

A new population screening program for BRCA mutations in Israel – Attitudes and barriers among Ashkenazi Jewish women

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Abstract

Israeli Jewish women of Ashkenazi ancestry have a high BRCA mutation carrier rate. Therefore, recently, Israel included free genetic testing among all Jewish women with Ashkenazi ancestry, 25 yrs. and older in its public health system. The aim of this study was to assess the intention of eligible women to be tested for BRCA mutations, and to find factors that may affect their decision.

We distributed an online survey to a panel of participants in a commercial research institute. The survey included socio-demographic characteristics, attitudes towards preventive actions, views related to benefits and limitations of performing the BRCA test, worry regarding cancer morbidity, knowledge about breast cancer morbidity and hereditary breast cancer genetics. The survey concluded with a question regarding the woman's interest in undergoing the BRCA test.

The results showed that among the 506 respondents, 250 (49%) were interested in BRCA testing, 42 (8%) objected and 214 (43%) were undecided. In comparing the undecided to the other groups, we found that most presented a positive attitude towards screening tests and preventive medicine, they showed acceptable knowledge about the proposed test, and yet were interested in learning and further expanding the knowledge and the consequences of doing the test. Most respondents of all groups expressed concern of breast cancer morbidity and were reluctant to perform the test for reasons of reducing uncertainty, implications for children and implications for their own health.

Within all groups, many women expressed their desire to consult with a medical professional about the test. We conclude that aiming to improve the performance of BRCA genetic testing, women need a thorough explanation about its implications. The main way to inform them would be by medical professionals, especially in primary care. This implies that front line nurses and physicians need to become more knowledgeable and committed to this subject.

Introduction

BRCA mutations are associated with elevated risk of breast and ovarian cancer, accountable for a high percentage of familial breast and ovarian cancers as well as other peritoneal originating malignancies [1-3]. Among the Jewish community in Israel, Jewish women of Ashkenazi ancestry have a high BRCA mutation carrier rate, mainly of three well known mutations [2,4,5]. Several studies estimated 2.5% carrier rates, whereas other studies lower rates due to different population inclusion criteria and additional factors [4,6,7].

In high-risk populations such as these, early detection strategies, close follow-up, and preventive interventions are recommended. For those who are carriers of the BRCA mutation, preventive mastectomy and/or oophorectomy can significantly reduce breast cancer morbidity and mortality [3,8]. Therefore, screening for BRCA mutations has been suggested as part of any prevention program [3,6,9].

Nevertheless, until recently, screening for BRCA mutations was limited to persons with a family history of cancer. This strategy leaves as many as 40-70% of women who carry the mutation, not included in screening [2,10]. This has been explained by limited communication between family members of BRCA carriers, lack of awareness, small size families, male siblings and paternal inheritance [5,6].

Based on the effectivity of screening for BRCA mutations within high-risk populations, Israel became one of the first countries in the world to include free genetic testing among all Jewish women with Ashkenazi ancestry, 25 yrs. and older, in its public health system screening recommendations.

This approach is consistent with WHO and USPTS recommendations for genetic screening [2,10]. In a study by Michaan et al., this screening approach was exhibited as cost effective for a population carrier rate of 2.5% (such as the rate among Ashkenazi Jews) as well as a lower carrier rate of 0.75% representing the general Israeli Jewish population [11,12].

Successful implementation of genetic screening, such as BRCA screening, within a population is challenging, and relies on a wide range of factors [1]. Of paramount importance are the candidate's perception of the test, as expressed by beliefs, attitudes and barriers to being screened [10,13].

Several studies examined population screening for BRCA mutations. A Canadian single arm study by Metcalfe et al. [7] and an Israeli study by Lieberman et al. [4] found high rates of satisfaction among women tested, although cancer related distress scores were higher among those who were discovered as BRCA carriers. A randomized controlled study conducted in London by Manchanda et al. compared the benefits and disadvantages of genetic testing for BRCA mutations using a classic family history (FH) approach versus population screening (PS) [6]. No significant differences were found regarding psychological aspects such as anxiety, distress, depression, and quality of life [14]. Within both study groups personal characteristics such as age, income and marital status affected levels of anxiety, distress, and quality of life [6]. In these studies participants were recruited voluntarily through self-referral, using several modalities, such as newspaper items, telephone, and recruiting through posters in hospitals and medical clinics [4,6,15]. This might cause a selection bias towards women with a higher level of awareness and inclination towards screening tests.

