Contemporary Clinical Trials Communications 16 (2019) 100433

Contents lists available at ScienceDirect

Contemporary Clinical Trials Communications

journal homepage: www.elsevier.com/locate/conctc

Study protocol: Randomized controlled trial of web-based decision support tools for high-risk women and healthcare providers to increase breast cancer chemoprevention

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ARTICLE INFO

Keywords:
Breast cancer risk
Chemoprevention
Decision support

ABSTRACT

Background: Chemoprevention using selective estrogen receptor modulators and aromatase inhibitors has been shown to reduce invasive breast cancer incidence in high-risk women. Despite this evidence, few high-risk women who are eligible for chemoprevention utilize it as a risk-reducing strategy. Reasons for low uptake include inadequate knowledge about chemoprevention among patients and healthcare providers, concerns about side effects, time constraints during the clinical encounter, and competing comorbidities.

Methods/design: We describe the study design of a randomized controlled trial examining the effect of two web-based decision support tools on chemoprevention decision antecedents and quality, referral for specialized counseling, and chemoprevention uptake among women at an increased risk for breast cancer. The trial is being conducted at a large, urban medical center. A total of 300 patients and 50 healthcare providers will be recruited and randomized to standard educational materials alone or in combination with the decision support tools. Patient reported outcomes will be assessed at baseline, one and six months after randomization, and after their clinic visit with their healthcare provider.

Discussion: We are conducting this trial to provide evidence on how best to support personalized breast cancer risk assessment and informed and shared decision-making for chemoprevention. We propose to integrate the decision support tools into clinical workflow, which can potentially expand quality decision-making and chemoprevention uptake.

Trial registration: NCT03069742.

1. Introduction

Breast cancer imparts significant morbidity and mortality upon women in the United States, and the primary prevention of this disease would substantially improve public health. Several randomized controlled trials provide evidence that chemopreventive agents, such as selective estrogen receptor modulators (SERMs; tamoxifen and raloxifene) and aromatase inhibitors (AIs; exemestane and anastrozole) given for 5 years, reduce breast cancer incidence by up to 40–65% among high-risk women [1–3]. For this reason, the U.S. Preventive Services Task Force (USPSTF) and other professional organizations recommend that clinicians have discussions with women at increased breast cancer risk about chemoprevention [4–6]. Despite this evidence, uptake of chemoprevention remains low among eligible women in the

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https://doi.org/10.1016/j.conctc.2019.100433
Received 1 May 2019; Received in revised form 11 August 2019; Accepted 19 August 2019
Available online 22 August 2019

United States. An estimated 10 million women between the ages of 35 and 70 years are eligible for chemoprevention in the United States [7]; however, fewer than 5% of high-risk women who are offered a SERM decide to initiate the medication [8]. Barriers to adoption include concerns about side effects, insufficient knowledge about chemoprevention among patients and providers, and an inability to efficiently assess breast cancer risk in primary care.

Many women choose not to begin a chemoprevention regimen because they and their physicians do not perceive SERMs and AIs to offer a favorable risk-benefit profile [9–12]. Concerns about potential side effects—such as endometrial cancer, thromboembolic events, and menopausal symptoms—are the main barriers to patient uptake and physician prescription of SERMs [9–11,13–16]. Such considerations, however, are often more complicated than a simple pros-cons calculation: whereas the protective effect on breast cancer risk persists beyond 10 years after discontinuation, the side effects often diminish after stopping SERMs [17]. Unlike other primary prevention strategies, which often require chronic therapy throughout a patient's lifetime, 5 years of chemoprevention can significantly reduce lifetime breast cancer risk with negative effects limited to active treatment. Moreover, risk and benefit estimations can differ between women and the types of chemoprevention offered.

Such complexity requires effective strategies to identify high-risk women and inform them about the risks and benefits associated with chemoprevention. After the patient is adequately informed, a detailed patient-provider deliberation based upon the patient's personalized risk estimates and values can help ensure the patient is taking the course of action that is best for her. Both of these efforts often prove too difficult or time-consuming to undertake during a standard medical encounter. While communicating with a provider is among the most influential factors to impact SERM use [9,11,18], providers often lack the information and time they need to initiate such a conversation. Further, physicians who feel insufficiently knowledgeable about risk-reducing options are less than half as likely to prescribe a SERM than physicians who feel sufficiently trained [19]. Patient support alone is therefore insufficient in promoting chemoprevention uptake among eligible women; providers also need timely support and facilitation in administering these needed discussions.

Chemoprevention and other breast cancer risk-reducing strategies are also less likely to be utilized by women from racial/ethnic minorities, and uninsured women are less likely to seek breast cancer preventive care [20,21]. These differences can lead to increased health disparities as underutilization of breast cancer risk assessment, chemoprevention, and other risk-reducing strategies may contribute to higher rates of late-stage diagnosis among minority groups [22–24]. In a study of 1700 women from four racial/ethnic groups seen in mammography centers, recognition of any breast cancer prevention strategy (chemoprevention, genetic testing, or prophylactic surgery) among high-risk white women was 96% compared to 74% among Hispanic women [20]; discussion with a physician about risk-reducing strategies was particularly limited among non-English-speaking women [20].

