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Self-Rated Family Health History Knowledge Among *All of Us* Program Participants

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Abstract

Purpose: Disparities in access to genetics services are well-documented. Family health history is routinely used to determine whether patients should be screened for heritable conditions. We sought to explore variation in levels of self-rated family health history knowledge as a possible driver of this disparity.

Methods: We performed a cross-sectional analysis of survey data from the *All of Us* Research Program. We compared the characteristics of participants who reported “none”, “some”, and “a lot” of family health history knowledge using multinomial logistic regression.

Results: Self-rated family health history data was available for 116,799 participants. The minority of survey participants (37%) endorsed “A lot” of knowledge about their family health history (N=43,661). The majority of participants (60%) endorsed “Some” family health history knowledge (N=69,914), and 3% (N=3,224) endorsed “None.” In adjusted analyses, compared to those who endorsed “A lot” of knowledge, those indicating “Some” or “None” were more likely

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Ethics Declaration

Participants in the *All of Us Research Program* are consented and enrolled in the Program according to the *All of Us* research protocol, which was approved by the *All of Us* Institutional Review Board: https://allofus.nih.gov/about/who-we-are/institutional-review-board-irb-of-all-of-us-research-program. Only de-identified participant data is made available for researcher access on the secure Research Hub platform, and several measures are taken to encrypt participant data: https://www.researchallofus.org/privacy-security-protocols/. Access to the de-identified data required registering with the Program, completion of ethics training, and agreeing to a code of conduct for responsible data use. In addition, our local Mass General Brigham Institutional Review Board deemed use of the de-identified *All of Us* Research Program data non-Human Subjects Research.

to be assigned male sex at birth, possible gender and sexual minorities, have a self-reported race other than White, have lower household annual income (<$25,000), and report lower educational attainment (<high school graduate), compared to reference groups.

Conclusion: Family health history knowledge may be limited, especially among traditionally underserved populations.

Introduction:

Disparities in access to genetics services, including genetic counseling and testing, are well-documented.[1] Traditionally, racial and ethnic minorities and individuals of lower socioeconomic status have routinely been under counseled, under referred, and under tested for heritable diseases.[2,3]

One possible driver of this disparity is a lack of knowledge about one's family health history. Family health history is routinely used to determine whether an individual should be screened for heritable diseases;[4] thus, individuals with poor knowledge of their family health history may not be referred for genetics services. Additionally, insurance reimbursement for genetic testing is strongly linked to having a high-risk family history of heritable disease,[5,6] creating a financial barrier to accessing genetics services in the absence of family health history awareness. The extent to which a lack of or insufficient knowledge about one's family health history drives disparities in access to genetics services is unknown.

The *All of Us* (*AoU*) Research Program is a novel longitudinal cohort enrolling U.S. adults ages 18 and up from across the United States, with an emphasis on promoting inclusion of diverse populations, including gender and sexual minorities, racial and ethnic minorities, and participants with low levels of income and educational attainment.[7] Using the diverse *AoU* cohort, we tested the hypothesis that family health history knowledge may be lower among these historically underrepresented groups, which could exacerbate disparities in access to genetics services.

Materials & Methods:

We conducted a cross-sectional analysis of responses to participant surveys included in the *AoU* v5 Curated Data Repository, which includes data collected between May 6, 2018 and April 1, 2021. Details about the *AoU* study goals and protocols, including survey instrument development,[8] participant recruitment, data collection, and data linkage and curation were previously described in detail.[9,10] Upon enrollment, participants gain access to the first three surveys, including "The Basics Survey", which includes questions about participants' sex at birth, gender identity, sexual orientation, race, ethnicity, annual household income, and educational attainment. Another set of surveys, including the "Family Health History Survey," are made available to participants who have completed the initial three surveys. A total of 329,011 *AoU* participants who had Basics Survey data available were included in this analysis.

Measures:

Participant characteristics of interest were ascertained from responses to the *AoU* Basics survey, and were defined *a priori* to capitalize on *AoU* inclusion of groups traditionally underrepresented in biomedical research[7] as a way to better understand the diverse population of the cohort. Whenever possible, missing covariate data was specified, and those with missing covariate data were included in analyses. However, privacy protections at the level of the *AoU* data release prevented being able to distinguish those who skipped questions, indicated prefer not to answer, or selected a response consistent with having a gender or sexual minority status for analyses.