In this original research we used an internet panel as an efficient method of accessing a large and standardizable population sample [16]. We interviewed women who are eligible for genetic testing for BRCA through the Israeli public health plan, as to their intention to be tested, and various factors that may affect their decision. Understanding these factors and their effect on the candidate population is an important step towards successfully implementing screening for BRCA mutations within the population.

Materials and Methods

The study was approved by the ethics committee of the Ben-Gurion University of the Negev. Data was collected through an online survey during June 2021 by a commercial research institute. The number and identity of potential participants from the total number registered in the company's database were determined to achieve a suitable socio-demographic distribution.

Participants

Inclusion criteria for survey participation were: Women of Ashkenazi descent (at least one of her grandparents of Ashkenazi descent), between ages of 25 and 70, with no prior diagnosis of breast cancer, or previous completion of BRCA genetic testing.

Surveys included 6 categories that might influence the decision

to conduct BRCA genetic screening test:

1. Socio-demographic characteristics: Age, marital status, family composition, education, socioeconomic status, and family history details: family history of cancer or of other genetic syndromes and close accompaniment of a person with a malignant disease.

2. Attitude towards preventative actions: We asked the participants to refer to four preventative actions- recommended screening tests (mammogram and PAP test), pre-natal genetic counseling and vaccinations. Eligible responses were: I support, I'm conflicted, I object or I am not familiar with the measure.

3. Positions towards 14 statements, expressing the views related to performing BRCA1/2 testing. Based on 18-items questionnaire used by Manchanda et al. [2] (Supplementary Table S1). Six items assessing perceived benefits of testing and 8 items assessing perceived limitations/risks [2]. Response options for each statement were: agree, disagree or not relevant.

4. Worry regarding cancer morbidity was estimated using the Cancer Worry Scale (CWS), a four items questionnaire. Each item is scored on a 4-point Likert scale, from 1 to 4. Higher scores indicate greater worry of developing cancer [3].

5. Knowledge was assessed using a specially developed six-item questionnaire (score range 0-10) about breast cancer screening, morbidity and hereditary breast and ovarian cancer (HBOC) genetics based on a questionnaire used previously (Supplementary Table S2). In addition, we used two subjective questions regarding knowledge: "I fully understand the meaning of BRCA1/2 testing", and "I am interested in additional knowledge regarding the test and its implication". Another question was used to assess the inclination to consult with others: physicians, friends, and relatives.

The survey included a question about the interest in undergoing BRCA testing: "Since the test is available in all HMOs in Israel free of charge, do you intend to undergo this test?" Response options were yes, no and I am undecided.

Due to a misunderstanding, one item of the CWS was dropped from the survey. As a result, supplement questionnaires were sent to the respondents a month later. We analyzed the three CWS items that existed in both questionnaires by paired t-test, and found that their means were similar (4.34 vs. 4.33, $p=0.876$). Therefore, we used the CWS scores from the supplement questionnaire in this study analysis.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics (version 26). The mean value of continuous variables was compared using the t-test. Frequencies of categorical variables were compared using the chi-square test. Paired t-test were used to compare paired continuous data. For multivariate analysis, linear regression and logistic regression were used for continuous and categorical variables, respectively. P values are two-tailed with 95% confidence intervals.

Results

The on-line questionnaire was sent to 1860 women. Only 740 began to respond to the survey. Of these, 171 did not meet the inclusion criteria (i.e., were not of Ashkenazi descent, were diagnosed with cancer, or had already undergone a BRCA test). In addition, 63 did not complete the survey, resulting in 506 women remaining. Of

Table 1: Sociodemographic characteristics of study participants: interested in BRCA testing, not interested and un-decided.