In order to address these barriers, facilitate chemoprevention uptake, and expand risk assessment and risk-reducing options to diverse populations of high-risk women, this trial seeks to evaluate patient and provider decision support tools that are integrated into clinic workflow. We hypothesize that the tools will improve accuracy of breast cancer risk perceptions and other decision antecedents, improve decision quality, facilitate referrals for specialized risk management, and, ultimately, increase chemoprevention uptake. Given the demonstrated efficacy of breast cancer chemoprevention in high-risk populations, higher uptake may significantly reduce the public health burden of this disease [1–3].

2. Trial objectives

Our study objective is to assess the effect of standard educational materials combined with web-based decision support tools, *RealRisks* and *BNAV (Breast cancer risk NAVigation)*, for high-risk women and their healthcare providers, respectively, on chemoprevention uptake compared to standard educational materials alone. *RealRisks* is a patient-centered, web-based decision aid (DA) that calculates a woman's 5-year and lifetime risks for developing breast cancer according to the Gail model [25], determines her eligibility for chemoprevention and other breast cancer risk-reducing options, provides tailored education based upon her personalized risk profile, and elicits the patient's preferences and values surrounding breast cancer prevention decisions [26–28]. *BNAV* is a provider-centered decision support tool that delivers summaries of patient risk profiles and preferences along with educational resources in order to support provider decision-making surrounding breast cancer risk reduction [29,30]. Secondary study objectives include determining whether these tools improve decision antecedents (accuracy of breast cancer risk perceptions, chemoprevention knowledge, decision self-efficacy), decision quality (informed choice, decision conflict, shared decision-making), and appropriate referrals to a high-risk breast clinic.

3. Methods

3.1. Study design

Our study design (Fig. 1) is a randomized controlled trial (RCT), which aims to recruit 300 women, ages 35–75 years, with a 5-year invasive breast cancer risk ≥1.67% or lifetime risk ≥20% according to the Gail model [25] or a personal history of lobular carcinoma *in situ* (LCIS). Potential participants are initially screened to determine eligibility for chemoprevention and other study criteria. After confirmation of eligibility, interested participants go through an informed consent process in-person, via telephone, or online.

Following consent, participants are administered the baseline survey and then are randomized to the active or control arms. All enrolled patients are given standard educational materials either in-person, by mail, or by email. These standard educational materials

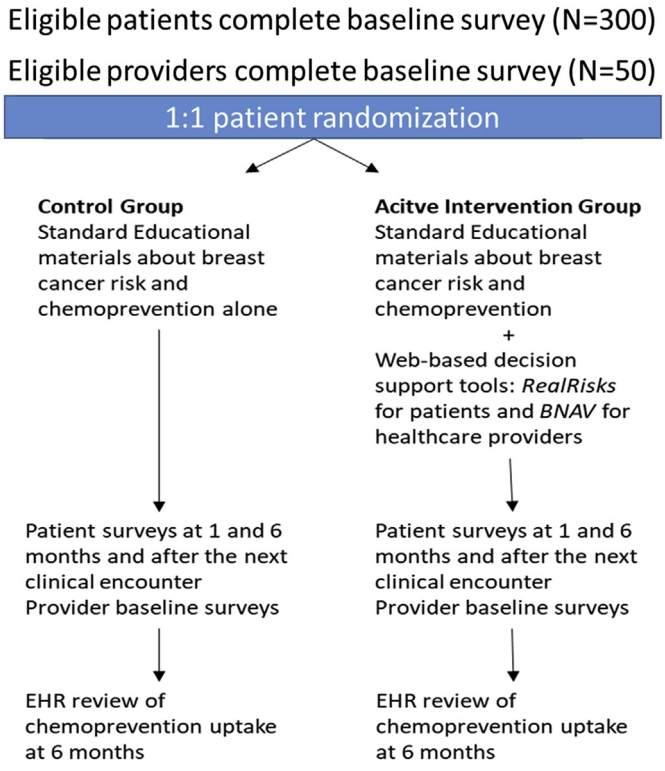

Fig. 1. Study schema.

include: 1) a brochure to the Columbia University Irving Medical Center (CUIMC) Breast Cancer Prevention Program; 2) a Susan G. Komen brochure about risk-reducing drugs for women at an increased risk of breast cancer (https://ww5.komen.org/uploadedFiles/_Komen/Content/About_Breast_Cancer/Tools_and_Resources/Fact_Sheets_and_Breast_Self_Awareness_Cards/Risk-Lowering%20Drugs%20for%20Women%20at%20Higher%20Risk%20of%20Breast%20Cancer.pdf); and 3) a personalized risk letter explaining that the participant is at increased risk for breast cancer and eligible to take pills to reduce breast cancer risk. Those randomized to the active intervention are then sent a link to the *RealRisks* website, and, once the patient completes the decision aid, their personalized risk report is sent to their healthcare provider at CUIMC via secure health messaging. Participants then complete surveys one month and six months after randomization and a fourth survey after the patient's next clinic appointment with her CUIMC healthcare provider.

