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Pilot Testing of a Psycho-educational Telephone Intervention for Women Receiving Uninformative BRCA1/2 Genetic Test Results

Christine Maheu, Wendy S. Meschino, Weiming Hu, Joanne Honeyford, Ingrid Ambus, Meredith Kidd, Aronela Benea, Xin Gao, Madhis Azadbakhsh, Christian Rochefort, Mary Jane Esplen

Evidence suggests that women who receive uninformative results for breast and ovarian cancer (BRCA1/2) gene mutations may experience as much distress as women whose results indicate the presence of a gene mutation. No intervention to reduce distress after receipt of uninformative results has yet been tested. The purpose of this study was to test the feasibility and preliminary effects of a psycho-educational telephone (PET) intervention to reduce distress in women who receive uninformative BRCA1/2 results. A single group with repeated measures was used to assess the impact of the intervention on 72 such women. After receiving the results, most of the women continued to feel uncertain about their carrier genetic status. However, their distress significantly decreased between receipt of uninformative results and 3 months post-intervention (p = 0.01). The preliminary findings suggest that a PET uncertainty intervention is clinically feasible and may reduce the distress of receiving uninformative results.

Keywords: breast cancer, BRCA1/2, genetic testing, uninformative results, pilot intervention study

Résumé

Essai pilote d'une intervention psycho-éducative par téléphone pour les femmes ayant reçu des résultats non concluants après des tests de dépistage génétique concernant BRCA1 et BRCA2

Christine Maheu, Wendy S. Meschino, Weiming Hu, Joanne Honeyford, Ingrid Ambus, Meredith Kidd, Aronela Benea, Xin Gao, Madhis Azadbakhsh, Christian Rochefort, Mary Jane Esplen

Les données permettent de croire que les femmes qui obtiennent des résultats non concluants à la suite de tests de dépistage d'une mutation des gènes liés aux cancers du sein et des ovaires (BRCA1 et BRCA2) sont susceptibles d'éprouver une détresse aussi importante que celles dont les résultats indiquent la présence d'une mutation génétique. Aucune intervention visant à atténuer le sentiment de détresse après réception de résultats non concluants n'a encore été mise à l'essai. L'objectif de la présente étude est d'évaluer la faisabilité et les effets préliminaires d'une intervention consistant en un appel psycho-éducatif destiné à réduire la détresse de femmes ayant reçu des résultats de dépistage génétique non concluants concernant les gènes BRCA1 et BRCA2. Un groupe unique sondé à plusieurs reprises a été étudié afin d'évaluer l'effet d'une telle intervention sur 72 femmes. Après la réception de leurs résultats, la plupart éprouvaient toujours de l'incertitude concernant leur statut de porteuse ou non d'une mutation génétique. Toutefois, une diminution considérable de leur détresse a été observée entre la réception des résultats non concluants et une période de trois mois après l'intervention par téléphone ($p = 0{,}01$). Les constatations préliminaires donnent à penser qu'une intervention psycho-éducative par téléphone à propos de l'incertitude est réalisable et permet de réduire la détresse des femmes dont les résultats sont non concluants.

Mots-clés : cancer du sein, BRCA 1/2, dépistage génétique, résultats non concluants, essai pilote d'une intervention

Introduction

Genetic testing is becoming increasingly more available for mutations of two genes, BRCA1 and BRCA2 (BRCA1/2), that place carriers at increased risk for breast and ovarian cancer. Members of families with a history of breast or ovarian cancer (i.e., affected individuals) who undergo testing for BRCA1/2 can receive four possible test results: (1) BRCA *positive:* carrying a pathogenic familial genetic mutation; (2) BRCA *negative/true negative:* not carrying a familial pathogenic mutation; (3) BRCA *variant of uncertain significance* (VUS): identified gene mutation with an unknown effect; or (4) BRCA *uninformative:* absence of known familial mutation despite striking but unexplained personal and/or family history of cancer (Culver et al., 2013; Leblond et al., 2011). Most individuals who are tested (75% or more) receive uninformative results (Culver et al., 2013; Schwartz et al., 2004). Current evidence suggests that individuals who receive such results exhibit distress levels similar to those of mutation carriers who test positive (van Dijk et al., 2006). Further, it appears that the distress among individuals who receive uninformative results does not follow the descending trend observed in the recipients of true-negative test results (Schwartz et al., 2002).

