In Search of New Perspectives in Cancer Genetics Services: Exploring Use of Genetic Counseling Among a Group of Young Breast Cancer Survivors

by

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ABSTRACT

Breast cancer associated with mutations in the breast cancer genes *BRCA1* and *BRCA2* often occurs at an earlier age and individuals with a mutation have increased risk for developing breast, ovarian, and other cancers. The cancers may be more difficult to treat, have higher rates of recurrence, and have poor outcomes. Genetic counseling can facilitate informed decision-making about risk-reducing strategies that have shown to be effective but carry their own risks. However, genetic counseling use is low, even among individuals considered high risk for having a *BRCA* mutation. The reason for this is not clear. Existing knowledge is limited by 1) inconsistent findings, 2) potential bias from highly selected samples (e.g., recruited only African American women, or only Hispanic women, or patients at a cancer risk evaluation clinic at an academic facility), 3) inadequate representation of rural populations, 4) small sample sizes, and 5) cross-sectional design.

This dissertation describes a secondary analysis of existing data from a group of young breast cancer survivors identified using a state cancer registry. Of 859 participants, 281 (32.7%) used genetic counseling. Of 546 participants who did not use genetic counseling, 357 (65.4%) reported that “No one ever suggested it.” In fact, genetic counseling is recommended for all participants in this study due to their personal diagnosis of breast cancer at age younger than 50.

There was no significant difference in genetic counseling use between medically served and underserved participants (α=.05, p=.32). However, the analysis was underpowered and this finding should be interpreted with caution. Variables that showed positive associations with counseling use could be interpreted as facilitators and were the same for served and underserved groups: perceived positive consequences for family, perceived positive consequences for self, and provider recommended. The associations were moderate to strong with Pearson's r>.50. Variables that showed negative associations could be interpreted as barriers. The strongest associations were still weak with Pearson's r<-.25. These were: perceived negative consequences to self (among served) and convenience factors (among underserved).

Logistic regression was done using data from the entire sample. The following were significant and increased odds of using genetic counseling: having an additional risk factor (OR=2.292; 95% CI=1.604-3.275; p=.000), income (OR=1.356; 95% CI=1.091-1.686; p=.006). Knowledge of breast cancer genetics also showed increased odds of using genetic counseling (OR=1.208; 95% CI=1.137-1.282; p=.000) but because 32.7% of participants already received genetic counseling at the time of the study, the knowledge score may be an outcome of genetic counseling rather than a predictor. Motivation to comply with healthcare provider showed lower odds of using genetic counseling (OR=.360; 95% CI=.162-.803; p=.013). Challenges in operationalizing variables due to being a secondary analysis led to exclusion of some variables from analyses and were a limitation of the study. Triandis's model of

interpersonal behavior still shows promise as a framework for guiding research on the predictors (barriers and facilitators) of cancer genetic counseling use.

To prevent worsening disparities in the context of having a heritable mutation for cancer, additional work needs to ensure equitable opportunity to use genetic counseling. Prospective studies might oversample for rural populations and individuals of racial and ethnic minority background. Integration into the health care system, measured by regular use of preventive health services, may be a helpful criterion for determining underserved status in the context of the specialized health service of cancer genetic counseling.

CHAPTER I

Introduction

The burden of cancer can be described in multiple ways and from many perspectives. Cancer is the second leading cause of death in the United States; medical costs and lost productivity from cancer cost the United States an estimated $263.8 billion in 2010; approximately 575,000 people died of cancer and more than 1.5 million people had a diagnosis of cancer in 2011 (http://www.cdc.gov/chronicdisease/resources/publications/aag/dcpc.htm). Extending beyond these numbers, however, is the emotional burden of cancer for individuals and their families. By this measure, hereditary cancers arguably claim one of the highest burdens associated with cancer. Some characteristics suggestive of hereditary cancers that contribute to burden include younger-than-usual age at tumor diagnosis, multiple or recurrent cancers in one individual, and same or related tumors present in multiple family members (Lindor, McMaster, Lindor, & Greene, 2008). Hereditary breast and ovarian cancer (HBOC) is one syndrome associated with increased risk for cancers due to heritable mutations. With HBOC, carrying a mutation in the breast cancer gene *BRCA1* or *BRCA2* substantially increases risk for cancer of the breast, ovary, prostate, and others (Antoniou et al., 2003a; Chen and Parmigiani, 2007a). Existing strategies have been associated with significant reductions in risk of developing cancer due to inherited mutations and reducing associated morbidity (Nelson et al., 2013a). However,

some strategies such as risk-reducing surgeries can have severe consequences, affecting future fertility, body image, and other morbidity. The decision to implement these strategies must be an informed one and tailored to individuals at greatest risk. Genetic counseling and genetic testing can reduce the potential for developing cancer among individuals with the known risk factors. However, disparities may exist in who uses the genetic services that can lead to informed decision-making.

Approximately 1 in 8 women in the US will develop invasive breast cancer at some point in their lifetime, making breast cancer the most common cancer among women in the United States excluding skin cancer (ACS, 2015). A very small segment of the general population, between 0.2 - 1%, has a mutation in one of the breast cancer susceptibility genes *BRCA1* and *BRCA2* (Kurian, 2010). In the U.S., where there were an estimated 233,000 cases in 2012 (women only) (http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx), approximately 2,330 individuals carry one of the mutations increasing their susceptibility to cancer of the breast, ovary, prostate, pancreas, and other cancers. These mutations account for approximately 5-10% of all female breast cancers, 5-20% of male breast cancers, and 15-20% of familial breast cancers (ACS, 2015). *BRCA1/2* mutations are found at higher rates among certain ethnic or other groups whose ancestors or "founders" were geographically isolated for a period of time. Rare mutations in these populations became more common within the group as a result of isolation and interbreeding.

Founder mutations have been identified among European populations, including: Ashkenazi Jewish, Icelanders, Norwegians, Finns, Swedes, French, Dutch, and Italians from Calabria and Italians from Sardinia; they have also been identified among non-

European populations, including: French-Canadians from Quebec, Hispanics from South California, Hispanics from Columbia, Afro-Americans, South Africans, Iraqi/Iranian Jewish, Chinese, Japanese, Malaysians, Filipinos, and Pakistanis (Ferla et al., 2007). A review of these and additional studies consisting of clinic-based samples, population-based samples, and individuals with and without strong family history of cancer, concluded that the prevalence of of *BRCA1/2* mutations among individuals of African, Asian, white, and Hispanic descent is comparable (Kurian, 2010a). This finding is supported in a recent study with a national commercially insured sample (Armstrong et al., 2015).

BRCA1 and *BRCA2* are tumor suppressor genes. Each has its own mechanism of action but both play important roles in the maintenance of genome stability through DNA damage signaling, DNA repair, chromatin remodeling and transcription. Carrying a mutation in the *BRCA1* or *BRCA2* genes means a substantially increased risk of developing cancer of the breast, ovary, prostate, pancreas, and others. Having a mutation in the *BRCA1* gene can increase lifetime risk of developing breast cancer to 57-65% and risk of developing ovarian cancer to 39-40% (Antoniou et al., 2003a; Chen and Parmigiani, 2007a). For *BRCA2* mutation carriers, risk for breast and ovarian cancers are slightly lower with lifetime risk for breast cancer being 45-49% and risk for ovarian cancer being 11-18%. However, these risk levels are still substantially higher than the general population risk (those who do not carry a mutation associated with increased susceptibility to cancer) of 12.3% for breast cancer and 1.3% for ovarian cancer. (Howlader N, Noone AM, Krapcho M, Garshell J, Miller D, Altekruse SF, Kosary CL, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ,

Cronin KA (eds). SEER Cancer Statistics Review, 1975-2012, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2012/, based on November 2014 SEER data submission, posted to the SEER web site, April 2015.).

Although the prevalence of cancer due to a *BRCA1/2* mutation may seem low, the potential burden to individuals who develop these cancers is no less significant. In addition to increased risk of developing a variety of cancers as mentioned above (though breast and ovarian are most common), individuals who carry *BRCA1/2* mutations may get multiple or recurrent cancers (Lindor et al., 2008). Compounded with an uncertainty of when or if one will develop cancer, when or if a cancer will recur, and the shock of cancer onset at a young age, being at risk for having a *BRCA1/2* mutation can prove to be a challenge. Although the risks associated with having a mutation seem significant, a recent review of the literature (Lynn C. Hartmann & Lindor, 2016) supports previous findings on the efficacy of risk-reducing surgeries for the prevention of breast and ovarian cancers. With the exception of one study which did not show a significant reduction in the risk of subsequent breast cancer after bilateral mastectomy (Skytte et al., 2011), recent additional studies (Domchek et al., 2010; Evans et al., 2009; Heemskerk-Gerritsen et al., 2007) support the findings of studies done between 1999 and 2004 (L. C. Hartmann et al., 1999, 2001; Meijers-Heijboer et al., 2001; Rebbeck et al., 2004) that showed a reduction of 90% or more in the risk of subsequent breast cancer among women who underwent prophylactic mastectomy. Additionally, one meta-analysis and seven efficacy studies on risk-reducing salpingo-oophorectomy also support previous findings of significant reduction in risk for ovarian cancer – approximately 80% among *BRCA1* and *BRCA2* mutation carriers (Domchek et al.,

2006, 2010; A. Finch et al., 2006; A. P. M. Finch et al., 2014; Kauff et al., 2002, 2008; Rebbeck et al., 2002; Rebbeck, Kauff, & Domchek, 2009). As in the case of prophylactic mastectomy to reduce the risk of breast cancer, it should be noted that a substantial decrease in risk for ovarian cancer results from risk-reducing salpingo-oophorectomy, but some risk does remain. Although there are advantages to these surgeries, some of the risk-reducing strategies such as surgery carry their own risks such as infection and other morbidity. The risk-reducing surgeries can be considered drastic and must be weighed with the individual's level of risk as well as awareness of remaining risk and potential complications after risk-reducing approaches. Genetic counselors can facilitate discussions about these and similar factors to consider in order for individuals to make informed decisions and arriving at a plan that minimizes risk are of utmost importance.

Genetic counselors' expertise in evaluating risk and discussing strategies to minimize risk and potential outcomes can be invaluable. However, the proportion of individuals receiving genetic counseling is far from optimal. Data from the National Health Interview Survey (NHIS) and the Centers for Disease Control and Prevention, National Center for Health Statistics (CDC/NCHS) found only 34.6% of women with a family history of breast and/or ovarian cancer received genetic counseling in 2005 (http://www.healthypeople.gov/node/4502/data_details#revision_history_header). The US Preventive Services Task Force (USPSTF) recommended in 2005 in that all women with a family history suggestive of increased risk for clinically significant mutations in the *BRCA1* or *BRCA2* genes be referred for genetic counseling and evaluation for mutation testing (U.S. Preventive Services Task Force, 2005a). Yet, as recently as 2015, studies

where all participants met criteria for genetic counseling are still reporting that fewer than 50% of study participants pursued genetic counseling (Anderson et al., 2012a; Armstrong et al., 2015; Cragun et al., 2015a). In one of these studies (Cragun et al., 2015a), a mere 35% were referred for genetic counseling despite all participants meeting national guidelines for referral. Of the 440 participants who completed surveys, 91 saw a genetic counselor. This translates to 21% of the sample.

Although use of genetic services (genetic counseling and genetic testing if applicable) may be relatively new, disparities in the use of genetic services may be next in contributing to persistent disparities in health and health outcomes. Breast cancer mortality rates have been decreasing since 1989 (ACS, 2015), with the overall decline being attributed largely to early detection and better treatments (Berry et al., 2005). Declines in mortality rate, however, have been greater for some segments of the population than for others. For example, mortality rates have been reported as declining by 1.8% in whites, 1.5% in Hispanics, 1.4% in blacks, and 1.0% in Asians/Pacific Islanders, but have been unchanged among American Indians/Alaska Natives (Howlader et al., 2012; http://seer.cancer.gov/csr/1975_2012/). The difference in rates of decline is likely due to a combination of factors including biological factors (e.g., tumor characteristics, genetic predisposition to cancer, obesity, age at first live birth, breastfeeding), social factors (e.g., cultural beliefs, historical influences, concerns about discrimination), and structural factors (e.g., insurance coverage, access to care which can influence stage at diagnosis and treatment) (De Ridder et al., 2016; Friebel, Domchek, & Rebbeck, 2014). These factors may also contribute to disparities in mortality among the subpopulations who may carry mutations in the *BRCA1/2* genes.

An analysis of a testing repository of individuals who underwent clinical full-sequence DNA testing for mutations in the *BRCA1* and *BRCA2* genes between 1996 and 2006 (through Myriad Genetic Laboratories, Inc., the only company in the United States offering this testing from 1996 to June 2013) found that women of African ancestry and Latin American ancestry had significantly higher prevalence of deleterious *BRCA1/2* mutations (15.6% [OR 1.3 (1.1-1.5)], and 14.8% [OR 1.2 (1.1-1.4)], respectively) compared to women of Western European ancestry (12.1%) (Hall et al., 2009). *BRCA1* mutations have been found to be less prevalent among African Americans compared to whites but African Americans diagnosed with breast cancer under 35 years of age have the highest rate of *BRCA1* mutations (16.7%) than any other racial/ethnic group except Ashkenazim (66.7%) in age-matched analyses (John et al., 2007). About 69% of breast cancers that develop in individuals who carry a *BRCA1* mutation are estrogen-receptor (ER)-negative, progesterone-receptor (PR)-negative, and human epidermal growth factor receptor 2 (HER2)-negative, or "triple-negative breast cancers". Triple-negative breast cancers tend to be more aggressive and are associated with poorer prognosis (Lacroix & Leclercq, 2005; Mavaddat et al., 2012; Rakha, Reis-Filho, & Ellis, 2008).

A review of the studies reporting the above findings, along with other studies, highlights important differences in the prevalence of *BRCA1* compared to *BRCA2* between racial/ethnic groups and differences in frequency of results containing variants of unknown significance (VUS) between racial/ethnic groups (Kurian, 2010a). In addition to the finding of higher prevalence of *BRCA1*-associated tumors among African American women under 35 years of age mentioned above (John et al., 2007),

individuals of African descent showed VUS nearly three times more than did whites (16.5% in African Americans compared with 5.7% in whites) (Hall et al., 2009). Individuals of Hispanic descent showed VUS nearly two times more than whites (10.1% in Hispanics compared with 5.7% in whites).

The scientific community has acknowledged the effects that inadequate knowledge about certain groups can have on health outcomes. One breast cancer risk assessment tool, for example, states that the original version was based on data from white women but has been updated as additional data has become available (http://www.cancer.gov/bcrisktool/about-tool.aspx). The tool now more accurately estimates risk for African American and Asian/Pacific Islander women. However, risk estimates may not be accurate for American Indian, Alaskan Native, and Hispanic women as the calculations are based on data from white women. For recent immigrants from some parts of Asia, risk is stated to be “probably” lower than predicted by the model.

In recent literature, scientists have also called for greater participation among groups traditionally underrepresented in research, such as ethnic minorities. One area in which this has been recognized, for example, is in clinical trials on cancer therapies. Without sufficient participation from groups of diverse backgrounds, treatment effects would be uncertain and perhaps suboptimal. Studies in genetics and genomics face a similar challenge of having the majority of knowledge coming from non-Hispanic whites. For example, the frequency of VUS in individuals of African and Hispanic descent is much higher than that in whites because of lack of information from individuals of African and Hispanic descent. A VUS is, as its name suggests, a variation from a gene

sequence that has been defined as the normal, and the significance of this variation is unknown. The variations often are single nucleotide polymorphisms or alterations to noncoding regions of the gene and may or may not affect the function of the resulting protein. Receiving a result of a VUS is not clinically useful. In some cases, receiving a result of a VUS can be distressing due to the ambiguous, uninformative nature of the finding. The tests to identify a mutation in the *BRCA1/2* genes developed from gene sequences of white individuals and thus have the gene sequences of white individuals as the "normal". Interestingly, the reported frequency of *BRCA1/2* VUS in a population is inversely proportional to the dissemination of genetic testing (Kurian, 2010a). *BRCA1/2* mutation prediction models, again developed largely from samples of white individuals, have also shown to be better in white individuals. The high rate of VUS and greater inaccuracy of mutation prediction models for groups other than non-Hispanic whites can be discouraging and potentially lead to less use of testing and further disparities.

A recent meta-analysis of 11 genome-wide association studies (Michailidou et al., 2015) reports identifying 15 new susceptibility loci for breast cancer, increasing from the 68 susceptibility loci for breast cancer identified in a prior report (Michailidou et al., 2013). The previous meta-analysis had reported that further analyses suggested more than 1,000 additional loci could be involved in breast cancer susceptibility. Genetic variants at these loci include the widely known *BRCA1* and *BRCA2* mutations. Development of tests for mutations at these newfound loci may increase the relevance and utility of testing to a broader range of individuals. One caveat of these findings, however, is that they are based on controls that were of European ancestry; application

to individuals not of European ancestry is unclear. While potentially useful for individuals with European ancestry, the findings carry the potential to furthering disparities in risk assessment for individuals and groups of other ancestry.

Recognition by the scientific community of factors that may further widen disparities in health and health outcomes is an important step in ameliorating the long-standing problem. However, it is insufficient. Policy also can also influence disparities. Guidelines for breast cancer screening, for example, have been a widely controversial topic for at least the past decade. In 2009, the United States Preventive Services Task Force (USPSTF) released breast cancer screening recommendations, recommending against mammography for women aged 40 to 49 years (US Preventive Services Task Force, 2009). The USPSTF is an independent group of experts in prevention and evidence-based medicine who assign recommendations for preventive services based on rigorous reviews of peer-reviewed evidence. The recommendations are intended to help primary care clinicians and patients decide whether a preventive service is right for each patient. Although the USPSTF recommendations themselves do not make statements about whether preventive services should be covered by insurance, the Affordable Care Act (ACA) does use the recommendations to determine what services private insurance companies are required to cover without cost sharing (The Henry J. Kaiser Family Foundation, 2015).

The 2009 USPSTF breast cancer screening recommendations were the topic of many heated debates by clinicians, scientists, politicians and patients alike. The recommendations were released at a time when soaring healthcare costs were becoming clearly unsustainable and health care reform was vital. Inefficiency and

waste were suspected and led to questions about overtreatment. The USPSTF recommendations were made taking into consideration reports about the harms associated with false-positive findings on mammograms (e.g., biopsies, pain and anxiety associated with biopsies, prophylactic mastectomy and associated morbidities). The USPSTF recommended against routine screening mammography in women aged 40 to 49 years, and stated that rather, the decision to start screening should be an individual one, taking into account each individual patient's context, including the patients values regarding specific benefits and harms. The backlash following the recommendations involved accusations about rationing of health care and concerns about whether mammograms would be covered by insurance for individuals under 49 who may still wish to get annual mammograms. The latter concern still exists today, with the recent release of the new guidelines for breast cancer screening from the American Cancer Society (ACS) (Oeffinger et al., 2015). The ACS guidelines recommend that women with an average risk of breast cancer – which is most women – should begin yearly mammograms at age 45, then decrease to every other year at age 55. However, the recommendation also states that women should be able to start the screening as early as age 40 if they want to, that women age 55 should be able to continue having yearly mammograms if they want to, and that they can continue to do so as long as they are in good health with a life expectancy of 10 years or longer. The 2016 USPSTF recommendations are for biennial screening mammography for women aged 50 to 74 years; women who place higher potential benefit on potential harms may choose to begin biennial screening between the ages of 40 and 49 years. The two organizations provide different recommendations. If insurance companies base

coverage criteria on these recommendations, differences in type of insurance can worsen existing health disparities.

The effects of the ACS and USPSTF recommendations can be particularly important to individuals at high risk for having a *BRCA1/2* mutation. Although genetic counseling and *BRCA* testing, if appropriate, are considered a preventive service and must be made available without cost-sharing under the Affordable Care Act, "if a recommendation or guideline does not specify the frequency, method, treatment, or setting for the provision of that service, the plan or issuer can use reasonable medical management techniques to determine any coverage limitations" (https://www.cms.gov/CCIIO/Resources/Fact-Sheets-and-FAQs/aca_implementation_faqs12.html#fn7). If one chooses not to get genetic testing and instead opts for frequent surveillance, there may be challenges with insurance coverage for services. Furthermore, if receipt of these services is dependent on an individual's personal financial resources, this can also worsen existing health disparities. Reflecting the increasing scientific evidence on the benefits of family health history and genetic tests, "Genomics" was created as a new topic area of Healthy People 2020 (http://www.healthypeople.gov/2020/topics-objectives/topic/genomics/objectives). Two objectives were set: 1) increasing the proportion of women with a family history of breast and/or ovarian cancer who receive genetic counseling, and 2) increasing the proportion of persons with newly diagnosed colorectal cancer who receive genetic testing to identify Lynch syndrome (or familial colorectal cancer syndromes. This proposed study will focus on the first objective.

The lost opportunity from identifying an individual as a mutation carrier only after cancer has developed has been regarded as a failure of cancer prevention (King, Levy-Lahad, & Lahad, 2014). Mary-Claire King (2014), a pioneer in the field and awarded for "bold and imaginative contributions to medical science and society," one of which was her discovery of the *BRCA1* gene, has proposed population-based genetic screening. King cites that World Health Organization criteria for population screening for genetic predisposition to disease (the disease is an important public health burden in the target population; risk of disease due to mutations in the screened genes is known; and effective interventions exist to reduce morbidity and mortality among genetically susceptible individuals) (Khoury, McCabe, & McCabe, 2003) are met in *BRCA1/2*-related cancers, and highlights flaws in existing mutation probability models (Weitzel et al., 2007). Smaller families, fewer opportunities for the mutations and/or cancer to manifest, have been considered akin to missing data (Weitzel et al., 2007). Thus, probability models cannot be relied on for determining eligibility for mutation analysis. King suggests that there are too many missed opportunities for cancer prevention. Clinical practitioners and the health care system may not yet be prepared to handle population-based genetic screening, as part of routine medical care, but King's bold proposal highlights the potential for disease prevention, flaws that need to be addressed in order to prepare for population-based genetic screening, and a glimpse of the possibilities in the future of genomics.

Genetics research has consistently ranked second highest in NIH-funded research after Clinical Research since at least 2011 (http://report.nih.gov/categorical_spending.aspx). However, the low uptake of genetic

services indicates that the benefits of current research efforts may not be fully being realized. While genomics carries a potential to improve health outcomes through predictive genetic testing and implementation of risk reducing strategies, the potential for widening disparities in health outcomes due to inequitable access and utilization of services also exists. In order to prevent further widening of long-standing and persistent disparities in health outcomes, equitable use of cancer genetic services that evaluate risk and guide the use of risk-reducing strategies must be ensured. Multiple factors and pathways can lead either to using genetic services or away from using genetic services. Because of the number and entwined relationships of some of those factors, the reason why genetic service use is low is still poorly understood. This information, however, is essential for developing interventions to address the causes among individuals who may benefit.

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CHAPTER II

Theoretical Framework and Literature Review

The Triandis model of interpersonal behavior

Multiple factors can influence the use of genetic services. These factors can occur at the individual level, interpersonal or social level, and structural level. Culture can play a role at each of these levels. Harry C. Triandis, from the field of sociology, has done extensive research on behavior and the role that culture can play. The relationship between culture and behavior in the context of using genetic services is an important one but is not yet well understood. From Triandis's extensive work on culture, he distinguished between individualistic and collectivistic cultures. Much of this work contributed to the development of his theory of interpersonal behavior (Triandis, 1977). The theory considers the complex interplay of human cognition, emotion, social influences, and physical or structural barriers in predicting behavior and shows potential for being applicable in the context of predicting the use of genetic services. In order to further explore the theory's applicability in the context of using genetic services, a literature review was conducted using the theory as an organizing framework.

Triandis conducted extensive work on individualistic and collectivistic cultures which increased the understanding of norms, values, attitudes, and behaviors among individuals from diverse ethnic and cultural backgrounds (Berman, 1990). Hui and

Triandis (1986) found that members of collectivist cultures have greater concern about the results of their actions on others. This is in contrast to individualist cultures, which place greater value on individual self-development, autonomy, and privacy, and regard the individual as the basis of society. Collectivism is often internalized to the extent that members act according to in-group norms automatically, without doing any calculation about the benefits and consequences to themselves (Berman, 1990). The resulting behaviors may or may not be congruent with what their preference would be if they were to do a calculation of benefits and consequences for themselves. Principles of individualism and collectivism can vary at multiple levels, including the individual, interpersonal, and societal levels. Presently, which of these levels is most influential in the use of genetic services is not known. However, culture may likely play an overarching role in the use of genetic services.

According to Triandis, the components that contribute to a behavior are: habit hierarchies, social factors, affect, the value of perceived consequences, and facilitating conditions. The model posits that the probability of a behavior depends on three major factors: 1) the strength of the habit of producing a behavior, which is indexed by the number of times the behavior has already occurred in the history of the individual, 2) the intention to produce the behavior, and 3) the presence or absence of conditions that facilitate performance of the behavior. Triandis distinguishes between behaviors that are done with little thought and are almost automatic (resulting largely from habit), and behaviors that are more deliberate, requiring more thought and planning (involving greater intention). The habit and intention components are dynamic, fluctuating in the amount of influence they have on a behavior. The components might vary according to

individuals, type of behavior, and context such as life stage. To account for this variation, Triandis weights variables according to importance.

