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Patient actions and reactions after receiving negative results from expanded carrier screening

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Abstract

With the expansion of carrier screening to general preconception and prenatal patient populations, most patients will receive negative results, which we define as indicating <25% risk of having a child with a genetic condition. Because there is limited experience with expanded carrier screening, it is important to understand how receiving negative results affects patients, especially as providers, payers, and policymakers consider whether to offer it. In this mixed-methods study, we asked preconception patients enrolled in the NextGen study about their expectations and experiences receiving negative expanded carrier screening results. Participants completed surveys at study enrollment (n=110 women, 51 male partners), after receiving carrier results (n=100 women, 38 male partners), after receiving secondary findings (n=98 women, 36 male partners), and 6 months after receiving results (n=95 women, 28 male partners). We also interviewed a subset of participants 12–24 months after receiving results (n=24 women, 12 male partners). We found minimal negative emotional impact and privacy concerns, increased confidence in reproductive plans, and few changes to health behaviors, although some patients made health decisions based on misunderstandings of their results. These findings suggest that expanded carrier screening causes minimal psychosocial harms, but systems are needed to reduce the risk of misinterpreting results.

Keywords

Genetic carrier detection; genomics; interview; preconception care; psychosocial factors; surveys and questionnaires

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CONFLICT OF INTEREST STATEMENT

All authors declare they have no conflicts of interest.

INTRODUCTION

As the cost of sequencing decreases, expanded carrier screening, defined as simultaneously screening for a large number of genetic variants, is expected to be available to an increasing number of patients.[1] Carrier screening is used to identify a patient or couple's likelihood of passing on a genetic condition to their child and has historically targeted specific subpopulations of individuals who are at increased risk of specific genetic conditions, but it is becoming more common to offer screening for a limited number of conditions to the general preconception and prenatal patient populations.[1–4] As costs decrease for expanded carrier screening, there will likely be more couples receiving such screening. However, even with expanded screening that can screen for hundreds of conditions, the conditions tested for are still collectively rare and there is a low likelihood that both partners in a couple will be carriers for the same condition.[4–6] Because of this, the vast majority of patients will receive negative results indicating they and their partners are at relatively low (which we define as <25%) risk of passing on a genetic condition to their children.

While it is well recognized that patients who are found to be at risk of having a child with a particular genetic condition should have access to high-quality genetic counseling,[1–2] there is a need to understand how patients who receive negative results from expanded carrier screening will be affected and what kind of support they need, as they will represent the vast majority of carrier screening patients. In contrast to single-disease screening, where receiving negative results has been shown to cause minimal long-term harm,[7–10] expanded carrier screening has the potential to raise additional challenges due to its ability to screen for more conditions among a broader population. For example, the inclusion of many conditions and the lack of knowledge about their implications could cause negative psychological or emotional effects during and after the screening process.[2,11–12] This may be especially true if patients learn about conditions they did not want to know about. Another concern is that the increase in conditions tested for may increase the potential for patients to misunderstand their results, due to the impracticality of providing details about every condition on a panel during the consent process[13] as well as the limited availability of genetic counseling services that would be needed to thoroughly counsel patients about each condition.[11–12,14] Additionally, it is possible that patients may misinterpret their results to mean they have no risk of carrying any genetic conditions or that their child will not be susceptible to harm, causing them to have a false sense of security about their child's future.[11,15] In particular, the perception of expanded carrier screening as "whole" or all-inclusive, combined with the limits of informed consent, may heighten the potential for misunderstanding beyond the well-desecribed misunderstanding of residual risk in the context of single-disease testing.[16] However, there is no empirical evidence demonstrating the extent to which these speculative concerns about expanded carrier screening will affect patients in practice.

This study describes patients' experiences receiving negative (<25% risk) expanded carrier screening results. We present mixed-methods findings from surveys and interviews with healthy preconception patients who received negative results in the context of a research study of expanded carrier screening using genome sequencing. Our findings shed light on

patients' emotional reactions and privacy concerns, as well as reproductive and healthcare decision making, across different time points before and after receiving their results.