After informed consent, 50 healthcare providers complete a one-time survey. If a provider's patient is in the intervention arm, he or she is instructed to access the educational content on the *BNAV* website, which is embedded within an Ambulatory Medicine dashboard in the electronic health record (EHR). Prior to an intervention patient's next appointment, her provider is also sent the personalized risk report by email and secure health message and is given access to the patient's personalized risk report in the *BNAV* tool. Treating providers are sent this alert regardless of whether or not they consented to complete the one-time survey. All providers are able to view the 5-year invasive breast cancer risk according to the Gail model for all enrolled patients through an embedded notice in the EHR as well as a link-out to the *BNAV* website.

3.2. Conceptual model

RealRisks incorporates two complementary approaches, shared decision-making (SDM) and self-determination theory (SDT), to engage women in planning a preference-sensitive course of action to make decisions about chemoprevention (Fig. 2). SDM differs from other models of medical decision-making in that it incorporates patient values and decision self-efficacy, which have an important influence on what is the "right" decision for that patient at that time, particularly in decisions with no clear clinical path [31–36]. Decision-making is "shared" in that the model is often applied to the patient-provider context (that is, power is shared between the provider and the patient). The clear provision of comprehensive information that is inclusive of personalized risk estimates and the explicit incorporation of clarification, expression, and integration of patient values and preferences is central to SDM [37]. In decisions about chemoprevention, these facets are essential.

SDT posits that people have a basic and universal need when making decisions: self-efficacy, which refers to an individual's own perceived ability to perform a specified behavior [38,39]. We expect that the decision aid, particularly the components that focus on communicating risk, eliciting patient preferences, and modeling a patient engaging in decision-making, will enhance self-efficacy for decision-making and engaging in an informed decision. As shown in Fig. 2, the secondary outcomes for the study are those most proximal to the decision aid including decision antecedents (*i.e.,* accurate risk perceptions) and decision quality (*i.e.,* informed choice). The model also shows that we will measure chemoprevention intent and uptake (primary endpoint).

3.3. Study setting

The catchment area of CUIMC encompasses the Washington Heights and Inwood neighborhoods of New York City. These neighborhoods are home to 350,000 people, 85% of whom are Hispanic or black [40]. Hispanics in our sample predominantly have Dominican and Caribbean backgrounds. We are targeting women seen in the Internal Medicine, Family Medicine, and Gynecology practices of the New York-Presbyterian Ambulatory Care Network (ACN), as well as those seen at the primary care, radiology and breast clinic practices of the Columbia Doctors network in Upper Manhattan.

3.4. Eligibility criteria

Patient eligibility criteria include: 1) women, age 35–75 years; 2) 5-year invasive breast cancer risk ≥1.67% or lifetime risk ≥20% according to the Gail Model (Breast Cancer Risk Assessment Tool) [25] or a personal history of LCIS; 3) No prior use of a SERM or AI; 4) No personal history of breast cancer; 5) No active cancer diagnosis; 6) Healthcare provider at CUIMC; 7) English- or Spanish-speaking; 8) Access to the internet; 9) Access to text messaging or email; and 10) Able to provide informed consent. Providers are identified and

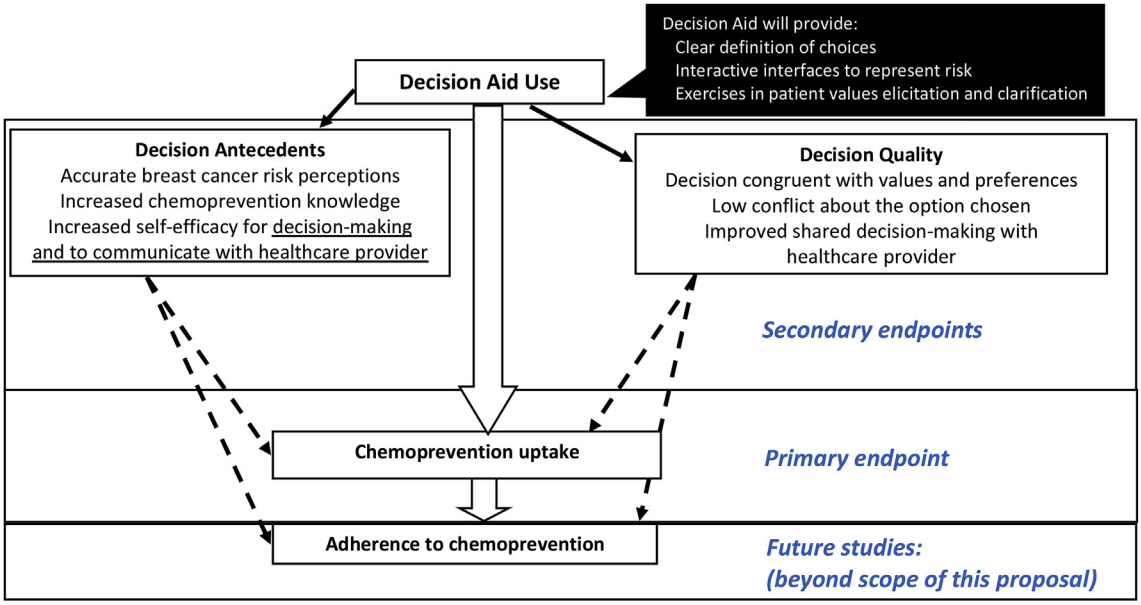

Fig. 2. Multidisciplinary framework based on Shared Decision-Making (SDM) and Self-Determination Theory (SDT).

recruited when one of their patients is identified as being potentially eligible for enrollment.

