# Uptake of Genetic Research Results and Patient-Reported Outcomes With Return of Results Incorporating Web-Based Predisclosure Education

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## ABSTRACT

**PURPOSE** We developed a web-based education intervention as an alternative to predisclosure education with a genetic counselor (GC) to reduce participant burden and provider costs with return of genetic research results.

**METHODS** Women at three sites who participated in 11 gene discovery research studies were contacted to consider receiving cancer genetic research results. Participants could complete predisclosure education through web education or with a GC. Outcomes included uptake of research results, factors associated with uptake, and patient-reported outcomes.

**RESULTS** Of 819 participants, 178 actively (21.7%) and 167 passively (20.4%) declined return of results; 474 (57.9%) were enrolled. Most (60.3%) received results although this was lower than the 70% uptake we hypothesized. Passive and active decliners were more likely to be Black, to have less education, and to have not received phone follow-up after the invitation letter. Most participants selected web education (88.5%) as an alternative to speaking with a GC, but some did not complete or receive results. Knowledge increased significantly from baseline to other time points with no significant differences between those who received web versus GC education. There were no significant increases in distress between web and GC education.

**CONCLUSION** Interest in web-based predisclosure education for return of genetic research results was high although it did not increase uptake of results. We found no negative patient-reported outcomes with web education, suggesting that it is a viable alternative delivery model for reducing burdens and costs of returning genetic research results. Attention to attrition and lower uptake of results among Black participants and those with less formal education are important areas for future research.

ACCOMPANYING CONTENT

Appendix

Protocol

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## INTRODUCTION

Genetic sequencing studies involving biobanked DNA raise questions about the obligation to share individual research results with participants.[1-7] Arguments supporting return appeal to the principles of beneficence, autonomy, reciprocity, respect for persons, and clinical utility.[4,7-9] Arguments opposing return raise concerns about the distinction between research and clinical care, the actionability of results, the right not to know, and costs.[5,7,9-13] Although debates are ongoing, the consensus favors returning results that could be relevant to participants' health.[2,4,5,14-16]

Research participants have reported high interest in receiving research results.[16-25] However, lower uptake has been reported,[26] particularly in studies involving biobanks for which return of results was not emphasized during enrollment.[27-34] There are limited patient-reported outcomes (PROs) in the research setting[27-29,35] although some genomic implementation studies have reported no psychological harms with return of genetic findings.[36,37] In RESPECT1, we found favorable cognitive (eg, knowledge) and affective (eg, distress and uncertainty) responses with return of results among patients with breast cancer, but low uptake of results.[38] In addition, we found that one third of participants reported that a

## CONTEXT

**Key Objective**

Is web-based education a viable alternative delivery model for predisclosure education for return of individual genetic research results?

**Knowledge Generated**

Uptake of web-based predisclosure education for return of individual genetic research results was high among enrolled participants. Among those who completed predisclosure education, most received their research results, which did not differ by web-based education versus education with a genetic counselor. No negative patient-reported outcomes with web education were found.

**Relevance *(S.B. Wheeler)***

As return of genetic test results to patients continues to increase with clinically relevant genetic information becoming more widely available, appropriate and timely education to support interpretation is key. This study offers a potentially impactful and efficient approach to providing that education via web-based platforms.*

*Relevance section written by *JCO* Associate Editor Stephanie B. Wheeler, PhD, MPH.

self-directed web platform would be an acceptable alternative to speaking with a genetic counselor (GC) and could reduce steps in receiving results.[39]

In this multicenter, observational return of results study (RESPECT2), we developed a web-based predisclosure education intervention (web education) as an alternative to speaking with a GC to reduce participant burdens and steps in receiving genetic research results. Our primary aim was to evaluate uptake of genetic research results among research participants who provided a biospecimen for genetic research when using an alternative delivery model incorporating web education. We hypothesized that 70% would receive their results after predisclosure education. Secondary aims included understanding participant factors associated with uptake of results, changes in PROs, and whether outcomes differed by the method of predisclosure education (GC *v* web education).

## METHODS

Participants were English- or Spanish-speaking adult women who had provided a biospecimen for genetic research (11 studies) at the University of Pennsylvania (UPenn), University of Chicago (UChicago), or Columbia University (Columbia) and had not previously had clinical multigene panel testing. Original consents stated that results that could affect participant health would be returned (n = 7) or would not be returned (n = 4). Individuals in the latter group were contacted so as not to assume that they would not want results.

Sequencing included 25 high- and moderate-penetrance genes (*APC, BRCA1, BRCA2, CDH1, CDKN2A, PMS2, PTEN, MLH1, MSH2, MUTYH-homozygous, MSH6, STK11, TP53, ATM, BAP1, BARD1, BMPR1A, BRIP1, CHEK2, MRE11A, MUTYH-heterozygous, NBN, PALB2, RAD50, RAD51C, RAD51D*) that had potential clinical relevance when the study was conducted. Sequencing was performed in institutional research laboratories. Clinical confirmation testing was recommended to participants for results that could potentially affect medical care (see below).

Institutional Review Board approval was obtained at all sites. Study invitation letters (English and Spanish versions at Columbia) explained that research testing had been completed and that participants could enroll to learn their research results. In eight studies (n = 1,583), the research team could follow up with participants by phone (three to five calls per site standards). In three studies (n = 379), original consents stated that results would not be returned and participants had to call or mail back a response card to be contacted.

### Predisclosure Education by Web Intervention or Genetic Provider

On the basis of participant feedback in RESPECT1, we developed a self-directed web-based alternative for predisclosure education.[39] The intervention was developed to cover the same content as predisclosure genetic counseling. Informed by the tiered-binned model, GCs reached consensus on indispensable tier 1 information that should be presented to all participants and additional or optional tier 2 information that could be provided to support variable information needs.[40] The intervention and genetic counseling checklists included the same tier 1 content. The intervention consisted of seven modules and optional videos and was available in both English and Spanish (Appendix Table A1, online only).

Predisclosure, participants were offered access to web education or a GC session (conducted by seven GCs via phone or

in person).[38,40] GCs were blinded to participants' research results at predisclosure and completed counseling checklists to ensure fidelity to tier 1 content.[41,42]

### Disclosure of Genetic Research Results

Participants received results by phone or in person with a GC. The result disclosure visit was separate from the education visit. Fidelity was assessed in 20% of counseling sessions, with a mean fidelity to checklists of 89% (predisclosure sessions) and 88% (disclosure sessions). On the basis of institutional policies, participants at Columbia with a positive result were told that there was a genetic finding but not the specific gene. Participants with a variant of uncertain significance (VUS) or negative result were told that there were no findings that could affect their health. UPenn and UChicago allowed participants with positive or VUS results to learn the specific gene and informed them that they should not change medical care until after confirmation testing.

### Confirmation Testing in a Clinical Laboratory Improvement Amendments-Certified Laboratory and Clinical Follow-Up

Participants with a pathogenic or likely pathogenic research result in any gene were recommended to have clinical confirmation testing. We also recommended confirmation for VUS results in high-penetrance genes since a reclassification to pathogenic or likely pathogenic could affect medical care. This approach provided confirmation of the result along with an additional opinion regarding variant calling as clinical laboratories have access to additional data. It also allowed clinical laboratories to be responsible for updates to VUS results. The need for confirmation testing and the importance of not altering medical management until after confirmation was shared in predisclosure education and at disclosure. For discordant results, recommendations for medical management were based on the participant's clinical result and personal and family history, consistent with clinical care. GCs and research staff provided reminders and support to complete confirmation testing. Research funds covered all costs of confirmation testing at UChicago and costs not covered by insurance at UPenn and Columbia. Confirmation testing was completed by mailed saliva kits or phlebotomy during a clinical visit. Confirmation testing results were shared by phone or in person. All participants were recommended to return for follow-up care.

