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ORIGINAL ARTICLE

A Lack of Information About Family Health History Motivates Adopted Individuals to Pursue Elective Genomic Testing

Madison R. Hickingbotham[1] | Megan Bell[2,3] | Emilie S. Zoltick[1,4] | Dylan Platt[2,3] | Jennifer R. Leonhard[2] | Catherine Hajek[2,5] | Robert C. Green[6,7,8] | Hadley Stevens Smith[1,4,9] | Kurt D. Christensen[1,4,8]

[1]Department of Population Medicine, Harvard Pilgrim Health Care Institute, Boston, Massachusetts, USA | [2]Sanford Imagenetics, Sioux Falls, South Dakota, USA | [3]Department of Genetic Counseling, Augustana University, Sioux Falls, South Dakota, USA | [4]Department of Population Medicine, Harvard Medical School, Boston, Massachusetts, USA | [5]Helix Inc, San Mateo, California, USA | [6]Mass General Brigham and Harvard Medical School, Boston, Massachusetts, USA | [7]Ariadne Labs, Boston, Massachusetts, USA | [8]The Broad Institute of Harvard and MIT, Cambridge, Massachusetts, USA | [9]Center for Bioethics, Harvard Medical School, Boston, Massachusetts, USA

Correspondence: Megan Bell (megan.bell@sanfordhealth.org)

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ABSTRACT

Elective genomic testing (EGT) for medically actionable disease predispositions may help adopted individuals (adoptees) with limited knowledge of family health history (FHH) information understand their inherited risks. In this prospective cohort study, patients who participated in Sanford Health's EGT program were surveyed at the time of enrollment between August 2020 and April 2022 about their motivations for pursuing EGT and perceived risks for three conditions. Data from self-reported adoptees and nonadoptees were analyzed using bivariate analyses. Of the 5799 eligible patients, 197 (3.4%) reported that they were adopted. Adoptees were more likely than nonadoptees to report lack of information about FHH as a very important motivation for pursuing EGT (81% vs. 32%, $p < 0.001$) and were more likely to rate it as their most important motivation (45% vs. 5%; $p < 0.001$). Other motivations, including learning about personal disease risk (72% vs. 61%; $p = 0.016$) and providing disease risk information to children (69% vs. 57%; $p = 0.003$), were also more likely to be rated as very important by adoptees than by nonadoptees, respectively. No differences in risk perceptions were observed. A lack of FHH information is an important reason why adoptees pursue EGT. Adoptees may hope that EGT will identify inherited risks for disease.

1 | Introduction

Elective genomic testing (EGT) for medically actionable disease predispositions is increasingly available in clinical settings (Lu et al. 2019), and may be of particular interest to individuals who are adopted (adoptees) (May et al. 2015). Adoptees often lack the knowledge about their family health history (FHH) that predicates guidelines for indication-based genetic testing, where identification of monogenic risk informs enhanced surveillance and early intervention to reduce or eliminate risks of associated disease (May et al. 2016). EGT provides opportunities for monogenic risk identification without meeting indication-based testing criteria, but little is currently known about its use among adoptees.

Understanding whether and how adoptees' motivations for pursuing EGT differ from those of nonadoptees is important to ensure that enrollment and result communication protocols account for their particular needs. Studies of adoptees' use of EGT to date have primarily been limited to experiences with direct-to-consumer (DTC) genetic testing. Qualitative studies suggest that adoptees often employ DTC genetic testing to fill

Hadley Stevens Smith and Kurt D. Christensen are co-senior authors.

information gaps (Kay and Taverner 2022; Strong et al. 2017). Surveys to assess adoptees' experiences with DTC testing and interest in EGT have found that adoptees are strongly interested in genetic health risk assessment and/or pharmacogenomic applications (Baptista et al. 2016; Edgar et al. 2022; Lee et al. 2021), although across studies, there appeared to be greater interest in nonhealth applications such as ancestry and finding genetic relatives.

An improved understanding of the motivations of adoptees for pursuing EGT as a clinical service may help health systems adapt their programs to address the particular needs of adoptees with limited knowledge of FHH information. To fill this knowledge gap, we compared the motivations of adoptees and nonadoptees who participated in a large EGT program administered in a clinical setting.

