Social and Behavioural Research in Clinical Genetics

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Patient satisfaction and cancer-related distress among unselected Jewish women undergoing genetic testing for BRCA1 and BRCA2


It is not known to what extent participation in a genetic testing program for BRCA1 and BRCA2, which does not include an extensive pre-test counselling session, influences cancer-related distress, cancer risk perception and patient satisfaction. Unselected Jewish women in Ontario were offered genetic testing for three common Jewish BRCA mutations. Before testing and 1-year post-testing, the women completed questionnaires which assessed cancer-related distress, cancer risk perception, and satisfaction. A total of 2080 women enrolled in the study; of these, 1516 (73%) completed a 1-year follow-up questionnaire. In women with a BRCA mutation, the mean breast cancer risk perception increased from 41.1% to 59.6% after receiving a positive genetic test result (p = 0.002). Among non-carriers, breast cancer risk perception decreased slightly, from 35.8% to 33.5% (p = 0.08). The mean level of cancer-related distress increased significantly for women with a BRCA mutation, but did not change in women without a mutation; 92.8% expressed satisfaction with the testing process. The results of this study suggest that the majority of Jewish women who took part in population genetic screening for BRCA1 and BRCA2 were satisfied with the delivery of genetic testing and would recommend testing to other Jewish women. However, women with a BRCA mutation experienced increased levels of cancer-related distress.

Conflict of interest
None declared.

There are two mutations in BRCA1 and one mutation in BRCA2, which together are present in up to 2.5% of Ashkenazi Jewish women (1, 2). These mutations are responsible for approximately 12% of breast cancers and 35% of ovarian cancers in the Jewish population. Carriers of a BRCA1 mutation (5382insC or 185delAG) face a lifetime risk of breast cancer of approximately 70% and a risk of ovarian cancer of 30–40% (3). Carriers of the BRCA2 mutation (6174delT) have a risk of breast cancer of approximately 50% and a risk of ovarian cancer of approximately 20% (4).
Because these three mutations comprise the majority of deleterious mutations in the Jewish population, genetic testing for the ‘founder’ panel is relatively straightforward and inexpensive.

Given the high frequency of mutations in the Jewish population at large, it has been proposed that the entire female Jewish population be eligible for testing (5, 6). However, only 1–2% of tested patients are likely to be positive and it is inefficient to offer extensive pre-test counselling to all. Prior to recommending population screening in which standard pre-test genetic counselling is not offered, it is important to gauge the level of satisfaction with such a program. Previous research has shown that women who present for genetic testing do not experience increased levels of distress after receiving a positive genetic test result, but these studies have been based on women with a strong family history of breast cancer (7–14). It is important to assess the impact of receiving a positive test result on cancer-related distress in women who may or may not have a personal or family history of breast or ovarian cancer. We conducted testing for BRCA mutations in 2080 unselected Jewish women from Ontario (15) and we reported that 1.1% of the patients had a positive result. It has been a minimum of 1 year since the patients received their result. In this study, we report on satisfaction with the genetic testing process and on the cancer-related distress levels and cancer risk perception before and after receiving genetic test results.

Methodology

Study population

The study protocol received full ethical approval from the research institute. Eligible subjects were women who self-identified as (Ashkenazi or Sephardic) Jewish, who were between the ages of 25 and 80 years, and who resided in Ontario. Women with a family or personal history of cancer were not solicited, but were not excluded. Study subjects were recruited through an article that was published in a national newspaper (on a single occasion) in May 2008. Women were invited to call the study office if they were interested in participating. At the initial phone call, the study was explained and the woman was asked if she wished to participate. If she was interested, she was given an appointment to come and provide a blood or saliva sample. Prior to the appointment, each subject was mailed a study package, which included a study consent form, an information brochure on BRCA1 and BRCA2, a family history questionnaire, and a study-specific questionnaire. They were asked to complete and return the relevant documents at the time of their blood/saliva collection appointment.

Women were not offered in-person genetic counselling at the time they provided a DNA sample for this study. However, all women were provided with a pamphlet on genetic testing for BRCA1 and BRCA2. Topics covered in the pamphlet included information on basic genetics and BRCA1 and BRCA2, management options for mutation carriers, genetic testing in the Jewish population, implications of genetic testing, and information about the study and the study team (materials available upon demand). Before signing the consent form, each woman was asked if she had read the pamphlet and if she had any questions or concerns. A genetic counsellor was available to answer any questions about the testing process or implications of testing.

