Development of a family-based intervention for BRCA carriers and their close biological relatives: Focus groups, feasibility, and usability testing

Short Title: Family Gene Toolkit©

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Abstract

Background: Carriers of BRCA mutations are asked to communicate genetic test results to their close biological relatives and advocate for genetic services. This process is highly variable from family to family. Interventions that support communication of genetic test results, coping, and offer decision support in families that harbor a pathogenic variant may contribute to more effective management of hereditary cancer.

Objective: This paper describes the development of the Family Gene Toolkit©, a web-based intervention targeting BRCA carriers and untested biological relatives, designed to enhance coping, family communication, and decision-support.

Methods: We present findings from focus groups regarding intervention acceptability and participant satisfaction, and findings from a pre-post pilot study with random allocation to a wait listed control group regarding intervention feasibility and usability.

Results: The Family Gene Toolkit© was developed by a multidisciplinary team as a psycho-educational and skills-building intervention, including two live webinar sessions and a follow-up phone call guided by a certified genetic counselor and a Master’s prepared oncology nurse. Each live webinar includes two modules (total four modules) presenting information about BRCA mutations, a decision-aid for genetic testing, and two skills-building modules for effective coping and family communication. Participants in focus groups (n=11) were highly satisfied with the intervention, reporting it was useful and illustrative of pertinent issues. From the n=12 dyads recruited in the pre-post pilot study (response rate 23%), completion rate was 71% and 20% for the intervention and wait-listed control group, respectively.

Conclusions: Acceptability and satisfaction with the Family Gene Toolkit© is high. Based on usability and feasibility testing, modifications on timing, delivery mode, and recruitment methods are planned.
Keywords: BRCA families, family-based intervention, web-based, psycho-educational and skills-building intervention, communication and coping, decision-aid for genetic testing
Introduction

Women with germline mutations in the Breast Cancer 1 (BRCA1) and Breast Cancer 2 (BRCA2) genes (hereafter BRCA) have a 55%-70% chance of breast cancer and 17-59% chance of ovarian cancer by age 70, when the corresponding lifetime risks in the general population are 12% and 1.3% [1]. They also have an increased risk for early cancer onset, before screening recommendations apply, and for triple-negative tumors [2]. Germline BRCA mutations are inherited in an autosomal dominant manner with incomplete penetrance, following Knudson’s two hit hypothesis for cancer development. For every BRCA carrier, first-, second-, and third-degree relatives have 50%, 25%, and 12.5% risk, respectively, for inheriting the mutation [3]. The availability of genetic testing for BRCA mutations is a significant milestone for effective cancer control, since close biological relatives can be tested with almost 100% accuracy [4]. Genetic counseling and testing provide information about available risk management options (e.g., cancer screening at a younger age, etc.). Testing also confirms the non-inheritance of a well-characterized mutation preventing unnecessary early-onset screening in “true negative” relatives [5].

Underutilization of genetic testing among close biological relatives indicates that its potential benefits are not being effectively communicated [6-10]. Barriers to family communication include lack of understanding of genetic information, often hampering the ability of the family to cope with health threats associated with the pathogenic mutation [11]. Lack of communication skills and non-helpful coping (e.g., avoidance) inhibit disclosure of test results to relatives [12-14]. While helping family members learn more about their cancer risk is a leading motivation among women pursuing genetic testing [15, 16], positive
test results may also generate conflicts. Poor communication about the implications of increased cancer risks associated with the pathogenic mutation may leave family members unaware of the need for genetic counseling. Poorly informed decisions motivated by anxiety, fear, exaggerated perceptions of risk, together with lack of knowledge often lead to decisional conflict among close biological relatives [17-22]. Interventions supporting disclosure of genetic test results and enhancing helpful coping (e.g., information seeking) in mutation-harboring families could contribute to more open communication about cancer risks, informed decisions for genetic testing, and better management of hereditary breast and ovarian cancer (e.g., prophylactic mastectomy and/or salpingo-oophorectomy in mutation carriers).