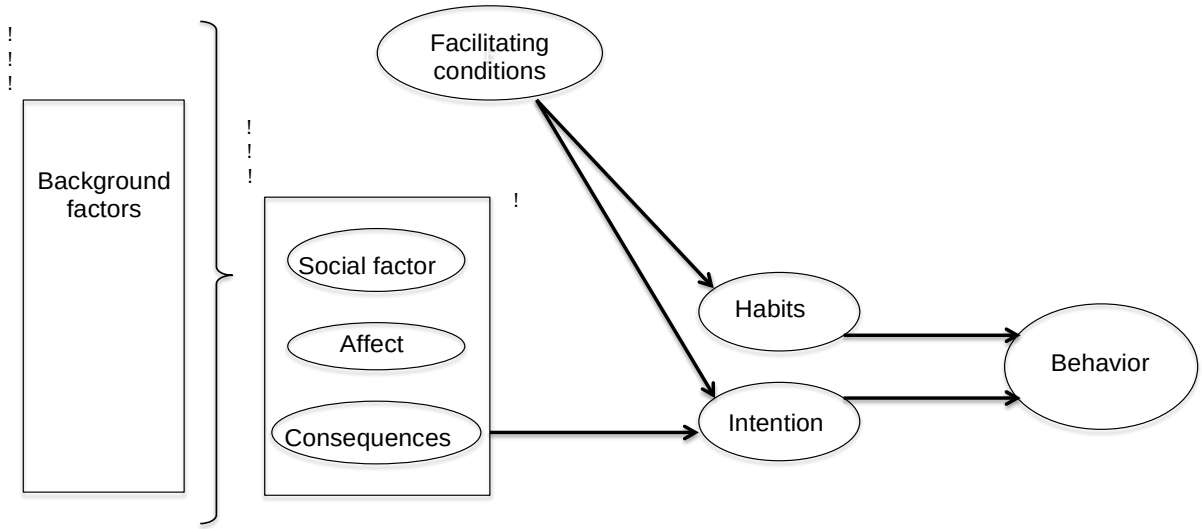
The model also describes determinants of behavioral intentions. These are: 1) social factors which include norms, roles, social contracts, self-monitoring, and self-concept, 2) affect associated with the behavior, and 3) the value of the perceived consequences. Triandis proposes that the value of perceived consequences is derived from first identifying the consequences that an individual perceives as likely to follow a behavior, then summing up how likely they perceive each of those consequences to occur and how much they value those consequences. Conceptual definitions and details about how values for each of the variables can be considered are shown in Table 2.1. The relationship of concepts based on Triandis's theory are shown in Figure 2.1.

Table 2.1. Concepts of Triandis model defined

Concept	Conceptual definition	Related concepts
Habits	Behaviors that occur with frequency	Number of times the person has committed a behavior
Facilitating conditions	Conditions that enable the person to carry out a behavior	Includes the person's ability, arousal, and knowledge to carry out a behavior
Intention	Cognitive antecedent of a behavior	Product of social factors, affect attached to the behavior, value of the perceived consequences of the behavior, and the weights of each
Social factors	Influential factors derived from the relationship between the person and other people	Includes norms, roles, contractual arrangements, self-monitoring, self-concept
Affect	Emotions that the person feels at the thought of the behavior, can be positive (pleasant) or negative (unpleasant), and strong or weak	
Perceived consequences	Subjective probability that certain consequences will follow a behavior; may differ from actual consequences	
Value of perceived consequences	How good or bad one would feel if a particular consequence actually happened	Sum of the products of the subjective probabilities that particular consequences will follow a behavior, and the values of (or affect attached to) those consequences

Source: *Interpersonal Behavior* by H.C. Triandis (1977).

Figure 2.1. Conceptual framework of Triandis's theory



According to Triandis, cultures differ significantly on the emphasis they place on the individual being part of and belonging to a "collective", with mainstream US culture being extremely individualistic (Triandis, 1977). From very impressionable ages, individuals learn behaviors that stem from the attitudes and beliefs of their culture. These attitudes and ways of thinking are ingrained into individuals starting from a very young age. As memberships and roles in various groups with their own subcultures evolve, so do the individuals' attitudes and beliefs. These experiences and their consequences shape an individual and their behaviors.

Reports of study findings about a particular racial or ethnic group may imply that the participants' race or ethnicity had a direct role in an outcome when in fact cultural beliefs may not have been measured, and race/ethnicity may simply be a background factor or at most associated with an outcome, not predictive of it. Participants' race or ethnicity may have been drawn from a simple question in a questionnaire. This

presents limitations, for example among multi-cultural/multi-ethnic individuals, and it does not address differences in level of acculturation and assimilation within the sample. Furthermore, comparison of studies, replication, and verification of findings involving specific races/ethnicities can be challenging due to limited numbers of specific cultural/ethnic populations in some geographic areas. Using characteristics of cultures – such as collectivist versus individualist cultures – as a way of defining groups and exploring the association with and effect on an outcome is an alternative approach that has yet to be explored.

Measures of collectivism and individualism are not readily found in research on the use of health services. However, medical underservice is a more recognizable characteristic and may be suitable as a proxy for culture. Medical service (not living in a federally designated medically underserved area) will be used as a proxy for individualist culture, and not having medical service (living in a federally designated medically underserved area) will be used as a proxy for collectivist culture. The medical service (alternatively, underservice) piece incorporates socioeconomic and system-related structural factors; using these as a proxy for the traits of individualist and collectivist cultures, respectively, will incorporate the cultural piece, presenting a multidimensional analysis of the influence of culture in the use of genetic counseling.

Literature review

The act of using genetic services is multi-faceted and still not well understood. As mentioned earlier, the proportions of individuals who are at high risk for carrying a BRCA1/2 mutation and for whom genetic counseling is appropriate are far below

optimal. In a population-based study of women diagnosed with breast cancer before age 50, widely recognized as a red flag for possible hereditary mutation such as *BRCA1* or *BRCA2*, fewer than 50% of women pursued genetic counseling (Anderson et al., 2012). Even more recently, in another study where Black women diagnosed with invasive breast cancer were at or below age 50, 49% of participants were neither referred for genetic counseling nor accessed genetic services, and a mere 35% were referred for genetic counseling despite all participants meeting national guidelines for referral (Cragun et al., 2015). To understand more about the barriers and facilitators around the use of genetic services, a review of the literature was conducted in Medline, Scopus, and CINAHL and included the key terms genetic testing, genetic counseling, intention, BRCA, decision making, psychology, social support, health knowledge, attitudes and practice. The use of genetic services is the primary interest of this review. Both genetic testing and genetic counseling were used because counseling may not necessarily precede testing and testing may not necessarily follow counseling. However, important lessons may be learned from literature in both cases. Decision making, psychology, social support, health knowledge, and attitudes were chosen to retrieve studies on the cognitive aspect of determining a preference to use genetic testing and genetic counseling. Practice was included to retrieve studies on the actual uptake of services. The search using this combination of terms produced results with the highest relevance to the aim of this review. Reports of the link between the BRCA genes and increased predisposition to breast, ovarian, and other cancers were reported in the late 1990s (Miki et al., 1994; Wooster et al., 1994). Articles published between 2000 and 2014 were included. Abstracts were reviewed for applicability. Articles were

chosen if they examined factors that influenced the use of genetic testing or genetic counseling for hereditary breast cancer. Because genetic tests for other syndromes with hereditary links to breast cancer such as Cowden's and Li-Fraumeni syndrome are not as well established, results were limited to articles on *BRCA1/2* mutations. Some related articles from search results were also included. Both qualitative and quantitative studies were included.

The findings of the review can be found in Appendix A. Findings are organized by the constructs of the Triandis model (habits, facilitating conditions, social factors, affect, and perceived consequences) in the rows, and categories under which the influential factors derived from the literature search fit (personal factors/characteristics, social and cultural influences, healthcare system factors, government policy, and the industry/market) in the columns.

Social factors

This concept encompasses the various relationships between a person and other people that can be influential. The social factors associated with or found to predict use of genetic services in the literature can be categorized under two variables: 1) perceived expectations and 2) motivation to comply with perceived expectations. The most commonly reported reasons for using genetic services, whether genetic counseling or genetic testing, is to benefit the family in addition to identifying risk for oneself (Anderson et al., 2012; K. Armstrong et al., 2000; Thompson et al., 2002). Among Latinas, a perceived expectation that was commonly reported as influencing the use of genetic services was in prioritizing the family's needs over one's personal needs (Glenn,

Chawla, & Bastani, 2012; Sussner, Jandorf, Thompson, & Valdimarsdottir, 2013). This has been reported as a cultural belief in multiple studies. Among Asians, stigma of having “bad genes” was a common theme for concerns about using genetic services to obtain genetic information (Glenn et al., 2012). In that culture, where family approval of a suitable marriage partner involved asking about the family’s medical history, there was an expectation to keep the medical record free of such information.

A common theme found across different backgrounds was stigma from having a *BRCA1/2* mutation. Among some Ashkenazi-Jewish, there is concern that increased awareness of higher frequency of this mutation occurring among individuals with this background will lead some to associate the group with having bad genes or inbreeding (Davis, 2000). Stigma of having bad genes is also associated with concern for abuse in the context of eugenics and denigrating groups, particularly among African-Americans who have experienced similar abuses in the past (Glenn et al., 2012). Other than among Ashkenazi-Jewish, concerns about social factors like these are not reported among non-Hispanic white participants. A gap in knowledge is whether these or similar social factors are not significant concerns among non-Hispanic whites or simply that studies exploring this topic have involved primarily understudied and underrepresented groups in research.

Although some interesting themes have emerged from studies on this topic, important limitations of studies mentioned above are 1) small sample sizes and 2) limited ability to corroborate findings due to few comparable studies.

Affect

Relief and worry are the predominant themes for emotions that influence the use of genetic services. Existing literature primarily involves the emotions from anticipated consequences to the self, with some literature on emotions related to consequences to family. Positive emotions associated with getting genetic counseling and testing included feeling relief from a negative result (not having a mutation) (Chin et al., 2005; Thompson et al., 2002) and having a better sense of personal control (Chin et al., 2005). Negative emotions included worry about passing a mutation on to children and for relatives who may be carriers, fear of positive results (having a mutation), and not wanting to hear bad news (Chin et al., 2005; Thompson et al., 2002). Knowing the truth or receiving a diagnosis makes some feel empowered with the opportunity to then take actions that can potentially affect their outcome. However, the truth may be disabling if they were to become consumed with worry. This finding emerged from a study within the context of end-of-life care (Blackhall, Frank, Murphy, & Michel, 2001) but may be applicable in the context of using genetic services to identify predisposition to cancer. Individuals who do not wish to know the truth about their risk may choose to forego genetic services. Worry about whether their children or other family members are carriers has been a top perceived barrier to genetic testing (Thompson et al., 2002). Another possible emotion is guilt about passing a mutation on to children, not having the mutation though a family member might, or causing burden or worry to family by being diagnosed with a mutation (Glenn et al., 2012; Sussner et al., 2013). Existing literature suggests that individuals with ethnic minority background, particularly African-American

and Asian backgrounds, may be more likely to experience worry. However, this may vary with level of acculturation to Western attitudes and practices.

Perceived consequences

Triandis describes the value of perceived consequences as the sum of the products of the subjective probabilities that particular consequences will follow a behavior, and the values of (or affect attached to) those consequences (Triandis, 1977). No studies were found assessing or reporting subjective probabilities of particular consequences occurring. However, some studies report percentages of participants who agree or strongly agree with a factor being important (Thompson et al., 2002) or report most frequently reported reasons (Anderson et al., 2012). 'Benefits to the family's future' has been among the most frequently reported reasons for receiving genetic counseling in multiple studies (Anderson et al., 2012; Chin et al., 2005; Glenn et al., 2012). The negative consequences frequently reported are loss of privacy and potential discrimination. There are no studies, however, on which of the following influence the use of genetic services more: positive perceived consequences or negative perceived consequences, and whether consequences to the self or to family/others are more influential. These findings present an important gap in the literature which may be useful in identifying targets for interventions aiming to increase the use of genetic services to decrease cancer risk.

Intention

The literature search did not yield studies measuring intention to use genetic services. Intention has long been part of theories of behavioral change such as the Theory of Reasoned Action (Fishbein & Ajzen, 1975) and the Theory of Planned Behavior (Ajzen & Fishbein, 1980), which have been widely studied, evaluated, and used in predicting behavior change. If the use of genetic services is considered a health behavior, theories aiming to predict the behavior (use of genetic services) should include intention. Triandis has theorized that intention is derived from an individual considering 1) social factors, 2) affect or emotions at the thought of engaging in the behavior, and 3) perceived consequences (Triandis, 1977). However, the relationship of these three factors with actual intention has not been studied in the context of using genetic services.

Facilitating conditions

Perhaps the largest amount of literature regarding the use of genetic services is on facilitating conditions. According to Triandis, facilitating conditions enable an individual to follow through with a desire to engage in a behavior. Regardless of the habits or intention to engage in a behavior, the facilitating conditions must be present and sufficient. Provider recommendation has been cited as one of the most consistent predictors of genetic counseling (Anderson et al., 2012) and genetic testing (McCarthy et al., 2013; Marc D. Schwartz et al., 2005). A recent large, population-based study aimed at evaluating rates and predictors of physician recommendation for *BRCA1/2*

testing among patients with breast cancer found the correlation between provider recommendation and undergoing testing to be greater than .9 (McCarthy et al., 2013). Over 80% of women who reported receiving a provider recommendation had testing, while fewer than 6% of those not receiving a recommendation went ahead to pursue testing. Individuals with limited access to a knowledgeable healthcare provider or extensive network of individuals with personal experience may be at a disadvantage when it comes to receiving appropriate recommendations. Individuals living in medically underserved areas, by definition, have more limited access to healthcare providers (http://www.hrsa.gov/shortage/mua/). Therefore, they may be less likely to receive a provider recommendation and less likely to use genetic services. However, no studies in this review of the literature explored the relationship between individuals living in medically underserved areas and receiving a recommendation from their provider for genetic services, and subsequently whether the individuals went on to get genetic services. Additionally, no studies are known to have explored the relationship between the existence of facilities providing genetic services, proximity of these facilities to residence, and use of genetic services. Little is known about the presence or absence of facilities offering genetic services in medically underserved areas.

Having received a referral for genetic counseling, perceived risk, availability of transportation and childcare, and social support have been described as facilitators (Anderson et al., 2012; Chin et al., 2005; Sussner et al., 2013); while lack of knowledge about genetic services and next steps, and being too busy or viewing other things as being more important, have been reported as barriers (Anderson et al., 2012; Chin et al., 2005; Glenn et al., 2012). Each of these can be considered a facilitating condition;

variables reported in the literature as facilitators can also be thought of as having been identified as present and sufficient by the study participants, while the the absence or shortage of the same variables were reported as barriers.

Knowledge about how to navigate the health care system may be another facilitating condition. Among a sample of Arab-American women where some participants were recent immigrants, use of genetic services was negatively influenced by difficulty navigating the system (Mellon, Gauthier, Cichon, Hammad, & Simon, 2013). Insufficient knowledge of how to navigate the system may be a barrier for others who lack experience with it. The medically underserved, for example, who may have insufficient knowledge about or experience with navigating the system, may find that it is a barrier also, especially with more specialized health care services such as genetic counseling or genetic testing. The experience of medically underserved in this respect is lacking in the literature.

Characteristics of the healthcare system can be facilitators or barriers in the use of genetic services. For example, the availability of female physicians may influence women who have strong beliefs related to modesty during physical exams and other interactions (Mellon et al., 2013). Concerns about insurance coverage and cost of counseling and testing have been frequently reported in the literature as a barrier (Anderson et al, 2012; Glenn et al., 2012). Having a clinic close to home, having a clinic with flexible hours, and the provision of services by phone have also been reported to facilitate use of genetic counseling (Anderson et al., 2012). It is plausible that having a clinic close to home, or proximity to a clinic that provides these services may facilitate use of genetic services. However, other factors may be necessary or increase the

ability of proximity to influence use of genetic services. For example, living within walking distance to a clinic may be helpful but without financial resources, lack of perceived risk, or provider recommendation, the proximity to the clinic may be insignificant. In that case, flexible hours and availability of services by phone may be irrelevant as well. Whether the availability of clinics providing genetic services close to home would make a significant difference and what factors may work synergistically with that remains largely unexplored. However, some researchers have cited the potential for genetic counseling via telephone to increase reach and access, and to maximize cost savings (Kinney et al., 2014; M. D. Schwartz et al., 2014). Noninferiority trials of telephone counseling compared to usual care in the context of genetic counseling and testing for *BRCA1/2* mutation have found telephone counseling to be noninferior to usual (in-person) counseling. Both studies found lower uptake of genetic testing with groups receiving telephone counseling. The difference was not statistically significant, but approximately 10% (95% CI = 3.9% to 16.3%).

Another interesting finding from one of the studies (Kinney et al., 2014) was that uptake of testing was higher among rural participants compared with urban participants. Although not statistically significant, the authors of the study believe that this suggests that rural participants – for whom geography may be a barrier – may have genetic screening interests that are underserved by existing health care systems. Individuals living in federally designated medically underserved areas (MUAs) may experience similar barriers and a similar increased uptake of genetic counseling and testing when the opportunity to receive the services is made more readily available. Because there are a variety of ways to define rural, using residence in an MUA as a study variable may

more comprehensively capture underserved individuals for whom interventions can be aimed.

Having family that is supportive and helpful can facilitate the use of genetic risk assessment and counseling among those who wish to do so (Mellon et al., 2013). Individuals who were married were more interested in *BRCA* testing (Schwartz et al., 2001) but the reason behind this is unclear. Conversely, lack of social support, for example by family members or cultural beliefs may influence an individual to not use genetic services (Sussner et al., 2013).

Important limitations of the studies above are small sample sizes and lack of multiple similar studies to corroborate the findings. The findings of the single study with an Arab-American sample described above demonstrates how cultural beliefs that are different from the majority can be a barrier. In the context of using genetic services, there were no other studies that support these findings among another Arab-American sample. Studies with Hispanic women also show culturally-related factors that influence use of genetic services, but again, these are few in number. The opportunity for individuals or groups to benefit from the value of genetic services cannot be deferred until they become better represented in the literature, however. One approach to explore differences in behavior related to deep-seated influences such as culture, may be through a lens of individualist and collectivist cultures.

Nations with more individualist traits are developed, wealthy, have more economic development, have modern industry, urbanization, and greater social mobility. Nations that show more collectivist traits are underdeveloped, poor, have less economic development, are more agricultural, and have less social mobility (Triandis, 1977).

Triandis's extensive study of the influence of culture and cross-cultural psychology led to recognition of differences in aspects of the self and social behavior among individuals from individualist compared to collectivist cultures (Triandis, 1977). The variable of living in a medically underserved area may provide a similar lens through which differences in the use of genetic services may be examined. Designation as a medically underserved area (MUA) by the federal government includes consideration of demand for and access to primary care, infant mortality rate for a specified area, and prevalence of poverty in an area (http://www.hrsa.gov/shortage/mua/). Medically underserved areas, which have higher demand and lower access to primary care, higher infant mortality rates, and higher poverty, can be compared to the traits of collectivist nations. Areas that are not medically underserved may be comparable to individualist nations which, related of greater wealth and being more developed, may offer better access to primary care, lower infant mortality rates, and lower poverty.

Habits

According to Triandis, habits stem from behaviors that occur with certain frequency and can be identified by assessing the number of times the individual has committed the behavior in the past. By this definition, genetic services would need to have been used more than once. Repeat testing may be useful for individuals who received a result indicating a variant of unknown significance (VUS), for which ongoing scientific developments may lead to reclassification of the VUS as deleterious or pathogenic. Reclassification may have implications for clinical management recommendations such as surveillance with mammography or risk-reducing surgeries

(G. F. Schwartz et al., 2009). However, there were no studies that discussed use of genetic services as a habit. A related question is whether individuals who engage in health maintenance behaviors such as recommended screenings, may be more likely to use genetic services. For example, a predisposition to use health services was found to be associated with higher likelihood of breast cancer screening behaviors (Katapodi, Pierce, & Facione, 2010). A limitation of the study reporting this was that there were a limited number of participants over age 40 and therefore eligible to receive a recommendation for breast cancer screening. Examining the relationship may be more informative with a sample who is high-risk, for whom screening is indicated, and for whom screening could be a health-maintenance behavior.

Lack of a personal and family history of using health services can result in little knowledge about one's health history. Some feel ill-equipped for using genetic services which would involve assessment of personal and family past medical history and therefore may defer doing so (Glenn et al., 2012). These findings are limited by the few number of studies and small sample sizes, and the relationship between use of health services in general, and cancer screening or risk assessment services requires further investigation. Future studies may identify approaches for system-related interventions to facilitate use of health services in the context of genetic services.

Background factors

The USPSTF put forth a recommendation statement for *BRCA*-related risk assessment (U.S. Preventive Services Task Force, 2013). Contained in that recommendation statement is a referral screening tool wherein personal and family

history of breast and ovarian cancer are assessed (from (Bellcross, Lemke, Pape, Tess, & Meisner, 2009). Individuals indicating yes to two or more items should receive a referral for genetic counseling and, if indicated after counseling, genetic testing. The tool asks about breast cancer at ≤50 years or ovarian cancer at any age among self, mother, sister, daughter, mother's side grandmother, aunt, father's side grandmother, aunt, ≥2 cases of breast cancer after age 50 years on the same side of the family, male breast cancer at any age in any relative, and Jewish ancestry. Some other professional organizations that have put forth guidelines for referral to genetic counseling are the American College of Medical Genetics and Genomics (ACMG) and National Society of Genetic Counselors (NSGC), National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO), The American College of Obstetricians and Gyncologists (ACOG), American Cancer Society (ACS). The USPSTF guidelines are based on a comprehensive systematic review of literature by content experts following a protocol consistent with the Agency for Healthcare Research and Quality (AHRQ) methods for systematic reviews, and posted for public comment for 4 weeks. The process described in the statement put forth by the USPSTF seems to be of sufficient rigor. Therefore, the criteria listed in the referral tool described above will also be used in data analyses to be described further below for this proposed study.

Summary

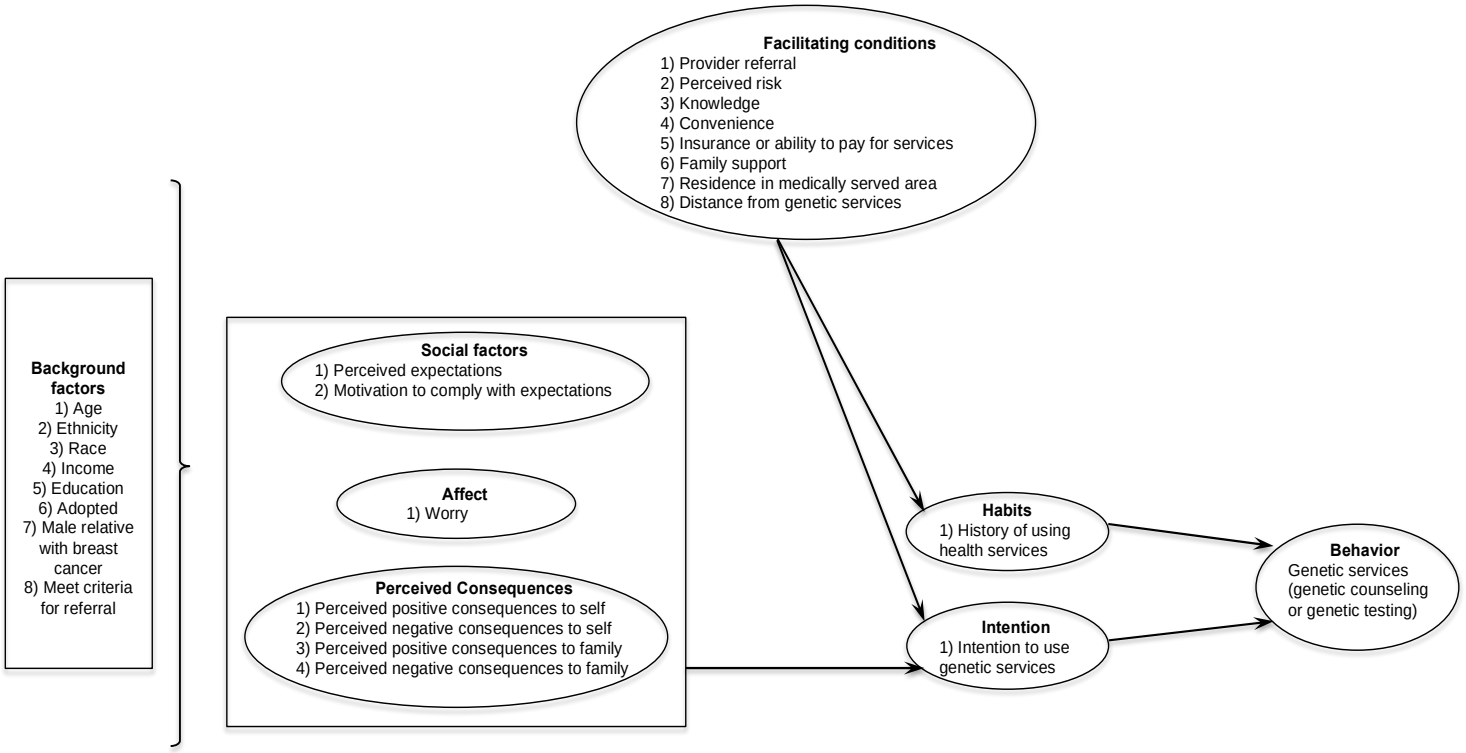
This review of the literature shows a significant amount of the literature is on facilitating conditions. Study findings are largely limited by small sample sizes and lack of a large number of studies that are comparable in participant characteristics and study

focus. Despite the number of studies exploring various facilitating conditions, there is still a lack of understanding of what factors – and in what combination – predict use of these services. One observation that emerged from the review of the literature is that women with ethnic minority backgrounds are more likely to refuse genetic services than are non-Hispanic white women, for a variety of reasons. The reasons include: having competing demands; having perceived role expectations that are incompatible with undergoing genetic services and associated physical exams and clinic visits; concerns about stigma from positive results; concerns about inadequate knowledge related to lack of family history from not using health care previously, unfamiliarity with navigating the health care system, or discomfort with aspects of the system (e.g., preferring a female provider, distrust due to racially-related reasons). Although these reasons for not using genetic services comes from women with ethnic minority backgrounds, they may not be limited to or always true for women with an ethnic minority background. From a broader perspective, there seems to be a theme of requiring the support or approval of a community, whether that is the spouse, family, community where one lives and works, and/or compatibility with broader ethnic/cultural beliefs. This resembles beliefs of collectivist cultures. Therefore, studying medically underserved samples (who share characteristics of collectivist cultures as described earlier) may inform about a focus for interventions aimed at individuals who do not use genetic services but who could benefit from them.

