Controlled Trial of Pretest Education Approaches to Enhance Informed Decision-Making for BRCA1 Gene Testing

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Background: **In response to the isolation of the BRCA1 gene, a breast–ovarian cancer-susceptibility gene, biotechnology companies are already marketing genetic tests to health care providers and to the public. Initial studies indicate interest in BRCA1 testing in the general public and in populations at high risk. However, the optimal strategies for educating and counseling individuals have yet to be determined.** ***Purpose:*** **Our goal was to evaluate the impact of alternate strategies for pretest education and counseling on decision-making regarding BRCA1 testing among women at low to moderate risk who have a family history of breast and/or ovarian cancer.** ***Methods:*** **A randomized trial design was used to evaluate the effects of education only (educational approach) and education plus counseling (counseling approach), as compared with a waiting-list (control) condition (n = 400 for all groups combined). The educational approach reviewed information about personal risk factors, inheritance of cancer susceptibility, the benefits, limitations, and risks of BRCA1 testing, and cancer screening and prevention options. The counseling approach included this information, as well as a personalized discussion of experiences with cancer in the family and the potential psychological and social impact of testing. Data on knowledge of inherited cancer and BRCA1 test characteristics, perceived risk, perceived benefits, limitations and risks of BRCA1 testing, and testing intentions were collected by use of structured telephone interviews at baseline and at 1-month follow-up. Provision of a blood sample for future testing served as a proxy measure of intention to be tested (in the education and counseling arms of the study). The effects of intervention group on study outcomes were evaluated by use of hierarchical linear regression modeling and logistic regression modeling (for the blood sample outcome). All *P* values are for two-sided tests.** ***Results:*** **The educational and counseling approaches both led to significant increases in knowledge, relative to the control condition (*P*<.001 for both). The counseling approach, but not the educational approach, was superior to the control condition in producing significant increases in perceived limitations and risks of BRCA1 testing (*P*<.01) and decreases in perceived benefits (*P*<.05). However, neither approach produced changes in intentions to have BRCA1 testing. Prior to and following both education only and education plus counseling, approximately one half of the participants stated that they intended to be tested; after the session, 52% provided a blood sample.** ***Conclusions:*** **Standard educational approaches may be equally effective as expanded counseling approaches in enhancing knowledge. Since knowledge is a key aspect of medical decision-making, standard education may be adequate in situations where genetic testing must be streamlined. On the other hand, it has been argued that optimal decision-making requires not only knowledge, but also a reasoned evaluation of the positive and negative consequences of alternate decisions. Although the counseling approach is more likely to achieve this goal, it may not diminish interest in testing, even among women at low to moderate risk. Future research should focus on the merits of these alternate approaches for subgroups of individuals with different backgrounds who are being counseled in the variety of settings where BRCA1 testing is likely to be offered. [J Natl Cancer Inst 1997;89:148-57]**

In response to the isolation of a breast–ovarian cancer-susceptibility gene (BRCA1) (*1,2*), biotechnology companies are already marketing genetic tests to health care providers and to the public (*3*). The demand for genetic testing is expected to be very great among women in the general population and among those with an increased cancer risk (*4,5*). In two recent studies (*6,7*), more than 90% of women with a family history of breast or ovarian cancer reported that they wanted to have BRCA1 testing when available. This high level of interest in genetic testing was associated with a grossly overestimated sense of personal cancer risk, heightened breast cancer anxiety, and misunderstanding of the benefits, limitations, and risks of genetic testing (*6,7*). This finding suggests that motivation for genetic testing may diminish greatly following pretest education. This situation would be especially true among individuals at low to moderate risk of having a predisposing mutation, for whom the limitations and risks of testing may outweigh the benefits (*8*).

To test this hypothesis, we conducted a randomized trial comparing two alternate forms of BRCA1 pretest education with a waiting-list control condition: 1) an educational or ''informative'' approach, and 2) a counseling or ''interpretive'' approach (*9*). Participants in the educational arm of the study received all of the relevant information related to personal cancer risk factors,

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See ''Notes'' following ''References.''

the benefits, limitations, and risks of genetic testing, and cancer screening and prevention options. This approach, which is consistent with the standard medical model of patient decision-making, is based on the assumption that general information or education alone is sufficient for patients to make an optimal decision (*9*). The educational approach was contrasted with a counseling approach, which is considered standard of care in the genetic counseling community (*10*). The counseling arm of the study included education (as described above) and explored personal experiences with cancer in the family, potential psychosocial consequences of positive and negative results of genetic testing, and the impact of alternate decisions about genetic testing on participants' personal goals. Support for the expanded counseling approach can be found in behavioral models of decision-making (*11-13*). These models underscore the need for careful deliberation about the potential positive and negative consequences of alternate choices for the individual and significant others.