All DNA samples were tested for the three Jewish founder BRCA1 (185delAG and 5382insC) and BRCA2 (6174delT) mutations. The molecular technique that was used to identify carriers of Ashkenazi-specific mutations in BRCA1 and BRCA2 was performed using a specific assay for Jewish mutations (16). All mutations found by this method were confirmed by direct sequencing.

Each woman’s pedigree was reviewed and women were assigned to one of the three categories: (1) no significant family history of breast or ovarian cancer (no first- or second-degree relative with breast or ovarian cancer), (2) moderate family history (first- or second-degree relative with breast or ovarian cancer with personal breast cancer risk less than double population risk based on Tyrer-Cuzick Model), or (3) strong family history (breast cancer risk greater than double population risk based on Tyrer-Cuzick Model).

The genetic test result was available to all women who wished to receive her result. If the woman was negative for the three BRCA1 and BRCA2 mutations and had no significant family history of breast or ovarian cancer, she received her negative genetic test result by mail. If the woman was negative for the genetic tests, but had a moderate or strong family history of breast or ovarian cancer, the result was given by a genetic counsellor over the telephone and a follow-up letter was sent. The letter summarized her breast cancer risk and provided recommendations for surveillance. If the woman had a positive genetic test, the result was disclosed by the genetic counsellor over the telephone. She was invited to come for a full genetic counselling session within 3 days of receiving her result.
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Study questionnaires

Study-specific questionnaire
This questionnaire was developed for this study; it included questions related to basic demographic information (age, cancer status, education, screening history, cancer preventive procedures), in addition to questions about personal cancer risk perception and satisfaction with genetic testing. Women were asked to estimate their lifetime risk of breast cancer between 0% and 100%. Satisfaction with experience of genetic testing was rated on a 5-point scale (1: very dissatisfied to 5: extremely satisfied).

Family history questionnaire
This questionnaire was completed by each woman and was reviewed with each woman by a member of the study team. This questionnaire is currently in use in our clinical department and inquires about cancer histories in relatives in order that cancer risk can be estimated using various cancer risk models.

Impact of Event Scale
The Impact of Event Scale (IES) (17) is a self-report measure designed to measure current subjective distress in relation to a specific stressor. In this study, the stressor was identified as ‘being at risk of breast cancer’. It measures the frequency of intrusive and avoidant phenomena. The scale consists of 15 items (7 intrusion items and 8 avoidance items). Participants rate the frequency of intrusive and avoidant behaviours using a 4-point frequency scale (0 = not at all, 1 = rarely, 3 = sometimes, 5 = often). The IES allows the calculation of a total score (with a possible range of 0–75), and separate scores of intrusion and avoidance subscales (with a possible range of 0–35 for intrusion, and 0–40 for avoidance). Cronbach’s α based on populations of patients with cancer, women with a family history of breast cancer, survivors of advanced Hodgkin’s disease, patients with malignant melanoma, individuals tested for Huntington’s disease, and patients experiencing bereavement are 0.78 for intrusion and 0.82 for avoidance. The IES has been found to have good validity and reliability when measuring cancer-related distress in women at increased risk of developing breast cancer (18).

Breast cancer and BRCA mutation risk estimation
For each woman, the probability of having a BRCA mutation was estimated using data derived from the family history questionnaire. The BRCA mutation probability and the breast cancer risk were calculated using the Tyrer-Cuzick model (19). This model utilizes Bayes’ theorem to calculate the mutation probability and then refines the calculation by maximum likelihood estimates and incorporates risk factors such as age at menopause and menarche, weight, height, age, use of hormonal replacement therapy, and previous benign breast biopsies. When compared to the Gail, Claus, and Ford models, the Tyrer-Cuzick model has been shown to be the most consistently accurate model for prediction of breast cancer (20, 21), and BRCA mutation carrier status (22).

Statistics
Student’s t-tests were used to compare the mean value of continuous variables and chi-squared test was used to compare the frequency of categorical variables between sub-groups. Paired t-tests were used to compare the estimations of cancer risk and cancer-related distress, pre- and post-genetic testing. Statistical analyses were performed by sas (version 9.1.3; SAS Institute Inc., Cary, NC).