Lack of closure and relief after receiving uninformative BRCA1/2 test results has been observed in studies with this population (Ardern-Jones, Kenen, Lynch, Doherty, & Eeles, 2010; Dorval et al., 2005; Maheu & Thorne, 2008) and may explain partially the continued distress experienced by these individuals. The ambiguous nature of their true cancer risk in light of their uninformative BRCA1/2 result may further generate this distress (Maheu & Thorne, 2008). There are also the added cancer risk perception and personal and family cancer experiences that are closely correlated with emotional distress (Esplen et al., 2000; Leblond et al., 2011). In spite of these findings, studies tend to suggest that most individuals undergoing genetic testing for BRCA1/2 experience little clinical distress regardless of test result outcomes (Leblond et al., 2011; Meiser, 2005; O'Neill et al., 2009). However, we need more long-term studies on the psychological and behavioural impact of BCRA1/2 genetic test results (O'Neill et al., 2009; van Dijk et al., 2006; van Oostrom et al., 2003).

In a previous study (Maheu & Thorne, 2008), 17 of 21 women from families at high risk for breast cancer and with a previous breast cancer diagnosis (affected) interpreted their uninformative results as having a mutation that genetic testing missed, leaving them feeling distressed and in a state of limbo. Given the overexpressed cancer patterns in their families, these women were doubtful about the validity of their test results. This finding suggests the need for an intervention to reduce uncertainty

by providing support from health professionals so that women can more accurately interpret their uninformative genetic test results and experience less distress.

We designed an intervention based on Mishel's (1988) illness uncertainty theory, according to which uncertainty and distress are decreased if a frame of reference is provided, along with relevant information and organized and accessible support (Gil et al., 2006). Other means of reducing uncertainty include effective coping strategies and formal and informal social support, such as counselling by health professionals (Gil et al., 2006). Earlier research suggests that events in the cancer experience, such as testing for a gene mutation, may threaten personal perceptions of control and illness uncertainty (Stiegelis et al., 2004). Providing a psycho-educational telephone (PET) intervention, in addition to standard genetic counselling, has been found to reduce the distress and anxiety of mutation carriers in the short term (Graves et al., 2010). No such intervention has been tested with affected women who receive uninformative BRCA1/2 test results. This article reports on a pilot intervention aimed at reducing distress among women with a personal and family history of breast or ovarian cancer who received uninformative BRCA1/2 test results. As no psycho-educational intervention has been evaluated for women who receive ambiguous test results, we considered a feasibility and acceptability pilot study with this design to be the most appropriate approach before proceeding to a full clinical trial (Feeley et al., 2009). The primary aim of the study was to test the feasibility, acceptability, and preliminary effects of a standardized PET intervention for this group of women. The intervention was standardized through the development of a detailed manual created for this study. We hypothesized that our PET intervention would reduce distress in women receiving uninformative BRCA1/2 results. Our secondary aim was to identify predictors of distress among the women sampled in this study.

Methods

Study Design

The intervention and its evaluation took place in a hereditary cancer program (HCP) at North York General Hospital in Toronto, Canada. We used a single group with repeated measures whereby participants completed questionnaires at four time points: while waiting to receive the BRCA1/2 test results following their usual care genetic counselling session (T1), immediately after receiving uninformative results (T2), and at 3 months (T3) and 1 year (T4) post-intervention. All questionnaires, along with addressed, stamped return envelopes, were mailed to participants and completed by them at home.

