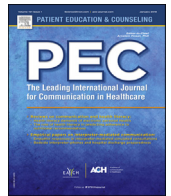




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The impact of the number of tests presented and a provider recommendation on decisions about genetic testing for cancer risk

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ABSTRACT

Objective: To determine how the method of presenting testing options and a provider recommendation can influence a decision about genetic testing for inherited cancer predispositions.

Methods: An online hypothetical vignette study was completed by 454 healthy volunteers. Participants were randomized to receive one of two survey versions which differed by genetic testing choice presentation. One group was shown three options simultaneously (no test, 5-gene or 15-gene), and a second group received the 15-gene option after choosing between the no test and 5-gene options. A preference-based provider recommendation was also incorporated. We examined the effect of these interventions on test selection.

Results: Participants in the simultaneous group were more likely to choose a genetic test than those in the sequential group (OR: 2.35, $p=0.003$). This effect was no longer observed when individuals who had selected no-test in the sequential group were told about the 15-gene test (OR: 1.03 $p=0.932$). Incorporating a provider recommendation into the hypothetical scenario led to more preference-consistent choices ($\chi^2 = 8.53$, $p < 0.0035$).

Conclusions: A larger menu of testing choices led to higher testing uptake. A preference-based clinician recommendation resulted in more preference-consistent choices.

Practice Implications: The structuring of testing options and preference-sensitive recommendations appear to facilitate informed testing decisions.

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1. Introduction

Rapid technological advancements in genetics have led to many new genetic testing (GT) options in a short period of time. Best practices in regard to the presentation of GT options have not been established and clinicians have little guidance on how to structure and present these choices to their patients [1,2]. This has the potential to influence the decisions that patients make and their subsequent medical care. The objective of the current study was to contribute to the evidence base regarding how the presentation of testing options—specifically the number of testing options presented together and the use of a personalized recommendation

from a health care provider – might influence choices about hereditary cancer GT likely to be made by patients.

1.1. Inherited cancers and genetic testing

It is believed that about 5–10 % of all cancers are caused by a hereditary cancer syndrome resulting from a germline genetic variant [2]. Individuals with a hereditary cancer syndrome have an increased lifetime risk to develop specific types of cancer, often at younger ages than the general population. A genetic diagnosis of a hereditary cancer syndrome can guide approaches to cancer screening, prevention and/or treatment and to help inform cancer risks in relatives.

Referral for genetic counseling and testing is often guided by personal and family health history. However, specific guidance for providers about which gene combinations to include on a panel test is lacking [3–5]. Genes differ by the degree of supporting

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evidence for use in clinical management and they are often grouped by the level of risk that a disease-causing variant in the gene confers [3–5]. Clinical testing of high-penetrance genes is supported by well-quantified associations and data-driven risk management strategies in certain populations [3]. One example is Hereditary Breast and Ovarian Cancer Syndrome (HBOC) which is caused by pathogenic variants in either the *BRCA1* or *BRCA2* gene [2]. This syndrome is associated with elevated lifetime risks of developing breast, ovarian, prostate and pancreatic cancers [6]. In contrast, some genes confer moderately increased risks for cancer (e.g. *ATM*, *CHEK2*, *BRIP1*) and the link between positive results and downstream health outcomes is less clear. Testing for some moderate penetrance genes remains controversial in the community and efforts to better understand these genes and their clinical utility are ongoing [3,7–13].

There is a wide assortment of gene combinations available through various commercial labs and the composition of genes on these panels is largely unregulated in the United States [3]. Clinicians generally employ one of four approaches to panel-based GT in the setting of a personal or family history of disease including the following:

- 1.) Syndrome specific test (e.g., testing for HBOC)
- 2.) Cancer-specific high penetrance gene panel (e.g., genes for several syndromes that cause a high-risk for breast cancer)
- 3.) Cancer-specific gene panel with both high and moderate penetrance genes (e.g., many genes that have some association with increased breast cancer risk)
- 4.) “Comprehensive” cancer panels that include genes associated with multiple cancer types or hereditary cancer syndromes [14].