To evaluate these two pretest education approaches, we examined changes in the key elements of models of decision-making and genetic counseling (*10-13*): knowledge, perceived risk, perceptions of the benefits, limitations, and risks of genetic testing, and testing intentions. Since genetic testing is not yet recommended outside families at high risk (*8*), provision of a blood sample for the explicit purpose of future testing served as a surrogate marker of testing decisions. We hypothesized that the two educational approaches would be equally beneficial, relative to the control condition, in enhancing knowledge about BRCA1 testing and decreasing perceived personal risk of having a mutation. However, we predicted that the counseling approach would lead to relatively greater decreases in perceived benefits of BRCA1 testing and increases in perceived limitations and risks of BRCA1 testing. These expectations were based on previous studies indicating that most individuals have inflated perceptions of their personal risk of cancer (*14*) and exaggerate the benefits of BRCA1 testing relative to its limitations and risks (*7,15*). Since the vast majority of participants were not at high risk for having a BRCA1 mutation, we also expected that counseling would lead to relatively greater reductions in intentions to have BRCA1 testing and to a lower rate of provision of a blood sample for future testing than education only. Information about the impact of alternate pretest education strategies on knowledge and other key components of the decision-making process could be valuable for designing standard pretest education and counseling protocols for BRCA1 testing and for testing for other cancer susceptibility genes.

Subjects and Methods

Participants

Subjects were women aged 18-75 years who had had at least one first-degree relative with breast and/or ovarian cancer. Women who had had a personal history of cancer (except basal cell or squamous cell skin cancers) were excluded.

Of 740 eligible women, 578 (78%) completed the baseline telephone interview. Of these 578 women, 128 completed an education session, 132 completed an education plus counseling session, and 180 were in the waiting-list control condition. (The overall response rate was 76% [440/578]; the response rate for education and education plus counseling was 65% [260/398].) Of these 440 women, 400 completed 1-month follow-up interviews (response rate = 91%). Thus, the sample for this interim report included 400 women. With this sample size, we had more than 90% power to detect between-group differences of 0.5 standard deviation in continuous outcome variables and to detect a 20% difference in rates of provision of a blood sample.

Procedures

Subjects were recruited from one of two cancer centers (Georgetown University Medical Center or the Washington Hospital Center, both located in Washington, DC). Institutional Review Boards at both centers had approved the study. Two recruitment mechanisms were used: patient referral and self-referral.

Patient-referred subjects were recruited through a living first-degree relative affected with either breast or ovarian cancer. Index cancer patients at the two cancer centers were contacted by telephone to be asked permission to contact their unaffected first-degree relatives about participation in the trial. Letters of introduction describing the program were mailed to unaffected first-degree relatives of the index patients who granted permission.

Self-referred women were informed about the program either by their physicians or through brochures located in both cancer centers and in the departments of obstetrics and gynecology at both Georgetown University Medical Center and Washington Hospital Center. The brochure provided general information about the content of the education program and eligibility requirements.

Both patient- and self-referred subjects were contacted to participate in a 20-minute baseline telephone interview. This structured interview was administered by a research assistant using a computer-assisted telephone interviewing system.

Following the interview, subjects were randomly assigned to one of three study conditions: 1) education only (E); 2) education + counseling (E + C); or 3) a waiting-list control (WLC) (*see* ''Description of Treatment Interventions'' *below*). All subjects provided written informed consent prior to the session. After the E or the E + C session, subjects were given an opportunity to provide a blood sample for future testing. [Since testing is not recommended for unaffected women outside families at high risk (*8*), actual testing was not offered at that time.] Specifically, subjects were told, ''We are giving women who are interested in BRCA1 testing an opportunity to provide a blood sample for BRCA1 testing in the future. Your blood sample will be stored in our laboratory. When BRCA1 testing becomes available, you would be among the first people to be tested by our center, if you are still interested. Your blood sample will not be tested now. When a test is available for your sample, we will contact you so that you could sign another consent form for testing. . . . It is important to understand that this blood sample is for future testing. You should not give a sample unless you wish to be tested for BRCA1 in the future. There is no other reason to give a blood sample.'' Subjects who wished to provide a blood sample signed a second consent form for blood sample storage.

Subjects randomly assigned to the E and E + C conditions were recontacted 1 month following the session to complete a follow-up telephone interview. Subjects randomly assigned to the WLC condition were recontacted for the follow-up interview 4-6 weeks following their baseline telephone interview (prior to receiving any education or counseling).

Description of Treatment Interventions

Intervention sessions (E or E + C) were completed by one of two trained oncology nurses (213 subjects) or a genetic counselor supervisor (23 subjects) during a 1- to 1½-hour individual visit.

Education Intervention (E)

The following specific topics were reviewed by use of structured protocol:

(*a*) Individual risk factors for breast and ovarian cancers: Qualitative descriptors were used to communicate risks associated with family history (i.e., the number of affected first-degree relatives and their ages at diagnosis) and other risk factors; e.g., ''. . . because you had your first child after age 35, your risk of breast cancer *may be increased* over a woman your age in the general population.''

(*b*) Patterns of inheritance of breast/ovarian cancer susceptibility: Participants' pedigrees were reviewed and described as: ''not suggestive,'' ''somewhat suggestive,'' or ''very suggestive'' of hereditary breast/ovarian cancer.

(*c*) Benefits of BRCA1 testing: These benefits include the potential for reducing uncertainty, learning about one's children's risks, and improving health behavior and surveillance.

(*d*) Limitations of BRCA1 testing: These limitations include accuracy of test

results and uncertainty associated with positive or negative results (i.e., concepts of incomplete penetrance and genetic heterogeneity).

(*e*) Risks of BRCA1 testing: These risks include potential discrimination by insurance companies or employers if genetic information is placed in medical records or disclosed by the participant to third parties, disclosure of nonpaternity (when multiple family members tested), stigmatization, changes in self-concept, and adverse psychosocial consequences.

(*f*) Limitations of options for breast and ovarian cancer prevention and surveillance.