2 | Materials and Methods

2.1 | Overview

We conducted secondary analyses of survey and electronic health record data from patients who enrolled in the Sanford Chip program, an EGT program at a large health system located in the upper Midwestern United States. All Sanford Chip recipients received pharmacogenomic panel testing with the option to be screened for medically actionable predispositions, defined as pathogenic or likely pathogenic variants in genes in the American College of Medical Genetics and Genomics secondary findings version 2.0 (ACMG SF v2.0) list (Kalia et al. 2017), excluding *NF2* and *WT1*. Details about the program, including the methods for genomic testing, provider education and experiences, and communication of results have been published previously (Christensen et al. 2021). Briefly, between 2018 and 2022, English-speaking adult patients with an active Sanford Health MyChart patient portal account were invited to enroll in the Sanford Chip program via messages sent through the portal. Invitation messages directed patients to a web-based platform that provided education about the program and general genetics, collected clinical consent for testing, offered the ability to opt out of screening for medically actionable predispositions, and collected a $49 testing fee if required. Some patients, such as military veterans and patients from underserved communities, received targeted invitations containing a coupon code to receive the test for free. A Sanford healthcare provider approved orders before a blood specimen was collected.

Patients who enrolled in the program after August 2020 completed a survey at the time of enrollment which collected information about personal characteristics, motivations for genetic testing, FHH of 11 conditions, and risk perceptions (Zoltick et al. 2024). To assess motivations, we adapted items from related studies (Carere et al. 2014; Zoltick et al. 2019) and asked patients to indicate which of 10 different reasons was most important in their decision to pursue the Sanford Chip. We also asked patients to rate the importance of each of the reasons, with response options of "not at all important," "somewhat important," "very important," and "not applicable." To assess FHH, patients were asked if any family members, specified to include first- and second-degree relatives and cousins, had a history of 11 conditions that may have a heritable component, with response options of "yes", "no", and "I don't know." Risk perceptions were assessed for three conditions for which Sanford Chip results may be informative: colon cancer, breast cancer, and heart attack. Items asked patients to rate their risk of developing each condition during their lifetime and to compare their risk to that of the average person of their same age, sex, and ethnicity. Adoption status was determined by response to the question "Are you adopted?". Patients also self-reported their race, ethnicity, household income, employment, education, marital status, and smoking status, and rated their health on a 5-point scale from "poor" to "excellent." Patients were also asked if they had a genetic condition. We abstracted data on patient age, sex, and clinical characteristics from medical records.

2.2 | Data Analysis

Descriptive summaries of the characteristics and attitudes of program participants have been published previously (Zoltick et al. 2024). All participants who completed enrollment in the Sanford Chip program after August 2020, had a record of release of genetic results, and completed the adoption question in the survey were included in analyses. We computed descriptive statistics for survey items, including means with standard deviations, medians with interquartile ranges (IQR), and counts with percentages. Bivariate analyses comparing adoptees and nonadoptees were conducted using Chi-Squared tests, Fisher's exact tests, Wilcoxon rank-sum tests, and *t*-tests as appropriate. Using logistic regression and correlation tests, we evaluated the association between the number of "I don't know" responses on FHH items and the likelihood of rating lack of FHH information as a very important motivation for pursuing EGT. Missing values were not imputed. Available case analyses were conducted using R and $p < 0.05$ was considered statistically significant. Data were de-identified by an honest broker prior to analysis. This study was approved by the Sanford Institutional Review Board (STUDY00001862), and a waiver of HIPAA authorization and a waiver of consent were granted.

3 | Results

3.1 | Patient Characteristics

Of 5799 patients included in analyses, 197 (3.4%) self-reported they were adopted. Adoptees were younger, more likely to report Hispanic, Latino, or Spanish ethnicity, had lower household incomes, had higher body mass indices, and had lower self-rated health status than nonadoptees (all $p < 0.05$; Table 1). Adoptees were more than twice as likely to report being a current smoker than nonadoptees (15.7% vs. 7.5%, $p < 0.001$). Adoptees were also more likely than nonadoptees to report prior genetic testing (19.3% vs. 13.1%, $p = 0.015$). Four adoptees (2.0%) were identified to have medically actionable disease predispositions.

3.2 | Family Health History and Risk Perceptions

Adoptees were more likely than nonadoptees to answer "I don't know" on all FHH questions (all $p < 0.001$; Table S1). For all 11

TABLE 1 | Patient characteristics.