A few existing studies have reported findings from samples of women who received a diagnosis of breast cancer at age younger than age 50 (Cragun et al., 2015; Levy et al., 2011). These individuals met multiple guidelines that recommend genetic

counseling at a minimum, then genetic testing if applicable, yet still showed low uptake of genetic counseling (approximately 30-36%). This population – women diagnosed with breast cancer at age younger than 50 – may be an ideal population to study because they have an identified risk factor that hints at the possibility of having a mutation that substantially increases risk for multiple and recurrent cancers. Furthermore, there appears to be consensus from professionals based on research and clinical experience that genetic services could be beneficial for them. However, this population is rather small; researchers must be careful not to burden the individuals belonging to this group with numerous requests for participation in research. Attempts should be made to obtain as much knowledge as possible from existing data. This proposal outlines the use of existing data on a population-based sample of young breast cancer survivors (diagnosed at younger than 50 years old) to understand more about the barriers and facilitators to using genetic services. Figure 2.2 on the following page shows the Triandis framework modified to include the specific variables that will be evaluated in this study.

Figure 2.2. Triandis framework with specific variables to be evaluated in this study



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CHAPTER III

Methods

Studies on predictors of using genetic services (either genetic counseling or genetic testing) are few in number, demonstrate incongruent findings, and have small or convenience samples, therefore, more research is needed on what predicts the use of genetic services. Understanding the experience around genetic services use in young breast cancer survivors may be particularly informative because women diagnosed with breast cancer before the age of 50 represent a group that is at high risk and could benefit from genetic services, as early diagnosis is one indicator of a potential BRCA1/2 mutation. Young survivors and their relatives may benefit the most from using genetic services and gaining knowledge about their risk (i.e., genetic predisposition to cancer). The proposed study will be a secondary analysis of existing data from women who received a diagnosis of breast cancer before the age of 50 (also known as a young breast cancer survivor, or YBCS). The outcomes will contribute to understanding about this important, yet scarce population.

The **specific aims** of this study are:

1. Evaluate whether genetic counseling use differs between medically underserved versus medically served. For this study, medically underserved is defined as resident of a HRSA designated medically underserved area (MUA) in Michigan.
    a. Hypothesis: YBCS who are from medically underserved areas will have reported less frequent genetic counseling use compared to YBCS who are not from medically underserved areas.
2. Identify the correlates of using genetic counseling for hereditary breast and ovarian cancer risk among the medically underserved YBCS versus not medically underserved YBCS.
    a. It is hypothesized that among the medically underserved segment of YBCS from this sample, using genetic counseling will be most strongly correlated with social factors (perceived expectations of relatives, motivation to comply with perceived expectations of relatives), perceived consequences (perceived negative consequences to family), and facilitating conditions (provider referral, insurance or ability to pay, family support, distance from facility offering genetic counseling), and habits (history of using health services).
    b. It is hypothesized that among the YBCS who are not medically underserved, using genetic counseling will be most strongly correlated with perceived consequences (perceived positive consequences to self, perceived negative consequences to self), habits (history of using health services), intention (intention to use genetic counseling).

3. Evaluate the ability of the Triandis model to explain the use of genetic counseling overall (based on data from the entire sample of YBCS) and for medically underserved YBCS.
    a. It is hypothesized that for the *entire sample of* YBCS, facilitating conditions, perceived consequences, habits, and intention, will explain the use of genetic counseling the most, i.e., account for a high percentage of variance for the outcome of genetic counseling. It is hypothesized that for the *medically underserved* YBCS, the addition of social factors will further increase variance explained for the outcome of genetic counseling.

Expected outcomes generated by this study will improve understanding about barriers and facilitators to using genetic counseling, in particular among individuals who have a risk factor for carrying a *BRCA1/2* mutation but did not use genetic counseling. The outcomes may inform potential targets for interventions aimed at increasing the use of genetic services among the underserved population, who may face unique and less understood barriers to using genetic services. This goal is consistent with the genetics objective of Healthy People 2020 – to increase the population of women with a family history of breast and ovarian cancer who receive genetic counseling.

Study overview

The proposed study will be a secondary analysis of data from a completed study on an intervention to increase breast cancer screening among young breast cancer survivors and their high-risk female relatives. The secondary analysis will use data from

the baseline surveys of young breast cancer survivors only. This group are established to be at high risk for having a genetic predisposition to cancer given their breast cancer diagnosis at age younger than 50 and genetic services are indicated for them. The purpose of this study is to gain an understanding of genetic services use among young breast cancer survivors (YBCS) who are at high-risk for having a heritable genetic predisposition to cancer and identify whether differences exist in genetic services use among YBCS living in a medically underserved area versus YBCS not living in medically underserved area.

Data source

The completed study on which the proposed secondary analysis will be done was chosen for its large sample of YBCS. The identification and recruitment of individuals using the Michigan Cancer Surveillance Program (MCSP) cancer registry allowed for a population-based sample, reducing the potential for bias from including only individuals who have access to centers conducting this type of research.

Sample

Participants for the completed study were identified and recruited from the Michigan Cancer Surveillance Program (MCSP), a central cancer registry for *in situ* and invasive malignancies. From approximately 9,000 cases of young women diagnosed with cancer *in situ* or invasive breast cancer between 20 to 45 years old from 1994 to 2008, a sample of 3,000 women were randomly selected; deceased YBCS were excluded. A total of 859 YBCS completed baseline surveys with 100-120 women (11.6-

14%) reporting having used genetic services (either genetic counseling or genetic testing). To increase inclusion of minority and underserved women, the sample was stratified by race and oversampled YBCS who are black and living in counties with the highest mortality rates for young women with breast cancer.

Inclusion criteria

The proposed study will explore only data from the YBCS from the original study. Participants had to be female, age 25-64 years old, diagnosed with unilateral or bilateral invasive breast cancer between 20 and 45 years old or diagnosed with unilateral or bilateral ductal carcinoma in situ between 20 and 45 years old, Michigan resident at time of diagnosis, and able to read and understand English.

Exclusion criteria

Women who were pregnant, incarcerated, or institutionalized at the time of the study were excluded because they may not have been able to follow recommendations for breast cancer screening and genetic counseling. Relatives of participants in the original study will be excluded from the proposed study because they may not have known about their increased risk of being a *BRCA1/2* mutation carrier prior to the study. Therefore, they may not have had adequate time to use genetic services.

Variable determination

The operationalization of the variables to be examined is described in Table 2 below. The variable “medically underserved,” shown in Figure 2 under Background

Factors was not measured in the original study. However, medically underserved groups may face additional barriers to using genetic services and experience disparities in health and health outcomes as a result. Because a long-term goal of this program of research is to develop interventions to improve health disparities related to health behaviors that will decrease cancer risk, including among traditionally underserved groups, extra effort was made to create a medically underserved variable to be included in analyses.

To guide the creation of a medically underserved variable for this proposed study, a search of the literature was conducted on how the term "medically underserved" is defined in studies on the use of genetic services. A search on PubMed yielded zero results and the search was therefore expanded with keywords "medically underserved" and "healthcare utilization." Limits were: publications from the past 5 years and printed in English. This yielded a total of 139 results. Fifty-six articles were excluded because they either reported on studies conducted outside of the United States (n = 32 articles) (Afridi, 2013; Arya & Agarwal, 2011; Austin et al., 2014; Ban, Karki, Shrestha, & Hodgins, 2012; Blumenthal et al., 2013; Canada, 2013; Eskandari et al., 2013; Fagan, Cannon, & Crouch, 2013; Frey et al., 2013; Haile, Ololo, & Megersa, 2014; Haque, Louis, Phalkey, & Sauerborn, 2014; Harrison & Britt, 2011; Hasselback et al., 2014; Hirayama et al., 2013; Holloway, Mathai, Gray, & Community-Based Surveillance of Antimicrobial Use and Resistance in Resource-Constrained Settings Project Group, 2011; Hurune, O'Shea, Maguire, & Hewagama, 2013; Kalter et al., 2011; Karari et al., 2011; Khanal, Sauer, & Zhao, 2013; Kuo, Loresto, Rounds, & Goodwin, 2013; Martiniuk et al., 2011; Mitton, Dionne, Masucci, Wong, & Law, 2011; Mohammed,

Elnour, Mohammed, Ahmed, & Abdelfattah, 2011; Na, Kim, & Lee, 2014; Qumseya et al., 2014; Sangeda et al., 2014; Timony, Gauthier, Hogenbirk, & Wenghofer, 2013; Turner, Mulholland, & Taylor, 2011; van Roosmalen & Meguid, 2014; Whitehead et al., 2012; Wong, Heng, Cheah, & Tan, 2012; Wood, Vial, Martinez-Gutierrez, Mason, & Puschel, 2013), did not give a definition (a few of these articles were brief commentaries or policy briefs) (n = 18) (Aksu, Phillips, & Shaefer, 2013; Genz et al., 2015; Jha, Orav, & Epstein, 2011; Lalude, Gutarra, Pollono, Lee, & Tarwater, 2014; Little, Motohara, Miyazaki, Arato, & Fetters, 2013; Runkle, Zhang, Karmaus, Martin, & Svendsen, 2012;) (Allen, 2011; Casamassimo, 2014; Delzell, 2013; Frellick, 2011; Merchant, 2011; Raduege, 2012; Sahota, 2014; Sprague, 2014; Waldman & Perlman, 2014; Weigel et al., 2015; Xiong et al., 2015); No authors listed (132), or the articles were not obtainable through the University's electronic library (n = 5) (Diringer & Phipps, 2012; Hawk, 2011; Rivera-Colón et al., 2013; Sederstrom, 2015; Tanner, Kim, Friedman, Foster, & Bergeron, 2015). One article (Chi, Momany, Jones, & Damiano, 2011) was excluded because the focus involved intellectual or developmental disability which may have involved additional barriers.

Eighty-two articles provided a definition of medically underserved in the study being reported. The majority of articles (n=45) defined medically underserved using multiple factors (Arvey, Fernandez, LaRue, & Bartholomew, 2012; Bazargan, Chi, & Milgrom, 2010; Beazoglou, Lazar, Guay, Heffley, & Bailit, 2012; Bocker, Glasser, Nielsen, & Weidenbacher-Hoper, 2012; Chodosh et al., 2015; Dodd, Logan, Brown, Calderon, & Catalanotto, 2014; Dragun, Huang, Gupta, Crew, & Tucker, 2012; Dumont, Brockmann, Dickman, Alexander, & Rich, 2012; Enard & Ganelin, 2013; Engelman et

al., 2011; Glassman, Harrington, Namakian, & Subar, 2012; Golbeck et al., 2011; Harris et al., 2011; Heffernan et al., 2011; Jerkins, Zarzaur, & Fabian, 2013; Kapoor & Thorn, 2014; Klein et al., 2013; Langellier, Guernsey de Zapien, Rosales, Ingram, & Carvajal, 2014; Larkey et al., 2012; LeMasters et al., 2014; Lobb et al., 2011; Lustria, Smith, & Hinnant, 2011; Lynch et al., 2014; McCullough, Zimmerman, Bell, & Rodriguez, 2014; Northington et al., 2011; Ogbuanu et al., 2012; Ogunwale et al., 2015; Onoye et al., 2013; Pieh-Holder, Callahan, & Young, 2012; Purnell et al., 2012; Remler et al., 2011; Rustveld et al., 2013; Sadowski, Devlin, & Hussain, 2011; Samantaray et al., 2011; Samuel, King, Adetosoye, Samy, & Furukawa, 2013; Shaw, Vivian, Orzech, Torres, & Armin, 2012; Snyder & Milbrath, 2013; Summerfelt, 2011; Valencia, Savage, & Ades, 2011; Vlahov, Bond, Jones, & Ompad, 2012; Wallack, Loafman, & Sorensen, 2012; Wells et al., 2013; Whitley, Main, McGloin, & Hanratty, 2011; Xierali, Phillips, Green, Bazemore, & Puffer, 2013; Ziller, Lenardson, & Coburn, 2012). Factors used included being under- or uninsured, “low-income” (not further specified), ethnic minority, receiving care at a community health center, safety net facility, public hospital, small practice, or federally qualified health care center (FQHC), living in a health professional shortage area (HPSA), living in an area with a shortage of particular specialist (e.g., surgeon, dentist, behavioral health providers, etc.), living in a particular state or region, living in a rural area, living in a geographic isolated area (specified in some cases as living in Appalachia, number of miles from residence to a health care center or metropolitan center, and other times not specified at all), being a migrant or resort worker, homeless, and having limited access to care. Articles differed in number and type of factors used and there was no discernible pattern in choice.

The second largest group of articles (n=36) defined medically underserved using single criterion. The criterion included: being uninsured/underinsured without parameters (n=6) (Chi & Leroux, 2012; Hwang, Liao, Griffin, & Foley, 2012; Kamimura, Christensen, Mo, Ashby, & Reel, 2014; Montealegre et al., 2015; Notaro et al., 2012; Schiefelbein, Olson, & Moxham, 2014); "economically disadvantaged," parameters not defined (n=1) (Franklin et al., 2014); enrolled in Medicaid (n=1) (Chi & Raklios, 2012); received care through a "safety net program" (n=1) (Bailit & D'Adamo, 2012); live in a specified urban area (n=1) (Handy et al., 2013); live in an urban community with poor health status and high emergency department use (n=1) (Song, Hill, Bennet, Vavasis, & Oriol, 2013); total distance travelled to reach the healthcare center (n=1) (Pfeiffer et al., 2011); availability of providers (e.g., supply of subspecialists per county or radius of specific number of miles) (n=2) (Grindlay, Lane, & Grossman, 2013; Ray, Bogen, Bertolet, Forrest, & Mehrotra, 2014); live in a state with incidence and mortality for particular condition that is higher than the national rate (n=1) (Greene et al., 2012); live in a geographically isolated or remote area (specifically, Appalachia) (n=2) (Head, Vanderpool, & Mills, 2013; Wilson, Kratzke, & Hoxmeier, 2012); live in a "rural" area with no parameters defined (n=1) (Siminerio, Ruppert, Huber, & Toledo, 2014); live in a rural area defined by federally established Rural Urban Commuting Area Codes (RUCA Codes) (http://www.ers.usda.gov/data-products/rural-urban-commuting-area-codes.aspx) (n=3) (Doescher, Andrilla, Skillman, Morgan, & Kaplan, 2014; Gruca, Nam, & Tracy, 2014; Keenum et al., 2013); ethnic/racial minority without supporting rationale (n=2) (Christopher Gibbons, 2011; Roman et al., 2014); ethnic/racial minority with supporting rationale such as incidence, mortality, lower rates of screening than non-

Hispanic Whites (n=1) (Holt et al., 2013), ethnic/racial minority with the rationale of minority group having disproportionately higher mortality versus White women (n=1) (Ochoa-Frongia, Thompson, Lewis-Kelly, Deans-McFarlane, & Jandorf, 2012). One article defined medically underserved as living in a health professional shortage area (HPSA) (Brown et al., 2011). Seven articles defined medically underserved as receiving care at a federally qualified health center (FQHC) (Benkert et al., 2014; Connolly & Crosby, 2014; Hanson, West, Thackeray, Barnes, & Downey, 2014; Hoffman et al., 2015; Olayiwola, Sobieraj, Kulowski, St Hilaire, & Huang, 2011; Walker, Clarke, Ryan, & Brown, 2011; Young et al., 2012), and four articles defined medically underserved as receiving care in an area federally designated as a medically underserved area (a.k.a. "MUA") (Coughlin, Kushman, Copeland, & Wilson, 2013; Holt et al., 2013; Ogbuanu, Goodman, Kahn, Long, et al., 2012; Zach, Dalrymple, Rogers, & Williver-Farr, 2012).

The results of this review of recent literature on healthcare utilization among the medically underserved show a lack of consensus around the definition of the term "medically underserved" and that a minority of studies use a definition consistent with any established definition. One established definition that relates to the medically underserved has been developed by HRSA. HRSA designates an area as an MUA based on a set of measures collectively termed the Index of Medical Underservice, or IMU. The IMU consists of four variables: 1) ratio of primary care medical care physicians per 1,000 population, 2) infant mortality rate for a service area or for the county or subcounty area which includes it, 3) percentage of the population with incomes below the poverty level, and 4) percentage of the population age 65 or older (http://www.hrsa.gov/shortage/mua/). Because FQHCs must be in MUAs, the articles

defining medically underserved in terms of FQHCs and MUAs, if considered together, total 11 articles that could be considered to use the HRSA definition and is the most frequently used definition. The index score provided by the IMU seems to comprehensively capture medically underserved groups and provides a clear and measurable definition that can facilitate identification of groups. The ability to comprehensively capture the medically underserved is important for exploring whether being part of a medically underserved population (via living in a medically underserved area) plays a role in the use of genetic services. Having a medically underserved variable defined in this way will allow for exploration about whether the underserved are more or less likely to use genetic services than those who are not considered underserved, and then to identify variables that the underserved and not underserved have in common along with differences in the variables between the underserved and not underserved. This information will help identify ways that interventions can facilitate use of genetic services among those for whom genetic services are appropriate yet may be unattainable due to unknown variables.

The distinction as medically underserved or not medically underserved, as discussed in the beginning of Chapter 2 (along with discussion of Triandis's theory), is serving as a proxy for the concepts of collectivism and individualism, respectively. No published studies have thus far been identified as taking this approach. However, one study with a medically underserved population did report the importance and preference for programs or interventions with collectivist underpinnings (Lana Sue Ka'opua & Anngela, 2005). These findings were used in the development of a breast cancer screening intervention for native Hawaiian women (L. S. Ka'opua, 2008). Studies

reporting the importance of considering collectivist and individualist ideologies in understanding behavior and designing interventions have specifically obtained participants belonging to groups who are at risk for being medically underserved (e.g., Mexican immigrants) (Sampson, Kim Witte, Kelly Morrison, 2001). One article discussed the importance of considering collectivist and individualist values in understanding behavior and designing interventions for women whose individual cultural background are incongruent with that of the majority, or the culture of the larger society in which they live (Haj-Yahia & Sadan, 2008). The authors explore the challenges of addressing abuse in women with collectivist backgrounds yet living in an individualist context and being treated according to individualist norms and ideologies. The authors of the article state that their discussion does not refer only to remote cultures, but rather "to collectivist communities that exist within and alongside individualist cultures". The findings of the studies above highlight the importance of considering collectivist and individualist traits and ideologies in understanding behavior, preferences, and designing interventions. The choice of the medically underserved or groups at risk for being medically underserved to represent collectivist cultures in some of the studies above lends support for hypothesizing a link between medically underserved areas and collectivist traits.

Another variable that will require development is distance to genetics services. The website for the National Society of Genetic Counselors (http://nsgc.org/p/cm/ld/fid=164) offers the ability to search for genetic counselors by state or within up to a 50-mile radius of a zip code. Search results list work setting. These workplaces will be contacted and asked to verify that genetic counseling and/or

genetic testing were offered at the facility in 2012-2013 when the parent study was open. Distance will be calculated from participants' zip codes to the zip codes to the facilities. The minimum and maximum distances from YBCS zip code to facility zip code will be used in analyses. Number of facilities within a 50-mile radius will also be reported. The search results from the NSCG website will only list members of the NSGC, therefore facilities employing only genetic counselors who are not members of the NSGC may be missed. To account for this, other websites will be searched and contacted in the same manner as above to verify whether genetic counseling and/or testing were provided in 2012-2013. These websites are: the American College of Medical Genetics (https://www.acmg.net/ACMG/Find_Genetic_Services/ACMG/ISGweb/FindaGeneticService.aspx?hkey=720856ab-a827-42fb-a788-b618b15079f9), Myriad (https://ms360.myriad.com/patient-resources/find-a-provider/), the National Cancer Institute (http://www.cancer.gov/about-cancer/causes-prevention/genetics/directory), and GeneTests (https://www.genetests.org/clinics/?region=usa).

Variables to be controlled for: age, ethnicity, race, insurance, whether participant was adopted, and male relative with breast cancer. If the number of participants who report being adopted and having a male relative with breast cancer are very low, these will be dropped from the model. Age will be controlled for because the inclusion criteria of YBCS may mean a larger number of younger women. Race and ethnicity will be controlled for because the findings of the literature review discussed above suggests that women with an ethnic minority background are less likely to use genetic services than are women of a non-Hispanic White background. Having insurance will be

controlled for because lack of insurance or ability to pay has been frequently reported to be a barrier and has been found to be a predictor of not using genetic services. Whether a participant was adopted will also be controlled for. Lack of family history has discouraged use of genetic services. Although the evidence behind this is limited, it is a plausible confounding factor. Finally, having a male relative with breast cancer will also be controlled for as this is very rare and a red flag for carrying a *BRCA1/2* mutation.

Power analysis

Post hoc power analyses were conducted since this was a secondary data analysis. Effect size is hypothesized to be small (d=0.2). No reports of effect size were found among studies on increasing the use of genetic counseling or genetic testing. The effect size is hypothesized to be small due to persistently low rates of BRCA1/2 mutation testing, approximately 30-36% (Levy et al., 2011; Cragun et al., 2015). Using a small effect size will err on the conservative side. This is preferable to using a larger effect size in calculating sample size, which may lead to underpowered findings. G*Power was used post hoc to calculate the approximate power obtained.

Data analysis

Data analysis will begin with examination of data for missing data, outliers, and other abnormalities that could affect statistical procedures. Descriptive statistics of each independent variable and dependent variable will be done first for the entire sample of YBCS. Descriptive statistics of each variable will then be further analyzed by group with medically underserved defined as YBCS living in a federally designated medically

underserved area (MUA) and medically served defined as YBCS not living in an MUA. The HRSA website http://datawarehouse.hrsa.gov/tools/analyzers/muafind.aspx will be used to determine whether participants' residential zip code is designated as being in a medically underserved area.

Aim 1: Evaluating whether genetic counseling use differs between medically underserved and medically served.

The outcome variable, genetic counseling, will be dichotomous, treated as categorical. For this level of measurement, test of proportions will be used to evaluate whether there is a significant difference in genetic counseling between medically underserved and medically served. Significance level will be set at p=.05. This calculation will be done using SPSS v.24.

Aim 2: Identifying the correlates of using genetic counseling for hereditary breast and ovarian cancer risk among the medically underserved versus medically served in this sample of YBCS.

Point-biserial correlation coefficients will be determined for all of the independent variables in Table 2.2 and the outcomes of genetic counseling. Point-biserial correlations are selected because the independent variables are quantitative and the dependent variable is dichotomous.

Aim 3: Explore the ability of the Triandis model in explaining the use of genetic services.

First, univariate logistic regression will be done with each independent variable being regressed on the dependent variable, genetic counseling. Variables with p-value < 0.10 (according to convention) will be candidates for a first multivariable model. The variables will be examined critically for clinical or practical importance. Variance inflation factors (VIF) will be checked as an indicator of multicollinearity.

Next, model building will be done by conducting a series of logistic regressions. Regressions will confirm relationships between theoretical constructs. Variables will be added to regression equations according to construct groups of the Triandis theory. For example, variables under the Facilitating Conditions construct with p-value < 0.10 (established above) will be regressed on the variable(s) under the Habits construct. (For simplicity, "variables under the *x* construct" will hereafter be indicated as "X".) Habits will be regressed on Behavior, and Facilitating Conditions will also be regressed on Behavior. Significance will be set at $p<0.05$.

A regression with the background factors being controlled for will serve as a base model. Background factors found to be significant will be included in subsequent models. Next, Habits and Background Factors will be regressed on Behavior (genetic counseling). This will be compared with Intention and Background Factors regressed on Behavior. See below for more examples.

Model0: Behavior = Constant only
Model1: Behavior = Background Factors
Model2: Behavior = Background Factors + Social factors + Affect + Perceived Consequences
Model3: Behavior = Background Factors + Social factors + Affect + Perceived Consequences + Facilitating conditions
Model4: Behavior = Background Factors + Social factors + Affect + Perceived Consequences + Facilitating conditions + Intention
Model5: Behavior = Background Factors + Social factors + Affect + Perceived Consequences + Facilitating conditions + Intention + Habits
Model6: Behavior = Statistically significant variables from Model 3 (determined most parsimonious) + Intention + Habits
Model7: Behavior = Background Factors + Social factors + Affect + Perceived Consequences + Facilitating Conditions + Habits

The above models are only a few examples of the regressions that will be done. Model performance will be evaluated using multiple fit measures: Omnibus test of model coefficients, -2 Log Likelihood values, pseudo R^2 values from Cox & Snell R^2 and Nagelkerke R^2, and classification accuracy. Model fit will be evaluated by likelihood ratio test and receiver operating characteristic (ROC) curve values. The model showing greater area under the ROC curve will indicate the better model. Improvements in the -2 Log likelihood values, pseudo R^2s, and classification will be used to determine the most parsimonious yet accurate model.

Triandis's theory suggests a directional flow or path of relationships (i.e., Social Factors, Affect, and Perceived Consequences leading to Intention; then, Intention leading to Behavior). These and other paths and relationships between constructs will be evaluated with Structural Equation Modeling. One example of why doing SEM will be useful is in the following: Triandis's theory states that behaviors that are performed rather frequently come to require little thinking. In these instances, habits are more likely to predict the behavior than is intention. However, when the behavior is not one

that is performed frequently, more thought is likely to be required, and intention becomes more important in predicting behavior. Findings of the SEM may be helpful in understanding the relationships of these and other constructs in the context of using genetic counseling among this sample of young breast cancer survivors.

Expected outcomes and next steps

This study will contribute to understanding use of genetic services among a high-risk sample from medically underserved areas. Because the original study oversampled for blacks living in counties with the highest mortality rates for young women with breast cancer, findings are expected to contribute to knowledge about use of genetic services among two currently underrepresented groups in research on the topic: one or more ethnic minority groups and perhaps a segment of the rural population in Michigan.

