The *All of Us* Genetic Counseling Resource Call Center: Integrating Genetic Counseling in the Return of Non-clinical Genetic Results

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Introduction

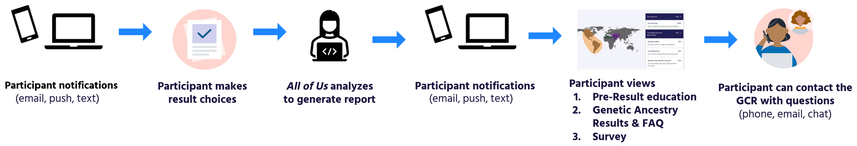
Non-clinical genetic results like genetic ancestry are widely available to the public; however, research shows sweeping differences in how individuals understand and react to these results, and few are returned with genetic counseling support.[1-4] The NIH *All of Us* Research Program is an ongoing, large-scale, national research program focused on including people historically underrepresented in biomedical research that reflect the rich diversity of the United States.[5] Upon enrollment, participants consent to *All of Us* studying their DNA for research. *All of Us* also values returning genetic results directly to participants so they can access their information, learn about their own health, and continue to actively participate in the program.

The *All of Us* Research Program felt that returning non-clinical genetic results such as genetic ancestry would be a good entry point to educate participants about genetic concepts, including uncertainty and penetrance, and could help foster participant engagement. *All of Us* recognized that participants may get unexpected or unpleasant information when they receive their results, and that genetic counselors are beneficial in augmenting genetic return of results to increase participant understanding and contextualization. Subsequently, *All of Us* provides genetic counseling support to all participants via the Genetic Counseling Resource (GCR) through a multi-tier triage system. Here we describe the return of results process for genetic ancestry and traits results, with a specific focus on participant engagement and feedback through the GCR Call Center.

Methods

Figure 1. Participant contact, consent and return of non-clinical genetic ancestry results

All of Us participants who consented and submitted a valid DNA sample were notified about the option to receive genetic ancestry results. After viewing digital information on the benefits and risk of receiving genetic ancestry results, participants could select yes, no, or maybe later to receiving results. Participants who chose yes were notified again when results were ready, and were then guided through a series of digital pre-results information reminding them of the genetic analysis performed and the types of information they may receive. Once a participant viewed their *All of Us* genetic ancestry results and supporting information, they had the option to fill out a brief satisfaction survey within their online portal. Participants were reminded they could contact the GCR with any questions or concerns several times throughout the notification and return of results processes.



The *All of Us* Support Center triaged genomic-related inquiries to the GCR Call Center for resolution. When the GCR received a participant contact, genetic counselors documented the inquiry topics and quotes in detail through internal notes in the *All of Us* secure electronic case management system. Participant contact data between November 2, 2020 and April 30, 2022 was generated in aggregate and inquiries were coded thematically by a single GCR genetic counselor. Coding was performed by GCR team consensus if categorization was ambiguous. Some individual participant contacts contained multiple inquiries; each inquiry was counted and coded as it arose. Results shown were produced using descriptive statistics.

Conclusions

- As expected, GCR Call Center uptake was low (286/81,131 = 0.4%) in return of genetic ancestry results to *All of Us* participants.
  - Those that did seek genetic counseling support were able to discuss how to interpret their results and other complex topics like unexpected results, which genetic counselors are well suited to discuss.
- Almost all (272/286 = 95%) participants who contacted the GCR Call Center had their inquiries resolved satisfactorily with one call, on average 14 minutes. Few participants had inquiries that required multiple contacts or long phone calls.
- *All of Us* health-related genetic results and counseling appointments will be available to the first participants starting in the end of 2022. We expect high engagement in future genetic results given that many of the GCR Call Center participants (51/286 = 17.8%) asked when health-related genetic results or genomic sequence data would be available.
- Future work will assess genetic counseling participant engagement with the return of health-related genetic results.

Results

Figure 2. *All of Us* Genetic Ancestry result uptake and engagement

Between November 2, 2020 and April 30, 2022, *All of Us* participants who provided primary research program consent and submitted adequate DNA samples were notified of their choice to receive non-clinical genetic results. The majority went on to view their genetic ancestry results, which included a high-level composition of geographic regions and supplemental information explaining how ancestry was calculated. One-third completed the result satisfaction survey, and participants expressed high satisfaction with results on a 5-point Likert scale.