METHODS

Sample

We surveyed and interviewed patients who took part in a clinical study of preconception carrier screening using genome sequencing, referred to as the "NextGen" study, at Kaiser Permanente Northwest (KPNW), an integrated healthcare delivery system in the Portland, Oregon metropolitan area.[17] NextGen was part of the Clinical Sequencing Exploratory Research consortium funded through the National Human Genome Research Institute. Patients who presented for clinical preconception carrier screening and whose provider ordered carrier testing were identified through chart review and invited to join NextGen by non-clinician research staff. Participants were randomized to receive usual clinical care (i.e., only the test their provider had ordered for them) or expanded carrier screening using genome sequencing. From the genome sequence, we reported 728 gene-condition pairs for carrier status and 114 for medically actionable secondary findings, which were identified and categorized by an advisory committee of national experts on genetics and genomics.[18]

Primary study participants were all female patients with healthcare coverage through KPNW. Participants' male partners were invited to join NextGen regardless of where they received their healthcare, with genome sequencing costs covered by the study, if the primary participant received any positive carrier screening result. All participants were provided an introductory genetics session at the time of consenting to NextGen, and individuals with carrier results received an in-person genetic counseling session including, when possible, an estimate of residual risk. Overall, NextGen included 383 participants, of whom 132 women and 71 male partners received genome sequencing. The NextGen study was approved by the KPNW Institutional Review Board.

Definition of "negative" results

For this analysis of the disclosure of negative results, we defined participants with negative results as those who had received genome sequencing and had less than a 25% risk of having a child that could be affected by a specific genetic condition. This included individuals or couples for whom (1a) both participants in a couple were tested but were not carriers of the same autosomal recessive condition or (1b) only the female participant was tested, (2) no individual in the couple who was tested had an autosomal dominant secondary finding, and (3) the female participant was not found to be a carrier of any X-linked condition. In contrast, individuals or couples with positive results included those for whom (1) both partners were carriers of the same autosomal recessive condition, (2) either partner had an autosomal dominant secondary finding, or (3) the female participant was a carrier of an X-linked condition. However, this definition does not exclude the possibility that a participant still could have been a carrier of a condition that we did not report despite being categorized as having a negative result for purposes of this analysis.

Data collection

NextGen included a series of surveys: one at the time of study enrollment ("enrollment (EN) survey"), one two weeks after receiving carrier results ("carrier results (CR) survey"), one two weeks after receiving medically actionable secondary findings ("secondary findings (SF) survey"), and one six months after enrollment (usual care group) or receiving carrier results (genome sequencing group) ("follow-up (FU) survey"). Genome sequencing participants were given all four surveys. Usual care participants did not receive genome sequencing results, so they were given only the EN survey and a modified version of the FU survey. Participants received $10 for each survey they completed, and an additional $20 for completion of all surveys.

Our review of the literature did not uncover validated measures for assessing psychosocial effects specific to receiving results from genome sequencing, so we used some items that we developed in a previous study that were adapted from published measures, as well as some that we developed for this study, to address uncertainty, decisional impact, and expected and actual reactions to results.[17,19] Items were either yes-no or were scored on a five-point scale from 1 (strongly disagree) to 5 (strongly agree). We did not conduct any formal validity analyses on these items. The surveys also included validated scales for anxiety (State-Trait Anxiety Inventory-6 (STAI-6))[20] and depression (Patient Health Questionnaire-8 (PHQ-8)).[21] The STAI-6 consists of six questions about the magnitude of anxiety symptoms, which are each scored from 1 (not at all) to 4 (very much), summed, and prorated against the original 20-item scale, for a minimum score of 20 and maximum of 80, with higher scores indicating greater anxiety. The PHQ-8 consists of eight questions about the frequency of depression symptoms, which are each scored from 0 (not at all) to 3 (nearly every day) and summed, for a minimum score of 0 and a maximum of 24, with higher scores indicating greater depression.

We also conducted and analyzed interviews with a subset of genome sequencing participants between 12 and 24 months after results disclosure. Our goal was to engage approximately 40 participants who had received results in an in-depth reflection about their expanded carrier screening experience. Interviews were conducted in person or by phone, and couples were interviewed primarily separately but sometimes together, based on participants' preferences. We developed a semi-structured interview guide that explored participants' recall of results; reflections on their feelings before, immediately after, and months after result disclosure; perceived concerns about or utility of results; actions taken after learning results; and views on the overall experience.[17] Interviews were audio recorded, transcribed verbatim, and de-identified for analysis.

Quantitative data analysis

For those items that were only asked of the genome sequencing group and at two time points, we used paired t-tests to determine whether there was change over time. Because depression, anxiety, and the item asking whether participants would like their doctor to know the outcome were collected from both the genome sequencing and usual care groups at both baseline and follow-up, we used generalized estimating equations to test whether there was a differential change between groups over time (i.e., time by arm effect). A significant

coefficient for the time by arm product term would indicate that one arm changed more than the other from enrollment to follow-up. We examined significant interactions using the estimated marginal means to graph and interpret the nature of the differential change. All statistical tests were evaluated at a two-tailed alpha level of .05, and we present 95% confidence intervals for all estimates. Because of multiple comparisons, which can result in increased likelihood of committing type I errors, we used the Benjamini-Hochberg procedure to adjust p-values.[22]