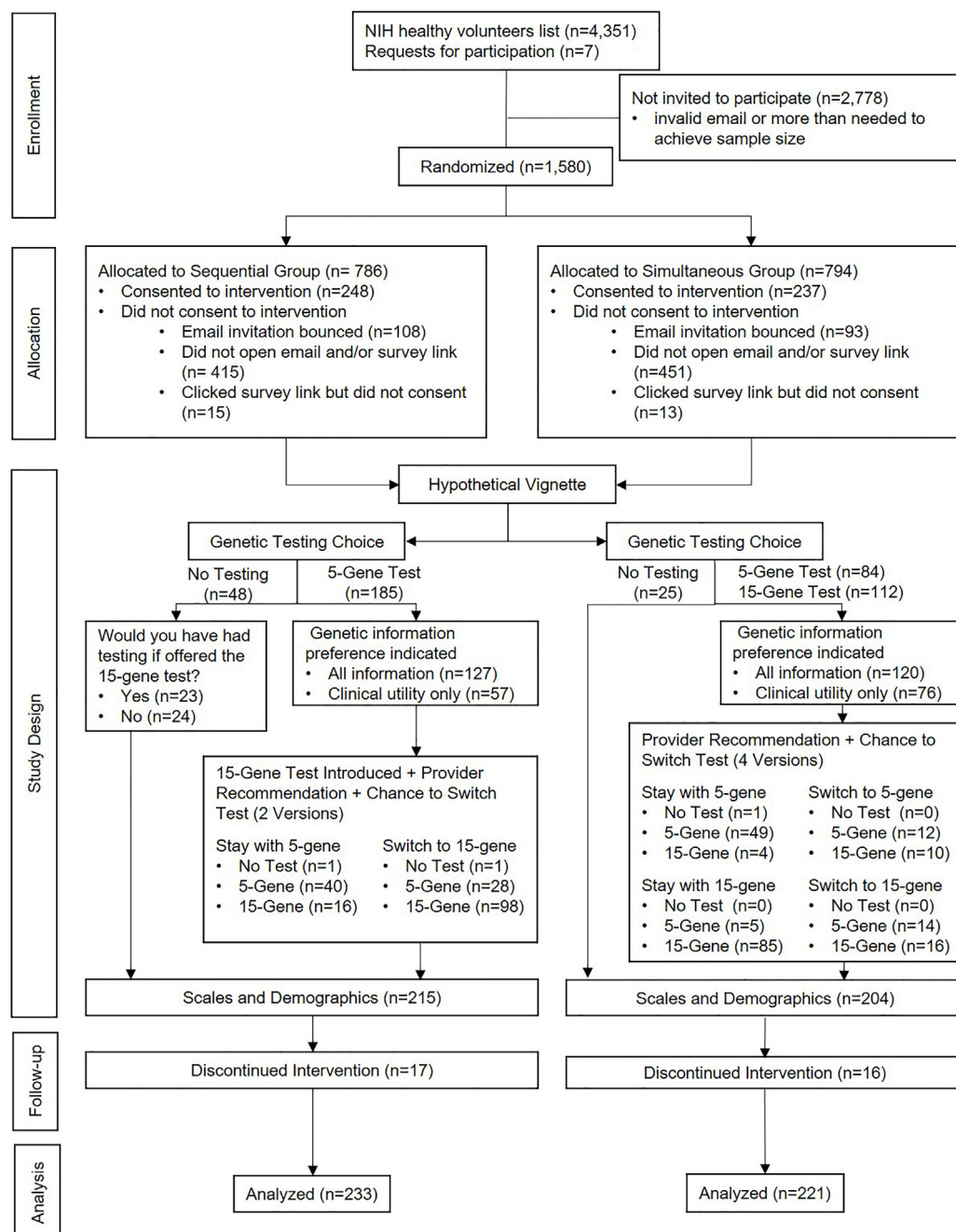


Fig. 1. Flow chart of study design. Survey logic was used to administer personalized follow-up questions to the initial genetic testing decision.

This survey is based on a choice that is possible but not actually available to anyone. This survey should not be used as a source of medical fact. You cannot return to previous pages in the survey after hitting ">>" at the end of each page.

Your Situation

Please imagine that you have visited your family doctor to talk about your chance of having or developing cancer. You have told him that your mother, uncle and grandfather all had cancer, either breast or prostate cancer, when they were around 40 years of age. Your doctor is concerned about your family history and suggests that you see a genetic counselor to learn about genetic testing. The purpose of genetic testing is to see if you have a faulty gene that puts you at high risk for certain types of cancer.

When you visit the genetic counselor she asks you questions about your family's cancer history. Based on this, she says that you qualify for genetic testing. She says that not everyone wants genetic testing because the results can be upsetting. It is up to you to decide if you want genetic testing or not. In the next question you will be asked to make a (hypothetical) decision about undergoing genetic testing. Below is some information about genetic testing to help you with your decision.

What You Could Learn from Genetic Testing

You can get three types of results:

<i>Type of Result</i>	<i>Explanation</i>	<i>Meaning for your Cancer Risk</i>
Positive Result	You have a <u>faulty gene</u>	You are at higher risk to get certain cancers in your lifetime than people without a faulty gene. For the faulty gene with the biggest cancer risk, about 8 in 10 people will get cancer. Some cancers you could learn you are at risk for are breast, prostate, pancreatic and ovarian cancers.
Negative Result	<u>No faulty gene</u> was found	You may not have inherited a faulty gene that gives you a high risk to have certain cancers. However, your family history may still put you at higher risk than the general public to get certain cancers. You could still have a faulty gene that was not tested.
Inconclusive Result	You have a change in a gene but it is <u>unclear</u> if this increases your risk of cancer.	An unclear result means that the test cannot help determine your cancer risk at this time. Your family history may still put you at higher risk than the general public to get certain cancers. You could still have a faulty gene that was not tested.

What Would Happen if You Have a Positive Result

If you have a positive result (faulty gene found):

- You will be told about your chance to develop certain cancers.
- Doctors may recommend that you have certain tests to look for cancer (such as a mammogram or PSA testing), or surgeries to prevent cancer.
- There may not be ways to find early and prevent every cancer you could be at high risk for.
- Each of your children would have a 50% chance of having the same faulty gene.
- Other family members may also have the same faulty gene and a high cancer risk.

Logistics

- Genetic testing is done on a tube of your blood.
- There is 100 dollar copay for any type of genetic testing.

Fig. 2. Hypothetical vignette as it appeared to all study participants.

