Genetic testing for breast and ovarian cancer has been publicly available since the mid-1990 discovery of two breast/ovarian cancer susceptibility genes named BRCA1 and BRCA2. Although many professionals say that genetic testing may be the best available preventative medicine breakthrough, controversy abounds over whether the medical benefits of BRCA1/2 mutation testing outweigh the psychological and financial costs. This study uses three models to analyze 104 women’s responses to a self-designed questionnaire: a logit regression model, an ordered probit regression model, and a cost effectiveness model. The regression models use questionnaire responses to learn how the benefits and costs of genetic testing affect a woman’s decision to get genetically tested for breast/ovarian cancer susceptibility at price points that correspond to no insurance, 20% coinsurance, and full insurance. The cost effectiveness model determines for whom BRCA1/2 mutation testing is cost effective by evaluating average and individual utilities for post-genetic test treatment strategies. The results of this study indicate that women’s level of risk and the price of the BRCA1/2 mutation test affect women’s responsiveness to testing. Overall, as price decreases, more women who should not be genetically tested (from a social cost effectiveness perspective) want to get tested. In addition, women’s preferences for post-genetic test treatment options matter in determining women’s cost effectiveness of testing. In fact, customizing cost effectiveness by individual preferences (in contrast to using average utilities for post-test surgeries) makes BRCA1/2 mutation testing cost effective for more women. By evaluating how well the normative cost effectiveness model and descriptive regression models match up, this study ultimately determines that genetic testing for breast/ovarian cancer susceptibility is being underdone when patients pay the full cost or 20% of
the cost of the genetic test itself, and overdone when the costs of the test are completely covered by insurance.

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Genetic testing for breast and/or ovarian cancer\footnote{Notation for rest of paper: breast/ovarian cancer.} has been publicly available since 1996, after the discovery of two breast/ovarian cancer susceptibility genes named BRCA1 (1994) and BRCA2 (1995)\footnote{BReast CAncer Gene I and BReast CAncer Gene 2.} Although the procedure of offering predictive DNA testing to individuals at high risk of developing specific diseases has been applied successfully to several inherited cancers, application of this procedure for breast/ovarian cancer susceptible individuals has engendered much controversy. The current debate focuses on the implications of a positive or negative BRCA1/2 result, the moral and psychological effect, and the financial barriers to genetic testing.

In the United States, more than 180,000 women are diagnosed annually with breast cancer and 26,000 women are diagnosed annually with ovarian cancer (National Cancer Institute, 1997, Pub No. 97-4252). Only 5-10\% of these breast/ovarian cancers are caused by inherited gene mutations, namely BRCA1 and BRCA2 (Claus, Risch, and Thompson, 1991). According to the American Cancer Society (\textit{Genetic Testing}, 2001), about 50-80\% of women with inherited BRCA1/2 mutations will develop breast cancer by the age of 70. In contrast, only 12-13\% of women in the general population will develop breast cancer by the age of 85. Women with BRCA1/2 mutations also have an increased risk of developing ovarian cancer. Whereas 20-40\% of women with BRCA1/2 mutations will develop ovarian cancer, only 1-2\% of women in the general population will develop ovarian cancer over the course of their lifetime. Having a BRCA1/2 mutation also increases a woman’s risk of developing several other cancers. For many women, however, the value of the BRCA1/2 mutation test remains ambiguous.
Knowing about a BRCA1/2 mutation allows a woman to know that she is at high risk of developing breast/ovarian cancer. She, in turn, has the opportunity to make lifestyle choices, share information with her family, contribute to research, and make decisions about preventative treatments. Preventative treatment options for BRCA1/2 mutation carriers include: early and frequent breast exams, mammography and MRI screenings, oral contraception use, chemoprevention, pelvic ultrasound, pregnancy, and prophylactic surgeries (namely, removal of breasts or ovaries). None of these preventative measures, however, reduces a woman’s chance of getting breast/ovarian cancer completely. Therefore, knowing that one is at high risk of developing a fatal disease may have serious psychological repercussions. Some researchers (Devilee, 1999, and Kodish et al., 1998) argue that not having an effective strategy to treat BRCA1/2 mutation carriers only augments the psychological, social, and financial burden of a mutation carrier. Thus, until medical tests and therapies are designed to provide total prevention or cure, the cons of receiving a positive BRCA1/2 mutation result might outweigh the pros of knowing the genetic test outcome.