		Non-interested	Interested	Un-decided	Total	Uni-variant analysis	Multi-variant analysis								
							interested vs. not interested		Interested vs. un-decided		Un-decided vs. not interested				
							OR	p	OR	p	OR	p			
		N=42	N=250	N=214	N=506										
Age	mean (SD, range)	50.64 (14.1, 41)	43.8 (12.5, 45)	43.6 (13.2, 45)	44.3 (13.3, 45)	I vs. NI, 0.006 I vs. UD 0.006	0.93	<0.001		NS	1.07	NS	<0.001		
Marital status		N (%) ^a	N (%) ^a	N (%) ^a	N (%) ^a										
	Never married	10 (23.8)	33 (13.2)	35 (16.4)	78 (15.4)	0.001	1								
	married / partnership	20 (47.6)	192 (76.8)	158 (73.8)	370 (73.1)			NS							
	Divorced or widowed	12 (28.6)	25 (10)	21 (9.8)	58 (11.5)		0.2	0.039							
Has children ^b	Yes	26 (66.7)	196 (83.1)	158 (79.4)	380 (80.2)	NS	6.7	0.001		NS	4.8	NS	0.005		
	No	13 (33.3)	40 (16.9)	41 (20.6)	94 (19.8)										
Education	High school	7 (16.7)	32 (12.8)	31 (14.5)	70 (13.8)	NS		NS				NS		NS	
	Beyond high school	7 (16.7)	43 (17.2)	46 (21.5)	96 (19)										
	Academic	28 (66.7)	175 (70)	137 (64.0)	340 (67.2)										
Socioeconomic - Income	Lower than average	24 (57.2)	91 (36.4)	97 (45.3)	212 (41.9)	0.051		NS				NS		NS	
	Average	7 (16.7)	69 (27.6)	58 (27.1)	134 (26.5)										
	Higher than average	11 (26.2)	90 (36)	59 (27.5)	160 (31.6)										

the remaining, 450 (89%) women responded to the supplementary questionnaire. A total of 506 women met the inclusion criteria and completed the questionnaire.

Sociodemographic characteristics are shown in Table 1. Participants' mean age was 44.3y (SD 13.3). Of all participants, 370 (73%) were married or in partnership and 380 (80%) had children. Family history of any cancer was reported by 310 (61.3%) and 131 (25.9%) had HBOC family history (including breast, ovarian and pancreatic cancer), 91% of whom had only one affected relative.

Regarding BRCA testing, 250 (49%) responded they were interested in BRCA testing, 42 (8%) objected and 214 (43%) reported they were undecided. We summarized the findings we reviewed under 5 key categories, depending on the respondents' answer regarding their intention to perform the test. We performed analyzes that included the above three groups, with an emphasis on the undecided group, which should attract the major focus of this study.

The socio-demographic characteristics of respondents who were interested and undecided were very similar and did not significantly differ in statistical analysis. Only two significant factors significantly differed between undecided participants and those uninterested: Younger age (OR=1.07 per year, $p<0.001$) and having children (OR=4.83, $P=0.005$) (Table 1).

In the univariate model higher socio-economic status (higher income) had a positive correlation with interest in BRCA testing ($p=0.051$). Family history of cancer in general as well as HBOC family history were not correlated with the interest in BRCA testing. Having other genetic syndromes in the family, as reported by panel participants (e.g., Familial Mediterranean fever, Retinitis Pigmentosa, Cardiomyopathy, Gaucher's disease), had a positive correlation with test interest ($p=0.03$) (Table 1).

Following respondents' positions toward screening tests and preventive medicine, it was found that the majority of participants reported high support for preventive medicine: 92% supported mammography, 95% supported PAP testing, 89% supported prenatal genetic counseling, and 87.6% supported vaccination (Table 2). Comparing the undecided group to the other two groups, it was found that support for prenatal genetic counseling was the only predictor of the tendency to perform the test ($p=0.005$). The attitude towards mammography and PAP screening were predictors of being undecided vs. not interested (0.007 and 0.01, respectively) (Table 2a). Interestingly, despite supporting these health preventative measures, of the 24 women who reported they were referred by a physician for onco-genetic counseling only 7 (29.2%) reported they actually completed genetic counseling.

Table 3 describes the results of the attitudes scale. In a multivariate analysis, all six considerations which expressed perceived benefits positively influencing performance of the test, significantly predicted interest vs. the undecided groups. For example: "reduction of uncertainty" (OR=28.3, $p<0.001$), "To know if I need to get cancer screening tests more often" (OR=18.9, $p<0.001$) and "To be reassured" (OR=12.9, $p<0.001$). Among the 8 items that expressed potential barriers 4 were found to predict lower inclination to being tested: "I am worried about loss of confidentiality" (OR=0.4, $p=0.01$), "I am concerned about the effect it would have on my family" (OR=0.6, $p=0.012$), "I am concerned that I could not

handle it emotionally" (OR=0.4, $p<0.001$) and "I am concerned about the test medical implications" (OR=0.6, $p=0.01$) (Table 3).

