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Title: Development and Testing of a Decision Aid for Unaffected Women with a BRCA1 or BRCA2 Mutation

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Abstract

For women who are unaffected carriers of a pathogenic BRCA mutation, cancer risk management requires ongoing education, counseling and support from an interdisciplinary team of medical specialists, genetic counselors and nurses specializing in genomics. The purpose of this study was to develop and pilot test an educational, patient focused decision aid to facilitate shared decision-making. A steering committee developed the prototype aid after an extensive review of the literature. The aid was designed at the ninth-grade reading level, to be consistent with internationally accepted clinical guidelines and inclusive of all risk management options and psychosocial issues important to cancer risk management decision making. The aid was tested with twenty-three participants: eight experts and fifteen end users. Eleven survey items were asked related to organization, clarity, usefulness, comprehensiveness, ease of understanding and relevance to the cancer risk management decision making process. Mean scores were 3 or higher on Likert scales of 1-4 (high) for each of the eleven items. Two open-ended questions elicited general comments, and suggestions for additions, deletions or revisions to the decision aid. The steering committee made final revisions to the aid based on participant feedback and committee consensus.

Keywords: BRCA1/2, genetics/genomics, hereditary breast and ovarian cancer syndrome, decision aid, educational material

Introduction/Background

Research in genomics continues to rapidly transform health care. Through the Healthy People 2020 initiative, the U.S. federal government calls for the translation of genomic recommendations into practice and the development of decision support resources [19]. Well-designed decision aids are needed in clinical settings and may improve the effectiveness and efficiency of preventive care for germline mutation carriers. Female carriers of a deleterious BRCA1 or BRCA2 mutation, whose care warrants specific interventions for risk management of hereditary breast and ovarian cancer syndrome (HBOC), are one such population. Average lifetime risks for women with a deleterious BRCA1/2 mutation range from 69-72% for breast cancer and 17-44% for ovarian cancer. Additionally, other cancer risks might also be present, such as risk for pancreatic cancer or melanoma. Age, familial factors and mutation location help to determine more precise individual risks [12]. In 2000, the patient advocacy and support organization Facing our Risk of Cancer Empowered (FORCE) coined the term *previvor* to depict the needs, concerns and difficult decisions faced by those at high risk for cancer, and to differentiate between them, the general population, and cancer survivors. The term has since gained increasing use by women with HBOC risk, healthcare providers and researchers [5]. Previvors often experience anxiety, fear, and a sense of urgency to make decisions to prevent cancer [7]. International guidelines provide evidence-based recommendations for cancer risk reduction and early detection. Choices include prophylactic surgeries, chemoprevention and intensive surveillance [14, 16]. Decision making requires a complex analysis of clinical factors and individual preferences that impact quality of life across the lifespan.

Optimal risk reduction is obtained with prophylactic surgeries done at specified ages, and a survival benefit occurs especially in the context of oophorectomy. According to the National Comprehensive Cancer Network (NCCN), prophylactic mastectomy reduces the risk for developing breast cancer by more than 90%; salpingo-oophorectomy reduces the risk of developing ovarian cancer by at least 80% and the risk of breast cancer by 50%. Chemoprevention (Tamoxifen or Raloxifene) reduces breast cancer risk by 50%; with evidence of greater efficacy in those with BRCA2 mutations. Oral contraceptives (OCs) reduce the risk for developing ovarian cancer in BRCA mutation carriers by 53% if taken for five years, with greater risk benefit associated with longer use [16]. Although intensive surveillance does not reduce cancer risk, there is a survival benefit to early detection. Screening reduces breast cancer mortality [25]; however, ovarian cancer screening methods are not effective for early detection or improving survival [6]. The complexity of decision making lies in analyzing cancer risk and survival along with the

consequences of risk management choices, such as surgical menopause, infertility, body image changes, and anxiety. Decisions necessitate a complex, personal analysis of issues and may change over time, thus a decision aid may be helpful.