Existing interventions targeted confirmed mutation carriers or women at risk for carrying a pathogenic mutation, and complemented the genetic counseling process by addressing primarily decision-making for genetic testing [23-38]. Other intervention outcomes include improving understanding of cancer genetics during counseling [37, 39-46]; enhancing carriers’ well-being after testing [23, 47-50]; and supporting them during disclosure of genetic test results [51-54]. Genetic information was delivered with an information booklet [29], a CD-ROM [25, 29, 38], a phone call [42, 48], a computer-based program [25, 27], and with peer-educators [54]. Modes of delivery included a one-day retreat to provide updated information [50], a short follow-up session [46], pre-counseling materials [34, 38, 43], virtual reality technology [44], and phone counseling for psychological support to carriers and their sisters [42, 48]. Outcomes included satisfaction with the intervention, knowledge improvement, intention to use genetic testing, and reducing emotional burden. Five interventions were designed to reduce emotional distress and enhance helpful coping with
consequences of positive test results [31, 32, 36, 47, 49], but results were inconsistent regarding coping with decisions related to risk management [32, 36]. Four interventions addressed communication of genetic results from carriers to relatives [51-53, 55]. A six-step skill building strategy [53] and a personalized communication toolkit for BRCA carriers [52] did not report significant effects on disclosing genetic test results or on use of genetic testing among relatives.

Although the above interventions achieved positive outcomes (e.g., communication of hereditary cancer risk), most targeted only mutation carriers and did not include close biological relatives. Communication of genetic test results in families is a two-way exchange that takes place between mutation carriers and relatives. It depends on understanding and processing of genetic information, communication skills, and coping competencies of all parties involved. Enhancing communication skills to explain genetic information should be most effective when combined with helpful coping for cancer risk (e.g., seeking expert advice) and decreasing decisional conflict for genetic testing in close biological relatives.

In short, BRCA mutations affect the whole family and genetic testing can cause tensions among family members [56, 57]. Few interventions address the complex communication and coping needs of BRCA families. To address this gap, the specific aims of this study were to develop a communication, coping, and decision-support intervention targeting BRCA carriers and close biological relatives (Family Gene Toolkit©); determine the acceptability of the intervention and participant satisfaction using focus groups; and examine usability and feasibility of the intervention in a pre-post pilot study.
Development of the Family Gene Toolkit©

The development of the Family Gene Toolkit© and selection of outcomes were based on the theory of stress and coping [58] adapted to reflect the needs of BRCA families. The model integrates bio-psychological family adaptation in genetic illness [59]; consequences of genetic testing from a stress and coping perspective [60]; and decision-making and decision support for genetic testing associated with hereditary breast and ovarian cancer [61]. Stress occurs when primary appraisals of a health problem threaten a person’s psychological and physical well-being. Secondary appraisals regarding risks and benefits associated with the health problem and the availability of coping resources can either exacerbate stress or mitigate it. For example, perceived lack of family support regarding genetic testing may increase stress after a pathogenic variant has been identified, while self-efficacy in managing cancer risks may reduce stress. The theoretical framework guiding the study has been developed and evaluated with 168 families pursuing testing for hereditary breast and ovarian cancer ([11]. (Figure 1).
The Family Gene Toolkit© is a psycho-educational and skills-building intervention targeting BRCA families. It was developed by a multidisciplinary team, including three expert nurses in psychosocial oncology, communication, and executive cognitive function, one genetic
counselor, and one physician expert in BRCA mutations. The content was based on empirical findings from a descriptive study with 168 at-risk families [11, 62]; a meta-analysis of interventions targeting cancer patients and their family caregivers [63]; feedback from a psychologist, expert in decision-making for genetic testing, not involved in the development in the intervention; and feedback from two BRCA families (two female carriers and two female relatives). The intervention prototype targets family dyads consisting of a female mutation carrier and a female close biological relative.

The four modules of the Family Gene Toolkit cover the following topics (Figure 2).

- **Module 1: Breast Cancer and Genetics** provides background information about breast cancer development and the role of heredity (Module 1A). It explains the epidemiology and probabilities of the disease with and without a germline BRCA mutation, and other cancers associated with BRCA mutations in both genders. A module for **Ovarian Cancer and Genetics** (Module 1B) was developed for ovarian cancer patients.

- **Module 2: Genetic Counseling and Testing** provides decisional support for genetic testing to relatives, including a description of the counseling process, potential risks, benefits, limitations of genetic testing, and possible results. It incorporates formal elements of decision aids based on the International Patient Decision Aids Standards criteria [64] and patient testimonials about accepting or refusing testing.