Psychosocial assessment

Cancer worries: In the entire cohort the mean CWS was 6.28/16. The only socio-demographic factor that was found to be related to CWS level was positive family history of cancer which increased CWS score by 0.52 points ($p=0.014$). By univariate as well as by multivariate analysis it was found that higher CWS is correlated with being more interested vs. not interested in being tested (OR=1.8, $p<0.001$) and among undecided vs. not interested (OR=1.4, $p=0.017$) (Table 2b).

Knowledge: In the entire cohort the mean knowledge score was 6.2 (SD 2.6). The only socio-demographic factor that was found to affect knowledge level was higher education which increased knowledge by 0.76 points (<0.001). Regarding the inclination to BRCA testing, undecided participants represented the lowest knowledge level (5.2) vs. women who were interested (6.6) ($p<0.001$) and vs. not-interested (6.3) (NS). In multivariate analysis greater knowledge was a predictor for being interested vs. un-decided (OR=3.9, $p=0.002$) (Table 2b).

The average knowledge score of women who said they fully understood the meaning of the BRCA test was higher than the knowledge scores of those who reported they didn't fully understand (7.1 vs. 5.8, $p<0.001$). Among participants who desired to be tested the proportion of women who felt they fully understood was higher (48%) than those who were uninterested (38.1%), whereas the rate of women who were undecided was the lowest (28.5%) ($p<0.001$) (Table 2b). Thus, according to the logistic regression, those who reported they fully understood the test are 2.4 times more inclined to actually perform it (vs. undecided) ($p=0.002$).

Regarding the desire to gain knowledge about the test and its implication: The knowledge score of those who wanted to gain knowledge was significantly lower than the score of those who did not want to know more (7.2 vs. 6.2) ($p=0.025$). Women who want to do the test want to know more about it (90.8%) more than those are not interested (21.4%) vs women who were hesitant (74.3%) ($p<0.001$). When comparing those hesitating with those who are positively inclined, the interest in gaining knowledge was found to be a significant positive predictor (OR= 2.318, $p=0.094$).

Consulting others regarding the BRCA testing, 139 (27.5%) reported they would like to consult with relatives, 46 (9.1%) friends and the vast majority 463 (91.5%) would like to consult medical staff. The proportion of women who wanted to consult medical staff was higher in those who said they did not understand the meaning of the test compared with those who said they understood it well (96.8% vs. 88.4, $p=0.051$). In addition, 79.7% of women who want to know more, want to consult medical staff compared to 6.7% of those who do not want to know more and compared to 13.8% of women who are undecided on this issue ($p<0.001$).

By crosschecking this data by logistic regression, the significant predictors for consulting medical staff were intention to be tested or undecidedness (OR=10.08, 9.227 respectively, $p<0.001$) and not fully understanding the test. Those who declared they fully understand the significance of testing and those uninterested will consult less (OR=0.255, $p=0.045$).

Table 2: Attitudes towards preventative health measures, cancer worry and knowledge: correlations with the desire to be tested.

									Multi-variant analysis ^a				
									Interested vs. not interested	Interested vs. undecided	Undecided vs. not interested		
									P value		P value		P value
Part A: Attitude regarding other health behaviors:													
		N (%) ^a	N (%) ^a	N (%) ^a									
Mammography^b													
	Against	3 (7.3)	0	2 (1)	5 (1)								
	For	31 (75.5)	237 (96)	187 (91.2)	455 (92.3)								8.88 0.046
	Not sure	7 (7.1)	10 (4)	16 (7.8)	33 (6.7)								
PAP test^c													
	Against	2 (5)	0	1 (0.5)	3 (0.6)								
	For	34 (85)	239 (96.8)	192 (95)	465 (95.1)								67.5 0.003
	Not sure	4 (10)	8 (3.2)	9 (4.5)	21 (4.3)								44.7 0.015
Pre-natal GC^d													
	Against	4 (10.8)	2 (0.8)	2 (1)	8 (1.7)								
	For	26 (70.3)	224 (94.9)	172 (86.9)	422 (89.6)								30.2 0.004
	Not sure	7 (18.9)	10 (4.2)	24 (12.1)	41 (8.7)								<0.001 0.005

Table 3: Attitudes towards BRCA testing: correlations with the desire to be tested.