Altering the size and gene composition of a panel also alters the risks and benefits associated with the test, leading to clinically relevant trade-offs [15]. Testing more genes increases the chances of a positive finding with potential health consequences but also increases the chance of identifying variants of uncertain significance (VUS) [16]. Additionally, some expanded tests can increase the chance of a finding in a gene with unclear clinical validity or related to an unanticipated cancer syndrome. In these instances, the variant may not explain a patient's personal or family history of cancer. Generally, in the United States, it is up to providers to decide what tests to offer and how to offer them, and up to patients to decide if they would like to have GT and which test to have when there are multiple appropriate options [1].

1.2. Decision making

Most patients who make GT decisions prefer an active or collaborative role over a passive role [17]. Patients also have differing opinions on subtle aspects of the GT process such as whether they prefer a single recommended course of action or want all available options before deciding [18]. One method to assist with GT choices is the use of decision-support tools. However, despite being valued by patients, many such tools are limited and have failed to keep pace with clinical advances [19]. Provider recommendations are an additional resource to help patients choose an option. One survey of women considered at-risk for breast cancer found that 82 % wanted their providers to make a recommendation about whether or not to have breast cancer susceptibility testing or provide an opinion after discussing the pros and cons of testing [20]. However, recommendations for or against testing are not practiced by all providers and some still use a non-directive approach [15]. A provider-guided values clarification exercise is another tool that can be used to help patients decide [25,26]. There are limited data about the role and influence of providers in helping patients decide which test to choose in the setting of multiple appropriate GT options.

There are also some unusual financial incentives in the GT process. GT is often presented as an elective medical test so discussions of the out-of-pocket cost are routine [21,22]. To simplify cost discussions, many GT laboratories in the United States have set billing policies that involve a flat out-of-pocket maximum, or a blanket self-pay price [15,23,24]. The same price can apply across similar tests which means that a patient may expect to pay the same for a 10-gene panel or a 40-gene panel.

Additionally, when patients are presented with additional testing options the complexity of the decision increases. It has been well characterized in other contexts that the number and similarity of options presented to individuals can influence choice. When deciding between several options, individuals must determine what information they find important, compare options across the relevant dimensions and integrate that information to come to a decision. The process of comparing different items or attributes of an item can influence how individuals evaluate the options and their ultimate choice [27]. There has been little work to study how the structural aspects of a choice can influence decisions in the context of GT. This study was designed to examine if the way GT options were introduced (simultaneously or sequentially) or the addition of a provider recommendation based on a values clarification question would influence a hypothetical decision about GT for hereditary cancer predisposition. Specifically, we sought to examine (1) whether presenting multiple tests simultaneously would influence the likelihood of choosing to undergo GT and (2) if providing a personalized recommendation would improve the chance that individuals would make choices consistent with their stated preferences.

2. Methods

2.1. Study population and randomization

A list of potential study participants was obtained from the healthy volunteers database at the National Institutes of Health (NIH). A subset of people from this list were selected for email invitation using random number generation with oversampling of older age groups (relative to a census representative distribution) to account for anticipated differences in internet usage patterns by age. Potential participants were randomized to an experimental group (sequential or simultaneous) using random number generation. Exclusion criteria included being under 18 years of age and not having a valid email address.

2.2. Survey distribution

Potential participants received an email invitation to participate in the study with a personalized link to the online survey. Each link enabled one-time completion of the survey with the ability to return to the survey after a delay. The survey was active for 17 days in August and September 2014 and was closed when the desired

Table 1

Genetic testing options and descriptions presented to study participants and an example of a provider recommendation as it was presented to participants.

Genetic Testing Options		
No Genetic Testing	5 Gene Test	15 Gene Test
Description	Looks at the 5 best-studied genes that can cause breast and prostate cancers	Looks at the 5 best-studied genes that can cause breast and prostate cancers and 10 other genes that have been tied to breast or prostate cancers
Quality of information and recommendations if a positive test	Clear guidelines telling your cancer risks and suggestions for screening	Clear guidelines telling your cancer risks and suggestions for screening for 5 genes. Meaning of a positive result for the 10 other genes is not well-established.
Chance of an inconclusive result	2 in 100 people have an inconclusive result	15 in 100 people have an inconclusive result
Time it takes to get your results	3 weeks	8 weeks
Provider Recommendation Example:		
Since you said the amount of information is more important to you than the meaning of that information she thinks the 15 gene test is the best option for you. Would you like to change from your first answer of the 5 gene test to the 15 gene test?		
o Yes, I would like to switch to the 15 gene test		
o No, I would like to stay with my original answer of the 5 gene test		
o No, I don't want genetic testing at all		

sample size of 400 participants had been achieved and participation dropped to zero. Participants received a \$10.00 gift card incentive for survey completion.

2.3. Study design and survey instrument

This study was a randomized trial with two experimental groups (Fig. 1). Each group was presented with a hypothetical GT vignette followed by a series of questions about GT decisions, measures designed to capture preferences, other personal characteristics, and demographic questions (Fig. 2, B.2–4, Table 1). Groups differed by the questions that elicited GT decisions; however, the hypothetical vignette and all other survey questions remained constant.

The experimental portion of the study had two components. The first component was designed to determine the impact of the number of options on the likelihood of undergoing GT. The second component was to investigate the impact of a personalized provider recommendation on test choice.

2.3.1. Hypothetical vignette

A hypothetical vignette was generated based on data about GT for hereditary cancer predisposition in the literature, the author's clinical experience, and the design of prior hypothetical vignettes used in research [28] (Fig. 2). The scenario was loosely based on the constellation of cancers seen in HBOC with an overemphasis on prostate cancer to enhance relevance to male participants. In addition to their involvement in HBOC, these cancers were chosen because they are common and likely to be familiar to members of the general population. Before launch, five individuals without a medical background reviewed the survey and language modifications were made based on their feedback.