### PROs

As previously described, the selection of relevant outcomes after the receipt of genetic research results was informed by our conceptual model,[38,40,41] which is grounded in the Self-Regulation Theory of Health Behavior.[43,44] Our model proposes that uptake of genetic research results and response to (eg, psychosocial adjustment) and use of (eg, performance of health behaviors) genetic information are products of an individual's understanding (eg, knowledge of genetic disease) and perception of disease threat (eg, cancer risk).[41,43] Participants completed surveys at baseline (T0), after predisclosure education (T1), after disclosure counseling (T2), and at 6 months (T3).

*Knowledge of genetic disease* was evaluated (T0-T3) using an adapted version of the Cancer Genetics Knowledge Scale and ClinSeq knowledge scale[45-47] and included knowledge of inheritance and test interpretation (nine items), benefits (three items) and limitations (six items) of multigene testing, and differences between research and clinical testing (five items; Cronbach's $\alpha$ = .79-.83).[38]

*Perceived risk of cancer* (T0) was measured on a Likert scale in relation to the average woman (much higher, higher, same, lower, much lower) and, in a second item, as a numerical lifetime risk (0%-100%) of getting breast cancer (or breast cancer again).

*Psychosocial adjustment* included the following: (1) state anxiety (T0-T2), measured with the 20-item State Inventory[48,49] (Cronbach's $\alpha$ = .94-.95); (2) general anxiety and depression (T0-T3), assessed with the Hospital Anxiety and Depression Scale[50] (Cronbach's $\alpha$ = .83-.85 and .81-.83); and (3) cancer-specific distress (T0-T3), evaluated with the 15-item Impact of Events Scale[51] (Cronbach's $\alpha$ = .86-.89).

*Satisfaction with genetic services* was measured (T2) with a 13-item scale used in related research[38,42,52,53] (Cronbach's $\alpha$ = .81-.83).

*Uncertainty* was assessed (T0-T3) using a three-item scale adapted from the Multi-Dimensional Impact of Cancer Risk Assessment[54] (Cronbach's $\alpha$ = .84).

*Perceived utility* was assessed (T0-T3) with a novel scale developed to evaluate patient perceptions of the utility of genetic results, including two 12-item subscales evaluating medical and personal utility, both now and in the future (Cronbach's $\alpha$ = .96-.97).[38,55]

### Statistical Analyses

We characterized the samples using means, standard deviations, and proportions. We used logistic regressions to examine characteristics associated with responding to enrollment status groups and completion of the intervention. For psychosocial outcomes, we examined linear regressions of change scores between baseline and follow-up times (ie, follow-up minus baseline scores). In regressions, we controlled for variables that were found or hypothesized to be associated with longitudinal follow-up. These included site, Hispanic ethnicity, education, number of children, age, and number of relatives with previously diagnosed cancer. We used multiple imputation methods with 100 multiply imputed data sets to account for missing data in the regression analyses.[56] Analyses were conducted in STATA (StataCorp, College Station, TX) and SAS (SAS Institute, Cary, NC).

