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Dated: April 29, 2017

BREAST CANCER CHEMOPREVENTION AMONG WOMEN: EFFECT OF INVOVEMENT AND RISK COMMUNICATION

By

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BREAST CANCER CHEMOPREVENTION AMONG WOMEN: EFFECT OF INVOVEMENT AND RISK COMMUNICATION

To the Faculty of the University of Houston, College of Pharmacy: The members of the committee appointed to examine the dissertation of find it satisfactory and recommend that it be accepted on May 10, 2017

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Dedicated to

Mom (Nimisha Bhansali)

and

Dad (Hiren Bhansali)

Abstract

Objective: The purpose of this study was to test the effect of patient involvement levels, developed using different breast cancer risk scenarios and message format on their intention to initiate breast cancer chemoprevention.

Method: In this experimental field study involvement was manipulated at 2 levels (high and low) and was developed using two scenarios. Breast cancer risk levels were considered using the Gail risk score. A breast cancer risk level of 16% with family history was used for low risk scenario and breast cancer risk level of 55% with family history and a breast biopsy was used for high risk scenario. Message format was manipulated 2 levels (graphic and written) and was developed using concepts of chunking and picture superiority. Women across the Houston metropolitan area evaluated two chemoprevention drug decision aids after reading scenarios simulating high and low involvement. A pre-validated, self-administered survey instrument was used to measure their perceived susceptibility to breast cancer, perceived severity to breast cancer, perceived benefits, perceived adverse events and intention to start chemoprevention using a Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree). ANCOVA and post-hoc analyses were done using SAS® 9.3.

Results: Of the 320 women included in the study (81.4% response rate) majority were married 144 (46.45%), white 160 (51.61%) with a mean age of 40.25 (± 11.27) years. Majority 182 (58.52%) had at least one family member with a history of cancer. A univariate and post hoc analyses indicated women with high involvement level had significantly higher mean (4.14 ± 0.99) intention to start chemoprevention when compared to women in a low involvement scenario (2.52 ± 1.1). Message format had a direct effect of perceived susceptibility to breast cancer. There was an indirect effect of message format on perceived severity to breast cancer,

perceived benefit of chemoprevention and perceived adverse events of chemoprevention. There was a mediating effect of perceived susceptibility to breast cancer. There was a direct and indirect effect of message format on intention to start chemoprevention.

Conclusion: Patient involvement manipulated using breast cancer risk levels plays an important role in intention to initiate chemoprevention. Message format plays a role on intention to start chemoprevention. Interventions can be targeted among women emphasizing on their breast cancer risk.

CHAPTER ONE

Introduction

Dissertation Overview

Breast cancer (BC) is an abnormal growth of epithelial cells present in the duct and lobules within the mammary glands.(Chemicals et al. 2011) It is the most common malignancy among women around the world, with very low incidence in men.(Benson et al. 2009) It is also the leading cause of cancer associated mortality.(Hortobagyi et al. 2005) Approximately 1.38 million cases were detected in 2008, which comprises of about 23% of incident cases of cancer.(Ferlay et al. 2010) While in 2012, approximately 1.7 million incident cases of breast cancer were diagnosed worldwide, which accounted for 25% of all cancer cases in women, showing and increasing trend of new cases (Colditz and Bohlke 2014).

Breast cancer has a huge financial burden on the society, while severely affecting the quality of lives. Direct medical costs associated with breast cancer treatment per patient, over a period of 16 months has been shown to be approximately $35,164 (Maitino et al. 2003; Rao, Kubisiak and Gilden 2004). Approximately, $4.2 billion per year is attributed as direct medical costs for treatment of breast cancer within the United States (Freedman et al. 2003).

Several risk factors have been identified of which family history and age are the most common.(Ralph et al. 2014) Multiple studies have depicted modifiable risk factors like radiation exposure, (Land et al. 2003) alcohol consumption, (Longnecker 1994) lack of physical activity and obesity (Bober et al. 2004).

Breast cancer incidence and prevalence is mostly in post-menopausal women. Most of the tumors developed are hormone receptive or due to gene mutation of BRCA1 and BRCA2 (Benson et al.

2009). While there are several ways to reduce risk, not all are feasible. Diet and alcohol consumption can be controlled. However obesity and radiation exposure is difficult.

Breast cancer prevention has not been the focus of the healthcare industry but requires attention (Colditz and Bohlke 2014). Where the concept of 'Prevention is better than cure' is applied for cardiovascular and infectious diseases, a similar approach is the only hope to attenuate the global burden of breast cancer (Vogelstein et al. 2013).

Chemoprevention plays a major role in risk modification. Selective estrogen receptor modulators (SERM) and Aromatase Inhibitors are the two major drug classes used for chemoprevention. Tamoxifen is currently the most widely used SERM.(Visvanathan et al. 2009) Two clinical trials have indicated the reduction in incidence of breast cancer by 50%. Raloxifene another drug launched after tamoxifen has been shown to reduce the incidence of breast cancer by 75% in the MORE trial. When seen over a period of 8 years it reduces the incidence by 68%.(Goss et al. 2011)

Tamoxifen is also associated with rare cases of thromboembolism and endometrial cancer due to its mechanism of action. It is also known to reduce the risk of fractures and osteoporosis in post-menopausal women. The MORE trial for raloxifene showed a reduced risk of adverse events, better breast cancer prevention and better bone protective effect compared to tamoxifen. However, the STAR trial showed both tamoxifen and raloxifene to be equally efficacious (Goss et al. 2011).

Aromatase inhibitors (AI) are typically used for chemoprevention for women with high plasma estrogen levels. Aromatase inhibitors prevents more contralateral breast cancer with fewer side effects as compared to tamoxifen and raloxifene. Exemestane an aromatase inhibitor, due to its anti-estrogenic activity such as bone resorption was considered to be a chemo-preventive agent. Tamoxifen is the current gold standard for prevention of breast cancer in high risk women,

however the current guidelines state Raloxifene to be more beneficial among post-menopausal women (Wood, Smith and Dowsett 2003).

Several risk management strategies have been adopted among women with high risk of breast cancer, including preventive surgeries and risk-reducing drugs like selective estrogen receptor modulators (SERM) and aromatase inhibitors (AI).

However, there is a strong concern associated with the use of these drugs with respect to their side-effects, including an increased incidence of endometrial cancer, deep vein thrombosis, cataract and several cardio-vascular diseases. American Society of Clinical Oncology (ASCO) and the Oncological Drug Advisory Board have recommended the use of SERMS (tamoxifen®, raloxifene®) among high risk women upon discussion with their physicians about the potential risks and benefits (Taylor and Taguchi 2005).

Several randomized clinical trials have shown a 50% reduction in incidence of invasive breast cancer and a higher reduction in hormone-receptor positive breast cancer (Cuzick et al. 2007; Fisher et al. 1998). Risk-reducing drugs taken over a period of five years reduces the risk of breast cancer by 38%. About 15% of women in the United States could benefit from these drugs. However, the uptake of these drugs is considerably low (Ralph et al. 2014). The reason can be lack of explanation by the physician of the potential benefits and patient characteristics.

The study intended to study factors governing patient decision making to initiate chemo-prevention and develop a decision aid to help patients make an informed decision. The study will help tailor interventions while giving an insight into the minds of the patients. Cancer is a complex disease and severely hampers the lives of the patients. It is not just the patient, but the disease

negatively impacts their respective families, employers, including work hours lost, which as a whole affects the society.

We have tested written and graphic decision aids. The level of patient involvement governs their self-motivation towards preventive action. By simulating real life scenarios and manipulating patient involvement levels, the study tested the effect of graphic and written decision aid on the manner in which patients appraise risk and their intention towards preventive action. The study aim was to develop a model to improve patient understanding and reduce decisional conflict while creating realistic outcome expectations.

In forthcoming chapters, the following will be discussed:

Chapter 2: A detailed review on breast cancer etiology, economic and societal burden, breast cancer risk factors, breast cancer preventive methods, chemo-prevention uptake, importance of patient information leaflet in chemo-prevention decision making.

Chapter 3: Discussion of theories and concepts applied in this research. Hypotheses were stated, based on theoretical discussion.

Chapter 4: A detailed explanation of the methodology used to test the hypotheses.

Chapter 5: Results of the statistical tests

Chapter 6: Study discussion, implications, strengths, limitations and future studies

CHAPTER TWO

Literature Review

Breast Cancer Etiology

The American Cancer Society has defined cancer as a group of cells that have mutated from their original function, grown out of control and formed a mass (2013; Benson et al. 2009; Chlebowski et al. 2002). Based on the location from where the mutated cells began growing the cancer is named, such as breast cancer. Since the body cannot regulate the growth of these cells, they multiply out of proportion and cancer can spread to other locations throughout the body. When cancer is diagnosed, the severity of the disease can be determined by the spread of the disease. Local staged tumors are confined to the breast, regional staged spread to surrounding tissue or nearby lymph nodes, and metastatic tumors have spread to distant organs (Benson et al. 2009; Colditz and Bohlke 2014).

Breast Cancer Burden

Societal Burden

The growing incidence of breast cancer has an effect on every strata of the society. With healthcare services being restructured and more of breast cancer patients opting for home services over hospitals, the burden increases on family caregivers. Caregivers often suffer a psychological, occupational and economic impact while assisting a patient diagnosed with breast cancer. Anxiety and depression is commonly experienced among family, friends and caregivers of breast cancer patients. Feelings of burden have often been associated among close relatives of patients with breast cancer. Caregivers of breast cancer patients have reported an increased inability to work regular hours due to the demands of the disease.

Economic Burden

Advances in medical care has improved breast cancer survivorship. Magnitude of health care service utilization and increasing costs of cancer care is expected to result in a greater burden of cancer in the future. Costs for breast cancer may account for as much as 20% of the $228 (Ferlay et al. 2010). About 1 billion in total costs of breast cancer care, with estimates in the United States yielding highly variable results. Breast cancer associated costs increased significantly with morbidity, costs were higher immediately after diagnosis of recurrence and in the terminal months of life than during the continuing-care phase.

Breast Cancer Risk Factors

Gender:

Breast cancer is caused when mammotropic hormones interact with mammary gland mass. Based on the amount of estrogen production in later life and its interaction with the mammary gland cells, the risk associated with gender can be explained (Benson et al. 2009). Females are more susceptible to breast cancer due to higher mammary gland mass and estrogen production in a lifetime.

Age:

The incidence of breast cancer increases rapidly with age during the reproductive years and then increases at a slower rate after about age 50 years, which is the average age at menopause

Age at Menarche:

For each 1-year delay in menarche, the risk decreases by around 5%. There is also evidence that, although age at menarche is related to breast cancer risk at all ages, the effect may be stronger in younger (premenopausal) women.

Age at Menopause:

A later age at menopause necessarily prolongs exposure to ovarian hormones. A surgical menopause confers more protection than a natural menopause at the same age because bilateral oophorectomy eliminates the gonadal source of estrogens abruptly, whereas natural menopause is typically characterized by a gradual decline in estrogen levels.

Two main factors are linked with a higher risk of cancer after menopause:

- Increased exposure to hormones, such as estrogen, which increases the risk of uterine cancer and breast cancer.
- Increased number of ovulations, which increases the risk of ovarian cancer. Ovulation is the time in a woman's cycle in which the ovary releases eggs.

As women menstruate longer, they have more ovulations and are exposed to hormones for longer. This means that woman who start menopause after age 55 are more likely to get breast cancer (Benson et al. 2009).

Age at first full-term Pregnancy:

A pregnancy is accompanied by many-fold increases of estrogens and other mammotropic hormones that can boost already initiated clones but also makes a large fraction of previously

susceptible cells refractory to carcinogenesis after undergoing terminal differentiation. When the first pregnancy occurs at an early age, fewer cells are likely to have already been initiated. In addition, the period of protection covers a larger fraction of the remaining life span. The transient increase in risk following a pregnancy explains a longstanding enigma, namely, why breast cancer risk is higher among parous than among nulliparous women of premenopausal age.

Obesity and premenopausal breast cancer:

The prevalence of high-risk mammograms, that is, mammograms with a high fraction of total breast size occupied by mammary gland tissue, as opposed to fat, is four times higher among lean women than among obese women, as the large study by Byrn et all has conclusively demonstrated (Case et al. 2004). The inverse association between obesity and breast density underlies the inverse association between obesity and breast cancer risk among premenopausal women, because the associations of breast density with obesity and breast cancer risk inverse and positive, respectively are both strong. It has been argued that obese women are at lower risk for premenopausal breast cancer because they have a higher frequency of anovulation, but the relations of anovulation to obesity and breast cancer risk positive and inverse, respectively are, at best, weak (Colditz and Bohlke 2014).

Exogenous Estrogens and Oral Contraceptives:

The risk of breast cancer is increased by around 25% in current users of combined oral contraceptives, but the excess risk falls after cessation of use, such that 10 or more years after use stops, no significant increase in risk is evident. Risk does not vary significantly with duration of use, nor does the effect of combined oral contraceptives vary significantly according to other risk factors. The effect on risk of breast cancer does not vary with the type of estrogen or

progestogen used. Although data on progestogen-only oral contraceptives are limited, their effects seem to be broadly similar to those of combined preparations. Use of combined oral contraceptives is associated with a larger excess of localized cancers than those that have spread beyond the breast. This finding has raised the possibility that the increased risk of breast cancer in recent users of oral contraceptives may be partly due to increased surveillance.

Because breast cancer is rare at young ages when use of oral contraceptives is common, most use of these agents does not result in a large number of extra cases. However, use of oral contraceptives late in a woman's reproductive life will result in an increased relative risk of breast cancer at a time when the background risk is becoming appreciable. Thus, the later the use of oral contraceptives, the larger the number of resulting excess cases of breast cancer

Diet:

Adult diet has a minimal effect on breast cancer risk when compared to other risk factors. There are indications that consumption of certain vegetables and fruits, olive oil, and soy-based foods may have preventive potential, due to their antioxidant properties. However, there is no established association between these food items and breast cancer prevention.

Family History:

A familial component to breast cancer incidence has been determined for many years. Multiple studies have tried to quantify risk, however it is dependent on several individual factors. The risk associated with a positive sister history lead to a higher risk as compared to a positive mother history. The relative risk to a woman under 50 with a mother affected before the age of 50 is 2.5 to 2.8 while the same woman with a sister history of breast cancer before age 50 has a relative risk of 3.3. It is known that a high proportion of high-risk breast cancer families are due to either

of the genes BRCA1 or BRCA2 (Miki et al. 1994; Wooster et al. 1995). The risk of breast cancer associated with a family history is higher in younger women, particularly in women under 40. However, it is one of the leading factors even in post-menopausal women (Warren, Harvie and Howell 2004).

Breast Cancer Prevention Methods

Prevention programs for breast cancer require general breast cancer awareness, population-based breast cancer risk assessment, and individual patient breast cancer risk assessment. If a woman's personal breast cancer risk has been established as moderate or high, a personalized prevention and screening plan can be developed. Frontline health professionals need expertise in breast cancer risk assessment and counseling (including prevention counseling) or must be able to refer women for risk assessment and counseling. Frontline health professionals should understand available breast cancer prevention strategies, including lifestyle modification, or preventive or protective medical therapy for select moderate- to high-risk women or preventive surgery for select high-risk women.

Lifestyle Modification

Lifestyle recommendations can improve overall health and include increased exercise, avoidance of weight gain (particularly during menopause), encouragement of breastfeeding, avoidance of harmful use of alcohol (more than one drink per day for women) and physical activity. Although not a known breast cancer risk factor, all women should avoid tobacco use (Chlebowski et al. 2002).

Surgery Prophylaxis

Surgical interventions, such as prophylactic mastectomy and/or oophorectomy (removal of ovaries), should only be considered for high-risk women with known or highly suspected genetic predisposition to breast cancer. Candidates must understand the irreversible effects of such treatment. Total mastectomy with breast reconstruction is currently the procedure of choice in HICs among some high-risk women (Veronesi et al.). The psychological implications can be substantial and include anxiety regarding body appearance, sexual relationships and psychosocial issues. Bilateral prophylactic mastectomy is the complete removal of both breasts, including the nipple-areolar complex (total mastectomy) or as much breast tissue as possible while leaving the nipple-areolar complex intact (nipple-sparing or subcutaneous mastectomy). In HICs, in moderate- to high risk women, this reduces the risk of breast cancer by 90-95%. Immediate breast reconstruction, if available and desired, should be performed after adequate pre-operative counseling (Kedar et al. 1994). Patient regret regarding the decision to undergo prophylactic mastectomy is not common in HICs (approximately 5-6%). Prophylactic oophorectomy, after age 35 and child bearing has been completed, should be reserved for high-risk women such as those with a known deleterious BRCA mutation. The potential benefits include a reduction in both breast and ovarian cancer. Oophorectomy in women younger than 35 years old is associated with an approximately 50% reduction of breast cancer risk and an 85% risk reduction of ovarian cancer. Surgically induced menopause carries its own concomitant risks, including premenopausal symptoms (e.g., hot flashes, night sweats, and vaginal dryness), osteoporosis, and increased risk of cardiovascular disease (Cuzick et al. 2007).

Medical Prophylaxis (Chemo-prevention)

Medical prophylaxis with tamoxifen and raloxifene, both selective estrogen receptor modulators (SERMs), has been shown to reduce breast cancer risk in select patients, but has not been well-

accepted by health professionals or patients. It requires careful consideration and in-depth discussions regarding the benefits and risks of therapy.

Current Chemo-prevention

Selective Estrogen Re-uptake Modulator (SERM)

Tamoxifen citrate and raloxifene hydrochloride are selective estrogen receptor modulators that respectively have been approved by the US Food and Drug Administration for prevention of breast cancer and osteoporosis. The acceptability of drugs that are used for prevention often rests on their efficacy as well as their adverse-effect profiles. Selective estrogen receptor modulators bind competitively with the estrogen receptor in various tissues and can have properties of both an estrogen antagonist and agonist.

- Tamoxifen:

  FDA approved for the treatment of metastatic breast cancer and adjuvant treatment of breast cancer and to reduce the risk of invasive breast cancer in premenopausal or postmenopausal women with DCIS and/or women at high risk of developing breast cancer (Cuzick et al. 2003; Cuzick et al. 2007; Kedar et al. 1994).

- Raloxifene:

  FDA approved for the treatment and prevention of osteoporosis in postmenopausal women and to reduce the risk of invasive breast cancer in postmenopausal women with osteoporosis and/or postmenopausal women at increased risk of breast cancer (Cuzick et al. 2003).

Aromatase Inhibitors (AIs)

- Exemestane:

  FDA approved for the adjuvant treatment of ER-positive early breast cancer in postmenopausal women and for treatment of ER-positive advanced breast cancer in postmenopausal women whose disease has progressed after tamoxifen therapy or in combination with everolimus after failure of treatment with letrozole or anastrozole (Aktas et al. 2016). Exemestane is not approved by the FDA for breast cancer prevention.

- Anastrazole:

  FDA approved for adjuvant treatment of hormone receptor–positive early breast cancer in postmenopausal women, for first-line treatment of postmenopausal women with hormone receptor–positive or hormone receptor–unknown locally advanced or metastatic breast cancer, and for the treatment of advanced breast cancer in postmenopausal women with disease progression after tamoxifen therapy. Anastrozole is not FDA approved for breast cancer prevention (Chlebowski et al. 2002).

Current Guidelines

The American Society of Clinical Oncology guidelines recommend that women should consider the harms and benefits of tamoxifen or raloxifene during their decision making. Considering the drug profile, its potential benefits and risks, women are likely to experience difficulty making this decision (2013; Taylor and Taguchi 2005; Tchou et al. 2004; Visvanathan et al. 2009). Support for decision-making may be provided through counselling supplemented by decision aids.

Risk/ Benefit of Chemo-prevention

Net Benefits:

Premenopausal women. For tamoxifen, there were no new publications evaluating the risk-benefit profile in premenopausal women. Gail et al4 previously demonstrated, based on the NSABP-P1 data, that the greatest clinical benefit with the least adverse effects, for tamoxifen compared with placebo, occurred in younger women (between ages 35 and 50 years) who were at elevated risk of breast cancer. Postmenopausal women. Freedman et al conducted a post hoc retrospective analysis that included data from the STAR and NSABP-P1 trials (Cauley et al. 2001; Razzaboni et al. 2013). In postmenopausal women, the risk-benefit profile for both tamoxifen and raloxifene was found to vary by age, race (white non-Hispanic, black, and Hispanic), level of breast cancer risk, and history of hysterectomy (Powles et al.). Overall, the most favorable risk-benefit profile is seen in women at greatest risk of developing breast cancer. Postmenopausal women with an intact uterus were found to have a better risk-benefit index for raloxifene compared with tamoxifen (Cuzick et al. 2003; Veronesi et al.). For postmenopausal women without a uterus, the risk-benefit ratio was not statistically significant between the two chemoprevention agents. More detailed estimates of risk-benefit profiles stratified by age and race are available in their article (Cummings et al. 2002; Lippman et al. 2001). Additionally, Cuzick et al conducted a meta-analysis based on individual-level data from nine randomized trials that compared SERMs with placebo or another drug in women without breast cancer (Cauley et al. 2001; Cuzick et al. 2003). Eight of these trials were placebo controlled trials, and one compared tamoxifen with raloxifene. Overall, there was a 38% reduction in breast cancer incidence, with 42 women needing to be treated to prevent one case of breast cancer, over a 10-

year follow-up period. The largest risk reduction was observed in the first 5 years. There has been a significant increase in the incidence of thromboembolic disease with all SERMs (odds ratio [OR], 1.73; 95% CI, 1.47 to 2.05) and a significant reduction in the incidence of non-vertebral fractures (OR, 0.66; 95% CI, 0.59 to 0.73) (Cauley et al. 2001). In summary, when considering tamoxifen and/or raloxifene as chemopreventive options, both the risks and benefits should be discussed, and the discussion should be tailored to the individual patient. Providing information on net health benefits such as those described here can also be helpful in the decision making process (Cuzick et al. 2007).