Characteristics of interest included age on the date the participant completed "The Basics Survey" and sex assigned at birth (Male/Female/Other [Intersex, prefer not to answer, or skipped]), possible sexual and gender minority status (non-straight sexual orientation, gender identity other than male/female, or non-binary sex at birth, or participants who either skipped these questions or indicated prefer not to answer[11]), self-reported race (Asian, Black or African American, Other (Indicates collapse of the response choices another single population, more than one population, or none of these into one group so that cell sizes would remain above count of 20 in the smallest cell), or White), self-reported Ethnicity (Hispanic or Latino, Not Hispanic or Latino, None of These, or Missing), annual household income (<$25,000 versus ≥$25,000), and educational attainment (< high school graduate versus ≥high school graduate).

The primary outcome was based on the participant's response to the first Family Health History survey question: "How much do you know about illnesses or health problems for your parents, grandparents, brothers, sisters, and/or children?" Response choices included "A lot", "Some", and "None at all." Participants who either did not respond to the question or did not participate in the Family Health History Survey were considered to have missing outcome data.

Analyses:

Data was accessed through the *AoU* Researcher Workbench platform. This cloud-based analytic platform was built on the Terra platform.[12] Upon completion of a 3-step process including registration, completion of ethics training, and attesting to a data use agreement attestation, researchers gain access to the platform.[13]

Participant characteristics were initially compared across response groups using descriptive statistics (Pearson's Chi-square). Initially ordinal logistic regression was considered to compare the association between participant characteristics and the outcomes of interest; however, the model violated the proportional odds assumption. Therefore, multivariate multinomial logistic regression was used instead. We compared the associations between those who indicated "None" or "Some" family health history knowledge against those who indicated "A lot" of family health history knowledge. All covariates of interest determined *a priori* were included in the multivariate model. Associations were deemed significant at an $\alpha<0.05$. Adjusted odds ratios (aOR), 95% confidence intervals (CI), and p-values are presented for regression models. Analyses were performed on the *AoU* Researcher

Workbench in Jupyter Notebooks[14] using R programming language. Results are reported in compliance with the *AoU* Data and Statistics Dissemination Policy. All code used to generate analyses was saved in the project Jupyter Notebook and can be made available on request to registered researchers.

Results:

A total of 329,011 participants with "The Basics Survey" data were included in the analyses. The majority (N=212,212) did not participate in the family health history survey (Table 1). Of the participants with family health history survey data available (N=116,799), only 37% (N=43,661) indicated "A lot" of family health history knowledge. The majority (60%, N=69,914) indicated "Some" knowledge and 3% (N=3224) indicated "None." Participants' characteristics varied significantly by self-rated family health history knowledge.

The results of the multinomial logistic regression models are found in Table 2. Compared to those who endorsed "A lot" of self-rated family health history knowledge, both those who indicated "None" and "Some" knowledge were more likely to be male than female, identify as possible gender or sexual minorities, self-report Asian, Black or African American, or Other race compared to White race, be from households with an annual income of <$25,000 and have a less than high school graduate level of education, compared to reference groups. Participants in older age groups were less likely to indicate "Some" or "None" compared to the youngest participant age group (18–34 years old). The effect sizes for significant associations were generally smaller when testing those who indicated "Some" versus "A lot" of knowledge compared to those who indicated "None" versus "A lot" of family health history knowledge.

Discussion:

In this analysis, we found that the minority (37%) of *AoU* Participants completing the Family Health History survey reported "A lot" of family health history knowledge; the majority indicated "Some" knowledge, and only 3% indicated "None." While it is important to highlight that the majority of participants did report some or greater knowledge about their family health history, this knowledge may be limited as only 37% of respondents indicated the highest level of family health history knowledge. It is not clear if and to what extent self-rated family health history knowledge correlates with medically actionable family history knowledge.

It is notable that possible gender and sexual minorities, racial and ethnic minorities, and participants with lower socioeconomic status measures were disproportionately represented among respondents with less family health history knowledge, compared those who indicated "a lot." Family health history can play a key role in identifying individuals at higher risk of disease who should consider genetic testing for heritable disease and consider intensified screenings for diseases with heritable risk. It can also be used both to facilitate communication about disease risk with patients and families, as well as aid interpretation of genetic testing to allow clinicians to translate test results into clinically actionable next steps for patients. The disproportionate representation of higher educated, more affluent, White

non-Hispanic, and non-gender and sexual minority groups among those with the highest level of self-reported family health history knowledge ("A lot") in this analysis does warrant mindfulness that being overly reliant on patient-reported family health history to determine who may benefit from preventive genetic screening could inadvertently restrict screening for populations who have traditionally faced barriers to healthcare access.

Although clinical guidelines have endorsed using family history as a criterion for determining who to screen for heritable conditions,[4] the risks and benefits of population-based genetic screening programs that are not dependent on self-reported family history and/or knowledge are being investigated.[15] Additionally, movement towards using screening modalities that are more appropriate for ancestrally diverse or mixed populations are growing, given the concern that knowledge of one's family history and ancestral lineage may be incomplete, incorrect, or insensitive.[16] Several population-based genetic screening programs have been modeled to be cost-effective.[17–19] As the movement towards equity in accessibility to genetic screening grows, considering disparities in family health history knowledge when designing screening strategies is important for combating these inequities.