The financial burden of the BRCA1/2 genetic test might also deter high risk women (those with a strong familial history of breast/ovarian cancer) from getting genetically tested. Myriad Genetics, Inc is a biopharmaceutical company that focuses on discovering and commercializing genes involved in cancer, cardiovascular disease and central nervous system disorders. Myriad is currently the only company that provides breast/ovarian cancer susceptibility testing, called BRACAnalysis®. For a complete analysis of BRCA1/2 (only necessary for individuals for whom their familial mutation has not yet been identified), the genetic test costs $2,760. The cost of the genetic test, though, is just one of the financial pressures a person faces upon pursuing BRCA1/2 mutation testing.
When a physician believes a woman is at high risk of carrying a BRCA1/2 mutation, he/she often advocates that their patient visit a genetic counselor. Genetic Counselors are Masters’-degree trained professionals in Clinical Genetics. The philosophy of genetic counseling has typically been to present information in an unbiased or neutral fashion in order to allow the potential genetic testing participant to make his/her own decision about genetic testing. Benefits, risks, costs, and limitations of testing are discussed. Depending on the genetic counselor and the clinic to which he/she attends, a woman may be advised to have several sessions with the genetic counselor before undergoing genetic testing. Multiple genetic counseling sessions may cost an individual hundreds of dollars. Moreover, many women undergoing genetic testing for breast/ovarian cancer prefer paying for the counseling sessions and the genetic test out-of-pocket (instead of asking their health insurance company to cover the expenses) in order to avoid potential genetic discrimination.

The fear that genetic testing will engender genetic discrimination in the workplace and insurance markets, has received much publicity. Most researchers believe that public fear of genetic discrimination is unwarranted, for there have been several policy proposals designed to address the potential genetic discrimination problem. Nonetheless, even though approximately 40 states have enacted anti-genetic discrimination legislation, many people are unaware of these laws. As a result, many women facing genetic testing still believe that genetic discrimination may limit their choice of insurance companies, increase their premiums, or decrease the amount of their coverage.

Much research has addressed the efficacy, psychological repercussions, and economic implications of the BRCA1/2 genetic test and its post-test treatment options. Nonetheless, insufficient research has been conducted on several BRCA1/2-related issues. First, few studies
attempt a decision analysis that quantifies the factors that influence a woman’s decision to undergo genetic testing for breast/ovarian cancer susceptibility. Second, no study (that I am aware of) has yet addressed the issue of moral hazard with respect to BRCA1/2 mutation testing. In other words, how many more women want to get genetically tested as the price of the test decreases due to insurance? Lastly, no quantitative analysis has focused on whether or not regulators of the BRCA1/2 mutation test are over-testing or under-testing high risk women. This study tackles all three of these information gaps by using three models to analyze 104 women’s responses to a self-designed questionnaire: a logit regression model, an ordered probit regression model, and a cost effectiveness model.

This study uses the Sanders et al.’s model to evaluate the cost effectiveness of screening for a BRCA1/2 mutation in different groups of women. In Sanders et al.’s model, cost effectiveness is determined by how much a woman values the post-genetic testing treatment options after accounting for the possible decreases in quality-of-life engendered by such treatments. Questionnaire responses are used to determine women’s patient-specific variables (i.e. which sample a woman belongs to—general population, Ashkenazi Jewish, or high familial risk-- and her disutility of mastectomy and oophorectomy) and, in turn, to determine for whom the BRCA1/2 genetic test is cost effective. The cost effectiveness model determines for whom BRCA1/2 mutation testing is cost effective by evaluating women’s average and individual utilities for BRCA1/2 mutation treatment strategies.

According to Sanders et al., women should only be tested if they think that there is some value to finding out that they are positive. For example, if a high risk woman highly values mastectomy as a preventative treatment option (meaning: she believes that this invasive surgery will significantly reduce her risk of getting breast/ovarian cancer without decreasing her quality-
of-life significantly), then getting genetically tested for BRCA1/2 may be worthwhile (or cost effective) for her. In other words, the cost effectiveness model determines which women “should” be genetically tested, from a social perspective. Nonetheless, I am ultimately interested in seeing if there is a mismatch between a rational economic determination of who should be tested for BRCA1/2 and an individual’s personal determination.

There are some women who might refuse genetic testing, but for whom genetic testing is beneficial (or cost effective). The regression models use questionnaire responses in order to calculate a woman’s probability of undergoing BRCA1/2 mutation testing at various price points, which correspond to no insurance, 20% coinsurance, and full insurance. By evaluating how well the normative cost effectiveness model and descriptive regression models match up, I am able to determine the optimal insurance coverage for BRCA1/2 mutation testing (based on a cost effective standard), and whether or not genetic testing for breast/ovarian cancer susceptibility is currently being overdone or underdone.

**Literature Review**

*Genetic Testing for a BRCA1/2 Mutation: Who’s At Risk?*

Genetic testing is conducted to see if a person has a certain gene change (mutation) known to increase his/her risk of developing a specific condition or disease (such as breast or ovarian cancer). Predictive gene testing is used to identify people who are at high risk of getting a disease before any symptoms appear. Testing for a BRCA1/2 mutation in a woman whose mother and sister had breast cancer is an example of predictive testing. Predictive gene testing is available for high risk people who are at least 18 years-old. Once a woman has signed an
informed consent form, blood or tissue samples are drawn, and specific laboratory tests are done to look at the gene(s) of interest.