A combination of oral presentation, flip-chart visual aids, and printed handouts was used to illustrate key points and ensure standardization. The average time for completion of the E intervention was 45-60 minutes.

Education Plus Counseling Intervention (E + C)

Subjects assigned to this intervention received the education and materials described above. After the education, they also received nondirective counseling. The following specific issues were addressed using a semi-structured protocol: (*a*) experience with cancer in the family, including psychosocial impact; (*b*) anticipated impact of positive or negative BRCA1 test results, including impact on psychological and functional status, personal relationships, and medical outcomes; (*c*) anticipated outcomes of deciding not to be tested; (*d*) perceived coping resources and skills to adapt to different testing outcomes; and (*e*) intentions regarding communication of test results to family, friends, and others. The average time for completion of the E + C intervention was about 75-90 minutes.

Waiting-List Control Condition (WLC)

A WLC was utilized to control for the effects of media exposure and secular trends. Subjects randomly assigned to this condition were scheduled for an educational visit 6-8 weeks after the baseline phone interview. This procedure allowed sufficient time to conduct the 1-month follow-up interview before these subjects received any education or counseling.

Measures

Controlling Variables

Sociodemographics. Age, education level, ethnicity, marital status, and income level were assessed during the baseline telephone interview.

Family history. The number of first-degree relatives affected with breast and/or ovarian cancer was assessed during the baseline telephone interview. Because the presence of ovarian cancer and/or multiple affected relatives is associated with a higher likelihood of having a BRCA1 mutation (*16*), this variable was dichotomized as one first-degree relative with breast cancer versus one first-degree relative with ovarian cancer and/or two or more first-degree relatives with breast or ovarian cancer.

Referral variables. The site (Washington Hospital Center versus Georgetown University Medical Center) and source (patient referral versus self-referral) of subjects were determined.

Outcome Variables

Knowledge. Knowledge about breast cancer genetics and BRCA1 testing was assessed at baseline and at 1-month follow-up by use of an 11-item true–false scale. One point was given for each correct answer (range, 0-11). This measure was developed as part of a core set of instruments for a consortium of the National Institutes of Health-funded genetic testing projects (Cancer Genetic Studies Consortium) and has been used in previous research (*15*).

Perceived risk of having a BRCA1 mutation. Perceived risk was assessed at baseline and at 1-month follow-up by use of a single Likert-style item used in previous research (*6*). Subjects were asked, ''In your opinion, how likely is it that you have an altered breast–ovarian cancer susceptibility gene?'' (1 = not at all likely, 2 = somewhat likely, 3 = very likely, or 4 = definitely).

Perceptions of the benefits, limitations, and risks of BRCA1 testing. Perceptions of the benefits, limitations, and risks of genetic testing were measured at baseline and at 1-month follow-up by use of a 14-item Likert-style scale that was adapted from previous research (*7,15*). Subjects were read a series of benefits, limitations, and risks of BRCA1 testing and were asked to rate the level of importance (1 = not at all important, 2 = somewhat important, or 3 = very important). Principal component factor analysis of the scale indicated that this measure consisted of two independent subscale factors: 1) perceptions of the benefits of BRCA1 testing (seven items) and 2) perceptions of limitations and risks of BRCA1 testing (seven items) (*15*). Both subscales were internally consistent in this sample (Cronbach's α's = .74 and .75 for benefits and limitations–risks, respectively).

Genetic testing intention. Intention to have BRCA1 testing was assessed at baseline and at 1-month follow-up with a single Likert-style item used in previous research (*6*). Subjects were asked, ''At the present time, which of the following statements describes you best?'' (1 = haven't thought about it/not considering genetic testing; 2 = considering genetic testing; 3 = probably will have genetic testing; or 4 = definitely will have genetic testing).

Provision of a blood sample. As mentioned above, provision of a blood sample for storage for future testing (yes, no) was used as a surrogate marker of testing decisions for participants in the E or E + C conditions.

Analysis Plan

The analysis plan was conducted in three stages. First, chi-squared tests were done to compare study participants with nonparticipants and to compare participants in the three study groups in terms of baseline characteristics. Second, responses to individual items for the knowledge scale, the perceived benefits scale, and the perceived limitations–risks scale were compared by study group at baseline and at 1-month follow-up by use of chi-squared tests. Third, between-group differences in changes in the outcome measures were evaluated by use of repeated measures analyses of variance (ANOVAs). The fourth step was to test the effect of study group on the outcomes at 1-month follow-up in hierarchical linear regression models. Referral source (self versus patient), site (Washington Hospital Center versus Georgetown University Medical Center), and all demographic and family history variables having univariate associations ($P<.10$) with a particular outcome were considered for inclusion as confounder variables in the first step of the models. However, only those variables accounting for a significant amount of variance (as determined by Wald statistics) were retained in the models. Family history was controlled in all models because of the a priori importance of this variable in the genetic testing process. The baseline level of the outcome variable was also included in step 1 in all models. In the second step, dummy variables were created for group effects (E versus WLC; E + C versus WLC). Groups by controlling variable interactions (e.g., group by family history and group by ethnicity) were tested in the final step of all models. The ΔR^2 reflects the increment in variance that is accounted for by the addition of variables in each successive step. Logistic regression modeling was used to compare the E group with the E + C group in terms of provision of a blood sample for future testing.