Qualitative data analysis

Interview data were analyzed using a content analysis approach.[23–24] Interview transcripts were loaded into a qualitative analysis software tool,[254] and an experienced qualitative researcher (JS) generated reports of interview text related to relevant interview questions pertaining to recall, emotional reactions, impact on family planning, actions taken, concerns, and utility. Using an iterative process, reports were reviewed multiple times and checked against the raw interview transcripts to categorize and summarize content into key themes. Summaries were shared with the research team and discussed to achieve consensus on interpretation.[26]

RESULTS

Participant characteristics

Limiting analysis of survey data to participants who received negative results, there were 110 women and 51 male partners in the EN survey, 100 women and 38 male partners in the CR survey, 98 women and 36 male partners in the SF survey, and 95 women and 28 male partners in the FU survey. Statistical calculations for each survey item excluded missing responses, with the n for each item reported in tables. We interviewed 36 participants from the negative results cohort, including 12 female/male couples and 12 women without participating partners. Demographics for survey and interview participants are shown in Table 1.

Emotional impact of results

Surveys—Across all surveys (Table 2), participants were mostly glad that they decided to get expanded carrier screening (means ranged from 4.0 to 4.5 on a five-point scale). Mean scores for female participants were slightly higher at 6 months after results disclosure compared to immediately following disclosure of carrier results (b=−0.13, 95% CI [−0.25, −0.02], p=.03), but this difference was not significant after adjusting for multiple comparisons. Across surveys, participants also indicated that they felt they could cope with the results (means ranged from 4.2 to 4.7), had a low level of worry about the accuracy of the test results (means ranged from 1.7 to 2.0), and had a low level of concern about what the results would mean for their families (means ranged from 2.2 to 2.3).

Additionally, participants' anxiety scores, which were assessed at all four survey time points, did not differ significantly across time for either women or male partners (Table 3). Mean depression scores, which were assessed only in the EN and FU surveys, increased slightly from 2.63 to 2.99 (p=.02) among women, while male partners' depression scores did

not differ across time. In addition, we found a significant interaction for the time by arm effect, which reflects the difference in the change from EN to FU between women in the usual care and genome sequencing groups, for both anxiety (b=−7.6, 95% CI [−10.7, −4.6], p<.001, Cohen's d=0.78) and depression (b=−0.96, 95% CI [−1.74, −0.18], p=.02, Cohen's d=0.35). The nature of the interaction for anxiety was such that the usual care group increased from EN to FU (30.6 to 35.9) and the genome sequencing group decreased (31.9 to 29.5), but both groups' mean scores fell on the lower half the STAI scale of 20–80.[20] For depression, the usual care group had a greater increase from EN to FU (2.31 to 3.82) than the genome sequencing group (2.60 to 3.14), but all of these means were very low on the PHQ scale of 0–24.[21]

Interviews—The interviews asked participants with negative results to reflect on their emotional reactions at three different time points: just before receiving results, just after receiving results, and at the time of the follow-up interview (12–24 months after receiving results). Participants' patterns of emotional reactions fell into four distinct groups (Table 4). One group (39%, n=14) said they were not worried, neutral, and/or curious before they received their results, and felt "good" and pleased to have the knowledge just after receiving results. A second group (42%, n=15) described feeling mild worry or anxiety before receiving results, then relieved and curious about their results afterwards. A third group (11%, n=4) said they felt significant anxiety or stress before receiving results, followed by relief nothing serious was found. Some participants in this group also commented that the sequential design of testing, which had male partners tested only after the primary female participant received her results, had created two distinct timeframes of anxiety as they waited to see if their partner's results would match their own. Finally, a fourth group (8%, n=3) said they felt neutral or were "in waiting mode" before receiving results, then were surprised at their results because they either believed they would not have found anything (in the case where a recessive gene was found in one partner but not the other) or expected to find more. However, participants in all four groups converged to all report feeling good about their results by the time of the follow-up interviews 12–24 months later and to express that the knowledge they received was beneficial.

Privacy concerns

Surveys—Across all time points, participants indicated a low level of concern about their privacy or confidentiality (means ranged from 1.9 to 2.1 on a five-point scale; Table 2). Among female participants, privacy concerns were greater at 6 months following disclosure compared to immediately after receiving carrier results (b=−0.27, 95% CI [−0.43, −0.11], p=.002) or secondary findings (b=−0.25, 95% CI [−0.49, −0.01], p=.04). However, only the change from the CR to FU survey remained significant after adjusting for multiple comparisons.