Characteristic	Adoptees ($n = 197$)	Nonadoptees ($n = 5602$)	p
Age, median (IQR)	48.7 (17.7) years	52.0 (25.9) years	0.044*
Sex			
Female	119 (60.4%)	3530 (63.0%)	0.457
Male	78 (39.6%)	2072 (37.0%)	
Body mass index, mean (SD)	33.6 (9.1)	31.6 (8.4)	0.001*
Current smoker	31 (15.7%)	418 (7.5%)	< 0.001*
Currently married	126 (64.0%)	3847 (68.7%)	0.170
Number of children, mean (SD)	1.93 (1.4)	1.8 (1.4)	0.339
Self-reported race			
American Indian or Alaska Native	8 (4.1%)	25 (< 1%)	< 0.001*
Asian	< 5 (< 3%)	28 (< 1%)	
Black or African American	< 5 (< 3%)	27 (< 1%)	
Native Hawaiian or Pacific Islander	< 5 (< 3%)	< 5 (< 1%)	
White	170 (86.3%)	5344 (95.4%)	
Other race	< 5 (< 3%)	34 (< 1%)	
Two or more races	10 (5.1%)	119 (2.1%)	
Self-reported ethnicity			
Hispanic, Latino, or Spanish origin	9 (4.6%)	107 (1.9%)	0.008*
Not of Hispanic, Latino, or Spanish origin	186 (94.4%)	5476 (97.8%)	
Educational attainment			
High school/GED or less	26 (13.2%)	772 (13.8%)	0.236
Post high school training (vocational, technical)	21 (10.7%)	535 (9.6%)	
Some college or associate's degree	63 (32.0%)	1497 (26.7%)	
College degree	56 (28.4%)	1841 (32.9%)	
Master's degree	21 (10.7%)	699 (12.5%)	
Doctoral degree	7 (3.6%)	221 (3.9%)	
Full time employed	123 (62.4%)	3305 (59.0%)	0.318
Household income			
Less than $10,000	10 (5.1%)	102 (1.8%)	0.041*
$10,000 to $19,999	9 (4.6%)	195 (3.5%)	
$20,000 to $34,999	23 (11.7%)	392 (7.0%)	
$35,000 to $49,999	17 (8.6%)	521 (9.3%)	
$50,000 to $74,999	34 (17.3%)	887 (15.8%)	
$75,000 to $99,999	13 (6.6%)	799 (14.3%)	
$100,000 to $149,999	36 (18.3%)	934 (16.7%)	
$150,000 to $199,999	16 (8.1%)	356 (6.4%)	
$200,000 or above	10 (5.1%)	367 (6.6%)	
Prefer not to answer	29 (14.7%)	1049 (18.7%)	

(Continues)

TABLE 1 | (Continued)

Characteristic	Adoptees ($n=197$)	Nonadoptees ($n=5602$)	p
Patient reports a known genetic condition	34 (17.3%)	743 (13.3%)	0.097
Self-reported health status			
Excellent	10 (5.1%)	299 (5.3%)	0.014*
Very good	47 (23.9%)	1704 (30.4%)	
Good	91 (46.2%)	2501 (44.6%)	
Fair	35 (17.8%)	912 (16.3%)	
Poor	14 (7.1%)	162 (2.9%)	

Note: p-values represent bivariate comparisons of adoptees and nonadoptees.
*Statistically significant at $p<0.05$.

conditions, at least half of adoptees reported a lack of knowledge of FHH information, while fewer than 26% of nonadoptees reported a lack of knowledge of FHH information for all conditions except colon polyps (49.6%). In instances where respondents indicated a knowledge of their FHH by answering "yes" or "no" (Table S1), adoptees were more likely than nonadoptees to report a positive family history of ovarian cancer (28.6% vs. 15.0%, respectively; $p=0.002$) and uterine cancer (17.2% vs. 8.6%, respectively; $p=0.015$). We observed no differences between adoptees and nonadoptees in risk perceptions of developing colon cancer, developing breast cancer, or having a heart attack (all $p>0.05$; Table S2).

3.3 | Motivations

Nearly half (45.2%) of adoptees ranked interest in learning about their genetics due to a lack of information about FHH as their most important reason for pursuing EGT (Figure 1). In contrast, only 4.8% of nonadoptees ranked this as their most important motivation ($p<0.001$).

Adoptees assigned much greater importance to a lack of FHH information as a motivation for pursuing EGT than nonadoptees, with 80.7% of adoptees rating this as a very important motivation compared to 32.0% of nonadoptees ($p<0.001$; Table S3). Adoptees also assigned greater importance than nonadoptees to learning their personal disease risks, providing risk information for children, EGT as a fun opportunity, and providers' recommendations about testing (all $p<0.05$; Table S3).