2.3.2. Genetic testing options and personalized recommendations

The three options fell into the following categories: (1) no testing, (2) a 5-gene cancer-specific high penetrance gene panel, and (3) a 15-gene cancer-specific gene panel with high and moderate penetrance genes. The 15-gene test was inclusive of all genes on the 5-gene test. The tests differed on three dimensions: the likelihood of an uncertain result, the likelihood of a result with unclear implications for cancer risk management and turn-around time (Table 1). The two genetic tests had the same patient out-of-pocket cost which is consistent with some United States GT laboratory billing practices [15,23,24].

The two study groups were presented with these three options differently. The sequential group was presented with an option for no testing or the 5-gene test. Those who had selected the 5-gene test were asked a values clarification question to determine if they preferred “(a) only genetic information with clear meaning for future health care” or “(b) having all possible genetic information”. They were then introduced to the 15-gene test, presented with a corresponding ‘provider’ recommendation based on their information preference (IP) (option (a) with the 5-gene test, option (b) with the 15-gene test) and given the opportunity to change their selection. Those who first selected ‘no genetic testing’ were asked if they would have wanted testing if they had been offered this 15-gene test. This group of participants was not given the IP question or an opportunity to switch tests based on a recommendation.

In contrast, the simultaneous group was presented with all three options together. After selecting an option, those who selected a genetic test were asked the same values clarification question and were provided with a personalized recommendation for a test based on their answer including an option to switch their test (Table 1).

The specific text of the GT questions with the recommendation differed based on an individual's group, initial test selection, and

specified IP (six versions). Individuals in the simultaneous group who selected the 5-gene test were presented with one of two frames: (1) an introduction to the 15-gene test and recommendation to choose that test. (2) an introduction to the 15-gene test and recommendation to stay with the 5-gene test. Individuals in the sequential group who chose a genetic test were presented with one of four questions. Individuals who selected the 5 gene test were either given (1) a recommendation to stay with the 5-gene test or (2) switch to a 15-gene test. Individuals who selected the 15-gene test were either presented with (3) a recommendation to stay with the 15-gene test or (4) switch to the 5-gene test. All questions also included the option to switch to no GT. Individuals in both groups who initially selected ‘no genetic testing’ were not presented with a recommendation intervention.

Recommendations in this setting were focused on which test to choose rather than whether to have testing at all. Recommendations for or against testing are less relevant among populations with high baseline desire for testing and may not occur if providers counsel using a non-directive approach. Test-specific recommendations among those who express an interest in genetic testing are understudied and patients who want testing may be unsure how different tests can influence results.

2.3.3. Measures and demographics

Demographic information, data about personal experiences with cancer and perceptions of personal health status were collected. Four scales were used to measure intolerance for uncertainty, genetic literacy, subjective numeracy, and decisional conflict for use in descriptive analyses and as covariates (Fig. B.4). Intolerance for uncertainty was measured because of the probabilistic nature of genetic decisions using the Short Form of the Intolerance for Uncertainty Scale (12 items, possible score range 12–60, Cronbach's $\alpha = 0.88$) [29]. Genetic familiarity was measured using a version of the Rapid Estimate of Adult Literacy in Genetics (REAL-G) [30] modified for survey form [31,32] (8 items, possible score range 1–7, Cronbach's $\alpha = 0.97$). Genetic comprehension was measured using questions created using the words from the REAL-G (8 items score range 0–100 % correct, Kuder-Richardson 20 = 0.60) [32]. Numeracy was measured using the Subjective Numeracy Scale (8 items, possible score range 1–6, Cronbach's $\alpha = .80$) [33,34]. Decisional conflict was measured using a modified version of the decisional conflict scale (16-items, possible score range 0 (extremely informed)–100 (extremely uncertain about best choice) Cronbach's $\alpha = .93$) [35,36].

An author-generated item was included to measure self-reported understanding of the hypothetical vignette. Participants responded to “I feel like I understood the medical scenario and genetic testing choice” on a Likert scale (1–5).

2.3.4. Outcomes

There were three overarching outcomes of interest: the likelihood of undergoing GT, genetic tests chosen, and the concordance between stated IP and test choice. There were four binary outcome variables calculated to investigate the likelihood of undergoing GT. The initial likelihood of undergoing GT was determined by whether a person selected any genetic test or not in the initial GT question. The final likelihood of undergoing GT was calculated in the same way using the genetic test selections made after the recommendation intervention. Individuals who selected ‘no genetic testing’ in the initial testing question (no recommendation received) were counted as no testing with respect to the final likelihood of undergoing testing. Two individuals who did not complete all applicable testing questions had their initial choices carried forward. A second variation of each of these two outcomes was also calculated to account for the follow-up answers of individuals in the simultaneous group who

selected ‘no genetic testing’ but indicated interest in the 15-gene test in a follow-up question.

The overall distribution of genetic tests chosen was calculated in the same way as the final likelihood of undergoing GT except the 5-gene test and 15-gene tests were not collapsed together into one category. Two versions of this variable were calculated, one that accounted for the follow-up answers of simultaneous group initial non-testers and one that did not.