Results

Demographics
A total of 2080 women enrolled in the study and provided a DNA sample. The mean age at enrollment was 49.3 years (range 23–79 years); 162 women reported a personal history of cancer (including 6 with invasive breast cancer, 9 with ductal carcinoma in-situ (DCIS) or lobular carcinoma in-situ (LCIS), 2 with ovarian cancer, and 147 with other forms of cancer); 1886 women reported 100% Ashkenazi Jewish ancestry, 105 women reported 75% Ashkenazi Jewish ancestry (3 grandparents), 56 women reported 50% Ashkenazi Jewish ancestry (2 grandparents), 3 women reported 25% Ashkenazi Jewish ancestry (1 grandparent) and 17 women were of Sephardic Jewish ancestry. Twenty-two women were identified as having a BRCA mutation. Of those who did not have a mutation, 64.5% had no family history of breast or ovarian cancer, 26.2% had a moderate family history, and 9.3% had a strong family history of breast/ovarian cancer.

A total of 1516 women completed a 1-year follow-up questionnaire (72.9%). Of the 1516 women, 18 had a mutation in BRCA1 (n = 8) or BRCA2 (n = 10). There were no significant differences in response levels in terms of cancer status (77.8% of affected women vs 72.5% of unaffected women; p = 0.14) or BRCA mutation
status (81.8% of carriers vs 72.8% of non-carriers; p = 0.34). There was a significant difference in age between responders and non-responders (47.5 vs 50.0 years, respectively; p < 0.0001).

Breast cancer risks

A total of 1077 women estimated their lifetime risk of developing breast cancer and 969 estimated the risk of ovarian cancer prior to genetic testing. The remaining women answered 'do not know'. Objective lifetime breast cancer risk estimates were generated for each woman using the Tyrer-Cuzick model. When objective and subjective breast cancer risks were compared, women significantly over-estimated their breast cancer risk prior to genetic testing. The mean subjective lifetime risk for breast cancer was 35.9% (range 0–100%) compared with the mean computer-generated risk of 11.4% (range 1–49%) (p < 0.0001).

The women were asked to re-estimate their breast cancer risk 1 year after receiving their genetic test result; 1073 women estimated their breast cancer risk and 976 women estimated their ovarian cancer risk. For non-carriers, the mean pre-test genetic lifetime breast cancer risk estimate was 35.8% (range 0–100%) compared with the mean post-test genetic risk of 33.5% (range 0–100%) (p = 0.08). There were significant differences in the subjective follow-up breast cancer risk compared with the mean computer-generated risk of 10.6% (range 1–49.7%) (p < 0.0001). For carriers, the mean pre-test genetic risk was 41.1% (range 10–80%) and the mean post-test genetic risk was 59.6% (range 20–86%) (p = 0.002 for difference; Table 1).

Cancer-related distress

Cancer-related distress was measured using the IES. A total of 2074 women completed the IES before genetic testing and 1505 women completed it after testing. The mean total score pre-testing was 11.1 (range 0–75). The mean scores for the pre-test intrusion and avoidance sub-scales were 4.5 (range 0–35) and 6.5 (range 0–40), respectively. There were no differences in pre-test cancer-related distress between carriers and non-carriers (p = 0.58 for avoidance sub-scale, p = 0.29 for intrusion sub-scale, and p = 0.39 for total scale).

Cancer-related distress was measured 1 year following genetic testing. The mean total score post-testing was 10.9 (range 0–66). The mean scores for the post-test intrusion and avoidance sub-scales were 4.6 (range 0–35) and 6.3 (range 0–4.0), respectively. Cancer-related distress did not change significantly in women without a BRCA mutation. However, distress scores increased significantly for women with a BRCA mutation (Table 2; Fig. 1). For women with a BRCA mutation, the mean total distress score was 25.3 (range 2–51). Three of the carriers (16.7%) scored in the sub-clinical range (0–8), five women (27.8%) scored in the mild range (9–25), seven women (38.9%) scored in the moderate range (26–43), and three women (16.7%) scored in the severe range (44+).