Notably, adoptees and nonadoptees often differed in the likelihood that they reported specific motivations as "not applicable." Adoptees were less likely than nonadoptees to classify a lack of FHH information as not applicable ($p<0.001$; Table S3). Adoptees were more likely than nonadoptees to classify potential genetic medical conditions in the family, provider recommendations, and other family members receiving the Sanford Chip as not applicable (all $p<0.05$; Table S3).

3.4 | Correlation Between Family Health History and Motivation

Overall, participants with many "I don't know" responses on FHH items were more likely to have rated lack of FHH information as a very important motivation for pursuing EGT; correlation tests indicated a statistically significant positive association between the number of "I don't know" responses on FHH items and rating lack of FHH information as a very important motivation for pursuing EGT ($r=0.19$, $p<0.001$). However, adoption status was not a significant effect modifier; logistic regression on the likelihood of reporting lack of FHH information as a very important motivation for pursuing EGT showed no significant interaction between adoption status and the number of "I don't know" responses on FHH items ($p=0.394$).

4 | Discussion

Our study is one of the first to provide insight into the characteristics and motivations of adoptees who pursue EGT. We found that adoptees who enrolled in the Sanford Chip program tended to self-identify as more ethnically diverse than nonadoptees and tended to report lower socio-economic status and worse health despite being younger. They typically lacked FHH information for common conditions, and this lack of information was the most important reason they pursued EGT. They were also highly motivated to learn about personal disease risks and potential risks for their children, and often assigned greater importance to these reasons for testing than nonadoptees. Taken together, our findings show notable differences between adoptees and nonadoptees who pursue EGT as a clinical service, with adoptees having strong desires to address informational gaps that they recognize may have important implications for the health of themselves and potential offspring.

As expected, the majority of adoptees in our study reported a lack of knowledge about their FHH. Considering some adoptees report frustration and sadness when completing FHH paperwork in a healthcare setting (Williams et al. 2023), programs implementing EGT should be cognizant of how questions about FHH are framed. Just as importantly, a substantial proportion of adoptees did indeed have knowledge about their FHH. In the context of EGT and healthcare decision-making, health care providers should take care to avoid assuming adoptees have no FHH information available.

Strengths of our study include a focus on characteristics and attitudes of adopted patients who received EGT in a clinical setting, as opposed to DTC testing or hypothetical interest in