- **Module 3: Coping with Cancer Risk** discusses common challenges faced by BRCA families, including an overview of different coping styles, the importance of active coping, and practical tips to facilitate active coping with different personal and family challenges. It is designed to enhance active coping and family support about hereditary cancer risk and includes narratives from mutation carriers to support these points.
• *Module 4: Family Communication* presents testimonials about the responsibility to share test results, the importance of open family communication about the mutation, common issues that arise during this process, and practical ways to avoid conflicts. It provides five-steps training designed to enhance communication skills in family members.
The Family Gene Toolkit© is delivered over a period of four weeks by two expert clinicians (i.e., a certified genetic counselor and a Master's prepared oncology nurse) using two live webinars (PowerPoint presentations with live audio) and one brief follow-up phone call. Dyads log in to a password-protected website synchronously (same time on different...
computers) to attend the live webinars. The first webinar includes Module 1 and Module 2 and is facilitated by a certified genetic counselor. The second is offered a week later; it includes Module 3 and Module 4 and is facilitated by a Master’s prepared oncology nurse. Each webinar lasts 60 minutes (45 minutes presentation and 15 minutes for questions and answers). Each participant also receives a 15-minute phone call with the genetic counselor and the nurse to address individual concerns (Figure 3).

**Figure 3. Procedures of the Family Gene Toolkit©**

<table>
<thead>
<tr>
<th>Informed Consent</th>
<th>Week 1 T₀</th>
<th>Week 2</th>
<th>Week 3</th>
<th>Week 4</th>
<th>Week 5 T₁</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mutation Carrier</td>
<td>Baseline Survey</td>
<td>Joined Session 1 Webinar Module 1 &amp; Module 2</td>
<td>Joined Session 2 Webinar Module 3 &amp; Module 4</td>
<td>Session 3 Phone call</td>
<td>Follow-up Survey</td>
</tr>
<tr>
<td>Relative</td>
<td>Baseline Survey</td>
<td>Joined Session 1 Webinar Module 1 &amp; Module 2</td>
<td>Joined Session 2 Webinar Module 3 &amp; Module 4</td>
<td>Session 3 Phone call</td>
<td>Follow-up Survey</td>
</tr>
</tbody>
</table>

- Mail self-administered survey
- Email Log In and Webinar Tip Sheet
- Email Log In and Webinar Tip Sheet
- Mail self-administered survey
Focus group study: Assessing acceptability and participant satisfaction

Methods

The Institutional Review Board (IRB) of a university-affiliated Comprehensive Cancer Center approved the study. A purposeful sample of 25 BRCA carriers from a genetic risk clinic were asked to participate in the focus groups. Three focus groups were conducted (N=11; 10 mutation carriers and 1 niece) to determine the acceptability of the Family Gene Toolkit© and patient satisfaction. Focus groups included women who were older than 18 years; were identified as BRCA mutation carriers OR were female relatives (first- or second-degree, or first cousin) who did not have genetic testing. All participants were Caucasian and between 32 – 60 years old (mean age 46±12); most were married/partnered (n=8), college educated (n=9), with annual family income greater than $80,000 (n=6).

Focus groups were shown a prototype of the Family Gene Toolkit© as a PowerPoint presentation by a certified genetic counselor (Module 1 and Module 2) and a Master’s prepared oncology nurse (Module 3 and Module 4) in a two-hour, face-to-face session. Discussions were audiotaped and transcribed verbatim. Transcripts were analyzed for commonalities in participants’ responses and verified in team meetings. A 6-item survey assessed intervention acceptability: ease of use, clarity, appropriate length, level of detail, relevance, interest, and satisfaction on a Likert-scale (1=Low to 7=High) [65, 66]. Participants were asked to rate their overall satisfaction with the content, the extent it could help with communication and decision-making, and the format and appearance of the program. Suggestions for improvement were discussed at the end.
Results