Usual care at the HCP consists of initial genetic counselling for all individuals who qualify for BRCA1/2 testing, followed by a second counselling visit to discuss the results. The initial counselling includes general explanations of genetic inheritance and the implications of positive, negative, or uninformative results. In the study, the two-step PET intervention began following the receipt of T2 questionnaires, which were completed immediately after receipt of the BRCA1/2 results. In step 1, an information booklet and a relaxation compact disc (CD) were given to each woman at her second genetic counselling appointment, when she received her genetic test result. In step 2, 1 month after each woman received her result, telephone follow-up care was provided. The telephone follow-up care represented step 2 of the PET intervention and was delivered by one of the two genetic counsellors from the HCP, who also provided the usual genetic counselling care to the women enrolled in the study.

Study Population

Between 2007 and 2012, women scheduled to receive BRCA1/2 results were approached through the HCP. Those who met four inclusion criteria were given a package inviting them to enter the study: (1) a breast cancer (BC) diagnosis (affected women), (2) a significant family history of BC, (3) a scheduled appointment to receive their test result, and (4) ability to understand and read English. Excluded from the study were women who had an identified BRCA1/2 mutation in the family at the study's beginning or received notice of one during the course of the study. The final sample comprised 68 women.

Measures: Outcome Variables

The baseline questionnaire asked participants for basic demographic and lifestyle data (e.g., alcohol intake, smoking habits, and health/lifestyle behaviours, such as making changes to improve weight, diet, and exercise). Psychosocial functioning was assessed using measures of cancer-specific distress (T1–T4), genetic-testing distress (T2–T4), risk perception (T1–T4), and interpretation of uninformative results (T2–T4).

Feasibility and Acceptability

Participant retention, satisfaction with intervention (i.e., proportion who completed the PET intervention and who voiced satisfaction with the intervention), and completion of study measures were monitored as indicators of feasibility and acceptability of both the intervention and the study methods.

Cancer-Specific Distress

To assess our primary outcome of distress from undergoing genetic testing, the Impact of Event Scale (IES) was used (Horowitz, Wilner, & Alvarez, 1979). The IES has been extensively used to measure distress among women with BC (Appleton et al., 2004; Esplen et al., 2000), with good internal consistency for the total score and subscale scores (Cronbach's α = 0.91, 0.88, and 0.84 for the total scale, intrusion and avoidance, respectively) (Thewes, Meiser, & Hickie, 2001). The IES is a 15-item questionnaire rated on a four-point Likert scale (0, 1, 3, 5), with two subscales that measure intrusive thoughts (7 questions; score: 0–35) and avoidance of certain thoughts, feelings, or situations (8 questions; score: 0–40). The total IES score combines the two subscales, for a possible score of 0 to 75. Although no clinical cut-off has been validated, total scores over 27 indicate risk of post-traumatic stress disorder (PTSD) and scores over 35 a probable diagnosis of PTSD (Reed, 2007). Participants' IES total scores were obtained at T1 to T4. Cronbach's alpha for the IES score at T1 was 0.89.

Genetic-Testing Distress

To measure the impact of result disclosure after genetic testing, the Multidimensional Impact of Cancer Risk Assessment (MICRA) questionnaire was used. MICRA comprises 25 items that incorporate three subscales measuring distress associated with genetic test results (6 items), uncertainty associated with test results and future plans (9 items), and positive experiences with genetic testing (4 items). A total score is built from these three subscales, with two additional global items and four conditional items, to produce a score ranging from 0 to 125. Acceptable reliability of the total score and the three subscales has been reported in a sample of women with BRCA1/2 test results (Cronbach's α = .84 [Graves et al., 2010]) for total score, .87 for distress, .84 for uncertainty, and .82 for positive experience (Halbert et al., 2011). Unlike other standardized measures of psychological distress, MICRA was specifically developed to measure distress associated with disclosure of genetic test results (Cella et al., 2002). Consequently, MICRA was administered following result disclosure such as at T2, T3, and T4. Cronbach's alpha for the MICRA total score at T2 was 0.90.