Genetic counselors and breast and gynecologic oncology specialists are among the team members important to managing cancer risk while maximizing quality of life [23]. Providers and patients alike are challenged by limited resources to address decisional needs. Previvors seek guidance balancing cancer risk and survival with fertility, body image and sexuality, hormonal balance, and other health issues. Psychological distress is inherent in the decision-making process. Evidence indicates that fear and worry are related to risk perception, complexities of cancer risk management, and memories of close family members' cancer experiences [7, 23]. Previvors seek a holistic, comprehensive approach from an engaged, informed health care team sensitive to their individual needs [9]. They are empowered by knowledge and choice in the decision-making process [3].

Healthcare trends suggest a preference for shared decision making in groups such as previvors who face complex health-related decisions [1]. Patient decision aids facilitate shared decision making by engaging patients and clinicians in making choices that have the most beneficial outcomes and are based on individual patient preferences. Such aids supplement, not replace, clinicians' counseling and have shown to improve patients' knowledge and clarity about a health situation, improve the congruence of choices with personal values, normalize risk perception, and reduce decisional conflict [22]. Decision aids have been shown to increase knowledge and reduce decisional conflict in women making treatment decisions about breast cancer [17]; and in women making cancer risk management decisions related to HBOC [15, 20] .

The purpose of this study was to develop and pilot test an evidence-based patient-centered decision aid for previvors, consistent with internationally accepted guidelines; inclusive of all options for breast and ovarian cancer risk management related to HBOC, and psychosocial issues relevant to the decision-making process.

Methods

Decision Aid Development

The Ottawa Decision Support Framework [8] guided development of the decision aid based on International Patient Decision Aid Standards [10] and a method recommended by Coulter and colleagues [2]. The three-step process agreed upon by the steering committee is shown in Figure 1. Approvals were obtained from the Committee for the Protection of Human Participants in Research at Emmanuel College, the executive director of

FORCE, and the regional FORCE support group chairperson. Informed consent was obtained from all individual participants included in the study.

Step 1

The steering committee convened to determine the purpose, aims, target audience and scope of the project. The committee was composed of two PhD-prepared nurse researchers with expertise in instrument and decision aid development; two PhD-prepared advanced practice nurses with experience in adult oncology and genomics; and one master's-prepared oncology nurse executive (also a previvor).

Step 2

A comprehensive review of clinical guidelines, decision aids, and outcomes of cancer risk management choices for previvors in current literature was conducted using Medline and CINAHL databases. Varied limitations were found in decision support resources for previvors. International organizations provide evidence-based guidelines for HBOC syndrome management to help guide decision making [14]. These are geared toward clinical decision making and are written for health professionals' use. The (NCCN) (2018) guide for clinicians is perhaps the most frequently updated and is available free of charge to those who register on the NCCN website. The document is over eighty pages in length, written at a college graduate reading level according to Microsoft Word 2010® Flesch-Kincaid readability analysis, and requires specialized knowledge for interpretation. These complex guidelines are not amenable to general patient use. Healthcare professionals are challenged to interpret guidelines and provide patients with the education and support that leads to a full understanding of risk management choices.

Based on our literature review, decision aids available for patient use in the context of HBOC are limited with regard to the following: 1) Exclusion of one or more options available to previvors [11, 16] or addressing breast or ovarian cancer risk only [15, 24], resulting in a tool that is incomprehensive; 2) Inclusion of both affected and unaffected mutation carriers' issues and outcomes, making it difficult to differentiate these populations [20]; or 3) Exclusion of important psychosocial issues impacting the decisional process [18, 13].

In addition to the literature review, a previously conducted qualitative study by Jabaley and Mawn (2015), as well as professional and personal experiences of the steering committee, helped to inform the decisional needs of previvors from multiple perspectives. Four iterative designs of the format were developed, and content was reviewed and revised over a four-month period by the committee. Clinical probabilities and psychosocial aspects of the decision-making process were included, as well as a means for prioritization of issues and values clarification by the

end user. Content was analyzed and reinterpreted using the Microsoft Word 2010® Flesch-Kincaid readability analysis to reduce the reading level to 9th grade.