Results

Analysis of Participation Bias

To assess participation bias, we compared women who completed a baseline interview but who declined to participate in the intervention sessions with those who completed a baseline interview and participated in the intervention sessions. Women who declined to participate in the intervention sessions were more likely to have less education (chi-squared = 19.0; $P<.001$), to be unmarried (chi-squared = 4.0; $P<.05$), to be African-American (chi-squared = 10.1; $P<.001$), to have lower incomes (chi-squared = 11.5; $P<.003$), and to have only one first-degree relative affected with breast cancer (chi-squared = 7.0; $P<.05$). We also compared women who completed the intervention sessions and 1-month follow-up interviews with those who were lost to follow-up. No statistically significant differences were found.

Characteristics of the Study Population

As Table 1 shows, there were no statistically significant differences in referral source, demographic characteristics, or fam-

ily history between the three study groups. Overall, 70% of women were self-referrals, 91% had education beyond high school, 72% were white, 63% were married, and 63% had incomes over $50 000. Ninety-one percent had only one first-degree relative affected with breast or ovarian cancer. Two hundred eighty-two women (70%) were recruited from Georgetown University Medical Center, and 118 (30%) were recruited from the Washington Hospital Center.

Descriptive Data for Individual Items Constituting Scales for Knowledge, Perceived Benefits, and Perceived Limitations and Risks by Study Group

Responses to the individual knowledge items at baseline and at 1-month follow-up are shown in Table 2. With the exception of one item, there were no baseline between-group differences in the proportion of participants responding correctly. However, significant between-group differences in knowledge were found at 1-month follow-up for nine out of the 11 items. For example, at baseline, only 51% of E, 52% of E + C, and 49% of WLC participants knew that a ''father can pass down an altered BRCA1 gene to his children.'' At 1-month follow-up, 85% of E, 78% of E + C, and 38% of WLC participants answered this item correctly. Most items showed improvements in knowledge in the E and E + C group that were equally clinically significant (i.e., >20% increases in the proportion of participants responding correctly).

Table 3 shows responses to the individual items for the perceived benefits and perceived limitations–risks. Responses to most of the perceived benefit items showed 10%-20% decreases in the proportion of E and E + C participants rating the benefit as ''very important.'' However, statistically significant between-group differences at follow-up were observed for only two of the seven perceived benefits items. For example, at baseline, 63% of E, 55% of E + C, and 60% of WLC subjects endorsed reassurance as a very important testing benefit. At follow-up, 51% of E, 34% of E + C, and 47% of WLC participants rated reassurance as very important. Statistically significant between-group differences at follow-up were observed for three of the seven perceived limitations–risks items. For example, at baseline, 16%-18% of participants in all study groups rated insurance discrimination as a very important limitation–risk of testing. At 1-month follow-up, 24% of E, 30% of E + C, and 17% of WLC participants rated it as very important. Similar between-group differences were observed for risks associated with loss of confidentiality and stigmatization. However, other limitations and risks were endorsed as very important by few participants either at baseline or at 1-month follow-up.

Between-Group Differences in Changes in Continuous Scores for Knowledge, Perceived Personal Risk of Having a BRCA1 Mutation, Perceived Benefits, Limitations and Risks of Testing, and Testing Intentions

As Table 4 shows, the results of ANOVAs showed statistically significant between-group differences in changes from baseline to 1-month follow-up in knowledge ($F = 64.10$; $P = .0001$), perceived personal risk of having a BRCA1 mutation ($F = 3.16$; $P = .04$), and perceived limitations and risks of testing ($F = 5.61$; $P = .004$). Participants in both the E and E + C interventions showed increases in knowledge, whereas participants in the WLC condition showed decreases. Post-hoc tests of change scores showed that both the E and E + C interventions were significantly different from the WLC condition in terms of

Table 1. Characteristics of sample by study group

Variable	Level	Study group*		
		Waiting-list control (n = 164)	Education (n = 114)	Education + counseling (n = 122)
Referral	Self-referral	107 (65)	82 (72)	90 (74)
	Patient referral	57 (35)	32 (28)	32 (26)
Age	18-34 y	19 (12)	17 (15)	20 (16)
	35-49 y	94 (58)	63 (55)	72 (59)
	⩾50 y	50 (30)	34 (30)	30 (25)
Education	⩽High school	20 (12)	6 (5)	14 (11)
	>High school	144 (88)	107 (95)	108 (89)
Ethnicity	White	107 (66)	84 (74)	92 (75)
	African-American	49 (30)	29 (25)	28 (23)
	Other	7 (4)	1 (1)	2 (2)
Marital status	Married	100 (61)	74 (65)	76 (62)
	Unmarried	64 (39)	40 (35)	46 (38)
Income	⩽$35 000	30 (19)	22 (20)	27 (23)
	$35 001-$50 000	33 (21)	17 (15)	17 (14)
	⩾$50 001	95 (60)	73 (65)	75 (63)
Family history	1 first-degree relative with breast cancer	135 (82)	90 (79)	93 (76)
	1 first-degree relative with ovarian cancer	18 (11)	14 (12)	14 (12)
	⩾2 first-degree relatives with breast or ovarian cancer	11 (7)	10 (9)	15 (12)

*Values in columns = number (%). Values do not always add up to total number of study subjects because of missing values.