Adverse Events and Adverse Effects:

Tamoxifen: Serious adverse events associated with tamoxifen use include endometrial cancer, stroke, transient ischemic attack, venous thromboembolism, deep vein thrombosis, and pulmonary embolism (Chlebowski et al. 2002; Fisher et al. 1998). A systematic review and analysis of data from women in the NSABP-P1, IBIS-I, and Royal Marsden trials demonstrated that women age less than 50 years who took tamoxifen for breast cancer prevention had a lower risk of endometrial cancer, deep vein thrombosis, and pulmonary embolism than women age more than 50 years (Chlebowski et al. 2002; Powles et al.). The risk decreased from the active phase to follow-up phase of treatment. Vascular and vasomotor adverse effects were observed to decline post-treatment across all ages (Cuzick et al. 2007; Kedar et al. 1994; Powles et al.). Two studies have also identified specific subgroups of women at increased risk of developing venous thromboembolism while on tamoxifen: women who are immobilized in the prior 3 months and/or women who have body mass index (BMI) less than 25 kg/m2. Of note, women were not eligible to join the STAR trial if they had: increased risk of thromboembolic disease from uncontrolled atrial fibrillation; uncontrolled diabetes; uncontrolled hypertension; or prior history

of stroke, deep venous thrombosis, or pulmonary embolus (Breuer and Anderson 2000; Powles et al. ; Visvanathan et al. 2009).

Raloxifene: Raloxifene was associated with a more favorable adverse effect profile compared with tamoxifen in the STAR trial, including a significantly lower risk of thromboembolic disease (statistically significant only for deep vein thrombosis) and uterine cancer and lower incidence of benign uterine hyperplasia, cataracts, and cataract surgery (Breuer and Anderson 2000). A retrospective analysis of data from the NSABP-P1 and STAR trials on the incidence of gynecologic conditions in postmenopausal women demonstrated that women who received raloxifene also had a statistically significant lower incidence of ovarian cysts, endometrial polyps, hot flashes, vaginal discharge, and vaginal bleeding and had fewer gynecologic procedures performed compared with women who received tamoxifen (Reis et al. 2001). Results of a substudy, known as Co-STAR, to assess cognitive differences between women in the tamoxifen arm compared with the raloxifene arm were also published (Powles et al.). The analyses included follow-up data on two thirds of the patients at 1 year and one third at 2 years. No significant differences in mean cognitive scores between women taking tamoxifen and raloxifene were observed at baseline or during subsequent visits. The women who took part in this study were younger and it should be noted that they were more likely to have attended some college, undergone a hysterectomy, reported prior estrogen usage, and had hypertension or diabetes compared with women who did not participate in Co-STAR (Banegas et al. 2013; Powles et al.).

Systematic Literature Review

The studies (K=9) in our review primarily focused on the real or hypothetical decision towards uptake of chemoprevention among women at high risk of breast cancer (Appendix 1). Since

uptake rates was not measured in a uniform way throughout all studies reporting of uptake was different across the studies. Uptake rate was lowest (4.7%) in a prospective survey post-intervention carried out at Memorial Sloan –Kettering Cancer center (Table 2). The overall decision to start chemoprevention ranged from 4.7-47% affirmative in the reviewed studies. About an average of 70% women declined chemoprevention. Only 1 study measured the uptake of chemoprevention immediately after the intervention, while others did after a follow up of 3months to 14 months (Table 2). The studies defined uptake as participants' decision to start chemoprevention therapy. Study 2 required their participants to discuss the therapy with their physicians and further their decision to start therapy. The presence of a control group indicates a stronger study design. Only three studies had a control group to test the true effect of intervention. The uptake rates were about 10% on an average in the target population.

Breast Cancer Risk Assessment:

According to the NCCN women ≥ 35 years of age without a BRCA 1/2, TP53, or PTEN mutation; a strong family history of breast cancer; a history of thoracic radiation before age 30; or a history of LCIS should have their risk for breast cancer estimated using the Gail model. A woman with 1.7% or greater 5-year actuarial breast cancer risk as defined by the Gail model are eligible for risk-reducing strategies (Bober et al. 2004).

What is the probable solution?

Pre-cursors to effective decision making regarding chemoprevention

Disease Factor

- Lack of appropriate breast cancer risk communication.
- Ineffective breast cancer risk perception.

Drug Factor

- Inappropriate information presentation.
- Higher risks compared to benefits.

Individual Trait

- Inherent attitude towards risk.
- Individuals' behavior towards prevention.
- Inability to make complex risk benefit decisions

Previous Knowledge

- Just knowledge about the adverse events of chemoprevention may be highly aversive.
- Complete patient knowledge is important.

The factors and barriers to chemo-prevention should be studied.

Drug Risk Communication

Risk communication when done effectively can improve awareness of health risks and promote risk-reducing behavior in support of health promotion and disease prevention. One of the many challenges to risk communication among patients is the difficulty in expressing complex information in an easily comprehensible manner. Universal cognitive limitations cause biases in interpreting numerical probabilities (Ancker et al. 2006). A well designed visual display can reduce the amount of mental computation by replacing it with automatic visual perception.

Two main approaches to communicating statistical risk information especially for diseases like breast cancer (i.e., visual and verbal representations) have been used and disseminated in a variety of ways. As with nonverbal communication, which may function to complement, substitute for, emphasize, contradict, or repeat verbal content—visual representations of evidence likely serve varied purposes with different outcomes as well. Use of scientific evidence, which often resides in statistics, frequently forms a foundation for judgments and decision making relating to many domains, including health risk appraisals associated with genetics. In health communication, statistics are frequently used to gain attention and to provide a context within which individuals can evaluate their personal health status with regard to what is defined as “normal”.

Perceivers are likely to judge the quality of evidence in part by whether they regard it to be comprehensible, with comprehension defined as understanding based on the integration of the ideas with related frame-works of meaning (Hughes, Whittlesea and Luscombe 2002). Thus, comprehension likely undergirds subjective constructions of meaning associated with the use of evidence and relates to the strategies used to communicate ideas in a message, as well as individual experience with efforts to assimilate or construct meaning based on these strategies.

Davis and colleagues, for example, conducted a randomized trial to test the effects of different printed pamphlets on receipt and perceptions of immunizations, finding that the addition of instructional graphics to illustrate the process and procedures raised comprehension scores.

Graphic Information Representation

A systematic review showed no differences in behavior after viewing asterisk and face displays. A qualitative study found that women considered human figure icons to be more meaningful, easier to understand, and easier to identify with than bar charts (Schapira, Nattinger and McAuliffe 2006). A focus group comprising of women, with lower mean age and educational level, perceived risk of breast cancer as larger when it was shown as a part-to-whole human icon display than when it was shown as a part-to-whole bar graph. When multiple icons were represented, they perceived it to be population risk while a single icon was perceived as individual risk. With visual forms of communication found that judgments related to comprehension include “clarity,” “salience”, and “complexity” (Childers and Houston 1984). With increasing frequency, researchers outside the field of communication have advanced the premise that visual representations of health information can substitute for/or complement verbal information to promote comprehension and retention of message content

Text Information Representation

One of the studies indicated, text descriptions of statistical data about interactions between disease and genetics were better understood and perceived as higher quality evidence than bar charts of the same data (Ancker et al. 2006). Poor comprehension was associated with impressions that the evidence was of poor quality and was not persuasive.

What is a Decision Aid?

Patient decision aids are interventions for preparing patients and assist in decision making about professional care options. Decision aids are defined as 'interventions designed to help people make specific and deliberative choices among options by providing (at a minimum) information on the options and outcomes relevant to the person's health status. Effective message formats have been known to improve knowledge (Ravdin 2010). They create realistic expectations by providing a complete picture of the benefits and risks, reduce decisional conflict and enhance reader participation in the decision-making process (Childers and Houston 1984). Decision aids are effective tools in healthcare. They have been used to assist decision making in various cancer therapies, preventive therapies like Hepatitis B vaccine and hormone therapy at menopause, clinical trial entry decisions and end-of life decisions such as resuscitation in seniors. The most effective way to build a decision aid is an effective message format.

An effective decision aid should:

1. Effectively communicate the disease risk
2. Reduce confusion among patients by information presentation
3. Motivate change towards preventive action

4. Provide appropriate prevention information
5. Enable tailoring of risk based on interventions

Need for Effective Message Format

According to the factors in the Gail risk score, about 21% women in America are defined as 'high risk' of getting breast cancer, they have a relative risk of 1.66 or higher (Freedman et al. 2003). However, these women are subject to a process of conflicting decision making. Women who consider an option of chemoprevention require:

1. A true understanding of their personal breast cancer risk
2. Complete information on lifestyle changes, breast screening, benefits and harm associated with chemoprevention
3. Guidance with decision making

A decision tool will help practitioners disseminate information on chemoprevention in an effective manner. Presenting a decision aid will help reduce physician time while providing information in an efficient way. The NCCN guidelines mandates counselling about chemoprevention when a woman has a Gail model 5-year breast cancer risk ≥1.7% or a history of LCIS (Freedman et al. 2003).

A study in Canada used a decision aid for Tamoxifen. The study developed a decision aid for a safer drug approved by the FDA for chemoprevention, raloxifene. The tested written and graphic decision aids (Bober et al. 2004). The aim of developing an updated decision aid is to improve patient understanding and reduce decisional conflict while creating realistic outcome expectations. Previous study combined decision aid with counselling.

Significance

Several studies have looked at attitudes of women towards BC prevention and chemoprevention, and physician prescribing behavior of these chemo-preventive agents. However, none have looked at the underlying factors governing the low uptake amongst high risk women. Is the adverse event profile or the lack of appropriate knowledge governing the current behavior? This study will provide a deeper understanding of the beliefs that govern the current behavior, while giving a glimpse into this multifaceted issue of BC chemoprevention. It will help us understand the barriers to uptake of therapy and factors enhancing the acceptance of this highly effective prevention therapy within our target population.

The study will help tailor interventions while giving an insight into the minds of the patients. Cancer is a complex disease and severely hampers the lives of the patients. It is not just the patient, but the disease negatively impacts their respective families, employers, including work hours lost, which as a whole affects the society.

Several factors could be a pre-cursor to the low uptake. It could be attributed to patients' reluctance to take the therapy. A small study showed only two out of 43 eligible women agreed to take chemo-preventive therapy (Waters et al. 2010). An alternate reason could be, the patients feel that the potential adverse events outweigh the benefits. Calculating the risk and the benefits is a very complex decision dominated by several factors.

While patient education plays a big role in healthcare, just knowledge about the adverse events of chemoprevention may often be highly aversive, leaving women with an assumption that the potential of adverse events may be higher than the risk of developing breast cancer. Informing women about the potential risk and highlighting the number of people saved by this treatment

could affect their perceptions and may address this issue of low uptake (Waters et al. 2010; Waters et al. 2007). However, communicating the risks and benefits of treatment should be done with careful consideration of patient autonomy.

A major factor is that only 37% of physicians prescribe chemoprevention therapy, but a probable reason maybe the lack of acceptance of such a therapy by the patients (Ravdin 2010). As literature repeatedly points that, weighing the potential risks and benefits and producing an estimate of the net benefit is a complex process and it is possible that very few physicians and patients engage in this process in a thoroughly informed way. The circumstance is in dire need of further research to understand the patient which further influence their physicians.

This study could help develop a tool or an intervention to make women more cognizant of the more-complex end points, like the subjective measures in relation to their quality of life. While there are several tools to measure risk of breast cancer among women, similar tools for chemoprevention can have a significant impact on the uptake of chemoprevention (Ravdin 2010). Reducing the perceived barriers and enhancing the perceived benefits and cues to action can influence their uptake.

This study would precede the development of educational interventions tailored to reduce the burden of BC mortality and in turn improve the patient quality of life. This view is consistent with the observed decline in mortality due to early detection and use of preventive therapies (Cyrus-David et al. 2009). From the economic perspective, prevention of breast cancer will save billions of dollars not just in direct medical costs but also indirect costs. The study benefits the manufacturers, regulatory personnel by increasing patient safety and managed care.

This study will help improve comprehension of the materials and decision aid provided to women, by understanding their perceptions and improving comprehension. It will help physicians reduce their time and effort while providing information in a more efficient manner. The NCCN guidelines requires a practicing oncologist to calculate the breast cancer risk of their patients. Based upon the Gail Risk Score, they have to counsel patients about chemoprevention.

While this study adds to the existing literature, more research is needed to implement a nationwide program that can affect millions of lives.

CHAPTER THREE

Theoretical Framework

Theory Used

Self-protective behavior among humans is the key to survival and evolution. Expectancy-value models are very heavily used to explain these behaviors and beliefs. Commonly used expectancy-value models include protection motivation theory (PMT), theory of planned behavior (TPB) and health belief models (HBM) (Ajzen 1991; Ajzen and Fishbein 1977; Ralph et al. 2014; Rosenstock, Strecher and Becker 1988).

While preventive behavior in BC has been described by various theoretical model, a scant few have looked at chemoprevention specifically. The low acceptance of chemoprevention negates the effect of subjective norm, hence making TPB less favorable. Social support theory describes cancer and preventive behavior as stress enhancing agents, which can be alleviated by a strong support system. Most of the studies in breast cancer prevention are using HBM, making it the most suitable choice for studying chemoprevention.

Cognitive transactional model of stress expresses prevention as a way to cope with anxiety associated with BC. Other models focus on locus of control and a belief that coping and prevention of the disease is beyond their volition of control. Another concept looked at prevention as a dynamic process moving through various stages of contemplation to action within the trans-theoretical model.

Health belief model (HBM) is one of the most widely used model to understand human behavior. According to the assumptions of the model, people engage in healthy behavior and health promotional activities as they value health (Rosenstock, Strecher and Becker 1988). Its widespread

use in vaccine uptake, prevention therapy will help us understand the barriers to uptake of chemoprevention (Reiter et al. 2009; Yarbrough and Braden 2001).

HBM is a multidimensional, interactive, multifactorial framework which expects the reduction in susceptibility and severity to a disease serves as a motivational factor to practice preventive behavior. Beliefs about benefits of chemoprevention are weighed against the barriers, mainly the adverse events of chemoprevention. Cues from the environment shape their beliefs about the benefits and barriers (Rosenstock, Strecher and Becker 1988; Strecher and Rosenstock 1997; Yarbrough and Braden 2001).

The model is best utilized with respect to its ability to predict behavior, thereby providing healthcare professionals with a blue print for intervening with women at high risk of developing BC and their response to the uptake of chemo-preventive therapy.

Perception:

Perception is a process by which humans interpret and organize sensation to produce a meaningful experience of the world (Lindsay and Norman 2013). For example, when a person confronts a situation or stimuli, they interpret it into something meaningful based on their prior experience and overall understating of that situation or stimuli. However, the reality may be different from what the person perceives or interprets.

Decision Making

Decision making involves probabilistic information involving the risks and benefits. Communication of probabilistic information is difficult and essential. It is difficult for people to comprehend concepts of probability and uncertainty. Individuals today are posed with a complex decision of cancer chemoprevention. Ideally, individuals are required to understand not only

their cancer risks but also the relative harm and benefit associated with each possible course of action that they might choose (chemoprevention, prophylactic surgery). This understanding involves two important steps:

1. Knowing which risks are small and which ones are large (i.e., a "quantitative assessment" of risk)
2. Considering more thoroughly the multitude of factors that may influence those risks or result from them (i.e., a "qualitative assessment" of risk).

An information source that is developed on well-known cognitive principles is likely to be more effective and cognitively accessible (Day 1988; Day 2006).

Graphic and visual elements along with verbally oriented elements not only convey a message about a product but also attract consumer attention (Houston, Childers et al. 1987). Holbrook and Moore argue that, in general, pictures promote a more holistic and integrative form of processing, than do words (Holbrook and Moore 1981). Research on the inclusion of pictures could be broadly classified into two categories specifically, one that tests effects of pictures on consumer attitudinal response and other that tests effects of pictures on consumer memory. It is worthy to study the effects of pictorial information on memory because the impact of internal information throughout the consumer decision process (Houston, Childers et al. 1987). Research in cognitive psychology provides substantial evidence that in a wide variety of memory tasks pictures are remembered better than words (Paivio 1971; Alesandrini 1983). Patients exposed to text combined with pictured warnings as compared to text-only warnings had better compliance. Similarly, Young and Wogalter reported that pictorial icons improved recall and comprehension (Young and Wogalter 1990).

A literature done on picture-text learning, and describe the effects of supplementing text with pictures as being "positive, potent and pervasive" (Levin and Lesgold 1978). Levin (Levin 1979) suggests that combining pictures with text results in the following positive functions:

1. Motivation – pictures may have a motivating effect, thereby increasing the likelihood that the text will be read carefully,
2. Reiteration – pictures may repeat the information presented in the text providing additional exposure (redundancy) to the textual concept. Levin describes this as the "two exposures are better than one" concept,
3. Organization – pictures may help to organize the content of the text into meaningful groupings,
4. Interpretation – pictures may serve to make relatively abstract or difficult concepts more understandable,
5. Transformation – pictures are in a form which facilitate long-term memory, and
6. Representation – pictures make the material more specific, and provide a second modality through which the text information can be cognitively represented.

The transformation and representation functions have received empirical support, and are best summarized by Pavio's Dual Code theory (VIGILANTE 2003).

Conceptual Model of Patient Use of Healthcare Information for Healthcare Decisions

What happens during information seeking? How do people search for health information? The Health Information Acquisition Model offers explanations to these questions. This model was developed by Freimuth et al. (1989), who were National Cancer Institute researchers evaluating the dissemination of cancer information to the public (Freimuth, Stein et al. 1989).

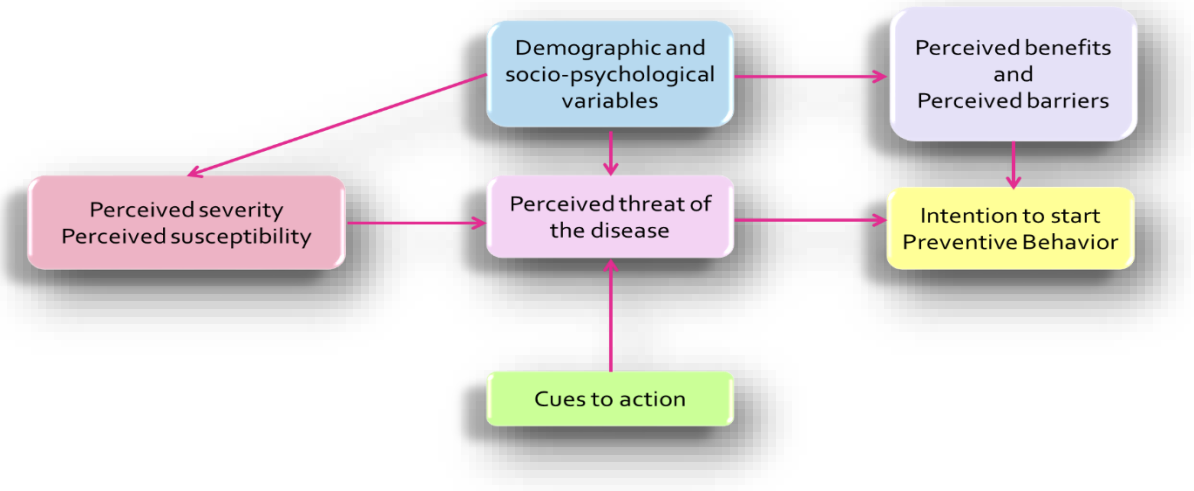
The model is a flow chart depicting the sequence of actions during health information seeking. It is particularly valuable for identifying factors shaping search outcomes. The model accommodates active information seeking as well as passive information acquisition (e.g., television public service announcements).

Health Risk Appraisal

High risk appraisals resulted in a remarkable increase in preventive behavior. The importance of perceived risk, therefore, is its presumed significance as a motivator of behaviors to prevent, detect, and manage cancer in cases other than those involving public policy or medical or employment requirements for compliance. It is assumed that perceptions of risk are related to motivation to act and to action, and that increasing the match between perceived risk (beliefs) and actual risk (reality) will encourage individuals to initiate and maintain preventive and treatment behaviors at a level that is appropriate to their actual risk and its source.

Health Belief Model

Figure 2: Health Belief Model



The Health Belief Model states that behavior change is a function of perceived threat of a negative health outcome and the perceived benefits minus barriers to taking some course of preventive action (Rosenstock, Strecher and Becker 1988). When perceived threat is high, the relative balance of benefits and barriers determines the likelihood of change occurring. The risk information generally provided HRA feedback might influence a user's perceived susceptibility, but it has no means of addressing perceived benefits and barriers. What is the effect of heightening perceived risk without addressing the barriers to reducing the risk?

Perceived susceptibility- Individuals vary widely in their feelings of personal vulnerability to a condition (in the case of medically-established illness, this dimension has been reformulated to include such questions as estimates of re-susceptibility, belief in the diagnosis, and susceptibility to illness in general'). Thus, this dimension refers to one's subjective perception of the risk of contracting a condition.