Testing positive for a BRCA1/2 mutation means a woman has a higher probability of eventually having breast and ovarian cancer. Breast cancer is currently the leading type of non-skin cancer among women, affecting 1-in-8 women, or 12-13%, during their lifetime. Risk factors in developing breast cancer include: a personal history of breast abnormalities, age, age at menarche, age at first live birth, age at menopause, breast cancer among first-degree relatives, number of breast biopsies, race, Ashkenazi Jewish descent, density of breast tissue, use of birth control pills or hormone replacement therapy, a high-fat diet, alcohol, radiation exposure, and environmental pollutants (National Cancer Institute, 1998). Ovarian cancer currently afflicts 1-in-70 women, or 1-2% (National Cancer Institute: Cancer.gov, 2000). Risk factors in developing ovarian cancer include: history of ovarian cancer in immediate family members, age, not giving birth, a personal history of breast cancer, race, Ashkenazi Jewish descent, infertility drug use, and a high fat diet (Johns Hopkins Pathology, 2001). It is important to realize, however, that a person who does not fit into any of the risk factor categories mentioned above is still at risk of getting breast and ovarian cancer.

Risk factors for having a BRCA1/2 mutation differ somewhat from the risk factors for getting breast/ovarian cancer. Hereditary breast/ovarian cancer only accounts for 5-10% of total breast/ovarian cancers, which means that only 1-in-800 women from the general population have a BRCA1/2 mutation (Milunsky, 2001). The best predictor of a BRCA1/2 mutation is a strong family history of the disease, especially when coupled with Ashkenazi Jewish descent. A family history of breast/ovarian cancer is defined by the National Cancer Institute (Cancer.gov, 2000) as having family members who: (1) are affected with both breast and ovarian cancer, (2) have two
or more primary breast or ovarian cancers, or (3) got breast cancer at an early age. Nonetheless, having multiple first-degree relatives with breast/ovarian cancer is often the strongest (and simplest) indicator that a familial BRCA1/2 mutation might exist. For example, having one first-degree relative (mother, sister, daughter) with breast cancer approximately doubles a woman’s risk of having a genetic mutation, and having two affected first-degree relatives increases a woman’s risk five-fold (American Cancer Society, Genetic Testing, 2001). Easton, Bishop, Ford, and Crockford (1993) estimate that 45% of families with a familial history of breast/ovarian cancer have the BRCA1 mutation. In 1997, Gayther et al. predicted that 35% of breast cancer found in such high risk families is accounted for by BRCA2. Therefore, about 1-in-3 women with a familial risk of breast/ovarian cancer have the BRCA1/2 gene. Although family history and a BRCA1/2 mutation are correlated, a BRCA1/2 mutation is a stronger predictor of breast/ovarian cancer susceptibility than a family history of breast/ovarian cancer.

Being of Ashkenazi Jewish descent is also a strong predictor of a BRCA1/2 mutation carrier. About 1-in-38 Ashkenazi Jewish women, or 3%, have one of three recurrent mutations in BRCA1/2 (Milunsky, 2001). An Ashkenazi Jewish woman with a close relative affected with breast/ovarian cancer is considered to be at higher risk than a non-Ashkenazi Jewish woman with an affected relative (Egan et al., 1996, and Steinberg et al., 1998). Nonetheless, family history and Ashkenazi Jewish descent still do not perfectly predict BRCA1/2 mutation carriers.

Several models have been developed to evaluate breast/ovarian cancer susceptibility risk; the three most commonly-used models include: the Claus Model, Gail Model, and BRCAPRO. The Claus Model uses data from the Cancer and Steroid Hormone Study conducted by the Centers for Disease Control. The Claus Model determines a woman’s breast cancer susceptibility by analyzing how many of her first or second-degree relatives have had breast
cancer, and the ages at which they were diagnosed. The main disadvantages of the Claus Model are that it can only accommodate up to two affected family members, and does not incorporate other risk factors commonly associated with breast cancer. The Claus Model is, therefore, not suitable for women who belong to very high-risk families containing three or more first/second-degree relatives with breast cancer. (Pergament and Fiddler, 2001)

The Gail Model uses data from the Breast Cancer Detection and Demonstration Project and differs from the Claus Model in that it incorporates four non-genetic measures of breast cancer risk (current age, age at menarche, number of breast biopsies, and age at first live birth) in addition to including the number of first-degree relatives with breast cancer in a family. The main disadvantages of the Gail Model include: the data is based on women undergoing mammography, and affected relatives’ age at diagnosis are not taken into account. Therefore, the Gail Model is also not appropriate for women with a strong familial history of breast cancer. (Pergament and Fiddler, 2001)