Interviews—Most interview participants (75%, n=27) said they had no concerns about privacy, including any potential effects on health insurance coverage from having their results documented in their medical record. Some noted that their negative results had contributed to this lack of concern, with one participant commenting that "the chance of me having a child that has a mutation is not really possible with my current partner, and so it is

not something that I think would be held against me in any way." The remainder of participants (25%, n=9) said they had some mild concerns about privacy at the onset of the study, but once they knew their results these concerns were resolved. For example, one participant said she "might have had some concerns if something came up to where my information got out and it affected my insurance or something, but I don't think with my result that would be an issue."

Reproductive planning

Surveys—Across all surveys, nearly all participants reported that their results did not affect their plans for having a child (97%–100%; Table 5).

Interviews—In the interviews, 61% (n=22) of participants confirmed that they did not change their plans to have children or become pregnant in response to their results, although about half of those said that if the results had been different (i.e., revealing them to be at higher risk of passing on a genetic condition), they would have deliberated more about their plans to become pregnant. The other 39% (n=14) said their results made them feel more confident moving forward with their reproductive plans, with one saying it "takes some worry off the table" and another noting that she and her partner seemed to be a "good genetic match."

When asked to elaborate on how the results shaped their family planning experience, 31% (n=11) of participants indicated the results had no influence, often stating they were planning to start a family no matter the results of their expanded carrier screening. In contrast, 69% (n=25) of participants said they felt their results shaped their family planning experience by providing "peace of mind" or additional confidence to feel prepared to start a family, or as one participant put it, to "go full steam ahead." Additional ways these 25 participants described how their results impacted their family planning experience included believing the testing process encouraged them to think more than they otherwise would have about the genetic conditions they could pass on (n=9), feeling the results would be good information to share with their providers should anything "unknown" arise during a pregnancy or in a child's life (n=6), and generating discussion with their partner about other family planning options to consider depending on the test's outcome (n=4). For some, their family planning experience was mildly and temporarily impacted by concern that the results would reveal or confirm a genetic issue (n=5).

In terms of the effect of the results on perceptions of a future child's health, 39% (n=14) of participants in the interviews said the results did not change anything. The other 61% (n=22) said their results had somewhat affected their perception, with most of those (47%, n=17) saying the results gave them a sense of relief that there would be no big genetic health surprise in their child's life, and a few (14%, n=5) saying they might consider genetic testing for their child when they were older if it was appropriate. Additionally, 44% (n=16) said the results slightly lowered their perception of the risk of having a child with a problem, saying they "feel better about it" but understand that some risk is always present.

Changes to insurance, healthcare, and lifestyle

Surveys—Across all surveys, nearly all participants reported that they were not planning to change their life or health insurance coverage or their financial plans based on the information they received (98%–100%; Table 5).

Interviews—No interview participants reported making changes to long term care or disability or life insurance after receiving their results, and only two (5%) reported making minor lifestyle changes: increasing water intake due to a carrier result (*SLC3A1*, cystinuria) pertaining to kidneys, and monitoring environmental exposures due to a secondary finding (*SERPINA1*, Alpha-1 Antitrypsin Deficiency) pertaining to lungs. Of those who were pregnant during the study (n=25), the majority (84%, n=21) said the results had not affected their medical decisions or screenings during pregnancy and that they would make the same choices regarding care whether they knew the information or not. One participant added that the results gave her more confidence to proceed with the prenatal screening her provider offered. However, the results did alter some pregnant participants' decisions (16%, n=4), who said they decided to turn down some or all prenatal genetic screening (e.g., first trimester screening, non-invasive prenatal testing, quad screening) after getting their carrier results.

Sharing results with provider

Surveys—When comparing the change over time between the genome sequencing and usual care groups on the degree to which they would like their doctor to know the results of their genome sequencing, we found a significant interaction for the time by arm effect (b= −0.30, 95% CI [−0.53, −0.07], p=.009, Cohen's d=0.37). The nature of the interaction was such that the usual care group remained relatively stable from EN to FU (4.36 to 4.40), whereas the genome sequencing group decreased (4.36 to 4.11). Nevertheless, mean scores for both groups on both surveys indicated an overall high level of agreement on the desire to share results (Table 2).

Interviews—Half (n=18) of participants interviewed said they did not actively share their results with their provider, commenting that they did not see a need to do so because they had received negative results or because they assumed the results were already documented in their health record and therefore visible to their provider. Of those who did share their results (36%, n=13), most shared them with their obstetrician or midwife and one with a pediatrician. For the other 14% (n=5), their provider proactively brought up their results based on seeing information in the medical record.