All 11 participants rated their level of comfort and skills using computers as very high (1=Low to 7=High, 6.7±0.48 and 6.1±0.32, respectively) and their level of comfort and skills using the internet as very high (1=Low to 7=High, 6.6±0.52, 6.1±0.57, respectively). Participants were highly satisfied with the Family Gene Toolkit© (6.80±0.42); pleased (6.88±0.35); and contented (6.63±0.52). The content in each module was rated highly on importance and usefulness and was not confusing or uncomfortable. Participants also reported high satisfaction with the communication training module and the decision-aid for genetic testing. (Table 1). Participants valued the narratives and testimonials used to illustrate relevant content, and reported that the intervention could reduce a current gap in healthcare delivery, was useful, and relevant. Satisfaction with the appearance and length of the modules was high. They suggested including more information about testing children, how to support relatives who test negative and husbands, and management of cancer risk. They preferred live webinars involving contact with an expert to a website, as a more effective educational tool. However, they pointed that scheduling could interfere with the success of this approach. When asked about the best time frame to intervene (e.g., immediately after the diagnosis), some participants indicated they would prefer the program immediately after they were identified as BRCA carriers; others thought this would be an added burden. Consensus on timing was not reached. (Table 2). Information from the focus groups and the content experts was incorporated in the prototype of the intervention.
Table 1. Satisfaction with the Family Genetic Toolkit© - Focus Groups Short Survey
(n = 11 participants: 10 Mutation Carriers; 1 female relative)

<table>
<thead>
<tr>
<th>Category</th>
<th>Survey - Satisfaction with Family Gene Toolkit</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Item</td>
<td>n</td>
</tr>
<tr>
<td></td>
<td>Frequency</td>
<td>N</td>
</tr>
<tr>
<td>Overall Satisfaction</td>
<td>How do you feel about your overall experience with this program;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dissatisfied - Satisfied</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Displeased - Pleased</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Frustrated - Contented</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Important</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>The information I received in the program was important to me</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Content</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>The information I received in the program was confusing</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>I thought that the program was easy to understand</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>The program was too complex</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Uncomfortable</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>The information in the program made me feel uncomfortable</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Helpful for Family Communication</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>The program made me think about ways to help my family</td>
<td>0</td>
</tr>
</tbody>
</table>
The program helped me learn how to communicate with my family about cancer

<table>
<thead>
<tr>
<th>Theme</th>
<th>Interview Questions</th>
<th>Excerpts from Focus Group Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Satisfaction</td>
<td>Overall, what do you think about the information covered?</td>
<td>“…those quotes, those actual experiences, were so eye-opening for me. I was like, wow!” [quote related to everybody will see me as the bearer of bad news. …]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>“…depends on [the] audience. Researchers want everything. But some people don’t want in detail. Tell me what I have to know.”</td>
</tr>
<tr>
<td>Content</td>
<td>What did you like or dislike the most?</td>
<td>“That is a little shallow…. Maybe that is an issue in some families, though. It wouldn’t be in mine…. I have a hard time [believing that] anybody would ever think those things. Who would think someone’s going to blame me? Just, in my situation, I just can’t see these families saying this.”</td>
</tr>
<tr>
<td></td>
<td>What did you value the most from the content we covered?</td>
<td>“… finding this info is very freeing. … just knowing that there was a genetic reason why my cancer occurred, was very freeing for me. Certainly quelled the anger factor a bit. And it helps to explain my father’s death, my grandmother’s death, and this long history of early deaths in that side of the family.”</td>
</tr>
<tr>
<td></td>
<td>Do you think the intervention is useful and relevant to the care you received?</td>
<td>“… the coping module was extremely significant. …. I’ve been on the cancer world for a very long time. That was the first time I’d seen that information presented that way. … it was extremely helpful and one of the best I’ve seen…”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>“…this is the information that you want your family members to have…”</td>
</tr>
<tr>
<td></td>
<td>We used the term “damaged gene.” Was this confusing?</td>
<td>“I liked it because “mutation” sounds different, it sounds painful, there’s something wrong with you.”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>“Damaged” makes it less dangerous sounding. Like, you can deal with it.”</td>
</tr>
</tbody>
</table>
|                                          |                                                                                     | “It depends on [the] slide. If the information is from [a

Table 2. Acceptability of the Family Genetic Toolkit© - Focus Groups Interview Questions
(n = 11 participants : 10 Mutation Carriers ; 1 Relative)