Step 3

A paper version of the prototype aid was used for testing. The first testing group consisted of three genetic counselors, one physician and four advanced practice nurses specializing in the genomics of breast and ovarian cancer. These clinicians were recruited from a large medical center in the Northeast and through referral sampling. The prototype aid and evaluation forms were sent and returned by email or regular postage-paid mail.

The second group consisted of a convenience sample of end users, fifteen previvors recruited from a regional meeting of Facing our Risk of Cancer Empowered (FORCE), a support group for those with HBOC syndrome. Eligibility criteria included being female, an unaffected BRCA mutation carrier by self-report, age eighteen or older, English speaking, and having completed informed consent. The primary investigator attended the FORCE meeting to answer questions and provide study forms to potential participants. Meeting attendees took study information packets and voluntarily returned them in sealed, postage-paid envelopes provided with each packet. A twenty-five-dollar stipend was given to each participant as compensation for time and effort.

Evaluation surveys developed by the steering committee for both groups included eleven Likert scale items to rate the decision aid for organization, clarity, usefulness, comprehensiveness, ease of understanding and relevance to the cancer risk management decision making process of previvors. Reviewers were invited to make suggestions for content and format revisions to the decision aid by answering two free form questions and/or writing on the decision aid itself. Data were analyzed and reported using descriptive statistics. Data obtained from open-ended questions were analyzed for repetitive thematic elements. The steering committee reviewed survey results and made final revisions to the decision aid.

Findings

End user participants in step 3 were all Caucasian, and all reported at least two years of college education. Seven reported a BRCA1 mutation, seven reported a BRCA2 mutation, and one reported mutations on both BRCA1 and 2. The median age was 45 years; with a range of 33-62 years. The median time since receiving a positive BRCA mutation testing result was 4.8 years, with a range of 1 month to 15 years. Four participants reported previously having prophylactic mastectomy and oophorectomy; five reported prophylactic mastectomy alone; one reported prophylactic oophorectomy alone; five reported surveillance alone and were undecided about prophylactic surgery.

Survey results are presented in Tables 1 and 2. Participants and experts alike expressed enthusiasm about using the decision aid; and many agreed that the aid was no more complex than the decision-making process itself. One expert thought that the numerical ratings entered into the tool by participants were confusing since there was no meaning to individual, summed scores. Most end users reported that the decision aid increased their knowledge and was useful in sharing information with family members. The final decision aid is available at https://www.brcadecisionaid.com/.

Discussion

Survey results from experts and end users suggest several strengths of the decision aid for use in the risk management decision making process of women who are unaffected BRCA mutation carriers. Survey results were generally high; the lower relevance ratings for the prophylactic oophorectomy and chemoprevention sections from end users might allude to participants' consideration of the option's relevance to them personally. In similar studies, participants have preferred bar graphs as opposed to other graphics such as faces, or individualized calculations, to present risk [4]. Similarly, participants in our study found the first section of the aid, which includes risk information displayed in graphs, easy to understand and highly relevant. Findings indicate a need for the decision aid in clinical practice to support shared decision making among patients and their care providers. Although we did not test the decision aid in the clinical setting, both patients and clinicians made statements indicating a desire to use the aid as a resource at the time of diagnosis.

The steering committee agreed upon a paper version of the aid, to be made available publicly online after pilot testing. Others have agreed that a paper decision aid is preferable due to its ease of use among patients and families in the clinical setting [4]. Several studies have used electronic formats for decision aids; however, these can be difficult to share in primary care settings and can be expensive to update [11, 22], Unlike other decision aids for previvors, the inclusion of all options for decision making and the differentiation of unaffected carriers from carriers who were cancer survivors was thought to be a strength of the aid. It was hoped that providing patients with the opportunity to reflect on and include their personal concerns and priorities would help previvors to better prepare for clinical visits and maximize their time with providers. Others have recognized the need to integrate care among physicians, genetic, and other genomics specialists [21]. This aid's instructions explicitly state that it is designed to promote a discussion between patients and clinicians. The steering committee envisioned that ideally the aid would be initiated by clinicians; however, designed with the possibility of being initiated by patients themselves.