The concordance between stated IP and test choice was generated from these two variables. A test choice was considered concordant if a person selected either (a) only genetic information with clear meaning for future health care AND the 5-gene test OR (b) having all possible genetic information AND the 15-gene test. The final concordance was calculated by making this comparison between the IP and GT choice after the recommendation intervention. For sequential group participants, an initial concordance was also calculated by comparing the IP with the first genetic test chosen. Concordance assignments were not applicable to individuals who initially selected ‘no genetic testing’ and thus did not receive a recommendation.

2.4. Data analysis

Data analyses were performed using Stata12 IC. The impact of group assignment on the likelihood of choosing to undergo GT and the likelihood of a test choice matching IPs were investigated using bivariate and multivariate logistic regressions. The impact of group assignment on the final genetic test chosen was investigated using multinomial logistic regression. Backward elimination ($p = 0.1$) was performed during logistic regressions to identify covariates of interest [37]. Covariates were reviewed and those retained in more than one model were used for the final multivariate analyses as this list included diverse, potentially relevant covariates and allowed for cross-comparison of results. Sex did not meet other inclusion criteria but was added to the model by convention (Table 3). The changes in GT choices before and after a provider recommendation were examined using a McNemar test and a McNemar Bowker Test of Symmetry using only the data from the simultaneous group. Only the simultaneous group was included in this analysis because the GT options presented did not differ before and after the provider recommendation.

Table 2

Study participant characteristics. N presented by category to account for survey non-completion.

Demographics	Sequential Group	Simultaneous Group
Age (% N = 211, 201)		
18–44	46.0	44.3
45–64	33.6	29.9
65+	20.4	25.9
Sex (% Female, N = 214, 204)	58.9	59.8
Race (% N = 212, 203)		
White	59.0	70.0
Black or African American	30.2	20.7
Other	11	9.5
Ethnicity (% Hispanic, N = 214, 204)	5.1	3.4
Associates Degree or Higher (% N = 214, 204)	76.6	77.9
Employment (% N = 213, 204)		
Part-time or full-time	65.7	66.2
Retired	15.5	19.1
Unemployed or disabled	14.1	10.8
Job free by choice	4.7	3.9
Native English Speaker (% N = 214, 204)	86.9	89.7
Relationship Status (% N = 214, 202)		
Married/Domestic Partnership	44.4	39.1
Divorced/Separated/Widowed	15.4	19.8
Single	40.2	41.1
Biological Children (% with, N = 213, 204)	50.7	46.1
Reported Personal and Family Health History		
Personal History of Cancer (% yes, N = 215, 206)	7.9	7.8
One or More First Degree Relatives with Cancer History (% yes, N = 215, 206)	45.1	45.1
Personal History of any Cancer Screening (% yes, N = 214, 206)	81.3	85.0
Personal or Family History of Cancer Genetic Testing (% yes, N = 214, 206)	10.3	9.7
Perceived Cancer Risk Relative to People of Same Age and Gender (% N = 214, 206)		
Higher	10.7	11.2
Lower	52.3	52.9
Same	36.9	35.9
Level of Anxiety about Developing Cancer (% N = 214, 206)		
High	1.9	4.9
Moderate	23.4	27.7
Low	74.8	67.5
Perceived Health (% Good or Excellent, N = 214, 206)	93.5	94.7
Knowledge and Literacy		
Mean Subjective Numeracy Score (mean, N = 215, 207)*	4.76	4.80
% Correct Genetic Comprehension Questions (mean, N = 215, 207)	92.2	92.5
Genetic Familiarity Score (mean, N = 217, 208)*	5.9	5.8

* Higher score correlates with higher numeracy (maximum = 6), genetic familiarity (maximum = 7).

3. Results

3.1. Sample description

30.7 % of invited individuals consented to the study and 26.5 % completed the survey in its entirety (Fig. 1). 454 individuals completed the questions about GT choice and were included in the analysis even if they did not complete all demographic questions and scales. Characteristics of the sample appear in Table 2. Most individuals (93 %, $n = 437$) indicated they agreed or strongly agreed with the statement “I feel like I understood the medical scenario and genetic testing choice”. Individuals who indicated limited understanding were not excluded from the reported findings as the inclusion of their data did not alter study conclusions.

3.2. Impact of the number of genetic testing options

When first asked, 79.4 % (185/233) of sequential group participants (none vs 5-gene) and 88.7 % (196/221) of simultaneous group participants (none vs 5-gene or 15-gene) chose to undergo GT. The likelihood of undergoing GT was significantly different by group with a higher percentage of simultaneous group participants selecting a genetic test (OR:2.31, 95 % CI:1.31–4.06, $p = 0.004$) (Table 3). Among simultaneous group participants who decided to undergo testing, 38.0 % (84/221) chose the 5-gene test and 50.7 % (112/221) chose the 15-gene test. Sequential group participants who did not opt for testing were then asked if they would have wanted GT if presented with an additional option. 48.9 % (23/47) of these individuals said they would have wanted GT if they had been told about the 15-gene test. If these individuals are counted as

choosing to undergo GT, there is no longer a statistically significant difference in the likelihood of undergoing GT by group (OR:0.917, 95 % CI:0.494–1.70, $p = 0.785$) (Table 3).

3.3. Impact of a provider recommendation based on values clarification

Responses of simultaneous group participants were used to determine the influence of a provider recommendation on GT choice. A provider recommendation did not lead to a significant difference in the overall distribution of genetic test choices ($\chi^2 = 1.24$, $p = 0.537$). However, test choice after a provider recommendation was significantly more likely to match the participant's indicated IP than before ($\chi^2 = 8.53$, $p = 0.0035$) (Table 4).