<table>
<thead>
<tr>
<th>Theme</th>
<th>Interview Questions</th>
<th>Excerpts from Focus Group Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Helpful for Decision Making for Genetic Testing</td>
<td>The program helped me learn how to communicate with my family about cancer</td>
<td>0 0 1 0 6.4±0.70</td>
</tr>
<tr>
<td></td>
<td>The program made me feel more satisfied with my decision OR</td>
<td>0 1 1 6.5±1.08</td>
</tr>
<tr>
<td></td>
<td>The program helped me make up my mind about genetic testing</td>
<td>0 1 1 0 6.5±1.08</td>
</tr>
<tr>
<td>Helpful for Family Communication</td>
<td>What did you think about the communication module?</td>
<td></td>
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<tr>
<td>----------------------------------</td>
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<tr>
<td></td>
<td>“...what different scenarios can develop when you’re talking with family...it’s important to give the information and not tell them, or expect them to tell you, how they’re going to use it. You can’t control how your family member is going to use the information. That’s their decision.”</td>
<td></td>
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<tr>
<td></td>
<td>“I like how you say that there’s a duty [to share genetic test results]. It’s a responsibility, regardless how it’s fallen on your lap.”</td>
<td></td>
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<tr>
<td></td>
<td>“I really loved the slide that said that they [relatives] also have a responsibility, that it’s not all on you. ...There is cohesiveness because of it. ... when the whole family knows, they can support each other, and you address it, but it’s even bigger than that. ...you’re facing something severe and dangerous. It’s nice to know you have some control and some power....”</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Helpful for Decision Making for Genetic Testing</th>
<th>Regarding the pros and cons of genetic testing, do you think we covered most of them or at least the main ones?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>“...it pretty much tracks my decision-making process. Certainly weighed most of the pros and cons. ... These were pretty much the factors we weighed in our decision-making process.”</td>
</tr>
<tr>
<td></td>
<td>“I don’t know if the pros are strong enough. My sister was tested after myself and when she had her ovaries removed, they had cancerous changes. When my niece was tested, she had had childhood leukemia, and when she tested positive she decided to have her children younger. So the pros are kind of nice but maybe they could be more assertive.”</td>
</tr>
<tr>
<td></td>
<td>“I like this [decision making worksheet]. We can do our own. ... We can discuss how they [relatives] feel, how they rate those options.”</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Format (appearance, length)</th>
<th>If this program was offered in different formats, which ones would you prefer?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Internet: 6*</td>
</tr>
<tr>
<td></td>
<td>CD/DVD: 5</td>
</tr>
<tr>
<td></td>
<td>In-person: 2</td>
</tr>
<tr>
<td></td>
<td>Any format: 1</td>
</tr>
<tr>
<td>What did you thing of the presentation?</td>
<td>&quot;I liked the way they [slides] looked. Didn’t lose my attention.&quot;</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mode of Delivery</th>
<th>What you think is the best way to deliver this intervention? Do you think that a webinar and logging on at the same time is feasible, considering distance and time zones? Or would it better to record the webinar and the family members can view this information on their own time?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>“Probably that [recorded presentations]... Getting everyone together is always hard...if we could provide them [relatives] with links that they could go to online so that they could review information, and maybe educate themselves more and understand better, then they would go and take the steps to get tested.”</td>
</tr>
<tr>
<td></td>
<td>“My nieces are busy, they’re doing this and that, but if I... say “look, take a few minutes, you can go online, you can look at it, and get additional information, it’s all in one place, and you could do it during your own time” they might be more apt to do it.”</td>
</tr>
</tbody>
</table>
“I like the idea of a live person. [It is] not effective alone, [it is a] better impression.”

<table>
<thead>
<tr>
<th>Missing Information</th>
<th>Is there additional information we need to address?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>“[Explaining probabilities and risk] was very important ... in my decision-making process. How pathogenic is pathogenic? Am I closer to inconclusive? Or, am I high on the “this is a bad thing to have” scale.... Another graphic for women with mutation.”</td>
</tr>
<tr>
<td></td>
<td>“…one slide talking to my children. When should [we] tell them, …when should [we have] them get tested?”</td>
</tr>
<tr>
<td></td>
<td>“…it would be really neat in the coping module to speak to the unique challenges faced by spouses, and/or parents. Certainly, my cancer was much more difficult emotionally for my husband and my mom.”</td>
</tr>
<tr>
<td></td>
<td>“Certainly, for males – our fathers, husbands, and sons – they feel it’s a woman’s world. ... Maybe in some pictures you can incorporate some men so that ... they have [the] sense that they belong, it’s not just women talking to women.”</td>
</tr>
<tr>
<td></td>
<td>“…about open communication, make the pictures more general, include more men. This is really hard on husbands....on marriages. Any kind of feminine cancer takes a toll on a marriage.”</td>
</tr>
<tr>
<td></td>
<td>“… there is nothing, if tested negative, what is next?”</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Timing of Intervention</th>
<th>When is the best time to deliver this information?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>“I guess it depends. For me I wasn’t going through cancer treatment. I would say like a week later.”</td>
</tr>
<tr>
<td></td>
<td>“The way I’m wired, I would’ve said Yes, sign me up, right away.”</td>
</tr>
<tr>
<td></td>
<td>“I would’ve waited. ... I was going through a lot of different things. I would’ve been like Oh, I’ve got too much right now.”</td>
</tr>
<tr>
<td></td>
<td>“...maybe a month or two, after my major treatment was over.”</td>
</tr>
</tbody>
</table>