3.5. Recruitment

Potential patient participants are recruited from several different sources. Recruitment flyers are distributed throughout the medical center, in the community, and online. In-person recruitment and breast cancer risk assessment was completed during screening mammography [41]. Women undergoing screening mammography who met high-risk criteria were also identified through the EHR, based upon data extraction of breast cancer risk factors [42]. Additionally, using ICD-9/10 codes in the EHR, we have identified women at high-risk due to a diagnosis of atypical hyperplasia or LCIS [43]. Finally, we are also screening high-risk women scheduled to be seen in the breast surgery and medical oncology clinics, using EHR data to prioritize patients at the highest risk. When a high-risk patient is identified, her provider will be invited to participate as well. Even if her healthcare provider does not enroll, the provider will still receive the risk reports and alerts.

3.6. Interventions

In addition to the standard educational materials, patients randomized into the intervention arm are given access to a web-based decision support tool. *RealRisks* is designed to empower women to engage in dialogue about chemoprevention. To compliment *RealRisks*, the *BNAV* toolbox ensures providers are prepared by providing them with their patients' personalized risks and preferences prior to the clinical encounter.

RealRisks is designed to improve: 1) accuracy of risk perceptions; 2) self-efficacy in engaging in dialogue about breast cancer risk and chemoprevention; and 3) informed choice. The tool is structured around a narrative that is based on a fictitious character named Rose, who is a 40-year-old mother of two daughters. Breast cancer has affected several people in her life, including her mother at age 48. She visits her doctor and plans to ask the doctor about breast cancer. The narrative then proceeds into the following modules: 1) Risk (what is risk and what is breast cancer and its risk factors); 2) Chemoprevention (chemopreventive agents and risk/benefit profiles).

RealRisks is tailored to a woman's risk, so she reviews only the modules that are relevant to her. Each module has a dense and light narrative (Fig. 3). The dense sections are detailed text explanations of specific breast cancer topics whereas the light sections present the same information in the style of a graphic novel. To account for low health literacy, patients are able to hover over text to view definitions for key terms in the narrative. Each page also has audio buttons that allow the user to hear the text read aloud, as well as Spanish translations. Explanatory videos are placed throughout different sections of the website to help the user navigate through the tool.

Two experience-based, interactive games based upon our previous work are embedded within the narrative of *RealRisks.* [44] The first game illustrates breast cancer risk for an average 50-year-old woman and conveys how time (5-year and lifetime risk to age 90) affects breast cancer risk; the second game displays the participant's personalized breast cancer risk (5-year and lifetime) according to the Gail model. Both games are presented visually as a group of 100 women. Players click on these women (*i.e.,* sample from a population of 100 women) until they uncover one who is predestined to develop breast cancer. In this way, players are able to experience the meaning of a probability (*e.g.,* 12 out of 100 women or 12%). The chemoprevention module then depicts the benefits of chemoprevention and the risks of side effects based on each user's personal profile. Our data suggests that this experience-based format for representing risk improves accuracy of risk perception in low-numerate populations [45].

The whole tool has been developed in both English and Spanish after usability and pilot testing [28,46]. Based upon feedback from our focus groups, we were able to identify unacceptable and confusing language along with missing information needed to fully represent the important issues of breast cancer risk and chemoprevention [26]. To enhance completion rates of *RealRisks*, we have implemented a number of strategies, including text-message and phone call reminders, financial incentives, and technical assistance. The *RealRisks* architecture is designed to include additional modules that can be added over time for breast cancer screening, risk-reducing surgeries, and lifestyle modification.

The Breast Cancer Risk Navigation (*BNAV*) tool includes modules that present healthcare providers with resources on how to manage women at high risk for breast cancer (Fig. 4). The *BNAV* tool uses a two-pronged approach to improve knowledge among healthcare providers about breast cancer risk assessment and chemoprevention. After patients complete *RealRisks*, a tailored action plan is generated for providers, who will also be invited to access the web-based *BNAV* toolbox. Modeled on the Theory of Planned Behavior [47], the toolbox is a repository of information and resources that includes: 1) standard guidelines and a self-paced interactive educational guide with slide presentations and audio (attitudes); 2) case-based learning modules with quizzes (subjective norm); 3) a repository of their patients' breast cancer risk information, along with action plans based upon their patients' interactions with *RealRisks* (perceived behavioral control). The *BNAV* chemoprevention module includes information on breast cancer risk assessment, risks and benefits of chemoprevention, and how to manage side effects of SERMs and AIs. Over time, additional modules have been added to *RealRisks* (genetic testing, screening, lifestyle modification) and *BNAV* (genetic testing, screening, patient-centered care) to provide self-directed learning outside of the clinical encounter. Each module takes about 10–20 min to complete and can be viewed during multiple sittings. Multiple reports have stressed the importance of supporting user workflow to improve efficiency in the clinic setting [48–50]. Using *BNAV's* secure database, the patients' breast cancer risk status and eligibility for chemoprevention are also displayed in the EHR Ambulatory Medicine dashboard. Through the *BNAV* notice in the EHR dashboard, the alerts that are sent prior to the clinical encounter, and the communication of patient-entered data to the treating provider, both *RealRisks* and *BNAV* are integrated into clinic workflow. All providers at CUIMC have access to the educational modules within *BNAV* through the link-out in the iNYP Ambulatory Medicine dashboard. However, providers only view personalized risk reports from their patients who are randomized to the active intervention; control patients' risk profiles and action plans are not included in *BNAV*.