In contrast to the Claus and Gail Models, BRCAPRO is well-suited for high-risk people. BRCAPRO is a computer program that assesses an individual’s risk of carrying a BRCA1/2 mutation. Unlike the Claus and Gail Models, BRCAPRO does not assess breast/ovarian cancer risk. The main advantages of BRCAPRO are that it incorporates a person’s family pedigree, age at breast/ovarian cancer diagnosis, presence of bilateral breast cancer, male breast cancer, and Ashkenazi heritage in estimating the probability of carrying a BRCA1/2 mutation. (Berry et al., 1997). While BRCAPRO looks promising, this model has yet to be validated by the medical community. In addition, just because a woman has a strong likelihood of carrying a BRCA1/2 mutation, does not necessarily mean that she should be genetically tested.
**BRCA1 and BRCA2**

In order to understand how BRCA1/2 mutations increase a woman’s risk of getting breast/ovarian cancer, one must first understand the cell process of tumorigenesis. There are currently over 100 different types of cancer. A cell becomes cancerous after several separate gene changes. These gene changes result in uncontrolled growth, allowing a tumor to form. Tumors can be benign (non-cancerous) or malignant (cancerous). Malignant tumors are the ones that can invade and destroy neighboring tissues, spread to other parts of the body, and lead to death. (U.S. Department of Health and Human Services, 1999).

BRCA1/2 are tumor suppressor genes, which slow down cell growth and repair DNA mistakes. Breast cells that lack BRCA1/2 accumulate DNA abnormalities. Such abnormalities can disrupt the health cell cycle and, in turn, cause a tumor. (American Cancer Society, 2001, *Oncogenes and Tumor Suppressor Genes*). For a woman in the general population, there is only about a one-in-a-million chance that a specific tumor suppressor gene will be mutated in a given cell. Nonetheless, tumorigenesis requires that both genes in a cell be affected. The chance of both genes in a given cell becoming affected is approximately one-in-a-billion. So, if a woman inherits a BRCA1/2 mutation, one of her two genes already does not function properly. Thus, her likelihood of getting breast/ovarian cancer increases by one million, because her second (and only remaining) gene is one million times more likely to completely lose functionality. (Weinberg, 1998)

Although genetic testing holds promise, many ambiguities and uncertainties remain. Clinical BRCA1/2 mutation testing is highly accurate for detecting DNA sequence variation. It does not, however, detect all mutations that affect BRCA1/2 function and may miss 10-20% of large DNA rearrangements or non-coding mutations. Furthermore, many sequence variations in
these large genes have yet to be defined as to whether they are disease-related or benign variations. BRCA1/2 mutation testing can thus result in uninterpretable results in 10-15% of cases. More recent data suggest that BRCA1/2 mutations only account for about 84% (at most) of hereditary breast cancer cases, and about 70% of hereditary ovarian cancer cases (Milunsky, 2001). Therefore, a high risk person who tests negative for a BRCA1/2 mutation may, in fact, be positive for a different genetic mutation not yet discovered.

For those who test positive for a BRCA1/2 mutation, their risk of developing breast and ovarian cancer increases substantially. Women with a BRCA1/2 mutation have a cumulative lifetime risk of breast cancer (up to the age of 70 years) of 55 to 85 percent, and of ovarian cancer of 15 to 65 percent” (Ford et al., 1998). In addition, BRCA1/2 mutation carriers have an increased risk of getting prostatic, pancreatic, gall bladder, bile duct and stomach cancers, and melanoma (Breast Cancer Linkage Consortium, 1999). Unlike many other genetic diseases, not all women who inherit a BRCA1/2 mutation will for sure develop cancer. It is therefore important that a woman contemplating BRCA1/2 mutation testing understand, prior to testing, exactly what the test can and cannot do.

The Psychological Impact

The BRCA1/2 mutation test can only tell a person what might happen, and not what will happen. Undergoing BRCA1/2 mutation testing could therefore have severe direct and indirect psychological impacts on a woman. The direct psychological effects stem from having to cope with the genetic test result itself. Learning that one has or might develop a serious disease is frightening (especially if family members have already died from the disease in question). On the other hand, learning that one does not have an inherited familial mutation is relieving (a
negative BRCA1/2 mutation result indicates that a woman only has a 1-in-8 lifetime chance of getting breast cancer--the same chance a woman from the general population has). The indirect psychological effects originate from having to cope with family and friends’ reactions to the genetic test result. While some women might experience relief from the ambiguity of not knowing if they have inherited a predisposed gene mutation and feel more confident proceeding with decisions to manage their risk once their status is clarified, such decisions might affect relationships with a spouse, siblings, children, or other family members. Furthermore, testing negative for a BRCA1/2 mutation may engender “survivor’s guilt” if a woman’s siblings or other relatives test positive. Although a certain degree of stress may be normal, too much can be incapacitating. Thus, as more women opt for genetic testing, it is increasingly important that medical services provide pre- and post-test counseling, assure long-term emotional support, and help improve communication and family dynamics.