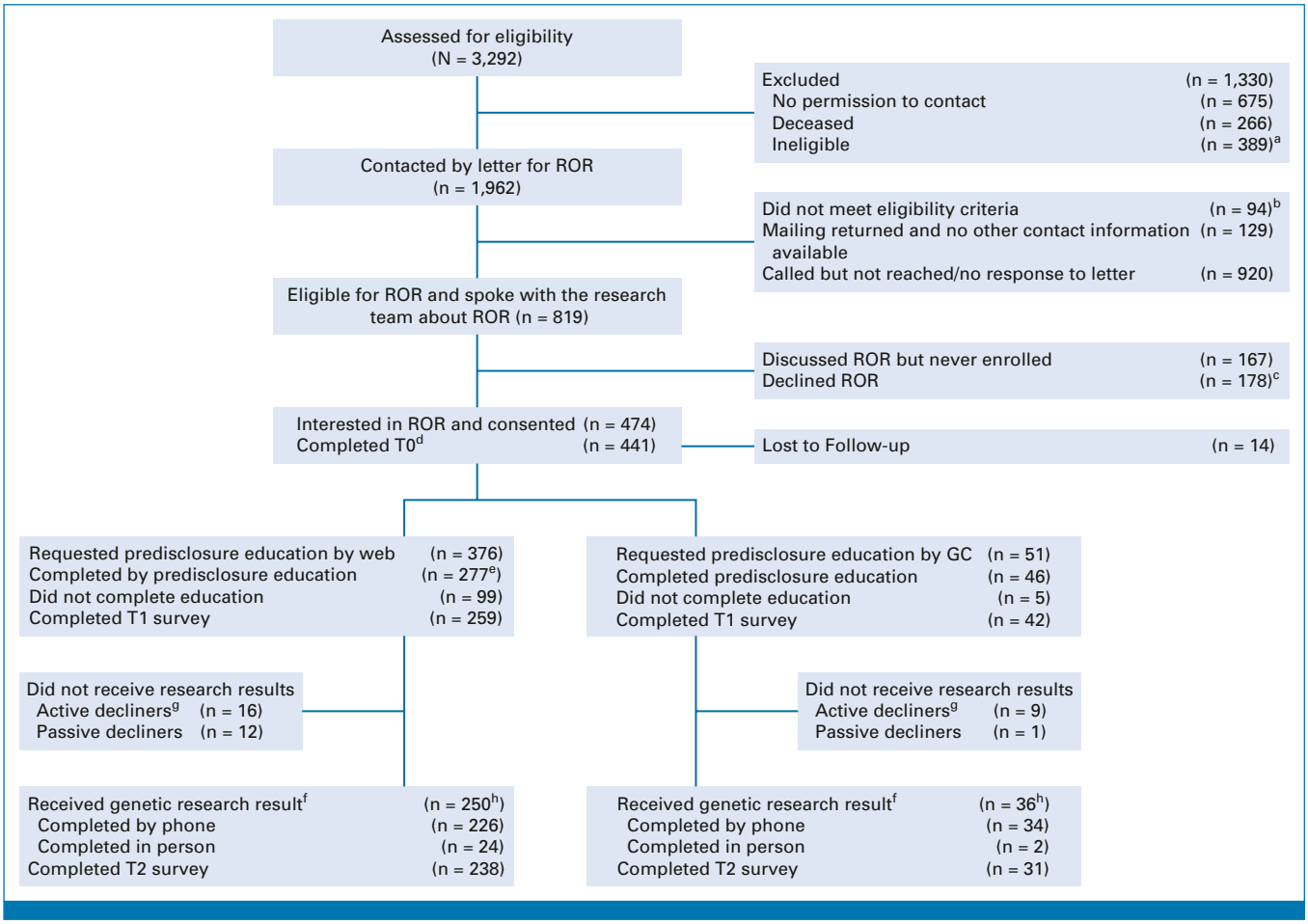


**FIG 1.** CONSORT diagram. [a]Twelve patients already had clinical MGPT, 155 had missing contact information, 103 research samples were not available, 38 were already known to be clinically BRCA+, and 81 were living abroad. [b]Thirty-four patients were found to be deceased, 47 already had clinical MGPT, two were previously disclosed, three had language barriers, two did not have decision making capacity, and six did not have valid consent. [c]Reasons for declining included privacy concerns, concerns about time burdens, not being interested in genetic information, only wanting actionable results, preferring clinical testing, and concerns about uncertainty or distress. [d]The time from baseline survey to web education link being sent to participants was a median of 1.0 days and a mean of 4.98 days (SD, 16.06). [e]Twenty-one were completed with a GC. [f]Fourteen pathogenic or likely pathogenic variants (positive result) were returned, including five high-penetrance genes (BRCA1 [2], BRCA2 [2], MSH6) and nine moderate-penetrance genes (ATM [2], BARD1, CHEK2 [4], NBN, PALB2, RAD51D). There were 23 results with at least one VUS (14 variants in moderate-penetrance genes and nine in high-penetrance genes where confirmation testing was recommended). There were two additional VUS results as a second finding. There were 250 with no findings. One individual received results without completing visit 1. [g]Sixteen withdrew from the study. [h]Two hundred twenty-nine of 256 who ultimately completed by web received results, and 56 of 67 who ultimately completed by GC received results. MGPT, multigene panel testing; ROR, return of results; T0, baseline; T1, after predisclosure counseling; T2, after disclosure counseling; VUS, variant of uncertain significance.

We hypothesized that among 1,200 participants, 70% could be reached, 50% would enroll, and 70% would receive results. With 50% enrollment, we would be able to estimate the true uptake with at least a precision of approximately 4.9%. For secondary analyses, we aimed for a sample size of 420 to have 85% power to detect a standardized odds ratio of 1.5 in logistic regressions. We set the type I error rate and *P* value to 1% (two-sided) to partially account for multiple hypothesis testing. Additional power calculations are provided in our Protocol (online only).

## RESULTS

### Participants

Across three sites, 1,962 potential participants were contacted (April 2015-October 2019; Fig 1). Some letters were returned (6.6%), and 94 participants were found to be deceased or ineligible, leaving 1,739 eligible mailings. We were not able to communicate with 920 research participants to discuss the option to receive research results

**TABLE 1.** Characteristics of All Potential Research Participants Contacted

| Characteristic | Declined (active and passive; n = 345) | Consented and Did Not Receive Results (n = 188) | Consented and Received Results (n = 286) | Total (n = 819) | P[a] |
|---|---|---|---|---|---|
| Site, No. (%) | | | | | <.001 |
| Penn | 72 (21) | 39 (21) | 102 (36) | 213 (26) | |
| Chicago | 61 (18) | 53 (28) | 68 (24) | 182 (22) | |
| Columbia | 212 (61) | 96 (51) | 116 (41) | 424 (52) | |
| Age, years, median (range)[b] | — | 61.89 (13.13) | 62.44 (10.97) | 62.26 (11.71) | .654 |
| Race, No. (%) | | | | | <.001 |
| White | 210 (61) | 113 (36) | 243 (85) | 566 (69) | |
| Black | 51 (15) | 36 (19) | 34 (12) | 121 (15) | |
| Asian | 4 (1) | 2 (1) | 0 (0) | 6 (<1) | |
| Others | 8 (2) | 15 (8) | 9 (3) | 32 (4) | |
| Unknown | 72 (21) | 22 (12) | 0 (0) | 94 (12) | |
| Ethnicity—Hispanic, No. (%) | | | | | <.001 |
| Hispanic | 53 (15) | 47 (25) | 21 (7) | 121 (15) | |
| Non-Hispanic | 184 (53) | 140 (74) | 243 (85) | 567 (69) | |
| Unknown | 108 (31) | 1 (1) | 22 (8) | 131 (16) | |
| Education, No. (%) | 43 (13) | 20 (11) | 13 (5) | 76 (9) | <.001 |
| HS or less vocational/tech | 4 (1) | 7 (4) | 5 (2) | 16 (2) | |
| Some college | 37 (11) | 26 (14) | 32 (11) | 95 (12) | |
| College graduate or higher | 161 (47) | 92 (49) | 192 (67) | 445 (54) | |
| Unknown | 100 (29) | 43 (23) | 44 (15) | 187 (23) | |
| IRB permitted the research team follow-up after invitation letter | | | | | .587 |
| Yes | 306 (89) | 172 (92) | 255 (89) | 733 (90) | |
| No | 39 (11) | 16 (9) | 31 (11) | 86 (11) | |
| Marital status, No. (%) | | | | | <.001 |
| Married | 50 (15) | 116 (62) | 206 (72) | 372 (45) | |
| Not married | 41 (12) | 56 (30) | 73 (26) | 170 (21) | |
| Unknown | 254 (74) | 16 (9) | 7 (2) | 277 (34) | |
| Has children, No. (%) | | | | | <.001 |
| Yes | 93 (27) | 117 (62) | 191 (67) | 401 (49) | |
| No | 42 (12) | 69 (37) | 94 (33) | 205 (25) | |
| Unknown | 210 (61) | 2 (1) | 1 (0) | 213 (26) | |
| History of cancer, No. (%) | | | | | .825 |
| Yes | 213 (62) | 122 (65) | 186 (65) | 521 (64) | |
| No | 131 (38) | 66 (35) | 99 (35) | 296 (36) | |
| Unknown | 1 (<1) | 0 (0) | 1 (0) | 2 (<1) | |
| Had previous BRCA1/2 testing,[c] No. (%) | | | | | <.001 |
| Yes | 77 (22) | 96 (51) | 185 (65) | 358 (44) | |
| No | 55 (16) | 68 (36) | 87 (30) | 210 (26) | |
| Unknown | 213 (62) | 24 (13) | 14 (5) | 251 (31) | |
| Age at first cancer among those with cancer history, mean (SD) | 50.88 (13.49) | 47.27 (11.08) | 46.57 (9.42) | 47.81 (11.11) | .007 |
| No. of FDR/SDR with breast cancer, mean (SD) | 1.58 (1.47) | 1.19 (1.34) | 1.24 (1.20) | 1.30 (1.31) | .038 |
| No. of FDR/SDR with any cancer, mean (SD) | 3.39 (2.52) | 2.22 (2.31) | 2.93 (2.26) | 2.80 (2.37) | <.001 |
| Years since the sample was received, mean (SD), range, years[d] | 7.83 (4.48), 2.6-16.6 | 8.80 (4.43), 1.3-17.4 | 9.99 (4.46), 0.1-16.9 | 8.75 (4.55), 0.1-17.4 | .002 |

Abbreviations: FDR, first-degree relative; IRB, institutional review board; SD, standard deviation; SDR, second-degree relative.

[a]*P* values by ANOVAs and chi-squared tests for the joint test of equality among the three columns.

[b]Participant age was not available for many potential participants until after consent.

[c]Given standards at the time, all participants who had previous *BRCA1/2* testing would have had pretest counseling. Participants who had previous *BRCA1/2* testing had a 1.6-unit increase in the baseline knowledge score ($P = .05$) although previous *BRCA1/2* testing was not associated with uptake of education or receipt of research results.

[d]Among those with available dates for when the original sample was received. Original studies enrolled patients from 1999, and many were still open at the time of RESPECT2 (2015).