3.7. Outcomes

Table 1 provides a summary of the schedule of study evaluations. The primary and secondary outcomes of interest are described below and are assessed at multiple time points in the active intervention and control groups.

3.8. Primary outcome

1. Chemoprevention uptake

Proportion of patients who initiate a SERM or AI for breast cancer chemoprevention at 6 months after randomization. Electronic health records and self-report measures are used to track chemoprevention uptake.

3.9. Secondary outcomes

1. Perceived breast cancer risk and accuracy of risk perceptions

4 items measuring the patient's estimate of her comparative and absolute 5-year and lifetime risks of breast cancer. Comparative risk is

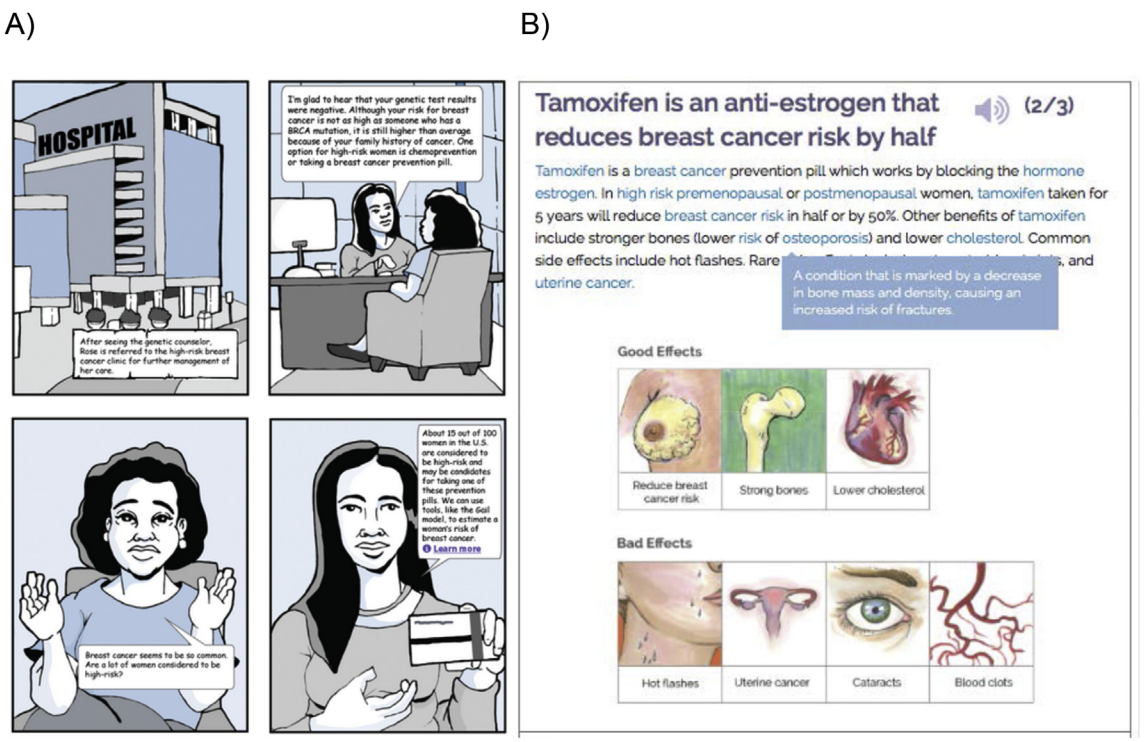

Fig. 3. Sections of the *RealRisks* decision aid: A) Light narrative in graphic novel style, which include audio and Spanish translations; B) Dense narrative with key information about breast cancer risk and chemoprevention, including roll-overs with definitions of terms.

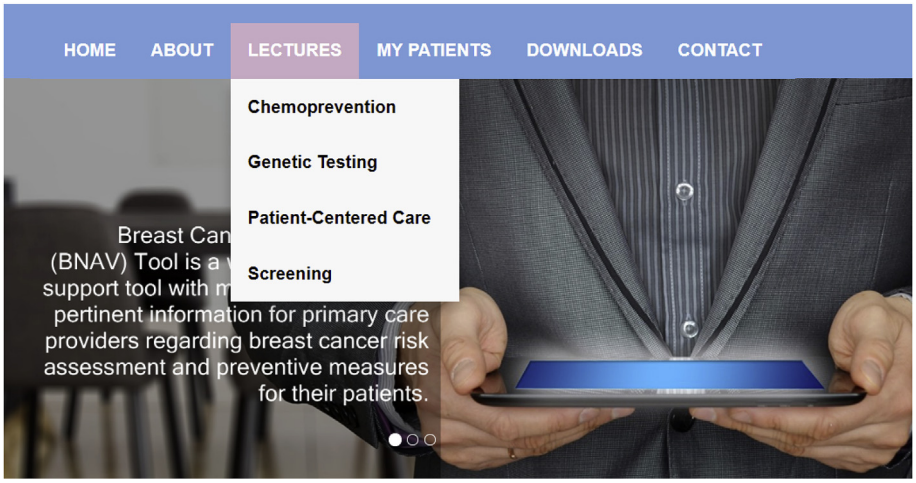

Fig. 4. The *BNAV* toolbox.