Strengths and limitations

A strength of this proposed study is that it will contribute to multiple knowledge gaps in the literature. It will contribute to knowledge about barriers and facilitators of YBCS in medically underserved areas versus YBCS in areas not defined as medically underserved. Discrepancies exist in the current literature regarding predictors of using genetic services, and only few studies contribute knowledge about 1) rural and other underrepresented populations, and 2) the perspectives of YBCS, who have been diagnosed with breast cancer between the ages of 20 and 45, for whom genetic services are indicated but underutilized. Secondly, this study uses the HRSA definition of medically underserved area to define medically underserved groups. The HRSA designation of an MUA seems to more comprehensively capture medically underserved

groups rather than choosing rural or urban setting, poverty level, race/ethnicity, or insurance type alone or in some combination. Furthermore, using the HRSA designation of MUA provides a clear and measurable definition that can facilitate identification of groups in further research. Because the proposed study is a secondary analysis, findings may present an area for further, prospective studies in the future.

Another strength of this study is the use of a centralized state cancer registry for the identification and recruitment of study participants. This is favorable because it allows for a population-based sample and minimizes bias resulting from including only individuals who have access to centers conducting this type of research. This study may serve as a model for the use of other cancer registry databases to explore the same questions among geographically different samples, enabling stronger conclusions to be drawn. This knowledge can be used toward developing intervention studies to increase the use of genetic services among those at high risk for an inherited predisposition to cancer who may be interested in using genetic services but face additional or unique barriers as a result of living in medically underserved areas.

Several limitations of the proposed study are related to the nature of a secondary analysis. First, the data being analyzed are only from the baseline surveys and therefore are cross-sectional data. Prospective studies would be needed to verify any conclusions and additional hypotheses drawn from the proposed study. Additionally, because the original study was not designed with the specific aims of the proposed study, the secondary analysis will be using data obtained with measures that may not be optimal for the questions being asked in the proposed study. However, given the limited numbers of YBCS and keeping in mind the burden on these individuals resulting

from multiple requests for participation in research, using existing data to gain further knowledge about the group and develop hypotheses should be considered. Another limitation of the proposed study is that a different theoretical framework was used to develop and design the original study. Therefore, some of the concepts are not exactly the same as those in the proposed study, some variables were measured differently, and some of the variables of interest for the proposed study were not in the original study (and therefore had to be omitted). However, the concepts are similar and related. Triandis's theory of interpersonal behavior may show greater potential for predicting behavior in the context of using genetic services. Findings from this study may present a different perspective and new insights for further exploration. An additional limitation of the proposed study which is that the data are from participants only from the state of Michigan and therefore findings may be generalizable only to the Michigan population. However, lessons learned from conducting the secondary analysis may be applied to exploring the same questions in other states.

Table 3.2 Table of Triandis concepts, variables, and measures

Triandis concepts	Variables, from lit. rev.	Specific variable-measure, from dataset	Calculated score	Level of measurement	Rationale for using measure
Dependent variable					
Behavior	1) Use of genetic counseling or genetic testing	Variable from dataset: Current screening practices. Instrument: Behavioral risk factors surveillance system. Q114. Have you ever had cancer genetic services? (No, Yes, Don't know) Q118. Have you ever had genetic testing for a gene mutation connected to breast or ovarian cancer? (No, Yes → Age: __ yrs old, Don't know)	Q114 2=Yes=1 1,3=No=0 Q118 2=Yes=1 1,3=No=0	Dichotomous	Measures engagement in behavior of interest
Independent variables					
Social factors	1) Perceived expectations from family 2) Perceived expectations from healthcare provider	Variable from dataset: Perceived family expectations about breast cancer screening. Instrument: (developed from Ajzen and Fischbein: Understanding attitudes and predicting behavior; 1980). Q155. Do you believe that your relatives want you to get mammograms and other tests to find cancer at an early stage? (Definitely no=1, No=2, Somewhat no=3, Neutral=4, Somewhat yes=5, Yes=6, Definitely yes=7) Q156. Do you believe that your doctor or other healthcare provider wants you to get mammograms and other tests to find cancer at an early stage? (Definitely no=1, No=2, Somewhat no=3, Neutral=4, Somewhat yes=5, Yes=6, Definitely yes=7)	Q155 As marked (for greater sensitivity) Q156 As marked (for greater sensitivity)	Ordinal	Triandis defines social factors as influential factors derived from the relationship between the person and other people. Relationships with relatives and/or healthcare provider can be considered social factors. Analyze items separately since one does not necessarily influence or is the same as the other
	1) Motivation to comply with expectations of family 2) Motivation to	Variable from dataset: Motivation to comply with family members' expectations Instrument: (developed from Ajzen and Fischbein: Understanding attitudes and predicting behavior; 1980).	Q157 As marked (for greater sensitivity) Q158	Ordinal	Literature suggests motivation to comply with expectations as predictor in some

	comply with expectations of healthcare provider	Q157. How often do you try to do what your relatives want you to do about finding cancer at an early stage? (Never=1, Almost never=2, Sometimes=3, Neutral=4, Most times=5, Almost always=6, Always=7) Q158. How often do you try to do what your doctor or other healthcare provider wants you to do about finding cancer at an early stage? (Never=1, Almost never=2, Sometimes=3, Neutral=4, Most times=5, Almost always=6, Always=7)	As marked (for greater sensitivity)		groups (e.g., Hispanic). Include this variable to explore relationship further among this sample
Affect					
	1) Worry	Variable from dataset: NA Instrument: Q118d: (Q118: Have you ever had genetic testing for a gene mutation connected to breast or ovarian cancer?) If no, please tell us why you have not had genetic testing (check all that apply): No one ever suggested it; The genetic counselor told me it was not the right test for me; Issues with medical insurance coverage (no coverage, too high cost out-of-pocket); I am worried the result could be used against me (by employer, health insurance); **I would rather not know if I have a mutation connected to cancer**; Family members would not want me to go; Family members might be upset with test results; Cultural and/or religious beliefs do not support genetic testing; I did not know that genetic testing existed; A healthcare provider told me not to have the test; Other – please explain.	If Q118=No Q118d 5=Yes=1 1,2,3,4,6,7,8,9,10=No=0	Dichotomous	In literature, "rather not know" has been discussed in context of worry
Perceived consequences	1) Perceived consequences *to self* - Positive	Variable from dataset: NA Instrument: Q118b: (Q118: Have you ever had genetic testing for a gene mutation connected to breast or ovarian cancer?) If you had genetic testing, what helped you decide to have testing (check all that apply): I wanted to know if I have a mutation connected to cancer; **I wanted to learn more about my future cancer risk; Results may change my cancer treatment (preventive surgery, chemotherapy, etc.)**; I already know someone in my family who has a mutation connected to cancer; Results will benefit my family; Using cancer genetic services seemed very important; Family members wanted me to; My healthcare provider suggested that I	If Q118=Yes, Q118b 2 or 3=Yes=1 1, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15=No=0	Dichotomous	**I wanted to learn more about my future cancer risk; Results may change my cancer treatment (preventive surgery, chemotherapy, etc.)** are perceived positive consequences to oneself. These have been

		do; The clinic was close to home; I have available transportation; I have available child care; I was able to obtain these services by phone; My medical insurance covered the visit; My medical insurance covered the cost of the test; Other – please explain			associated with use of genetic services in existing literature.
	- Negative	Variable from dataset: NA Instrument: Q118d: If no, please tell us why you have not had genetic testing (check all that apply): No one ever suggested it; The genetic counselor told me it was not the right test for me; Issues with medical insurance coverage (no coverage, too high cost out-of-pocket); **I am worried the result could be used against me (by employer, health insurance)**; I would rather not know if I have a mutation connected to cancer; Family members would not want me to go; Family members might be upset with test results; Cultural and/or religious beliefs do not support genetic testing; I did not know that genetic testing existed; A healthcare provider told me not to have the test; Other – please explain ___.	If Q118=No Q118d 4=Yes=1 1,2,3,5,6,7,8,9,10,11 =No=0	Dichotomous	**I am worried the result could be used against me (by employer, health insurance)** is a perceived negative consequence to oneself. This has been reported in existing literature as influencing use of genetic services.
	2) Perceived consequences *to family* - Positive	Variable from dataset: NA Instrument: From Q118b: I wanted to know if I have a mutation connected to cancer; I wanted to learn more about my future cancer risk; Results may change my cancer treatment (preventive surgery, chemotherapy, etc.); I already know someone in my family who has a mutation connected to cancer; **Results will benefit my family**; Using cancer genetic services seemed very important; Family members wanted me to; My healthcare provider suggested that I do; The clinic was close to home; I have available transportation; I have available child care; I was able to obtain these services by phone; My medical insurance covered the visit; My medical insurance covered the cost of the test; Other – please explain	If Q118=Yes Q118b 5=Yes=1 1,2,3,4,6,7,8,9,10,11 ,12,13,14,15=No=0	Dichotomous	**Results will benefit my family** is a perceived positive consequence to family. This has been reported in existing literature as predictor of using genetic services.
	- Negative	Variable from dataset: NA Instrument: From Q118d: No one ever suggested it; The genetic counselor told me it was not the right test for me; Issues with medical insurance coverage (no coverage, too high cost out-of-pocket); I am worried	If Q118=No, go to Q118d Q118d 7=Yes=1	Dichotomous	**Family members might be upset with test results** is a perceived negative

		the result could be used against me (by employer, health insurance); I would rather not know if I have a mutation connected to cancer; Family members would not want me to go; **Family members might be upset with test results**; Cultural and/or religious beliefs do not support genetic testing; I did not know that genetic testing existed; A healthcare provider told me not to have the test; Other – please explain ___.	1,2,3,4,5,6,7,8,9,10, 11=No=0		consequence to family. This has been reported in existing literature as predictor of using genetic services.
Intention	1) Self-reported intention	Variable from dataset: Intention to pursue mammography, CBE, cancer genetic services (when applicable). Instrument: (developed from Ajzen and Fischbein: Understanding attitudes and predicting behavior; 1980). Q115: During the next 12 months, how likely are you to ask your healthcare provider if genetic testing for a gene connected to hereditary cancer is a right test for you? (Very unlikely=1, Likely=2, Somewhat unlikely=3, Neutral=4, Somewhat likely=5, Likely=6, Very likely=7, Does not apply=NA).	As marked. Range 1-7	Ordinal	This approach to measuring intention has been widely used and accepted by Ajzen and Fischbein in studies to predict behavior. Keep all options for greater sensitivity of measure.
Facilitating conditions	1) Provider referral	Variable from dataset: NA Instrument: Q114a: (Q114: Have you ever had cancer genetic services?) If no, please tell us why you have not used cancer genetic services – check all that apply: **No one ever suggested it;** I am too busy; I cannot get time off work; My disability makes it difficult to carry out daily activities; Lack of transportation; Lack of child care; Clinic hours do not fit my schedule; Clinics are too far away; Other life issues that come up are more important; I am too sick from cancer treatment; Other – please explain. From Q118b: I wanted to know if I have a mutation connected to cancer; I wanted to learn more about my future cancer risk; Results may change my cancer treatment (preventive surgery, chemotherapy, etc.); I already know someone in my family who has a mutation connected to cancer; Results will benefit my family; Using cancer genetic services seemed very important; Family members wanted me to; **My healthcare provider suggested that I do**; The clinic was close to home; I have available transportation; I have available child care; I was able to obtain these services by phone; My medical insurance covered the visit; My medical insurance covered the cost of the test; Other – please explain	If Q114=No Q114a 1=Yes=1 2,3,4,5,6,7,8,9,10,11 =No=0 If Q118=Yes Q118b 8=Yes=1 1,2,3,4,5,6,7,9,10,11 ,12,13,14,15=No=0	Dichotomous	**No one ever suggested it; My healthcare provider suggested that I do.** Provider recommendation has been reported in existing literature as predictor of using genetic services.

	2) Perceived risk	Variable from dataset: Perceived breast cancer risk. Instrument: Developed from: *Verbal*: "Rate your chances of developing breast cancer from 0–10," coupled with verbal anchors: 0–1 (definitely not), 2–3 (probably not), 4–6 (50/50), 7–8 (probably will), and 9–10 (definitely will). *Numeric*: "Rate your lifetime chances of developing breast cancer from 0% (absolutely no chance) to 100% (definitely)" (Katapodi et al., 2009). PMID: 19403452 (Cronbach's alpha=0.9) *From article: The verbal scale had low sensitivity (0.37) but high specificity (0.93) in identifying women with very high perceived risk as well as high sensitivity (0.81) and specificity (0.93) in identifying women with very low perceived risk. The comparative scale had high sensitivity (0.90) and specificity (0.99) in identifying women with very high perceived breast cancer risk as well as high sensitivity (0.89) and specificity (0.91) in identifying women with very low perceived breast cancer risk. In the present study, internal consistency reliability between the two scales was high (Cronbach alpha = 0.78). Q153: On a scale from 0 (Definitely Will Not) to 10 (Definitely Will), please circle a number that best describes what you believe is **your chance** for getting breast cancer.	As marked. Range 0-10	Ordinal	This approach to measuring perceived risk has been used and found to be acceptable in prior research. (Katapodi et al., 2011; Katapodi, Dodd, Lee, & Facione, 2009)
	3) Knowledge	Variable from dataset: Knowledge of breast cancer genetics. Instrument: Knowledge of breast cancer gene inheritance. A 17-item instrument with questions about causes of breast cancer, breast cancer genetics, genetic testing, and methods to reduce breast cancer risk (Cronbach's alpha=0.72). (Appendix A: Knowledge Assessment Questionnaire. (Wang et al., 2005). PMID: 15690408	Sum correct answers. Range 0-17.	Interval	This measure has been used in prior research in similar context and has demonstrated reliability.
	4) Convenience	Variable from dataset: NA Instrument: Q114a: (Q114: Have you ever had cancer genetic services?) If no, please tell us why you have not used cancer genetic services – check all that apply: No one ever suggested it; **I am too busy; I cannot get time off work;** My disability makes it difficult to carry out daily activities; **Lack of transportation; Lack of child care; Clinic hours do not**	Q114=No Q114a 2,3,5,6,7,8=Yes=1 1,4,9,10,11,12=No=0	Dichotomous	These have been reported in literature as reasons for not using genetic services.

		fit my schedule; Clinics are too far away; Other life issues that come up are more important; I am too sick from cancer treatment; Other – please explain. Q118b: (Q118: Have you ever had genetic testing for a gene mutation connected to breast or ovarian cancer?) If you have genetic testing, what helped you decide to have testing (check all that apply): I wanted to know if I have a mutation connected to cancer; I wanted to learn more about my future cancer risk; Results may change my cancer treatment (preventive surgery, chemotherapy, etc.); I already know someone in my family who has a mutation connected to cancer; Results will benefit my family; Using cancer genetic services seemed very important; Family members wanted me to; My healthcare provider suggested that I do; **The clinic was close to home; I have available transportation; I have available child care; I was able to obtain these services by phone**; My medical insurance covered the visit; My medical insurance covered the cost of the test; Other – please explain	Q118=Yes Q118b 9,10,11,12=Yes=1 1,2,3,4,5,6,7,8,13,14,15=No=0		
	5) Insurance or ability to pay for services	Variable from dataset: NA Instrument: Q118b: (see above) I wanted to know if I have a mutation connected to cancer; I wanted to learn more about my future cancer risk; Results may change my cancer treatment (preventive surgery, chemotherapy, etc.); I already know someone in my family who has a mutation connected to cancer; Results will benefit my family; Using cancer genetic services seemed very important; Family members wanted me to; My healthcare provider suggested that I do; The clinic was close to home; I have available transportation; I have available child care; I was able to obtain these services by phone; **My medical insurance covered the visit; My medical insurance covered the cost of the test**; Other – please explain	Q118=Yes Q118b 13,14=Yes=1 1,2,3,4,5,6,7,8,9,10,11,12,15=No=0	Dichotomous	These have been reported in literature as reasons for using genetic services.
	6) Family support	Variable from dataset: Perceived family support for breast cancer screening. Instrument: Q51-75. [cited in protocol paper: Social support for breast cancer screening. Described in Katapodi et al., 2002. Item 1: "When I need suggestions on how to deal with a personal problem, I have someone I can turn to."	Sum of responses. 25 items: 1=Never true; 2=Almost never true; 3=Seldom true; 4=Sometimes true; 5=Often true;	Ordinal, being treated as interval	This measure has been used in a prior study (Katapodi, Facione, Miaskowski, Dodd, & Waters, 2002)

		Item 2: "If I was sick, I could easily find someone to help me with my daily work." Item 3: "There is at least one person I know whose advice I really trust." Item 4: "I often do not have anyone to turn to" Item 5: "I do not know anyone whom I can confide in" (Cronbach's alpha=0.81).]	6=Almost always true; 7=Always true. Range 25-175.		
	7) Live in medically underserved area	Variable from dataset: County/Zip code Instrument:		Nominal, treated as Categorical	
	8) Distance from facility offering genetic services	Variable from dataset: [to be created] Distance between Zip code of YBCS and Zip code of facilities offering genetic services within a 50-mile radius will be calculated. Minimum and maximum distances will be used in analyses.		Ratio	Explore the following: 1) availability of facilities offering genetic services in medically underserved areas, 2) possible effect on use of genetic services, 3) whether residence in MUA helps explain use of genetic services
Habits	1) History of using health services .	Variable from dataset: Current screening practices. Instrument: from Behavioral risk factors surveillance system Q80. A clinical breast exam is when a doctor or nurse checks the breasts for lumps. Have you ever had a clinical breast exam? (No, Yes, Don't know). Q80a. If yes, how often did you have a clinical breast exam over the past 12 months? (Every 3-4 months, Every 6 months, Every 12 months, It has been more than 12 months since my last clinical breast exam, Don't know, Other – please explain). Q81. A mammogram is an x-ray of each breast to look for breast cancer. Have you ever had a mammogram? (No, Yes, Don't know). Q81a. If yes, how often did you have a mammogram over the past 12 months? (Every 3-4 months, Every 6 months, Every 12 months, It has been more than 12 months since my last mammogram, Don't know, Other – please explain).	Q80 2=Yes=1 1,3= No=0 Q80a 1,2,3=Yes=1 4,5,6=No=0 Q81 2=Yes=1 1,3,=No=0 Q81a 1,2,3=Yes=1 4,5,6,=No=0 Q82	Dichotomous	Having had any of these services creates/increases history of using health services. These measures will explore relationship between having a history of using health services and using genetic services. Analyze each separately since use of one may not mean use of

		Q82. A breast MRI, or magnetic resonance image, involves lying on your stomach on a bed that moves into a tunnel-shaped machine. You may have an IV during the procedure, and images of your breasts are taken. Have you ever had a breast MRI? (No, Yes, Don't know). Q82a. If yes, how many breast MRIs have you had over the past 12 months? (Every 3-4 months, Every 6 months, Every 12 months, It has been more than 12 months since my last breast MRI, Don't know, Other – please explain).	1,2,3,4=Yes=1 5,6=No=0		another.

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CHAPTER IV

Results of specific aim 1: Use of Genetic Counseling for Hereditary Breast Cancer in the United States: An Integrative Review

The results of aim 1 are described in this first manuscript.

Use of Genetic Counseling for Hereditary Breast Cancer in the United States: An Integrative Review

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INTRODUCTION

Cancer imposes a significant burden on individuals, their families, and to society because of economic impact, premature death, and disability. Mutations in the breast cancer genes, *BRCA1* and *BRCA2,* are two of a few clinically actionable mutations where identification of risk alters recommendations to prevent or treat disease. A mutation in the *BRCA1* or *BRCA2* gene translates to a significantly higher risk of developing breast and other cancers compared to the general population [1]. For a woman with a *BRCA1* mutation, the risk of developing breast cancer can be four to five times higher than the risk for a woman who does not carry the mutation [2,3]. Mutation carriers also have an increased risk for cancers in the ovary, prostate, and pancreas, and have a higher chance that their breast cancer is “triple negative” [4]. Triple negative breast cancers lack the three main hormone receptors that the most effective therapies for breast cancer target and therefore generally have a poorer prognosis [5]. Individuals with mutations in the *BRCA1/2* genes tend to develop cancer at younger than 50 years of age, when cancer is less expected and surveillance is less likely to be occurring. Furthermore, small families and paternal inheritance can reduce suspicion of risk for carrying a mutation [6].

Engaging in preventive strategies can reduce morbidity and mortality, but the benefits may be greatest before cancer occurs. There is limited evidence for the effectiveness of lifestyle modification at this time [7]. Observational studies have found that risk-reducing bilateral mastectomy reduced diagnoses of breast cancer among high-risk women and women with *BRCA* mutations by 85 to 100%[8–10]. However, risk-reducing surgery can be considered an aggressive strategy due to physical

complications and psychosocial sequelae[11]. An individual's risk should therefore be assessed properly and risk management strategies tailored to the appropriate individuals. Population screening for *BRCA1/2* mutations, though currently controversial, is on the horizon with some prominent leaders in the field advocating for it [12]. Implementing population screening could overwhelm limited resources such as genetic counselors and genetic testing facilities, as well as increase morbidity from surveillance (e.g., mammography) false positives, morbidity from prophylactic surgeries, and unfavorable sequelae of other risk-reducing strategies. National guidelines [13,14] and several professional groups [15–17] recommend genetic counseling for individuals with certain risk factors. Predictive genetic testing can determine whether an individual has an increased risk of developing a disease prior to experiencing any symptoms. Effective use of genetic services has the potential to minimize onset of cancer, in some cases multiple cancers or particularly aggressive cancers, and the physiological, emotional, and financial burden of treatment could be reduced substantially. However, among individuals for whom genetic counseling is indicated, based on widely accepted national guidelines [13,14], rates of counseling use are often below 50% [18–21]. Counseling use can have a multitude of implications, including ability to notify family members, increased frequency and/or intensity of screening, prophylactic drug therapy, prophylactic surgeries. Alternatively, individuals could do nothing if that is their preference. The decision on action to take, however, should be based on a solid understanding of potential benefits and risks.

There is evidence of potential disparities in who engages in genetic services. In many studies of predictors of genetic counseling use, participants are largely non-

Hispanic White, college educated, insured individuals with higher household income. These studies report non-Hispanic White women being more likely than women of other races or ethnicities to receive referral for genetic counseling or testing [18,22] and being more aware or informed about the *BRCA* genes and mutation testing [23,24]. While cancer genetics carries a potential to improve health outcomes, it also carries the potential for widening health disparities. Recently, studies are focusing on subgroups that have been traditionally underrepresented in genetics and genomics research, including ethnic minorities, residents of rural areas, low-income, and uninsured individuals. Predictors of uptake of genetic counseling are not well understood among more widely studied groups and may be even less well understood among groups traditionally underrepresented in research.

The purpose of this literature review is to explore factors predicting the use of genetic services, both testing and counseling. Uptake of genetic counseling for a heritable mutation associated with a substantial risk for cancer is multi-faceted and can involve influences from and implications on interpersonal relationships. A model of interpersonal behavior [25] which considers the complex interplay of human cognition, emotion, social influences, and physical or structural barriers in predicting behavior was used as a guiding conceptual framework for this review.

CONCEPTUAL FRAMEWORK

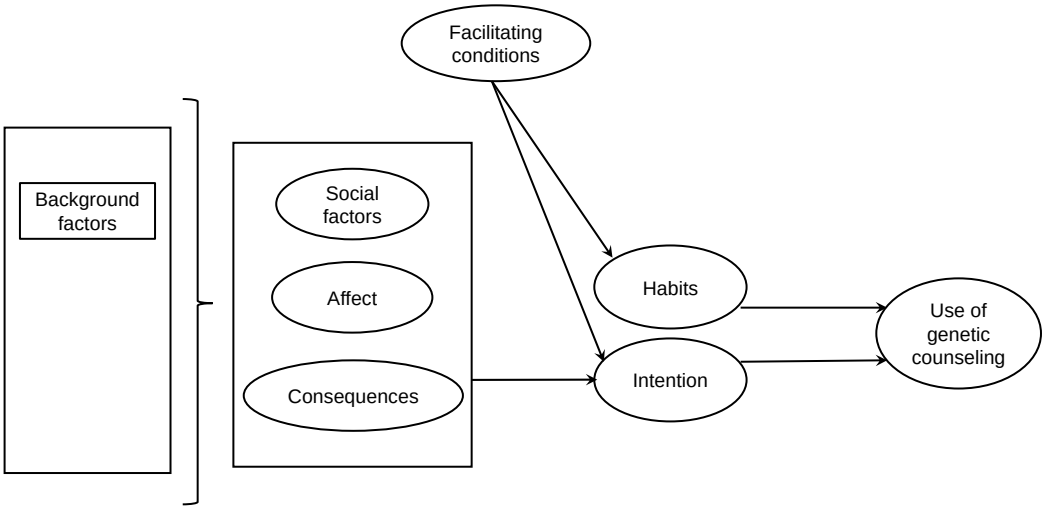
The Triandis model of interpersonal behavior

Triandis has done extensive work leading to the establishment of cross-cultural psychology as a discipline [26,27]. His work on how culture affects the way people think,

feel, and act may be helpful in the context of understanding the use of genetic counseling, for which the effect of culture is poorly understood. Culture has been defined as “the ideas, customs, and social behavior of a particular people or society.” [28] Culture is often associated with race or ethnicity. However, a culture can exist among other group classifications such as geographic location. Triandis’s theory allows for various ways that the influences of culture can manifest. Figure 4.1 shows how the concepts of Triandis’s theory may be related to the area of genetic counseling use.

Triandis’s model includes several aspects of what the literature suggests may be associated with use of genetic counseling. Constructs range from background factors which are primarily sociodemographic factors such as age, race, income, and education, to those with a cognitive aspect such as perceived consequences, to emotions such as worry. There is also a time component in the constructs of habit (past) and intention (future). Furthermore, variables can span from individual level, interpersonal, or broader societal. Whether factors are at the individual, interpersonal, or broader societal level may be less important, however, as they may be intertwined and separation may be unrealistic. Culture may affect behavior on an individual level, interpersonal level, and societal level. For the purpose of identifying an area of focus for facilitating use of genetic counseling, the way that concepts are organized may be helpful.