Satisfaction

Satisfaction with delivery of genetic testing was assessed among 1497 women who completed a post-test satisfaction questionnaire. Satisfaction was measured using a Likert scale, from 1 to 5 (with 1 being very dissatisfied and 5 being extremely satisfied). The mean satisfaction score was 4.2 (SD = 1.0; range 1–5). There were no significant differences in satisfaction scores between the carriers and non-carriers (3.8 vs 4.2; p = 0.11). One hundred and seven (7.2% of the 1497) of the women expressed dissatisfaction (score 1 or 2), 283 women (19%) said they would have preferred to have had a face-to-face meeting with a genetic counsellor before undergoing genetic testing and 81% of the women were satisfied with the printed materials. There was a significant difference in this response between carriers and non-carriers; 10

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### Table 1. Change in cancer risk perception

<table>
<thead>
<tr>
<th></th>
<th>Pre-test cancer risk estimate (SD) (range)</th>
<th>Post-test cancer risk estimate (SD) (range)</th>
<th>p-Valuea</th>
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</thead>
<tbody>
<tr>
<td>BRCA mutation carriers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast cancer</td>
<td>41.1 (24.7) (10–80)</td>
<td>59.6 (21.2) (20–86)</td>
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<td>Ovarian cancer</td>
<td>35.6 (27.3) (3–90)</td>
<td>26.2 (20.5) (0–60)</td>
<td>0.41</td>
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<tr>
<td>Non-carriers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast cancer</td>
<td>35.8 (23.1) (0–100)</td>
<td>33.5 (20.8) (0–100)</td>
<td>0.08</td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>26.2 (21.8) (0–100)</td>
<td>25.7 (20.8) (0–100)</td>
<td>0.65</td>
</tr>
</tbody>
</table>

BRCA, breast cancer, early onset.
aPaired t-test was performed on subjects for whom both measures were available.
Patient satisfaction and cancer-related distress

Table 2. Cancer-related distress pre- and post-genetic testing

<table>
<thead>
<tr>
<th>BRCA mutation carriers (n = 18)</th>
<th>Post-genetic testing score</th>
<th>p-Value a</th>
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</thead>
<tbody>
<tr>
<td>Intrusion score</td>
<td>Mean (SD) (range)</td>
<td></td>
</tr>
<tr>
<td>BRCA mutation carriers (n = 18)</td>
<td>2.5 (6.4) (0–27)</td>
<td>0.0003</td>
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<tr>
<td>Avoidance score</td>
<td>Mean (SD) (range)</td>
<td></td>
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<tr>
<td>Total score</td>
<td>7.1 (12.9) (0–39)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Non-carriers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intrusion score (n = 1484)</td>
<td>4.2 (6.3) (0–35)</td>
<td>0.21</td>
</tr>
<tr>
<td>Avoidance score (n = 1482)</td>
<td>6.2 (7.8) (0–36)</td>
<td>0.88</td>
</tr>
<tr>
<td>Total score (n = 1482)</td>
<td>10.4 (13.0) (0–59)</td>
<td>0.48</td>
</tr>
</tbody>
</table>

BRCA, breast cancer, early onset.

aPaired t-test.

Fig. 1. Course of cancer-related distress levels in carriers and non-carriers.

(55.6%) of carriers would have preferred a pre-test counselling session compared with 273 (18.3%) of non-carriers (p < 0.0001).

All of the women with a BRCA mutation were given in person post-test genetic counselling as part of this study. Of the 1494 women with a negative test result, 324 (21.7%) would have preferred to have received their genetic test result in a face-to-face meeting with a genetic counsellor, rather than by telephone or mail.

Almost all subjects (98.4%) said that they would recommend genetic testing for BRCA mutations to other Jewish women (94.4% of carriers and 98.5% of non-carriers); 96.1% of subjects felt that genetic testing should be available to all Jewish women (88.9% of carriers and 96.2% of non-carriers).

Discussion

This is the first study to assess satisfaction, cancer-related distress, and cancer risk perception in self-selected women who underwent genetic testing for BRCA1 and BRCA2 mutations without formal pre-test genetic counselling. The women in this study were eligible to undergo genetic testing for BRCA mutations because of their Jewish ancestry. The mean lifetime breast cancer risk (based on the Tyrer-Cuzick model) for this group of women was comparable to that of the general population risk in North America.