Risk Perception

To examine risk perception, we asked each woman to estimate her personal risk of BC compared with women of a similar age, using a five-point Likert scale (1 = *much less likely*; 5 = *much more likely*) at T1 to T4. We also asked each woman to rate her perceived risk of carrying an

inherited mutation on an eight-point Likert scale (1 = *non-existent*; 8 = *very high*) at T1 to T4. Cronbach's alpha for the scale was calculated from the four time points as the scale has only one item. Cronbach's alpha was greater than 0.83.

Interpretation of Uninformative Results

We asked participants how they interpreted their uninformative results at T2 to T4 using the following four lay-interpretation options (Maheu & Thorne, 2008): (1) I am certain that **I have** an inherited mutation; (2) I am certain that **I have** an inherited mutation, **but** the current testing procedures could not detect it; (3) I think that **I may or may not have** an inherited mutation, but the current testing procedures could not detect it; and (4) I am certain that **I do not have** an inherited mutation. The third option represents the proper medical interpretation of uninformative results, in that they do not exclude the possibility of an inherited mutation. This interpretation produces uncertainty for recipients of test results (Leblond et al., 2011; Maheu & Thorne, 2008).

Psycho-educational Telephone Intervention

The two-step PET intervention provided cognitive and behavioural coping strategies to help women understand and manage complex genetic information stemming from uninformative test results. The intervention was begun after participants completed the T2 questionnaire.

Step 1 consisted of (1) a 33-page information booklet to address participants' need for knowledge about cancer genetics and to clarify information they received in their genetic counselling sessions, and (2) a relaxation CD to help them manage their anxiety. The booklet, modelled on Stiegelis et al.'s (2004) study, contained three levels of information. Level 1 consisted of facts about BC risk, genetic testing for BRCA1/2, and clarifying information to help women interpret their genetic test results. Level 2 comprised relaxation strategies and techniques based on cognitive-behavioural therapy, including guided imagery from the relaxation CD, calming self-talk phrases, and coping strategies drawn from an uncertainty self-management intervention (Gil et al., 2006). Level 3 contained stories, drawn from a previous study (Maheu & Thorne, 2008) co-led by the first author, about other women who received uninformative BRCA1/2 test results and had to make sense of them. According to uncertainty theory (Mishel, 1988), stories about others who went through a similar experience facilitates event congruency, thus reducing uncertainty. As with Stiegelis et al.'s (2004) study, only positive stories of receiving uninformative BRCA1/2 test results were included.

The level 2 information mirrored another uncertainty intervention study (Gil et al., 2006) by recommending the use of calming self-talk

phrases whenever uncertainty triggered negative thoughts; for example, "While I am scared, I can cope. I have a health care team who looks after me." Use of this coping strategy can decrease anxiety by reframing intrusive negative thoughts with more comforting thoughts. Use of the relaxation CD was also recommended for when uncertainty triggered negative thoughts. The booklet recommended that participants play the CD at least once a day for 21 days.

Step 2 consisted of a telephone follow-up care session lasting 5 to 15 minutes and taking place 1 month after the women received their uninformative test results. All the women were contacted by one of the two counsellors who provided usual care for the initial genetic counselling and issuing of results. The goal of step 2 was to answer any questions the women might have and to address any misinformation or confusion concerning their test results. According to illness uncertainty theory (Mishel, 1988), contact with a trusting, caring, credible authority can reduce overall uncertainty. Both of the genetic counsellors conducting the follow-up care session used a two-step guide: (1) review the woman's understanding of the test results, the booklet, and the relaxation CD; and (2) ask whether she used the CD and the coping strategies suggested in the booklet. Two weeks before the session, a research assistant contacted the women to remind them to review the booklet and practise some of the relaxation exercises and also to schedule the session.

Sample Size

To achieve 80% power to detect a same-group difference of 2.7, with a SD of 9, from pre- and post-intervention IES scores at alpha 0.05, we estimated a sample size of 68. This calculation was based on change in total IES observed in a previous randomized controlled trial (RCT) group intervention for women at high risk for BC (Lerman et al., 1996). However, we could have considered a smaller sample size, since the study on which we based our calculation was an RCT.