Shaw, Abrams, and Marteau (1999) provide a literature review on the direct psychological (emotional, cognitive, and behavioral) impact of predicting people’s risk of various illnesses. Although the authors examined 54 studies that ranged in design (experimental, prospective, longitudinal, and cross sectional) and disease (risk of cardiovascular disease, AIDS, cancer, Huntington’s disease, diabetes, spinocerebellar ataxia, and osteoporosis), the overall conclusions of the studies were similar. Shaw, Abrams, and Marteau’s (1999) results indicate that a positive genetic test result is associated with increased, short-term (four weeks after testing) psychological distress, anxiety, and depression, and no significant long term (more than one month after testing) psychological effects. The results further show that the manner in which genetic test results are revealed to a patient, and the availability of post-test emotional support, mitigate post-test mood disturbances. Receipt of a negative result did not engender adverse
psychological effects.) Shaw, Abrams, and Marteau’s (1999) findings can be generalized to potential BRCA1/2 mutation carriers because, as the authors themselves argue:

While it seems likely that responses will be shaped by the nature of the condition for which an individual has undergone a risk assessment, there are good grounds for believing first, that individuals’ responses reflect a sense of threat that transcends disease type, and second that disease type, particularly clinical severity, is often a poor predictor of psychological responses. (p. 1579)

Although Shaw, Abrams, and Marteau (1999) only show short-term psychological duress, the severity and length of post-genetic testing stress might vary woman-to-woman, for genetic testing affects more people than just the one getting tested.

BRCA1/2 mutation testing is not an independent process; when it comes to getting genetically tested, the potential carrier is usually not the only one in a family experiencing anxiety. For example, genetic testing is most informative if a mutation can be identified in an affected relative. By testing an affected relative first, experts can (hopefully) locate the disease-causing mutation; in turn, they can determine if definitive testing is available to unaffected. Genetic testing currently has an 80% sensitivity rate. This means that 20% of the time a woman tests negative for BRCA1/2, she is, in fact, positive. If, however, the "family" mutation is identifiable (meaning: a family member has already tested positive for a BCA1/2 mutation), the test's sensitivity increases to 99% (France et al., 1999). Furthermore, Croyle, Achilles and Lerman (1997) suggest that women already diagnosed with cancer actually cope better with genetic information (since such women have already dealt with their psychological distress upon receiving their initial cancer diagnosis) than healthy women at high risk. Regardless, genetically testing of the already-diagnosed-with-breast-cancer woman may be just as stressful for the “high-risk, worried-well woman” (France et al., 1999). For example, if a mother (who already has
breast cancer) gets genetically tested for a BRCA1/2 mutation, the daughter may experience just as much anxiety during the waiting period for the test results. If the mother tests positive, the daughter will need to be genetically tested herself; if the mother tests negative, the daughter will not need to be tested, but still might be at high risk for getting cancer. The situation is further complicated if the mother has several children, both male and female.

Smith et al. (1999) address these indirect, short-term psychological effects of BRCA1/2 mutation testing by genetically testing 87 males and 125 females, and analyzing their psychological stress in a follow-up interview 1-2 weeks after receipt of test results. Their findings were similar to those of Shaw, Abrams and Marteau (1999) in that BRCA1/2 mutation-positive women experienced more test-related distress than BRCA1/2 mutation-negative women. On the other hand, Smith et al. (1999) showed that test-related distress is even higher when all siblings tested positive or when siblings had mixed (positive and negative) test results. Smith et al. (1999) explain the large, indirect sibship impact on psychological grief by suggesting that women testing positive might feel isolated from and envious of non-carrier family members. Another rationale for post-genetic test psychological disturbance is that genetic testing forces patients to make life-altering decisions based on estimates of risk, not diagnosis. Since many women simply do not understand statistics, they might interpret their high risk status incorrectly by considering their positive BRCA1/2 mutation result as a breast/ovarian cancer diagnosis. As Julie Goldstein (2001), a BRCA1 mutation carrier, says about her life as a genetically predisposed woman living in the margins between the sick and well:

I do not have cancer. I am a healthy woman... Yet two weeks after learning my status I had my own oncologist and breast surgeon, underwent my first mammogram and breast magnetic resonance scan, and had my first biannual transvaginal ultrasound. Between the sick and the well is the uncertain, and that is where I now found myself. (p. 92)
Therefore, as Devilee (1999), Kodish et al. (1998), and Fasouliotis and Schenker (2000) suggest, "the potential risks of psychological and emotional harm to the patient, lack of long-term data on appropriate management plans, and genetic discrimination . . . [due to] predictive testing for hereditary cancer syndromes is [possibly] doing more harm than good” (Matloff et al., 2000, p. 2485).

The Financial Burden and Genetic Discrimination

Genetic testing for breast cancer has both psychological and economic costs. The current charge for a complete analysis of both BRCA1/2 genes is around $2,600. Nonetheless, with three U.S. patents and eight international patents, Myriad Genetics has the monopolistic power to control consumer prices. In fact, the BRACAnalysis® test has achieved an average growth rate of greater than 25% quarter-to-quarter since its introduction in late 1996 and contributed significantly to the 103% growth in Myriad's revenue in 2001 (Myriad Genetics, 2001). High risk women considering BRACAnalysis®, however, face more than the $2,600 cost of the genetic test itself; such women face potential insurance and employment discrimination.