assessed on a 3-point Likert scale that asks the patient to compare her chances of developing breast cancer to the average women her age. Response options include "much lower," "about the same," and "much higher." 5-year and lifetime absolute breast cancer risk estimates are measured on a numeric scale ranging from 0 to 100%. Patients are also asked to rate their chance of developing breast cancer on a 5-point Likert scale ranging from "very low" to "very high." Accuracy is assessed by comparing the difference between a patient's perceived absolute lifetime breast cancer risk, measured on a scale of 0–100%, and their actual risk based on the Gail model. Patients are defined as having accurate breast cancer risk perceptions if their perceived lifetime risk is within ± 10% of their Gail model risk score [51]. Breast cancer risk perceptions are assessed at baseline, 1 month, and 6 months.

2. Breast cancer worry

2 Likert-style items asking the patient how often she worries about developing breast cancer and how much does worrying about developing breast cancer interfere with her everyday life [52,53]. Response options range from "None of the time" to "All of the time." Breast cancer worry is assessed at baseline, 1 month, and 6 months.

3. Chemoprevention knowledge

8-item scale assessing knowledge about the risks and benefits of tamoxifen and raloxifene. The multiple-choice items ask the patient to identify whether each medication will make her more or less likely to experience hormonal symptoms, cataracts, broken bones, and breast cancer. The patients also have the option to indicate that the medications will have no effect on the likelihood of experiencing these conditions. Adequate knowledge is defined as at least 50% correct responses [54]. Chemoprevention knowledge is assessed at baseline, 1

Table 1
Schedule of study evaluations.

Patient-Reported Outcomes	Baseline	1 month	6 months	Post-clinic
Baseline Characteristics				
Demographics/breast cancer risk factors	X			
Health literacy/numeracy	X			
Decision Antecedents				
Perceived breast cancer risk	X	X	X	
Breast cancer worry	X	X	X	
Chemoprevention knowledge	X	X	X	X
Decision self-efficacy	X	X		
Decision Quality				
Decision conflict		X	X	X
Attitudes/Informed choice		X	X	X
Shared decision-making				X
Clinical Outcomes				
Chemoprevention intention/decision		X	X	X
Referral to high-risk clinic			X	
Chemoprevention uptake[a]			X	
Provider-Reported Measures	Baseline			
Personal/professional characteristics/practice patterns	X			
Confidence in risk communication	X			

[a] Primary endpoint.

month, 6 months, and after the clinical encounter.

4. Decision self-efficacy

11-item scale measuring how confident the patient is in performing different behaviors involved in making an informed choice about chemoprevention. The 5-point response options range from “not at all confident,” to “very confident.” [55] Self-efficacy is assessed at baseline and 1 month.

5. Decision conflict

10-item, low-literacy version of the Decision Conflict Scale, which measures how conflicted a patient feels about her chemoprevention decision. Response options include “yes,” “no,” and “unsure.” [56] Decision conflict is assessed at 1 month, 6 months, and after the clinical encounter.

6. Chemoprevention intention/decision

Intention is assessed at 1 month using a 5-point Likert Scale ranging from “very unlikely” to “very likely”. Responses of 1 and 2 are interpreted as unlikely to adopt chemoprevention, responses of 4 and 5 are interpreted as likely to adopt chemoprevention, and a response of 3 is interpreted as neutral [54]. Chemoprevention decision is assessed at 6 months and after the clinical encounter and specifically queries about the initiation and current use of SERMs or AIs.

7. Attitudes/Informed choice

5-point item that asks the patient how good of a choice chemoprevention is for her [54]. Responses range from “for me, it is not a good choice at all” to “for me, it is an extremely good choice.” An informed choice is defined as one that is based upon adequate knowledge (which is defined as $\geq$50% of the chemoprevention knowledge items correct) with the patient's attitudes towards taking chemoprevention congruent with their intention or decision [54]. Therefore, a patient is considered to have made an informed choice if she has adequate knowledge and one of the following: 1) positive attitudes (*i.e.*, a score of 4 or 5 on the attitudes measure) and an intention or decision to adopt chemoprevention; 2) negative attitudes (*i.e.*, a score of 1 or 2 on the attitudes measure) and an intention or decision to not adopt chemoprevention; 3) neutral attitudes (*i.e.,* a score of three on the attitudes measure) and a neutral intention or no decision on chemoprevention adoption. These measures are assessed at 1 month, 6 months, and after the clinical encounter.

