet]. Available online: <https://www.joinallofus.org/journey-and-events> [Accessed Aug., 20, 2018.]

²¹All of Us Research Program Investigators. The "All of Us" Research Program. *New England Journal of Medicine*. 2019 Aug 15;381(7):668-76.