Typically, genetic counselling and testing involves a 1 hour pre-test genetic counselling session. Such an approach would be costly if applied to the general population, as the vast majority of individuals would not carry a genetic mutation. In the current study, women were not offered standard pre-test genetic counselling, but were given a detailed brochure on BRCA1 and BRCA2. A genetic counsellor was available to answer any questions at the time of DNA sample provision, although less than 5% of women had questions. For those who did, the most common concern was regarding insurance implications. All positive genetic test results were given by the genetic counsellor over the telephone, and an in-person counselling appointment was offered for carriers within 3 days. For those with a negative genetic test result, the disclosure of genetic test results was given in one of two ways. For those with a family history of breast or ovarian cancer, negative results were given over telephone, followed with a written letter summarizing the results and screening recommendations. For those without a family history of cancer, the results were given in a letter, which provided information on recommended general population breast screening guidelines. All women were provided with their lifetime breast cancer risk estimate.

Overall, at 1 year following genetic testing, the majority of women rated their satisfaction with the genetic testing process to be high or very high (92.8%). There were no significant differences in mean satisfaction scores between women with and without a BRCA mutation. However, there was a difference between carriers and non-carriers regarding counselling preferences. Overall, the vast majority of women were satisfied with the counselling process, but one half of the women who were found to carry a BRCA
The women estimated their breast cancer risk to be, on average, 35.9% compared with a computer-generated mean risk of 11.4%. After being given a negative genetic test result, the mean risk estimate remained elevated (33.9% estimated lifetime risk). This is perhaps surprising, given that every woman received a personalized letter that included her breast cancer risk. It is possible that continued over-estimation of breast cancer risk was due to women not receiving formal genetic counselling. However, previous research has shown that, despite attending a genetic counselling session, women continue to misinterpret their lifetime cancer risk. It is not clear if this is due to a failure in understanding or in retaining risk information (30).

There are several limitations to our study. The group of women who participated in this study self-selected and may not be representative of the entire Jewish population. The 1-year follow-up response rate of 73% is good for a mailed survey; however, greater responses may have impacted on the study results. Although 82% of the women with a BRCA mutation completed the follow-up questionnaires, limited conclusions can be made on the impact of testing without pre-test genetic counselling. In addition, we did not collect data on women’s preferences for the delivery of genetic testing prior to receiving genetic test results and although we did collect post-testing related distress scores (measured using IES) for unaffected relatives with a positive genetic test result, the mean distress score was 18 for unaffected relatives. They then measured cancer-related distress at 6-month post-genetic testing. The unaffected relatives with a positive genetic test result had a mean distress score of 18 and the unaffected relatives with a positive genetic test result had a mean score of 15. This represented a decreased distress level in the unaffected probands, and no change in the unaffected relatives. In contrast, in our study of low-risk women, distress levels increased significantly for women who were found to carry a BRCA mutation. This may be explained by the fact that the positive test result was unanticipated. Alternatively, this could be due to the fact that these women did not receive pre-test genetic counselling. In the present study, it was not possible to distinguish between these alternatives and future studies may address this question. Furthermore, we will measure distress levels at 2-year post-testing in these women to determine if distress levels remain elevated over time.

Many women over-estimate their breast cancer risk. These include women with and without a family history of breast cancer (23–29). Breast cancer risk perception in women at high risk of developing the disease is accurately reported between 9% and 57% of the time (24–29). In the current study, breast cancer risk was greatly over-estimated by many women prior to genetic testing. The women estimated their breast cancer risk to be, on average, 35.9% compared with a computer-generated mean risk of 11.4%. After being given a negative genetic test result, the mean risk estimate remained elevated (33.9% estimated lifetime risk). This is perhaps surprising, given that every woman received a personalized letter that included her breast cancer risk. It is possible that continued over-estimation of breast cancer risk was due to women not receiving formal genetic counselling. However, previous research has shown that, despite attending a genetic counselling session, women continue to misinterpret their lifetime cancer risk. It is not clear if this is due to a failure in understanding or in retaining risk information (30).

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The results of this study suggest that Jewish women who took part in population genetic screening for BRCA1 and BRCA2 were satisfied with the delivery of genetic testing and would recommend testing to other Jewish women. Owing to the high frequency of BRCA mutations in the Jewish population and the relatively low cost of performing the genetic test for the three common Jewish founder mutations, it may be time to consider offering population-wide screening for Jewish individuals.

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References


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