Perceived severity- Feelings concerning the seriousness of contracting an illness (or of leaving it untreated) also vary from person to person. This dimension includes evaluations of both medical/clinical consequences (e.g., death, disability, and pain) and possible social consequences (e.g., effects of the conditions on work, family life, and social relations).

Perceived benefits.-While acceptance of personal susceptibility to a condition also believed to be serious was held to produce a force leading to behavior, it did not define the particular course of action that was likely to be taken; this was hypothesized to depend upon beliefs regarding the effectiveness of the various actions available in reducing the disease threat. Thus, a sufficiently-threatened individual would not be expected to accept the recommended health action unless it was perceived as feasible and efficacious (Cyrus-David et al. 2009).

Perceived barriers.-The potential negative aspects of a particular health action may act as impediments to undertaking the recommended behavior. A kind of cost benefit analysis is thought to occur wherein the individual weighs the action's effectiveness against perceptions that it may be expensive, dangerous (e.g., side effects, iatrogenic outcomes), unpleasant (e.g., painful, difficult, upsetting), inconvenient, time-consuming, and so forth (Strecher and Rosenstock 1997).

The combined levels of susceptibility and severity provided the energy or force to act and the perception of benefits (less barriers) provided a preferred path of action. However, it was also felt that some stimulus was necessary to trigger the decision-making process. This so-called cue to action might be internal (i.e., symptoms) or external (e.g., mass media communications, interpersonal interactions, or reminder postcards from health care providers or in the current study a decision aid). Unfortunately, few HBM studies have attempted to assess the contribution of cues; to predicting health actions. Finally, it was assumed that diverse demographic, socio-

psychological, and structural variables might, in any given instance, affect the individual's perception and thus indirectly influence health-related behavior.

The concept of decision making is derived from the work of Janis and Mann (1977) that indicates the ways in which people weigh the costs and benefits. Decision making is the concept of an implicitly innate psychological cost/benefit mechanism that is important in driving and/or directing (health) behavior.

Rohrmann's Risk Model:

According to the Rohrmann's risk model it is important to be conscious of differences between physical and psychological phenomena, and to distinguish between people's judgments, attitudes and behaviors with respect to risk situations. The conceptualization of "risk" should be a multi-disciplinary. It connects insights from domains like engineering, geography, economics and psychology in order to create suitable and valid characterizations.

The model describes risk perception, risk attitudes and risk communication as a precursor to risk management.

Risk perception refers to people's judgments and evaluations of hazards they (or their facilities, or environments) are/or might be exposed to. Such perceptions steer decisions about the acceptability of risks and are a core influence on behaviors before, during and after a disaster. People's risk appraisals are a complex result of hazard features and personal philosophies.

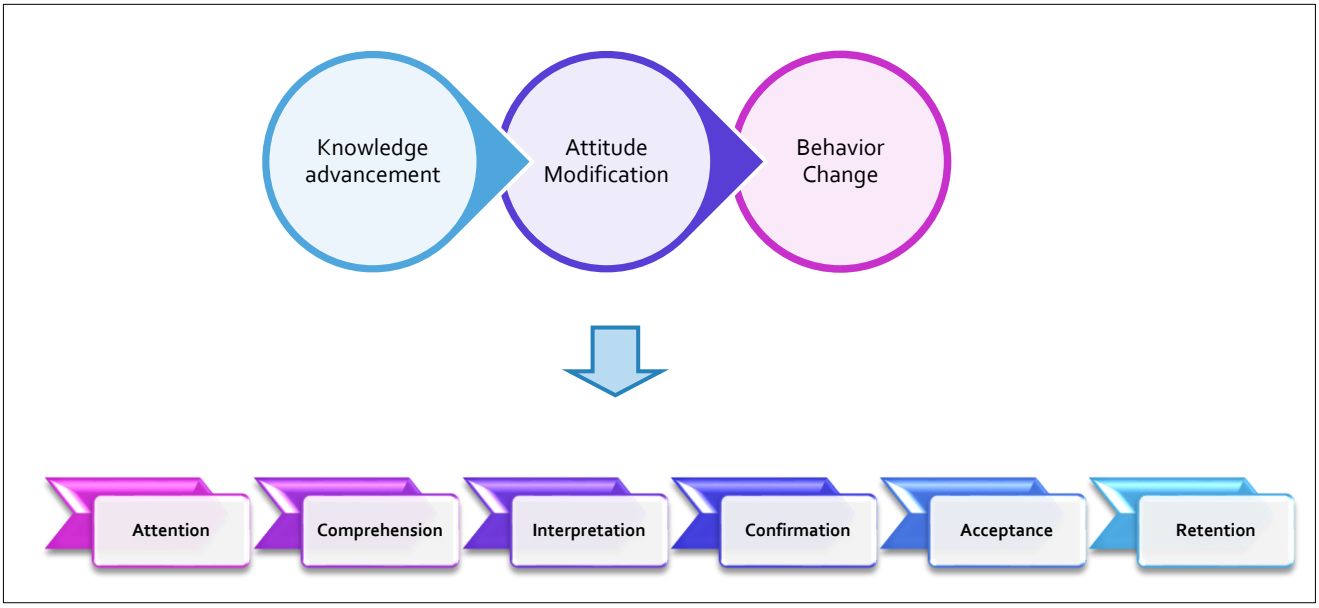
Risk attitudes are people's intentions to evaluate a risk situation in a favorable or unfavorable way and to act accordingly. The underlying traits are risk propensity and risk aversion, i.e. cautiousness. High risk propensity can induce hazards; on the other hand, risk management

activities may require some risk propensity. However, risk attitudes are neither necessarily stable, nor homogeneous across hazard types.

Risk communication is a social process by which people become informed about hazards, are influenced towards behavioral change and can participate in decision-making about risk issues in an informed manner. Such activities are part of almost all emergency management efforts. For effective risk communication, a sound understanding of risk perceptions and attitudes is indispensable.

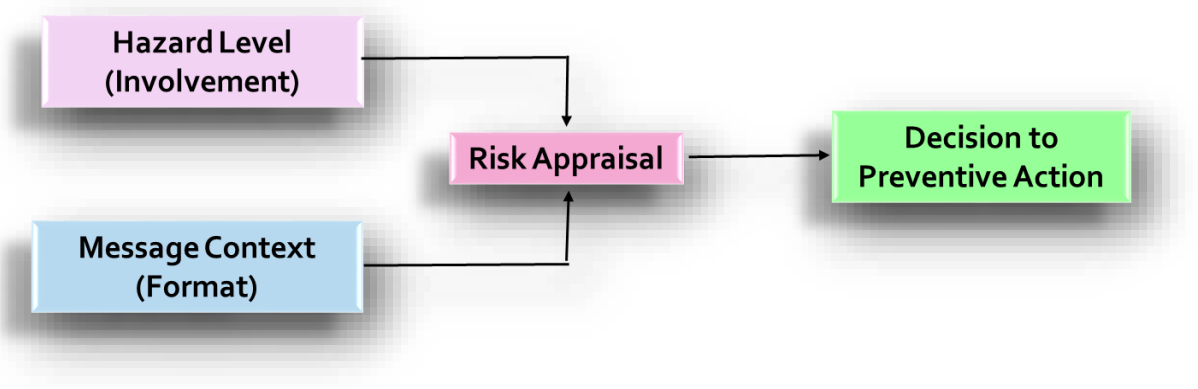
Risk management are manifold procedures for reducing risks (either the hazard itself or its consequences) to a level deemed tolerable by society; this includes monitoring, control and public communication. For people exposed to a hazard (residents, employees, commuters, consumers, etc.), their preparedness is the critical goal, regarding both the occurrence and the impacts of an accident/disaster. This cannot be achieved without skillful risk communication.

Figure 2a: Process of Risk Persuasion



The main question to be answered is 'What factors govern the outcomes of hazard information and education efforts; what determines success or failure?' There are multiple factors which affect these outcomes and preventive actions. These can be analyzed with respect to the principal steps of persuasion and attitude change processes. Attention + comprehension + interpretation + confirmation + acceptance + retention (+ behavior change). Difficulties are both technical and psychological in nature, ranging from information distribution and storage problems to lack of involvement and inertia. Biased risk perception, overconfidence in the existing safety level and "optimism bias" add to the problem. Authorities might believe in a path "knowledge advancement - attitude modification - behavior change" but obviously such a process cannot be relied on.

Figure 2b: Risk Communication Process Framework



Involvement

Involvement is a concept that is borrowed from the motivation theory. Motivation explains the process of individual behavior. The concept of involvement was linked to marketing following Krugman's (1967) measurement of involvement with advertising. Since then, and especially in the 1980's, intensive attention from consumer researchers has generated a bulk of literature which has conceptualized and measured involvement in multiple contexts including involvement with: a product class (e.g., (Laurent and Kapferer 1985; Zaichkowsky 1985; Rahtz and Moore 1989; Kapferer and Laurent 1993; Zaichkowsky 1994; Michaelidou and Dibb 2006) a purchase decision (e.g.(Slama and Tashchian 1985; Mittal and Lee 1989; Smith and Bristor 1994), a service (Keaveney and Parthasarathy 2001) advertising or message processing (Mitchell 1981; Petty, Cacioppo et al. 1983; Vaughn 1986; Laczniak, Muehling et al. 1989; Zaichkowsky 1994). Zaichkowsky (1985) defined involvement as "a person's perceived relevance of the object based on inherent needs, values and interests" (p. 342). Celsi and Olson (1988) further explicate involvement as essentially perceived personal relevance. Perceived relevance is a function of a consumer's perceptions of his/her needs, goals and values and their congruence with the consumer's knowledge of the product category. More specifically, the personal relevance of a

product is represented by the perceived linkage between an individual's needs, goals, values (self-knowledge) and their product knowledge (attributes and benefits). The greater the perceived linkage, the stronger are the feelings of personal relevance to the product category. Irrespective of the specific variations in defining involvement, there is a consensus among many researchers that the essence of involvement is perceived personal relevance (Petty, Cacioppo et al. 1983; Zaichkowsky 1985; Celsi and Olson 1988; Higie and Feick 1989).

Involvement can be viewed as the motivation to process information (Sansgiry, Cady et al. 2001). Involvement refers to "the level of perceived personal importance and/or interest evoked by a stimulus (or stimuli) within a specific situation". This definition implies that aspects of the person, the product, and the situation all combine to determine the consumer's motivation to process product related information at a given point in time. It has been suggested that an individual's level of involvement affects product-related information searching and decision-making (Engel, Kollat et al. 1973) as well as his/her processing of persuasive communications and resultant attitude change (Petty, Cacioppo et al. 1983). Highly involved consumers process information actively (Krugman 1965; Engel, Kollat et al. 1973) and therefore their attitudes would be expected to polarize.

When consumers are intent on doing what they can to satisfy a need, they will be motivated to pay attention and process any information felt to be relevant to achieving their goals. On the other hand, a person may not bother to pay any attention to the same information if it is not seen as relevant to satisfying some need. To the degree that there is a perceived linkage between a consumers' needs, goals, or values, and product knowledge, the consumer will be motivated to pay attention to product information. When relevant knowledge is activated in memory, a

motivational state is created that drives behavior (e.g., shopping). Thus, type of information processing depends upon the consumer's level of involvement. It can range from simple processing, where only the basic features of a message are considered to the one all the way to elaboration, where the incoming information is linked to one's preexisting knowledge systems.

While consumer researchers have adopted various conceptualizations of involvement, it is commonly accepted that there are following two distinct types of involvement (Houston and Rothschild 1978; Laurent and Kapferer 1985; Richins, Bloch et al. 1992).

Enduring involvement (EI) is defined by Richins & Bloch (1986) as "an ongoing concern with a product," and is due to internal consumer characteristics that define certain products as inherently interesting to an individual (Childers and Houston 1984). Enduring involvement is also referred to as intrinsic involvement. It indicates the level of interest a consumer has in a product. This involvement is generally stable and cannot be changed easily.

a. **Situational involvement** (SI), "occurs only in specific situations, such as a purchase". SI reflects adaptation to external circumstances, rather than individual characteristics, and is often heightened by the need to make a choice regardless of enduring involvement with the product (Bhansali et al. 2016). In the current, SI will be manipulated and measured.

Involvement Level

In most contexts the notion "risk" stands for a danger of unwanted and unfortunate events, not just uncertainty about the potential outcomes of an incident. Accordingly, "risk" can be defined as the possibility of physical and/or social and/or financial harm/ detriment/ loss due to a hazard

within a particular time frame. "Hazard" refers to a situation, event or substance that can become harmful for people, nature or human-made facilities. A hazard is a physical entity while risk is not; it is an inference about the implications of a hazard for people (or nature, or assets) exposed to it (Rohrmann 2002; Taylor and Taguchi 2005). People at risk might be residents, employees in the workplace, consumers of potentially hazardous products, travelers/ commuters and/or the society at large.

Message Format

The format in which information is communicated has been shown to influence comprehension and its impact on perception and health outcomes. Moreover, certain formats have been shown to affect decision making. The most widely used graphical formats for numerical information are tables and graphs. There seems to be general agreement that graphical formats, in comparison with textual information, are better able to accurately communicate risk information, although contradictory evidence has also been published. Communicating quantitative risk information in the clinical setting is a difficult task. The use of numeric terms and graphic displays may increase the specificity of information provided but also may introduce format effects on risk perceptions. Health communicators should be consistent in their use of format in order to minimize unintended effects while enhancing patient understanding and ability to participate in the decision-making process (Schapira, Nattinger and McAuliffe 2006).

Graphic Format

Graphic and visual elements along with verbally oriented elements not only convey a message about a product but also attract consumer attention.(Childers and Houston 1984) Holbrook and Moore argue that, in general, pictures promote a more holistic and integrative form of processing, than do words.(Moore et al. 2007) Research on the inclusion of pictures could be

broadly classified into two categories specifically, one that tests effects of pictures on consumer attitudinal response and other that tests effects of pictures on consumer memory. It is worthy to study the effects of pictorial information on memory because the impact of internal information throughout the consumer decision process (Childers and Houston 1984). Research in cognitive psychology provides substantial evidence that in a wide variety of memory tasks pictures are remembered better than words (Paivio 1971). Patients exposed to text combined with pictured warnings as compared to text-only warnings had better compliance. Similarly, Young and Wogalter reported that pictorial icons improved recall and comprehension.(VIGILANTE 2003) The transformation and representation functions have received empirical support, and are best summarized by Pavio's Dual Code theory.

Written Format

An alternate evidence suggests, graphic information when presented should match the schema of the minds of its readers as the original intention of the graphic. The icons and figures may not represent what it originally intended to. The perceived information may differ in the minds of the end readers. It had been commonly examined in pictograms presented in healthcare. Since every individuals differ, even a widely tested graphic may cause conflict in the minds of different individuals. The role of gender, race, ethnicity, economic background and region have a significant effect on perception of graphic information.

The theory of Chunk hierarchy and Retrieval structures (CHREST) indicates, when information is presented in a logical manner, it is comprehended more effectively. This is due to improved processing of information. When written information is presented in a manner that matches the schema in the minds of the readers, it leads to representational congruence. Thus when numbers

and statistical information representing like information (eg. benefits or risks) should be chunked together (Bhansali et al. 2016). Using the theories of information processing and CHREST a written decision aid was developed.

Risk Appraisal

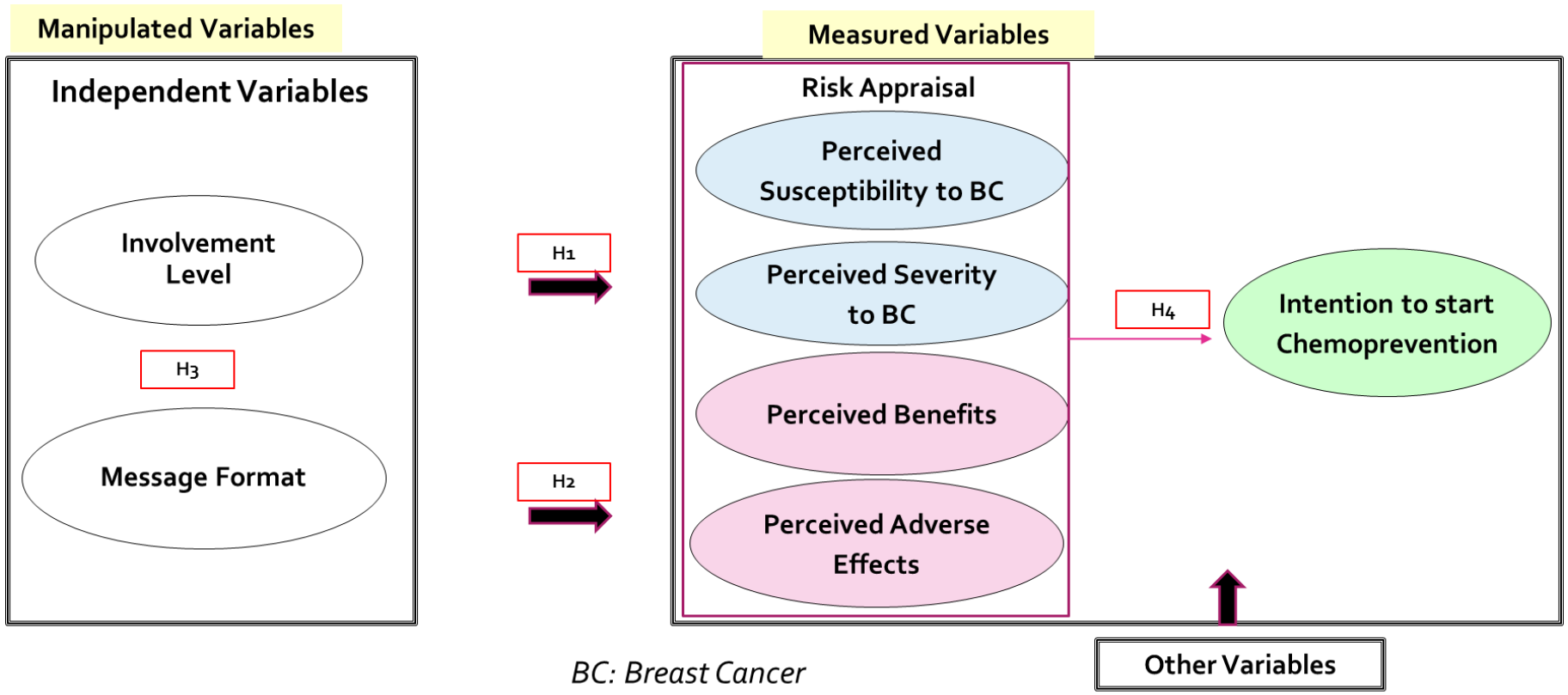
People's judgments and evaluations of hazards they (or their facilities, or environments or diseases) are or might be exposed are called "risk perception". Risk perceptions are interpretations of the world, based on experiences and/or beliefs. They are embedded in the norms, value systems and cultural idiosyncrasies of societies.(Rohrmann 2002; Rohrmann 2005) Every human is occupied with risk perception most of the time, whether driving a car or thinking about residence safety or worrying about fires in an environment and so on. It is notable that most people have views about every risk, regardless of whether they are exposed to it or not. Strictly speaking risks cannot be “perceived” (like a size or speed or the weather). Yet "risk perception" has nonetheless become the standard label of the respective research topic. Risk perceptions steer decisions about the acceptability of risks and are a core influence on behaviors before, during and after a disaster. However, neither perceptions of nor attitudes towards risk should be taken as equivalents of actual behavior. People's risk appraisals are a complex result of hazard features and personal philosophies. The conceptual risk perception model shown in Figure 2 reveals the multiple influences which affect responses to risk exposure.

Proposed Model

The proposed model is developed using the Rohrmann’s risk model and the health belief model. The hazard level here is the involvement level. Hazard was defined as the source of risk, which was breast cancer as a disease. According to the Rohrmann’s risk model the level of hazard in

association with the risk communication affects the manner in which individuals appraise their risk. Risk communication was the message format of the drug used to lower the hazard. The manner in which risk is appraised is a pre-cursor to the drug their risk reducing behavior which is our model is intention to start chemo-prevention. The constructs of health belief model have been used to measure the way risk is perceived and appraised. Risk appraisal was measured using constructs: Perceived susceptibility to breast cancer, perceived severity to breast cancer, perceived benefits of chemoprevention and perceived risks of chemoprevention. Finally the outcome of intention to initiate preventive action was measured. Several factors were controlled for, including the effect of comprehension of the drug risk information provided in the form of a decision aid (graphic and written) for drug A (Raloxifene) and Drug B (Control) on the risk perception. The effect of individuals overall health status and perception towards preventive action was also measured and controlled for. The intrinsic behavior of patients can have an effect on the manner in which patients decide to start chemo-prevention. The study, examined the factors and barriers that affect patients decision to start Raloxifene, and if the content and context of the message impact the decision making process.

Figure 4: Operational Model



Operational Definitions

Perceived Susceptibility: subjective perception of the risk of developing breast cancer (4 items)

Perceived Severity: evaluations of both clinical and social consequences of developing breast cancer (3 items)

Perceived Benefits: beliefs regarding the effectiveness of chemoprevention in reducing breast cancer threat (2 items)

Perceived Adverse Events: Potential negative aspects of a chemoprevention may act as impediments to undertaking the recommended behavior (4 items)

Other Factors:

Patient related:

- Age
- Race
- Level of education
- Current menopause status
- Overall health status
- Marital Status
- Product Knowledge

Cancer related:

- Previous breast biopsy
- Previous hysterectomy
- History of breast cancer
- History of chemoprevention
- Family history of breast cancer

- Friends experience with breast cancer

Knowledge related:

- Previous knowledge about chemoprevention
- Previous knowledge about Raloxifene

Research Hypothesis

Considering the above model developed and the constructs discussed, following hypotheses will be tested.