Figure 4.1. Conceptual framework developed from Triandis model of interpersonal behavior[25]



METHODS

A review of the literature was conducted in PubMed (includes Medline), Scopus, and CINAHL and included the key terms *genetic testing, genetic counseling, intention, BRCA, decision making, psychology, social support,* and *health knowledge, attitudes and practice*. Both *genetic testing* and *genetic counseling* were used because counseling may not necessarily precede testing and testing may not necessarily follow counseling. However, important lessons may be learned from the literature in both cases. *Decision making, psychology, social support, health knowledge, and attitudes* were chosen to retrieve studies on the cognitive aspect of determining a preference to use genetic testing and genetic counseling. *Practice* was included to retrieve studies on the actual uptake of services. The search using this combination of terms produced results with the highest relevance to the aim of this review. Reports of the link between

the *BRCA* genes and increased predisposition to breast, ovarian, and other cancers were reported in the late 1990s [29,30], therefore articles published between 2000 and 2017 were included. Abstracts were reviewed for applicability. Articles were chosen if they examined factors that influenced the use of genetic testing or genetic counseling for hereditary breast cancer. Because genetic tests for other syndromes with hereditary links to breast cancer such as Cowden's syndrome and Li-Fraumeni syndrome are not as well established, results were limited to articles on *BRCA1/2* mutations. Studies conducted outside of the United States were excluded due to differences in procedures for using genetic services. Some related articles from search results were included. Both qualitative and quantitative studies were included.

The findings of the review are summarized in Table 4.1. Table 4.1 is organized by the constructs of the Triandis model (social factors, affect, perceived consequences, facilitating conditions, habits, and intention) in the left column, and variables associated with use of genetic counseling or testing reported in the literature in the right column.

Social factors

Triandis theorized that intention to engage in a behavior results from three concepts: social factors, affect or emotion associated with the behavior, and perceived value of consequences. Social factors are derived from the relationship between a person and other people [25]. In the context of genetic counseling for a *BRCA1/2* mutation, social factors in the literature have shown a more negative influence on using genetic counseling than a positive one.

Some of the reasons for not using counseling are related to religious or cultural beliefs. For example, some women of Arabic background will allow only female healthcare providers to do physical examinations. In one qualitative study Arab American women reported that cultural beliefs about modesty can discourage them from undergoing examinations performed by a predominantly male physician workforce [31]. This potentially precludes them from obtaining clinical information often obtained prior to genetic counseling. More than one study, including another qualitative study, reported Latino cultural beliefs and expectations about prioritizing care of the family over care of oneself [32,33]. Genetic counseling would be considered a personal need and therefore deferred when faced with family responsibilities. These studies, each consisting of participants with a single, specific ethnic minority background, tended to be qualitative with small sample sizes. A strength of the studies is the qualitative design which yielded rich information -- valuable when little is known about a topic. However, the ability to generalize the findings is limited by the number of participants in each study.

Individuals of African American [33,34] and Ashkenazi Jewish [35–37] backgrounds have reported concerns about stigma of having a mutation, potential discrimination resulting from a breach in privacy, and shame related to perceiving a mutation as a flaw. The association with having a mutation can affect close interpersonal relationships as well as the broader perception of the ethnic group as a whole. These concerns are important given the atrocities committed against the groups historically – the eugenics movement and forced sterilization in America, and the Holocaust in Germany. Some members of the Ashkenazi Jewish community value the increased awareness and higher likelihood of referral to appropriate services. For some, the potential benefits of testing could outweigh the negative effects of discrimination. However, some members of the Ashkenazi Jewish community have expressed concern about stigma and discrimination resulting from studies highlighting their increased risk [35,36], with some believing that the recent focus on the Ashkenazi Jewish community is "giving the world the impression that we have all the bad genes" (Rabbi M. Tendler in [36]). For fear of being associated with a group that "carries bad genes" or implications of inbreeding, individuals from other communities that also have founder mutations may be discouraged from disclosing important family history and other relevant risk factors to healthcare providers or from seeking other necessary support. Consequently, they lessen their chances of managing an increased risk appropriately.

Concerns about stigma have been found in small, qualitative studies [33], and also in slightly larger quantitative [34] and population-based studies [35]. In the slightly larger quantitative study of African American women, approximately 20% of the sample of 80 participants declined genetic counseling and also reported concerns about stigma as a

reason for not using counseling. In this study, counseling was offered without cost and counseling sessions were conducted by an African American genetic counselor. The population-based study with participants of Ashkenazi Jewish ancestry was slightly larger with a sample of 200 participants. The proportion of individuals reporting concerns about stigma in this study was 5%. This was a minority of the sample but nonetheless deserves recognition as it may be an underlying concern among others.

Because of the genetic and social link with each other, family members can be influential in the decision to get genetic counseling and/or testing. In a study of high-risk women who received a diagnosis of cancer at younger than 50 years of age – suggestive of risk for carrying a predisposing mutation -- benefitting the family's future was reported as a top reason for getting genetic counseling. This was a moderately-sized population-based study of women considered high-risk and for whom genetic counseling is indicated. Using genetic testing to obtain information about children's risk was associated with increased interest among another moderately-sized population-based sample. This was a sample of 200 Ashkenazi Jewish women [35], also considered at increased risk due to their ancestry.

The motivation for using genetic counseling or testing to benefit the family may be altruistic, but this may not always be the case. Completion of genetic counseling at the request of family has been reported by a small portion of high-risk participants [20]. It is unclear, however, whether the request was made to benefit the study participant, or whether the request was made in order to help identify risk for other family members.

Affect

Affect, the emotions that a person feels at the thought of using genetic services, likely plays a role in whether individuals use genetic services. The emotions can vary widely, ranging from relief and empowerment in knowing and having the ability to act, to shame, anger, fear, and distress. Existing literature related to affect is largely on emotions related to anticipated consequences to the self, but literature on emotions related to consequences to family is also noteworthy.

Positive emotions associated with getting genetic counseling and testing included feeling relief from a negative result (not having a mutation) [34]. However, although knowing the truth or receiving a diagnosis would make some feel empowered with the opportunity to then take actions to potentially affect their outcome, to others, the truth may be disabling if they were to become consumed with worry. This finding came from a relatively large survey of individuals from four different ethnic groups followed by more in-depth qualitative interviews of a small fraction of the sample found differences in telling the truth about a diagnosis of cancer and prognosis [38]. Participants of European-American and African-American backgrounds tended to prefer to know, reporting that it would be distressing not to know. Korean-American and Mexican-American participants, however, felt it would be distressing to know that one had been diagnosed with cancer and the prognosis, and one would feel pain in knowing. This study presented a hypothetical scenario about cancer in general but its findings may apply in the context of possibly having a mutation associated with cancer. The findings of the study are somewhat limited by the involvement of only older adults and the smaller sample size of the qualitative portion. However, medical anthropologists who were of the same ethnic

background were available and could conduct the in-depth interviews in the participant's language of choice. This suggests that special efforts were made to increase comfort level and elicit genuine, in-depth responses from participants. Moreover, responses viewed as atypical were explored further to obtain additional insight into diversity within groups.

Other studies' findings have supported the underlying role of culture in the emotions associated with genetic counseling and genetic testing. Among studies with Latinas [32,39], a sense of guilt or selfishness was reported if they were to get genetic counseling. Getting genetic counseling would be putting their health ahead of the needs of their families. Found among Caucasians, another type of guilt termed "survivor guilt" has been found among noncarriers of a *BRCA* mutation in families where there is a carrier [40]. Among Asians, when it came to genetic testing, some Asians reported discomfort with Western preventive medicine as a potential discouraging factor, finding it too foreign and dissimilar to their traditional practices [33]. Distress from learning that one carries a cancer-predisposing mutation has also been reported from a relatively large qualitative study of Ashkenazi Jewish women [37]. Knowledge about influential factors among understudied populations such as ethnic minorities is increasing but the knowledge is still in its early development. At this stage, the studies are few and often qualitative, generally with smaller sample sizes. No strict conclusions can be made about beliefs of ethnic groups since there is potential for within-group diversity but it is important for clinicians to understand that preferences may vary by ethnic group even in emotional response. Literature may provide some general idea but it will still be important to assess anticipated emotions on an individual basis.

Perceived consequences

Triandis describes the value of perceived consequences as the sum of the products of the subjective probabilities that particular consequences will follow a behavior, and the value of (affect attached to) those consequences [25]. Perceived consequences of genetic counseling and genetic testing ranged from anticipated consequences to the self and family to science and society at large. Several perceived or anticipated positive as well as negative consequences (hereafter referred to as perceived positive or negative consequences) have been reported (shown in Table 4.1).

Along with the many positive consequences identified by individuals for themselves, positive consequences for family members are considered as well [20,23,35,39]. The positive consequences perceived by individuals for the family are likely highly valued. Positive consequences to family has been reported as the most frequently reported[20] or primary reason [39] for getting genetic counseling. In one study, 87% of participants would be willing to undergo *BRCA* testing for the sole purpose of helping their family [23]; another study reported mean score of 8.5 for value of obtaining information about children's risk (scale of 1 to 10 where 10 indicates 'extremely valuable') [35]. The ability to contribute to science and society has also been reported [33,35] but how highly this is valued and extent to which it motivates use of genetic counseling or testing was not discussed.

Perceived negative consequences have been reported by individuals as well, such as possible depression [33], anger or potential hopelessness and despair [34], shame [33], stigmatization and discrimination [31,33–35]. Negative consequences related to concerns about privacy and potential discrimination are a concern for both individuals and their

family members and seems to be important or have a high value for some [33–36]. Perceived negative consequences were similar, whether with respect to consequences to the individual or to family members. These concerns were reported in studies on genetic counseling alone [20,39], genetic testing alone [23,33,35], and counseling and testing together [34].

Similar perceived positive consequences have been reported by multiple groups of different racial and ethnic backgrounds. For example, benefitting family has been reported by samples that are largely non-Hispanic White [20,23,35], Ashkenazi Jewish [35], Hispanic [39], and African American [34]. Some differences by race or ethnicity were found in the anticipated potential negative consequences. However, sample sizes were not sufficiently large or diverse to allow for any conclusions at this time.

Facilitating conditions

Perhaps the largest amount of literature regarding the use of genetic services is on facilitating conditions. According to Triandis, facilitating conditions enable an individual to follow through with a desire to engage in a behavior. Regardless of the habits and intention to engage in a behavior, the facilitating conditions must be present and sufficient. The facilitating conditions for using genetic services can be categorized into personal, interpersonal, and societal areas.

Personal

Individual factors such as the availability of transportation and childcare, perceived risk, and having received a referral for genetic counseling have been described as facilitators [20,32]; whereas lack of knowledge about genetic services and

next steps, and being too busy or viewing other things as being more important, have been reported as barriers [20,33]. The factors listed as facilitators can just as likely be barriers. Breast cancer genetics knowledge, for example, has been significantly and positively associated with genetic counseling and testing in a sample of ethnic minority breast/ovarian cancer survivors considered at risk for hereditary breast cancer [41]. If a factor aligns with the individual's desire to use genetic services or enables the individual to use services, it is considered a facilitator. If the factor does not align with the individual's desire to use genetic services or if the factor is not present, the factor is considered a barrier. Individuals who were married were more interested in *BRCA* [42] testing but the reason behind this is unclear. This finding was from a moderately sized study with a family history suggestive of hereditary breast cancer. From a large multisite randomized controlled trial of high-risk women, having a spouse or partner has been suggested as possibly creating a conducive environment for *BRCA1/2* testing and subsequent decision-making about risk-management strategies if genetic counseling is received [43].

Interpersonal

Having family that is supportive and helpful can facilitate the use of genetic risk assessment and counseling among those who wish to do so. In a study exploring the knowledge, attitudes and beliefs of Arab-American women regarding inherited cancer risk, many of the women reported family support, especially from the husband, after a cancer diagnosis [31]. Some anecdotal experiences were shared by the women that illustrated family support and several women mentioned the importance of getting friends and family involved in discussions about cancer and inherited risk. The study

was a qualitative focus group, with a small sample size. The sample was community-based, recruited from a community center of one region with a high concentration of Arab Americans, through a trusted worker at the center. Participants had a personal or family history of breast cancer. No restrictions were placed with family members participating in the focus groups and there was no mention how many participants were relatives. A group of related individuals reporting on their experience could bias reported experiences to seem more prevalent among the sample. However, the perspective of a group which is so underrepresented in the literature is still important for understanding and as groundwork to build upon.

Related family support may be the concept of family hardiness. Family hardiness is a measure of family resiliency, which is defined as cohesion and ability to cope with adverse events [44]. Family hardiness has been positively associated with genetic testing in a moderately sized sample of family dyads recruited from hereditary cancer genetics clinics at a large comprehensive cancer center [45].

Structural

Lack of familiarity with the healthcare system presents a barrier that can be difficult to overcome, especially among underserved groups. Recent immigrants may lack experience with or knowledge about the healthcare system and may also have language barriers or cultural differences. Lacking insurance or sufficient income also present barriers. As described earlier, Asians reported in one study a discomfort or lack of familiarity with Western preventive medicine and genetic testing for the prevention of disease was a foreign concept [33]. Compounding this problem is the lack of ethnic and

cultural diversity among genetic specialists. Reports of efforts being made by the healthcare system to reach individuals facing these barriers are lacking in the literature.

The literature reports some ways that healthcare providers can be facilitators or present barriers to using genetic services. Provider recommendation has been cited as one of the most consistent predictors of genetic counseling [20] and genetic testing [42,46]. A recent large, population-based study aimed at evaluating rates and predictors of physician recommendation for *BRCA1/2* testing among patients with breast cancer found the correlation between provider recommendation and undergoing testing to be greater than .9 [46]. Over 80% of women who reported receiving a provider recommendation had testing, while fewer than 6% of those not receiving a recommendation went ahead to pursue testing. The same study suggests that a significant percentage of women at high risk of carrying a *BRCA1/2* mutation may not receive a recommendation for testing from their provider. Women aged 51 years to 64 years had >5 times the odds of not receiving a recommendation, even though the study criteria based on current guidelines identified them as high-risk. Provider knowledge of cancer genetics [18,47,48], knowledge of genetic testing for *BRCA1/2* mutations [24], and comfort level with cancer genetics risk assessment [49,50] were identified as facilitators to genetic counseling or testing. Lack of recommendation or discussion by the provider [18,51], provider lack of knowledge or confidence [52], lack of follow-up on discussion about genetic testing [53], and being told by a provider not to go[20] were associated with not using genetic counseling.

Individuals without access to a knowledgeable healthcare provider or extensive network of individuals with personal experience may be at a disadvantage when it

comes to receiving appropriate recommendations. This vulnerability can be significant given what seems to be the current state of knowledge and practices among healthcare providers in the area of genetic services. A systematic review of the literature on the integration of genetic/genomic knowledge into clinical practice [54] found the most consistent barrier to be the "self-assessed inadequacy of the primary care workforce to deliver genetic services." The most important and consistent finding was that the primary care workforce, which will be at the front lines of the integration of genomics into the regular practice of medicine, "feels woefully underprepared to do so." More recent studies continue to report lack of knowledge among providers in the appropriate identification of high-risk individuals, screening, testing, test result interpretation [47], interpretation of risk and referral to genetic counseling [55]. These studies have the strengths of large sample sizes, a national sample, or looking at practices at high-volume, internationally renowned medical centers.

Characteristics of the healthcare system can also be facilitators or barriers in the use of genetic services. Insurance coverage, having a clinic close to home, having a clinic with flexible hours, and the provision of services by phone have been reported to facilitate use of genetic counseling [20]. These same factors can be barriers when they are not present or available to those who wish to use genetic services. Concerns about insurance coverage and cost of counseling and testing have been frequently reported in the literature as a barrier [20,33]. These concerns will likely remain uncertain for the next several years while healthcare reforms are made. It will be important to assess the use of genetic services with the policy changes that theoretically increase access to these services. The psychological and emotional effects resulting from an inability to act on

knowledge gained from genetic testing may be more harmful than helpful. This is a gap in the literature and in policy.

In order to meet a need among those who find the cost of genetic testing to be prohibitive or otherwise inaccessible, a market has developed that provides genetic testing direct-to-consumer (DTC). DTC testing for BRCA mutations have evolved and garnered attention for some time. Although direct-to-consumer advertising is felt by some to be helpful as a means of providing information, study participants still preferred to have the professional input and personalized guidance of their provider when deciding to undergo testing [56].

Habits

According to Triandis, habits can contribute to the likelihood of a behavior occurring. Habits stem from behaviors that occur with certain frequency and can be identified by assessing the number of times the individual has committed the behavior in the past. Although improvements in the predictive ability of genetic testing technologies may attract some individuals who have previously undergone genetic testing to get tested again, genetic testing for a hereditary condition is unlikely to occur frequently enough to be considered habitual. One study found a predisposition to use health services to be associated with higher likelihood of breast cancer screening behaviors [57]. The participants were not necessarily at increased risk for having a cancer-predisposing mutation. However, it was a moderately sized, community-based, culturally diverse sample. The relationship between use of health services in general and use of genetic

services more specifically is unclear. Table 4.1 shows very few studies related to this topic.

In one qualitative study with an ethnically diverse sample, the sparse understanding of one's health history resulting from the lack of using health services was reported by some individuals to make them feel inadequate, lacking information to share with their provider [33]. A benefit of its qualitative design, this study provided insight into cultural factors and perceived barriers to testing among underrepresented ethnic groups not well-documented in the literature. The study was not limited to women eligible for genetic testing per se, but focused on participants with a history of breast or ovarian cancer or were first degree relatives of survivors. It is possible that a predisposition to use health services may translate to a higher likelihood of using genetic services but this relationship needs further investigation.

Intention

Triandis defines intention as "the cognitive antecedent of a behavior" [25]. He posits that intention is a product of social factors, affect, and perceived consequences. Few recent studies, within the past ten to fifteen years, have identified intention to pursue genetic counseling or testing as a specific outcome. A recent study of women in the general population recruited through a large multispecialty clinic in one urban area, found the following to be significantly associated with intention: awareness of genetic testing, cancer worry, insurance coverage of testing cost, and just wanting to know whether she possessed a mutation in the *BRCA1/2* gene [58]. In another study, with a sample whose risk was considered to be moderate to high, factors significantly

associated with intention to undergo testing in a regression model were more specific to personal risk: number of relatives with a history of breast and/or ovarian cancer and perceived risk of having a *BRCA1/2* mutation [59]. Although belief in the benefits of testing was high over limitations and risks, intention defined as a response of "would definitely get tested" was reported by only a small fraction of the sample -- 30%. The findings of this study suggest a disconnect between belief in benefits and intention. This was a small sample of African American women recruited through a variety of approaches (i.e., provider referral from a large health system and community clinics, health fairs, support groups, and newspaper ads).

LIMITATIONS

This review was limited to studies examining factors that influence the use of genetic counseling or genetic testing related to a *BRCA1* or *BRCA2* mutation. Articles may have been missed if they were indexed with key words that are different from the ones described in the search strategy of the Methods section above or did not have any key words for indexing. The search strategy used for this review did include 'intention' initially, along with 'BRCA'. 'BRCA' was used rather than 'hereditary breast cancer' in order to filter out articles on genetic counseling or testing related to Cowden's syndrome, Li-Fraumeni syndrome, and other conditions related to hereditary breast cancer. However, 'hereditary breast cancer' was added later when the search yielded no articles with intention as a variable of interest. Relevant results from the past two years were included in this review. Limiting studies to those conducted in the United States, presents another limitation, as well and should be explored in another paper.

CONCLUSION

The existing literature illustrates the complexity in the act of using genetic counseling. Not only are individual factors involved, but interpersonal and structural factors also seem to be important factors. The factors reported in the literature as influencing use of genetic counseling can be categorized under the concepts of Triandis's interpersonal theory. This suggests that the theory may be helpful for further exploration of the relationships between the various factors. In turn, the theory may be helpful in understanding the use of genetic services among individuals from a variety of backgrounds.

The largest number of factors reported to influence use of genetic services fit under the concept of facilitating conditions, with social factors and perceived consequences following closely. One of the most compelling factors under the concept of facilitating conditions involves providers in the healthcare system. The association between use of genetic counseling and having had genetic counseling recommended by a provider has been found to be strong in a large population-based study [46]. Coupled with a number of studies finding provider knowledge or comfort to be lacking [22,47,49], providers' knowledge and appropriate recommendation for genetic counseling could be a focus for interventions.

The influence of family also has been demonstrated in several studies. Though many of these may have had small sample sizes, several studies have reported family considerations. The limitation of small sample sizes can be mitigated by the number of studies reporting similar findings, as well as the depth with which family influence was described.

Another important theme across many of the studies that were part of this review is the underlying effect of culture. Many studies on the influence of culture are small with a qualitative design. Furthermore, there are none or only a limited number of studies for some cultures (for example, in this review, there was only one study on Arab Americans; two studies reported beliefs and attitudes of a small sample of Asian Americans). Although there was no identified influence of culture seen in the perceived positive consequences of using genetic counseling, culture did have a presence in the perceived negative consequences. Because these may be barriers to using genetic counseling among individuals who could benefit, more efforts to understand perceived negative consequences in more cultures could be beneficial in supporting or anticipating needs of those groups.

A clear gap in the literature is in the studies on underserved groups. Ethnic minorities are often associated with underserved. However, ethnic minorities are not always underserved, and underserved are not always ethnic minorities. There were no studies that described samples as rural. Current knowledge may be limited by a sort of selection bias with samples many times having been recruited from breast cancer clinics or even hereditary cancer risk assessment clinics. Population-based approaches (e.g., recruitment using state cancer registries) seem to be more popular recently. However, this approach may still exclude individuals who are not fully integrated into the healthcare system and who may have additional or unique set of needs or beliefs that influence their use of genetic services.

In summary, further studies should focus on the relative amounts of importance that individuals place on the factors determining use of genetic services. New

approaches to reaching underserved and underrepresented populations should also be pursued.

Table 4.1. Variables associated with the use of genetic counseling or testing and the constructs of the Triandis model.

Constructs of the Triandis model	**Variables associated with use of genetic counseling or testing**
Social factors Influential factors derived from the relationship between the person and other people; includes norms, roles, contractual arrangements, self-monitoring, self-concept	Concerns about modesty, availability of female providers [31] Concerns about being a burden [32] Traditional cultural beliefs (e.g., machismo, fatalism, destino among some Latinas; younger women may be less likely to ascribe to these) [33,39] Prioritizing family responsibilities over personal needs [32,33] Mistrust of medicine and research [33] Mistrust related to privacy, mishandling of information [33,37] Ability to contribute to science and society Requested by family [20]
Affect Emotions that the person feels at the thought of an act; can be positive (pleasant) or negative (unpleasant), and strong or weak	Fear [32] Distress [32,37,43] Uncertainty about next steps [56] Shame related to implications of inbreeding [36] Shame of having the mutation (seen as a flaw) [48] Anger [48] Relief from negative result (not having the mutation) [48] Positive and negative views about truth-telling [38]
Perceived consequences What might happen from a behavior (Note: Triandis defines this as how good or bad one might feel is a particular consequence actually happened. However, this was not measured in any studies. Therefore, only actual perceived consequences found in the literature are listed here.)	*Negative* Stigma, discrimination against self [33,35,48] Stigma, discrimination against children and relatives [33] Anticipated negative emotional response [48] Family would be worried [32,33] Potential benefits outnumbered by risks and limitations *Positive* Information might help guide or affect treatment [20,23] Obtain information to reduce cancer risk [33,48,59] Help make life plans (e.g., marriage, children, career) [48]

	Knowledge of negative results (not a carrier) would lead to relief [48] Just having the information [35] It would benefit their family [20,23,35,39]
Facilitating conditions Conditions that enable the person to carry out an act; includes the person's ability, arousal, and knowledge to carry out an act	*Barriers (lack of enabling conditions)* Lack of clinician recommendation or not discussed by provider [18,51] Told by provider not to go [20] Provider lacked knowledge or confidence [52,54,61] Provider did not follow up on discussion about testing [53] Risk not recognized by provider [22] Cost [23,32,33] Lack of insurance coverage [20,32] Lack of knowledge about where to go [32] Requirement of affected individual to be the proband [62] Competing demands (too busy taking care of family, other things to worry about) [20,32,39] Limited use of services resulting in limited knowledge [33] Difficulty navigating the system [31] Currently undergoing treatment [63] *Facilitators* Received a referral or discussed with provider [19,20,32] Provider felt comfortable or qualified [49,50] Family history [24,51] Personal history [51] Perceived risk [32,43] Knowledge about breast cancer genetics or BRCA genes [18,41,43,48] Knowledge about genetic testing [24] Have transportation, childcare [20] Insurance covered services [20] or having private insurance [19] Clinic close to home [20] Clinic hours flexible, fit patient's schedule [20] Services by phone [20] Perceived risk [32] Marital status [42]

	Have social support [31] Self-efficacy [41] Telephone counseling [43]
Habits Behaviors that occur with frequency; number of times the person has committed the act	Family hardiness [45]
Intention The cognitive antecedent of a behavior	Awareness of genetic testing [58] Cancer worry [58] Insurance coverage of testing cost [58]

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CHAPTER V

Results of specific aim 2: The relationship between residence in a medically underserved area and use of genetic counseling among a sample of young breast cancer survivors in the United States

The results of aim 2 are described in this second manuscript.