Several legal efforts have been made to diminish public fear of genetic discrimination. Recent federal (Health Insurance Portability and Accountability Act, 1996) and state legislation now make it illegal to discriminate (for purposes of employment and health insurance) against presymptomatic people. The Americans with Disabilities Act (ADA) currently offers some employment protection, and the Equal Employment Opportunity Commission (EEOC) expanded the definition of "disabled" to include individuals who carry genes that put them at higher risk for genetic disorders (National Action Plan on Breast Cancer, 1997, Fact Sheet). Nonetheless,
although 42 states have enacted laws prohibiting the health insurance industry from using genetic test results, 5 states have minimal genetic discrimination protections in health insurance, 21 states have legislative protections against genetic discrimination in employment, 8 states have some level of legislative protections against genetic discrimination in disability insurance, and 7 states have limited legislative protections against genetic discrimination in life insurance (Genetic Discrimination Laws, 2000). None of these laws, however, have been tested in the courts. So, concerns about potential genetic discrimination persist.

In spite of the insufficient laws protecting individuals against genetic discrimination, Wingrove et al. (1996) believe that consumers overestimate the incidence of genetic discrimination. Strohmenger and Wambach (2000) go even further by suggesting that sharing genetic test results with insurance companies would mitigate asymmetric information, and thus might be welfare improving. Perhaps the most important study that has addressed the genetic discrimination issue is the one by Hall and Rich (2000). Hall and Rich (2000) conducted a comparative case-study across seven states that provided protective legislation against genetic discrimination and found no substantial evidence of genetic discrimination before or after legislation was enacted. Hall and Rich (2000) also conducted a market test by creating a fictitious employer with a BRCA1/2 mutation-positive patient and tested how difficult it was for the fictitious group to acquire health insurance. The authors used interviews with regulators, insurance agents, insurees, and genetic counselors to supplement their market study. The shortcomings of the Hall and Rich (2000) study consist of: it only addressed genetic discrimination in the health insurance market, the market test only addressed potential genetic discrimination for a small-group employer (not for a single person desiring health insurance), and interviews with health insurance personnel about a hypothetical woman with a BRCA1/2
mutation may not represent the actual occurrence of discrimination. Lastly, the authors concede that although their study finds that genetic discrimination is not currently a substantial issue, evidence suggests that genetic discrimination might become more of an issue in the future.

Several experts have hypothesized about the reasons for and against genetic discrimination. Stephenson (1999) suggests that the absence of genetic discrimination in the health insurance industry is due to the high turn-over rate in health insurance policies; since people only stay in a health plan for a few years, chances of developing a disease during that period are slim. On the other hand, Simon (2000) argues that genetic discrimination does exist, but the evidence is only anecdotal (which leads some researchers to think that genetic discrimination is not as large of an issue as people have made it out to be). Simon (2000) argues the difficulty in providing hard evidence of genetic discrimination:

Complicating matters is the problem of distinguishing between two different, but related, potential arenas for discrimination—health insurance and employment. Also, documenting cases of genetic discrimination is problematic because it’s difficult to prove and many people are afraid to come forward” (1).

Whether or not it should be, genetic discrimination is a realized fear.

Fear of genetic discrimination has led some women to pay for the genetic test out-of-pocket (with their own money) or use an alias when undergoing genetic testing so that their health/life insurance company will not have access to their genetic test results. Nonetheless, women undergoing genetic testing might not be able to keep their genetic test results private. For example, imagine a woman pays for the BRCA1/2 mutation test out-of-pocket or uses an alias when undergoing testing. Four weeks later she finds out that she tested positive. She meets with an oncologist and a breast surgeon who suggest prophylactic surgery. This presymptomatic, healthy woman cannot afford to pay for the suggested surgery, yet her health insurance company
refuses to cover the “unnecessary” treatment costs. This woman, or her physicians, may have to release her genetic susceptibility information in order to reason with her health insurance company. Thus, a woman’s genetic information may not remain confidential after all. In short, proper protective legislation needs to be enacted so that fear of genetic discrimination will not deter individuals from getting genetically tested.

Factors That Affect the BRCA1/2 Mutation Testing Decision:

Implications for Genetic Counseling

Many studies have explored the factors that influence a woman’s decision to get genetic testing for breast/ovarian cancer susceptibility. Phillips et al. (2000) used a questionnaire to address factors that influenced Canadian Jewish women’s decision to get BRCA1/2 mutation tested. The authors found the largest motivators for testing to be: a desire to contribute to research, potential benefit to other family members, curiosity, and the potential relief if found not to be a carrier. The largest setbacks included: fear of insurance discrimination, confidentiality and accuracy concerns, interpretability of test results, and potential impact on marriage prospects. Another Canadian study was conducted by Surh et al (1999), who used a questionnaire to examine the psychological and social determinants for Canadian women deciding whether or not to get genetic testing for breast/ovarian cancer susceptibility. Surh et al. (1999) found a woman more likely to want to be tested if: she had breast cancer, had greater (fewer) perceived benefits (costs) of testing, and was more concerned about family members developing breast cancer.