The inclusion of patients with experiences from all decisional options was thought to be a strength of the sample, reflecting a variety of patient perspectives. All end users were members of an HBOC support group; thus it was expected that all participants had some degree of exposure to risk management prior to participation in the study. The timing and format of delivery for previvors at different ages and phases of life needs further evaluation. Several limitations of the study should be noted. The small, convenience sample was recruited from one support group in one region of the U.S. Demographic data revealed a homogeneous sample in terms of ethnicity, socioeconomic and educational status, and our findings cannot be generalized to more diverse populations. Although a 9th grade reading level was easy to understand by this sample, reading comprehension level could be reduced for other end users. A ceiling effect may have occurred due to the nature of the sample being self-selected women from a support group. Participants were all woman and included only those with BRCA 1 and 2 mutations; no other HBOC syndrome mutation carriers were sampled. The decision aid was developed for breast and ovarian cancer risk management only. We did not include discussion of risk for pancreatic cancer, as there are currently no evidence-based prevention or early detection measures. Neither did we include discussion of melanoma risk. Cancer risk management for men with HBOC differs regarding breast and ovarian cancer risk. The decision aid was designed for women; issues for men were not addressed. Feasibility testing was not conducted in a clinical setting due to resource limitations. Future studies should focus on evaluating the decision aid in clinical settings in randomized clinical trials to evaluate effects on patient knowledge, decisional conflict and anxiety.

A diverse group of stakeholders assessed the decision aid favorably and found it to be a useful addition for clinical practice. More research is needed to evaluate the efficacy of the aid and how to best implement it in clinical practice. The BRCA Decision Aid provides a means for facilitating patient-focused, interdisciplinary, holistic care for women who are previvors. The authors recognize the importance of being able to revise the decision aid as pertinent research findings emerge.

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Table 1 Survey Results

Survey Item	Experts (N=8)			End Users (N=15)		
	$\bar{X}$	**Mode**	**Frequency of Rating Good or Excellent**	$\bar{X}$	**Mode**	**Frequency Of Rating Good or Excellent**
Organization	4	4	100	3.53	3	100
Clarity	3.67	4	100	3.47	4	93
Usefulness	4	4	100	3.60	4	79
Comprehensiveness	4	4	100	3.73	4	100
Ease of Understanding	3.67	4	100	3.33	4	79
Relevance (By Section)						
General Information	4	4	100	3.47	4	93
1st Option: Intensive Surveillance	4	4	100	3.87	4	100
2nd Option: Prophylactic Mastectomy	4	4	100	3.80	4	100
3rd Option: Prophylactic Oophorectomy	4	4	100	3.60	4	93
4th Option: Chemoprevention	4	4	100	3.27	4	79
Resources	4	4	100	3.47	4	93

Possible Range:1-4 (high) for organization, clarity, usefulness, comprehensiveness, ease of understanding; and relevance of each section of the decision aid

Table 2 Repeating Thematic Elements with Supporting Comments from Open-ended Responses

An Exigent Need for the Decision Aid
Supporting Comments from Experts: "This is definitely something I could use in my practice." *Advanced Practice Nurse* "Please send me the final version to use in the clinic; we have nothing." *Genetic Counselor* Supporting Comments from End Users: "It's about time we had something like this for patients and families." “I learned so much from reviewing this. Can I take it home with me? I need it for my husband and daughter.”
The Importance of a Patient-focused Decision Aid
Supporting Comment from Experts: “I like the idea of the patient being in control.” *Advanced Practice Nurse* Supporting Comment from End Users: “I would choose many 3s [indicating very important] because it’s all very important and relevant to me.”
The Importance of a Comprehensive Decision Aid
Supporting Comment from Experts: “It’s overwhelming to try to convey all of this to patients. This would be a great resource.” *Genetic Counselor* Supporting Comments from End Users: “This [chemoprevention section] is often left out in discussions with medical professionals.” “This is the first information about this option [chemoprevention section] that I have ever received.”
Data from survey free form response item: Please make suggestions for additions, deletions or revisions to the BRCA Decision Aid in the space below. Feel free to write comments on the Decision Aid itself and return it with this survey

Fig 1 Development Process for the Decision Aid