The relationship between residence in a medically underserved area and use of genetic counseling among a sample of young breast cancer survivors in the United States

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Medically underserved, genetic counseling, young breast cancer survivors, BRCA

Introduction

More than 20 years have passed since mutations in the *BRCA1* and *BRCA2* (hereafter *BRCA*) cancer susceptibility genes were linked to breast cancer (Miki et al., 1994; Wooster et al., 1995). Yet, current research suggests that opportunities to use this information in clinical care are being missed, and many women are not getting genetic services that could be lifesaving. Mutations in the *BRCA* genes are estimated to be present in 0.2-1% of the general population (Kurian, 2010). The lifetime risk of being diagnosed with breast cancer for the general population is 12.4% (American Cancer Society, 2017). For carriers of a mutation in the *BRCA1* and *BRCA2* genes, this risk is increased to 57-65% and 45-49%, respectively (Antoniou et al., 2003; Chen & Parmigiani, 2007; Risch et al., 2006). For individuals at high risk, risk-reducing strategies have shown promise. Prophylactic mastectomy, for example, has demonstrated a 90% or more reduction of risk (Domchek et al., 2010; Evans et al., 2009; Hartmann et al., 1999, 2001; Heemskerk-Gerritsen et al., 2007; Meijers-Heijboer et al., 2001; Rebbeck et al., 2004). The decision to undergo a prophylactic mastectomy, however, carries its own risks and potentially unfavorable sequelae related to surgery, and should be undertaken only with a solid understanding of risks and benefits.

Genetic counselors can facilitate discussions about risks, benefits, and associated concerns that are key to individuals making informed decisions about minimizing risk. However, rates of genetic counseling are unfortunately low. In 2005, one large national survey reported that only 34.6% of women at risk for carrying a *BRCA* mutations received genetic counseling (HealthyPeople.gov, 2013). That same year, the United States Preventive Services Task Force (USPSTF) recommended that

"women whose family histories are associated with increased risks for clinically significant, or deleterious, mutations in the *BRCA1* or *BRCA2* gene be referred for genetic counseling and evaluation for mutation testing" (Nelson, Huffman, Fu, Harris, & U.S. Preventive Services Task Force, 2005). Yet, as recently as 2015, studies where participants had either a personal history of breast cancer younger than 50 years of age (Anderson et al., 2012; Cragun et al., 2015) or whose healthcare provider felt genetic testing was indicated (J. Armstrong et al., 2015) still reported that fewer than 50% of study participants pursued genetic counseling. In one study, 21% of the at-risk sample saw a genetic counselor and only 35% of the entire sample had been referred for genetic counseling (Cragun et al., 2015).

Predictors of genetic counseling use remain unclear. Provider recommendation has been reported as a strong facilitator and motivator (Anderson et al., 2012; Chin et al., 2005; Morgan, Sylvester, Lucas, & Miesfeldt, 2009), whereas lack of provider recommendation has been reported as the most commonly reported reason for not receiving genetic counseling (Anderson et al., 2012; J. Armstrong et al., 2015). The role of other factors such as race, ethnicity, income, and insurance coverage is either inconsistent, or studies had small sample sizes, or were too few to be conclusive (K. Armstrong, 2005; Thompson et al, 2002; Glenn, Chawla & Bastani 2012; Anderson, et al, 2012). For example, a case-control study of 408 women found African American women to be significantly less likely to undergo genetic counseling for *BRCA* testing than their white counterparts, a difference which was not explained by differences in the probability of carrying a mutation, socioeconomic status, attitudes about testing, discussions with their physicians about testing, or cancer risk perception and worry (K.

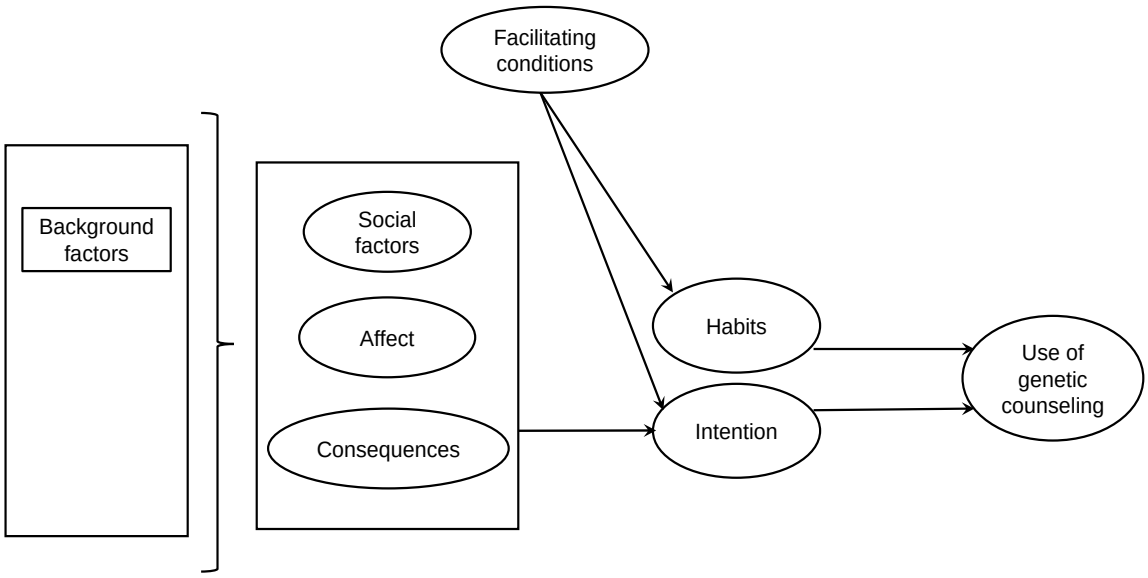
Armstrong, 2005). In a study of Hispanic women, concerns about insurance coverage were prominent, with most participants wanting to ensure insurance coverage prior to making an appointment for genetic counseling (Sussner, Jandorf, Thompson, & Valdimarsdottir, 2013). Income has not been reported as a significant factor when using genetic counseling. Taken together, findings from these studies suggest that uptake of genetic counseling is not consistently linked to ethnicity, income, insurance coverage, or other singular factor (Anderson et al., 2012; K. Armstrong, 2005; Glenn, Chawla, & Bastani, 2012; Thompson et al., 2002). Residence in a medically underserved area may capture a composite or set of variables which, when combined, may be related to use of genetic counseling for a heritable cancer syndrome. Some social behavioral theories (Triandis, 1993) may also suggest this.

While the diagnosis of cancer at any age can be tumultuous, a diagnosis of cancer at younger than 50 years old, as is often the case in those with *BRCA* mutations, may be especially challenging. There may be numerous barriers such as reproductive considerations, time off work and travel time to appointments, coupled with additional demands of young families, that can add to an already difficult balancing act (Hamilton, Innella, & Bounds, 2016). Little is known about the key predictors of getting genetic services, so effective intervention strategies cannot be efficiently explored. The purpose of this study was to understand genetic service use among young breast cancer survivors who are at high risk for having a heritable predisposition to cancer, and in particular, whether there is a relationship between residence in a medically underserved area and use of genetic counseling services. The specific aims of the study were to evaluate whether use of genetic counseling differs between participants

living in medically underserved areas versus medically served areas; and to evaluate variables associated with use of genetic counseling and differences between medically underserved and medically served participants.

An interpersonal theory developed by Triandis (1977) was used to guide this study. This model was selected because of Triandis's extensive work on differences in behavior from observations of different cultures (Triandis, 1993). Culture is not one particular construct in the theory; rather, the underlying influence of culture is understood to be pervasive, manifesting through cognition and emotion, social factors such as norms and expectations, habits, and facilitating conditions. Cultural effects can manifest on a personal, interpersonal relationships, as well as societal level. Triandis's model includes several important concepts associated with genetic counseling use as reported in the literature and therefore may help explain relationships between variables that predict genetic counseling use. A conceptual framework developed from Triandis's theory is shown in Figure 5.1. Variables explored in this study were determined based on variables associated with use of genetic counseling in existing literature and these fit into the model as depicted below. Residence in a medically underserved area (or not) is considered a facilitating condition in this study and its influence may be seen on habits and intention.

Figure 5.1. Conceptual framework developed from the Triandis model of interpersonal behavior (Triandis, 1977)



Methods

Sample

The study used baseline data from a randomized trial designed to increase cancer surveillance and use of genetic services among women diagnosed with breast cancer younger than 50 years of age (Katapodi et al., 2017; Katapodi, Northouse, Schafenacker, et al., 2013). The purpose of this study was to explore whether residence in a medically underserved area is related to use of genetic counseling for a *BRCA* mutation. Participants were recruited from the Michigan Cancer Surveillance Program (MCSP). This state-based cancer registry was established in 1984 and collects reports of cases of *in situ* and invasive malignancies. From 9,000 cases

reported between the years of 1994 and 2008, 3,000 women diagnosed with breast cancer between the ages of 20 and 45 were stratified for Black vs. White/Other race and were randomly selected. The study oversampled for Black women (1500 randomly selected) who also live in counties with the highest mortality rates for young women with breast cancer to increase the representation of minority and underserved women. Women who were pregnant, incarcerated, or institutionalized at the time of the study were excluded because they might not have been able to follow recommendations for breast cancer screening or genetic counseling.

Variables and measures

The study asked participants to complete a self-administered paper questionnaire adapted from previously-validated measures (Anderson et al., 2012; "Centers for Disease Control and Prevention: Behavioral Risk Factor Surveillance System: 2001 Survey Questions," 2002; Katapodi, Dodd, Lee, & Facione, 2009; Katapodi, Facione, Miaskowski, Dodd, & Waters, 2002; Katapodi, Northouse, Milliron, Liu, & Merajver, 2013; Wang, Gonzalez, Milliron, Strecher, & Merajver, 2005) that included questions on demographics, personal and family history, perceived expectations and motivation to comply with expectations of relatives and healthcare providers, worry related to possibly having a genetic mutation related to cancer, perceived consequences of genetic testing to self and to relatives if testing was indicated, and convenience factors. The survey also assessed intention to use genetic counseling, and history of using health services. There were items on perceived expectations of relatives and healthcare providers with respect to "mammograms and

other tests to find cancer at an early stage" and also items on motivation to comply with expectations of relatives and healthcare provider. Variables ranged from individual factors to interpersonal, broader structural factors. The outcome of interest was use of genetic counseling, assessed by "Have you ever had cancer genetic services?" The description of cancer genetic services given in the survey was as follows: "Cancer genetics services help people know if their own cancer or the cancer in their family might be due to heredity (due to genes that can be passed down in the family, from one generation to the next). Genetic services usually involve meeting with a genetic counselor or doctor who takes your family history, talks about your risk for hereditary cancer and gives you information about genetic testing and cancer screening." Other variables and instruments included in this study are shown in Table 5.1, organized by the constructs of the Triandis model.

Table 5.1. Variables and measures used in this study

Variable	Measure
Demographics including personal and family history	
Age Race Ethnicity Ashkenazi Jewish background Income Education Adopted Family history of male breast cancer Number of pregnancies	Adapted from the Behavioral Risk Factors Surveillance System ("Centers for Disease Control and Prevention: Behavioral Risk Factor Surveillance System: 2001 Survey Questions," 2002)
Additional risk factors* *in addition to* breast cancer onset at age ≤ 50	Examined this study. List of risk factors from U.S. Preventive Services Task Force (U.S. Preventive Services Task Force, 2005). Referral to genetic counseling indicated if 'yes' to ≥2 of the following: • Ovarian cancer, at any age: self mother sister daughter maternal grandmother maternal aunt paternal grandmother paternal aunt • Breast cancer at age ≤ 50 y.o.: self mother sister daughter maternal grandmother maternal aunt paternal grandmother paternal aunt
Social factors	
Perceived expectations of relatives Perceived expectations of healthcare provider	Adapted from Ajzen et al. (Ajzen & Fishbein, 1980) *Ex.: "Do you believe that your relatives want you to get mammograms and other tests to find cancer at an early stage?"*

Motivation to comply with relatives Motivation to comply with healthcare provider	*Ex.: "How often do you try to do what your relatives want you to do about finding cancer at an early stage?"*
Affect	
Worry	Examined in this study *Ex.: "Have you ever had genetic testing for a gene mutation connected to breast or ovarian cancer? If no, please tell us why you have not had genetic testing (check all that apply)."* *Worry was indicated if the following was checked:* *"I would rather not know if I have a mutation connected to cancer."*
Perceived consequences	
Perceived positive consequences to self Perceived negative consequences to self Perceived positive consequences to family Perceived negative consequences to family	Examined in this study *Ex.: "Have you ever had genetic testing for a gene mutation connected to breast or ovarian cancer? If you had genetic testing, what helped you decide to have testing (check all that apply).* *Perceived positive consequences to self was indicated if the following were checked:* *"I wanted to learn more about my future cancer risk; Results may change my cancer treatment (preventive surgery, chemotherapy, etc.)"*
Facilitating conditions	
Provider recommended genetic counseling	Examined in this study *Ex. "Have you ever had cancer genetic services? If no, please tell us why you have not used cancer genetic services – check all that apply"* *Provider recommended if the following was checked:* *"My healthcare provider*

	suggested that I do."
Perceived risk	Previously used (Katapodi et al., 2009; Katapodi, Northouse, Milliron, et al., 2013) *Ex. "On a scale from 0 (Definitely Will Not) to 10 (Definitely Will), please circle a number that best describes what you believe is **your chance** for getting breast cancer."*
Knowledge of breast cancer genetics	Adapted from Knowledge Assessment Questionnaire (Wang et al., 2005); (Cronbach's alpha=0.72)
Convenience	Previously used (Anderson et al., 2012) *Ex. "Have you ever had cancer genetic services? If no, please tell us why you have not used cancer genetic services – check all that apply."* *Convenience variable was created if the following were checked:* *"I am too busy; I cannot get time off work; Lack of transportation; Lack of child care; Clinic hours do not fit my schedule' Clinics are too far away"*
Insured	Previously used (Anderson et al., 2012) *Ex. "Have you ever had genetic testing for a gene mutation connected to breast or ovarian cancer?) If you have genetic testing, what helped you decide to have testing (check all that apply)* *Participant considered insured if the following were checked:* *"My medical insurance covered the visit; My medical insurance covered the cost of the test"*
Family support	Previously used (Katapodi et al., 2002); Social support for breast cancer screening (Cronbach's

	alpha=0.81)
Residence in a medically underserved area	Examined in this study Geocoded U.S. Census Tracts and HRSA designation as a medically underserved area (MUA) (Yes/No)
Distance to genetic counseling	Examined in this study Distance to nearest facility offering genetic counseling
Intention to use genetic counseling	Adapted from Ajzen et al. (Ajzen & Fishbein, 1980) *"During the next 12 months, how likely are you to ask your healthcare provider if genetic testing for a gene connected to hereditary cancer is a right test for you?"*
History of using health services	Adapted from the Behavioral Risk Factors Surveillance System ("Centers for Disease Control and Prevention: Behavioral Risk Factor Surveillance System: 2001 Survey Questions," 2002) Participant considered to have a history of using health services if answered yes to any of the following: *Have you ever had a clinical breast exam?; Have you ever had a mammogram?; Have you ever had a breast MRI?*

For the purposes of this analysis, some variables were created from the baseline data of the original study. A variable for residence in a medically underserved area was created using the definition offered by the Health Resources & Services Administration (HRSA). HRSA designates an area as "medically underserved" (MUA) according to a set of variables termed the Index of Medical Underservice, or IMU. IMU is comprised of four variables: 1) ratio of primary care medical care physicians per 1,000 population, 2)

infant mortality rate for a service area or for the county or sub county area which includes it, 3) percentage of the population with incomes below the poverty level, and 4) percentage of the population age 65 or older. For this study, medically underserved was defined as being a resident in a U.S. Census Tract designated by HRSA as an MUA (Yes/No) and was determined using Geocoded U.S. Census data.

Another variable that was created was that for additional risk factors indicating a referral for genetic counseling. The variable was created from the 2005 USPSTF Referral Screening Tool (U.S. Preventive Services Task Force, 2005), one of the main recommendation guidelines offered at the time of data collection for the parent study. The tool recommends a patient complete the checklist if she has a family history of breast or ovarian cancer; the patient should receive a referral for genetic counseling if two or more items are marked 'yes'. A reproduction of the Referral Screening Tool is shown in Figure 5.2.

Figure 5.2. Referral Screening Tool. Reproduced from the 2005 USPSTF recommendation statement for genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility (U.S. Preventive Services Task Force, 2005)

Risk Factor	Breast Cancer at Age ≤ 50 y	Ovarian Cancer at Any Age
Yourself		
Mother		
Sister		
Daughter		
Mother's side		
Grandmother		
Aunt		
Father's side		

Grandmother		
Aunt		
≥2 cases of breast cancer after age 50 y on the same side of the family		
Male breast cancer at any age in any relative		
Jewish ancestry		

Statistical analyses

Research question 1: Evaluate whether use of genetic counseling differs between participants living in medically underserved area versus medically served areas. Chi-square test was used to assess for the difference in the use of genetic counseling by medically served and underserved groups. The response variable for use of genetic counseling was dichotomous with "yes" or "no" responses. "Don't know" was treated as missing data.

Research question 2: Evaluate what variables are associated with use of genetic counseling and whether any differences exist between medically underserved and medically served participants. Point-biserial correlations determined strength and direction of relationships between explanatory variables and the response variable. This special type of Pearson's product-moment correlation was used because the response variable (use of genetic counseling) is dichotomous. Interpretation of association strength was based on Cohen (1988).

Approximately 3% of all values were missing. Two variables had greater than 10% of responses missing: Intention (36% missing), and Income (14% missing). Perceived risk and ethnicity had 8% and 7% missing, respectively; all other variables had less than 5% of values missing. No multiple imputation was done. Analysis of

missing values by SPSS suggests no pattern in missing values. Data are thus assumed to be missing at random.

G*Power 3.1.9.2 (Faul, Erdfelder, Lang, & Buchner, 2007) was used to calculate the power for these analyses. Power for the outcome of using genetic counseling (Yes/No) was calculated post-hoc based on the numbers in this secondary analysis. Power was determined to be 16%, likely due to the large imbalance in the number of medically served versus underserved participants (n=790 and n=68, respectively).

Results

A total of 859 women diagnosed with breast cancer younger than 45 years old completed the baseline survey. Participants ranged in age from 30 to 63 years old with a mean of 51 years (±5.9). Over half of participants were White/Other (63%); 37% were Black. Over half of the participants (59.5%) had either some college or completed a college education. Slightly less than half reported incomes above $80,000 (43%). Additional characteristics of the sample can be found in Table 5.2.

Analyses considered two groups: participants who were residents of medically underserved areas and those who were not. There were fewer participants in medically underserved areas (n=68) than not (n=790). Characteristics of the two groups were reviewed and are shown alongside characteristics of the entire sample in Table 5.2. The demographics of the two groups are similar proportionally for the most part, with one exception being a higher proportion of adopted participants in the medically underserved group.

Table 5.2. Characteristics of participants

	Entire sample (n, %) N=859	Medically underserved (n, %) n=68	Medically served (n, %) n=790
Age			
Mean (SD)	50.9 (5.9)	50.1 (6.0)	51.0 (5.8)
Self-reported race, n (%)			
White	503 (58.6%)	44 (64.7%)	459 (58.1%)
Black	314 (36.6%)	22 (32.3%)	292 (37.0%)
American Indian	22 (2.6%)	1 (1.4%)	21 (2.7%)
Asian or Southeast	11 (1.3%)	1 (1.4%)	10 (1.3%)
Asian	3 (0.3%)	0 (0 %)	3 (0.4%)
Arab-American	1 (0.1%)	0 (0%)	1 (0.1%)
Hawaiian	21 (2.4%)	1 (1.4%)	20 (2.5%)
Prefer not to answer			
Ethnicity			
Hispanic or Latina	14 (1.8%)	0 (0%)	14 (1.8%)
Not Hispanic or Latina	705 (88.5%)	59 (86.8%)	646 (81.8%)
Prefer not to answer	45 (5.6%	3 (4.4%)	42 (5.3%)
Don't know	33 (4.1%)	2 (2.9%)	31 (3.9%)
Income			
<$40,000	253 (29.5%)	24 (35.3%)	229 (29.0%)
$40,000-79,999	237 (27.6%)	20 (29.4%)	217 (27.5%)
$80,000-119,999	133 (15.5%)	9 (13.2%)	124 (15.7%)
$120,000 or higher	114 (13.3%)	8 (11.8%)	106 (13.4%)
Don't know or Missing	122 (14.2%)	7 (10.3%)	115 (14.5%)
Education			
High school/Tech school grad or less	199 (23.2%)	13 (19.1%)	186 (23.8%)
Some college, no degree or completed college	512 (59.6%)	45 (66.2%)	467 (59.6%)
Postgraduate degree	138 (16.1%)	8 (11.8%)	130 (16.6%)
Missing	10 (1.16%)	2 (2.9%)	8 (1.0%)
Marital status			
Single	338 (39.3%)	25 (37.9%)	313 (39.7%)
Married/life partner	516 (60.1%)	41 (62.1%)	475 (60.3%)
Adopted	23 (2.7%)	6 (8.8%)	17 (2.2%)
Number of times pregnant			
Mean (SD)	2.6 (±1.7)	2.7 (±1.9)	2.5 (±1.7)
Has family history of male breast cancer	17 (2.0%)	1 (1.5%)	16 (2.0%)
Age at first cancer diagnosis			
Mean (SD)	39.89 (±4.98)	39.33 (±4.70)	39.94 (±5.01)

Had at least one other risk factor in addition to breast cancer diagnosis ≤ 50 yrs. old	196 (23%)	14 (20.6%)	182 (23.2%)
Used genetic counseling			
Yes	281 (32.7%)	25 (36.8%)	256 (32.4%)
No	547 (63.7%)	38 (55.9%)	509 (64.4%)
Don't know	25 (2.9%)	3 (4.4%)	22 (2.8%)
Missing	6 (0.7%)	2 (2.9%)	4 (0.5%)

Overall, use of genetic counseling was reported by 281 participants and was higher among medically underserved participants (36.8%) compared to medically served participants (32.4%). However, the difference between groups is not statistically significant (α=.05, p=.32). Numbers and frequencies of genetic counseling use are shown in Table 5.3.

Table 5.3. Number of participants that used genetic counseling

	Entire sample (n, %) N=859	**Medically underserved (n, %) n=68**	**Medically served (n, %) n=790**
Used genetic counseling			
Yes	281 (32.7%)	25 (36.8%)	256 (32.4%)
No	547 (63.7)	38 (55.9%)	509 (64.4%)
Don't know	25 (2.9%)	3 (4.4%)	22 (2.8%)
Missing	6 (0.7%)	2 (2.9%)	4 (0.5%)

The variables that were highly correlated with genetic counseling use were: perceived positive consequences related to family (Pearson's r=.73 for served, r=.84 for underserved), perceived positive consequences to self (Pearson's r=.62 for served, r=.78 for underserved), and having genetic counseling recommended by a provider (Pearson's r=.55 for served, r=.57 for underserved). The correlations for these variables were positive and could be interpreted as facilitators.

Variables negatively correlated with counseling, which could be interpreted as barriers, showed only weak correlations. For the served, the strongest negative association was perceived negative consequences to self (Pearson's r=-.13). For the underserved, the strongest negative association was convenience factors (Pearson's r=-.24). Correlation coefficients for these and other variables can be found in Table 5.4.

Table 5.4. Correlation coefficients between all variables and use of genetic counseling. ***Correlation is significant at the 0.01 level (2-tailed); *Correlation is significant at the 0.05 level (2-tailed)*

Variables		Correlation coefficients, r			
		Medically underserved	**Sig.**	**Medically served**	**Sig.**
Background factors					
	Income	0.232		0.239	**
	Race	0.062		-0.108	**
	Education	0.096		0.125	**
	Ethnicity	0.038		0.011	
	Age	-0.381	**	-0.167	**
	Family history of male breast cancer	-0.146		-0.045	
	Number of pregnancies	-0.083		-0.047	
	Adopted	-0.042		-0.037	
	Ashkenazi Jewish	none		0.102	**
	Had at least one additional risk factor, in addition to breast cancer onset at age ≤ 50 y	.191		.186	**
Social factors					
	Perceived expectations of healthcare provider	0.163		-0.011	
	Perceived expectations of relatives	0.105		0.031	
	Motivation to comply with	0.079		0.096	**

	healthcare provider				
	Motivation to comply with relatives	-0.002		0.034	
Affect					
	Worry	-0.147		-0.121	**
Perceived consequences					
	Perceived positive consequences for family	0.841	**	0.728	**
	Perceived positive consequences for self	0.780	**	0.624	**
	Perceived negative consequences for family	-0.181		-0.05	
	Perceived negative consequences for self	-0.147		-0.132	**
Facilitating conditions					
	Provider recommended genetic counseling	0.567	**	0.546	**
	Knowledge of breast cancer genetics	0.150		0.294	**
	Family support	0.072		0.050	
	Convenience	-0.238		-0.088	*
	Minimum distance to facility offering genetic counseling	-0.218		-0.001	
	Perceived risk	-0.158		-0.033	
	Have insurance	-0.157		0.120	**
Habits					
	History of using health services	0.102		0.134	**
Intention					
	Intention	-0.037		0.082	

Table 5.5. Variables showing the strongest negative association with the outcome of genetic counseling (GC). Negative correlations indicate possible barriers to genetic counseling. Facilitating conditions may present largest barrier *(BF = background factor; SF = social factor; A = affect; PC = perceived consequence; FC = facilitating condition; H = habit; I = intention)*

Medically underserved		**Construct in Triandis model**						
Variables	**Correlation coefficients, r**	**BF**	**SF**	**A**	**PC**	**FC**	**H**	**I**
Age	-0.381							
Convenience factors	-0.238							
Minimum distance to facility offering GC	-0.218							
Perceived negative consequences for family	-0.181							
Perceived risk	-0.158							
Insurance	-0.157							
Medically served								
Variables	**Correlation coefficients, r**							
Age	-0.167							
Perceived negative consequences for self	-0.132							
Worry	-0.121							
Race	-0.104							
Convenience factors	-0.088							
Perceived negative consequences for family	-0.050							

Discussion

Findings suggest a possible difference in use of genetic counseling between medically underserved and medically served groups but not in the hypothesized direction. Regarding the actual use of genetic counseling, a slightly higher proportion of MUS used counseling compared to the MS. This finding was the opposite of what was

expected. However, the finding is slightly underpowered due to the low number of participants who were considered medically underserved, according to the HRSA definition. Thus, this finding should be interpreted with caution.