Analyses

Descriptive analyses were carried out, including distributions, means, and standard deviations on all demographic, lifestyle, and outcome data using the software SAS 9.3 and using 0.05 as the criterion for statistical significance. Using multivariate generalized estimating equation (GEE) modelling, data collected at T1, T2, T3, and T4 were analyzed for changes in distress levels between the different time points. Correlation analyses were also conducted, to assess relationships between potential predictors and distress measures.

Predictors of distress (IES) and impact of receiving test results (MICRA) were assessed using the multivariate regression models under

the GEE framework that can accommodate correlations among repeated participant measures. Potential predictors entered into the regression model were perceived BC risk, perceived inherited risk, age, education, employment status, and interpretation of test results. In our analysis, the missing data occurred at various time points. In order to assess the missing mechanism, we performed Little's (1988) MCAR test using R package "BaylorEdPsych." The test yields an insignificant p value of 0.5755, which indicates that the missing data occurred completely at random. As the missing proportion was above 5%, we performed multiple imputations to obtain multiple completed data sets using R package "mi" (Su, Gelman, Hill, & Yajima, 2011). We generated three imputed complete data sets and ran GEE on each data set and pooled the three sets of analyses into a single analysis using multiple imputation principles (Rubin, 1987).

Results

Intervention Acceptability and Feasibility

For the study, we approached 80 women, 75 of whom agreed to participate. Of these 75 women, 68 (91%) returned their T1 questionnaire. Three women tested positive and 72 received uninformative BRCA1/2 test results. Of the 72 who received uninformative results, 43 returned their T2 questionnaire. All 43 completed the intervention (received the booklet/CD and telephone follow-up), and 34 of those (79%) returned their T3 questionnaire. Finally, 33 of the 34 (97%) returned their T4 questionnaire. Overall, the retention rate at T2 was 60%; higher retention rates were observed at T3 and T4 (79%, or 34 out of 43, and 97%, or 33 out of 34, respectively).

Loss to follow-up was observed mainly at T2, when 40% of eligible women did not return their questionnaire package. The main reasons women gave for dropping out were not enough time to complete the questionnaire, feeling too ill, or changes in personal life. Overall, we recruited 75 women, meeting our sample-size requirement to obtain statistical power in this study. Dropouts occurred at different time points, leaving our sample smaller than the initial target of 68. However, even with the smaller sample, the study produced some significant results. This indicates that the actual effect size was larger than the speculated one in our preliminary sample calculation.

At the end of the telephone follow-up session, women who completed the intervention (i.e., booklet, relaxation CD, and telephone follow-up) were invited to comment on their overall acceptability of and satisfaction with the intervention, including use of the booklet and CD.

Of the 43 women who completed the intervention, 33 agreed to provide verbal feedback. Those who declined said they lacked time to extend the session beyond the telephone follow-up care review. Regarding the booklet, all 33 women had read it at least once and 10 had read it more than once. The women felt that the booklet's content was understandable and did not cover too much information but did cover their main areas of concern, such as how to interpret uninformative BRCA1/2 test results. Regarding coping skills such as calming self-talk and listening to the relaxation CD, although more than 80% of the women enjoyed learning and using the calming self-talk phrases to help them relax, they preferred the relaxation CD; however, they acknowledged that calming self-talk was more immediately accessible when they encountered anxiety triggers related to their state of uncertainty. While we recommended *daily* use of the relaxation CD, 80% of the 33 women said that they had used the relaxation CD at least once during the previous week and calming self-talk phrases at least three times during the previous week.

We asked the women to rate how much more relaxed they felt after using calming self-talk phrases and the relaxation CD on a scale from 0 to 10, with 0 being *not at all*. With the use of calming self-talk phrases, close to 73% of the women rated feeling more relaxed at 6 or above; with the use of the relaxation CD, close to 82% rated their increased relaxation at 7 or above. Overall, the women expressed gratitude for the additional opportunity to review their interpretation of the test results with a genetic counsellor via the telephone intervention.

Psychosocial Variables

We conducted independent sample *t* tests to compare participants who returned their questionnaire and those who did not at the four time points. The *t* tests did not reveal any differences in demographic characteristics or distress scores, as measured by total IES.