* Multiple responses possible

**Pre-post pilot study: Assessing usability and feasibility**

**Methods**

A pre-post pilot study with random allocation to a wait-listed control group was planned to assess usability and feasibility of the updated Family Gene Toolkit© delivered in a Webinar.
A different certified genetic counselor and a different Master’s prepared oncology nurse were trained to deliver the intervention. Webinars (PowerPoint presentations with live audio) and phone calls were recorded to assess protocol fidelity. The study was approved by all involved IRBs. The following sources were used to identify BRCA carriers over a period of 18 months: a cancer genetic risk evaluation program from a university-affiliated Comprehensive Cancer Center; the online Clinical Trial Registration Unit of the same center; a cancer genetic clinic affiliated with a tertiary hospital; a local online cancer support group; and another study assessing use of cancer genetic services in women with early-onset breast cancer [67]. Similar criteria applied for eligible mutation carriers and relatives: older than 18 years; identified as BRCA mutation carriers; OR female relatives (first- or second-degree, or first cousin) who did not have genetic testing; carriers willing to invite one female relative; could read and write in English, and provide consent. Mutation carriers who self-referred to the study via online support groups were screened by a trained project manager, and were asked to submit a copy of their test results or sign a release form, so that eligibility could be ascertained with the testing company.

**Figure 4: Pre-post pilot study design**

<table>
<thead>
<tr>
<th>Informed Consent</th>
<th>Week 1 (T₀)</th>
<th>Week 2 (T₁)</th>
<th>Week 3</th>
<th>Week 4</th>
<th>Week 5 (T₂)</th>
<th>Week 6</th>
<th>Week 7</th>
<th>Week 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family Gene Toolkit© Mutation Carrier</td>
<td>Baseline Survey</td>
<td>Session 1 Webinar</td>
<td>Session 2 Webinar</td>
<td>Session 3 Webinar</td>
<td>Session 3 Phone call</td>
<td>Follow-up Survey</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family Gene Toolkit© Relative</td>
<td>Baseline Survey</td>
<td></td>
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<td>Wait-listed Control Mutation</td>
<td>Baseline Survey</td>
<td>Follow-up Survey</td>
<td></td>
<td>Session 1 Webinar</td>
<td>Session 2 Webinar</td>
<td>Session 3 Phone call</td>
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Mutation carriers were sent an invitation letter from the Medical Director of the respective clinic and an informed consent form. Upon receiving the signed consent, a genetic counselor identified eligible relatives by contacting the carrier and obtaining her family history. Carriers received a letter explaining they could invite the relative of their choice among those included in the list. Once both members of the dyad (i.e., mutation carrier and relative) returned a signed consent, they were each mailed a paper and pencil baseline survey. Upon receipt of the completed survey, the webinars and the 15-minute phone calls were scheduled. The dyad was emailed a link to the webinar, along with information on how to log in to the website. One week after completing the webinars and the phone call, participants received the follow-up survey. Dyads randomly assigned to the wait-listed control group received the baseline and follow-up surveys four weeks apart.

Validated instruments assessed family communication, [68] knowledge of breast cancer risk factors [69] and breast cancer genetics [62], perceived breast cancer risk [70], fear of cancer recurrence [71, 72], decisional conflict [73], coping [74], self-efficacy [75] and intention for genetic testing [76, 77]. Access to genetic services was assessed with multiple response questions regarding a provider recommendation, “my doctor said I don’t need it”; availability of services, “clinics are too far away”; accessibility of services, “lack of transportation”; and acceptability of services, “I would rather not know if I have a mutation connected to cancer.”
Results

Over 18 months, 82 potentially eligible mutation carriers were identified for the pre-post pilot study. In approximately 35% of cases phone numbers were available; in these cases invitation letters were followed by a phone call three to four weeks later. Most mutation carriers were ineligible to participate either because all relatives had been tested, or because eligible relative refused participation. Signed consent forms were returned from 12 mutation carriers (response rate 23%) and 12 relatives (12 dyads; n=24), who were randomized either to the Family Gene Toolkit© (n=7 dyads) or to the wait-listed control (n=5 dyads). Since the research team did not have direct contact with relatives but only after they signed a consent form, reasons for relative non-participation are not known.