3.4. Impact of the overall method of testing presentation

After completing all GT decision-related questions the final testing choice for each participant was determined. 11.2 % (26/233) of individuals in the sequential group opted for no test, 29.6 % (69/233) opted for the 5-gene test and 59.2 % (138/233) opted for the 15-gene test. Among simultaneous group members, 11.8 % (26/221) opted for no test, 36.2 % (80/221) opted for the 5-gene test and 52.0 % (115/221) opted for the 15-gene test (Fig. 3, Table A.1). The difference in the overall likelihood of GT and distribution of the three GT options selected by group was not statistically significant in bivariate or multivariate analyses (Table 3). However, if individuals who had initially selected no test in the sequential group but later expressed interest in the 15-gene test are not counted as undergoing testing (as would be the case if expanded

Table 3
Genetic testing decision outcomes by survey group membership.

Likelihood of Undergoing Genetic Testing by Group (Binary)				
	Odds Ratio	95 % CI	Likelihood Ratio χ^2	P-Value
Initial Choice (Bivariate)	2.03	1.21–3.43	7.37	0.008*
Adjustment for 15-gene initial non-testers ⁺	0.942	0.524–1.70	0.04	0.843
Initial Choice (Multivariate [^])	2.31	1.31–4.06	46.73	0.004*
Adjustment for 15-gene initial non-testers ⁺	0.917	0.494–1.70	26.84	0.785
Final Choice (Bivariate)	2.05	1.22–3.43	7.77	0.006*
Adjustment for 15-gene initial non-testers ⁺	0.942	0.529–1.68	0.04	0.839
Final Choice (Multivariate [^])	2.35	1.35–4.12	52.29	0.003*
Adjustment for 15-gene initial non-testers ⁺	1.03	0.545–1.94	52.32	0.932
Final Distribution of Genetic Tests by Group (Default as 5-Gene Test)				
	Relative Risk Ratio	95 % CI	Likelihood Ratio χ^2	P-Value
Overall Distribution (Bivariate)			7.89	0.0194*
No Test	0.449	0.253–0.795	8.21	0.006*
15-Gene Test	0.870	0.576–1.04	8.21	0.509
Adjustment for 15-gene initial non-testers (Bivariate) ⁺			2.58	0.2751
No Test	0.863	0.459–1.62	2.59	0.646
15-Gene Test	0.719	0.479–1.08	2.59	0.111
Overall Distribution (Multivariate [^])			9.14	0.0104*
No Test	0.404	0.219–0.746	72.33	0.004*
15-Gene Test	0.917	0.598–1.41	72.33	0.691
Adjustment for 15-gene initial non-testers (Multivariate [^]) ⁺			1.93	0.381
No Test	0.815	0.412–1.61	75.97	0.557
15-Gene Test	0.743	0.488–1.13	75.97	0.166
Final Option Concordance with Information Preference by Group				
	Odds Ratio	95 % CI	Likelihood Ratio χ^2	P-Value
Bivariate	0.630	0.383–1.04	3.35	0.069
Multivariate [^]	0.619	0.366–1.05	27.03	0.074

* Statistically significant ($p \leq 0.05$).

⁺ Adjustment for 15-gene initial non-testers: Individuals in the sequential group who initially selected “No Genetic Test” but expressed interest in the 15-gene test in a follow-up question are counted as having the 15-gene test.

[^] Multivariate model controlling for sex, age, survey understanding, genetic comprehension, prior cancer screening, intolerance for uncertainty, native English speaker, has children.

Table 4

Changes to test choices after a personalized recommendation (simultaneous group participants).

Test selection after recommendation	No Change	Switch to 15-gene test	Switch to 5-gene test	Switch to no test	Total
Total number of participants (subset of change that fit recommendation)	158 ⁺	20 (16)	17 (12)	1 (0)	196 ⁺
Experimental Questions+	Test		χ^2	P	
Is test choice more likely to match with information preference after a provider recommendation?	McNemar Test		8.53	0.0035 [*]	
Is test distribution different before and after a provider recommendation?	McNemar-Bowker Test		1.24	0.5371	

⁺ Excludes 25 individuals who selected “No Test” that did not receive a personalized recommendation.

^{*} Statistically significant at ($p < 0.05$).