Table 2. Group differences in individual items for knowledge at baseline and at 1-month follow-up

Outcome	Time	Study group*			Chi-squared
		Waiting-list control	Education	Education + counseling	
True items					
Father can pass down an altered BRCA1 gene to his children.	Baseline	49	51	52	0.3
	1-mo follow-up	38	85	78	79.9†
Woman who does not have an altered BRCA1 gene can still get breast or ovarian cancer.	Baseline	94	92	92	0.4
	1-mo follow-up	81	93	95	16.6†
Woman who has an altered BRCA1 gene has a higher ovarian cancer risk.	Baseline	80	82	86	0.48
	1-mo follow-up	72	90	96	33.7†
Sister of a woman with an altered BRCA1 gene has 50% risk of having altered gene.	Baseline	67	49	57	9.8‡
	1-mo follow-up	66	64	74	3.2
Ovarian cancer screening tests often do not detect cancer until after it spreads.	Baseline	46	56	51	2.9
	1-mo follow-up	49	60	62	5.5
Woman who has breasts removed can still get breast cancer.	Baseline	68	61	70	2.3
	1-mo follow-up	66	77	84	13.2†
False items					
One half of breast cancer cases occur in women who have an altered BRCA1 gene.	Baseline	23	21	25	0.6
	1-mo follow-up	24	53	56	37.1†
All women who have an altered BRCA1 gene get cancer.	Baseline	82	79	78	0.5
	1-mo follow-up	73	87	90	16.4†
One in 10 women have an altered BRCA1 gene.	Baseline	9	16	14	3.8
	1-mo follow-up	10	36	28	29.9†
Having ovaries removed will definitely prevent ovarian cancer.	Baseline	29	25	16	7.1
	1-mo follow-up	24	59	55	42.7†
Early-onset breast cancer is less likely due to an altered BRCA1 gene than is late-onset breast cancer.	Baseline	47	54	50	1.4
	1-mo follow-up	40	59	52	10.0†

*Values in columns = percent responding correctly.
†Two-sided $P<.001$.
‡Two-sided $P<.01$.

knowledge changes. With respect to perceived personal risk of having a BRCA1 mutation, post-hoc tests showed that only the E intervention resulted in significantly greater decreases compared with the WLC condition. There were no significant between-group differences in changes in perceived benefits of BRCA1 testing.

Contrary to our predictions, there were no significant between-group differences in changes in the continuous measure of testing intentions (Table 4). In exploratory analyses, we examined the association of postintervention intentions to changes in knowledge, perceived personal risk, perceived benefits, and perceived limitations and risks of testing. Women who reported that they ''definitely'' wanted BRCA1 testing at 1-month follow-up had significantly greater increases in knowledge than women with weaker testing intentions (average change = 1.26 versus 0.63, respectively; Student's t test, $t = 2.5$; $P = .01$). In addition, women who definitely wanted BRCA1 testing had smaller increases in perceived limitations and risks compared with women with weaker intentions (average change = 0.11 versus 0.67; $t = -2.0$; $P = .04$). There were no significant associations of intentions with perceived personal risk or perceived testing benefits.

Between-Group Differences in Categorical Outcomes for Testing Intentions and Blood Sample Provision

Consistent with analyses of the continuous outcome for intentions, we found no evidence for an intervention effect on the categorical measure. At follow-up, 57% of participants in the E intervention and 61% of participants in the E + C intervention indicated that they probably or definitely would have BRCA1 testing, compared with 53% of WLC participants (and 55% of all participants at baseline). Examination of changes in intentions at the individual level showed that BRCA1 intentions were very stable over time. Of the E and E + C participants who reported at baseline that they probably or definitely would be tested, 71% reported this same level of intention at 1-month follow-up (compared with 75% of WLC subjects).

There were no statistically significant differences between the E and E + C interventions with regard to the proportion of participants providing a blood sample. Consistent with their intentions, 51% of participants in the E intervention and 52% of those in the E + C intervention provided a blood sample for future testing. Descriptive data from open-ended questions

Table 3. Group differences in individual items for perceived benefits and perceived limitations and risks at baseline and 1-month follow-up

Outcome	Time	Study group*			Chi-squared
		Waiting-list control	Education	Education + counseling	
Perceived benefits of BRCA1 testing					
Reassurance	Baseline	60	63	55	1.7
	1-mo follow-up	47	51	34	7.3†
Enhance cancer prevention	Baseline	85	82	82	0.6
	1-mo follow-up	74	73	60	7.3†
Learn children's risk	Baseline	71	76	79	1.6
	1-mo follow-up	64	52	58	2.8
Make surgery decisions	Baseline	50	52	51	0.1
	1-mo follow-up	46	39	36	2.9
Make childbearing decisions	Baseline	29	12	21	5.2
	1-mo follow-up	19	18	12	1.5
Increase cancer screening	Baseline	83	89	75	9.0†
	1-mo follow-up	74	80	76	1.3
Reduce uncertainty	Baseline	62	70	64	1.9
	1-mo follow-up	57	58	47	3.4
Perceived limitations and risks of BRCA1 testing					
Insurance discrimination	Baseline	18	17	16	0.1
	1-mo follow-up	17	24	30	7.0†
Loss of confidentiality	Baseline	11	10	7	1.1
	1-mo follow-up	11	15	23	7.6†
Stigmatization	Baseline	4	1	1	5.1
	1-mo follow-up	3	2	11	10.3‡
Lack of trust in modern medicine	Baseline	2	1	3	0.9
	1-mo follow-up	4	3	1	2.3
Can't prevent cancer	Baseline	2	2	3	0.2
	1-mo follow-up	4	4	3	0.8
Negative effect on family	Baseline	12	15	13	0.4
	1-mo follow-up	14	9	11	2.2
Couldn't handle it emotionally	Baseline	6	7	7	0.3
	1-mo follow-up	6	6	3	1.1

*Values in columns = percent responding ''very important.''
†Two-sided $P<.05$.
‡Two-sided $P<.01$.

showed that, when asked why they provided a blood sample, 77% of subjects reported that they did so to be tested or learn about their cancer risks, 12% did so to help research, and 11% reported other reasons. Of those who did not provide a blood sample, 37% reported that they remained undecided, 17% reported that they were not at very high risk of having a mutation, 16% reported insurance discrimination concerns, and 30% reported other reasons.