A completed baseline survey was returned from 10 dyads (n=20) at baseline. Of these 10 dyads, only first-degree relatives accepted participation (eight sisters; one daughter; one mother). All participants were Caucasian, between 18 - 62 years old (mean 41±13); most were college educated (n=16), worked full time (n=14), married/partnered (n=11), with family annual income greater than $80,000 (n=10). From the 10 BRCA carriers (mean years since genetic testing 4.4±3.2), four were diagnosed with invasive breast cancer; three with ductal carcinoma in situ (DCIS); one with ovarian cancer; two with other forms of cancer. Carriers were older than relatives (49±7 vs. 34±13, t=2.871, p=.010). A completed follow-up survey was returned from five dyads in the intervention group and from one dyad and two mutation carriers in the wait-listed control group. Completion rate was 71% and 20% for the
intervention and the control group, respectively. (Figure 5). Known reasons for participant withdrawal was scheduling conflicts (n=3 relatives) and pursuing genetic testing while in the intervention (n=1 relative).

Figure 5. Consort diagram for mutation carrier and relative recruitment and random assignment to Family Gene Toolkit© vs. Wait-listed control group

82 mutation carriers identified from all recruitment sites

Ineligible (n=30):
- Relatives have been tested (n=15)
- Relatives refused participation (n=10)
- Other (not BRCA) mutation (n=5)

No Response (n=40)

12 dyads consented (12 carriers and 12 relatives) (Response rate = 23%)

Randomization

Family Gene Toolkit© (n=7 dyads)
- Complete Baseline Survey (n=6 dyads & n=1 mutation carrier)
- Complete Follow-up Survey (n=5 dyads)

Wait-Listed Control (n=5 dyads)
- Complete Baseline Survey (n=4 dyads)
- Complete Follow-up Survey (n=1 dyad & n=2 mutation carriers)
Due to the small sample size, statistical evaluation of intervention effects was not undertaken. However, descriptive statistics were used to examine participants’ responses to the surveys. Facilitators of genetic testing listed by mutation carriers were a provider recommendation, acceptability of genetic services (e.g., “I wanted to know more about my future cancer risk”) (n=8), followed by accessibility of genetic services (e.g., “my medical insurance covered the cost of the test”) (n=4) and “the clinic was close to home”) (n=2).

Barriers for genetic testing listed by relatives were related to accessibility of genetic services (e.g., “I can’t get time off work”) (n=4), followed by acceptability of genetic testing (e.g., “I would rather not know if I have a mutation connected to cancer”) (n=3), and availability of genetic services (e.g., “clinics are too far away”) (n=1).

Discussion

This paper presents the development and pilot testing of a psycho-educational and skills-building intervention targeting BRCA families. The Family Gene Toolkit© is designed to provide comprehensive support to BRCA families for challenges faced by mutation carriers and untested relatives. It is a theory-based intervention that leverages the core factual knowledge of biology and medicine, the non-directionality of genetic counseling, and the expertise of nursing to foster coping with life-threatening diagnoses, and addressing the need for family cohesion in times of adversity. Participants provided valuable feedback for refining the Family Gene Toolkit©, which will be used in future testing. Assessment of acceptability, usability, and feasibility pointed to needed changes in intervention delivery. Acceptance of the intervention and high participant satisfaction suggests that the Family Gene Toolkit© appears to have the potential to meet the needs of these families. Sharing
information from the pre-post usability and feasibility testing assists in increasing scientific knowledge regarding intervention development and testing.

**Acceptability of the intervention: Participant satisfaction was high**

Focus groups valued the Family Gene Toolkit©. Participants were highly satisfied with the intervention and reported it was a needed service. They were highly satisfied with modules addressing coping and family communication, usefulness, and completeness of information. Satisfaction was high with module appearance, formatting, and the quotes used to illustrate pertinent content. The high levels of satisfaction suggest that BRCA families valued support for decision making, coping, and family communication, in addition to the support they receive from current healthcare services.