**TABLE 2.** Uptake of Research Results Hypothesized and Achieved

| Result | Hypothesized (No.) | Actual (No.) |
|---|---|---|
| Participants able to be reached | 70% (840/1,200) | 47.2% (819/1,739) |
| Participants enrolled | 50% (420/840) | 57.8% (474/819) |
| Participants who completed predisclosure education and receipt of results | 50% minimum (210/420) | 60.3% (286/474) |
| | 70% hypothesized (294/420) | |
| Uptake of research results among participants reached | 25% minimum (210/840) | 34.9% (286/819) |
| | 35% hypothesized (294/840) | |

NOTE. In RESPECT1 (n = 372 contacted), 51.6% were able to be reached, 55.7% enrolled, and 77.6% completed predisclosure counseling (all with a GC) and receipt of results. Uptake among all participants reached was 43.2%.
Abbreviation: GC, genetic counselor.

(ie, nonresponders; 52.9%). Of 819 participants who could be reached, 178 (21.7%) actively declined receipt, 167 (20.4%) passively declined (ie, expressed interest but were lost to follow-up), and 474 (57.8%) enrolled (Table 1).

### Uptake of Web-Based Predisclosure Education and Genetic Research Results

Most participants selected web education (88.5%) as an alternative to speaking with a GC for predisclosure education (Fig 1); 310 logged on, and 82.5% completed web education (Appendix Table A2). Research staff contacted participants who did not log on or complete to offer assistance or the option to speak with a GC. Among participants who selected to speak with a GC, 46 (90.2%) completed.

Among participants who consented to RESPECT2 to learn about receiving research results, 286 (60.3%) received results (Table 2). Most participants (88.2%) who completed predisclosure education received results, which did not differ by method (83.6% with a GC *v* 89.5% by web education; $P = .2$). Fourteen (4.9%) participants received a positive result, 23 received a VUS (8.0%), and 250 (87.4%) had no findings (Fig 1).

### Factors Associated With Uptake of Research Results

Research participants who could not be reached were more likely to be non-White, have lower education, have no history of cancer, have not allowed phone follow-up, and be at Columbia or UPenn. Research participants who actively or passively declined results were more likely to be Black, have lower education, not allow phone follow-up, and be at Columbia or UChicago (Appendix Table A3).

Enrolled participants who selected web education were more likely to have college education, be at UChicago or UPenn, not have children, have higher baseline knowledge, and have lower depression (Table 3). Completing predisclosure education was associated with selecting a GC, having college education, having higher baseline knowledge, having more relatives with cancer, and being at UPenn (Table 3). Completing predisclosure web education was associated with having higher education, having more relatives with cancer, and being at UPenn. Overall, uptake of research results among those who could be reached was associated with being White, allowing phone follow-up after letter notification, and being at UPenn or Columbia (Table 3).

### PROs

Knowledge increased significantly from baseline to all other time points (Appendix Table A4) and did not differ significantly by web versus GC education (Fig 2A). Similarly, there were no significant increases in distress for those who completed education by web versus GC. There was significantly greater reduction in short-term anxiety and uncertainty (T0-T1) and anxiety and depression (T0-T2) among those who completed by web versus GC although there were no significant differences in the long term (Figs 2A and 2B; Appendix Table A5).

Among participants with a positive result, knowledge increased and depression declined over time (Appendix Table A6). Among those with a VUS or negative result, there was a significant increase in knowledge after the receipt of results. There was also a significant reduction in general anxiety, perceived utility of results (VUS and negative), state anxiety, cancer-specific distress, and depression (negative only) after the receipt of results.

### Clinical Confirmation Testing

Most participants (82.6%) underwent recommended clinical confirmation testing (12 of 14 positive results, seven of nine VUS results in high-penetrance genes). Five of 14 (35.7%) participants with a VUS in a low- to moderate-penetrance genes had confirmation testing (testing optional). Among 17 participants for whom testing was submitted to insurance, three (18%) were not covered or had out-of-pocket costs and were covered by research funds.

Five of 24 samples (20.8%) sent for confirmation testing were discordant with research testing. These discordant results included a *BRCA2* variant, which was classified as

**TABLE 3.** Factors Associated With Interest in and Uptake of Individual Genetic Research Results in Multivariable Models

| Factor | OR (95% CI) | *P* |
|---|---|---|
| Factors associated with consenting to RESPECT2 to receive research results (n = 1,739) | | |
| History of cancer | 1.95 (1.72 to 2.21) | <.001 |
| Race | | |
| Black | Reference | |
| White | 3.09 (2.14 to 4.47) | <.001 |
| Allowed phone follow-up after letter | 3.33 (2.96 to 3.74) | <.001 |
| Site | | |
| Columbia | Reference | |
| UChicago | 3.26 (2.39 to 4.44) | <.001 |
| UPenn | 1.60 (1.26 to 2.03) | <.001 |
| Factors associated with selecting for web predisclosure education[a] (n = 427) | | |
| No children | 3.03 (1.34 to 6.84) | .008 |
| Education | | |
| High school education | Reference | |
| Some college | 4.46 (1.60 to 12.41) | .004 |
| College | 4.49 (2.33 to 8.65) | <.001 |
| Higher baseline genetic knowledge | 1.05/point[b] (1.01 to 1.10) | .015 |
| Lower depression | 0.86/point (0.78,0.95) | .003 |
| Site | | |
| Columbia | Reference | |
| UChicago | 5.85 (2.76 to 12.40) | .001 |
| UPenn | 3.27 (1.61 to 6.63) | .001 |
| Factors associated with completing predisclosure education[a] (n = 427) | | |
| Selecting GC predisclosure education as opposed to web education | 11.39 (5.03 to 25.81) | <.001 |
| Education | | |
| High school or less | Reference | |
| College | 3.20 (1.54 to 6.63) | .002 |
| No. of FDR/SDR with any cancer | 1.14 (1.01 to 1.29) | .031 |
| Higher baseline genetic knowledge | 1.05/point[b] (1.01; 1.09) | .026 |
| Site | | |
| Columbia | Reference | |
| UPenn | 1.85 (1.17 to 2.93) | .009 |
| Factors associated with receiving results among those who could be reached (n = 819) | | |
| Race | | |
| Black | Reference | |
| White | 2.56 (1.88 to 3.49) | <.001 |
| Allowed phone follow-up after letter | 2.84 (2.21 to 3.64) | <.001 |
| Site | | |
| Columbia | Reference | |
| UChicago | 2.03 (1.69 to 2.44) | <.001 |
| UPenn | 4.25 (3.60 to 5.03) | <.001 |

NOTE. We used multiple logistic regression models to assess relationships. Variables included in all models were site (Penn, Columbia, Chicago), race (White, Black, Asian/Other), ethnicity (Hispanic/Latino, not Hispanic/Latino), education (less than high school, vocational, some college, college degree, or higher), history of cancer (yes, no), marital status, and having children. The variable allowed phone follow-up after a mailed letter (yes, no) was included in the model of consent and receiving results.

Abbreviations: Columbia, Columbia University; FDR, first-degree relative; GC, genetic counselor; OR, odds ratio; SDR, second-degree relative; UChicago, University of Chicago; UPenn, University of Pennsylvania.

[a]Variables further included in the postconsent models were age, number of first/second degree relatives with breast cancer, web education versus GC education, and patient-reported outcomes (knowledge, anxiety, depression, distress, numerical lifetime perceived risk). We accounted for clustering by site in estimation. Postconsent models including perceived risk as a Likert scale (instead of the continuous scale) generated similar results.