Effect of Involvement level

H1: There is an effect of involvement on intention to start chemoprevention

H1a: There is an effect of involvement on perceived susceptibility to breast cancer

H1b: There is an effect of involvement on perceived susceptibility to breast cancer

H1c: There is an effect of involvement on perceived benefit to breast cancer chemoprevention

H1d: There is an effect of involvement on perceived risk to breast cancer chemoprevention

Effect of Message Format

H2: There is an effect of message format on intention to start chemoprevention

H2a: There is an effect of message format on perceived susceptibility to breast cancer

H2b: There is an effect of message format on perceived susceptibility to breast cancer

H2c: There an effect of message format on perceived benefit to breast cancer chemoprevention

H2d: There is an effect of message format on perceived risk to breast cancer chemoprevention

Interaction effect of Involvement and Message Format

H3: There is a combined effect of involvement and message format on intention to start chemoprevention

Note: Further evaluation of other interactions based on variables stated in subsections of hypotheses H1 and H2 will be conducted only if the interaction effect of involvement and message format is significant.

Effects within Dependent variables

H4: There is an association between perceived susceptibility, perceived severity, perceived risk and benefits with intention to use chemoprevention

CHAPTER FOUR

Methods

Due to the applied nature of this research, concepts from other fields such as marketing, psychology, and consumer behavior were used to develop the methodology. In order to determine the impact of hazard level and drug decision aid, following steps were accomplished:

1) Identification of the study design

2) Development of high and low scenarios to manipulate involvement

3) Development of drug information leaflet to manipulate message format

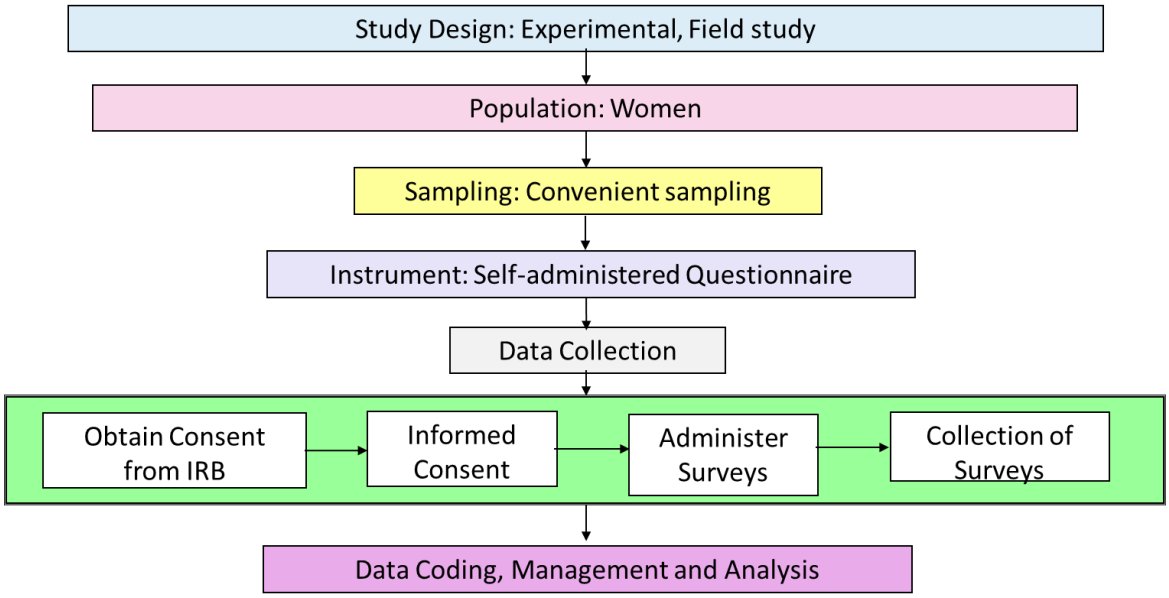
4) Development of instrument for measuring perceived risk susceptibility, perceived severity, perceived benefits of chemoprevention, perceived barriers to chemoprevention as well as respondent demographic characteristics.

5) Collecting the data from desired subjects

6) Data Coding and analysis.

Visual representation of overview of the methodology can be seen in figure 4. Each step will then be discussed in detail.

Figure 4: Summary of the methodology



Study Design

This study was a field experiment. It was a cross sectional study because it involved observation of population characteristics at one point of time. Field studies are strong in realism, significance, strength of variables, theory orientation and heuristic quality.(Kerlinger and Lee 1999) Field Experiments are done in the everyday (i.e. real life) environment of the participants. The experimenter still manipulates the IV, but in a real-life setting (so cannot really control extraneous variables). The advantages of a field experiment are:

i. Behavior in a field experiment is more likely to reflect real life because of its natural setting, i.e. higher ecological validity than a lab experiment.

ii. There is less likelihood of demand characteristics affecting the results, as participants may not know they are being studied.

Note, in a field experiment independent variable are called manipulated variables because the experimenter manipulates (i.e. changes) the variable. In the current study, breast cancer hazard level and drug information format were the manipulated variables. Breast cancer hazard level could occur at 2 levels: high risk level and low risk level and drug information format were manipulated using graphic and written format for raloxifene as Drug A and control as Drug B.

Manipulated Variables

1. Manipulated factor 1: Involvement Level

Involvement was manipulated at 2 levels. The involvement levels represent situations. These situations were based on actual clinical practice examples. The Breast Cancer Risk Assessment Tool or the Gail risk score calculator was used to calculate the risk score.

The Breast Cancer Risk Assessment Tool provides an estimate of a woman's risk of developing invasive breast cancer during the next 5-year period and up to age 90 (lifetime risk) based on the woman's age and the risk factor information provided. For comparison, the tool will then calculate 5-year and lifetime risk estimates for a woman of the same age who is at average risk for developing breast cancer. Lifetime risk estimates are higher than 5-year age interval estimates because breast cancer risk increases with years at risk.

Risk estimates calculated by the tool are estimates of absolute breast cancer risk. Absolute breast cancer risk is the chance or probability of developing invasive breast cancer in a defined age interval. One way to evaluate the accuracy of the risk estimate is to determine whether it

correctly predicts average risk in a group of women with the same risk factors and age. The Breast Cancer Risk Assessment Tool does predict such average risks well.

Although a woman's risk may be accurately estimated, these predictions do not allow one to say precisely which woman will develop breast cancer. In fact, some women who do not develop breast cancer have higher risk estimates than some women who do develop breast cancer.

The Breast Cancer Risk Assessment Tool may be updated periodically as new data or research becomes available.

The model uses a woman's own personal medical history, her own reproductive history, and the history of breast cancer among her first-degree relatives (mother, sisters, daughters) to estimate her risk of developing invasive breast cancer over specific periods of time. Data from the Breast Cancer Detection Demonstration Project (BCDDP), which was a joint NCI and American Cancer Society breast cancer screening study that involved 280,000 women aged 35 to 74 years, and from NCI's Surveillance, Epidemiology, and End Results (SEER) Program were used in developing the model. Estimates for African American women were based on data from the Women’s Contraceptive and Reproductive Experiences (CARE) Study and from SEER data. CARE participants included 1,607 women with invasive breast cancer and 1,637 without. Estimates for Asian and Pacific Islander women in the United States were based on data from the Asian American Breast Cancer Study (AABCS) and SEER data. AABCS participants included 597 Asian and Pacific Islander women with invasive breast cancer, and 966 women without breast cancer.

The Gail model has been tested in large populations of white women and has been shown to provide accurate estimates of breast cancer risk. In other words, the model has been "validated"

for white women. It has also been tested in data from the Women's Health Initiative for African American women, and the model performs well, but may underestimate risk in African American women with previous biopsies. The model has been validated for Asian and Pacific Islander women in the WHI and data from SEER. The model needs further validation for Hispanic women and other subgroups. Researchers are conducting additional studies, including studies with minority populations, to gather more data and to test and improve the model.

Other risk assessment tools are more appropriate for women who have a history of certain medical conditions. Below is a list of alternative resources for women with a medical history of:

- Breast cancer or lobular carcinoma in situ (LCIS) or ductal carcinoma in situ (DCIS).

Women with a history of breast cancer have risks of recurrence that depend on the type of breast cancer, its stage at diagnosis, and treatment. A cancer doctor can provide guidance on future risks for breast cancer survivors.

Women with a history of DCIS have risk of invasive breast cancer that depend on type of treatment for DCIS; a cancer doctor can provide information on this risk.

Women with a history of LCIS can use the IBIS Breast Cancer Risk Evaluation Tool to estimate the risk of invasive breast cancer or DCIS.

- Treatment with radiation to the chest for Hodgkin lymphoma

Women who had radiation to the chest for the treatment of Hodgkin lymphoma have higher than average risk of breast cancer.

- A known mutation in either the *BRCA1* or *BRCA2* gene

Women with a known mutation in either the *BRCA1* or *BRCA2* gene can use the BOADICE model to estimate their breast cancer risk.

- Other rare cancer-causing syndromes, such as the Li-Fraumeni syndrome

Women with a known or suspected inherited cancer-causing syndrome should consult a specialist in medical genetics.

The participants were given a risk scenario before they viewed each information leaflet. Scenarios were printed in black on A4 size white paper, double-spaced with 16-point font size. Each participant viewed both the low risk and high risk scenario.

Each risk scenario was developed on actual cases with the assistance of a practicing oncologist. The high risk scenario had a mention of both family history of breast cancer and pre-cancerous growth on a previous breast biopsy. It was also mentioned that their physician strongly suggests chemoprevention initiation. Their overall lifetime risk of getting breast cancer was 40% based on their risk score.

The low risk scenario had a mention of only family history. The patient had a biopsy with no abnormality. Their overall lifetime risk of getting breast cancer was 17% based on their risk score.

2. Manipulated factor 2: Message Format (Decision Aid)

While developing the decision aid the aim was to improve patient decision making process i.e. improve the drug benefit and risk perception to assist in a well-informed decision. The manner in which risk information is presented represents the message context. The information provided

will be for Raloxifene. The content of information was altered by less than 2% to develop a control. Comprehension of information is a pre-cursor to perception. To ensure patients understand the information presented, comprehension was measured and controlled for. However, since the same person will be viewing 2 formats (written and graphic information) of decision aid, a control is essential. The decision aid were developed to be printed on an A4 size paper. Based a previous studies, systematic reviews in risk information presentation in breast cancer and with the expert judgement of a panel of 3 oncologists, the decision aids were developed.

Graphic Information

Previously described well-known cognitive principles were used in development of the decision aid, so that it would assist decision making. Following concepts were adapted:

- **Off-loading** – Provide information through other route i.e. use of pictures or symbols. In the graphic decision aid, previously tested symbols were used to indicate reduction in breast cancer risk. The risk of adverse events was graphically represented. A review by Shapira et al. showed the superiority of representing adverse events using a bar graph. The used commonly identifiable pictures, previously tested in numerous studies to improve decision making.

- **Chunking of information or Segmentation**: Information was divided into sections of benefits and risks.

- **Coding/Naming:** Each section was titled to provide context of the information.

- **Color**: The graphic decision aid used colored icons to highlight the benefits and colored graphs to indicate adverse events. Reduction in breast cancer was indicated using the color pink as pink is associated with breast cancer awareness.

Dual coding theory represents the idea that cognitive processing takes place within the following two separate information processing systems:

1) A visual system that processes visual knowledge from illustrations
2) A verbal system that processes verbal knowledge mediated either by written or the spoken word.

The graphic decision aid was made for drug A (raloxifene) and drug B (raloxifene)

The content of drug information was taken from a meta-analysis of various clinical trials for raloxifene. It was approved by a panel of three oncologist and was tested for content validity by them.

Written Decision Aid

This decision aid were developed devoid of any pictures or graphic information. It consists of information only in the text and numeric form. The written only decision aid had the same quantity of information as compared to graphic information. Since there are no current decision aids in particular used in practice, there is no standard for development of these decision aids. This decision aid was developed using an A4 size paper, with the theoretical concepts of CHREST and information processing. The written decision aid was developed for Drug A (Raloxifene) and for Drug B (Control). Like information was chunked together and the information was presented in bullets.

Measured Variables

Overall there were 5 measured variables for the research model, specifically, perceived susceptibility to breast cancer, perceived severity of breast cancer, perceived benefit of the drug, perceived risk of the drug and intention to initiate the drug.

a. Perceived Susceptibility: Patients' opinion on chances of getting breast cancer based on their personal beliefs and family factors. Perceived susceptibility was measured using a 4-item 5-point likert scale (Cyrus-David et al. 2009).

b. Perceived Severity: Patients' opinion of how serious BC is and the effect of its consequences. Perceived severity was measured using a 3-item 5-point likert scale.(Cyrus-David et al. 2009)

c. Perceived Benefit: Patients' opinion on the efficacy of chemoprevention to reduce risk of breast cancer. This construct was measured using a 2-item, 5 point likert scale.(Cyrus-David et al. 2009)

d. Perceived Risk: Patients' opinion of tangible and psychological costs associated with chemoprevention. This construct was measured using a 4-item, 5 point likert scale.

e. Intention to initiate Drug: Likelihood that the patient will start drug A. Many studies in past have used validated scales to measure intention. This construct was measured using a 1-item, 5 point likert scale.

Manipulation check

The manipulated variables in this study were breast cancer hazard level and drug risk communication. Manipulation for the breast cancer hazard was measured using 5-point semantic differential scale having anchors like how involved, how interested and how motivated the participants felt. Similarly the colorful/colorless, not vivid/ vivid, confusing/ not confusing and easy to read/difficult to read were used to check the experiment manipulations

In addition to the above, the survey instrument also contained questions on demographic information, general health status and general risk perceptions.

Population and Sampling technique

Due to the exploratory nature of this study, random assignment was not possible and hence convenient sampling was deemed to be appropriate. A hypothesis testing type of field study was considered most appropriate for the research question in concern.

Pilot Study and Elicitation phases

Initial elicitations were taken from patients, breast cancer specialists, oncologists and research experts to design the drug information leaflet and finalize the content. After the development of the leaflet, it was submitted for review and suggestions from breast cancer oncologists. Modifications were made to revise the leaflet design and content based on their suggestions and then re-submitted for review. This process was continued until no changes were suggested.

Pilot studies were conducted as a replica of the experiment to determine the logistics and gather information that can improve the quality and efficiency of the questionnaire. The following pilot study protocol was adopted:(Peat, Mellis and Williams 2002; Van Teijlingen and Hundley 2002)

- Administer questionnaire to pilot subjects in exactly the same way as it will be administered in the main study
- Subjects were asked for feedback to identify ambiguities and difficult questions
- Time taken to complete the questionnaire was recorded
- Discard all unnecessary, difficult or ambiguous questions
- Assess whether each question gives an adequate range of responses
- Establish that replies can be interpreted in terms of the information that is required
- Check that all questions are answered
- Re-word or re-scale any questions that are not answered as expected
- Shorten, revise and, if possible, pilot again

Based on the above protocol 3 pilot studies were conducted. First study was conducted on 10 women above 18 years of age. Further, suggestions were obtained to revise the involvement scenarios. Based on the results of first pilot study the decision aids and the questionnaire were modified. After the participants successfully completed the survey, they were asked whether they understood all the questions and instructions in the survey, was the scale adequate and allowed for only one response to each question. If the respondent skipped any question, she was asked the reason for doing so. Also, information on whether any question was offensive or insulting

was obtained. A summary of all the queries was prepared and the questionnaire was edited accordingly.

Institutional Review Board Approval

This research protocol was reviewed and approved by the College of Health and Human Services Human Subjects Review Committee at University of Houston.

Instrument

Demographics Age, academic background, overall health status and breast cancer background were assessed in a self-reported questionnaire. The items included were patient related factors, cancer related factors, and knowledge related factors. Breast cancer backgrounds were distinguished by the following yes/no type questions.

Patient Related Factors

Age, Race, Level of education, Current menopause status, Overall health status, Marital Status

Cancer Related Factors

Previous breast biopsy, previous hysterectomy, history of breast cancer, history of chemoprevention, family history of breast cancer, friends experience with breast cancer

Knowledge Related Factors

Previous knowledge about chemoprevention, previous knowledge about raloxifene

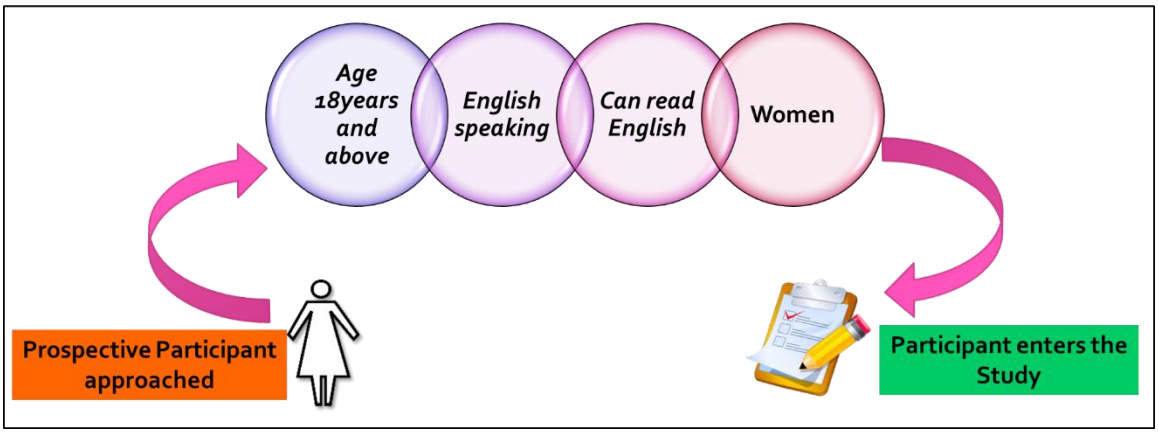
The instrument used to measure was adapted using Champion's health belief model constructs and Breast cancer risk reduction health belief scale. A five-point Likert Scale was used to measure responses. Strongly disagree was scored as one and strongly agree as five.

Risk Appraisal was represented using:

- Perceived susceptibility
- Perceived severity
- Perceived benefits
- Perceived risks

Sample Selection

Figure 6a: Sample Selection Process



As this was a field study a convenient sampling procedure was deemed appropriate. Participants from different areas across Houston were selected on the basis of a set rule. Locations were identified within a mall, parks, gathering areas. In each location, every second participant was approached. If participation was declined the next immediate woman above 18 years was approached. Only women greater than or equal to18 years of age and able to read English were included. Data were collected during all the weekdays and weekends from 9 am to 5.30 pm. The data was collected in the locations of parks and malls on weekdays and weekends alternatively. The aim was to avoid selection bias as much as possible.

Data Collection Process

Figure 6b: Experimental Procedure per participant

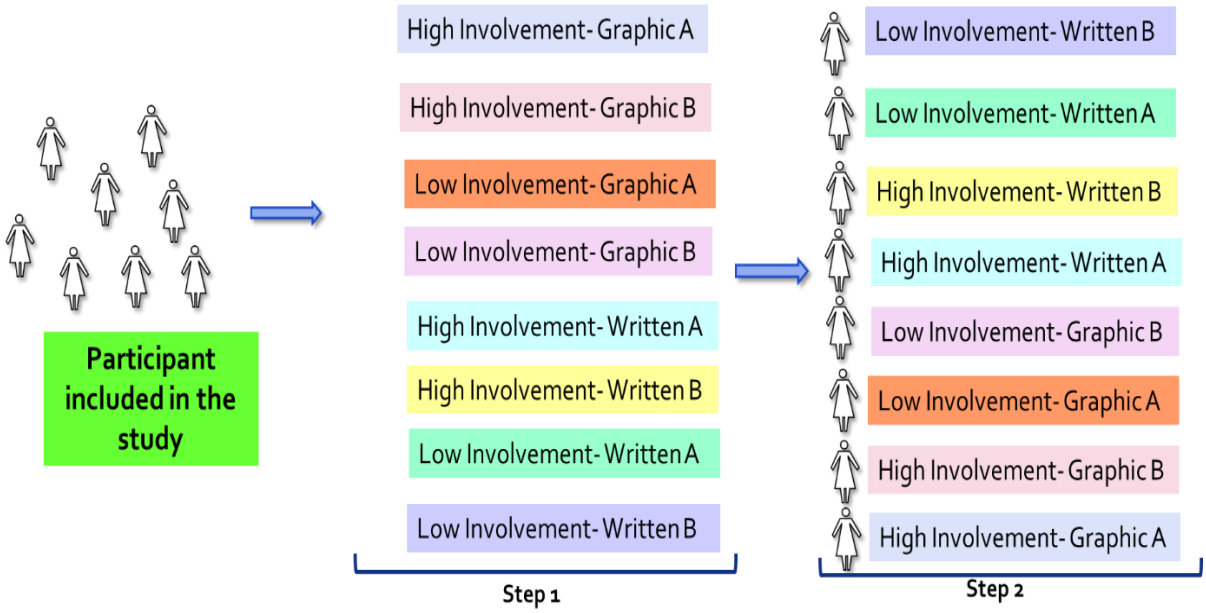


Figure 6 depicts the steps for the experimental process. The data collection procedure was similar to the one used by Grahn (1979) and Sansgiry and Cady (1996). Each individual was approached and requested to participate in the study by reciting a communiqué. After confirming consent to participate in the study, each participant was given a folder. Each participant evaluated 2 decision aid/ message format (graphic or written) for 2 drugs (Drug A and Drug B) at both levels of involvement (low and high). First the participant would read a general introduction to the experiment followed by a low risk scenario, after which they would evaluate the decision aid for Drug A. The participant was informed that s/he would have as much time as s/he needs to read the decision aid information. After the participant completes the evaluation s/he would respond to the questionnaire for that drug. This process would be repeated for the high risk scenario and a different drug decision aid. Finally the participants would respond to the patient, cancer and previous knowledge related questions.