One of the strongest associations between participant characteristics and self-rated family health history knowledge was for individuals with a total annual household income of less than $25,000 compared to those with $25,000 or more. While clinical grade preventive genetic testing is increasingly becoming available via direct-to-consumer models, many of these models require self-pay, making them practically inaccessible to low-income individuals,[20] and creating further barriers to care for this population.

Although this dataset is not nationally representative, *AoU* uses various approaches to recruit traditionally underrepresented populations in biomedical research.[9,10] However, disproportionately fewer individuals who identified as possible gender and sexual minorities, racial or ethnic minorities, with an annual household income of less than $25,000, and less than a high school graduate level of education completed the Family Health History Survey question about their self-rated family health history knowledge. This may be second to the nature of how surveys are distributed to *AoU* participants, in which a core set of three surveys is made initially available to participants, while additional surveys including the Family Health History Survey are released on a delayed basis.[10] The drop off in underrepresented in biomedical research participants seen in this analysis may suggest that improving longitudinal engagement of participants is necessary to maximize our ability to better understand these populations.

There are several limitations to this analysis. First, *AoU* does not ask participants about adoption status or conception using a donor gamete; therefore, it is unclear to what extent the number of individuals with limited family health history knowledge may reflect these populations. Given the option for *AoU* participants to opt-in to receive genomic results from the study,[10] it is possible that this would lead to enriched self-enrollment of individuals with an unknown family history who would like to learn from their genomic data. Another limitation of this analysis is that it does not assess the fidelity of self-rated knowledge with family health history. Therefore, it is possible that the traditionally underrepresented in research groups in these analyses either truly know less about their family health history, or

alternatively, there could be systematic underreporting of family health history for various reasons, such as institutional distrust in research and medical enterprises. Further analysis of potential explanation for disparities in self-reported family health history would be warranted.

However, whether the disparity represents either a true lack of knowledge, underreporting, or both, this could translate to a lack of actionable information to inform genetic screening recommendations. The release of genomic data for *AoU* participants could allow for further exploration between the degree of self-reported family health history and the presence of heritable pathogenic variants.[9]

In conclusion, we found that several groups traditionally underrepresented in biomedical research, were more likely to report limited knowledge of their family health history of disease. Attempts to improve equitable access to preventive screenings traditionally based on family history should consider these populations to avoid worsening disparities in access to care.

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Data Availability

All data used in this analysis are readily available to registered researchers in the *AoU* Researcher Workbench. Instructions for how to apply for access to the *AoU* Researcher Workbench can be accessed at: https://www.researchallofus.org/apply/

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Table 1.

All of Us Participants' characteristics by family health history knowledge (N=329011)

	Missing[a] (N=212212)		Family Health History Knowledge[b] (N=116799)					
			A lot (N=43661, 37%)		Some (N=69914, 60%)		None (N=3224, 3%)	
Characteristics	**N**	**Col %**	**N**	**Col %**	**N**	**Col %**	**N**	**Col %**
Age Group (years)								
18–34	50266	24%	6542	15%	13984	20%	869	27%
35–44	33438	16%	5431	12%	9603	14%	514	16%
45–54	39066	18%	6820	16%	10157	15%	631	20%
55–64	45545	21%	10507	24%	14119	20%	643	20%
≥65	43897	21%	14361	33%	22051	32%	567	18%
Sex Assigned at Birth								
Male	85779	40%	12683	29%	25342	36%	1380	43%
Female	123090	58%	30654	70%	44105	63%	1809	56%
Other/Unknown[c]	3343	2%	324	1%	467	1%	35	1%
Gender & Sexual Minority								
No	182153	86%	38911	89%	61194	88%	2674	83%
Yes/Unknown[d]	30059	14%	4750	11%	8720	12%	550	17%
Race								
Asian	7093	3%	1151	3%	2569	4%	227	7%
Black or African American	59215	28%	3099	7%	6056	9%	714	22%
Other[e]	7829	4%	1326	3%	2545	4%	155	5%
White	89133	42%	34640	79%	52362	75%	1502	47%
Missing[f]	48942	23%	3445	8%	6382	9%	626	19%
Ethnicity								
Hispanic or Latino	49046	23%	3761	9%	7082	10%	646	20%
Not Hispanic or Latino	156061	74%	39055	89%	61329	88%	2450	76%
None of these	2460	1%	338	1%	620	1%	63	2%
Missing[f]	4645	2%	507	1%	883	1%	65	2%
Annual Household Income								
≥$25,000	86407	41%	34709	79%	52486	75%	1540	48%
<$25,000	73429	35%	5214	12%	10410	15%	1137	35%
Missing[f]	52376	25%	3738	9%	7018	10%	547	17%
Educational Attainment								
≥HS Grad	29350	14%	688	2%	1771	3%	369	11%
<HS Grad	176146	83%	42702	98%	67640	97%	2786	86%
Missing[f]	6716	3%	271	1%	503	1%	69	2%

[a]Self-rated knowledge of participant's family health history not available;

[b] Based on response to the question: “How much do you know about illnesses or health problems for your parents, grandparents, brothers, sisters, and/or children?” Abbreviations: HS Grad = High school graduate; ref=reference.