[b]Per-point increase in the scale.

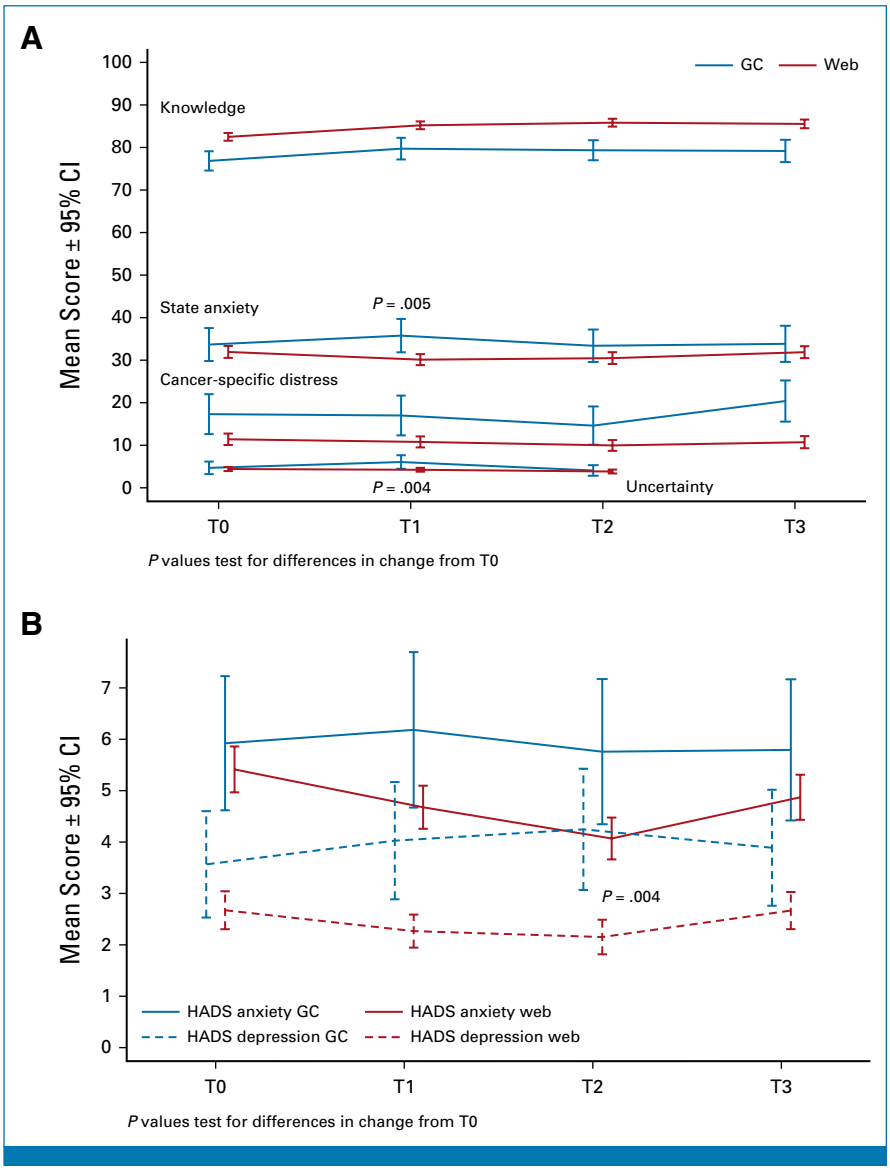


**FIG 2.** Change in patient-reported outcomes for web-based predisclosure education users relative to predisclosure education with a genetic counselor after predisclosure education and disclosure of results. The x-axis labels denote study wave, with T0 as baseline time point. The y-scale represents the absolute means of the scores. The range differs for each measure, which allowed us to present the results in the same figure to reduce space. The range and means at each time period are reported in Appendix Table A2. There were no significant differences in the percentage of participants who met cutoffs for clinically significant distress between groups. GC, genetic counselor; T0, baseline; T1, after predisclosure counseling; T2, after disclosure counseling; T3, at 6 months.

pathogenic by the research laboratory and as a VUS by the clinical laboratory (although this variant has been classified as pathogenic in ClinVar), and a common *CHEK2* variant, which was not detected by the clinical laboratory because of sample mix-up, or analytic error. Others included *MSH6*, *MUTYH*, and *PALB2* VUSs, which were not reported by the clinical laboratory. For these, we do not know if discordance was due to a difference in interpretation, sample mix-up or analytic error.

## DISCUSSION

To our knowledge, this is the first return of genetic research results study reporting uptake and PROs with a web-based alternative to predisclosure genetic counseling. Although we met our minimum hypothesized uptake of results, as in our previous return of results study, many participants could not be reached. In addition, 88% of participants chose web education although some did not complete it or receive their

results. Although uptake of results was not higher among those who requested web education, there was no evidence of misunderstanding or greater distress among those who chose web education as compared with a GC. This suggests that web education is a viable delivery alternative as long as completion rates can be addressed.

Interest in web education was higher than expected on the basis of stakeholder interviews,[39] but was still consistent with other studies of patients with cancer undergoing genetic testing.[57-60] Although most who selected web education completed the intervention, 26% did not and 18% never logged on. This finding is consistent with our stakeholder interviews in which some participants reported that they might be more likely to not complete a web alternative because it is not a scheduled appointment and therefore easier to forget to complete.[39] Participants who never logged on were more likely to have lower education and lower genetic knowledge, raising the concern that eHealth alternatives could increase health disparities. It is possible that staff resources for reminding participants to log on varied and that automated reminders, follow-up, or additional assistance (eg, digital navigators) could be beneficial. In addition, our data suggest that retaining the option to speak with a GC is important for some participants.

Although we expected that web education might decrease barriers and increase uptake of research results, receipt of results among eligible contacted participants was no higher than that in RESPECT1.[38] Other studies have similarly reported difficulty in recontacting research participants,[38,61] with passive or active decline of research results as high as 40%.[27,32-34,38,62] Site differences in reaching research participants and in uptake of research results suggest that the level of engagement with the research cohort may also be important. Lower uptake among non-White participants and those with lower education suggests that disparities continue to exist with respect to interest in receiving genetic information[32,38] and that providing the opportunity to decline genetic research results remains important.

Among those who completed predisclosure education, the majority (88%) chose to receive their research results, which did not differ by web versus GC education. Knowledge did not significantly differ by education method, and there were no increases in negative affective outcomes for web education. In addition, how participants used the intervention (eg, number of times accessed, content accessed) could be informative. More extensive secondary analyses addressing these questions are ongoing.

An additional challenge for research programs that are not sequencing in Clinical Laboratory Improvement Amendments-approved laboratories is the need to confirm research results. Four participants did not complete clinical confirmation testing even with significant support and coverage of costs, highlighting the importance of understanding barriers to confirmation testing.[27,28,38] The need for clinical confirmation was further underscored by the fact that we had at least one pathogenic result that was not confirmed and several results with discordant interpretations. Discordance in our study is likely partially related to the limited data and standards for variant calling at the time the study was conducted. Nevertheless, discordance is not uncommon, even in clinical testing, and provides additional rationale for confirmation testing, including for VUSs.[63]

We acknowledge several limitations. This was an observational study, and many research participants could not be reached, creating a potential nonresponse bias. Reaching participants when research results are not immediately available remains a real-world challenge, making understanding barriers to recontact especially important. Because the study was not randomly assigned, there may be unmeasured differences between groups on the basis of participant self-selection. In addition, the study only included women and was focused on those with a personal or family history of breast cancer. As we had few individuals with positive or VUS results, it is important to confirm findings for these subgroups. Although we used standardized counseling checklists, other differences in counseling could affect outcomes. Differences in levels of engagement with the research cohort and site policies regarding the number of follow-up calls may also be relevant. Finally, outcomes for web-based education could be affected by individual use of the intervention.