Race and ethnicity might help explain the unexpected finding of genetic counseling use among a higher proportion of the medically underserved than served. There was a higher percentage of Black, American Indian, Hispanic or Latina, and Arab-American participants in the MS group (42%) compared to the MUS group (33.9%). Thus far, no reports exist about use of genetic counseling among American Indian groups and only one with a sample of Arab-American women. However, studies have reported Black, Hispanic or Latina, and Arab-American women to decline or be less likely to use genetic counseling. Concerns reported by Black women include mistrust about confidentiality, possible discrimination, and lack of information about the family's health history due to less use of health services (Glenn et al., 2012; Thompson et al., 2002). Concerns reported by Hispanic and Latina women are related to cultural beliefs and attitudes that place the needs of the family before the woman's personal needs (Glenn et al., 2012; Sussner et al., 2015, 2013). Concerns reported by Arab-American women are related to cultural beliefs and attitudes involving modesty and lack of familiarity with the healthcare system (Mellon, Gauthier, Cichon, Hammad, & Simon, 2013). The lower proportion of genetic counseling use among the medically served group in this study may be a reflection of the higher percentage of Black, American Indian, Hispanic or Latina, and Arab-American women in that group.

Another variable that might help explain the unexpected finding of a higher proportion of MUS using genetic counseling is adopted status. A higher proportion of

the MUS group was adopted (8.8%) compared to the MS group (2.2%). It is possible that adopted participants had higher rates of using genetic counseling in order to gather more information about their risk if no family health history from their birth parents or other blood relatives was available. It is unclear whether the relationship results more from participants seeking out genetic counseling to obtain more information about their risk or whether healthcare providers are more likely to recommend counseling to adopted individuals who lack the health history suggesting a hereditary component. No reports about a possible association between adopted status and use of genetic counseling for a heritable predisposition to breast cancer have been found in existing literature. However, the possible association may be worth exploring in future studies to evaluate the driving forces in use of genetic counseling services.

The variables showing correlations with use of genetic counseling greater than .50 and .60 (moderately strong to strong) were the same for both groups: perceived positive consequences for family, perceived positive consequences for self, and provider recommended genetic counseling. These factors have been reported in existing literature to be important in whether one uses genetic counseling (Anderson et al., 2012). Of these three variables which were most strongly related to use of genetic counseling in both groups, two are rooted in the patient's perspective, and the third comes from the healthcare provider. The correlation between provider recommending genetic counseling and use of genetic counseling was between .55 and .57 for served and underserved, respectively. This suggests that the provider facilitates counseling use.

Perhaps more interesting, for the purpose of identifying barriers which can be the focus of interventions, are the variables showing negative associations with use of genetic counseling and the differences between groups. A negative association suggests a variable was a barrier or deterring factor to using genetic counseling. As acknowledged earlier, the strength of the associations could be regarded by some as relatively low. Although conclusions about those relationships cannot be made with certainty from these data also due to the small sample size of MUS breast cancer survivors, it is possible that there are real relationships there that are masked by unidentified or uncontrollable factors (Cohen, 1988).

For the MUS, convenience factors, minimum distance to a facility, and insurance were among the variables that showed the strongest negative associations. Multiple barriers may be faced by individuals. For example, in Michigan, where these data were collected, one of the largest cancer research and provider networks in Michigan with a long-standing tradition of genetic counseling is in the city of Detroit, an urban area with 38.1% (±0.7%) of individuals living below the poverty level at the time the data were collected (U.S. Census Bureau, 2012). Despite living in such proximity to the facility, an individual might still not be able to obtain services due to lack of insurance coverage. Interventions aimed at facilitating use of genetic counseling among the underserved, who may be more likely to face barriers related to access, likely need to be multifactorial and address insurance and convenience factors such as extended or alternate clinic hours, transportation, and child care.

For both groups, variables negatively correlated with genetic counseling use had correlations of -.24 or less. Age had a correlation of -.17 among the served and -.38

among the underserved. However, the importance of this is unclear since this age variable indicates age of the participant at the time of the study. Therefore, age will be excluded from further analyses.

Convenience factors had a correlation with use of genetic counseling of -.24 among the underserved. Among the served, the correlation of convenience factors with counseling was -.09. These are both considered weak but this would be an interesting relationship to explore further in future studies as Cohen (1988) stated that a real relationship might exist but might be masked by unidentified or uncontrollable factors. Further exploration of these factors in prospective studies could signal areas for intervention to facilitate genetic counseling use. Prospective studies could be done on convenience factors, for example, which included extended or alternative clinic hours, appointments by telephone, and childcare transportation.

Another interesting finding was that the survey-based measures were more consistently and significantly associated with genetic counseling use than other measures. This highlights the need for researchers and public health agencies to solicit information on barriers and facilitators to genetic service use from at-risk participants directly.

Limitations

The number of participants described as medically underserved (n=68) was the greatest limitation, making statistical analyses underpowered. The binary (yes or no) nature of the medically underserved status, as determined by HRSA definition, may have contributed to the low number of participants defined by medically underserved status. This study aimed to understand the behavior of women considered at high risk

for hereditary breast cancer through the lens of being medically underserved or not, based on residence in a HRSA-designated medically underserved area. HRSA designation as an MUA was the most consistent and reproducible way in which underserved has been defined in the literature, facilitating comparison of findings. However, given the low numbers in that category despite the original study oversampling Black women in high breast cancer mortality counties, it is unclear whether this was a sufficient methodology or whether HRSA designation of medically underserved is relevant in the context of cancer genetic services.

Residence in an area designated as a medically underserved area (MUA) may be an imperfect measure of whether an individual is actually medically underserved. The factors that make up the index defining an area as medically underserved (too few primary care providers, high infant mortality, high poverty, and large elderly population) may be less relevant in the context of using such a specialized health service such as genetic counseling. Additionally, there may be individuals living in MUAs who are not underserved. MUA designation may not be a specific and sensitive way to identify truly underserved individuals. Future studies might explore ways to develop a more sensitive and specific measure for identifying truly underserved individuals. In addition, residence was determined at the time of study participation, not at the time of diagnosis. Residence at the time of diagnosis is not known; if known and included, it may have yielded different results.

The way that other variables were operationalized for this study may have affected or limited the ability to detect some relationships as well. Variables were created using

existing data. Prospective studies might consider the use of the Triandis model to guide the selection of more sensitive and specific measures.

Conclusions

This study supports other studies' findings that recommendation for genetic counseling by a provider is related to use of genetic counseling. However, because receiving a recommendation from a provider is currently unreliable even when an individual has a red flag of a breast cancer diagnosis at age younger than 50, improving genetic counseling use may be further achieved by a better understanding of barriers faced by individuals (i.e., patients) and by empowering individuals and their family. Future research might aim at increasing access to services by exploring the effect of various convenience factors such as extended or shifted clinic hours (e.g., evening and weekend appointments), appointments via video conferencing or telephone, offering child care, or offering transportation. Future research might also explore approaches to including families in discussions and ways to elicit beliefs and attitudes from all parties on the risks and benefits of genetic services.

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CHAPTER VI

Results of aim 3: Exploring a theoretical framework to explain use of genetic counseling for hereditary breast cancer

The results of aim 3 are described in this third manuscript.

Exploring a theoretical framework to explain use of genetic counseling for hereditary breast cancer

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Introduction

Use of genetic counseling for a mutation in the *BRCA* cancer susceptibility genes, a heritable mutation that substantially increases one's risk of developing breast and other cancers, remains suboptimal with recent studies reporting rates of 50% or lower even among individuals considered high risk and for whom counseling is recommended (Anderson et al., 2012; J. Armstrong et al., 2015; Cragun et al., 2015; National Comprehensive Cancer Network., 2017). Incidence of *BRCA*-related cancer and mortality from the cancer may be reduced through interventions such as risk-reducing mastectomy and/or salpingo-oophorectomy (Domchek et al., 2010; Evans et al., 2009; Hartmann et al., 1999, 2001; Rebbeck et al., 2004), medications such as Tamoxifen and raloxifene (Cuzick et al., 2007; Fisher et al., 2005; Nelson et al., 2009; Nelson, Smith, Griffin, & Fu, 2013; Powles, Ashley, Tidy, Smith, & Dowsett, 2007; Veronesi et al., 2007), or increased surveillance. However, these interventions have their own risks and unfavorable sequelae and should be considered only by those for whom the potential benefits outweigh the risks. Genetic counseling involves evaluation of risk, patient education, discussion of benefits and harms of mutation testing, interpretation of results, and discussion of risk management options. It can facilitate understanding of the multiple facets of identifying and managing risk, and can reduce anxiety and depression (Braithwaite, Sutton, Mackay, Stein, & Emery, 2005; Pieterse, Ausems, Spreeuwenberg, & van Dulmen, 2011; Roshanai, Rosenquist, Lampic, & Nordin, 2009), and worry (Bennett et al., 2008; Bowen, Burke, Culver, Press, & Crystal, 2006; Brain, Parsons, Bennett, Cannings-John, & Hood, 2011; Braithwaite et al., 2005).

The benefits of genetic counseling are being realized by only a fraction of the appropriate individuals, however. The low rate of genetic counseling use leads to several questions, including whether some groups continue to face unique or unidentified challenges to using genetic counseling, and whether interventions being designed to facilitate use of counseling are addressing the most important barriers.

The most prevalent reasons for using genetic counseling have been consistently reported as 1) to obtain information to reduce risk (Chin et al., 2005; Glenn, Chawla, & Bastani, 2012; Thompson et al., 2002) or guide treatment decisions (Anderson et al., 2012), and 2) to benefit family members through identification and knowledge of risk (Anderson et al., 2012; K. Armstrong et al., 2000; Thompson et al., 2002). However, there is a gap in knowledge and understanding about the reasons for not using genetic counseling. Reported reasons for not using genetic counseling are numerous without clear and consistent findings. Furthermore, small sample sizes, highly selected samples, and few studies with similar approaches limit the ability to generalize and compare findings. Use of a theory-based conceptual model could aid comparison of findings across different populations by providing a clear and consistent framework for exploring the relationships between predictors. The model would guide variable selection, exploration of relationships, and formulation of subsequent research questions. Use of such a model currently seems to be lacking.

One example how a conceptual model might facilitate research and understanding about use of genetic counseling is through the use of a behavioral model developed by Triandis (Triandis, 1977). Triandis theorized that behaviors may be determined more by either habit or intention. Behaviors that occur only rarely or are

faced for the first time involve more mental processing and intention. In contrast, behaviors that have occurred before may be part of a habit. Habits may involve little or less thinking, and sometimes are done automatically. Genetic counseling for a *BRCA* mutation would likely require more mental processing and intention. However, it is possible that genetic counseling could be considered part of health maintenance behaviors, some of which have been accepted and are engaged in routinely. There is no direct evidence for this in existing literature. Having that knowledge might guide development of interventions that could facilitate use of counseling. Identifying a model that can be used as an organizing framework may help explore this and similar gaps in knowledge about the most important predictors of genetic counseling use and opportunities for interventions.

Information about predictors of genetic counseling use may be particularly informative coming from individuals for whom its use is relevant and recommended. Because mutations in the *BRCA1* or *BRCA2* genes are estimated to be present in only 0.2 to 1% of the general population in the United States (Kurian, 2010), the number of individuals for whom this topic is relevant and who are available for research studies, is limited. In order to maximize use of data already collected from this group, this study sought to explore whether the research questions could be answered from existing data.

The purpose of this study was to explore the ability of Triandis's theory of interpersonal behavior to explain genetic counseling use in the context of a heritable predisposition to breast cancer. The concepts included in Triandis's model may be sufficient to explain the predictors of genetic counseling use; however, it has not been

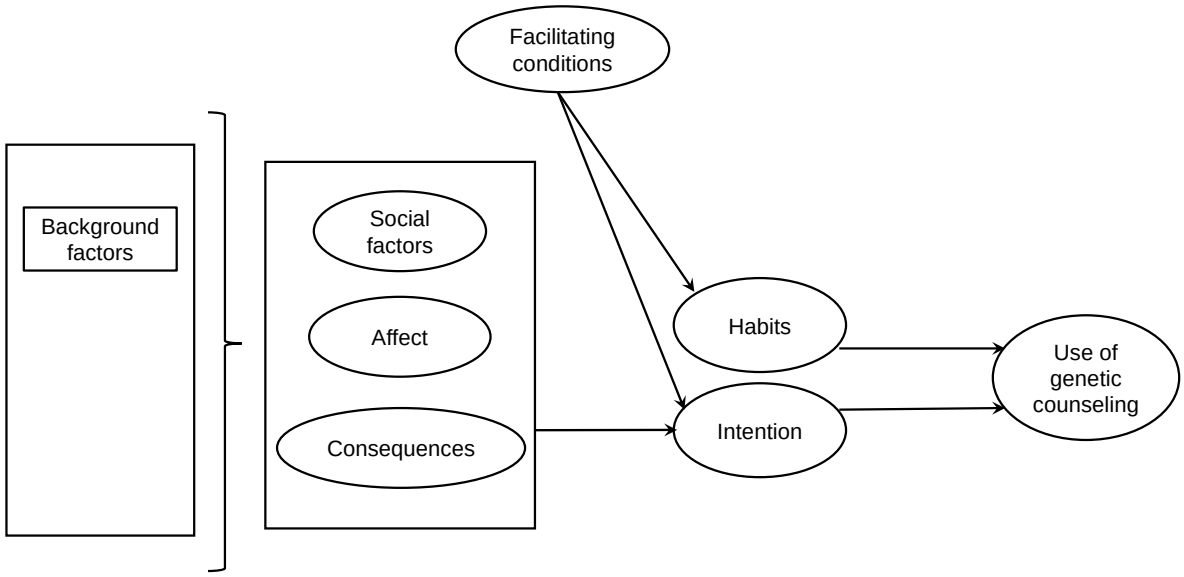
identified as a guiding framework in existing studies, nor have any studies evaluated its suitability. Modeling was done to explore what concepts and variables might be most important in determining use of genetic counseling and whether the model can adequately explain and predict use of counseling. It was hypothesized that all of the constructs in Triandis's model are relevant in predicting use of genetic counseling in this context of possibly having a mutation in the *BRCA1* or *BRCA2* genes, with significance being found in each construct.

Organizing framework

The Triandis model has roots in the role of culture in behavior (Triandis, 1977, 1989) and may help explore use of genetic counseling in a way that it has not been explored in existing literature. Attitudes of a particular race or ethnicity have been explored (Chin et al., 2005; Glenn et al., 2012; Sussner et al., 2015; Thompson et al., 2002). However, societies today are integrated and multicultural, and individuals are multiethnic and multiracial, making pinpointing behavior to a particular ethnic or cultural background challenging, if not impossible. The Triandis model considers the complex interplay of a host of factors which may be influenced by culture over time. For example, the model takes into consideration that ethnic or social cultural background can influence behavior through social factors – one's perceived expectations along with their motivation to comply with others' expectations. The model also considers influential factors to span from personal to interpersonal and broader societal factors. The model (Figure 5.1) organizes the factors that may predict a behavior by constructs such as background factors, social factors, affect or emotions, perceived

consequences, facilitating conditions, habits, and intention. Within those constructs are concepts that may be considered personal, interpersonal, or broader societal. The model suggests that whether factors are personal, interpersonal, or broader societal/structural is less important, however. Culture may affect them all, and separating them may be unrealistic. Interventions may be aimed toward specific facilitating conditions, habits, or perceived consequences, however, making understanding of these more actionable.

Figure 6.1. Conceptual framework developed from Triandis's model of interpersonal behavior



Methods

Study Sample and Recruitment

This study used data from the baseline survey of a randomized trial designed to increase cancer surveillance and use of genetic services among a group of young

breast cancer survivors, women diagnosed with breast cancer younger than 50 years old (Katapodi, Northouse, Schafenacker, et al., 2013; Katapodi et al., 2017). Participants were identified using the Michigan Cancer Registry. From the 9,000 cases of *in situ* and invasive breast malignancies reported between 1994 and 2008, 3,000 women diagnosed between the ages of 20 and 45 years old were randomly selected. The initial study oversampled for Black women residing in counties with the highest mortality rates for young women with breast cancer. This was done in order to increase the inclusion of minority and underserved women. The study excluded from participation women who were pregnant, incarcerated, or institutionalized at the time of the study because they might not have been able to follow recommendations for breast cancer screening or genetic counseling.

Variables and measures

The survey was a 187-item self-administered questionnaire from the initial study. It was mailed to participants along with an invitation letter to participate in the study. The variables and measures used were from previously used and validated measures where possible. Triandis's concepts and the way they were operationalized for this study are shown in Table 6.1.

Variables of interest for this secondary data analysis were chosen based on a review of literature on factors associated with use of genetic counseling or genetic testing that were consistent with Triandis's model. Two variables were created for this study. First, a medically underserved variable was created using U.S. Census Tract information and the Health Resources and Services Administration (HRSA) designation of Census tracts as a medically underserved area (MUA). Literature on the use of

health services by underserved groups reveals a multitude of ways in which "underserved" is defined. The clearest and most consistent was the HRSA definition. Medically underserved in this study was defined as being a resident in a U.S. Census Tract designated by HRSA as an MUA.

The second variable that was created was minimum distance from a facility offering genetic counseling. Facilities listed on the website of the National Society of Genetic Counselors were contacted and asked whether genetic counseling was offered at the facility at the time that data were being collected for the initial study. Distances were calculated based on a previously used methodology (Bliss, Katz, Wright, & Losina, 2012).

Table 6.1. Variables and how they were operationalized

Triandis concept	Variable	Measure
Background factors		
	Age Race Ethnicity Ashkenazi Jewish background Income Education Adopted	Adapted from the Behavioral Risk Factors Surveillance System (2002)
	Family history of male breast cancer Number of pregnancies Additional risk factors	Adapted from U.S. Preventive Services Task Force (U.S. Preventive Services Task Force, 2005b), individual meets criteria for referral to GC if 'yes' to ≥2 of the following: • Ovarian cancer, at any age: self mother sister daughter maternal grandmother

		maternal aunt paternal grandmother paternal aunt • Breast cancer at age ≤ 50 y.o.: self mother sister daughter maternal grandmother maternal aunt paternal grandmother paternal aunt
Social factors		
	Perceived expectations of relatives Perceived expectations of healthcare provider Motivation to comply with relatives Motivation to comply with healthcare provider	"Do you believe that *your relatives* want you to get mammograms and other tests to find cancer at an early stage?" (Definitely No/No/Somewhat No, Neutral, Somewhat Yes/Yes/Definitely Yes) "Do you believe that *your doctor or healthcare provider* wants you to get mammograms and other tests to find cancer at an early stage?" (Definitely No/No/Somewhat No, Neutral, Somewhat Yes/Yes/Definitely Yes) "How often do you try to do what *your relatives* want you to do about finding cancer at an early stage?" (Never/Almost Never/Sometimes, Neutral, Most times/Almost Always/Always) "How often do you try to do what *your doctor or other healthcare provider* wants you to do about finding cancer at an early stage?" (Never/Almost Never/Sometimes, Neutral, Most Times/Almost Always/Always) Adapted from Ajzen et al. (Ajzen and Fishbein, 1980b)
Affect		
	Worry	"Have you ever had genetic testing for a gene mutation connected to breast or ovarian cancer? If no, please tell us why

		you have not had genetic testing (check all that apply)." Worry was indicated if the following was checked: "I would rather not know if I have a mutation connected to cancer."
Perceived consequences		
	Perceived positive consequences to self	"Have you ever had genetic testing for a gene mutation connected to breast or ovarian cancer? If you had genetic testing, what helped you decide to have testing (check all that apply)." Perceived positive consequences to self was indicated if either of the following were checked: "I wanted to learn more about my future cancer risk; Results may change my cancer treatment (preventive surgery, chemotherapy, etc.)"
	Perceived negative consequences to self	"Have you ever had genetic testing for a gene mutation connected to breast or ovarian cancer? "If *no*, please tell us why you have not had genetic testing (check all that apply)." Perceived negative consequences to self was indicated if the following was checked: "I am worried the result could be used against me (by employer, health insurance)."
	Perceived positive consequences to family	"Have you ever had genetic testing for a gene mutation connected to breast or ovarian cancer?" Perceived positive consequences to family was indicated if the following was checked: "Results will benefit my family."
	Perceived negative consequences to family	

		"Have you ever had genetic testing for a gene mutation connected to breast or ovarian cancer? If *no*, please tell us why you have not had genetic testing (check all that apply)." Perceived negative consequences to family was indicated if the following was checked: "Family members might be upset with test results."
Facilitating conditions		
	Provider recommended genetic counseling	"Have you ever had genetic testing for a gene mutation connected to breast or ovarian cancer?" Provider recommended was indicated if the following was checked: "My healthcare provider suggested that I do."
	Perceived risk	"On a scale from 0 (Definitely Will Not) to 10 (Definitely Will), please circle a number that best describes what you believe is **your chance** for getting breast cancer." Likert-type scale, 0-10 for "Definitely Will Not/Probably Will Not/Equal Chances/Probably Will/Definitely Will Previously used (Katapodi et al., 2009b, 2013b)
	Knowledge of breast cancer genetics	For each item, "Please mark an X in the box that best describes whether these statements are true or false." (Options given were: True/False/Don't Know) Cancer can be caused by... ...chemicals and radiation ...a deleterious mutation that happens by chance during a person's life ...a deleterious mutation that is passed on from one generation to

		the next Breast cancer... ...affects about 1 in 8 women (12%) in the U.S. ...that is connected to heredity affects about 1 in 10 women (10%) who get breast cancer ...that is not connected to heredity is called “sporadic.” Most cases of breast cancer are sporadic ...that is sporadic, occurs earlier in life (younger than 50 years old) ...that is connected to heredity is caused mostly by deleterious mutations in the BRCA1 and the BRCA2 genes Families that have a deleterious mutation in the BRCA1 or BRCA2 genes are more likely than other families to have... ... cases of breast cancer in more than one generation ...women with cancer in both breasts ...cases of breast cancer diagnosed under the age of 50 ...cases of breast cancer in men Adapted from Knowledge Assessment Questionnaire (Wang et al., 2005); (Cronbach’s alpha=0.72)
	Convenience	“Have you ever had cancer genetic services? If no, please tell us why you have not used cancer genetic services – check all that apply.” Convenience variable was created if any of the following were checked: “I am too busy; I cannot get time off work; Lack of transportation; Lack of child care; Clinic hours do not fit my schedule; Clinics are too far away” Adapted from previously used (Anderson et al., 2012b)
	Insured	“Have you ever had genetic testing for a

		gene mutation connected to breast or ovarian cancer?) If you have genetic testing, what helped you decide to have testing (check all that apply) Insured if any of the following were checked: “My medical insurance covered the visit; My medical insurance covered the cost of the test” Adapted from previously used (Anderson et al., 2012b)
	Family support	Social support for breast cancer screening (Cronbach’s alpha=0.81) For each item, “Please read each statement below and decide which answer describes your family. You may skip any question(s) that make you feel uncomfortable or sad.” Likert-type scale of 1-7 for Never True, Almost Never True, Seldom True, Sometimes True, Often True, Almost Always True, Always True The people in my family... ...are willing to listen to me when I just need to talk ...give me a great deal of affection and warmth ...ignore or make light of my concerns ...support me as I try to cope with problems in my life ...change the topic when I discuss my concerns ...work as a team to manage concerns we have ...give me positive feedback for my attempts to cope with problems that I have ...offer to help me do things that are difficult for me to do ...do not like to talk about problems and concerns ...avoid talking about negative feelings

		and sad events ...disagree on how problems affect us ...disagree on how to solve problems we have ...hide their true feelings from each other ...make me feel comfortable when discussing my concerns ...make me feel that talking about my problems creates a lot of tension among us In our family, *when I have a health problem...* ...I have someone I can turn to ...I could easily find someone to help me with my daily work ...there is at least one person whose advice I really trust ...there is no one to turn to ...I can find someone to help me get to the doctor ...I can talk to someone about my concerns and fears ...there is someone helping me get the care that I need ...I can get help with costs and expenses ...there is no one to help me get theinformation that I need ...I don't have anyone I can confide in Previously used (Katapodi et al., 2002b)
	Residence in a medically underserved area	Geocoded U.S. Census Tracts and HRSA designation as a medically underserved area (MUA) Examined in this study
	Distance to genetic counseling	Distance to nearest facility offering genetic counseling Examined in this study
Habits		
	History of using health services	Participant considered to have a history of using health services if answered yes to any of the following: "Have you ever had a clinical breast

		exam?; Have you ever had a mammogram?; Have you ever had a breast MRI?" Adapted from the Behavioral Risk Factors Surveillance System (2002)
Intention		
	Intention to use genetic counseling	"During the next 12 months, how likely are you to ask your healthcare provider if genetic testing for a gene connected to hereditary cancer is a right test for you?" Likert-type scale, of 1-7 or NA for Very Unlikely, Likely, Somewhat Unlikely, Neutral, Somewhat Likely, Likely, Very Likely, Does Not Apply Adapted from Ajzen et al. (Ajzen and Fishbein, 1980b)

Data Collection and Analysis

Data from the baseline survey of the initial study were analyzed for the entire sample of 859 participants. Descriptive statistics characterized the sample in terms of sociodemographics, cancer-related medical history, perceived risk, perceived consequences, perceived expectations from family and healthcare provider, motivation to comply with those expectations, knowledge of breast cancer genetics, intention, and history of health services use. Bivariate correlations were assessed to rule out multicollinearity, defined as correlations of 0.9 or higher (Pallant, 2007). Prior to performing logistic regression, multiple imputation was done for missing data. Pooled data were used for regression analyses. Multiple imputation and all analyses were done using SPSS v. 24.

Logistic regression models for the dichotomous outcome were developed based on the Triandis model. Predictors for each model were added by block in order

according to the theoretical constructs of the Triandis model. The progression of model development is shown in Figure 2. The Omnibus test of model coefficients, Cox & Snell R^2 and Nagelkerke R^2 were used to evaluate how well a model fit the data relative to other models. Fit tests were analyzed to determine the most parsimonious model that might explain the use of genetic counseling in this sample of YBCS. Fit was assessed for each block addition and to compare models to the constant-only baseline model, model 0.