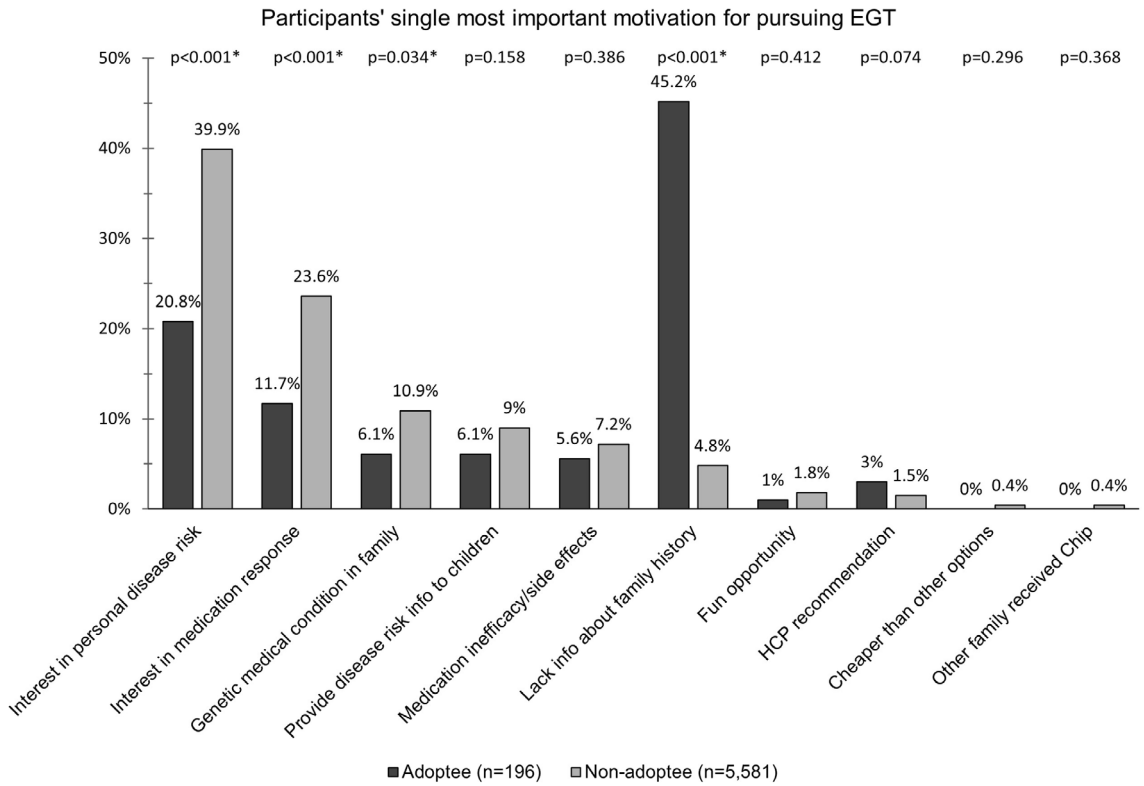

FIGURE 1 | Most important motivation for pursuing EGT. Percentages represent the proportion of adoptees and nonadoptees who selected each option as their single most important motivation when deciding to pursue elective genomic testing. Data were missing for 1 adoptee and 21 nonadoptees.

EGT. Our study included a larger number of adoptees than most other studies of attitudes towards genomic testing (Baptista et al. 2016; Edgar et al. 2022; Lee et al. 2021). Limitations included unequal sample sizes with limited power to control for potential confounding in analyses by demographic and clinical factors. Analyses of risk perceptions for breast cancer were agnostic to sex. Survey items were not validated, and self-reported data could not be verified. Survey questions and prompts did not explicitly use the wording of "family health history" (FHH), but rather used the phrase "family history"; thus, we are unable to determine with certainty that patients were interpreting the phrase "family history" to mean FHH. Findings that adoptees were more likely than nonadoptees to report a FHH of ovarian and uterine cancer may not be generalizable given the small number of adoptees in our study who were aware of their FHH. Lastly, we do not know the details of patients' adoptions, which is a factor that could significantly impact one's access to FHH information.

In conclusion, adoptees believe EGT can help them address their lack of FHH information and identify potential genetic risks. Clinicians at health systems with EGT programs should be sensitive to adoptees' potential lack of knowledge of FHH when considering whether testing is appropriate, and should tailor the way they communicate results to account for the lack of context that FHH information provides. Best practices for the communication of genetic risk information to adoptees are needed, and may resemble research and recommendations addressing communication strategies with those involved in reproductive donation (ESHRE Working Group on Reproductive Donation et al. 2022). Genetic risk information may hold greater meaning and value for adoptees than for most of the nonadopted population, for whom EGT results are likely not their only source of information on heritable disease risk. Future studies should explore the impact of EGT on psychosocial and health outcomes among adopted individuals.

Author Contributions

Conceptualization: Madison R. Hickingbotham, Hadley Stevens Smith, and Kurt D. Christensen. Data curation: Madison R. Hickingbotham and Kurt D. Christensen. Formal analysis: Madison R. Hickingbotham and Kurt D. Christensen. Funding acquisition: Kurt D. Christensen, Robert C. Green, and Catherine Hajek. Investigation: Madison R. Hickingbotham, Emilie S. Zoltick, Megan Bell, Jennifer R. Leonhard, Dylan Platt, and Kurt D. Christensen. Methodology: Madison R. Hickingbotham, Emilie S. Zoltick, Hadley Stevens Smith, and Kurt D. Christensen. Supervision: Catherine Hajek, Robert C. Green, and Kurt D. Christensen. Visualization: Madison R. Hickingbotham and Kurt D. Christensen. Writing – original draft: Madison R. Hickingbotham, Emilie S. Zoltick, Megan Bell, Dylan Platt, Jennifer R. Leonhard, Hadley Stevens Smith, and Kurt D. Christensen. Writing – review and editing: Madison R. Hickingbotham, Emilie S. Zoltick, Megan Bell, Dylan Platt, Jennifer R. Leonhard, Catherine Hajek, Robert C. Green, Hadley Stevens Smith, and Kurt D. Christensen.

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Disclosure

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Ethics Statement

This study was approved by the Sanford Institutional Review Board (STUDY00001862), and a waiver of HIPAA authorization and a waiver of consent were granted.

Conflicts of Interest

R.C.G. has received compensation for advising the following companies: Allelica, Atria, Fabric, Genomic Life, and Juniper Genomics; and is co-founder of Genome Medical and Nurture Genomics. H.S.S. has received consulting income from Illumina Inc. R.C.G., K.D.C., E.S.Z., and M.R.H. were supported by a research grant from Sanford Health. C.H. is an employee of Helix OpCo. All other authors declare that they have no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Data S1:** Supporting Information.