Changes in Psychosocial Variables

Over time, there were some significant decreases in distress following the intervention. Multivariate GEE modelling was conducted on the IES total (the study primary outcome) and the MICRA total score. Baseline scores for IES and MICRA were controlled in the GEE regression analysis. We found one significant effect between T2 and T3 (the intervention was administered after T2 and the first post-intervention measurement was taken at 3 months post-intervention, at T3) for IES total score (z value: -0.7094; $p = 0.01$), indicating a decrease in distress. Scores for IES were stable between T3 and T4 (12 months post-intervention), suggesting that any intervention effect was maintained (z value: -0.35; $p = 0.33$).

Mean IES total score for each time point measure were T1 = 24.08 (18); T2 = 21.74 (18); T3 = 16.39 (15); T4 = 19.25 (18). With the MICRA scale measuring impact of genetic testing, no significant differences were noted over time, including on the MICRA distress subscale.

From pre- to post-intervention (T1–T3), there was a statistically significant decrease in the percentage of women with a total IES score indicative of increased risk of PTSD ($p = 0.005$). Specifically, 38% fewer women had a score of 27 or higher (T1, $n = 25$; T3, $n = 6$). Of these, 53% fewer had a score of 35 or higher (T1, $n = 15$; T3, $n = 5$). This evidence of reduced distress is encouraging, considering that previous descriptive studies found that distress among women affected by cancer tended to remain elevated over time when left untreated (Carlson et al., 2004).

Personal Risk Estimates

Paired *t* tests were conducted on women's personal ratings of their risk of developing BC and carrying a gene mutation. There was a statistically significant decrease in mean perceived mutation-carrying risk between T1 and T2 ($p = 0.005$). This result suggests that women interpreted their uninformative results as not carrying an inherited breast and ovarian cancer gene mutation. However, no main effect over time was noted, which suggests that the intervention did not influence women's perceived risk of carrying a mutation. Following receipt of genetic test results, perceived risk of developing BC remained unchanged between T1 and T4.

Participants' Interpretations of Their Test Results

After receiving their test results (T2), most of the women (27 of 43) still felt ambiguous about their mutation-carrier status (options 2 and 3). Few (3 of 43) interpreted their results to mean that they were carriers (option 1), while the rest (13 of 43) felt that they were definitely not carriers (option 4). Between T2 and T4, the women's interpretations changed little. The proportion of women reporting each interpretation option is consistent with the results of previous studies (Cypowyj et al., 2009), except for option 4. In this study, a higher than average number of women interpreted their results as not carrying a pathogenic mutation with certainty.

One clinical concern with individuals interpreting uninformative BRCA1/2 test results as indicating certainty that they carry a pathogenic genetic mutation is that it could be associated with increased distress. However, we found that, although most women interpreted their results as ambiguous, there was no association between interpreting uninformative results as option 2 or option 3 and distress as measured by total IES score.

Predictors of Distress

Clinically, the ability to predict who is at risk for distress due to genetic testing is important in order to determine who may require additional emotional support and to offer timely interventions. We analyzed potential predictors of distress by examining IES total scores (distress associated with genetic testing). The scores were processed in a linear regression analysis with the following independent variables: baseline (T1) demographic and lifestyle data, perceived BC risk, perceived inherited-mutation risk, and interpretation of results. Significant Pearson correlations were observed and then multivariate GEE modelling was conducted on IES total scores. The result is described below.