In conclusion, we found high interest in a web-based alternative for predisclosure education for return of genetic research results although some patients did not complete web education or receive results. Notably, while uptake of results was not higher among those who requested web education, there was no evidence of misunderstanding or greater distress among those who chose web education. Attention to attrition and lower uptake of results among Black participants and those with less formal education are important areas for future research.

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## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

**Uptake of Genetic Research Results and Patient-Reported Outcomes With Return of Results Incorporating Web-Based Predisclosure Education**

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/jco/authors/author-center.

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

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## APPENDIX 1

**TABLE A1.** The Multimodality RESPECT2 Web-Based Predisclosure Education Intervention

| Module | Tier 1 Content[a] (No. of web screens) | Tier 2 Content (No. of web screens) | Tier 2 Videos[b] (minutes) |
|---|---|---|---|
| Introduction | Introduction to the RESPECT study and invitation to receive research results (1) | | What is the RESPECT study? (2:53) |
| | How to use the website (1) | | |
| Genetic research results *v* clinical testing | What are genetic research results, and how do they different from clinical testing? (2) | | What are the differences between research and clinical testing, and why is confirmation testing needed? (8:56) |
| | What is clinical confirmation testing? (4) | | |
| Cancer genes, risks, and medical management | | | Cancer genes and medical management (9:08) |
| Types of results being returned | Types of cancer genes: high, moderate, low/uncertain risk (1) | More about breast cancer genes (1) | GC explaining a VUS (3:47) |
| | Types of research results: positive, negative, VUS (2) | More about colon cancer genes (1) | |
| Clinical implications of results | How might my results change my clinical care if clinically confirmed? (1) | Medical management options by gene if results are confirmed (1) | |
| Benefits, risks, and limitations of receiving research results | Potential benefits of results (1) | | Benefits of research results (1:21) |
| | Limitations of research results and need for confirmation testing (1) | | Limitations of research results (2:07) |
| | Risks of results (1) | | Risks of receiving research results (2:07) |
| Option to decline results | You may choose to not receive results (1) | | |
| Participant choice | Log your decision (1)<br>Next steps and confirmation testing (1) | | |
| Optional content not included in modules above | | Glossary of terms (1) | Genetics 101 (3:59) |

NOTE. The intervention is informed by the tiered-binned model for genetic education and informed consent and was reviewed with a DAC of individuals with expertise in health disparities and health communication. It was also user and usability tested with five individuals from cancer risk research registries, two with less than a college degree and two who were non-White participants. Modifications on the basis of the DAC and user/usability testing included formatting to make the goals of screens clearer, text changes to increase use of plain language, clarifications to terms and descriptions identified as complex or difficult to understand, and additional content requested by users. The linear intervention includes eight modules and eight optional videos although participants can view modules for as long and as many times as desired and go back to previously viewed topics.

Abbreviations: DAC, Diversity Advisory Committee; GC, genetic counselor; VUS, variant of uncertain significance.

[a]Completing tier 1 content once takes approximately 15 minutes for the average user.

[b]Videos include a GC explaining specific topics. Content in some videos is intentionally redundant with tier 1 and tier 2 content and designed to provide an alternative method for reviewing content for participants with different learning preferences.

**TABLE A2.** Completion of Predisclosure Education by Web Versus Genetic Counseling (n = 427)

| Predisclosure Original Selection | Completed by Web Education Intervention[a] | Completed by GC |
|---|---|---|
| Requested web education (n = 376) | | |
| Logged on[b] (n = 310) | 256 | 13 |
| Never logged on (n = 66) | 0 | 8 |
| | Total Web group completed = 74% | |
| Requested GC (n = 51) | NA | 46 |
| | Total GC group completed = 90% | |

NOTE. Research staff contacted participants who did not log on to offer assistance or the option to speak with a GC although this varied by site and resources. The web education intervention remained open throughout the study, and passive decliners were recontacted a final time before study closure to let them know the intervention would be closing and no longer available. The median/mean time from completion of the baseline survey to completion of web education (19-49.35 days) did not differ significantly from completion of the baseline survey to completion of GC education (25-29.58 days; $P = .40$). But the time to completion was significantly longer for those who did not complete by web and were then contacted to assess barriers and ultimately completed by GC (81-104.68 days; $P \leq .022$ compared with web- or GC-only arms).

Abbreviations: GC, genetic counselor; NA, not available.

[a]Completing web education was defined as reviewing all tier 1 content (which is linear by design) and logging a decision on the participant choice screen.

[b]Logged on is defined as entering log-in information to access the site and includes viewing some but not all screens. The mean number of times that users logged on was 2.3 times (range, 1-12), and the mean total time on site was 49.7 minutes (range, 3.4-284.5).

**TABLE A3.** Factors Associated With Nonresponse and Declining Research Results

| Factor | OR (95% CI) | *P* |
|---|---|---|
| Factors associated with no response after receiving letter and follow-up phone calls[a] | | |
| No history of cancer | 2.03 (1.33 to 3.10) | .001 |
| Race | | |
| White | Reference | |
| Black | 2.55 (1.43 to 4.55) | .002 |
| Asian/Others | 1.81 (1.20 to 2.75) | .005 |
| Education | | |
| High school | 1.49 (1.10 to 2.03) | .011 |
| College degree or more | Reference | |
| Not allowed phone follow-up after letter | 2.24 (1.84 to 2.72) | <.001 |
| Site | | |
| UChicago | Reference | |
| Columbia | 2.03 (1.42 to 2.91) | <.001 |
| UPenn | 3.37 (3.00 to 3.78) | <.001 |
| Factors associated with active/passive declining after receiving letter and outreach by research staff if permitted[b] | | |
| Race | | |
| White | Reference | |
| Black | 2.04 (1.30 to 3.19) | .002 |
| Education | | |
| High school | 1.85 (1.08 to 3.19) | .026 |
| Some college | Reference | |
| Not allowed phone follow-up after letter | 2.83 (2.29 to 3.50) | <.001 |
| Site | | |
| UPenn | Reference | |
| UChicago | 1.28 (1.07 to 1.52) | .006 |
| Columbia | 3.83 (3.11 to 4.72) | <.001 |

NOTE. We used multiple logistic regression models to assess relationships. Variables included in both models were site (Penn, Columbia, Chicago), race (White, Black, Asian/Others), ethnicity (Hispanic/Latino, not Hispanic/Latino), education (less than high school, vocational, some college, college degree or higher), allowed phone follow-up after mailed letter (yes, no), history of cancer (yes, no), marital status, and children. Other variables, such as age, were not included because we did not have IRB approval for these variables before consent.

Abbreviations: Columbia, Columbia University; IRB, institutional review board; OR, odds ratio; UChicago, University of Chicago; UPenn, University of Pennsylvania.

[a]n = 1,739 with response data.