**Enhancing usability: The intervention is needed when the BRCA mutation is identified**

Information from about 35% of mutation carriers indicated that “timing” of intervention influenced the usability of the Family Gene Toolkit©. Many mutation carriers were not eligible to participate because all their relatives had been tested. Of the relatives who participated in the pre-post pilot study, none had genetic testing even though the mutation was diagnosed on average 4.4 year ago in their family. Relatives reported that genetic testing was not their priority and they would rather not know if they have a cancer-predisposing mutation. Relatives who did not accept participation in the study could have possibly refused genetic counseling several times in the past, and perhaps were not open to an intervention for family communication, coping, and decision support. These observations suggest that the optimal time for delivering the Family Gene Toolkit© is likely shortly after a positive test result; thus, future sessions are planned between three to six months after the
BRCA mutation is identified. Moreover, prospective recruitment of newly diagnosed BRCA families will help identify more mutation carriers whose relatives had not been tested, and may increase acceptance among relatives who are more open to accept expert information.

**Enhancing feasibility: The intervention should be delivered as an asynchronous website**

Focus groups indicated that live webinars with certified specialists are more credible and reliable sources of information, and could provide tailored answers to family members. However, the live webinars have to accommodate participants’ schedules, a significant challenge due to differences in lifestyles and time zones, which in turn affected the feasibility of the intervention. Reconfiguring the Family Gene Toolkit© as an “asynchronous” website (i.e., participants log in on their own without a live presentation) will also address the issue of optimal timing for intervention delivery, because mutation carriers and relatives can access the intervention when they are ready to discuss about the mutation with their family. Reconfiguration of the delivery mode has to capture the high relevance of a “live” information-providing session along with ease of using the web. Two possible approaches for an asynchronous website are envisioned. A targeted version involves recordings of the two webinars and provides all participants with the same information. This approach can be efficacious for increasing knowledge of cancer genetics [78]. A tailor-made approach involves an interactive website, which provides information according to cancer diagnosis, relationship of relative to the mutation carrier, etc. This approach, while more costly to develop initially, has been found more efficacious with another family- and web-based intervention [79].
**Enhancing recruitment: Personal contact to mutation carriers and relatives**

Although we have successfully used the same recruitment method (patient recruiting relative) in our prior studies targeting women completing genetic testing and young breast cancer survivors [11, 15, 80], the usability and feasibility study indicated that recruitment of mutation carriers and relatives for a family-based intervention requires personal contact and follow-up phone calls. The pre-post pilot study indicated that personal contact with mutation carriers is necessary first, to assess their eligibility to participate in the Family Gene Toolkit© (i.e., confirmed BRCA mutation, not all relatives have been tested) and second, to prepare them how to broach family participation in an intervention study with their relative, and help minimize relative refusal rate. Enhanced collaboration with clinicians and clinical settings will also increase participation in a family-based intervention.

**Limitations**

The prototype of the Family Gene Toolkit© was tested with a homogeneous sample of Caucasian, middle to upper class women, recruited from a single genetic clinic and one mid-western state. Thus, its acceptability and patient satisfaction cannot be guaranteed with diverse and minority families and families from lower socioeconomic status.

**Conclusion**

Expanding genetic care created a need for easy access to this information. Advances in technology are followed by an exponential increase in web-based health interventions, under the assumption that they provide easy and convenient access to this specialized information [81, 82]. Communicating hereditary cancer risks at the familial and professional
level poses several challenges at the medical and social level, and requires inter-professional collaboration. The Family Gene Toolkit®, although is not the only intervention targeting BRCA families, leverages expertise of a multidisciplinary healthcare team. Engaging the expertise of a multidisciplinary team is increasingly recognized as a necessary condition to address the complex needs of BRCA families at the individual, societal, and health policy level, and in finding sustainable solutions that optimize healthcare delivery.
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Conflict of Interest

Author Katapodi, MC, Author Jung, M, Author Schafenacker, AM, Author Milliron, KJ, Author Mendelsohn-Victor, KE, Author Merajver, SD, and Author Northouse, LL declare that they have no conflict of interest. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5). Informed consent was obtained from all participants included in the study.

Abbreviations

*BRCA1*: breast cancer 1

*BRCA2*: breast cancer 2
Reference list


78. Katapodi MC. Preliminary findings from an efficacy state-wide trial aiming to increase use of cancer genetic services among families at increased risk for breast cancer. International Society of Nurses in Genomics (ISONG) World Congress; November 6-8 2015; Pittsburg, PA, USA2015.