Predictors of Distress Associated With Undergoing Genetic Testing (IES Total Score)

The main objective of our GEE analysis was to assess the efficacy of the intervention. The GEE result suggested significant decreases in distress at T3 (3 months after intervention completion) compared with T2 (immediately after receipt of uninformative results) (OR = 0.5678: $p = 0.0215$), with T1 (baseline) average IES scores having a significant effect on IES level at all time points (log OR = 0.3109; $p < 0.0182$). Through GEE, we found several other predictors of distress associated with undergoing genetic testing. As the subgroup analysis explores a large number of predictors, the multiplicity issue can inflate the overall familywise type I error rate. Multiplicity adjustment was therefore needed, and we performed Bonferroni's correction to control the familywise type I error rate. As there were 13 predictors in the model, we adjusted the p value threshold to $0.05/13 = 0.0038$. Other significant predictors of distress were not planning lifestyle changes to improve health (OR = 5.7221; $p = 0.0006$) and greater time lapse between genetic testing and cancer diagnostic (OR = 1.0650; $p = 0.0011$). Significant protective factors predicting lower levels of distress were having university education (OR = 0.2817; $p = 0.0014$), having higher income (OR = 0.6947, $p = 0.0001$), not employed (OR = 0.0692, $p < 0.0001$), and a trend towards lower perceived risk of developing BC (OR = 0.2271; $p < 0.0452$). These findings from subgroup analysis can be used to generate hypotheses for future validation.

Discussion

The results of our pilot study suggest that a psycho-educational telephone intervention informed by illness uncertainty theory is feasible and acceptable in clinical practice. The intervention may be beneficial for women with BC and a family history of the disease who receive

uninformative BRCA1/2 test results and who are experiencing related distress. Of the women who took part in the interview at the end of the study, all provided strong support for the utility of the intervention. Overall, our preliminary results point to a marked decrease in distress between receipt of test results and 3 months post-intervention, as well as a sustained decrease in distress at 12 months post-intervention. Although this decreased distress may reflect a decrease in cancer-related distress rather than distress associated with receiving genetic test results, previous studies have shown that, when left untreated, general cancer distress tends to remain elevated (Carlson et al., 2004). Hence, considering that the IES scale used in the study was anchored on distress associated with undergoing genetic testing for BRCA1/2, it may be that the intervention did decrease genetic testing distress.

In contrast to the IES scores, the MICRA total score did not indicate a decrease in impact of genetic testing disclosure post-intervention. This may reflect a limitation of the scale, having only five items of distress to measure a multifactorial situation. For future studies, we recommend the use of a recently published validated tool, the Genetic Psychosocial Risk Instrument Scale (GPRS) (Esplen et al., 2013), which specifically measures genetic distress from a multifactorial angle. The GPRS also has the advantage of being able to screen for psychological risk before individuals receive their genetic test results, allowing for preventive action. This tool also contains a clinical cut-off score, while the MICRA scale does not.

Our results suggest that distress did not increase among participants between T1 (pre-testing) and T2 (following receipt of test results); therefore, uninformative results did not increase the women's distress. However, we did not find the substantial decrease in distress reported in previous studies among individuals who receive certain-negative results (Bish et al., 2002; van Dijk et al., 2006). Moreover, the psychological reactions of the participants receiving uninformative test results more closely resembled the reported reactions of those who receive positive results indicating the presence of a gene mutation.

The predictors of distress identified in this study are similar to those reported by other studies. Not uncommonly, distress decreased over time, and, consistent with the findings of previous studies, baseline (T1) distress predicted post-genetic-testing (T2) distress (den Heijer et al., 2013). Women who waited longer after their cancer diagnosis to obtain genetic testing and who were not exercising (Dorval et al., 2008) tended to experience more distress, while higher education, higher income, not being employed, and low perceived risk of developing BC seemed to provide a protective shield against high levels of distress.

Women who receive uninformative BRCA1/2 genetic test results remain a vulnerable and understudied group (Ardern-Jones et al., 2010).

The unresolved uncertainty about their BC risk and mutation-carrier status can impair their quality of life (Dorval et al., 2005). Similar to other researchers investigating the impact of uninformative results (Bish et al., 2002), we found that few women believed, after receiving uninformative results, that they were highly likely to carry an inherited BRCA1/2 mutation. Although most still interpreted their results as ambiguous, we conclude that, for the majority of participants, their perceived mutation risk and test-result interpretation did not result in increased distress. However, a small subset of women interpreted their results as indicating certainty of carrying an inherited mutation, and this interpretation predicted mutation-related distress.