8. Shared decision-making

The SDM-Q-9 questionnaire, which includes 9 Likert-scale items that reflect different aspects of shared decision-making. Response options range from “completely disagree” to “completely agree.” [57] Shared decision-making is assessed after the clinical encounter.

9. Proportion of high-risk patients who are referred to the breast clinic

Electronic health records are used to track patient referral to the high-risk breast clinic at 6 months.

The schedule of questionnaire evaluations was selected in order to assess the different facets of our intervention that occur at different time points. The baseline survey allows comparison between the two groups prior to study participation. Patients are sent the control materials and the *RealRisks* intervention tool shortly after enrollment, so the 1-month survey allows for examination of the short-term effects of the *RealRisks* tool. Because the intervention seeks to promote shared decision-making between the patients and providers, the post-clinical encounter survey allows for the examination of the effects on these clinical encounters. Finally, the 6-month evaluation allows the patient ample time to make a decision about chemoprevention and allows for the examination of long-term effects.

3.10. Statistical methods

The primary endpoint is uptake of a SERM or AI for breast cancer chemoprevention at 6 months in the intervention arm compared to the control arm. With a total sample size of 300 (150 per arm), assuming a Type 1 error of 5% and a 10% drop-out rate (effective sample size of 270), we will have > 80% power to detect a difference in chemoprevention uptake rate of 1% in the control arm (based upon data from our mammography screening population who met high-risk criteria for breast cancer [58]) and 10% in the active intervention arm.

After generating descriptive statistics, we will conduct chi-squared tests to determine associations between study arm and categorical outcome variables and t-tests to determine associations between study arm and continuous outcome variables. Depending on the scale of each outcome variable (continuous or binary) and the scale of the independent variable (categorical or continuous), we will also use ANOVAs, linear regression, Pearson's correlation coefficients, logistic regression, and—particularly when significant missing values are present—mixed effects models to identify the study variables that are associated with each outcome.

4. Discussion

Multiple trials have demonstrated that tamoxifen, a SERM, can reduce invasive breast cancer incidence in high-risk women by 30–50% compared to placebo when taken for five years [1,17,59–61]. Another SERM, raloxifene, has been shown to have similar effects in postmenopausal women [62,63]. Long-term raloxifene can be 76% as efficacious as tamoxifen in preventing invasive breast cancer among high-risk postmenopausal women with fewer serious side effects [64]. Based upon the results of these trials, the U.S. Food and Drug Administration (FDA) approved tamoxifen for breast cancer risk reduction in 1998 and raloxifene in 2007. In 2011 and 2014, the aromatase inhibitors (AI), exemestane and anastrozole, were demonstrated to reduce invasive breast cancer incidence by 50–65% compared to placebo among high-risk postmenopausal women [3,65].

Based upon this evidence, the U.S. Preventive Services Task Force (USPSTF), American Society of Clinical Oncology (ASCO), and the National Comprehensive Cancer Network (NCCN) distributed guidelines on breast cancer chemoprevention [4–6]. High-risk premenopausal and postmenopausal women, defined as those with a 5-year Gail risk score of ≥1.67% or those with LCIS, may take tamoxifen for five years to reduce breast cancer risk. Tamoxifen is most likely to benefit younger women (age 35–50 years), those who have undergone a hysterectomy, and those at higher risk for breast cancer. Women who have gone through menopause also have the option of raloxifene, anastrozole, or exemestane to reduce breast cancer risk.

Nonetheless, fewer than 5% of high-risk women in the U.S. who may be eligible for chemoprevention and are offered a SERM decide to take it [7,8]. Further, without the ability to effectively screen women in the primary care setting for an increased risk, a large proportion of high-risk women may be undetected. Low rates of chemoprevention uptake are influenced by concerns about side effects, the lack of time needed to provide patient counseling, and insufficient patient and provider knowledge of risk-reducing strategies [8,66]. Women of color are less likely to seek breast cancer preventive care [20,21], which can lead to poorer clinical outcomes in these populations compared with non-Hispanic whites [23,24,67].

Interventions involving reading materials or decision aids (DAs) that are designed to increase SERM uptake have been met with limited success [11,12,15,68,69]. In a randomized controlled trial of a web-based DA designed to educate women about the benefits and risks associated with SERMs [68], only 0.5% of 712 eligible participants decided to start taking raloxifene and none decided to take tamoxifen. In another study, primary care providers (PCPs) screened over 5700 women, age 35–70 years, with the Gail model and 868 (15.2%) were found to be eligible for a SERM; nevertheless, only 14.7% of these women received referral for specialized risk counseling, less than half completed the consultation, and only 2% started a SERM [70]. However, other studies that incorporated high-risk breast clinic consultations reported SERM use ranging from 11% to 58% [9,13,14,18,71–73]. This evidence suggests that higher uptake of chemoprevention may be achieved when patients and providers are adequately informed *and* when both parties are facilitated in discussing this issue during the clinical encounter.

