Engagement and Feedback on Genetic Ancestry and Trait Results from >100,000 *All of Us* Participants

Hannah Hoban[1], David Brazel[1], Cynthia L. Neben[1], Clara M Mbumba[1], Alexandra Myers[1], Anju Ondov[1], Bryanna Ellis[2], Leslie Westendorf[2], Anastasia Wise[2], Scott Topper[1], Alicia Y. Zhou[1]

1. Color Health, Burlingame, CA 2. National Institutes of Health, Bethesda, MD

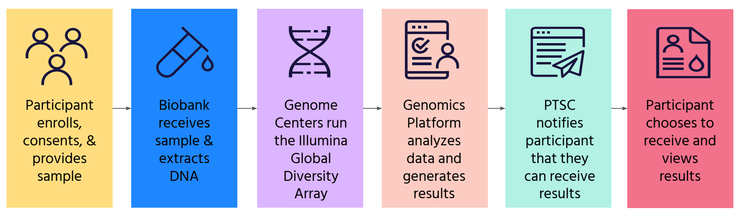
Introduction

The National Institutes of Health (NIH) *All of Us* Research Program (*All of Us*) 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[1]. *All of Us* is committed to creating a cohort that reflects the diversity of the US, with individuals who have traditionally been underrepresented in biomedical research (UBR). *All of Us* includes the following populations as UBR: racial and ethnic minority groups; children and seniors; sexual and gender minorities; people living with disabilities; people with barriers in access to care; people who have low income or low educational attainment; and rural residents. A key success metric of the program is to be of value to its constituents: participants, health care providers, and researchers.

Establishing authentic engagement with participants and providing value for them is important to long-term retention and continued recruitment of participants from diverse populations[1]. One opportunity to provide both value and authentic engagement is returning personalized genetic results to participants. In November 2020, the program launched the Genetics Engagement Module (GEM) on the Genomics Platform, to begin returning genetic results to participants. These include genetic ancestry and four non-clinical trait results (bitter taste perception, cilantro preference, ear wax type and lactose intolerance). Here we describe the return of results process as well as participant engagement and feedback.

Methods

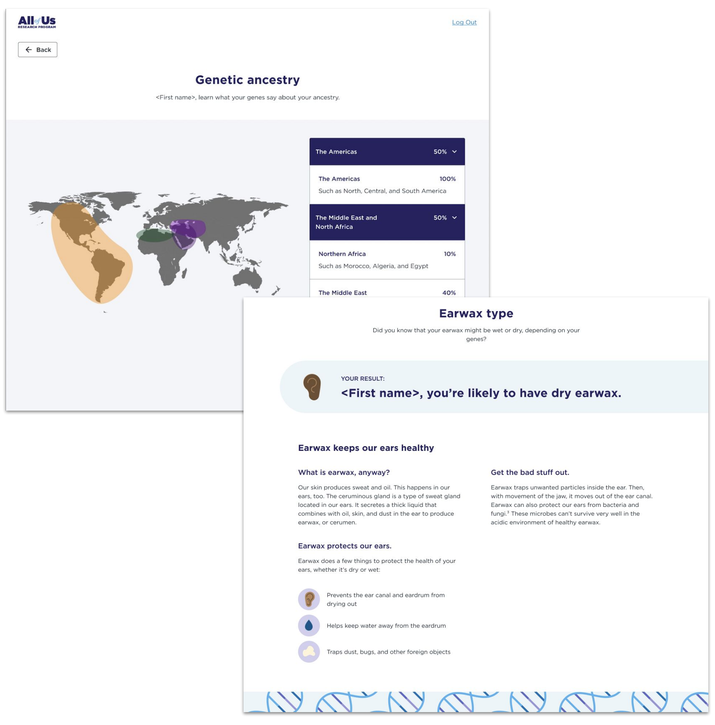
Figure 1. *All of Us* result generation process.



Result Generation and Participant Experience

All of Us participants enroll in and provide samples for the program through a variety of methods including in-person at Healthcare Provider Organizations and mobile clinics or online. Participants subsequently complete a consent for genomic return of results (gROR), including genetic ancestry and non-clinical trait results. Samples are stored and extracted at the Biobank (Mayo Clinic) and processed utilizing Illumina Global Diversity Array (GDA) at one of three Genome Centers (Baylor College of Medicine, Broad Institute of MIT and Harvard, University of Washington). Data is analyzed and results are generated by the Genomics Platform (Color). Participants are then notified either by email or SMS by the Participant Technology System Center (PTSC, Vibrent Health) that they are eligible to receive results. Participants complete an informing loop, or a series of screens with information on the benefits and risks, about receiving genetic ancestry and trait results. At the end of informing loops participants select 'yes', 'no', or 'maybe later' to receive results. Participants who selected 'yes' are then able to immediately view their genetic ancestry and trait results (Figure 2).