Telephone support in clinical contexts such as the one tested in this study is not new. Studies demonstrating the efficacy of telephone support report that participants view this approach as more "normal" than returning to the hospital to receive in-person support and thus are more satisfied with telephone support (Beaver et al., 2009; Beaver et al., 2011). In our study, the telephone intervention was delivered by the genetic counsellors who had counselled the women before their BRCA1/2 testing. The genetic counsellors were guided by a fully developed and manualized intervention collaboratively designed by the interdisciplinary research team — a strength of the study. All participants reached by telephone expressed satisfaction with their care and relief at having some closure. The intervention manual can be used as a guide for other trained health-care providers in genetics, such as genetic nurses working in hereditary cancer centres, in using the PET intervention with their population.

Limitations

Although the results of this preliminary study demonstrate that the PET intervention has the potential to reduce distress, the study has some limitations that need to be taken into consideration. Because of the absence of a randomized-control design, combined with the absence of a control group, the possibility of reduced distress over time without the intervention cannot be ruled out. However, the findings of previous studies show that post-genetic-test distress is unlikely to decrease without specific psychotherapy interventions (Graves et al., 2010). Thus, our findings provide some information on the changes that may have occurred among the women who received uninformative test results following the PET intervention.

Recommendations for Practice and Research

These results have direct implications for the care and quality of life of BC survivors who receive uninformative and ambiguous BRCA1/2

genetic test results. Targeted interventions for this group are greatly needed, considering the large proportion of individuals likely to receive uninformative results. Future research should investigate whether the telephone counselling alone, or the full intervention, produced significant changes in the variables measured in this study. In summary, this is an important study because of the subject matter and its essential preliminary design in obtaining important information that will allow for a subsequent RCT. A pilot study based on an RCT design could make an important contribution to the nursing literature. These small-scale pilot RCTs can reveal significant trends that can stir clinical debate and even shape clinical practice.

Conclusion

Preliminary evidence suggests that a psycho-educational telephone intervention, consisting of a psycho-educational information booklet, a relaxation CD, and a telephone follow-up care session, is clinically feasible and could minimize the potential negative psychological impact of receiving uninformative BRCA1/2 test results. Although a cause-and-effect relationship between the intervention and reduced distress could not be established in this pilot study, the results are promising and provide evidence of the need to evaluate the effectiveness of the intervention's components in an RCT format.

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Christine Maheu, RN, PhD, is Associate Professor, Ingram School of Nursing, McGill University, Montreal, Quebec, Canada, and Clinical Scientist Butterfield/Drew Fellow, ELLICSR: Health, Wellness and Cancer Survivorship Centre, University Health Network, University of Toronto, Ontario, Canada. Wendy S. Meschino, MD, FRCPC, is Chief of Genetics and Program Medical Director, Genetics Program, North York General Hospital, Toronto, and Assistant Professor, Department of Paediatrics, University of Toronto. Weiming Hu, MA, is a PhD student in the Department of Mathematics and Statistics, York University, Toronto. Joanne Honeyford, RN, BScN, is Genetic Nurse, Genetics Clinic, North York General Hospital. Ingrid Ambus, MSc, CCGC, is Genetic Counsellor, Genetics Clinic, North York General Hospital. Meredith Kidd, MS, CGC, CCGC, is Genetic Counsellor, Genetics Clinic, North York General Hospital.

Aronela Benea, RN, MScN, is Advanced Practice Nurse, ACTT at Women's College Hospital, Toronto. Xin Gao, MA, PhD, is Professor, Department of Mathematics and Statistics, York University. Madhis Azadbakhsh, MA, is a PhD candidate in the Department of Mathematics and Statistics, York University. Christian Rochefort, RN, PhD, is Assistant Professor, Ingram School of Nursing, McGill University, and FRQ-S Junior 1 Investigator. Mary Jane Esplen, RN, PhD, is Executive Director, de Souza Institute, Toronto, and Clinician-Scientist and Professor, Department of Psychiatry, University of Toronto/University Health Network.