[b]n = 819 participants who could be reached. This adjusts for clustering by site.

**TABLE A4.** PROs With Receipt of Genetic Research Results (n = 286)

| Outcome Measure | Baseline (T0) | After Predisclosure Education (T1) | | *P* for Change From T0 to T1,[a] *P* for Change in % Who Met Clinical Cutoff | After Research Result Disclosure (T2) | | *P* for Change From T0 to T2,[b] *P* for Change in % Who Met Clinical Cutoff | 6 months After Disclosure (T3) | | *P* for Change From T0 to T3,[b] *P* for Change in % Who Met Clinical Cutoff |
|---|---|---|---|---|---|---|---|---|---|---|
| | Mean (SD), % Who Met Cutoff for Clinically Significant Distress | Mean (SD), % Who Met Cutoff for Clinically Significant Distress | Difference, Mean (95% CI) | | Mean (SD), % Who Met Cutoff for Clinically Significant Distress | Difference, Mean (95% CI) | | Mean (SD), % Who Met Cutoff for Clinically Significant Distress | Difference, Mean (95% CI) | |
| Knowledge (range, 22-107) | | | | | | | | | | |
| n = 323 | 81.86 (7.47) | 84.37 (7.50) | 2.51 (1.75 to 3.27) | <.001 | | | | | | |
| n = 286 | 81.78 (7.45) | 84.52 (7.49) | | — | 85.01 (7.46) | 3.23 (2.46 to 4.00) | <.001 | 84.74 (7.95) | 2.96 (2.13 to 3.79) | <.001 |
| State anxiety (range, 20-80) | | | | | | | | | | |
| n = 323 | 32.31 (11.38) | 31.47 (10.95) | −0.84 (−1.74 to 0.05) | NSS | | | | | | |
| n = 286 | 32.16 (11.28) | 30.84 (10.68) | | — | 30.85 (11.10) | −1.31 (−2.24 to −0.37) | .006 | 32.13 (10.89) | −0.03 (−1.11 to 1.05) | NSS |
| General anxiety (range, 0-21) | | | | | | | | | | |
| n = 323 | 5.61 (3.62), 11% | 5.08 (3.61), 7% | −0.52 (−0.80 to −0.24) | <.001, .02 | | | <.001, NSS | | | <.001, NSS |
| n = 286 | 5.48 (3.62), 10% | 4.87 (3.54), 6% | | — | 4.28 (3.41), 5% | −1.20 (−1.51 to −0.88) | | 4.99 (3.44), 7% | −0.49 (−0.82 to −0.16) | |
| General depression (range, 0-21) | | | | | | | | | | |
| n = 323 | 2.84 (2.97), 3% | 2.59 (2.75), 2% | −0.25 (−0.46 to −0.03) | .024, NSS | | | <.001, NSS | | | NSS, NSS |
| n = 286 | 2.79 (2.98), 3% | 2.49 (2.74), 2% | | — | 2.42 (2.87), 2% | −0.37 (−0.59 to −0.15) | | 2.82 (2.90), 2% | 0.04 (−0.20 to 0.27) | |
| Cancer-specific distress (range, 0-42) | | | | | | | | | | |
| n = 323 | 12.44 (11.65), 7% | 12.10 (11.15), 7% | −0.34 (−1.39 to 0.71) | NSS, NSS | | | | | | NSS |
| n = 286 | 12.15 (11.39), 6% | 11.57 (11.02), 7% | | | 10.55 (10.52), 4% | −1.61 (−2.81 to −0.40) | .009, NSS | 11.94 (11.70), 7% | −0.21 (−1.5 to 1.07) | NSS |
| Uncertainty (range, 0-15) | | | | | | | | | | |
| n = 323 | 4.60 (4.09) | 4.64 (3.89) | 0.04 (−0.36 to 0.44) | NSS | | | | | | |
| n = 286 | 4.45 (3.88) | 4.47 (3.84) | | — | 3.86 (3.55) | −0.59 (−1.08 to −0.10) | .020 | — | | |
| Perceived utility (now; range, 12-60) | | | | | | | | | | |
| n = 286 | 37.22 (8.63) | — | | — | 32.58 (10.00) | −4.63 (−5.65 to −3.61) | <.001 | 34.64 (9.47) | −2.58 (−3.74 to 1.42) | <.001 |
| Perceived utility (future; range, 12-60) | | | | | | | | | | |
| n = 286 | 38.69 (8.61) | — | | — | 33.85 (10.04) | −4.85 (−5.94 to −3.76) | <.001 | 35.91 (9.54) | −2.78 (−3.95 to −1.62) | <.001 |
| Satisfaction (range, 13-65) | | | | | | | | | | |
| n = 286 | — | — | | — | 39.82 (4.15) | | NA | | | |

NOTE. For participants at Columbia University with a positive or VUS finding (n = 12), PROs reported above were obtained after confirmation testing as their initial disclosure only shared that there is a potential finding that needs to be confirmed. Specific gene and result (positive or VUS) were only shared after confirmation testing as per institutional policies. Cutoffs for clinically significant distress were ≥11 for anxiety and depression and >32 for cancer-specific distress.

Abbreviations: NA, not available; NSS, not statistically significant; PROs, patient-reported outcomes; T0, baseline; T1, after predisclosure counseling; T2, after disclosure counseling; T3, at 6 months; VUS, variant of uncertain significance.

[a]n = 323 for change from T0 and T1.

[b]n = 286 for change from T0 to T2 and T0 to T3 as 286 received results.

**TABLE A5.** Change in Patient-Reported Outcomes for Web-Based Predisclosure Education Users Relative to Predisclosure Education With a GC After Predisclosure Education and Disclosure

| Outcome Measure | T0-T1 (after predisclosure education, predisclosure web *v* GC) | T0-T2 (after disclosure of results, predisclosure web *v* GC) |
|---|---|---|
| State anxiety | 2.79 (GC) *v* −1.45 (web), −4.15 (95% CI, −6.98 to −1.32; adjusted difference), $P = .005$ | −0.28 (GC) *v* −1.45 (web), −1.32 (95% CI, −4.37 to 1.73; adjusted difference)<br>NSS |
| General anxiety | 0.38 (GC) *v* −0.67 (web), −1.13 (95% CI, 2.03 to −0.22; adjusted difference), $P = .020$ | −0.16 (GC) *v* −1.34 (web), −1.14 (95% CI, −2.14 to −0.15; adjusted difference), $P = .035$ |
| Cancer-specific distress | 0.40 (GC) *v* −0.46 (web), −0.77 (95% CI, −4.18 to 2.65; adjusted difference)<br>NSS | −2.69 (GC) *v* −1.45 (web), 0.55 (95% CI, −3.39 to 4.50; adjusted difference)<br>NSS |
| Depression | 0.34 (GC) *v* −0.35 (web), −0.63 (95% CI, −1.32 to 0.06; adjusted difference)<br>NSS | 0.68 (GC) *v* −0.52 (web), −1.06 (95% CI, −1.76 to −0.36; adjusted difference), $P = .003$ |
| Knowledge | 2.47 (GC) *v* 2.52 (web), 0.29 (95% CI, −2.17 to 2.75; adjusted difference)<br>NSS | 2.52 (GC) *v* 3.33 (web), 1.29 (95% CI, −1.30 to 3.80; adjusted difference)<br>NSS |
| Uncertainty | 1.46 (GC) *v* −0.20 (web), −2.00 (95% CI, −3.30 to −0.70; adjusted difference), $P = .003$ | −0.62 (GC) *v* −0.58 (web), −0.14 (95% CI, −1.72 to 1.44; adjusted difference)<br>NSS |

Abbreviations: GC, genetic counselor; NSS, not statistically significant; T0, baseline; T1, after predisclosure counseling; T2, after disclosure counseling.