Two additional models were explored. First, only the variables that were significant in model 3 were tested with Intention and Habits. The second additional model was similar to model 4, but substituted Habits for Intention. Model 4 explored Triandis's theory that behaviors done less frequently would involve more thought and intention; the additional model explored whether a health maintenance habit could be better at explaining use of genetic counseling than intention. These are also shown in Figure 6.2.

Figure 6.2. Constructs of Triandis theory included in each model

Model 0	Model 1	Model 2	Model 3	Model 4	Model 5
Constant only	Background factors	Background factors + Social factors, Affect, Perceived consequences	Background factors + Social factors, Affect, Perceived consequences + Facilitating conditions	Background factors + Social factors, Affect, Perceived consequences + Facilitating conditions + Intention	Background factors + Social factors, Affect, Perceived consequences + Facilitating conditions + Intention + Habits

Model 6	Model 7
Statistically significant variables from Model 3 (determined most parsimonious) + Intention + Habits	Background factors + Social factors, Affect, Perceived consequences + Facilitating conditions + Habits

Fit measures

Multiple measures of fit were used to assess the performance of each model. The first, the Omnibus test of model coefficients, was used to evaluate significance compared to the previous block in the model, and significance for the whole model compared to constant-only model. Chi-square tests of significance were used to

indicate model fit. Nagelkerke R^2, a pseudo R^2, was also used to evaluate model fit with higher values indicating better model fit. Cox & Snell R^2, another pseudo R^2 was also assessed for comparison. The most parsimonious model was the one that showed greatest fit with the outcome of interest with only the most essential variables.

Results

Of the 859 participants who completed the baseline survey, all of whom were young breast cancer survivors, 32.7 % (n= 281) used genetic counseling. Age at first cancer diagnosis ranged from 25 to 50 years old; median age was 41. A majority of the sample was educated, with 62.1% having completed college or at least some college, and 21.4% reporting a postgraduate degree. Other characteristics of participants who used genetic counseling as well as those who did not are shown in Table 6.2.

Many participants (89%) believed that their relatives want them to get mammograms and other tests to find cancer at an early stage and most (92%) believed their doctor or healthcare provider wants them to get mammograms and other tests to find cancer at an early stage. Many participants (77%) try to do what their relatives want them to do about finding cancer at an early stage most times, almost always, or always; even more (91%) try to do what their doctor or other healthcare provider wants them to do about finding cancer at an early stage most times, almost always, or always.

The most selected reason for not having used cancer genetic services (understood as genetic counseling in this study) was that “No one ever suggested it”. This item was selected by 357 of the 546 participants (65.4%) who did not use genetic counseling. Mean score on the scale for Knowledge of Breast Cancer Genetics was

6.72 (SD 3.04) with most frequently occurring score being 9.0 (possible scores from 1 to 12). The second most chosen reason for not having used cancer genetic services, selected by 72 of the 546 participants (13.2%), was that out-of-pocket expenses are too high or not covered by insurance.

Table 6.2. Characteristics of participants who used genetic counseling and participants who did not. (Note: Participants reporting "Don't know" to use of genetic counseling n=25)

	Used genetic counseling (n, %) n=281	Did not use genetic counseling (n, %) n=546
Age		
Mean (SD)	49.4 (±6.0)	51.72 (±5.6)
Range	32-63	30-63
Race		
White/Other	192 (68.3%)	319 (58.3%)
Black	89 (31.7%)	228 (41.7%)
Ethnicity		
Hispanic or Latina	1 (0.4%)	10 (2.0%)
Not Hispanic or Latina	241 (89.9%)	447 (88.7%)
Prefer not to answer	15 (5.6%)	29 (5.8%)
Don't know	11 (4.1%)	18 (3.6%)
Ashkenazi Jewish	7 (2.5%)	2 (0.4%)
Income		
<$40,000	58 (23.2%)	178 (38.5%)
$40,000-79,999	69 (27.6%)	163 (35.3%)
$80,000-119,999	60 (24.0%)	71 (15.4%)
$120,000 or higher	63 (25.2%)	50 (10.8%)
Don't know or Missing	31	85
Education		
High school/Tech school grad or less	46 (16.4%)	138 (25.6%)
Some college, no degree or Completed college	174 (62.1%)	323 (59.9%)
Postgraduate degree	60 (21.4%)	78 (14.5%)
Marital status		
Single	127 (45.5%)	198 (36.4%)

Married/life partner	152 (54.5%)	346 (63.6%)
Adopted	6 (2.1%)	16 (2.9%)
Number of times pregnant Mean (SD)	2.4 (±1.6)	2.63 (±1.8)
Has family history of male breast cancer	9 (3.2%)	8 (1.5%)
Age at first cancer diagnosis Median Range	41 25-50	41 22-58
Had one or more additional risk factor other than breast cancer diagnosis at age younger than 50 years	96 (34%)	96 (17.7%)
Reside in a medically underserved area	25 (8.9%)	38 (6.9%)

Predictors of genetic counseling use

Twenty-nine variables in total were identified from the literature as possible predictors of genetic counseling use and were organized according to the constructs of the Triandis model (shown earlier in Table 6.1). Descriptive characteristics of each of these variables were explored, along with the relationship of each variable with other predictor variables and with the outcome. Four variables had very low number of participants and were excluded from the modeling. For example, there were only 9 Ashkenazi Jewish women in the sample. Other variables that were excluded due to having too few participants were: ethnicity, adopted, and having a family history of male breast cancer. Nine variables were excluded for too few responses in some categories. Too few responses can be problematic for statistical analyses which require the assumption of normality. Data for these nine variables are shown in Table 6.3. These variables were: worry, positive perceived consequences to the self, negative perceived consequences to the self, positive perceived consequences to the family, negative perceived consequences to the family, provider recommendation, convenience factors, habits, and

intention. Age was also excluded because this referred to the age of the participants at the time of the survey and was determined as lacking a strong theoretical relationship to the outcome. There was a total of 15 variables included in the model. These are shown in Table 4.

Table 6.3. Data for variables excluded due to having too few responses in a group

	Outcome (used genetic counseling)	
	No	Yes
Worry		
No	519	280
Yes	28	1
Perceived Positive Consequences to Self		
No	2	63
Yes	5	158
Did not apply	540	60
Perceived Negative Consequences to Self		
No	453	48
Yes	40	3
Did not apply	54	230
Provider recommended		
No	4	109
Yes	3	112
Did not apply	540	60
Habits		
No	36	2
Yes	507	275

	Outcome (used genetic counseling)	
	No	Yes
Convenience factors		
No	526	280
Yes	21	1
Perceived Positive Consequences to Family		
No	5	36
Yes	2	185
Did not apply	540	60
Perceived Negative Consequences to Family		
No	479	49
Yes	14	2
Did not apply	54	230
Intention		
1	301	8
2	68	3
3	152	9

Results of logistic regression

Variables were added in a stepwise fashion, by block, grouped by constructs of the Triandis model. Three variables were statistically significant predictors in the regression of the full model: having an additional risk factor, knowledge of breast cancer genetics, and motivation to comply with one's doctor or healthcare provider. Fit measures, shown in Table 6.4, suggest that the full model predicts use of genetic counseling better than background factors alone or background factors plus the social factors in Block 2. The results of logistic regression of the full model to predict genetic counseling use using the full model are shown in Table 6.5.

Table 6.4. Results of stepwise regression to predict use of genetic counseling using the full model

	Model 0	Model 1	Model 2	Model 3
Omnibus tests of model coefficients+				
Model		χ^2=41.671, p=.000	χ^2=50.270, p=.000	χ^2=80.114, p=.000
Block		χ^2=41.671, p=.000	χ^2=8.598, p=.072	χ^2=29.845, p=.000
Cox & Snell R^2		.082	.098	.151
Nagelkerke R^2		.111	.133	.206
Variables in model		**Variables significant in each model**		
Background factors				
1. Race				
2. Income		Income***	Income***	Income**
3. Education				
4. Number of pregnancies				
5. Additional risk factor		Additional risk factor***	Additional risk factor***	Additional risk factor***
Social factors				
6. Perceived expectations of relatives				
7. Perceived expectations of HCP				
8. Motivation to comply with relatives				
9. Motivation to comply with HCP			Motivation to comply with HCP**	Motivation to comply with HCP*
Facilitating conditions				
10. Perceived risk				
11. Knowledge				Knowledge***
12. Insured				
13. Family support				
14. Residence in MUA				
15. Minimum distance to facility offering GC				
***p<.001; **p<.01; *p<.05				

Table 6.5. Performance measures for full model to predict use of genetic counseling

Variable	B	SE	Exp(B)
Block 1			
Race	.100	.194	1.105
Income	.280	.093	1.323**
Education	-.036	.141	.964
Number of pregnancies	-.035	.049	.965
Additional risk factor	.829	.182	2.292***
Block 2			
Perceived expectations of relatives	-.130	.345	.878
Perceived expectations of HCP	.511	.383	1.668
Motivation to comply with relatives	.058	.234	1.059
Motivation to comply with HCP	-1.021	.408	.360*
Block 3			
Perceived risk	-.085	.106	.918
Knowledge	.189	.031	1.208***
Insured	.752	.423	2.122
Family support	.052	.069	1.053
Residence in MUA	.309	.291	1.363
Minimum distance to facility offering GC	.001	.003	1.001
***p<.001; **p<.01; *p<.05			

As shown in Table 6.4, among models 1, 2, and 3, model 3 fits the data better than models 1 and 2. Model 3 shows the highest χ^2 as well as highest Cox & Snell R^2 and Nagelkerke R^2. In this model, the variables that were significant at α=.05 were: income (p=.003), having an additional risk factor (p=.000), motivation to comply with their healthcare provider (p=.013), and knowledge of breast cancer genetics (p=.000).

As shown in Table 5, having an additional risk factor showed the highest odds for using genetic counseling. Individuals with an additional risk factor were 2.3 times more likely to use genetic counseling (95% CI=1.604-3.275; p=.000). Individuals with higher income were 1.3 times more likely to use genetic counseling (95% CI=1.091-1.686;

p=.006). Individuals with more knowledge about breast cancer genetics were 1.2 times more likely to use or have used genetic counseling (95% CI=1.137-1.282; p=.000). However, the direction of this relationship is unclear because some participants had already received genetic counseling at the time of the study. Therefore, higher scores on the knowledge measure may be an outcome of genetic counseling rather than a predictor of it. An unexpected finding was that participants with higher motivation to comply with their healthcare provider were 36% less likely to have used genetic counseling. The reason for this is unclear. This relationship may just be a result of the fact that many participants (63.6%) had not used genetic counseling and a majority of participants even more (91%) try to do what their doctor or other healthcare provider wants them to do about finding cancer at an early stage most times, almost always, or always.

Models with the habit and intention variables were unable to be explored because of their exclusion due to too few responses in some categories. Additional models were explored with variable selection based primarily on a conceptual basis with some consideration for which variables showed significant relationships in the full model. In addition to being described here, these models are shown in Table 6.6. Model 4 controlled for three background factors -- race, income, and education -- and explored the significance of all four social factors along with two facilitating conditions -- knowledge and insurance. Model 5 controlled only for income, and added the variable of additional risk factor to the other variables explored in Model 4. Model 6 controlled for two background factors -- income and education, and explored the facilitating

conditions of knowledge and insurance. Model 7 explored only additional risk factor, with the facilitating conditions of knowledge and insurance.

Table 6.6. Additional models tested to identify a more parsimonious model

	Model 4	Model 5	Model 6	Model 7
Omnibus tests of model coefficients+ Model	χ^2=88.728, p=.000	χ^2=104.371, p=.000	χ^2=85.417, p=.000	χ^2=97.486, p=.000
Cox & Snell R^2	.120	.140	.114	.112
Nagelkerke R^2	.165	.192	.156	.155
		Variables significant in each model		
Variables in model	1. Race 2. Income** 3. Education 4. Motivation to comply with relatives 5. Motivation to comply with HCP* 6. Knowledge*** 7. Insured	1. Income** 2. Additional risk factor*** 3. Motivation to comply with relatives 4. Motivation to comply with HCP* 5. Knowledge*** 6. Insured	1. Income** 2. Education 3. Knowledge*** 4. Insured	1. Additional risk factor*** 2. Knowledge*** 3. Insured*

Table 6.7. Results of regression to predict use of genetic counseling using Model 7

Variable	B	SE	Exp(B)
Block 1 Additional risk factor	.838	.177	2.312***
Block 2 Knowledge Insured	.209 1.011	.028 .408	1.233*** 2.748*
***p<.001; **p<.01; *p<.05			

Based on the χ^2 values, Cox & Snell R^2, and Nagelkerke R^2, model 5 fits the data better than models 4, 6, and 7. However, model 7, has the second highest χ^2, Cox & Snell R^2, and Nagelkerke R^2 values, has fewer variables, and would be considered the most parsimonious. In both models 5 and 7, additional risk factor and knowledge are statistically significant. In these and the other models, income is significant; if income is not in the model, insured is significant. In model 7, insured may be acting as a proxy for income or socioeconomic status.

Using model 7, insured seems to be quite important in predicting genetic counseling use; it suggests that insured individuals are 2.7 times more likely to use genetic counseling that individuals who are not insured. Having an additional risk factor also shows higher likelihood of using genetic counseling (2.3 times). These are shown in Table 6.7.

Limitations

The limitations of this study are in large part due to using an existing dataset from a study that was designed with different research aims and using a different theoretical framework. Some concepts that were of interest in this study were not included in the initial study and variables were operationalized based on concepts in that model. Inclusion of variables explored in this study were limited to what was collected in the initial study. Stigma and mistrust, for example, were unable to be included in the modeling done in this study because it was not part of the model used for the initial study, nor was there a suitable similar concept or measure. Similarly, other emotions may have been explored in addition to worry.

Additionally, there were items in the survey of the initial study that were relevant, but posed challenges when operationalized for this study. Positive and negative perceived consequences to self as well as family were concepts of interest in this study, as were habits and intentions. However, these variables were not of primary interest in the initial study. For this study, they were operationalized using responses to select items in the survey rather than complete validated measures. In light of the limited availability of young breast cancer survivors and the exploratory nature of this study, the potential limitations were accepted initially so as to maximize use of data already collected and to minimize research burden on this group.

Discussion

This study yielded interesting and important results. First, for this sample of young breast cancer survivors, for whom genetic counseling is relevant and recommended, only 32.7% of the women used genetic counseling. This is consistent with the low rates of counseling reported in other studies mentioned earlier. Additionally, the most reported reason for not having used genetic counseling was that "No one ever suggested it". This was reported by 65.4% of the participants who did not use genetic counseling, despite having received a diagnosis of cancer at a young age. This suggests that there is still much work to be done in getting healthcare providers to recognize the risk factors and recommending use of genetic counseling. Perhaps even better would be to ensure that the public is aware of the risk factors for having a mutation that can predispose one to developing cancer at a young age, thereby empowering the public with the knowledge.

The modeling also yielded interesting results. Income or being insured, and having an additional risk factor were statistically significant in all models. Knowledge of breast cancer genetics was also significant. However, this cannot be assumed as being a predictor to counseling use but instead may have been an outcome of using genetic counseling. The direction of this relationship is not clear as 33% of participants had already received genetic counseling at the time of the study.

The most parsimonious model is extremely pared down from the original model, suggesting that the original model is not suitable for predicting genetic counseling use. Although the data used for this study does not support the ability of the Triandis model to explain the use of genetic counseling use in the context of young breast cancer survivors, the model continues to show promise as a model for exploring relationships among other variables that were unable to be included in analyses for this study. Some variables, and in some cases entire concepts of the Triandis model, were excluded due to issues with the way that variables could be operationalized. In addition to this, not all constructs of the model had variables significantly associated with the outcome of genetic counseling use. A prospective study designed to explore the research questions and aims of this study specifically may yield different results.

Variables excluded due to unsuitable measures

The difference in the way that variables should have been operationalized for this study and the way that they were operationalized in the initial study could have contributed to lack of significance of variables in some constructs. For example, the intention and worry measures asked about these concepts with regard to genetic

testing. Intention to get genetic testing could be very different from intention to get genetic counseling, and worry due to genetic testing as opposed to genetic counseling may also be different. However, these were the closest measures available from the dataset. Other variables that involved measures pertaining to genetic testing were: positive perceived consequences to self, negative perceived consequences to self, positive perceived consequences to family, negative perceived consequences to family, and provider recommendation. The social factors construct was comprised of the four variables on perceived consequences. Therefore, this construct could not be analyzed effectively.

The measure for habit was also inadequate. There is little data from individuals who have used genetic counseling more than once. Therefore, breast health maintenance habits were used as a proxy. This was operationalized using survey items on prior mammography, clinical breast exam, and breast MRI. However, most of the study participants likely would have undergone these services due to their breast cancer diagnosis. In fact, this led to too few responses in a group for some categories and the habits variable was not able to be included in the model. Better measures for habit and intention would have perhaps resulted in their inclusion in the modeling.

Variables excluded due to few responses in a group

In addition to the measures for these variables pertaining to genetic testing, the variables were operationalized using select items that were not complete and validated measures. There were too few responses for the majority of these items (shown earlier

in Table 3), and the conclusions that could be drawn from the responses were not suitable for this study.

Conclusion

Although the Triandis model was not able to explain genetic counseling in this study, there were several limitations related to this being a secondary data analysis and the way that variables were operationalized. The ability of the Triandis model to explain or predict genetic counseling may be worth exploring further. The model includes concepts such as emotions, interpersonal relationships, societal norms, and factors related to the healthcare system (e.g., availability of a knowledgeable healthcare provider who recognizes the risk factors for a cancer-predisposing heritable mutation such as *BRCA1* or *BRCA2*) in addition to concepts found in more widely used health-specific behavior prediction models. Prospective studies, with the opportunity to operationalize variables and use measures chosen specifically for this research question and concepts of the Triandis model, might yield different results. Future studies would ideally also have a population-based recruitment strategy, such as through use of cancer registries, in order to maximize the potential for obtaining a diverse sample. A clear and consistent theoretically-based conceptual model to guide studies on predictors will be helpful in producing results that can be compared, thus enabling confidence in study findings, facilitating development of interventions and policies that can effectively make an impact on the use of genetic counseling. This will help the field move toward increasing genetic counseling use for individuals who could benefit from it.

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CHAPTER VII

Summary

Although there were some challenges related to doing a secondary analysis of existing data, this study yielded some interesting findings and highlighted ideas needing further exploration. The literature review found several possible predictors of genetic counseling use, some of which were also explored in this study. The findings of this study provide some support for existing knowledge. First, this study found provider recommendation, perceived positive consequences (i.e., benefits) to family and perceived positive consequences to self to be correlated with genetic counseling use with correlations over .5. These have been identified from existing literature as frequently reported reasons for using genetic counseling. However, these were some of the variables that were excluded from the logistic regression analyses. The findings in terms of predictors of genetic counseling use therefore requires some caution in interpretation since variables (some of which were highly correlated with counseling use with correlations over .60) were excluded from the analyses on predictors in this study.

Similar to a few studies described earlier, this study also found rates of genetic counseling to be suboptimal, even among individuals considered high risk, for whom it is recommended and for whom it could present life-saving benefits. Additionally, this study, like many existing studies, lacked a diverse sample. It oversampled for blacks and individuals residing in Michigan counties with the highest rates of mortality for

breast cancer. However, there were still few participants of other racial and ethnic backgrounds such as Hispanic and Arabic, though there are large numbers of individuals with those ethnic backgrounds residing in Michigan.

Among this group of women diagnosed with cancer at an early age (younger than 50), only 32.7% used genetic counseling; furthermore, the most reported reason for not using genetic counseling, reported by 65.4% of the participants who did not use counseling, was that “No one ever suggested it.” Education efforts to healthcare providers should continue but perhaps more fruitful may be empowering patients and the public with education about risk factors for having a cancer-predisposing heritable mutation, of which cancer at an early age is a hallmark.

Findings of this study suggest that socioeconomic factors such as income and insurance are likely important in whether one uses genetic counseling. In all regression models explored in this study, one or the other were significant. In this study, women were 1.3 times (32%) more likely to use genetic counseling if they had higher income. Related to this, women were found to be more likely to use genetic counseling if they had an additional risk factor other than breast cancer diagnosis at age younger than 50. Although genetic counseling is now covered without cost sharing as a preventive service for individuals with the appropriate risk factors, awareness of this and of one’s risk factors may still depend on how integrated an individual is with the healthcare system and having a knowledgeable healthcare provider who can identify risk factors and discuss appropriate next steps such as genetic counseling.

One finding of this study that deserves extra caution with interpreting is that participants with higher knowledge scores on the breast cancer genetics measure were

1.2 times (21%) more likely to have used genetic counseling. The direction of this relationship is unclear. Nearly 33% of participants had already received genetic counseling at the time of the study; more knowledge of breast cancer genetics may be a reflection of counseling use rather than knowledge predicting counseling use.

An unexpected finding of this study was that there was no significant difference in rates of genetic counseling use based on medically served or underserved status. The test to determine this was underpowered, however, so confidence in this finding is low. There are a few possible reasons for the lack of a significant difference in counseling use according to medically served or underserved status. First is the way in which medically served or underserved status was operationalized in this study. Underserved status was operationalized as residence in an area designated by HRSA as a medically underserved area (MUA). In existing literature on barriers faced by underserved groups, underserved is defined in a multitude of ways, making comparison and synthesis of findings challenging. HRSA designation as an MUA was chosen for its characteristic as a sort of standardized measure which could be used to facilitate comparison of findings among multiple future studies. However, this designation considers 1) population to provider ratio; 2) percent of the population below federal poverty level; 3) percent of the population over age 65; and 4) infant mortality rate. These criteria might not be highly relevant in the context of specialized services such as cancer genetic counseling.

Another possible reason for lack of a significant difference in counseling use between served and underserved groups might be the imbalance in number of served and underserved participants. There was a far larger number of medically served

participants than underserved. Participants were identified using a state cancer registry. This should help increase the chances of obtaining a diverse sample in terms of race and ethnicity as well as rural and urban residences. However, individuals may still decline to participate in the study leading to samples that lack in diversity. Recruitment of participants may need to be more purposive, oversampling for rural in addition to ethnic minority individuals.

The findings of the literature review, described in the first manuscript, were organized according to the conceptual framework and informed selection of variables of interest for this study. The correlation of these variables with genetic counseling use, described in the second manuscript, provided some insight into possible barriers and possible facilitators to counseling use based on positive or negative relationship with counseling use. The relationships between these variables and the outcome of counseling use were explored further using regression analyses in the final manuscript, and the conceptual framework was evaluated for its potential to guide future research in this area. However, the regression analyses could not include variables that had too few responses in some response categories. The variables identified as predictors to counseling use based on regression analyses were different from the variables showing correlations over .50 in the correlation analyses. Although the data used for this study did not support the framework as suitable for predicting counseling use (primarily because some variables and constructs were excluded from analyses due to too few responses for some categories), the framework still shows potential for use in future research on the topic.

Next steps

A prospective study to follow up on some of the findings of this secondary analysis would again recruit women who were diagnosed with cancer at age younger than 50. Young breast cancer survivors would be a target population because they have been identified as high risk; additionally, genetic counseling is recommended for them and could lead to decision-making about potentially life-saving approaches to reducing risk for developing cancers associated with a heritable mutation. Recruitment of women using state cancer registries may be an effective approach, oversampling for rural populations as well as individuals of racial and ethnic minority backgrounds. Additionally, recruiting from multiple state cancer registries may be helpful for maximizing potential of obtaining large numbers of diverse groups, increasing power of analyses. Participants should be diverse in sociodemographic characteristics such as racial and ethnic makeup, median income and poverty levels, proportion of insured to uninsured individuals, and large metropolitan as well as rural populations. Availability of a large cancer center in the state may be a variable of interest as well.

In line with obtaining a diverse sample and increasing inclusion of underserved individuals, an effort should be made to identify criteria for being underserved in the context of specialized health services such as cancer genetic counseling. This could build on the HRSA criteria for MUA, perhaps removing the criterion of percent of the population over age 65 and instead including the criterion of integration into the health care system. The measure for this could be regular use of preventive health services. Regular use of preventive health services could improve the chances that risk factors such as personal and family history of cancer are identified and followed over time.

Special attention should also be given to identifying validated measures previously used in studies on use of breast cancer genetic services among high risk individuals. If not available, then next preferable would be validated measures from studies on hereditary cancer, followed by breast cancer. Suitable measures also should include the assessment of barriers and facilitators at multiple time points since there are multiple times when decision-making about genetic counseling and genetic testing may be considered. There were some limitations in the ability to do some of the analyses for this study related to the initial study having been developed using a different conceptual framework. Some concepts of interest for this study were not part of the initial study. The relationship of stigma, emotions such as relief and fear, and locus of control (the extent to which one believes she has control over events and outcomes) with use of counseling might be interesting to explore in future studies. Furthermore, the use of conditional-type questions should be avoided if possible in order to maximize available data from each participant.

The magnitude of the work to be done is clear. The urgency is even more pronounced in light of calls by revolutionaries in the field such as Mary Claire King (King et al., 2014) for population-based screening. The findings of this study highlight the potential for existing disparities in health outcomes to worsen in the context of lack of understanding about risk and risk management related to a heritable cancer-predisposing mutation. Fortunately, there already exists several individuals and groups interested in identifying barriers to use of cancer genetics services for mutations in the *BRCA1* and *BRCA2* genes, specifically. However, the limitations of existing knowledge need to be addressed in order for progress to occur. Nursing could be playing a larger

role in research in this context. Nurses care for individuals with cancers associated with *BRCA* mutations at the bedside, in the clinics, and in the community, as bedside nurses or advanced practice nurses with certifications in Advanced Genetics. Nurses can play a key role in research as well as in the translation of research into clinical practice. There is great potential for reducing burden from cancer and great opportunities for turning potential into reality. Nursing's holistic approach, with its focus on individuals, families, and societies, is a natural fit for making this potential become reality.