Table 4. Results of repeated-measures analysis of study outcomes

Outcome	Time	Study group*			F‡	*P*§
		Waiting-list control†	Education†	Education + counseling†		
Knowledge (range = 0-11)	Baseline	5.93 (2.01)	5.90 (2.17)	5.84 (2.12)		
	1-mo follow-up	5.39 (2.39)[a]	7.74 (2.16)[b]	7.58 (2.09)[b]	64.10	.0001
Perceived personal risk of having a BRCA1 mutation (range = 1-4)	Baseline	2.10 (0.63)	2.12 (0.59)	2.20 (0.59)		
	1-mo follow-up	2.06 (0.56)[a]	1.88 (0.57)[b]	2.06 (0.62)[ab]	3.16	.04
Perceived benefits of BRCA1 testing (range = 7-21)	Baseline	17.65 (3.03)	17.92 (2.80)	17.63 (2.95)		
	1-mo follow-up	16.93 (3.29)	16.62 (3.56)	16.19 (3.37)	2.18	.11
Perceived limitations and risks of BRCA1 testing (range = 7-12)	Baseline	9.46 (2.46)	9.41 (2.62)	9.20 (2.43)		
	1-mo follow-up	9.50 (2.73)[a]	10.09 (2.82)[ab]	10.26 (2.93)[b]	5.61	.004
Intention to be tested for BRCA1 (range = 1-4)	Baseline	2.61 (1.07)	2.74 (1.06)	2.75 (1.05)		
	1-mo follow-up	2.60 (1.02)	2.73 (1.12)	2.77 (1.07)	0.02	.97

*Groups with different superscripted letters are significantly different in post-hoc tests of change scores.
†Values in columns = averages (standard deviations).
‡F statistic for time by treatment group interaction in repeated-measures analysis of variance.
§Two-sided test.

Multiple Regression Analysis of Study Outcomes

Table 5 shows the results of the hierarchical linear regression models that controlled for potential confounder variables.

In the model of continuous knowledge scores, the controlling variables contributed 35% of the variance; baseline knowledge, family history, ethnicity, and education all made significant independent contributions to knowledge at 1-month follow-up as evidenced by the final β weights. Increases in knowledge were significantly greater for women who had one first-degree relative with ovarian cancer or two or more first-degree relatives with breast or ovarian cancer, as compared with women who had only one first-degree relative with breast cancer. Knowledge increases were also greater for women who were white and those with education beyond high school. Both terms for intervention group were statistically significant, accounting for 18% of variance in the model. Thus, both the E and E + C interventions led to significantly greater improvements in knowledge compared with the WLC condition.

In the model of perceived personal risk of having a BRCA1 mutation, the controlling variables accounted for 22% of the variance. Women with family histories of ovarian cancer or two or more first-degree relatives with breast or ovarian cancer showed significantly greater increases in perceived risk than those with one first-degree relative with breast cancer. When we controlled for age and family history, the E intervention led to significantly greater reductions in perceived risk than the WLC condition; however, this group term added only 2% of additional variance to the model.

In the model of perceived benefits of BRCA1 testing, the set of controlling variables accounted for 30% of the variance. White women had significantly greater decreases in perceived benefits than African-American women. Only the E + C intervention led to significantly greater decreases in perceived benefits than the WLC condition; however, this group term contributed only 1% of additional variance to the model.

In the model of perceived limitations and risks of BRCA1 testing, the controlling variables accounted for 30% of the variance. Both family history and ethnicity contributed significantly to the model. Women with only one first-degree relative with

Table 5. Multiple regression analyses of study outcomes at 1-month follow-up

Dependent variable	Step No.	Predictor variables*	ΔR^2	Final β
Knowledge	1	Baseline knowledge		0.52†
		Family history‡		0.45§
		Ethnicity‖		1.10†
		Education¶		0.89#
			0.35†	
	2	Group (E + C versus WLC)		2.10†
		Group (E versus WLC)		2.17†
			0.18†	
Perceived personal risk of having a BRCA1 mutation	1	Baseline perceived risk		0.43†
		Family history‡		0.13§
		Age**		−0.10††
			0.22†	
	2	Group (E + C versus WLC)		−0.06
		Group (E versus WLC)		−0.18#
			0.02§	
Perceived benefits of BRCA1 testing	1	Baseline testing benefits		0.59†
		Family history‡		0.55
		Ethnicity‖		−0.73§
			0.30†	
	2	Group (E + C versus WLC)		−0.67§
		Group (E versus WLC)		−0.34
			0.01	
Perceived limitations and risks of BRCA1 testing	1	Baseline testing limitations and risks		0.59†
		Family history‡		−0.77#
		Ethnicity‖		0.92†
			0.30†	
	2	Group (E + C versus WLC)		0.90#
		Group (E versus WLC)		0.51††
			0.18#	
Intention to be tested for BRCA1	1	Baseline testing plans		0.46†
		Family history‡		0.43†
			0.27†	
	2	Group (E + C versus WLC)		0.08
		Group (E versus WLC)		0.08
			0.00	