Additional information

Surveys—Survey participants were mixed in terms of whether they wanted additional information about genetic testing (means ranged from 3.0 to 3.3 on a five-point scale) and genetic conditions (means ranged from 2.9 to 3.2) (Table 2). Over time (from SF to FU), female participants had less of a desire to learn more about genetic testing (b=−0.25, 95% CI [−0.48, −0.02], p=.03) and conditions (b=−0.33, 95% CI [−0.55, −0.12], p=.003) related to secondary findings. Only the change in desire to learn about genetic conditions related to secondary findings remained significant after adjusting for multiple comparisons.

Interviews—As suggested by their survey responses, interview participants were divided in terms of whether they had sought out additional information after receiving results. A slight majority (56%, n=20) said they had not done any additional research, because the information they had received was sufficient or they didn't want to create unnecessary worry. Another 39% (n=14) said they did some searching on the internet, mainly to further their understanding of the concepts and terminology, and 5% (n=2) said they did quite a bit of internet research to better understand a complex result.

DISCUSSION

Our findings suggest that there is little direct psychosocial harm to patients from providing negative (<25% risk) expanded carrier screening results. Our results show little, if any, negative long-term emotional impact on patients after receiving negative results, including slightly lower levels of anxiety and depression when compared to the usual care group, and low levels of concern about privacy and confidentiality across all time points. While our interview data show that worry or anxiety may be briefly heightened for some patients while they wait to receive results, they also suggest that those are temporary reactions that dissipate with time. This finding is similar to Beard and colleagues' finding that pregnant women with a positive carrier finding experienced anxiety and imagined the "worst case scenario" of an affected pregnancy, but that this anxiety subsided after their partner received a low-risk result.[27] These findings also align with prior studies showing minimal long-term psychosocial harms from receiving negative results in single-disease carrier screening, even after some heightened anxiety while waiting for results.[7–10] To minimize this temporary worry, some patients may find it helpful to have simultaneous, rather than sequential, testing of both members in a couple, so that there is only one period of time while they wait to learn results.[1,28]

Very few participants made any changes to insurance or healthcare decisions based on their negative results, and participants reported minimal changes in their reproductive planning or perceptions of their future child's health. The most pronounced outcome after receiving results was relief and an increase in confidence moving forward with family planning, with a few participants commenting that they had gained confidence in receiving prenatal screening. Among the participants whose perceptions had changed, most acknowledged that there was still a chance they could have a child with health problems, suggesting that concerns about false assurance are less problematic than anticipated based on the large number of studies demonstrating a lack of understanding of residual risk among patients who received negative cystic fibrosis screening results,[16] as well as previous outcomes suggesting that understanding of residual risk may decrease when screening for an increasing number of conditions.[12] While this may suggest that our efforts at informing patients were largely successful in this study, further study is warranted, particularly among patients who have less genetic knowledge and less access to genetic counseling services than our patient population.

Half of participants actively shared their genome sequencing results with their doctors, and in a few other cases, doctors brought up the results themselves. However, some participants never discussed the results with a provider, despite saying they wanted their provider to

know their results, because they either felt it was not important given their negative results or assumed their provider had already seen the results. While a lengthy conversation is likely unnecessary for most patients, and not feasible given clinical constraints, our findings highlight a small number of cases of misunderstanding where discussion could help forestall potentially problematic behaviors. For example, one interview participant commented that her carrier result for *SLC3A1* cystinuria inspired her to drink more water to prevent kidney problems; while her chosen course of action is not likely to cause her harm, it shows how patients may misinterpret carrier results as threats to their own health and take action accordingly. Other participants' comments suggested similar misunderstandings without accompanying behavioral changes, such as a patient who received a hemochromatosis carrier result and subsequently made reference to her own high iron levels. These findings replicate those of prior studies showing that patients may misinterpret carrier results as affecting their own health.[8,28–29]

Additionally, a subset of pregnant interview participants said they declined some prenatal screening because of their carrier results, suggesting they did not understand that prenatal screening looks for conditions in a specific pregnancy that are not covered by expanded carrier screening. We conducted manual chart review on all participants to obtain information on prenatal testing refusals and the reasons for those refusals, if documented, which revealed one case of a participant who declined prenatal screening based on a negative carrier result, only to later decide to have the screening after learning she had misunderstood the implications of her results. This case suggests that some patients may base their health care decisions on misinterpretations about the relationship between carrier and prenatal screening, as has also been shown elsewhere.[2] To alleviate these potential misunderstandings without overburdening clinicians, a potential solution might be for physicians to be aware of their patients' negative results in the medical record, and affirm to the patient that they are offering appropriate care and/or testing based on the negative results. If further discussion is needed, the physician could refer for genetic counseling.