	Not interested	Interested	Undecided	univariate analysis	Multi-variant analysis ^a			
					Interested vs. undecided		Undecided vs. not interested	
					N (%) ^b	OR	p	OR
Attitude:	N (%) ^b	N (%) ^b	N (%) ^b	p	OR	p	OR	p
To be reassured.	5 (21)	239 (98.8)	147 (86)	<0.001	12.9	< 0.001	24.1	< 0.001
To enhance cancer prevention.	14 (48.8)	236 (97.1)	160 (90.9)	<0.001	3.8	0.007	11.9	< 0.001
To learn about my children's risk	9 (40.9)	213 (95.1)	127 (81.4)	<0.001	6.3	< 0.001	6.9	0.001
To make childbearing decisions.	5 (26.3)	112 (78.3)	69 (60)	<0.001	2.7	0.001	3.3	0.065
To know if I need to get cancer screening tests more often	9 (36)	238 (99.2)	157 (86.7)	<0.001	18.9	< 0.001	20.7	< 0.001
To reduce uncertainty	6 (24)	235 (99.2)	140 (79.1)	<0.001	28.3	< 0.001	14.8	< 0.001
I am worried about losing my insurance.	3 (12)	82 (39.2)	58 (36.7)	0.027		NS	8.2	0.006
I am worried about loss of confidentiality.	4 (13.8)	22 (9.6)	34 (18.8)	0.024	0.4	0.01		NS
I am worried about stigmatization.	3 (9.1)	22 (9.2)	18 (9.6)	NS		NS		NS
I do not trust modern medicine.	10 (28.6)	43 (17.6)	29 (15.2)	NS		NS		NS
I believe that there is nothing that can be done to prevent getting cancer.	11 (29.7)	35 (14.3)	37 (19.5)	0.05		NS		NS
I am concerned about the effect it would have on my family.	8 (26.7)	65 (27)	68 (37.4)	0.063	0.6	0.012		NS
I am concerned that I could not handle it emotionally.	12 (35.3)	67 (27.6)	88 (45.1)	0.001	0.4	< 0.001		NS
I am concerned about the test medical implications.	15 (45.5)	126 (51.2)	118 (61.5)	0.051	0.6	0.01	2.2	0.075

^aall regression included the socio-demographic variables (age, marital status, Has children, Education, Socioeconomic Income, Family history of cancer). For each attitude a separate regression was performed; significant values are marked in boldface. P values are indicated in italics; ^bN and percentages are of those who agreed with the statement. The missing numbers for each item (by items order) are: 70 (13%), 58 (11.5%), 104 (20.6%), 229 (45.3%), 60 (11.9), 67 (13.2), 114 (22.5), 67 (13.2), 46 (9.1%), 36 (7.1%), 34 (6.7%), 53 (10.5), 34 (6.7%), 35 (6.9%). The rate of the missing was higher among those who were interested in BRCA test, lower in undecided and lowest in those who were not interested in testing. NS not significant

Discussion

This survey was conducted shortly after BRCA testing was integrated in Israel's public health plan. The study population resembles those eligible for the screening test in Israel. This reinforces the ability to deduce relevant information applicable for implementing the test. Previous studies enrolled volunteers, who are more prone to being interested in the test, and subject to selection bias.

The main findings in our study relate to the unique and significant group of the undecided, which was identified through the research questionnaire. Major characters of this group were being married, and mothers of children (>70%), having family history of cancer (61%), and a minority had family history of other genetic disease. Most presented a positive attitude towards screening tests and preventive medicine. This group showed acceptable knowledge about the proposed test, and yet were interested in learning and further expanding their knowledge and the consequences of completing the test. Most expressed concern of breast cancer morbidity and were reluctant to perform the test for reasons of reducing uncertainty, implications for children and implications for their own health. This unique group invites further intervention and response to the concerns raised, thus raising the possibility of achieving improvement in compliance with population screening.

As noticed, excluding marital status, having children and younger age, most sociodemographic data were not significantly related to participant's inclination to be tested for BRCA mutations. Similar results were found by Lieberman et al. [4] and Manchanda et al. [6] in their surveys in Israel and London respectively. Possibly, both younger women and women with children are more involved and interested in their future health and in family planning, which BRCA status could affect. Nevertheless, the finding that most sociodemographic parameters were not significantly related to intention to be tested, directs us to focus on other aspects of views and beliefs as a potential influencing factor on test performing decision.