The order in which the participant evaluated the package was randomized. After the participant completes the questionnaire the packet was collected back and questionnaires were collected and stapled. Participants were thanked for their participation and were given a token of appreciation. The Committee of Human Subjects Protection at University of Houston reviewed and approved the study.

Sample Size Determination

To determine the sample size, an *a priori* power analysis was carried out by using the G-Power statistical software, version 3.1. In *a priori* analysis, sample size N is computed as a function of the power required, the pre-specified significance level and the population effect size. It is an efficient method for controlling power before a study is actually conducted (Cohen 1988; Faul, Erdfelder et al. 2007).(Faul et al. 2009) While carrying out the analysis following 4 parameters are very important:

a) Sample size, n

b) Effect size, d

c) Power

d) Probability of Type 1 error/Significance level, α.

Alpha (α) is the probability of making a type I error i.e. rejecting the null hypothesis when it is true. By setting an acceptable level of α, this probability is controlled at the beginning of the experiment. Power is related to the type II error (β) i.e. failing to reject the null hypothesis when it is false. Power is thus expressed as

Power = $1 - \beta$

Thus, power refers to the ability of the test to reject the null hypothesis when it should be rejected which in turn refers to the ability of that test to detect statistically significant differences. Effect size (d) refers to the expected difference between the groups being compared. The value of effect size for small, medium and large magnitude varies for different statistical tests.

Each of the four parameters – alpha (α), effect size (d), power (1- β) and sample size (n) are inter-related. By knowing the value of any three of these parameters, the value of the fourth can be determined.(Cohen 1992) At a given value of first two, the only factor that can affect power is the sample size. If the sample size is too small the power of the statistical test will be too low to detect significant differences. On the other hand, if the sample size is very large, valuable time and resources are wasted, with minimal improvements in power. Therefore, it is very important to have the most appropriate sample size so that, for a given α and d, a sufficiently powerful design can be obtained without overuse of time and resources.

If multiple tests are to be conducted, then the sample size for each statistical test must be conducted. The final sample size of the study should be determined based on the test that requires highest sample size for achieving pre-specified power. For this study, MANOVA: Special effects and interactions were conducted. For MANOVA effect size of 0.0625 was used. According to Cohen 0.10 is considered as small, 0.25 as medium and 0.40 as large (Cohen 1988). Table 1 shows the various effect size and sample size required for MANOVA test at $\alpha = 0.05$, power = 0.95, no. of groups = 8, number of predictor variables= 2, number of response variables= 5.

Table 2: Summary of different effect size used for calculation of sample size for MANOVA

($\alpha = 0.05$; power = 0.95)

Effect size (d)	0.06	0.1 (small)	0.25 (medium)
Sample size (n)	208	127	54

The effect size of 0.06 was considered appropriate for the study.

Data coding:

The data obtained were coded and a codebook was prepared. Data were entered in Microsoft Excel (Version 2013).

Data Analysis

Reliability Analysis

Reliability is defined as the extent to which a measure is accurate and consistent. The instrument in this study measured each variable using several items on a standardized five point scale. For the instrument to be reliable, it is important for all items in a domain to be correlated with each other and to consistently measure the same thing. Reliability analyses were thus performed for all the domains by calculating and reporting inter-item correlations along with Cronbach's alpha.

Note, the survey questions were adopted from pre-validated questionnaire used in the past. Hence, formal validity analyses are not required. However, content validity was determined using expert judgments.

Calculation of Measured Constructs:

Perceived Susceptibility (P_SS) = Score based on the patients' opinion on chances of getting BC based on their personal beliefs. Total score was obtained by summing scores on all 7 questions.

$P\_SS = (A1 + A2 + A3 + A4) \div 4$

Perceived Severity (P_Sev) = Score based on patients' opinion of how serious BC is and the effect of its consequences. Scores were obtained as follows:

$P\_Sev = (B1 + B2 + B3) \div 3$

Perceived Benefits (P_B) = Score based on patients' opinion on the magnitude and effectiveness of the drug. Scores were obtained as follows:

$P\_B = (C1 + C2) \div 2$

Perceived Risks (P_R) = Score based on patients' opinion on the magnitude of adverse events associated with the drug. Scores were obtained as follows:

$P\_R = (D1 + D2 + D3 + D4) \div 4$

Intention to Start Chemo-prevention (I_C) = Score based on patients' readiness to practice preventive action.

Statistical Analyses

The data analysis process involved several methods. Frequency distributions and measures of central tendency and dispersions were used to describe the sample and participant responses on

the instruments. Given the repeated nature of the experiment, repeated measures analysis (MANCOVA – multiple DVs) was used to analyze the impact of breast cancer hazard level and drug risk communication format on measured variables. Post hoc analyses were conducted to determine which of the k means in a one-way ANOVA are significantly different. Statistical analyses were performed using SAS® Version 9.2 set at *a priori* significance level of 0.05. To test the proposed research model structural equation modeling was conducted using Mplus. Within-subjects ANOVA and paired t-test were conducted for manipulation check.

For repeated measures analyses, in addition to the assumption of normality, within-subject analysis of variance is based on assumptions about the variances of the measurements and the correlations among the measurements. Taken together, these assumptions are called the assumption of sphericity. Although a complete description of sphericity is beyond the scope of this text, there is sphericity if:

a) The population variances of the repeated measurements are equal and
b) The population correlations among all pairs of measures are equal. Other complex and unusual patterns of variances and correlations can also produce sphericity. Violation of the assumption of sphericity is serious: It results in an increase in the Type I error rate. Tests for normality and sphericity were also conducted.

Path Analysis was done to test the coefficients for each pathway. Mplus was used to test the model. The goal is to determine whether a hypothesized theoretical model is consistent with the data collected to reflect this theory. The consistency is evaluated through model-data fit, which indicates the extent to which the postulated network of relations among variables is plausible.

The adequacy of any proposed model would be determined by following stand-alone fit statistics:

i. *Chi-square:* The chi-square for the model is also called the discrepancy function, likelihood ratio chi-square, or chi-square goodness of fit. In some softwares, the chi-square value is called CMIN. If the chi-square is not significant, the model is regarded as acceptable. That is, the observed covariance matrix is similar to the predicted covariance matrix--that is, the matrix predicted by the model. If the chi-square is significant, the model is regarded, at least sometimes, as unacceptable. However, many researchers disregard this index if both the sample size exceeds 200 and other indices indicate the model is acceptable. In particular, this approach arises because the chi-square index presents several problems:

    - Complex models, with many parameters, will tend to generate an acceptable fit
    - If the sample size is large, the model will usually be rejected, sometimes unfairly
    - When the assumption of multivariate normality is violated, the chi-square fit index is inaccurate.

ii. *Relative chi-square:* The relative chi-square is also called the normed chi-square. This value equals the chi-square index divided by the degrees of freedom. This index might be less sensitive to sample size. The criterion for acceptance varies across researchers, ranging from less than 2 to less than 5 (Schumacker and Lomax 2004; Ullman and Bentler 2003).

iii. *Comparative Fit Index (CFI)*: The CFI compares the fit of a target model to the fit of an independent model--a model in which the variables are assumed to be uncorrelated. In this context, fit refers to the difference between the observed and predicted covariance matrices, as represented by the chi-square index. In short, the CFI represents the ratio between the discrepancies of this target model to the discrepancy of the independence model.

Let d = $\chi 2$ - df where df are the degrees of freedom of the model.

$$CFI = \frac{d(null\ model) - d\ (proposed\ model)}{d\ (null\ model)}$$

If the index is greater than one, it is set at one and if less than zero, it is set to zero. Values that approach 1 indicate acceptable fit. CFI is not too sensitive to sample size.(Fan, Thompson and Wang 1999) However, CFI is not effective if most of the correlations between variables approach 0 as the covariance explained is low (Fan, Thompson and Wang 1999).

iv. *Root Mean Square Error of Approximation (RMSEA*): This absolute measure of fit is based on the non-centrality parameter. If $\chi 2$ is less than df, then the RMSEA is set to zero. Like the TLI, its penalty for complexity is the chi square to df ratio. The measure is positively biased (i.e., tends to be too large) and the amount of the bias depends on

smallness of sample size and df, primarily the latter. The RMSEA is currently the most popular measure of model fit and it is now reported in virtually all papers that use CFA or SEM and some refer to the measure as the "Ramsey." MacCallum, Browne and Sugawara have used 0.01, 0.05, and 0.08 to indicate excellent, good, and mediocre fit, respectively (MacCallum, Browne and Sugawara 1996). However, others have suggested 0.10 as the cutoff for poor fitting models. These are definitions for the population. That is, a given model may have a population value of 0.05 (which would not be known), but in the sample it might be greater than 0.10. Use of confidence intervals and tests of PCLOSE can help understand the sampling error in the RMSEA. There is greater sampling error for small df and low N models, especially for the former. Thus, models with small df and low N can have artificially large values of the RMSEA. For instance, a chi square of 2.098 (a value not statistically significant), with a df of 1 and N of 70 yields an RMSEA of 0.126. For this reason, it is argued to not even compute the RMSEA for low df models (Kenny 2012).

v. *Standardized Root Mean Square Residual (SRMR)*: The SRMR is an absolute measure of fit and is defined as the standardized difference between the observed correlation and the predicted correlation. It is a positively biased measure and that bias is greater for small N and for low df studies. Because the SRMR is an absolute measure of fit, a value of zero indicates perfect fit. The SRMR has no penalty for model complexity. A value less than .08 is generally considered a good fit (Ullman and Bentler 2003).

Assumptions

The methodology and results of this study were based on the following assumptions:

1) Human beings are rational and make systematic use of information available to them (Ajzen 1991).

2) People consider the implications of their actions before they decide to engage or not engage in certain behaviors (Ajzen 1991).

3) The participants understood the questionnaire and responses indicated by the participants on the questionnaire truly reflected their personal opinions.

4) Respondents provided accurate information about their socio-demographic and socio-economic characteristics.

Variables such as information load, information anxiety, product knowledge, attitude towards leaflet and intention to read were continuous constructs that were analyzed at the interval level.

CHAPTER FIVE

RESULTS

The results of the study will be presented in this chapter. The chapter would be categorized in five broad sections starting with response rate sections, which would include details of the data collection period and final sample size. The second section will describe the details about the sample characteristics followed by section 3 on psychometric testing of the instrument, model adequacy and manipulation test results. Hypotheses testing of main effects of involvement and format type and interaction effects will be discussed in section 4. This section would also include post hoc testing and correlation analyses between outcome variables. Finally, the last part of this chapter will be results obtained from structural equation modeling.

Response Rate

A-priori sample size calculations revealed that 240 completed surveys would be required to test the hypotheses. Data was collected from October 28, 2016 to November 15, 2016. A total of 463 women were approached out of which 335 women agreed to participate in the study. The length of the survey and lack of time were cited the main reasons for denied participation.

Figure 11 outlines the sample attrition.

Thus, a total of 320 surveys were obtained at the end of the data collection. Four participants were not able to complete the entire survey and had to leave the study mid-way due to time constraints or prior commitments. Further, 11 complete surveys were discarded because they had a lot of missing variables. A total of 331 usable surveys were finally considered for analysis. The response rate of the study was 69.11% (320/463*100). Surveys were coded according to the codebook (Appendix H). The a-priori alpha level was set at 0.05 for all tests.

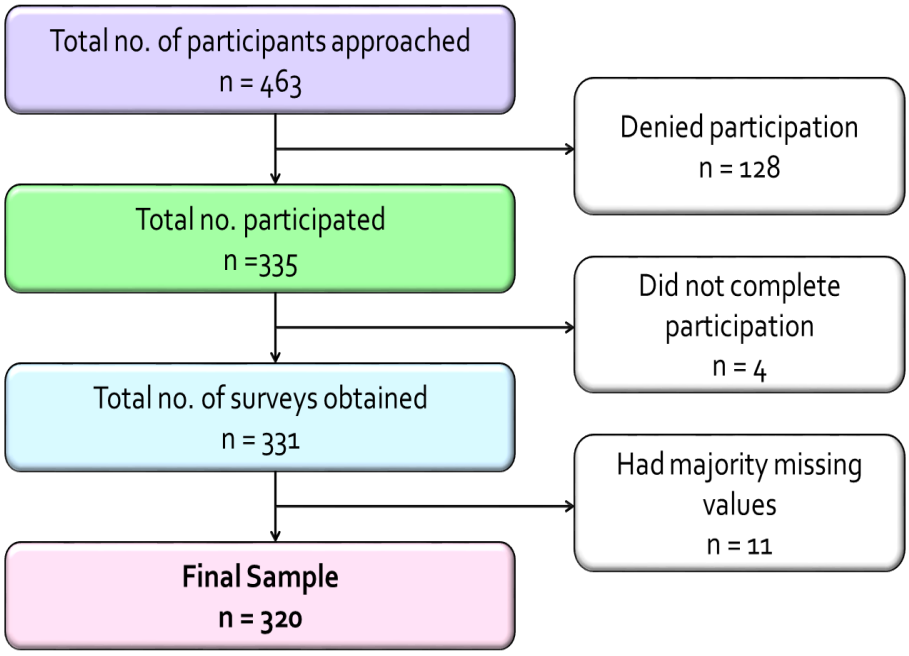


Figure 11: Participant Response Rate

Sample Characteristics

A summary of demographic and practice characteristic is provided in Table 2. The mean age of all respondents was 40.25 (±11.27) years with median equal to 39 years. The sample had a good mix of race/ethnicity with majority of Whites (52%) followed by Asian (16%), Hispanic (16%) and African American (12%) (Figure 12). All respondents indicated that they at least had high school education. Majority had some type of college education (63.99%). Majority of the participants were married (46%) (Figure 13).

About 11.9% of the participants had a history of breast biopsy, while 28.3% of the participants have heard of chemoprevention before.

Table 1: Participant Characteristics

Participant Characteristics	Frequency (N= 320)
Age, N (%)	
Mean (SD)	40.25 (11.27)
Median (Q1-Q3)	39 (31-50)
Education Level, N (%)	
High School	57 (18.32)
College	199 (63.99)
Graduate School	55 (17.68)
History of Breast Biopsy	
Yes	37 (11.9)
No	274 (88.1)
History of Hysterectomy	
Yes	14 (4.5)
No	297 (95.5)
Heard of Chemoprevention	
Yes	88 (28.3)
No	223 (71.7)
History of Chemoprevention	
Yes	8 (2.57)
No	303 (97.43)
Help read Material	

Never	151 (48.55)
Rarely	110 (35.37)
Sometimes	40 (12.86)
Often	8 (2.57)
Always	2 (0.64)
Overall Health Status	
Mean (SD)	3.55 (0.77)
Median (Q1-Q3)	3.57 (3.14-4.0)

Figure 12: Participant Marital Status

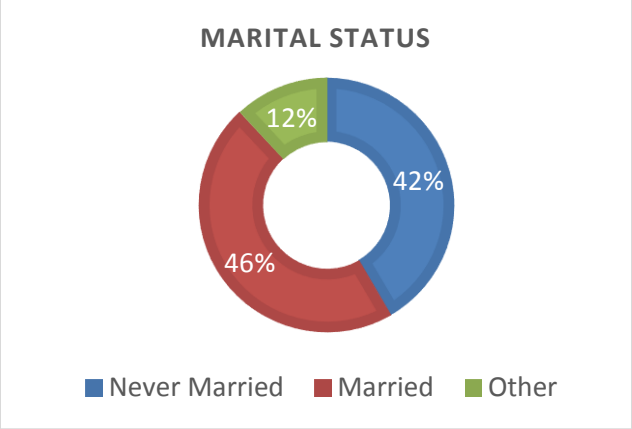


Figure 13: Race distribution across participants

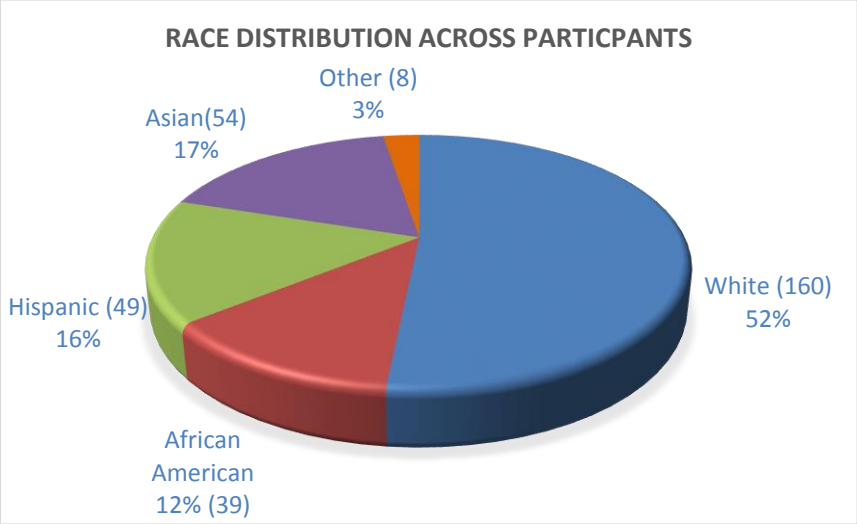


Figure 14: Heard of Chemopreventive Drugs

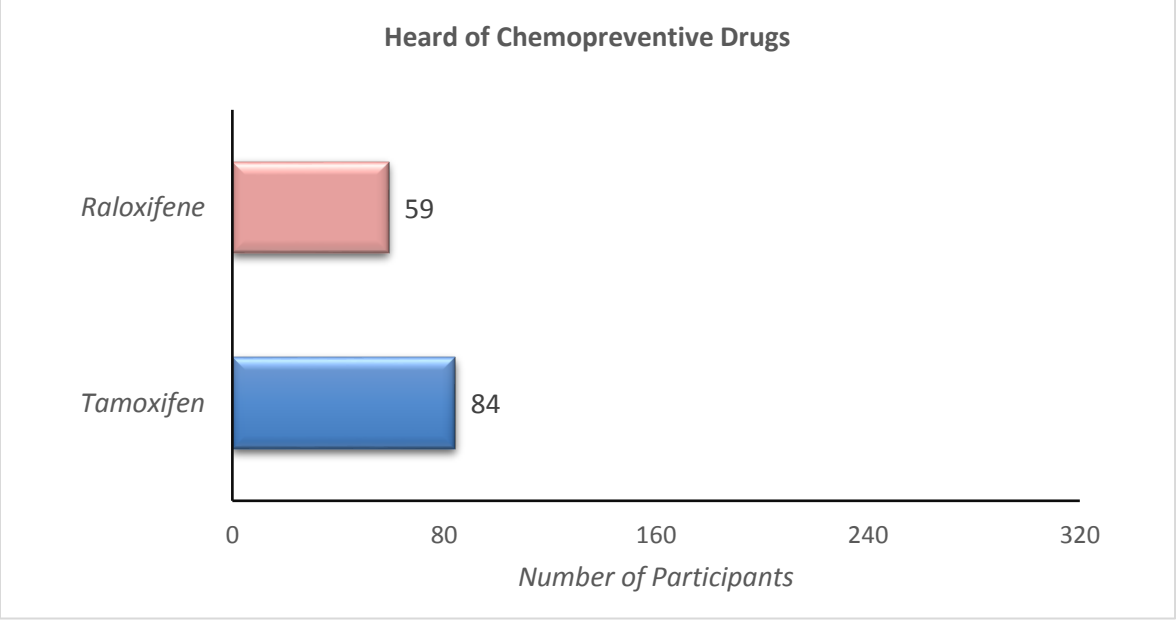
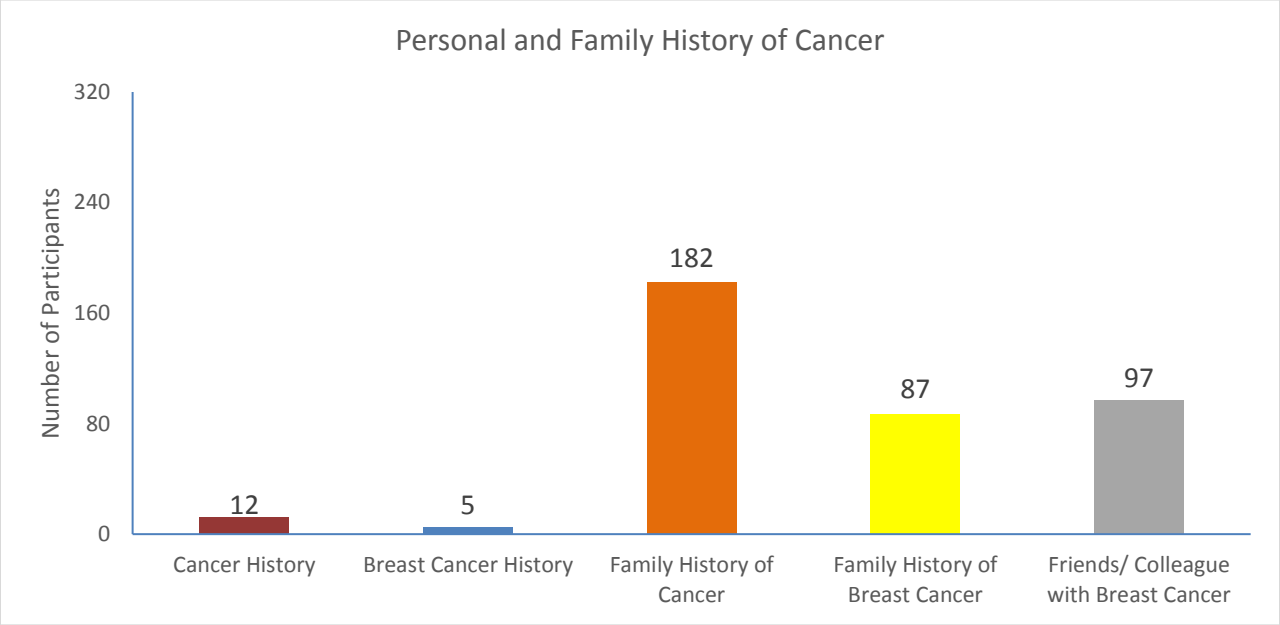


Figure 15: Cancer History



Reliability Analysis

Before a measure could be considered valid, it should be reliable. Reliability deals with the extent to which a measure is accurate and consistent. In other words, it is the ability of the survey or the questions to yield same results each time. Reliability can be tested using following methods:

1) Test-retest method – Same scale given at different times.
2) Alternate form method – two different scales measuring the same concept. One of the scales should be established as reliable and the other scale is the one which is to be tested.
3) Split-half method – Divide the scales and compare.
4) Internal Consistency method
    a. Homogeneity of scale items – Cronbach's Alpha
    b. Kuder-Richardson Method – Strictly for binary measures

As evident from the above, for this study Cronbach's alpha was considered more appropriate method over the others. Cronbach's alpha is an index of reliability associated with the variation accounted for by the true score of the "underlying construct." Its value can range from 0 to 1 and it indicates the internal consistency of the scale (Santos 1999). The higher the score, more reliable the generated scale is. For behavioral research, a value of 0.7 or above is acceptable but scales with lower threshold have been used in the literature (Nunnally 1978).