[a]Adjusted for baseline differences between groups. There were no significant differences in the percentage of participants who met cutoffs for clinically significant distress.

**TABLE A6.** Patient-Reported Outcomes With Receipt of Genetic Research Results by Test Result Among All Participants Regardless of the Pretest Education Method

| Outcome Measure | Baseline, Mean (SD) | After Predisclosure Counseling, Mean (SD) | After Result Disclosure, Mean (SD) | Change From T0 to T2, Mean (95% CI) | *P* for Change From T0 to T2 | 6 Months After Disclosure (T3), Mean (SD) | *P* for Change From T0 to T3 | Change From T0 to T3, Mean (95% CI) |
|---|---|---|---|---|---|---|---|---|
| Positive results (n = 13) | | | | | | | | |
| Knowledge total (range, 22-107) | 79.78 (5.76) | 81.80 (5.21) | 80.14 (5.78) | 0.36 (−3.19 to 3.91) | NSS | 84.40 (6.69) | .04 | 4.62 (0.19 to 9.05) |
| State anxiety (range, 20-80) | 35.74 (11.71) | 40.20 (12.38) | 37.86 (12.17) | 2.12 (−1.29 to 5.53) | NSS | 34.12 (10.94) | NSS | −1.62 (−5.92 to 2.68) |
| General anxiety (range, 0-21) | 7.54 (4.01) | 7.33 (3.83) | 6.43 (2.93) | −1.1 (−2.74 to 0.53) | NSS | 6.77 (3.23) | NSS | −0.77 (−3.01 to 1.47) |
| General depression (range, 0-21) | 4.54 (3.13) | 4.18 (2.82) | 3.36 (3.17) | −1.18 (−2.3 to −0.05) | .04 | 2.91 (3.20) | .05 | −1.63 (−3.3 to 0.04) |
| Cancer-specific distress (range, 0-75) | 14.92 (12.70) | 16.01 (13.35) | 14.62 (9.96) | −0.3 (−6.72 to 6.12) | NSS | 20.13 (15.02) | NSS | 5.20 (−2.42 to 12.82) |
| Uncertainty (range, 0-15) | 5.72 (4.68) | 5.29 (4.68) | 6.12 (4.08) | 0.4 (−2.25 to 3.05) | NSS | — | — | |
| Perceived utility (now; range, 12-60) | 38.92 (9.30) | — | 37.63 (10.16) | −1.29 (−5.74 to 3.15) | NSS | 38.06 (11.14) | NSS | −0.87 (−6.18 to 4.45) |
| Perceived utility (future; range, 12-60) | 40.62 (9.30) | — | 38.50 (10.48) | −2.12 (−7.03 to 2.78) | NSS | 40.16 (11.90) | NSS | −0.47 (−5.63 to 4.7) |
| Negative results (n = 250) | | | | | | | | |
| Knowledge total (range, 22-107) | 82.10 (7.39) | 84.80 (7.52) | 85.46 (7.45) | 3.36 (2.53 to 4.19) | <.001 | 85.01 (7.83) | <.001 | 2.90 (2.02 to 3.79) |
| State anxiety (range, 20-80) | 31.49 (10.92) | 30.21 (10.33) | 29.94 (10.43) | −1.55 (−2.49 to −0.6) | .001 | 31.85 (10.84) | NSS | 0.36 (−0.76 to 1.48) |
| General anxiety (range, 0-21) | 5.24 (3.45) | 4.69 (3.45) | 4.09 (3.22) | −1.15 (−1.47 to −0.83) | .000 | 4.94 (3.43) | .08 | −0.30 (−0.63 to 0.04) |
| General depression (range, 0-21) | 2.63 (2.96) | 2.32 (2.69) | 2.33 (2.84) | −0.3 (−0.53 to −0.07) | .01 | 2.79 (2.90) | NSS | 0.16 (−0.08 to 0.40) |
| Cancer-specific distress (range, 0-75) | 11.55 (11.02) | 11.18 (10.69) | 10.12 (10.47) | −1.43 (−2.7 to −0.16) | .03 | 11.56 (11.56) | NSS | 0.01 (−1.31 to 1.32) |
| Uncertainty (range, 0-15) | 4.31 (3.77) | 4.47 (3.82) | 3.72 (3.54) | −0.58 (−1.1 to −0.06) | .03 | | | |
| Perceived utility (now; range, 12-60) | 37.15 (8.72) | — | 32.30 (9.99) | −4.84 (−5.96 to −3.72) | .00 | 34.53 (9.40) | <.001 | −2.61 (−3.86 to −1.37) |
| Perceived utility (future; range, 12-600) | 38.60 (8.74) | — | 33.46 (10.12) | −5.14 (−6.33 to −3.95) | .00 | 35.61 (9.45) | <.001 | −2.99 (−4.24 to −1.74) |
| VUS results (n = 23) | | | | | | | | |
| Knowledge total (range, 22-107) | 79.46 (8.55) | 83.00 (8.10) | 82.91 (7.31) | 3.45 (0.8 to 6.09) | .01 | 82.05 (9.57) | NSS | 2.59 (−0.89 to 6.07) |
| State anxiety (range, 20-80) | 37.42 (13.41) | 32.41 (11.30) | 36.80 (14.39) | −0.62 (−6.16 to 4.92) | NSS | 34.02 (11.51) | NSS | −3.4 (−8.72 to 1.93) |
| General anxiety (range, 0-21) | 6.91 (4.51) | 5.41 (3.90) | 5.13 (4.95) | −1.78 (−3.47 to −0.1) | .04 | 4.49 (3.51) | .004 | −2.43 (−3.96 to −0.9) |
| General depression (range, 0-21) | 3.52 (2.89) | 3.33 (2.85) | 2.87 (2.97) | −0.65 (−1.46 to 0.15) | NSS | 3.14 (2.90) | NSS | −0.38 (−1.36 to 0.6) |
| Cancer-specific distress (range, 0-75) | 17.14 (13.51) | 13.37 (12.83) | 12.91 (11.02) | −4.23 (−9.41 to 0.95) | NSS | 11.48 (9.70) | .06 | −5.66 (−11.5 to 0.17) |
| Uncertainty (range, 0-15) | 5.35 (4.44) | 4.00 (3.63) | 4.12 (2.97) | −1.23 (−3.28 to 0.83) | NSS | — | — | −1.23 (−3.28 to 0.83) |
| Perceived utility (now; range, 12-60) | 37.00 (7.33) | — | 32.74 (9.68) | −4.26 (−7.3 to −1.23) | .01 | 33.88 (9.13) | NSS | −3.12 (−7.82 to 1.58) |
| Perceived utility (future; range, 12-60) | 38.61 (6.93) | — | 35.41 (8.25) | −3.2 (−6.36 to −0.04) | .05 | 36.75 (8.77) | NSS | −1.86 (−6.69 to 2.98) |

Abbreviations: NSS, not statistically significant; T0, baseline; T1, after predisclosure counseling; T2, after disclosure counseling; T3, at 6 months; VUS, variant of uncertain significance.