Assuming young women are more exposed to social networks and advertising information, may raise their awareness of morbidity and mortality data from common malignant diseases. Therefore, they tend to be more interested in conducting screening tests, including BRCA. Indeed, we found that specific beliefs and attitudes reflecting uncertainty and a desire for calmness were found to be have a significant effect on being tested. This assumption corresponds with their desire for reliable knowledge.

Both beliefs and attitudes scale and CWS score [17] showed concern and interest of breast cancer among most of the respondents. The vast majority responded they were concerned with preventing illness and its' consequences for their children. Prior studies presented decrease in CWS scores in long term follow-up, especially of those who tested positively for BRCA [18]. We can therefore conclude that these issues should be addressed when implementing the test.

The positive correlation between inclination to screening tests and preventive medicine with intention to perform the BRCA test suggests emphasizing raising public health awareness and attitudes towards screening tests and preventive measures in general, which could affect BRCA screening as well. The possibility of tying some of these screening tests together in terms of information, recruiting

patients or performing the test, might enhance public responsiveness. In the trial by Lieberman et al. [4] recruiting patients in different manners affected rates of participation and test performance.

Interestingly, only a small proportion of the women in the survey who were referred for genetic counseling actually performed the recommendation. This may be accounted for by low availability and low accessibility of genetic counseling in Israel, possible emotional factors, as well as other possible barriers to genetic testing. Assuming the more women are screened, the more will test positive and require genetic counseling, entitles this as an important factor to account for. Attitudes and barriers to genetic consultation need to be further investigated and are beyond the scope of this study.

In the age of the "involved patient", patients are expected to make medical decisions without having enough information about their benefit, therefore they rely on emotions, repress information that contradicts the opinion they have already formulated and get a misleading picture from media series or other unreliable sources [19]. The undecided participants desire for knowledge highlights the need for clear and comprehensive information regarding the test and its consequences.

Moreover, we found that most of the women wanted to consult a medical professional before performing the BRCA test. This would probably be a genetic counselor or a primary care physician or nurse, who would be the first to contact and consult. Further research is required about the attitudes of primary care physicians and nurses and their knowledge about the test and its consequences. Yet, it seems that the role of primary medicine is important in mediating and finding innovative ways for more available genetic knowledge, such as online counseling [2].

The limitations of this study are that conducting a computerized questionnaire, appeals to a population, which is based on knowledge and accessibility to answer in this media, and has chosen in advance to join public opinion polls [16]. This might cause a selection bias. On the other hand, it was found that the groups of women, based on all demographic parameters, presented in the survey, closely reflect their relative ratio in the Israeli population. There are questions, in which there is a possible recall or knowledge bias, we have done our best to obtain parallel information through access to a topic from several directions within the questionnaire. Most parts of the questionnaire are based on valid and accepted questionnaires in the world on this topic.

In conclusion, this study resumed two encouraging tendencies toward performing the BRCA screening test among Ashkenazi Jewish women in Israel. First, is the inclination of the largest group of respondents to perform the test, and the tendency of the second largest group to be undecided about it. The second trend expresses the desire of most respondents to know more and consult about the essence of the test and its consequences, which correlates with their intention of performing the test. Policymakers should consider an accessible and available escort system that will address this need, out of a desire to enable every woman to make an informed and clear decision regarding BRCA testing.

Authors' Contribution

Every author of the manuscript has made substantial contributions either to the planning of the work that led to the manuscript: A.S., L.S., B.A., L.A., and F.T. B.A. also contributed

to obtained funding to this research. A.S., L.S., B.A., L.A., and F.T. substantially contributed to study concept and design, acquisition of data; analysis and interpretation of data as well as drafting of the manuscript and critical revision of the manuscript.