In the United States, Tessaro et al. (1997) used a focus group setting with breast cancer patients and non-breast cancer patients who had affected relatives to better understand BRCA1/2 mutation testing decisions. Tessaro et al. (1997) found the main testing advantage to be the
ability to use information to make lifestyle choices and medical decisions about treatment. The main disadvantages included: concern about confidentiality, insurance coverage, controversial post-test treatment options, and post-test psychological stress. Similarly, Lerman et al. (1996) used interviews to determine that uptake of BRCA1/2 mutation testing is higher among women of a higher socioeconomic status (especially those with health insurance), those with more relatives affected with breast cancer, and those who are more knowledgeable about the benefits and costs of testing. In 1999, Lerman et al. also discovered that racial differences play a role in genetic testing uptake and post-test psychological distress. In contrast, Press et al. (2001) used interviews to find that genetic testing interest did not vary by ethnicity, level of education, or family history, but instead was affected by a woman’s feeling of vulnerability to breast cancer, her knowledge about genetic testing susceptibility, and how much she values the test information. Perhaps more interesting, Press et al. (2001) concluded that women were most interested in a genetic test that did not exist: high positive predictive value followed by effective, noninvasive, preventative therapy. In short, many studies have examined BRCA1/2 mutation testing decision-making, but the conclusions have differed and all the studies have been descriptive in nature. Therefore, as genetic testing for breast cancer becomes more available to healthy women at high risk, health professionals increasingly need to play a larger role in women’s genetic testing decision-making process.

The purpose of genetic counseling is to advise people on extremely controversial, personal, and life-changing decisions pertaining to genetic testing for a given disease. The typical genetic testing procedure, called 'non-directive,' is as follows. First, a woman receives a plethora of information. Second, she is guided into making a decision. The physician's goal in this approach is objectivity, for Wroe and Salkovskis (1999) illustrate that a potential BRCA1/2
participant may be highly influenced by (1) providing relatively positive versus relatively negative information, and (2) focusing on positive or negative issues, on anticipated choices and decisions associated with genetic testing for breast cancer. (Wroe and Salkovskis, 1999)

Wroe and Salkovskis (1999) interviewed 67 women passing by an American shop in Oxford. The women were randomly assigned to three study groups that manipulated information given to the women prior to genetic testing: the positive group, the negative group, and the control group. The positive and negative groups were provided information on genetic results, prevention, and early detection. The negative group was also told the limitations of genetic testing and their remaining options. The control group received no further information on breast cancer. After their respective session, the participants rated their likelihood of undergoing genetic testing.

The results show that information and focus-based manipulation significantly affected the anticipated likelihood of being tested, on anxiety levels, and on ratings of perceived severity. The positive group was more likely to undergo testing than the negative group, and the positive group showed significantly higher anxiety levels than the negative group. Wroe and Salkovskis (1999) account for this surprising result by hypothesizing that women in the negative group perhaps cope with negative issues (i.e., test limitations) by downsizing the severity of their cancer risk. Members of the positive group, however, are more likely to concentrate on their personal responsibility to preventing cancer that, in turn, induces an increased level of anxiety.

In effect, Wroe and Salkovskis’ (1999) study has large implications for pre-test counseling. Nonetheless, genetic counselors are in short supply. Approximately 12 million people in the United States need genetic counseling, but there are only about 1000-1500 trained counselors. Furthermore, only a small percent of these counselors specialize in cancer (Parens,
1997). Lastly, some evidence suggests that genetic testing may be under-utilized due to lack of physician knowledge about criteria and services for BRCA1/2 mutation testing or lack of communication between physicians and genetic counselors. According to the results from a survey completed by 135 oncologists and conducted by Culver et al. (2001), 79% of oncologists had discussed genetic testing for breast/ovarian cancer susceptibility with their patients, and 76% said they prefer potential genetic testing participants to see a genetic counselor. Nonetheless, only 29% of oncologists have made outside referrals to other medical departments or genetic counselors, or are appropriately equipped to offer BRCA1/2 mutation testing themselves. As more women undergo genetic testing for breast/ovarian cancer susceptibility, it is increasingly important to develop and offer services that help women make decisions about whether or not BRCA1/2 mutation testing is right for them.