Figure 2. *All of Us* genetic ancestry and trait results screenshots.



Survey Analysis

Once a participant has viewed their results, they can complete a brief set of survey questions within the Genomics Platform to share their experience, ask additional questions and provide generalized feedback. These survey questions include Likert-scale based questions, yes-no questions, and open ended, free text questions. We analyzed a random subset of 10,000 free-text surveys from January 2022 to October 2022. Participant responses were extracted and coded into predetermined categories to assess participant experience.

References and Acknowledgements

- [1]The All of Us Research Program Investigators (2019). The "All of Us" Research Program. NEJM, 381:668-676.
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Results

Figure 3. *All of Us* genetic ancestry and trait uptake.

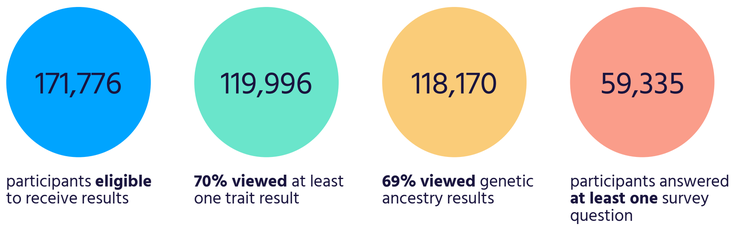


Figure 4. Uptake by participants who were determined to be underrepresented in biomedical research (UBR).

The rate of participants who were determined to be UBR remained steady through each step of the return of results process: 73.3% for gROR consent, 72.5% for participants' data analyzed and notified, 68.5% for trait informing loops, and 68.2% for genetic ancestry informing loops (IL).

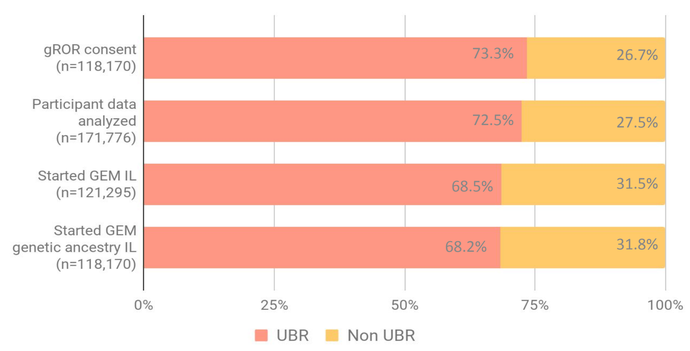
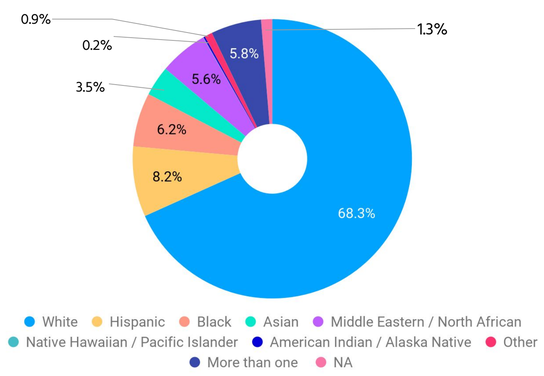


Figure 5. Demographic Information of participants who viewed their genetic ancestry results.

(A) 68.3% of participants that viewed their genetic ancestry results identified as White, of whom 31.4% were UBR by a different category. Additionally, 8.2% self-identified as Hispanic, 6.2% identified as Black, and 5.8% identified with more than one race or ethnicity.



(B) Genetic ancestry results were viewed equitably across all age brackets, with the largest age bracket being 65-74 year olds (21.5%) and the lowest being those 85+ (0.6%).

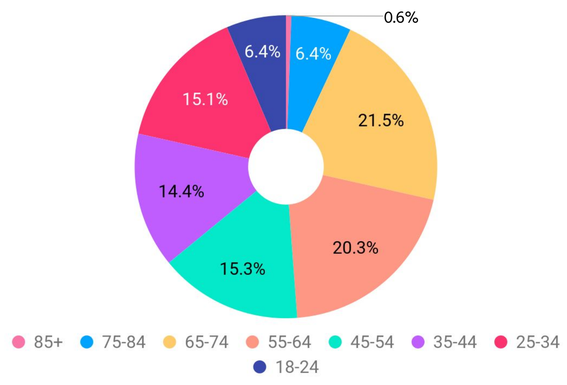


Figure 6. Participant satisfaction with receiving genetic ancestry and traits results

On average, participants were highly satisfied with their results; out of a 5-point Likert scale, participants were satisfied 4.3/5 overall, with the highest satisfaction rating on their genetic ancestry results and the lowest satisfaction rating on their cilantro preference results. That cilantro preference had the lowest satisfaction given was not necessarily surprising as there are many non-genetic components that can affect cilantro preference.