Reliability was tested for the measured variables specifically, perceived susceptibility, perceived severity, perceived benefits and perceived adverse events. Since intention was measured using one item, no coefficient was calculated. The correlation of each item in a domain with the total score for the domain was also determined.

Table 3: Reliability Analysis

Variables	Correlation (N= 640)	
	Crohnbach's Alpha	**(p-value)[a]**
Perceived Severity	0.73	<0.0001
Perceived Susceptibility	0.85	<0.0001
Perceived Benefits	0.86	<0.0001
Perceived Adverse Events	0.77	<0.0001

Validity Analysis

Validity refers to how well a test measures what it intends to. Since, all items for each domain were taken from literature and modified to address the question in concern, it was assumed to be valid. Content validity determines whether the content is representative of the whole concept. Expert judgments were considered for determining the content validity of the questionnaire.

Manipulation check results

Manipulation checks were conducted to identify whether the stimuli i.e. involvement and message format were manipulated successfully. As explained in methodology multi-item measures was developed for each stimuli. For manipulation check, the mean values were compared across the levels using ANOVA and t-test. The results showed a significant difference in means across the different levels indicating a successful manipulation. Both graphic and written formats were significantly different from each other.

Table 4: Manipulation Check

Stimuli	Conditions	Mean (±SD)	p-value
Involvement Level	High	4.18 (± 0.83)	<.0001
	Low	3.21 (± 1.07)	
Message Format	Graphic	4.21 (± 0.78)	<.0001
	Written	3.05 (± 0.89)	

Table 5: Means Across Dependent Variables

Dependent Variable	Mean (±SD)	Median
Perceived Susceptibility	2.94 (±1.07)	2.75
Perceived Severity	3.45 (±0.88)	3.67
Perceived Benefit	3.33 (±1.05)	3.50
Perceived Adverse Events	2.77 (±1.84)	2.75
Intention	3.20 (±1.40)	3.00

Model adequacy assumptions and testing

The analyses described in this chapter are mostly using parametric statistical tests. Before analyzing data with parametric statistical tests, data were evaluated to see if the assumptions of normality, homoscedasticity, variable independence and linearity were met. However, it should be noted that both the t-test and the F-test are robust enough to stand moderate deviations from these theoretical assumptions. Also when sample sizes are equal across the groups and large even major deviations from the above-mentioned assumptions can be tolerated (Zar 1984)

In this study the sample size was equal (360) across groups and the number was large (360 X 3). Residual analyses did not indicate any major deviations from normality, homoscedasticity and linearity assumptions. Normal probability plots, histograms and residual plots did not indicate any violation of model adequacy assumptions. Data transformation was not necessary. Where possible, non-parametric test were also conducted to check the consistency of results. Hence only parametric tests were used to report examined hypothesis.

Hypotheses testing

Results of MANOVA will be presented to test for hypothesis H1, H2 and H3. In other words MANOVA will help identify the effect (overall main effects and interaction effect) of cognitive effort and involvement on outcome variables specifically information load, information anxiety, product knowledge, attitude towards the leaflet and intention to read. Null Hypothesis (H_0) – There is no significant difference between the scores of information load, information anxiety, product knowledge, attitude towards the leaflet and intention to read across the 3 different leaflet and two levels of involvement. Table 7 shows the result for MANCOVA.

Table 7: MANCOVA- Test for the hypothesis of no overall effect of message format and involvement on dependent variables

Variable	Statistic	Value	F - Value	Pr > F
Involvement	Wilk's Lambda	0.45575093	145.69	<0.0001
	Pillai's Trace	0.54424907	145.69	<0.0001
Message Format	Wilk's Lambda	0.98367159	2.03	0.0734
	Pillai's Trace	0.01632841	2.03	0.0734
Involvement*Message Format	Wilk's Lambda	0.99068609	1.15	0.3342
	Pillai's Trace	0.00931391	1.15	0.3342
Cancer History	Wilk's Lambda	0.97312708	3.37	0.0052
	Pillai's Trace	0.02687292	3.37	0.0052
Help read Medical Information	Wilk's Lambda	0.97991923	2.5	0.0296
	Pillai's Trace	0.02008077	2.5	0.0296
Cancer Risk Information	Wilk's Lambda	0.90020866	13.52	<.0001
	Pillai's Trace	0.09979134	13.52	<.0001
Medicine risk perception	Wilk's Lambda	0.91933271	10.7	<.0001
	Pillai's Trace	0.08066729	10.7	<.0001

Since MANOVA indicated that the effect of involvement was significant on the dependent variables, ANCOVA were performed to determine the effect of the stimuli on each dependent variable. Since message format was one of the manipulated variables. As the interaction between involvement and message format was found to be not significant in MANCOVA, it was not included in each univariate analysis.

a. *Impact of involvement and message format on perceived susceptibility*

H_0: There is no statistically significant difference in perceived susceptibility scores between the two levels of involvement and 2 different message formats.

Results of this analysis show that there was a significant difference in perceived susceptibility scores across the two levels of involvement and 2 message formats. Table 10.1 and 10.2 presents the results for ANCOVA

Table 7a: ANCOVA to evaluate the effect of involvement level and message format on mean scores of perceived susceptibility

Source	DF	Type III SS	Mean Sq.	F value	Pr > F
Involvement	1	364.97	364.97	646.77	<.0001
Message Format	1	2.29	2.29	4.06	0.0442

Table 7b: Least square means for the effect of involvement level and Message format on mean scores of Perceived Susceptibility

Variable	LSMean	Pr > F
Involvement		**< .0001**
High	3.70	
Low	2.18	
Message Format		**0.0442**
Graphic	3.00	
Written	2.88	

b. *Impact of involvement and message format on perceived severity*

H0: There is no statistically significant difference in perceived severity scores between the two levels of involvement and 2 different message formats.

Results of this analysis show that there was a significant difference in perceived severity scores across the two levels of involvement however not across 2 message formats. Table 8.a and 8.b presents the results for ANCOVA

Table 8a: ANCOVA to evaluate the effect of involvement level and message format on mean scores of perceived severity

Source	DF	Type III SS	Mean Sq.	F value	Pr > F
Involvement	1	21.76	21.76	33.07	**<.0001**
Message Format	1	0.03	0.03	0.04	**0.8387**
Friend/ colleague with breast cancer	1	6.01	6.01	9.13	0.0026
Heard of Tamoxifen	1	5.90	5.90	8.97	0.0029
Cancer risk perception	5	51.11	10.22	15.54	<.0001

Table 8b: Least square means for the effect of involvement level and Message format on mean scores of Perceived Severity

Variable	LSMean	Pr > F
Involvement		**< .0001**
High	3.16	
Low	2.79	

c. *Impact of involvement and message format on perceived benefit*

H0: There is no statistically significant difference in perceived benefit scores between the two levels of involvement and 2 different message formats.

Results of this analysis show that there was a significant difference in perceived benefit scores across the two levels of involvement however not across 2 message formats. Table 9.a and 9.b presents the results for ANCOVA

Table 9a: ANCOVA to evaluate the effect of involvement level and message format on mean scores of perceived benefits

Source	DF	Type III SS	Mean Sq.	F value	Pr > F
Involvement	1	178.28	178.28	225.72	**<.0001**
Message Format	1	0.01	0.01	0.02	**0.9**
Cancer risk perception	5	12.27	2.45	3.11	0.0089
Medicine risk perception	5	18.14	3.63	4.59	0.0004

Table 9b: Least square means for the effect of involvement level on mean scores of perceived benefits

Variable	LSMean	Pr > F
Involvement		**< .0001**
High	3.59	
Low	2.52	

d. *Impact of involvement and message format on perceived adverse events*

H0: There is no statistically significant difference in perceived benefit scores between the two levels of involvement and 2 different message formats.

Results of this analysis show that there was a significant difference in perceived adverse events scores across the two levels of involvement however not across 2 message formats.

Table 10.a and 10.b presents the results for ANOVA

Table 10a: ANOVA to evaluate the effect of involvement level and message format on mean scores of perceived adverse events

Source	DF	Type III SS	Mean Sq.	F value	Pr > F
Involvement	1	39.33	39.33	66.91	**<.0001**
Message Format	1	0.06	0.06	0.1	**0.7579**

Table 10b: Least square means for the effect of involvement level and Message format on mean scores of perceived adverse events

Variable	LSMean	Pr > F
Involvement		**< .0001**
High	2.40	
Low	2.90	

e. *Impact of involvement and message format on intention*

H0: There is no statistically significant difference in intention scores between the two levels of involvement and 2 different message formats.

Results of this analysis show that there was a significant difference in intention scores across the two levels of involvement however not across 2 message formats. Table 11.a and 11.b presents the results for ANOVA

Table 11a: ANOVA to evaluate the effect of involvement level and message format on mean scores of intention

Source	DF	Type III SS	Mean Sq.	F value	Pr > F
Involvement	1	411.63	411.63	403.17	**<.0001**
Message Format	1	1.96	1.96	1.89	0.1703

Table 11b: Least square means for the effect of involvement level on mean scores of intention

Variable	LSMean	Pr > F
Involvement		**< .0001**
High	4.15	
Low	2.52	

Table 12a: Mean Involvement across the Dependent Variables

Variable	Involvement		Pr > F
	High	Low	
Perceived Susceptibility	3.70	2.18	< .0001
Perceived Severity	3.16	2.79	< .0001
Perceived Benefit	3.59	2.52	< .0001
Perceived Adverse Events	2.40	2.90	< .0001
Intention	4.15	2.52	< .0001

Table 12b: Mean Involvement across the Dependent Variables

Variable	Message Format		Pr > F
	Graphic	Written	
Perceived Susceptibility	3.00	2.88	0.04
Perceived Severity	2.97	2.98	0.8
Perceived Benefit	3.05	3.04	0.9
Perceived Adverse Events	2.78	2.76	0.7
Intention	3.35	3.47	0.107

Correlation Analyses

Past literature and theories have established that attitude, knowledge and intention are significantly related to each other. To identify the magnitude of association between product knowledge, attitude towards the leaflets and intention to read the leaflets in the current study, correlation analyses was conducted. Table X represents the Pearson correlation matrix along with the probability values across 3 different leaflet types.

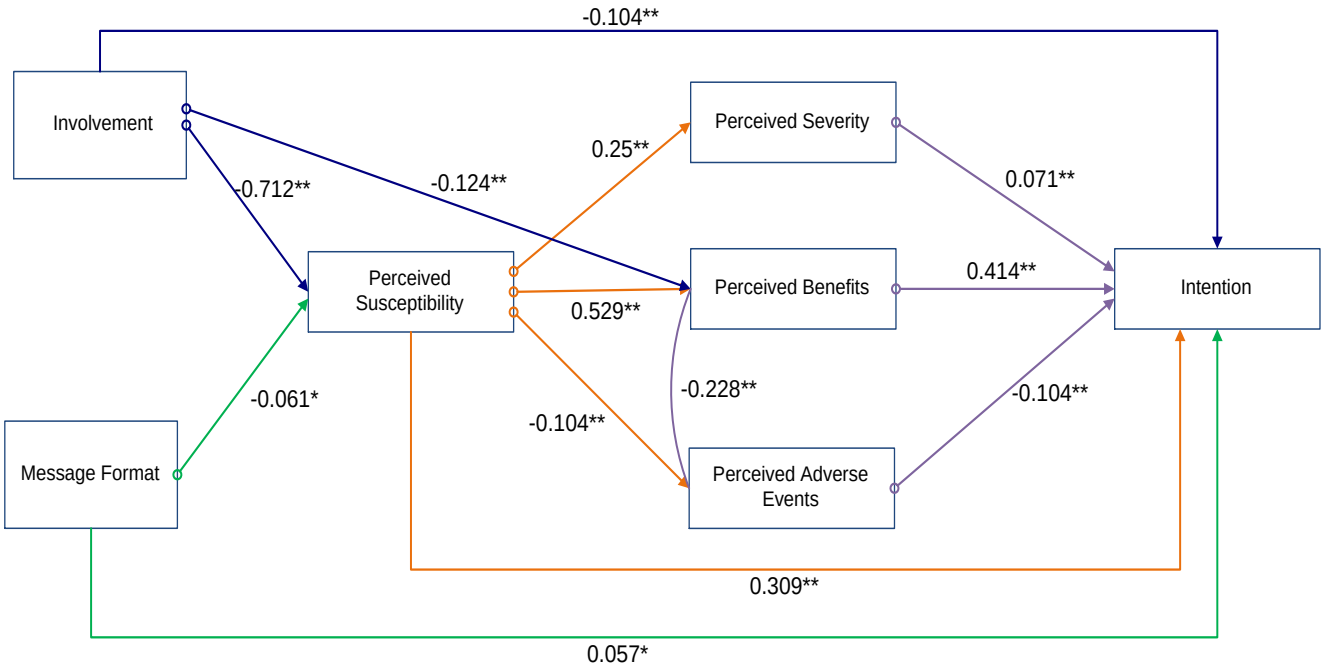
Table 13: Correlation Table

	Perceived susceptibility	**Perceived Severity**	**Perceived Benefit**	**Adverse event**	**Intention**	**Scene type**	**Format type**
Perceived susceptibility	1.00						
Perceived Severity	0.25	1.00					
Perceived Benefit	0.62	0.32	1.00				
Adverse event	-0.37	-0.10	-0.46	1.00			
Intention	0.68	0.31	0.72	-0.44	1.00		
Scene type	-0.71	-0.21	-0.51	0.30	-0.58	1.00	
Format type	-0.06	0.01	-0.01	-0.01	0.03	0.00	1.00

Comprehensive model testing

This section would present the results of evaluating the comprehensive model. The test was conducted using the concept and methodology of structural equation modeling. Mplus was used to test the proposed research model. The repeated nature of the study was taken into account by correlating data across different levels. Stand-alone fit statistics CFI, RMSEA, and SRMR were used to determine the adequacy of the proposed model. Figure 18 represents the result of the model testing.

Figure 19: Path Analysis- Final Model



The results of path analysis indicated that the proposed model had an acceptable fit. All the proposed paths were significant. Perceived susceptibility plays a mediating role between

message format and perceived severity, perceived benefits and perceived adverse events. The study deduced the above model upon the fit of the base model, correlation matrix and past literature. The SRMR value for the proposed model was 0.03 indicating a good fit. A value less than .08 is generally considered a good fit.

Table 14: Path Analysis- Indirect Effects

Indirect Effects	Estimate	S.E.	P-value
Involvement level-Perceived Susceptibility-Perceived Severity	-0.178	0.028	0.001
Message Format- Perceived Susceptibility-Perceived Severity	-0.015	0.007	0.037
Involvement level- Perceived Susceptibility-Perceived Benefits	-0.377	0.034	0.001
Message Format- Perceived Susceptibility-Perceived Benefits	-0.032	0.015	0.03
Involvement level-Perceived Susceptibility-Perceived Adverse Events	0.263	0.028	0.001
Message Format- Perceived Susceptibility-Perceived Adverse Events	0.023	0.01	0.031

Note: Chi- Square with 8 degrees freedom= 38.6 (p=0.001)

Root Mean Square Error of Approximation= 0.029 (p<0.05)

Standardized Root Mean Square Residual= 0.038

All pathways indicated were significant at p level 0.05

Table 15: Result Summary

Variable	Test	Perceived Susceptibility	Perceived Severity	Perceived Benefit	Perceived Adverse Events	Intention
Involvement	ANOVA	Significant	Significant	Significant	Significant	Significant
	Path Analysis	Significant	Significant	Significant	Significant	Significant
Message Format	ANOVA	Significant	Not Significant	Not Significant	Not Significant	Not Significant
	Path Analysis	Significant	Significant (Indirect)	Significant (Indirect)	Significant (Indirect)	Significant

CHAPTER SIX

DISCUSSION, RECOMMENDATION AND CONCLUSIONS

The aim of this research was to evaluate the effects of patient involvement and message format on perceived susceptibility to breast cancer, perceived severity to breast cancer, perceived benefits and risks to chemoprevention. This chapter begins with a discussion of the results and its implications to real world. The chapter ends with highlighting some strengths and limitations of the study along with recommendations for future research.

The discussion and implication of results will follows logical order starting with discussing the results of the demographic characteristics of the population and other extraneous variables. Further, the discussion would emphasize on results regarding the effects of the manipulated variables namely the cognitive effort and patient involvement followed by results of the model testing. The chapter concludes with a discussion of limitations and recommendations for future research.

Inferences from results of demographic characteristics

The results of this study could be directly applicable to young adult population because the mean age of the sample was approximately 40.25 (±11.27) years. The Statistics atlas provides the racial/ethnic make-up of the population in different cities across the country. The racial distribution of the study sample exactly mimicked the population in Houston metropolitan area indicating that there was no bias associated with race in sample selection. However, most of the respondents were naïve to the study medication. This could have affected the internal validity of the study. Respondents could have learned the medication information through his/her prior experience of taking the medication, from healthcare professionals etc. However the study

participants were asked later in the questionnaire if they have taken raloxifene or tamoxifen before. The majority of the sample was married. This could be true as the mean age of our population was above 35 years of age. The women indicated for SERMs are generally the age range of our sample. More than 50% of our population had a family history of cancer. This could have affected their perception towards breast cancer. In order to ensure their history and knowledge about breast cancer, they were also asked if they have a history of hysterectomy, breast biopsy, and previous history of breast cancer, family history of breast cancer and a friend or colleague with breast cancer. These factors were tested for any significant effect on all the measured variables.

The order randomization and repeated nature of the study appeared to be very effective to produce reliable results. The extraneous variables tested had no effect on the measured variables. The important message from the results of demographic variables was that approximately 30% of respondents did not read the leaflets (rarely or never). This number indicates that policy makers and manufacturers are not successful in capturing patient's attention/interest to these leaflets. Attention is the first and virtually the most important step of informed decision making. Use of pictures aimed to improve comprehension and lead to better understanding of complex information.

Effect of Involvement:

The first research question was to test the effect of involvement and message format on intention to start chemoprevention. Involvement was defined as situational involvement. Message format was information presentation in a graphic and written manner.

The level of involvement was manipulated as high involvement and low involvement using situations with altered breast cancer risk level. Patient with high involvement had a situation with both mother and sister with a history of breast cancer, a lump detected in their mammography and an abnormal growth detected in their breast biopsy. Based on the Gail risk score their total breast cancer risk was 55% in a lifetime. Patient with low involvement had a situation with a mother with a history of breast cancer. Their mammography indicate no abnormality and based upon the Gail risk score their total breast cancer risk was 16% in a lifetime. Women when under high involvement had a higher intention to start chemoprevention. Their perception towards breast cancer susceptibility was higher, they perceived breast cancer to be more severe compared to the same women in a low involvement scenario.

Past research has established that involvement enhances recall and recognition (Petty, Cacioppo and Schumann 1983). Highly involved individuals use central route of elaboration i.e. thoughtful and critical consideration to the information. They are more likely to understand and evaluate the information to make an informed decision. Due to better understanding and recognition their perception about a future risk is also higher.

Effect of Involvement on Perceived Susceptibility:

A study by Kash et al indicated that personal risk of a disease has a direct relationship with preventive behavior. Our study duplicates the above findings. Perceived susceptibility to breast

cancer has a direct association with intention to start chemoprevention. Women with high risk of getting breast cancer, feel more susceptible to breast cancer. They are more likely to start chemoprevention when compared to women at a low risk of getting breast cancer. There is a direct relationship between a personal risk of breast cancer used to manipulate the involvement levels and their perceived susceptibility to breast cancer.