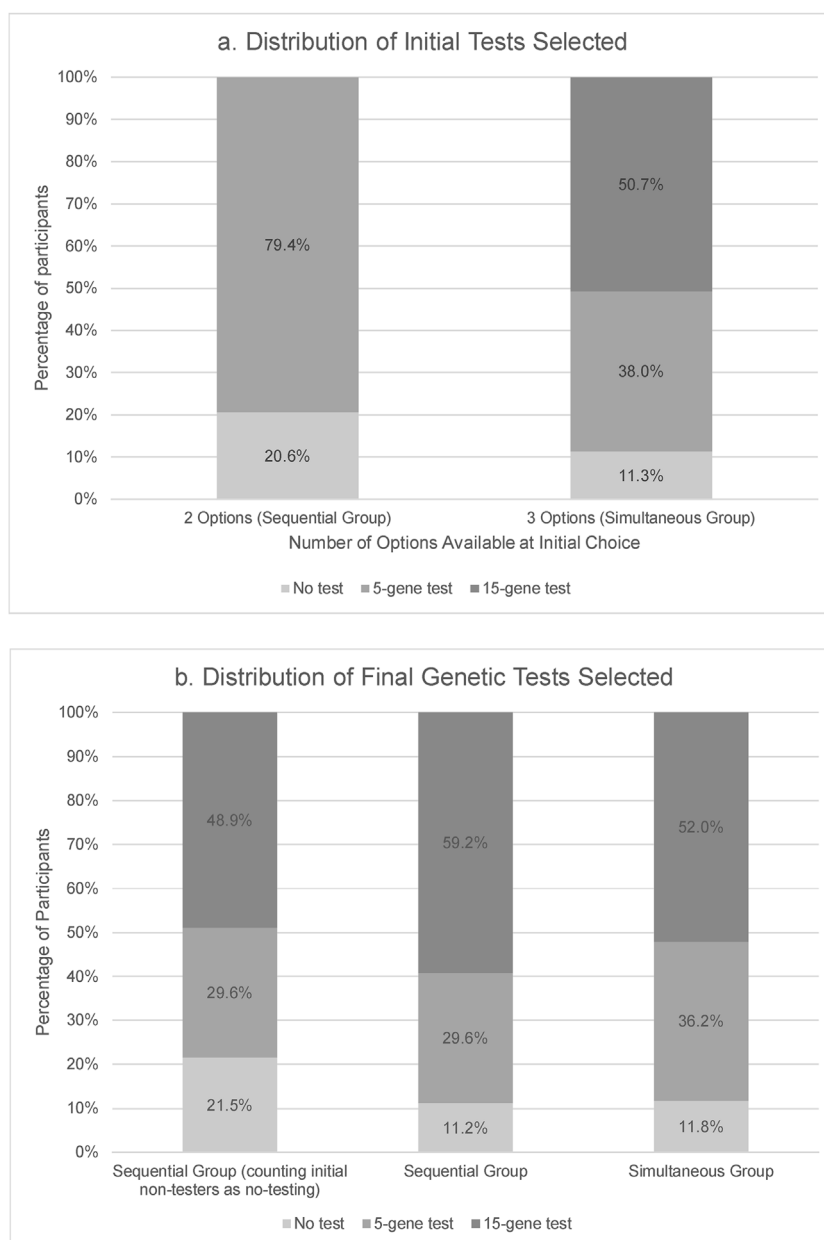


Fig. 3. Genetic testing options selected. a. The percentage of each option selected during the initial genetic testing choice by the number of testing options presented. b. The percentage of each genetic testing option selected for the final genetic testing choice by survey group.

testing is only offered to those interested in a high-penetrance gene panel) members of the simultaneous group were significantly more likely to choose a genetic test (either 5-gene or 15-gene) vs no genetic test than members of the sequential group (Table 3).

Additionally, the method of presenting genetic tests did not significantly influence the likelihood that the ultimate genetic test chosen matched the participant's information preference (OR:0.619, 95 % CI:0.366–1.05, $p = 0.074$) (Table 3).

4. Discussion and conclusion

4.1. Discussion

The overall method of offering testing did not significantly influence whether a person selected the 5-gene test or the 15-gene test with a sizable percentage of participants selecting each option. This indicates that a larger test is not universally more desirable. However, introducing three GT options rather than two options at the first decision-point made it more likely that a patient would undergo GT at that time. This effect was no longer seen when those who did not initially select a test were presented with a third option. Although it is unsurprising that people presented with more options are more likely to find an option they desire, this finding has potential consequences for medical care. If the primary goal of learning genetic risk information is to guide medical management, there should be limited circumstances in which people would decline a base test with high value medically relevant information but have interest in an expanded test which includes the same genes. Consequently, if providers offer testing through a tiered approach, where they first present a foundational genetic test and only offer expanded testing to those who express an interest, patients may be less likely to opt for GT than those who are presented with all options simultaneously. Findings from this study suggest that we should not assume that someone who declined testing in the past would not be interested in a different test in the future once additional testing options become available over time.

The finding that nearly half of individuals who declined GT in the sequential group expressed interest in the 15-gene test was unanticipated. There are several potential explanations for this finding. It is possible that these individuals evaluated the GT choice differently in the context of a comparator option. For example, the 15-gene test may have seemed like a good deal since the out-of-pocket cost was equivalent to the smaller 5-gene test. Furthermore, the phrasing of the question asked if they would have wanted the test had it been offered. The choice to say yes, may have been an expression of the desire to be offered all available options rather than a clear choice of the 15-gene test. Providing an additional option may have conveyed that it was normative to choose genetic testing leading to higher uptake. Alternatively, it is possible that participants did not engage as deeply with the decision since it was hypothetical. Regardless, participants offered more GT options had higher test uptake.

Our study also found a relatively high uptake of GT (>83 %). A meta-analysis of historical studies of uptake rates for breast cancer GT prior to 2002 (before panel tests were commonplace) found a wide range of uptake rates (25–96 %) with a mean of 56 % [38]. A more recent study of a clinical population offered several cancer panel options had high GT uptake (94.1 % of eligible patients) [15]. It is possible that the act of presenting multiple GT options is one factor that could explain higher rates of testing uptake.

Additionally, most individuals chose a test that matched their stated IP prior to a recommendation. This suggests that most people could determine which testing option best fit with their preference and then make an informed choice. However, a subset of individuals did not initially select a genetic test that matched their IP. The values clarification exercise and corresponding personalized recommendation significantly increased concordance rates between stated information preference and test selection. This indicates that using values clarification to guide a recommendation has the potential to affect individuals who would select a test that was inconsistent with their stated preference.