As an adjunct to communicating with providers, *RealRisks* is an important care component and can make chemoprevention accessible to underserved populations. Significant breast cancer risk factors include family history, reproductive factors such as early menarche and nulliparity, and lifestyle factors like consuming alcohol and obesity [74]. This data can be difficult to collect and analyze in a busy medical appointment. By providing education that is accessible to patients with varying health literacy and numeracy, collecting and analyzing patient-entered data, and communicating personalized risk profiles and patient preferences to the treating provider *before* the clinical encounter, *RealRisks* may help ensure that more high-risk women have crucial discussions on breast cancer risk-reduction with their providers.

Demonstrating this need, a study conducted by our research team revealed that patients categorized as having low numeracy were more likely than those who were categorized as having high numeracy to overestimate their risk and to report that their own risk was 50%, which may indicate uncertainty or confusion [45]. Such overestimation of breast cancer risk is not associated with a greater adherence to screening regimens or improved decision-making [75]. Some women are hesitant to adopt risk-reducing interventions due to exaggerated beliefs about side effects, even if breast cancer is one of their primary health concerns [76]. In other situations, it has been shown that women who have had both breasts removed to reduce their risk of breast cancer had overestimated their risk when they made their decisions [77]. Inappropriately high risk perceptions can lead to potentially harmful decisions and can increase cancer worry—a stressor that can impair ability to make good decisions [78–82].

Such challenges require effective DAs to make numbers more transparent and accessible for decision-making [83–86]. Most prior research that has attempted to explain risks to patients in narratives, numbers, or graphs has revealed that all of these media can bias perceptions and complicate risk communication [87–89]. People tend to overweigh rare events when probabilities are described to them, but assign them a lower weight when they learn probabilities through an experience such as drawing cards from a deck [90,91]. When participants used an experience-based dynamic interface to learn about and interpret risk in one of our previous studies, differences in risk perceptions associated with low numeracy were reduced [45]. The *RealRisks* DA incorporates a similar dynamic interface to communicate risk and reduce inaccurate risk perceptions.

Prior literature suggests that just targeting high-risk women or PCPs alone is ineffective at increasing chemoprevention uptake, and many patients and healthcare providers have limited knowledge about chemoprevention. Our study intervention differs from prior studies of decision support for breast cancer chemoprevention for the following reasons: 1) We are targeting high-risk women from different clinical settings, including screening mammography, primary care, gynecology, and breast surgery clinics; 2) We have developed decision support tools for both patients and healthcare providers, which include education about breast cancer risk, decision support for chemoprevention, and personalized risk reports; 3) The provider tool, *BNAV*, is embedded in the EHR to enhance dissemination, implementation, and sustainability; 4) Finally, our patient-centered DA, *RealRisks*, which is available in English and Spanish, has been rigorously tested in multi-ethnic high-risk women with varying educational backgrounds and health literacy.

Chemoprevention uptake is a preference-sensitive decision that is heavily dependent on a patient's personal beliefs and valued medical trade-offs. Deciding not to begin using chemoprevention could be due to a patient's lack of understanding of breast cancer risk and chemoprevention's risk-benefit profile, but it could also be the decision that is most closely aligned with a patient's preferences and informed choice. While improved decision antecedents and quality may not necessarily increase chemoprevention uptake, our analysis will attempt to assess the extent to which such a relationship exists. As noted above, much of the evidence surrounding the efficacy of SERMs has studied effects after five years of use. This trial is not able to assess long-term adherence, and is only able to evaluate uptake at six months. While we are mostly interested in helping patients make informed decisions on whether or not they should begin taking chemoprevention, the inability to assess adherence is a limitation in the study design. Future research should evaluate the effects of decision aids on long-term drug adherence.

Research to determine how best to assess and communicate personalized breast cancer risk and the risks and benefits associated with prevention options to high-risk women is needed in order to promote informed and shared decision-making on breast cancer risk-reducing strategies. Chemoprevention with SERMs and AIs is currently the most effective breast cancer prevention option apart from risk-reducing prophylactic mastectomies. Despite its demonstrated efficacy, chemoprevention uptake has been low due to the barriers of identifying high-risk women and a lack of understanding of its risks and benefits. Given that most women receive mammography referrals through PCPs, it is logical to enhance this interaction with a more comprehensive breast cancer risk assessment and decision support. If found to be effective in increasing chemoprevention informed choice or uptake, the *BNAV* tool and the web-based *RealRisks* DA may be widely disseminated.

Breast cancer incidence continues to increase in most countries and the U.S. is expected to spend increasing amounts of money on treatment due to greater intensity of healthcare usage and increasing costs of cancer care [92–99]. These rising costs can disproportionately impact minority, low-income, and under-insured women. Targeting high-risk populations is a key step in expanding breast cancer prevention services. *RealRisks* and *BNAV* can help promote informed decision-making and chemoprevention uptake among high-risk women and can help

shift clinical practice for breast cancer prevention towards a more personalized approach.

Trial status

We are currently implementing the study intervention at CUIMC and recruiting and enrolling patients into the trial. As of December 2018, we have enrolled 192 patients. We have completed recruitment of 50 healthcare providers.

This trial was registered in clinicaltrials.gov under trial number NCT03069742 on March 3, 2017.

Acknowledgements

This study is supported by the National Cancer Institute under R01CA177995, P30 CA013696-39, and by the National Center for Advancing Translational Sciences, National Institutes of Health under UL1 TR000040 and U01HG008680. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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