*E + C = education + counseling; WLC = waiting-list control; E = education.
†Two-sided $P<.001$.
‡Levels = ⩾2 first-degree relatives or 1 first-degree relative with ovarian cancer versus 1 first-degree relative with breast cancer.
§Two-sided $P<.05$.
‖Levels = white versus nonwhite.
¶Levels = >high school versus ⩽high school.
#Two-sided $P<.01$.
**Levels = >50 y versus 18-49 y.
††Two-sided $P<.10$.

breast cancer had greater increases in perceived limitations and risks than women with family histories of ovarian cancer or two or more first-degree relatives with breast or ovarian cancer. White women had significantly greater increases in perceived limitations and risks than African-American women. With these controlling variables in the model, the group variables accounted for an additional 18% of the variance. Only the E + C intervention produced significantly greater reductions in perceived limitations and risks when compared with the WLC condition.

In the model of intentions to have BRCA1 testing, baseline intentions and family history of cancer had statistically significant effects. Women with family histories of ovarian cancer or two or more first-degree relatives with breast or ovarian cancer reported greater increases in intention to be tested. There were no significant effects of either the E or E + C interventions on the intentions outcome variable. Likewise, in the logistic regression model of blood sample provision, only family history of cancer had a significant effect (odds ratio = 2.5; 95% confidence interval = 1.46-4.29); 47% of women with one first-degree relative with breast cancer versus 68% of women with one first-degree relative with ovarian cancer or two or more first-degree relatives with breast or ovarian cancer provided a blood sample. The E and E + C groups did not differ significantly with regard to the likelihood of providing a blood sample.

In all of the above models, terms for intervention group by controlling variable interactions (e.g., group by family history and group by ethnicity) were tested. However, none of these interactions was statistically significant; and therefore, these terms were not included in the final models.

Discussion

In this randomized trial, we examined the effects of alternate modes of BRCA1 pretest education on decision-making processes and outcomes in a sample of women at low to moderate risk who had a family history of breast or ovarian cancer. Pretest education (educational approach) and pretest education plus counseling (counseling approach) were each compared with a waiting-list condition that controlled for the influence of media exposure and secular trends. As predicted, compared with the control condition, the educational approach led to statistically significant increases in knowledge and small, but statistically significant, decreases in perceived personal risk of having a BRCA1 mutation. The results also showed that the counseling approach, but not the educational approach, was superior to the control condition in increasing the perceived importance of the limitations and risks of BRCA1 testing and in decreasing the perceived importance of the benefits of BRCA1 testing. However, neither the educational nor the counseling approach produced statistically significant changes in intentions to have BRCA1 testing in this population. Both before and after counseling, approximately 50% of participants stated that they intended to be tested, and 52% provided a blood sample for future testing.

Since comprehension of facts about genetic diagnosis is considered one of the most important goals of genetic counseling and informed decision-making (*17*), the improvement in knowledge produced by the educational and counseling interventions is very encouraging. Overall, levels of knowledge about inherited breast and ovarian cancers and BRCA1 testing increased by about 30% from baseline to 1-month follow-up, resulting in an average score of about 70% correct. In addition, increases in knowledge were associated with stronger intentions to have BRCA1 testing. This finding is consistent with results of a recent study (*15*) in which knowledge about inherited breast–ovarian cancer susceptibility predicted uptake of BRCA1 testing in members of hereditary breast cancer families. Therefore, educational strategies that enhance knowledge may also increase use of BRCA1 testing when it is more widely available.

In contrast to knowledge, perceived personal risk of having a BRCA1 mutation changed very little for participants in either intervention. This lack of a strong effect on perceived risk may be due to the fact that we did not provide numerical estimates of personal cancer risk to participants. However, change in risk perception resulting from provision of individualized breast cancer risks has also been shown to be very small (*14*). Likewise, previous studies of prenatal genetic counseling have shown that most individuals perceive their risks in binary form (e.g., ''I either will or will not get cancer'') (*18*) and that probability information about genetic inheritance has a limited impact on risk perception (*17*).

While risk communication is an important component of genetic counseling, deliberation about the potential positive and negative consequences of alternate choices is often considered the more essential feature of informed decision-making (*11,19*). As in previous studies (*7,15*), prior to counseling, most women rated the benefits of BRCA1 testing as much more important than its limitations and risks. The counseling intervention produced statistically significant decreases in the perceived benefits of BRCA1 testing and increases in its perceived limitations and risks, thereby changing the perceived benefit–cost ratio. In contrast, the educational approach produced little change in perceived benefits or limitations and risks. While the benefits, limitations, and risks of BRCA1 testing were reviewed in both interventions, only the counseling approach explored the implications of these consequences for the individual and her family. Thus, the more personalized nature of this approach appears to have facilitated a more thorough processing of the information provided during the session, thereby enhancing the decision-making process (*9,11*).