Effect of Involvement on Perceived Severity:

According to the health belief model (HBM), perception about the disease severity plays a significant role in the uptake of preventive behavior. A previous study indicated, women who perceive breast cancer to be a severe disease are more likely to have mammography screenings. Our study reiterates the findings in breast cancer chemoprevention. Women who perceive breast cancer to be a severe disease had a high intention to start chemoprevention. Our study also indicates that women with high involvement, feel breast cancer is more severe when compared to those in low involvement situations. Involvement which was manipulated using the risk of breast cancer in a lifetime indicates, play a significant role in perceived susceptibility too breast cancer and perceived severity of breast cancer.

Effect of Involvement on Perceived Benefits:

There is a direct effect of involvement level on the perceived benefits of chemoprevention. Involvement manipulated using breast cancer hazard level plays an important role in the benefit perception of preventive action. Women with a high risk of breast cancer perceived the benefits to chemoprevention to be higher than those with low risk of breast cancer. The model holds true when applied to any preventive action. Higher the level of involvement, higher perceived

benefits of a preventive action.

Effect of Involvement on Perceived Adverse Events:

There is a direct effect of involvement level on the perceived adverse events of chemoprevention. Involvement manipulated using breast cancer hazard level plays an important role in the adverse events perception of preventive action. Women with a high risk of breast cancer perceived the adverse event profile to chemoprevention to be higher than those with low risk of breast cancer. The model can be applied to any preventive action. When the level of involvement is manipulated the adverse event perception is affected.

Effect of Message Format:

Message format has a direct effect on perceived susceptibility to breast cancer. The manner in which information is presented has an effect on the ability of comprehend the information. When information is presented in a logical manner which matches the schema in the mind of the reader, the information is processed effectively (Sansgiry, Cady and Sansgiry 1998; Vigilante and Wogalter 1997). Graphic and visual elements along with verbally oriented elements not only convey a message about a product but also attract consumer attention (Houston, Childers et al. 1987). Holbrook and Moore argue that, in general, pictures promote a more holistic and integrative form of processing, than do words (Holbrook and Moore 1981). There was an indirect effect of message format on perceived severity of breast cancer. Perceived susceptibility played a mediating role. Women who feel susceptible to breast cancer feel breast cancer is more severe compared to women who feel less susceptible to breast cancer. When the information is processed easily, it leads to informed decision making (Sojourner and Wogalter 1998;

VIGILANTE 2003). Research on the inclusion of pictures could be broadly classified into two categories specifically, one that tests effects of pictures on consumer attitudinal response and other that tests effects of pictures on consumer memory. It is worthy to study the effects of pictorial information on memory because the impact of internal information throughout the consumer decision process (Houston, Childers et al. 1987).

Factors and Barriers to Chemoprevention

Perceived susceptibility to breast cancer, perceived severity to breast cancer, perceived adverse event to chemoprevention and perceived benefit to chemoprevention are the factors associated with intention to start chemoprevention (Rosenstock, Strecher and Becker 1988). Our findings are consistent with the literature, personal susceptibility to a disease is associated with increased likelihood of practicing preventive behavior (Strecher and Rosenstock 1997). Similarly perception about disease severity has a strong relationship with intention to start preventive behavior. Most patients undergo a complex decision making process. As indicated in consumer research studies, the benefit of performing an action should outweigh the risk associated with that action for positive confirmation. Similarly in our study perceived benefit of initiating chemoprevention and perceived adverse event associated with chemoprevention affect the intention to start chemoprevention.

Strengths and limitations

This study was conducted within the Houston metropolitan area. Thus, the generalizability of the study findings may be limited to population residing within Houston and those with characteristics similar to the sample. However, Houston is a large metropolitan city at which the

data was collected. A varied mix of ethnically diverse population is represented in the data sample with a good representation of different race/ethnic groups. It is well known that measuring behavior involves multi-dimensional concepts with many known and unknown variables that can affect the process or behavior under investigation. It is beyond the scope of any research to measure all the known variables that could affect a behavior. Further, there could be other unknown factors that had an effect on decision making for women in this experimental study. This study was a field-experiment where although the intent is to mimic natural process, but the participant activities and results would be generated in a controlled environment. For example: The participants read the decision aid because this study required them to read the decision aid and answer questions. In everyday practice probably they would never read leaflets. It is important to validate the study results in the real world patients. The manipulations i.e. cognitive effort and involvement were manipulated at fixed categorical levels but in reality they exist as a continuum. The data was collected using a self-administered survey. Respondents' tendency to report misleading response due to social desirability was possible. Also, the validity of the response at individual level could not be checked. However, emphasis on confidentiality of responses might have controlled this to an extent.

Future study recommendations

The results of this study can be built upon and considered for various future research projects. It would be extremely important to validate the study results in general consumers at national level. The model tested in this study is applicable and generalizable to different disease areas. The effect of involvement and the manner in which information is presented can be tested using for different preventive actions. The involvement level and the manner in which information is

presented affects the processing of complex information. Involvement when manipulated with risk levels play a significant role in decision making. The decision aid developed using the concepts of congruency, chunking and vividness can be tested among women in breast cancer clinics. The cost savings achieved due to effective patient communication could also be studied. Research is required on application of information processing model established by this study to develop effective physician-directed information sources also.

Conclusion

The results of the study showed that involvement manipulated using breast cancer risk level has a direct and indirect effect on intention to start chemoprevention. Effect of message format on intentions to start chemoprevention is mediated by perceived susceptibility to breast cancer. Perceived susceptibility to breast cancer, perceived severity to breast cancer, perceived benefits of chemoprevention and perceived adverse events to breast cancer are the factors associated with intention to start chemoprevention. The study model can be implemented in different disease areas, to understand various preventive behaviors. The decision aid developed is a basis for further studies to implement informed decision making. The study findings can be used to design targeted intervention among women at high risk of breast cancer.

Appendices

Appendix 1: Systematic Review Evidence Table on Chemoprevention Uptake Rates

Reference (Author name, Publication year,)	**Study Level**		**Intervention**		**Final Outcomes**				**Author conclusions**
	(Design, Location, enrollment years)	*Risk Determination, age (in years), Sample size*	*Chemoprevention Drugs*	*Received Intervention*	*Decision towards chemoprevention (Uptake rates)*			*Time to Measurement*	*Presence of a Control*	
					Yes	*No*	*Undecided /neutral*			
Decision Type: Real Decision (k= 7)										

Bilge Atkas et.al., 2015.	Chart review; Yale Breast Cancer Prevention Clinic, USA; November 2011-2012;	Breast Cancer Risk Assesment Tool (BCRAT); (41-79); 56 women	Exemestane, Tamoxifen, Raloxifene	Yes, Women were offered Tamoxifen.	13 (23%) women	43 (77%) women	NR	Immediately	No	Chemoprevention uptake rates of postmenopausal women in the setting of a breast cancer prevention clinic are higher than that reported in the general population.(Aktas et al. 2016)
Elisabetta Razzaboni	RCT; Modena Familial breast Cancer	Family history, previous benign disease,	NR	Yes, An educational and informational interview.	152 (47%) women	319 (53%) women	NR	Immediately	No	Decision to participate in a chemoprevention trial is based on beliefs and values and the

et.al., 2012	and Ovarian Cancer Center, Italy; June 2007-Novembe r 2010;	mammo graphic dysplasia ; (40-70); 471								potential benefits/ risks to promote an informed choice.(Razzaboni et al. 2013)
Pascal Pujol et.al.,20 12	RCT; Liber Trial, French National Cancer Institute,	Women with BRCA1/ 2; (40-70); 239	Aromat ase Inhibito r (Letroz ole)	Yes, Women were offered Tamoxifen.	75 (31.3%) women	134 (56.5%) women	NR	Immed iately	No	Women with with previous unilateral breast cancer or prior prophylactic oopherectomy are more likely to enter a medical prevention

	France; February 2008-March 2012;									trial.(Pujol et al. 2012)
Paul E. Goss et.al., 2011	RCT; International trial conducted in Canada, Spain, France, USA; Feb, 2004-	Gail Risk score >1.66/ prior atypical ductal or lobular hyperplasia or carcinom	Exemestane	Yes, Women were offered Tamoxifen.	2285 (were randomly assigned)	735 (32%) women (discontinued)	NR	Not clearly defined	Yes	Exemestane significantly reduced breast cancers in post-menopausal women at moderately increased risk of breast cancer.(Goss et al. 2011)

	March, 2010;	a in situ on breast biopsy.								
Ellen T. Matloff et.al., 2006	RCT; Yale School of medicine (USA);	1 first degree relative with history of breast cancer; 48 women	Hormone replacement therapy, Tamoxifen, Raloxifene	Yes, Women were given genetic counselling, informing their risk of breast cancer, heart disease, uterine cancer and osteoporosis.	2 of 48 (4%) women agreed for HT	46 (94%) women	NR	6 months post-intervention	Yes	A personalized risk assessment and genetic counseling intervention improves patient knowledge and risk perception, however, it is unclear that the intervention influenced menopausal treatment decisions.(Matloff et al. 2006)

Rebecca Taylor et.al., 2005	Survey, Intervention; Kingston (Ontario); April, 1991-March, 2001	Gail Risk Score; (35-80); 89 women	Tamoxifen, Raloxifene	Yes, The women were sent a letter explaining their risk and to discuss tamoxifen chemoprevention with their physicians. The physicians were sent a letter indicating the same with 3	1 of 89 women started Tamoxifen, 5 women started raloxifene	84 (94%) women	NR	49 days-14 months	No	Physicians recommend prophylactic tamoxifen to few women. Very few women chose to take it. Potential adverse effects is the major barrier for tamoxifen uptake.(Taylor and Taguchi 2005)

				published results of Tamoxifen trials.						
Julia Tchou et.al., 2004	Medical records review; September, 1998-October, 2002;	Gail Risk Score/ Claus Risk Score; (22-75); 137 women	Tamoxifen	Yes, Women were offered Tamoxifen.	57 (42%) women	80 (58%) women	NR	Reviewed over a period of 2 years (retrospectively)	No	The risk due to AH or LCIS were the main predictors of accepting Tamoxifen chemoprevention.(Tchou et al. 2004)
Decision Type: Hypothetical (k= 2)										

Elisa Rush et.al., 2001	Survey, Intervention; Memorial Sloan-Kettering Cancer Center;	Gail Risk Score; (39-74); 43 women	Tamoxifen	Yes, Neutral educational sessions and literature delineating the actual risks and benefits of tamoxifen therapy.	2 (4.7%) women	15 (34.8%) women	26 (60.5%) women were undecided	NR	No	Patients at high risk of breast cancer perceived the risks of taking tamoxifen to outweigh the benefits, declining therapy uptake.(Port et al. 2001)
Matthew Banegas et.al., 2013	RCT; National Cancer Institute, USA; August 2007-	Breast Cancer Risk Assesment Tool (BCRAT); (40-	Tamoxifen, Raloxifene	Yes, Patients were given a web-based, personally tailored decision aid developed to	NR	NR	NR	3 months post intervention	Yes	Guide to decide lowered decisional conflict and helped women at high risk decide whether to take prophylactic chemoprevention to

	March 2008	74); 690 women		inform women of risks and benefits of tamoxifen and raloxifen use. (guide to decide)						reduce risk.(Banegas et al. 2013)

Appendix 2a: Participant Consent

UNIVERSITY of HOUSTON
A CARNEGIE-DESIGNATED TIER ONE PUBLIC RESEARCH UNIVERSITY

Consent to Take Part in a Human Research Study

Title of research study: **Breast Cancer Chemoprevention among Women: Effect of Involvement and Message Format**

Investigator: This project is conducted by Ms. Archita H. Bhansali, a graduate student at University of Houston, as partial fulfillment of her doctoral degree requirements under the supervision of Dr. Sujit Sansgiry.

Why am I being invited to take part in a research study?

We invite you to take part in a research study because you are woman above the age of 18 years.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide, and can ask questions at any time during the study.

Why is this research being done?

The purpose of this study is to understand the manner in which participants make a decision. It will help us design effective interventions for patients in the near future.

How long will the research last?

We expect that you will be in this research study for 15 minutes.

How many people will be studied?

We expect to enroll about 250 people in this research study.

What happens if I say yes, I want to be in this research?

In this folder you will view: information on breast cancer, two scenarios and two decision aids. Please read the information provided carefully.

The steps to the data collection process is given below:

1) Review the flyer provided with information on breast cancer risk levels
2) After that please read the scenario provided
3) Following the scenario, you will view a decision aid.

Appendix 2b: Participant Consent

Consent to Take Part in a Human Research Study

4) Answer the questions with respect to the scenario and decision aid viewed.
5) Perform the same steps for the second scenario with a decision aid and the question that follows.
6) Debriefing to answer any questions you may have.

What happens if I do not want to be in this research?

You can choose not to take part in the research and it will not be held against you. Choosing not to take part will involve no penalty or loss of benefit to which you are otherwise entitled.

What happens if I say yes, but I change my mind later?

You can leave the research at any time and it will not be held against you.

If you stop being in the research, already collected data will be removed from the study record.

Is there any way being in this study could be bad for me?

There are no foreseeable risks related to the procedures conducted as part of this study. If you choose to take part and undergo a negative event you feel is related to the study, please inform your study team.

Will I get anything for being in this study?

There is no compensation for participation in the study.

Will being in this study help me in any way?

There are no known benefits to you from your taking part in this research. However, possible benefits to others include is understanding the process of decision making.

What happens to the information collected for the research?

Your taking part in this project is anonymous, and information you provide cannot be linked to your identity.

We may publish the results of this research.

Who can I talk to?

If you have questions, concerns, or complaints, or think the research has hurt you, you should talk to the research team at, (832) 842-8342 or at ahbhansali@uh.edu, or at (832) 842-8392. This research has been reviewed and approved by the University of Houston Institutional Review Board (IRB). You may also talk to them at (713) 743-9204 or cphs@central.uh.edu if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

Appendix 2c: Introduction to Data Collection

Introduction to the Data Collection Process

Dear Participant,

In this folder you will view: information on breast cancer, two scenarios and two decision aids. Please read the information provided carefully.

The steps to the data collection process is given below:

1) Review the flyer provided with information on breast cancer risk levels
2) After that please read the scenario provided
3) Following the scenario, you will view a decision aid.
4) Answer the questions with respect to the scenario and decision aid viewed.
5) Perform the same steps for the second scenario with a decision aid and the question that follows.
6) Debriefing to answer any questions you may have.

Appendix 2d: Risk Reduction Strategy Information

Please take a moment to review information in the table below. The table provides information on breast cancer risk* and risk reduction strategies.

National Comprehensive Cancer Network Guidelines

Breast Cancer Risk Category	Lifetime Risk of Breast Cancer	Recommendation for Risk Reduction
Usual/Normal Risk	12% or below	• Diet • Exercise
Low Risk	15-18%	• Diet • Exercise • Regular screening
Moderate Risk	19-29%	• Diet • Exercise • Regular screening • Prevention using medication (Drug A/ Drug B)
High Risk	30% and above	• Diet • Exercise • Regular screening • Prevention using medication (Drug A/ Drug B)

**Breast cancer risk is the chance of developing breast cancer in the future*

Appendix 3: Survey Questionnaire Part 1

Based on the table you read, please indicate your responses to following questions by **circling one number on the scale given below.**

Strongly Disagree (SD) 1	Disagree (D) 2	Neutral (N) 3	Agree (A) 4	Strongly Agree (SA) 5

	SD 1	D 2	N 3	A 4	SA 5
I read all the information provided in the table.	1	2	3	4	5
I clearly understood the information in the table.	1	2	3	4	5

Please turn over to the next page

Appendix 4a: Survey Questionnaire Part 2 (Drug A)

Breast Cancer Risk Questionnaire

SECTION 1: Based on the situation provided and your understanding of the decision aid, please indicate your responses to following questions by circling one number using the scale below.

Strongly Disagree (SD) 1	Disagree (D) 2	Neutral (N) 3	Agree (A) 4	Strongly Agree (SA) 5

The decision aid indicates that Drug A;	SD 1	D 2	N 3	A 4	SA 5
-reduces breast cancer by 62%.	1	2	3	4	5
-increases the risk of blood clots by 40%	1	2	3	4	5
-increases the risk of hot flashes	1	2	3	4	5
-improves baldness, reduces high cholesterol level and risk of fractures.	1	2	3	4	5
-causes glaucoma	1	2	3	4	5
-reduces lung cancer	1	2	3	4	5

Based on the situation and the decision aid I feel;	SD 1	D 2	N 3	A 4	SA 5
I have a high chance of getting breast cancer	1	2	3	4	5
My physical health makes it likely that I will get breast cancer.	1	2	3	4	5
My chances of getting breast cancer in a lifetime are good.	1	2	3	4	5
My own risk of getting breast cancer is too low to take Drug A.	1	2	3	4	5
When I think about breast cancer my heart beats faster	1	2	3	4	5
The thought of breast cancer scares me.	1	2	3	4	5
Getting breast cancer, would be more serious than other diseases.	1	2	3	4	5
Taking Drug A would give me peace of mind	1	2	3	4	5
I am sure that I will benefit from Drug A treatment	1	2	3	4	5
I am afraid that Drug A will make my health worse.	1	2	3	4	5
Drug A has some side effects that are unacceptable to me	1	2	3	4	5
Taking Drug A would be inconvenient for me	1	2	3	4	5
The period of therapy 5 years is too long.	1	2	3	4	5
I intend to start Drug A to reduce my future risk of breast cancer.	1	2	3	4	5

Please turn over to the next page....

Appendix 4b: Survey Questionnaire Part 2 (Drug B)

Breast Cancer Risk Questionnaire

SECTION 1: Based on the situation provided and your understanding of the decision aid, please indicate your responses to following questions by circling one number using the scale below.

Strongly Disagree (SD) 1	Disagree (D) 2	Neutral (N) 3	Agree (A) 4	Strongly Agree (SA) 5

The decision aid indicates that Drug B;	**SD 1**	**D 2**	**N 3**	**A 4**	**SA 5**
-reduces breast cancer by 61%.	1	2	3	4	5
-increases the risk of blood clots by 40%	1	2	3	4	5
-increases the risk of hot flashes	1	2	3	4	5
-improves baldness, reduces high cholesterol level and risk of fractures.	1	2	3	4	5
-causes glaucoma	1	2	3	4	5
-reduces lung cancer	1	2	3	4	5

Based on the situation and the decision aid I feel;	**SD 1**	**D 2**	**N 3**	**A 4**	**SA 5**
I have a high chance of getting breast cancer	1	2	3	4	5
My physical health makes it likely that I will get breast cancer	1	2	3	4	5
My chances of getting breast cancer in a lifetime are good.	1	2	3	4	5
My own risk of getting breast cancer is too low to take Drug B.	1	2	3	4	5
When I think about breast cancer my heart beats faster	1	2	3	4	5
The thought of breast cancer scares me.	1	2	3	4	5
Getting breast cancer, would be more serious than other diseases.	1	2	3	4	5
Taking Drug B would give me peace of mind	1	2	3	4	5
I am sure that I will benefit from Drug B treatment	1	2	3	4	5
I am afraid that Drug B will make my health worse.	1	2	3	4	5
Drug B has some side effects that are unacceptable to me	1	2	3	4	5
Taking Drug B would be inconvenient for me.	1	2	3	4	5
The period of therapy 5 years is too long.	1	2	3	4	5
I intend to start Drug B to reduce my future risk of breast cancer.	1	2	3	4	5

Please turn over to the next page....

Appendix 5: Survey Questionnaire Part 3

SECTION 3: Demographic Questions

- Please indicate the year you were born: 19__ __
- Please indicate the highest grade or years of school you have completed. Circle one number

0	1 2 3 4	5 6 7 8	9 10 11 12	13 14 15 16	17 18	19 20 20+
None	Elementary	Middle school	High School	College	Masters	Doctoral (PhD)

- Please indicate your racial/ethnic background: ◻ Asian ◻ Hispanic ◻ White (non-Hispanic) ◻ African American ◻ Native America ◻ Other (Please Specify)_____
- Current Marital Status: ◻ Never been married ◻ Married ◻ Widowed ◻ Divorced ◻ Separated ◻ Other (Please Specify)_____

Strongly Disagree (SD)	Disagree (D)	Neutral (N)	Agree (A)	Strongly Agree (SA)
1	2	3	4	5

SECTION 4: Based on your overall health status, please indicate your responses to the following questions by circling one number on the scale below.

	SD 1	D 2	N 3	A 4	SA 5
I have always been healthy	1	2	3	4	5
I frequently do things to improve my health	1	2	3	4	5
I take vitamins regularly	1	2	3	4	5
I search for new information related to my health	1	2	3	4	5
I always follow medical orders because they will benefit my state of health	1	2	3	4	5
I exercise regularly- at least three times a week	1	2	3	4	5
I always take my flu vaccines	1	2	3	4	5

SECTION 5: Medical History

- Do you have or ever had cancer? ◻ Yes ◻ No
- Do you have or ever had breast cancer? ◻ Yes ◻ No
- Do you have a family history of cancer? ◻ Yes ◻ No If yes then who _____
- Do you have a family history of breast cancer? ◻ Yes ◻ No If yes then who _____
- Do you have a friend or colleague with breast cancer? ◻ Yes ◻ No
- Have you had a breast biopsy before? ◻ Yes ◻ No
- Have you had your uterus surgically removed (complete/ partial hysterectomy) before? ◻ Yes ◻ No
- Have you heard of medications to prevent breast cancer (chemo-prevention) before? ◻ Yes ◻ No
- Do you have a previous history of chemo-prevention? ◻ Yes ◻ No
- Have you heard about Tamoxifen (Nolvadex)® before today? ◻ Yes ◻ No
- Have you heard about Raloxifene (Evista)® before today? ◻ Yes ◻ No
- How often do you need to have someone's help you when you read instructions, pamphlets or other written material from your doctor or pharmacy?