References

1. Winters S, Martin C, Murphy D, Shokar NK. Breast Cancer Epidemiology, Prevention, and Screening. *Prog Mol Biol Transl Sci.* 2017; 151:1-32.
2. Manchanda R, Lieberman S, Gaba F, Lahad A, Levy-Lahad E. Population Screening for Inherited Predisposition to Breast and Ovarian Cancer. *Annu Rev Genomics Hum Genet.* 2020; 21:373-412.
3. Bayraktar S, Arun B. BRCA mutation genetic testing implications in the United States. *Breast Edinb Scotl.* 2017; 31:224-232.
4. Lieberman S, Tomer A, Ben-Chetrit A, Olsha O, Strano S, Beeri R, et al. Population screening for BRCA1/BRCA2 founder mutations in Ashkenazi Jews: proactive recruitment compared with self-referral. *Genet Med Off J Am Coll Med Genet.* 2017; 19(7):754-762.
5. Hartge P, Struewing JP, Wacholder S, Brody LC, Tucker MA. The prevalence of common BRCA1 and BRCA2 mutations among Ashkenazi Jews. *Am J Hum Genet.* 1999; 64(4):963-970.
6. Manchanda R, Loggenberg K, Sanderson S, Burnell M, Wardle J, Gessler S, et al. Population testing for cancer predisposing BRCA1/BRCA2 mutations in the Ashkenazi-Jewish community: a randomized controlled trial. *J Natl Cancer Inst.* 2015; 107(1):379.
7. Metcalfe KA, Poll A, Royer R, Llacuachaqui M, Tulman A, Sun P, et al. Screening for founder mutations in BRCA1 and BRCA2 in unselected Jewish women. *J Clin Oncol Off J Am Soc Clin Oncol.* 2010; 28(3):387-391.
8. Forbes C, Fayter D, de Kock S, Quek RG. A systematic review of international guidelines and recommendations for the genetic screening, diagnosis, genetic counseling, and treatment of BRCA-mutated breast cancer. *Cancer Manag Res.* 2019 Mar 22; 11:2321-2337.
9. Newman L. US Preventive Services Task Force Breast Cancer Recommendation Statement on Risk Assessment, Genetic Counseling, and Genetic Testing for BRCA-Related Cancer. *JAMA Surg.* 2019; 154(10):895-896.
10. Evans O, Gaba F, Manchanda R. Population-based genetic testing for Women's cancer prevention. *Best Pract Res Clin Obstet Gynaecol.* 2020; 65:139-153.
11. Michaan N, Leshno M, Safra T, Sonnenblick A, Laskov I, Grisaru D. Cost Effectiveness of Whole Population BRCA Genetic Screening for Cancer Prevention in Israel. *Cancer Prev Res Phila Pa.* 2021; 14(4):455-462.
12. Patel S, Legood R, Evans DG, Turnbull C, Antoniou AC, Menon U, et al. Cost effectiveness of population based BRCA1 founder mutation testing in Sephardi Jewish women. *Am J Obstet Gynecol.* 2018; 218(4):431.e1-431.e12.
13. D'andrea E, Marzuillo C, De Vito C, Di Marco M, Pitini E, Vacchio MR, et al. Which BRCA genetic testing programs are ready for implementation in health care? A systematic review of economic evaluations. *Genet Med Off J Am Coll Med Genet.* 2016; 18(12):1171-1180.
14. Manchanda R, Burnell M, Gaba F, Sanderson S, Loggenberg K, Gessler S, et al. Attitude towards and factors affecting uptake of population-based BRCA testing in the Ashkenazi Jewish population: a cohort study. *BJOG Int J Obstet Gynaecol.* 2019; 126(6):784-794.
15. Metcalfe KA, Poll A, Llacuachaqui M, Nanda S, Tulman A, Mian N, et al. Patient satisfaction and cancer-related distress among unselected Jewish women undergoing genetic testing for BRCA1 and BRCA2. *Clin Genet.* 2010; 78(5):411-417.
16. Hays RD, Liu H, Kapteyn A. Use of Internet panels to conduct surveys. *Behav Res Methods.* 2015; 47(3):685-690. doi:10.3758/s13428-015-0617-9
17. Caruso A, Vigna C, Gremigni P. The Cancer Worry Scale Revised for Breast Cancer Genetic Counseling. *Cancer Nurs.* 2018; 41(4):311-319.
18. Manchanda R, Burnell M, Gaba F, Desai R, Wardle J, Gessler S, et al. Randomised trial of population-based BRCA testing in Ashkenazi Jews: long-term outcomes. *BJOG Int J Obstet Gynaecol.* 2020; 127(3):364-375.
19. Oxman AD, García LM. Comparison of the Informed Health Choices Key Concepts Framework to other frameworks relevant to teaching and learning how to think critically about health claims and choices: a systematic review. *F1000Research.* 2020; 9:164.