Finally, participants were split as to whether they wanted more information about genetic testing and conditions, but while some commented in the interviews that they had done some additional internet searches, most did not express a need for a lot more information. However, it is important to note that all the participants in our study were part of an integrated health care system and had access to genetic counselors as part of the NextGen study or via self-referral for clinical care, whereas many patients across the general patient population will not have similar access. Thus, further study is needed to identify gaps in information and understanding across a broader population and to ensure that all patients have access to trustworthy and accurate information.[27]

LIMITATIONS

Our study has several limitations. First, our sample over-represents high-income, highly educated, non-Hispanic white patients; there is a need for study among a more diverse cross-section of patients to generalize our findings beyond our patient population. Second, due to low numbers of male partners, statistical analyses among these patients were limited. Male partners were not tested if a woman, as the primary study participant, was a non-carrier or

did not have a male partner available for testing. Therefore, we focused our analyses on an individual basis, with the primary focus on the women, rather than on male/female couples as a unit. Consequently, we were unable to compare couples where both were non-carriers versus those where one was a carrier and the other was not. Third, the questions asked across surveys were not all identical, limiting some comparisons across time points. We also lacked a control group on questions that were only asked of the genome sequencing group, and therefore we were limited in our ability to attribute changes in our pre-post analyses to the experience of expanded carrier screening versus the natural passage of time.

In addition, this analysis only explored harms from patient perspectives and did not consider the impact on the healthcare delivery system. For example, these findings do not address how expanded carrier screening affects the capacity of genetic counseling services, including the possibility that it could detract from the provision of other important genetic counseling services. Similarly, these findings do not speak to the potential downstream effects of expanded carrier screening, such as additional visits for preconception or prenatal care, lengthened appointments, and increased costs. Consequently, while these results suggest that expanded carrier screening is not directly harmful to most patients who receive negative results, additional considerations must be taken into account before endorsing its widespread clinical use.

CONCLUSION

These results provide reassurance that expanded carrier screening using genome sequencing did not result in psychosocial harms in our patient population. While there were few potentially problematic patient behaviors, a small number of cases suggest there is a need for systems to prevent misunderstandings. Further research is needed to understand the overall impact of expanded carrier screening on the healthcare delivery system.

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Table 1

Demographics

	Surveys (At Enrollment)		Interviews	
	Women (n=110)	**Male Partners (n=51)**	**Women (n=24)**	**Male Partners (n=12)**
Age (years)				
Range	21 – 46	24 – 50	25 – 42	29 – 50
Mean (standard deviation)	32.6 (4.8)	33.8 (5.7)	32.1 (4.2)	36.2 (5.9)
Non-Hispanic white race/ethnicity	81 (73.6%)	43 (84.3%)	19 (79.2%)	12 (100.0%)
Education				
High school or less	3 (2.7%)	5 (9.8%)	0 (0.0%)	0 (0.0%)
Some college/Associate's degree	26 (23.6%)	13 (24.5%)	5 (20.8%)	3 (25.0%)
Bachelor's degree	43 (39.1%)	20 (39.2%)	10 (41.7%)	5 (41.7%)
Graduate degree	38 (34.6%)	12 (23.5%)	9 (37.5%)	4 (33.3%)
Prefer not to respond	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)
Gross annual income (US$)				
Less than 40,000	10 (9.1%)	4 (8.8%)	3 (12.5%)	0 (0.0%)
40,000–59,999	10 (9.1%)	6 (11.8%)	2 (8.3%)	0 (0.0%)
60,000–79,999	17 (15.5%)	2 (3.9%)	3 (12.5%)	0 (0.0%)
80,000–99,999	25 (22.7%)	8 (15.7%)	6 (25.0%)	3 (25.0%)
100,000–149,999	26 (23.6%)	19 (37.3%)	7 (29.2%)	6 (50.0%)
150,000+	15 (13.6%)	9 (17.7%)	3 (12.5%)	2 (16.7%)
Don't know/prefer not to respond	7 (6.4%)	3 (5.9%)	0 (0.0%)	1 (8.3%)
Employed or self-employed	91 (82.7%)	47 (92.1%)	21 (87.5%)	10 (83.3%)
Married	86 (78.1%)	41 (80.4%)	17 (73.9%)	9 (75.0%)

Table 2

Emotional impact of results; privacy concerns; sharing results with provider; additional information