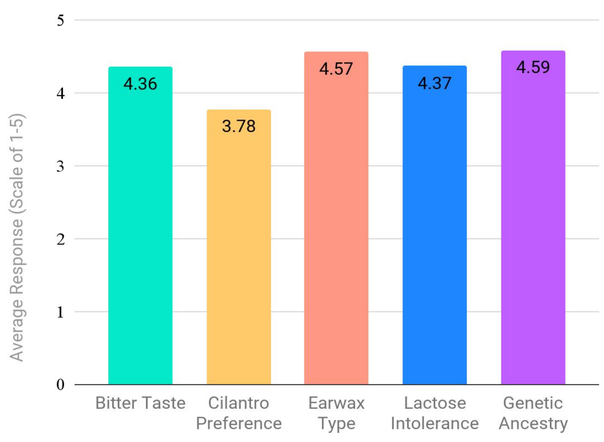


Figure 8. Participant understanding of their trait results.

Participants were asked "How easy or hard is it to understand your <trait/genetic ancestry> results?" with answers on a 5-point Likert scale. Participants responded that the results are easy to understand, with an average score of 4.6/5.

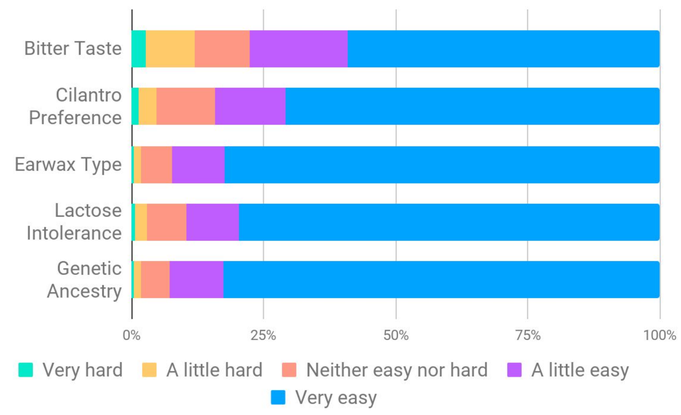


Table 1. Free text responses from participants to their trait results.

Participants were asked, "What questions do you still have about your [trait] results?" and "Is there any other feedback you want to share?". Participants had specific questions about certain traits but a common theme across all traits was not understanding the specific nucleotide results.

General confusion	• "I Don't feel like I entirely understand it." • "I get a bit lost on the gene part"
Specific trait questions	• "Would like to see more comprehensive list of bitter foods, to include those foods that people without this sensitivity may not experience, if possible." • What's the biological difference or importance of wet vs. dry earwax? Any evolutionary benefits or history?
Nucleotide questions	• "I don't understand what my "CC" result means." • "I'd like to understand what the DNA result "CC" actually means and what other results are possible. What other results would mean. There is no definition about what this CC should mean to me - can I not taste this PTF (was it?) or how is it related to it?"

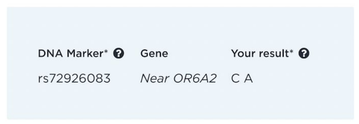


Table 2. Free text responses from participants about their genetic ancestry results.

Participants were asked, "Was there anything else you were hoping to learn about genetic ancestry?" and "Is there any other feedback you want to share?". Participants in general wanted more information about their genetic ancestry but also used this free text box to ask about future health information that they could receive and share they appreciated receiving results.

More specific information on my genetic ancestry	• "My family always told me we were Indian I would like to know if I am and which type, just to know." • "The modern composition that my genetic ancestry is likely to manifest itself as today. For example, I am Mexican American and I am curious to learn if other Latinx groups have similar percentages."
More information on health-related genetic results	• "Disease risk - I want to know my chances." • "I need medical history for various diseases" • "This is so helpful! I can't wait until the medical parts come out!"
Appreciation for results	• "A lot of it is way over my head, but very interesting. I like the way you break it down to a short answer at the top." • "I think the website looks great and like how the language is for a lay person. Embedded links to have certain terms explained is also fantastic for those that do not know much about genetics." • "I enjoy being a member of the All of Us research program. I have learned a lot about myself and life."

Conclusions

- Returning genetic ancestry and trait results to *All of Us* participants is highly effective at engaging research participants. On average 70% of participants clicked to view results when notified.
- Participants who viewed genetic ancestry results were from all races, ethnicities, and age brackets.
- Participants were satisfied with their genetic results, on average responding 4.3 out of a 5-point satisfaction scale. The majority (89%) of participants respond they were either a little satisfied or very satisfied with their genetic ancestry results.
- Participants on average found their genetic results easy to understand (4.6/5), but some have more questions, including about when they can receive health-related information. Participants will be eligible to receive health related results beginning in late 2022.