[c] Generalized Different Sex: The participant indicated not male, not female, prefer not to answer, or skipped the question: “What was your biological sex assigned at birth?”;

[d] Participant indicated either non-binary sex at birth, non-straight sexual orientation, gender identity other than male or female, indicated prefer not to answer, or skipped these questions.;

[e] Indicates another single population, more than one population, or none of these. These groups were collapsed so that cell sizes would remain above count of 20 in smallest cell.;

[f] None indicated, prefer not to answer, or skipped.

All Chi-square comparisons across covariate groups were significant at $p<0.001$

Table 2.

Adjusted associations with self-rated family health history knowledge[a] (N=116,799).

	None vs. A lot		Some vs. A lot	
	aOR (95% CI)	**p-value**	**aOR (95% CI)**	**p-value**
Age Group				
18–34 (ref)	1.00		1.00	
35–44	0.73 (0.65–0.82)	<0.001	0.84 (0.80–0.88)	<0.001
45–54	0.67 (0.60–0.75)	<0.001	0.70 (0.67–0.73)	<0.001
55–64	0.46 (0.41–0.52)	<0.001	0.63 (0.60–0.65)	<0.001
65+	0.37 (0.33–0.42)	<0.001	0.71 (0.69–0.72)	<0.001
Sex Assigned at Birth				
Female (ref)	1.00		1.00	
Male	2.42 (2.24–2.61)	<0.001	1.46 (1.42–1.50)	<0.001
Other/Unknown[b]	1.27 (0.87–1.86)	0.22	0.96 (0.83–1.12)	0.61
Gender or Sexual Minority				
No (ref)	1.00		1.00	
Yes/Unknown[c]	1.19 (1.07–1.32)	<0.001	1.05 (1.01–1.09)	0.01
Race				
White (ref)	1.00		1.00	
Asian	3.38 (2.89–3.95)	<0.001	1.32 (1.23–1.42)	<0.001
Black or African American	3.33 (3.00–3.69)	<0.001	1.24 (1.19–1.30)	<0.001
Other[d]	1.49 (1.19–1.87)	<0.001	1.15 (1.07–1.25)	<0.001
Missing[e]	1.79 (1.39–2.30)	<0.001	0.98 (0.89–1.08)	0.68
Ethnicity				
Not Hispanic or Latino (ref)	1.00		1.00	
Hispanic or Latino	1.24 (0.98–1.56)	0.07	1.10 (1.01–1.20)	0.03
None of these	2.16 (1.52–3.06)	<0.001	1.01 (0.87–1.18)	0.89
Missing[e]	1.33 (0.92–1.92)	0.13	1.16 (1.00–1.34)	0.05
Annual Household Income				
≥$25,000 (ref)	1.00		1.00	
<$25,000	2.98 (2.72–3.26)	<0.001	1.23 (1.19–1.28)	<0.001
Missing[e]	2.53 (2.26–2.82)	<0.001	1.23 (1.18–1.29)	<0.001
Educational Attainment				
≥HS Grad (ref)	1.00		1.00	
<HS Grad	3.15 (2.72–3.64)	<0.001	1.42 (1.29–1.56)	<0.001
Missing[e]	2.14 (1.61–2.84)	<0.001	1.08 (0.93–1.26)	0.30

Abbreviations: aOR = adjusted Odds Ratio; 95% CI = 95% Confidence Intervals; HS Grad = High school graduate; ref=reference.

[a]Based on response to the question: “How much do you know about illnesses or health problems for your parents, grandparents, brothers, sisters, and/or children?”

[b] Generalized Different Sex: For the question “What was your biological sex assigned at birth?” the participant indicated not male, not female, prefer not to answer, or skipped the question.

[c] Participant indicated either non-binary sex at birth, non-straight sexual orientation, gender identity other than male or female, indicated prefer not to answer, or skipped these questions.

[d] Indicates another single population, more than one population, or none of these. Groups were collapsed so that cell sizes would remain above count of 20 in smallest cell.

[e] None indicated, prefer not to answer, or skipped.