  ◻Never ◻ Rarely ◻ Sometimes ◻ Often ◻ Always
- How risky do you think cancer is as a disease? Please circle using the scale below.

  Not risky.....0 1 2 3 4 5.....Very risky
- How risky do you think it is to take medicine in general for any condition?

  Not risky.....0 1 2 3 4 5.....Very risky

Appendix 6a: Involvement Scenario A

Involvement Scenario (High)

Patient History:

Consider you have reached your menopause. You have a family history of breast cancer. Your mother and one of your aunts has breast cancer.

Patient Screening:

Due to your family history, you had a mammogram which indicated 2 lumps. You then got your first breast biopsy, which indicated an abnormal growth.

Physician Assessment:

Imagine you are at your physician's office. After examining your report and considering your family history the physician told you that you have a 55% risk of developing breast cancer in your lifetime. Your risk is more than 4.5 times higher than the risk of a normal woman. Please take a moment to think about this situation.

Physician Recommendation:

You then start enquiring with the physician about what should be done next. Your physician suggests you to consider taking Drug A immediately, to reduce your risk of getting breast cancer. Your physician strongly feels, starting Drug A is required at this time. It does not matter if you do/do not have insurance, there is no out of pocket costs for obtaining Drug A.

Patient Action:

Keeping the above situation in mind, please turn the page to view the drug decision aid provided by your physician.

Involvement Scenario (Low)

Patient History:

Consider you have reached your menopause. You have a family history of breast cancer. Your mother has been detected with breast cancer.

Patient Screening:

Due to your family history, you had a mammogram which was normal.

Physician Assessment:

Imagine you are at your physician's office. After examining your report and considering your family history the physician told you that you have a 16% risk of developing breast cancer in your lifetime. Your risk is almost similar to the risk of a normal woman. Please take a moment to think about this situation.

Physician Recommendation:

You then start enquiring with the physician about what should be done next. Your physician suggests Drug A is a possible option, to reduce your risk of getting breast cancer. Your physician does not feel, starting Drug A is required at this time. It does not matter if you do/do not have insurance, there is no out of pocket costs for obtaining Drug A.

Patient Action:

Keeping the above situation in mind, please turn the page to view the drug decision aid provided by your physician and answer the questions.

Appendix 6b: Involvement Scenario B

Involvement Scenario (High)

Patient History:

Consider you have reached your menopause. You have a family history of breast cancer. Your mother and one of your aunts has breast cancer.

Patient Screening:

Due to your family history, you had a mammogram which indicated 2 lumps. You then got your first breast biopsy, which indicated an abnormal growth.

Physician Assessment:

Imagine you are at your physician's office. After examining your report and considering your family history the physician told you that you have a 55% risk of developing breast cancer in your lifetime. Your risk is more than 4.5 times higher than the risk of a normal woman. Please take a moment to think about this situation.

Physician Recommendation:

You then start enquiring with the physician about what should be done next. Your physician suggests you to consider taking Drug B immediately, to reduce your risk of getting breast cancer. Your physician strongly feels, starting Drug B is required at this time. It does not matter if you do/do not have insurance, there is no out of pocket costs for obtaining Drug B.

Patient Action:

Keeping the above situation in mind, please turn the page to view the drug decision aid provided by your physician.

Involvement Scenario (Low)

Patient History:

Consider you have reached your menopause. You have a family history of breast cancer. Your mother has been detected with breast cancer.

Patient Screening:

Due to your family history, you had a mammogram which was normal.

Physician Assessment:

Imagine you are at your physician's office. After examining your report and considering your family history the physician told you that you have a 16% risk of developing breast cancer in your lifetime. Your risk is almost similar to the risk of a normal woman. Please take a moment to think about this situation.

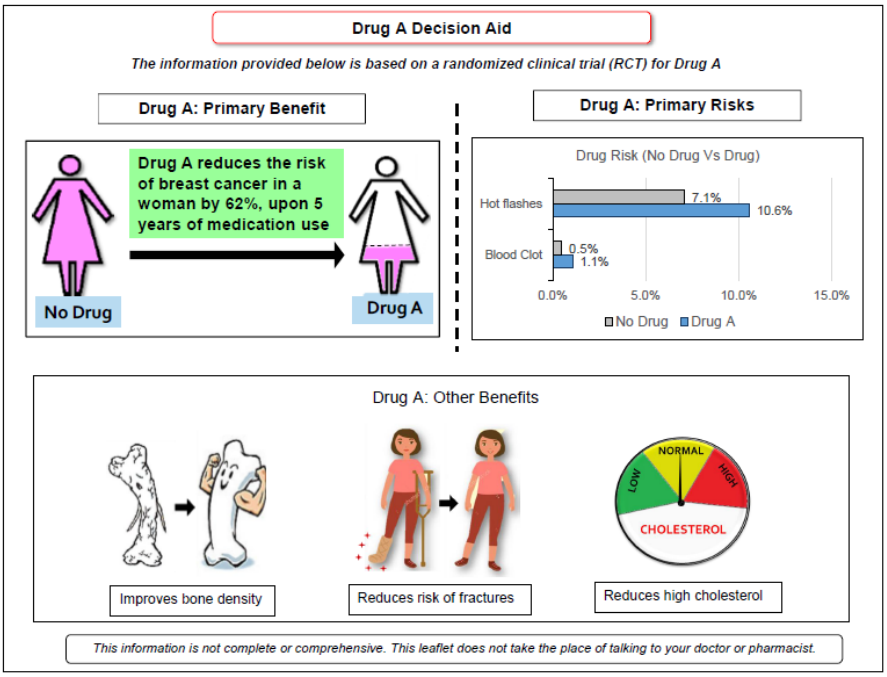
Physician Recommendation:

You then start enquiring with the physician about what should be done next. Your physician suggests Drug B is a possible option, to reduce your risk of getting breast cancer. Your physician does not feel, starting Drug B is required at this time. It does not matter if you do/do not have insurance, there is no out of pocket costs for obtaining Drug B.

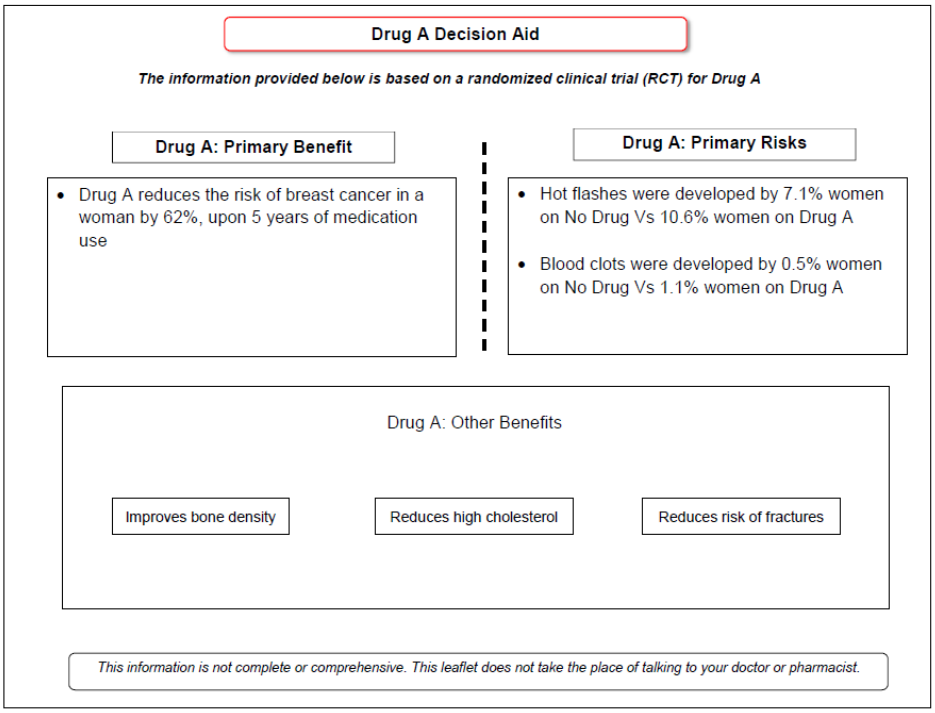
Patient Action:

Keeping the above situation in mind, please turn the page to view the drug decision aid provided by your physician and answer the questions.

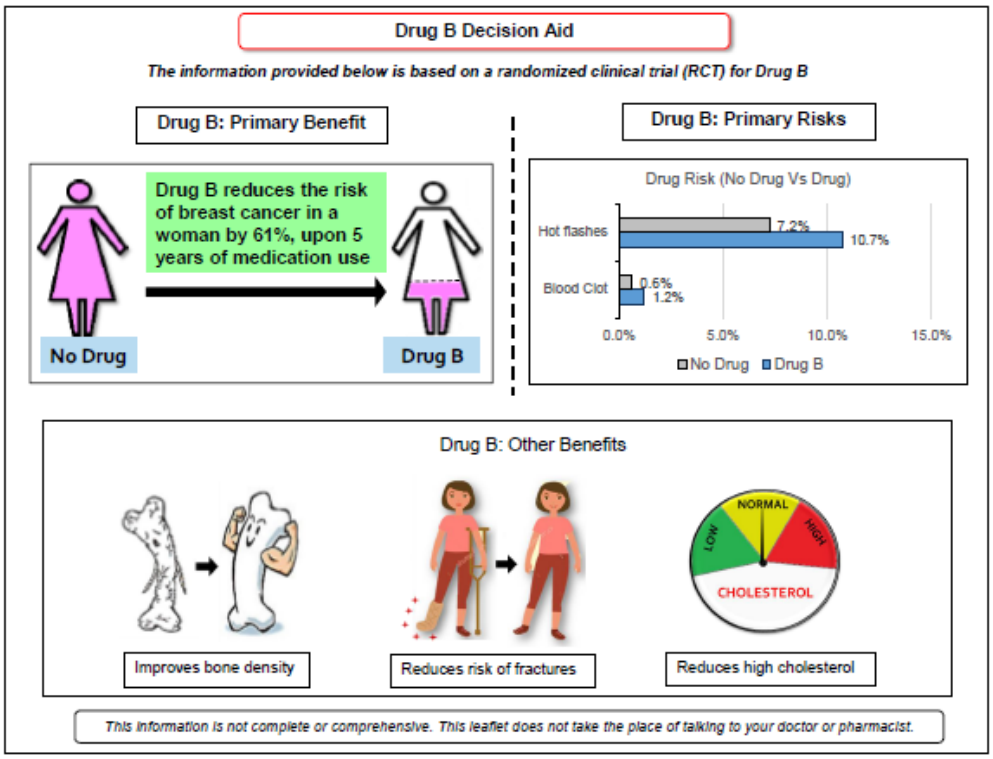
Appendix 7a: Message Format (Graphic)



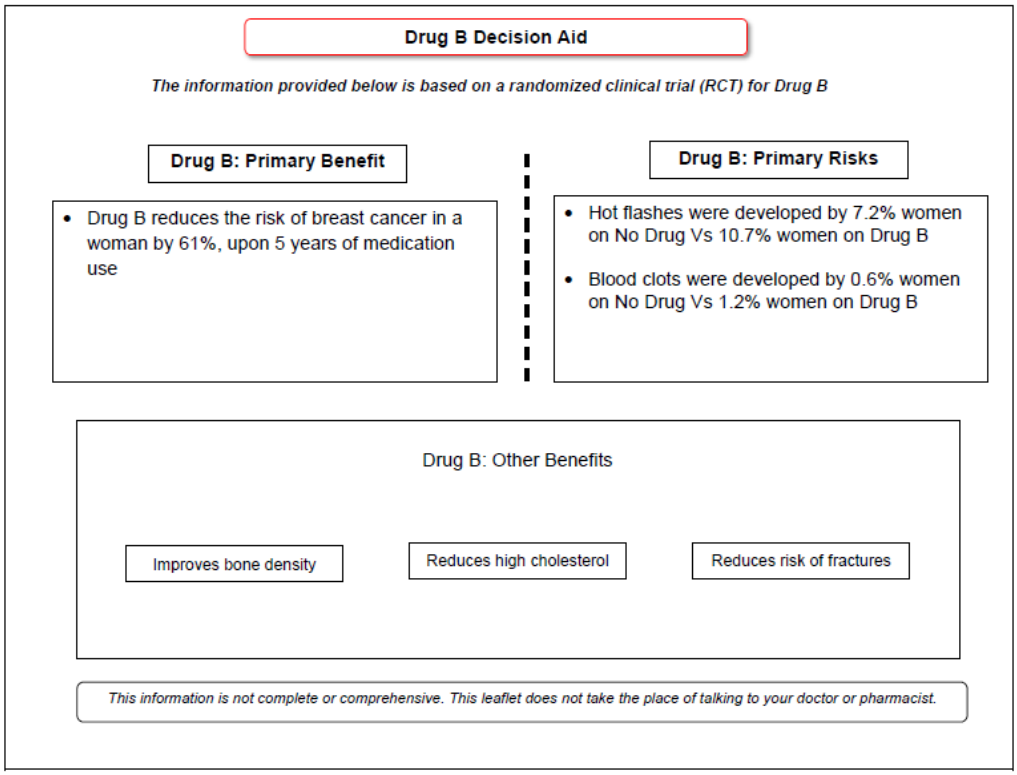
Appendix 7b: Message Format (Written)



Appendix 7c: Message Format (Graphic)



Appendix 7d: Message Format (Written)



Appendix 8a: Randomization and counterbalancing to minimize order effects

Sr. no.	Breast Cancer Risk Scenario	Drug Information Context based on Format	Breast Cancer Risk Scenario	Drug Information Context based on Format	Name
1.	High Risk	Written Drug A	Low Risk	Graphic Drug B	HWALGB
2.	High Risk	Written Drug B	Low Risk	Graphic Drug A	HWBLGA
3.	Low Risk	Written Drug A	High Risk	Graphic Drug B	LWAHGB
4.	Low Risk	Written Drug B	High Risk	Graphic Drug A	LWBHGA
5.	High Risk	Graphic Drug A	Low Risk	Written Drug B	HGALWB
6.	High Risk	Graphic Drug B	Low Risk	Written Drug A	HGBLWA
7.	Low Risk	Graphic Drug A	High Risk	Written Drug B	LGAHWB
8.	Low Risk	Graphic Drug B	High Risk	Written Drug A	LGBHWA

Appendix 8b: Codebook

Code Name	***Full Name***	***Description***	***Meaning of codes***
SECTION 1			
Pt_no	Patient number	Unique identification number given to each participant	1, 2, 3, 4…….
Time sec	Time in seconds	The amount of time taken by each participant to fill the label comprehension section.	
Order	Order of the experiment	The order in which the scenario, drug type and format given to each participant	
Set 8			1= HWALGB 2= HWBLGA 3= LWAHGB 4= LWBHGA 5= HGALWB 6= HGBLWA 7= LGAHWB 8= LGBHWA
Set			Same as above
Set24			Same as above

Q1	Table question1	I read all the information provided in the table	Same as above
Q2	Table question2	I clearly understood the information in the table	Same as above
Sc_typ1	Scene type 1	Level of Involvement	1= High 2= Low
Drg_typ1	Drug type 1	The dug information provided	1= A 2= B
Ft_typ1	Message format 1	The format of message content provided (Graphic/ Written)	1= Graphic 2= Written
pk11	Product knowledge 1	reduces breast cancer by 62%.	1= strongly disagree 2= somewhat disagree 3= Neutral 4= somewhat agree 5= strongly agree
pk12		increases the risk of blood clots by 40%	
pk13		increases the risk of hot flashes	
pk14		improves baldness, reduces high cholesterol level and risk of fractures	
pk15		causes glaucoma	
pk16		The product is used in indigestion.	
psus11	Perceived susceptibility 1	I have a high chance of getting breast cancer	Same as above
psus12		My physical health makes it likely that I will get breast cancer	

psus13		My chances of getting breast cancer in a lifetime are good	
psus14		My own risk of getting breast cancer is too low to take Drug A	
psev11	Perceived Severity 1	When I think about breast cancer my heart beats faster	Same as above
psev12		The thought of breast cancer scares me	
psev13		Getting breast cancer, would be more serious than other diseases	
pb11	Perceived Benefit 1	Taking Drug A would give me peace of mind	Same as above
pb12		I am sure that I will benefit from Drug A treatment	
ae11	Perceived adverse events 1	I am afraid that Drug A will make my health worse	Same as above
ae12		Drug A has some side effects that are unacceptable to me	
ae13		Taking Drug A would be inconvenient for me	
ae14		The period of therapy 5 years is too long	

int1	Intention to start chemoprevention	I intend to start Drug A to reduce my future risk of breast cancer	Same as above
inv11	Involvement manipulation check	Not involved to very involved	Scale of 1-5
inv12		Not at all interested to very interested	
inv13		Not at all motivated to very motivated	
mc11	Message context of format manipulation check	Colorless - colorful	Scale of 1-5
mc12		Not vivid - vivid	
mc13		Confusing – Not confusing	
mc14		Difficult to ready- easy to read	
Sc_typ2	Scene type 2	Level of Involvement	1= High 2= Low
Drg_typ2	Drug type 2	The drug information provided	1= A 2= B
Ft_typ2	Message format 2	The format of message content provided	1= Graphic 2= Written
pk21	Product knowledge 2	reduces breast cancer by 62%.	1= strongly disagree 2= somewhat disagree 3= Neutral 4= somewhat agree 5= strongly agree
pk22		increases the risk of blood clots by 40%	
pk23		increases the risk of hot flashes	
pk24		improves baldness, reduces high cholesterol level and risk of fractures	
pk25		causes glaucoma	

pk26		The product is used in indigestion.	
psus21	Perceived susceptibility 2	I have a high chance of getting breast cancer	Same as above
psus22		My physical health makes it likely that I will get breast cancer	
psus23		My chances of getting breast cancer in a lifetime are good	
psus24		My own risk of getting breast cancer is too low to take Drug A	
psev21	Perceived Severity 2	When I think about breast cancer my heart beats faster	Same as above
psev22		The thought of breast cancer scares me	
psev13		Getting breast cancer, would be more serious than other diseases	
pb11	Perceived Benefit 2	When I think about breast cancer my heart beats faster	Same as above
pb12		The thought of breast cancer scares me	
ae21	Perceived adverse events 2	Getting breast cancer, would be more serious than other diseases	Same as above
ae22		Taking Drug A would give me peace of mind	

ae23		I am sure that I will benefit from Drug A treatment	
ae24		I am afraid that Drug A will make my health worse	
int2	Intention 2	Drug A has some side effects that are unacceptable to me	Same as above
inv21	Involvement manipulation check	Not involved to very involved	Scale of 1-5
inv22		Not at all interested to very interested	
inv23		Not at all motivated to very motivated	
mc21	Message context of format manipulation check	Colorless - colorful	Scale of 1-5
mc22		Not vivid - vivid	
mc23		Confusing – Not confusing	
mc24		Difficult to ready- easy to read	
SECTION 3			
BDAY		Year in which participant was born	19_ _
Edu	Education	Level of Education	1= None 2= Elementary 3= Middle school 4= High school 5= College 6= Masters 7= Doctoral

MStat	Marital status	Marital Status of the subject	1= Never Married 2= Married 3= Widowed 4= Divorced 5= Separated 6= Other
Race		Racial Background	1= White 2= African American 3= Hispanic 4= Asian 5= Native American 6= Other
SECTION 4			
ohs1	Overall Health Status	I have always been healthy	1= strongly disagree 2= somewhat disagree 3= Neutral 4= somewhat agree 5= strongly agree
ohs2		I frequently do things to improve my health	
ohs3		I take vitamins regularly	
ohs4		I search for new information related to my health	
ohs5		I always follow medical orders because they will benefit my state of health	

ohs6		I exercise regularly- at least three times a week	
ohs7		I always take my flu vaccines	
canc	Cancer history	Do you have or ever had cancer	1= Yes 2= No
bcanc	Breast cancer history	Do you have or ever had breast cancer	Continuous number
fcanc	Family history of cancer	Do you have a family history of cancer	1= Yes 2= No
nfcanc	Number of family member with cancer	Number of family members with/ with history of cancer	Continuous number
fbcanc	Family history of breast cancer	Do you have a family history of breast cancer	1= Yes 2= No
nbcanc	Number of family member with breast cancer	Number of family members with/ with history of breast cancer	Same as above
cbcanc	Friend/ colleague with breast cancer	Do you have a friend or colleague with breast cancer	Same as above
bbio	History of breast biopsy	Have you had a breast biopsy before	Same as above

hyst	History of hysterectomy	Have you had your uterus surgically removed (complete/ partial hysterectomy) before	Same as above.
chem	Heard of chemoprevention	Have you heard of medications to prevent breast cancer (chemo-prevention) before	Same as above.
hchem	History of chemoprevention	Do you have a previous history of chemo-prevention	Same as above.
tamo	Heard of Tamoxifen	Have you heard about Tamoxifen (Nolvadex)® before today	Same as above.
ralo	Heard of Raloxifene	Have you heard about Raloxifene (Evista)® before today	
hlpread	Help read material	How often do you need to have someone's help you when you read instructions, pamphlets or other written material from your doctor or pharmacy	1= Never 2= Rarely 3= Sometimes 4= Often 5= Always
grisk1	General risk perception	How risky do you think cancer is as a disease	0= Not risky 5= Very risky
grisk2		How risky do you think it is to take medicine in general for any condition	Same as above.

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