Survey	Question	Women (Mean (SD))	Male Partners (Mean (SD))
EMOTIONAL IMPACT OF RESULTS			
Gladness (5=strongly agree, 1=strongly disagree)			
EN	If I received a normal genome sequencing result showing that I am not a carrier of a genetic condition, I expect that I would feel glad that I decided to get this test	4.4 (0.7) (n=110)	4.0 (0.7) (n=50)
CR†	I feel glad that I decided to get this test	4.3 (0.7) (n=100)	4.4 (0.6) (n=37)
FU†	Based on the results of my genome sequencing test, I am feeling glad that I decided to get this test	4.5 (0.6) (n=92)	4.4 (0.7) (n=28)
	Change over time (CR to FU)	−0.13 (0.57), 95% CI [−0.25, −0.02], p=.03 (n=89)	0.0 (0.68), 95% CI [−0.26, 0.26], p=.99 (n=27)
Coping (5=strongly agree, 1=strongly disagree)			
EN	I believe that I could cope with any results of genome sequencing	4.2 (0.8) (n=110)	4.5 (0.6) (n=50)
CR†	I believe I can cope with the results I received	4.6 (0.5) (n=100)	4.7 (0.5) (n=37)
Worry about accuracy (5=strongly agree, 1=strongly disagree)			
EN	If I received a normal genome sequencing result showing that I am not a carrier of a genetic condition, I expect that I would worry that the test might not be accurate	1.9 (0.9) (n=110)	2.0 (0.7) (n=50)
CR†	I worry that the test might not be accurate	1.7 (0.8) (n=100)	1.8 (0.7) (n=37)
FU†	Based on the results of my genome sequencing test, I am worried that the test might not be accurate	1.9 (0.8) (n=92)	2.0 (1.1) (n=28)
	Change over time (CR to FU)	−0.15 (0.72), 95% CI [−0.29, 0.00], p=.06 (n=89)	−0.04 (0.90), 95% CI [−0.38, 0.30], p=.83 (n=27)
Concern for family members (5=strongly agree, 1=strongly disagree)			
CR†	I am concerned about what the results mean for my family	2.3 (1.0) (n=100)	2.2 (1.0) (n=37)
FU†	Based on the results of my genome sequencing result, I am concerned that my family members may be at higher risk for genetic conditions	2.3 (1.0) (n=92)	2.2 (0.9) (n=28)
PRIVACY CONCERNS (5=strongly agree, 1=strongly disagree)			
Carrier results			
CR†	I am concerned about the privacy and confidentiality of the test results	1.9 (1.1) (n=100)	2.0 (1.2) (n=37)
FU†	I am concerned about the privacy and confidentiality of the test results	2.1 (1.2) (n=92)	2.1 (1.1) (n=28)
	Change over time (CR to FU)	−0.27 (0.78), 95% CI [−0.43, −0.11], p=.002 (n=89)	−0.22 (1.09), 95% CI [−0.63, 0.19], p=.30 (n=27)
Secondary findings			
	Change over time (SF to FU)	−0.25 (1.15), 95% CI [−0.49, −0.01], p=.04 (n=88)	−0.27 (1.19), 95% CI [−0.73, 0.19], p=.26 (n=26)
SHARING RESULTS WITH PROVIDER (5=strongly agree, 1=strongly disagree)			
EN	I would want my doctor to know the results of my genome sequencing	4.4 (0.8) (n=100)	4.1 (0.8) (n=49)
FU	I would want my doctor to know the results of my genome sequencing	4.1 (0.9) (n=90)	4.1 (0.9) (n=28)
	Change over time (EN to FU)	0.26 (0.84), 95% CI [0.08, 0.43], p=.005 (n=90)	0.0 (0.94), 95% CI [−0.36, 0.36], p=.99 (n=26)

Survey	Question	Women (Mean (SD))	Male Partners (Mean (SD))
ADDITIONAL INFORMATION (5=strongly agree, 1=strongly disagree)			
Genetic testing (carrier results)			
CR†	I plan to look for more information about genetic testing	3.1 (1.1) (n=100)	3.0 (0.9) (n=37)
FU†	Based on the results of my genome sequencing test, I am wanting more information about genetic testing	3.3 (1.0) (n=91)	3.1 (0.8) (n=28)
	Change over time (CR to FU)	−0.16 (1.11), 95% CI [−0.39, 0.07], p=.18 (n=88)	−0.15 (0.95), 95% CI [−0.51, 0.21], p=.43 (n=27)
Genetic testing (secondary findings)			
	Change over time (SF to FU)	−0.25 (1.09), 95% CI [−0.48, −0.02], p=.03 (n=87)	0.31 (1.16), 95% CI [−0.14, 0.76], p=.19 (n=26)
Genetic conditions (carrier results)			
CR†	I plan to look for more information about genetic conditions	3.2 (1.1) (n=100)	3.0 (0.8) (n=36)
FU†	Based on the results of my genome sequencing test, I am wanting more information about genetic conditions	3.1 (1.0) (n=92)	2.9 (0.8) (n=28)
	Change over time (CR to FU)	0.03 (1.12), 95% CI [−0.20, 0.27], p=.78 (n=89)	0.12 (0.86), 95% CI [−0.21, 0.45], p=.50 (n=26)
Genetic conditions (secondary findings)			
	Change over time (SF to FU)	−0.33 (1.03), 95% CI [−0.55, −0.12], p=.003 (n=87)	0.04 (1.31), 95% CI [−0.46, 0.54], p=.88 (n=26)