Not all individuals with a mismatched test and IP changed their testing choice in response to the recommendation. Their decision was likely based on a test attribute distinct from the information

provided by the test. For example, the time to result may have influenced choices because a shorter wait time may have been considered more valuable than information on a few additional genes (Table 1). Additionally, people often have difficulty accurately determining how they will respond to future information which makes values clarification that relies on affective forecasting an imperfect tool [39].

This study has several limitations. The hypothetical nature of the study differs from GT in the context of a provider interaction. Social accountability from the patient-provider relationship and the affective states of patients discussing personal and family histories of cancer may differ from the online context. Participants in the study would also not have anticipated the receipt of actual genetic test results. However, hypothetical vignettes have been commonly used in the setting of GT decision-making and this study used techniques associated with improved GT uptake accuracy such as introducing a test administrator and making the test seem more temporally imminent [28]. The findings from this study may not apply if a similar choice is presented differently, such as if extensive detail is provided for every syndrome and/or gene on a test.

Another limitation is that since this study was conducted in 2014, processing times have changed and the number of genes on a panel may not always increase the time to result. However, decisions about which genes to include on a panel and how to present GT choices to patients continues to remain relevant.

Additionally, individuals in the sequential group who expressed interest in the 15-gene test after initially selecting no testing were not subsequently presented with the values clarification/provider recommendation intervention. This was because the purpose of this question was intended only to gauge interest in this test since it is not customary to offer more genetic tests to those who initially decline. In retrospect, it would have been valuable to offer them the full intervention for better insight into this finding.

A major strength of the study is that it included individuals of different ages, races and education levels and nearly half of participants had a history of a close relative with cancer. However, healthy volunteers from a research database may differ from patient populations in other ways such as having a higher baseline interest in research or healthcare technologies.

4.2. Conclusion

This study provides evidence that GT decisions can be influenced by the way a provider presents testing options; the offer of a third alternative testing option to all individuals up-front may increase the likelihood that an individual will undergo GT relative to those who are only offered expanded testing after expressing an interest in a base test. In a real-life setting this could influence downstream patient care. Test uptake patterns were similar to those observed in an analogous clinical setting suggesting concurrent validity for this hypothetical scenario [15,40].

Although it is recognized that there are multiple types of medical decisions where more than one optimal treatment is available, most research has tied quality of choice to how informed the patient is, how consistent the choice is with values, and which choice is made and implemented [41]. A more thorough understanding of how structural aspects of medical decisions, such the number of options presented, can influence downstream medical outcomes in various contexts is needed and could help guide healthcare provider training or policies.

This study also suggests that a recommendation based on a values clarification exercise to discern patient IPs may be the most influential for people with an initial mismatch between their stated preference and choice made [15,20]. Historically, genetics

providers took a non-directive approach to the provision of services for several reasons including historical concerns about eugenics practices [42]. There has been a shift over time to incorporate new approaches such as a shared decision-making model; however, some providers continue the practice of non-directiveness in this context [15,17,43]. Although the extent to which genetic counselors employ values clarification questions in face-to-face interactions to patients remains unclear, decision support tools with a values clarification component have been utilized in the setting of GT [25,44]. A recommendation that relies on distilling the most important parts of GT and using that to elicit patient preferences such as that presented here is one tool to help facilitate shared decision making about GT.

4.3. Practice implications

Presenting multiple GT options may cater to the preferences of individuals who value different types of information. This is particularly relevant in settings with multiple medically appropriate tests with distinct trade-offs. Encouraging patients to talk through how they value these trade-offs and the different downstream implications of potential test results is one approach that can be used to help facilitate informed decision making and to give providers the information needed to make personalized recommendations when there are multiple medically appropriate options.

The way that providers present GT choices to patients may also influence the choices made. Although it is difficult to know how variation in offering tests to patients could lead to downstream psychosocial or clinical effects, this area is important as testing options continue to grow and alternative methods of obtaining GT emerge. There is increasing recognition that in-person pre-test counseling may not be necessary for all types of GT consent [45]. Although this vignette was designed to simulate a traditional pre-test counseling scenario, it still presented an electronic choice. Alternative test delivery models may employ software to help facilitate GT such as online portals or chatbots [46–48]. It will be important to have awareness of how GT choice design in these contexts may influence downstream outcomes.

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Informed consent and ethics approval

I confirm all patient/personal identifiers have been removed or disguised so the patient/person(s) described are not identifiable and cannot be identified through the details of the story.

The OHSRP determined this study to be excluded from IRB review per 45 CFR 46.101 (b) (2), OHSRP #12266. A copy of the consent form is available in Figure B.1.

Data statement

Data are available from the corresponding author by request

CRediT authorship contribution statement

Marci L.B. Schwartz: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Visualization, Writing - original draft. **William M.P. Klein:**

Conceptualization, Methodology, Supervision, Writing - review & editing. **Lori A.H. Erby:** Conceptualization, Methodology, Supervision, Writing - review & editing. **Christy H. Smith:** Conceptualization, Methodology, Supervision, Writing - review & editing. **Debra L. Roter:** Conceptualization, Methodology, Supervision, Writing - review & editing.

Declaration of Competing Interest

None.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.pec.2020.09.020>.

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