Despite these influences of education and counseling on knowledge and attitudes about BRCA1 testing, the participants' intentions related to BRCA1 testing changed little from baseline to 1-month follow-up. Research on patient decision-making about other risky medical procedures, such as bone marrow transplant, has also shown that patients' intentions and decisions are remarkably stable over time, even in the face of substantial risks and minimal expected benefit (*20*). In light of these findings, it has been suggested that the counseling process serves to reinforce and validate individuals' prior intentions rather than to contribute to the decision itself (*21*). This hypothesis is consistent with reports of prenatal genetic counseling showing that participants' decisions are frequently based on factors other than the facts presented during the session (*22*). The effectiveness of genetic counseling as a nondirective profession has usually been judged not on the basis of outcome (i.e., participants' decisions) but on the counseling process (i.e., whether participants carefully considered the consequences of alternate options) (*23*). The

latter criterion appears to have been met only by the addition of the counseling component.

Independent of the counseling interventions, individual factors had relatively consistent effects on decision-making processes and outcomes. Having a family history of ovarian cancer or having multiple affected relatives with breast or ovarian cancer is associated with a greater likelihood of having a BRCA1 mutation (*8,16*). Consistent with their elevated risk status, this subset of participants showed greater increases in knowledge, perceived personal risk, and intentions to be tested. They were also significantly more likely to provide a blood sample for future testing than women who had only one first-degree relative with breast cancer. It is curious, however, that family history of cancer did not interact significantly with intervention group assignment. In other words, the effects of family history of cancer were not stronger for women who received education and/or counseling than for those in the waiting-list control condition. It is possible that significant interactions were not revealed because of the relatively small numbers of women at higher risk in our population.

We also observed interesting differences between African-American and white women. These differences bear further study. For example, African-American, low-income, and less educated individuals who were invited to participate in the education or counseling sessions were less likely to do so. This result may reflect the general difficulty that many studies have in recruiting medically underserved populations to participate in clinical trials (*24*). It may also be related to concerns this population may have about genetic testing. For some, the possibility of being defined partly by one's genotype may be linked with other negative stereotypes that could have discouraged study participation (*25*). In addition, baseline data from this study have indicated that African-Americans who did participate started with less knowledge, more positive beliefs about the benefits of BRCA1 testing, and fewer concerns about the limitations and risks of testing, compared with white participants of largely European background (*26*). In this analysis, we found that these ethnic differences increased over time. Independent of intervention group or waiting list control group membership, African-American participants had smaller increases in knowledge, smaller reductions in perceived benefits of BRCA1 testing, and smaller increases in perceived risks and limitations of testing than white participants. It is possible that African-American participants gave greater weight to the potential benefits of testing because they had a higher degree of trust in the health professionals who succeeded in recruiting them than did the white patients. Further research is needed to help understand these potentially important differences between different ethnic groups.

Our study had some limitations. First, many other factors are likely to influence BRCA1 testing decisions, and all of these could not be examined in our study. For example, it is possible that differences in the backgrounds and training of the counselors influenced the outcomes of the study. Previous research, however, has shown that the type of counselor and years of experience do not influence the effects of genetic counseling on knowledge and risk perceptions (*17*). The fact that the vast majority of our participants were counseled by oncology nurses suggests that the results of this study will be generalizable to the setting where many individuals may receive BRCA1 testing in the future. An additional factor not accounted for in this study is psychological distress. Since distress has been shown to interfere with comprehension of breast cancer risk information (*14*), its role in BRCA1 test decision-making should be examined. A second limitation of our study is the possibility that differences between the educational and counseling approaches were due to differences in the amount of time spent with the counselor. However, length of contact has not been shown to influence the outcomes of genetic counseling (*17*). A third limitation is that stated intentions and provision of a blood sample for future testing were used as proxy measures of BRCA1-testing decisions (since it was not possible to actually offer BRCA1 testing at the time of the study). While some women may have given a blood sample for altruistic reasons, the vast majority reported that they did so to obtain future testing and to learn about their cancer risks. With improvements in the sensitivity and specificity of BRCA1 testing, it will soon be possible to offer testing to the broader population of unaffected women who are concerned about their cancer risks. It will be important at that time to determine whether the effects observed in our study can be replicated.

What can we learn from our study about the relative efficacy of the educational versus counseling approaches in enhancing informed decision-making for BRCA1 testing? This depends, in part, on how we define the goals and effectiveness of genetic counseling. If the primary goal is to increase knowledge and comprehension, then the education only approach could be deemed as effective as the education plus counseling approach. Given the desire to make BRCA1 testing more accessible and the fact that most health care providers lack the skills and the time to provide a more personalized approach to patient education (*9*), the educational approach may be sufficient in situations where genetic testing must be streamlined. On the other hand, it has been argued effectively that optimal decision-making requires not only knowledge, but also a reasoned evaluation of the positive and negative consequences of alternate choices (*11,23*). In our study, this goal appeared to be achieved only by the counseling approach. Perhaps the relative value of specific components of genetics education and counseling would best be judged by the long-term psychological consequences of participants' actual testing decisions and their satisfaction (*27*). The counseling approach, which explores participants' expectations about the impact of being tested, may be most critical in preparing individuals to cope with their test results (*23*). In reality, it is unlikely that a particular counseling approach will be more effective for all participants in all settings. Thus, what is needed is continued investigation of alternate counseling approaches and their merits for individuals with different ethnic and socioeconomic backgrounds who are being counseled in the variety of settings where BRCA1 testing is likely to be offered in the future.

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Notes

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