† These questions were asked with reference to carrier results. The SF and FU surveys also included these questions with reference to secondary findings, but data are not shown where responses did not differ.

Abbreviations: EN = Enrollment Survey, CR = Carrier Results Survey, SF = Secondary Findings Survey, FU = Follow-Up Survey

Table 3

Anxiety and depression

Survey	Women (Mean (SD))	Male Partners (Mean (SD))
ANXIETY (STAI-6). Scored by summing responses to 6 items (1=not at all, 4=very much) and prorating by multiplying by 20/6, for minimum=20 and maximum=80. Higher scores indicate greater anxiety.		
EN	31.93 (11.86) (n=109)	31.72 (9.31) (n=50)
CR	29.90 (10.38) (n=100)	32.43 (11.40) (n=37)
SF	29.84 (10.23) (n=96)	31.33 (9.88) (n=35)
FU	29.60 (9.95) (n=91)	32.50 (10.91) (n=28)
DEPRESSION (PHQ-8). Scored by summing responses to 8 items (0=not at all, 3=nearly every day) and summed, for minimum=0 and maximum=24. Higher scores indicate greater depression.		
EN	2.63 (3.05) (n=108)	3.78 (4.77) (n=50)
FU	2.99 (3.46) (n=89)	3.46 (3.33) (n=28)

Abbreviations: EN = Enrollment Survey, CR = Carrier Results Survey, SF = Secondary Findings Survey, FU = Follow-Up Survey

Table 4

Qualitative patterns of emotional reactions

Pattern of emotional reactions	Exemplar quote
Neutral or not worried (39%, n=14)	"I mean I was curious as far as everything goes. I wasn't worried about it or anything…and I felt a little more informed – it was good to know that there wasn't anything major in my genetic history to be too concerned about."
Mild worry or anxiety (42%, n=15)	"There was a little bit of nerves there [prior to result disclosure], but nothing major…it didn't both me and affect my daily life or anything."
Significant anxiety or stress (11%, n=4)	"It was super stressful for me. And the chances of getting pregnant were there, yet I didn't know what the results were going to be. And so that was probably the scariest thing."
Neutral yet surprised (8%, n=3)	"I wasn't nervous…but I was honestly surprised that more didn't come up. I think one kind of walks into it preparing for the worst. But I was comfortable with the results."

Table 5

Reproductive planning; insurance, healthcare, and lifestyle changes

Survey	Question	Women (% no[†])	Male partners (% no[†])
REPRODUCTIVE PLANNING			
EN	[If YES to: Do you know the results of your carrier status test that your provider ordered?] Has the information from the genetic testing for carrier status that your provider ordered altered your plans for having a child?	100% (n=79/79, excluding 37 who had not received results)	N/A
CR	Has the information from the genome sequencing for carrier status altered your plans for having a child?	97% (n=101/104)	98% (n=42/43)
SF	Has the information about the incidental findings altered your plans for having a child?	98% (n=98/100)	100% (n=36/36)
FU	Based on your genome sequencing results, have your original family plans changed?	100% (n=95/95)	96% (n=27/28)
INSURANCE, HEALTHCARE, AND LIFESTYLE CHANGES			
EN	[If YES to: Do you know the results of your carrier status test that your provider ordered?] Are you planning to change your health insurance coverage based on the information from the genetic testing for carrier status that your provider ordered?	99% (n=78/79, excluding 37 who had not received results)	N/A
CR	Are you planning to change your life or health insurance coverage based on the information from the genome sequencing for carrier status?	99% (n=103/104)	100% (n=43/43)
SF	Are you planning to change your life or health insurance coverage based on the information about the incidental findings?	100% (n=100/100)	100% (n=36/36)
FU	Did you change or are you planning to change your insurance coverage or financial plans based on the information from the genome sequencing for carrier testing?	98% (n=93/95)	100% (n=28/28)

[†]Denominator for each survey item excludes missing responses

Abbreviations: EN = Enrollment Survey, CR = Carrier Results Survey, SF = Secondary Findings Survey, FU = Follow-Up Survey