Figure 3. Most common participant inquiry topics

All of Us genetic counselors addressed participant inquiries and documented the inquiries in real time through notes in the respective internal electronic case log. Some participants had multiple inquiry topics addressed in one contact; therefore, inquiry topic count exceeds the total number of participant contacts. The vast majority of participants asked the GCR for additional help understanding the interpretation of their genetic ancestry results, such as the breakdown of ancestry region percentage presented. The 'Other' category includes inquiries related to general genetics and feedback.

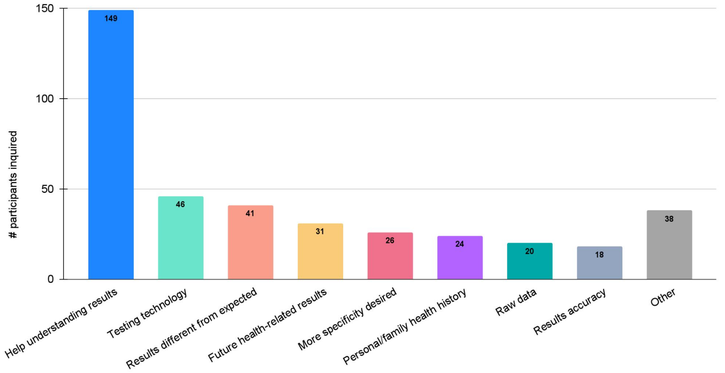


Table 1. *All of Us* GCR Call Center inquiry statistics

Data from all inquiries received by the GCR Call Center between November 2, 2020 and April 30, 2022 was generated in aggregate through the *All of Us* electronic support case management system and analyzed by two GCR genetic counselors.

		(n)	%
	Total Inquiries	**286**	**0.4%**
No. of contacts per participant	One	272	95.1%
	Two	11	3.8%
	Three or more	3	1.0%
Contact method	Phone	164	57.3%
	Email	70	24.5%
	Chat	52	18.2%
Duration of phone calls	Average	14 min	-
	Range	2.4 - 70.8 min	-
Participant language	English	284	99.3%
	Spanish	2	0.7%

Table 2. Participant inquiry quotes

Direct participant quotes received through GCR Call Center inquiries between November 2, 2020 and April 30, 2022.

Help understanding results	• "My brother had his DNA tested with one of the two major testing sites. His results show that he is 99% Ashkenazi Jewish. My results from *All of Us* show I'm 81% Ashkenazi Jewish. Does this mean we may have different parent(s)?" • "Can you help me understand my results? I want to be sure of what I'm looking at."
Testing technology	• "What type of chip will be used to process the genomic sequence for ancestry results?" • "Is *All of Us* doing whole genome sequencing?"
Results differed from expected	• "This report says I'm 10% Finnish but my family is for sure 100% Italian! My family knows their history. This is wrong." • "I thought I would be 25% Irish because my grandfather was 100% Irish, why does it say 35% Irish? That doesn't make sense." • "I don't think the DNA ancestry is accurate because I have the actual family tree."
Future health-related results	• "I thought when I got my DNA results it would include information about serious diseases that have DNA links such as Alzheimer's disease. So far all I have gotten is information on things like ancestry. Was I wrong?" • "When are my other DNA results going to be available?"
More specificity desired	• "I was hoping ancestry was being broken down further - I have been doing genealogy but can't afford to take an ancestry test." • "I got the initial DNA results but it's not specific, the part about ancestry anyway."
Personal or family health history	• "I was diagnosed with Ehlers Danlos in 2009. I was wondering if that showed up in my DNA, as I have heard that it is inherited." • "I have been diagnosed as bipolar and wonder if there is a genetic marker for it."
Raw data	• "Can you provide me more information of the genes so I can look further on my own?" • "Will I get my whole genome sequence?"
Results accuracy	• "How accurate are the ancestry results? Should I trust these or my family's story?"

References
[1]Hazel JW, Hammack-Aviran C, Brelsford KM, Malin BA, Beskow LM, Clayton EW. (2021) PLoS One. 16(11):e0260340.
[2]Rubanovich, C. K., Taitingfong, R., Triplett, C., Libiger, O., Schork, N. J., Wagner, J. K., & Bloss, C. S. (2021). 12(1), 37–52.
[3]Shim JK, Alam SR, & All of Usizerat BE. (2018). 37(1), 44–66.
[4]Kirkpatrick BE & Rashkin MD. (2017). Ancestry Testing and the Practice of Genetic Counseling. J Genet Counsel, 26: 6-20.
[5]The *All of Us* Research Program Investigators (2019). The "All of Us" Research Program. NEJM, 381:668-676.

Acknowledgments
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