**Testing Positive: What Now?**

Physicians and genetic counselors also play a large role in women’s decision-making process post-genetic testing. Once a woman has made the decision to undergo genetic testing for breast/ovarian cancer susceptibility and has received her test results, she has several treatment options. As Scheuer et al. (2002) showed, genetic counseling increased surveillance compliance and led to risk-reducing surgeries that, in turn, resulted in the detection of more early-stage tumors in BRCA1/2 carriers. In general, if a high risk woman tests negative for a BRCA1/2 mutation in a family with a defined mutation, she should continue following the age-specific guidelines for breast examinations and mammography screenings for women in the general population. If a high risk woman tests negative for a BRCA1/2 mutation when no familial mutation is defined or if a woman tests positive for a BRCA1/2 mutation her preventative
treatment options increase: risk avoidance, early and frequent breast exams, mammography and MRI screenings, use of oral contraceptives, chemoprevention, pelvic ultrasound, pregnancy, and prophylactic surgeries (complete removal of breasts and/or ovaries). None of these medical treatments, however, completely eliminate breast/ovarian cancer risk.

Some behaviors, such as smoking cessation, decreasing alcohol and caffeine consumption, and increasing exercise are examples of cancer risk avoidance measures. Unfortunately, effects of risk avoidance on BRCA1/2 mutation carriers are minimal. Thus, a healthy body based on good diet and exercise will not effectively prevent breast/ovarian cancer for a high risk woman.

A high risk woman is advised to self-examine her breasts every month (not during her menstrual cycle) and to receive a clinical-breast examination twice a year. Several new breast examination techniques have been explored, which have increased a woman’s likelihood of finding a lump in its early stages. Many genetic counseling clinics provide personal instruction on these new techniques. The goal of breast examinations is to catch breast cancer early in its development; the earlier breast cancer is discovered, the higher a woman’s likelihood of survival. The problem with using breast examination as a form of preventative treatment is that it is not very effective. By the time a woman can detect a lump with her hands, the lump might already be too large. Self-breast examinations can be unsuccessful if a woman is too self-conscious, nervous, or uninformed to discover a lump. Similarly, a physician might not be able to discover a lump as easily on large-breasted women.

Mammography is a good supplement to breast examinations. Most genetic counseling clinics recommend that BRCA1/2 mutation-positive women begin breast/ovarian cancer surveillance (breast examinations, mammography) ten years prior to the youngest first-degree
relative’s onset of breast/ovarian cancer or by age 25-30. The benefit of a mammogram is that the special x-ray can detect a mass before a person can feel a lump. The cons of mammography are that the test can still miss malignant tumors that are present, and can detect masses that turn out not to be malignant. Brekelmans et al. (2001) conducted a study on the effectiveness of surveillance (monthly breast self-examination, clinical breast examination, and yearly mammography) in BRCA1/2 mutation carriers and high risk women (women with a strong family history of breast/ovarian cancer). The highest breast cancer detection rates (33 per 1,000 person-years) were found in BRCA1/2 mutation carriers, but this group had a relatively unfavorable tumor stage at diagnosis and mean age at diagnosis was 40. Brekelmans et al. (2001) therefore advise that the screening methods used in their study might not effectively prevent breast cancer deaths among high risk women, especially women under age 40.

Since mammography is less effective in younger women with very dense breast tissue, magnetic resonance imaging (MRI) has recently been introduced as a complementary treatment to mammography in high risk women. According to preliminary results by Kuhl et al. (2000), the accuracy of MRI in detecting breast cancers in high-risk women is significantly higher than conventional screening detections. Although these results seem promising for BRCA1/2 mutation carriers, MRI still does not prevent a lump from occurring; it just potentially detects the mass at an earlier stage.

The impact of oral contraceptives on breast cancer has long been a source of controversy. The increased estrogen caused by oral contraceptives has long been considered to slightly increase breast cancer risk. Nonetheless, among BRCA1/2 mutation carriers, using oral contraceptives might decrease ovarian cancer risk more than they increase breast cancer risk (Narod et al., 1998). Nonetheless, Modan et al. (2001) found that, for Jewish women in Israel
with a BRCA1/2 mutation, each additional birth lowered a woman’s risk of getting ovarian cancer by 12%, whereas each additional year of oral contraceptive use only decreased ovarian cancer risk by 0.2%. Therefore, ambiguity remains over the effectiveness of oral contraceptives as a preventative treatment for BRCA1/2 mutation carriers.

Many women opt for chemoprevention as a preventative treatment measure. Although chemoprevention is more effective than surveillance (self/clinical breast-examinations, mammography, and MRI), it is not as effective as invasive surgery. The chemopreventative approach uses a 20-year-old pill named Tamoxifen. Tamoxifen combats breast cancer by interfering with estrogen activity, a female hormone that encourages growth of breast cancer cells. Nonetheless, the drug increases women's chances of developing four potentially life-threatening health problems: endometrial cancer (cancer of the lining of the uterus), deep vein thrombosis (blood clots in large veins), pulmonary embolism (blood clot in the lung), and stroke. (National Cancer Institute, 1998). According to King et al. (2001), Tamoxifen use beginning at age 35 reduced breast cancer incidence among healthy BRCA2 mutation carriers by 62%, but did not reduce breast cancer incidence among healthy BRCA1 mutation carriers. Nonetheless, the extremely small sample size raises questions about the generalizability of these study results: of eight patients with a BRCA1 mutation only 5 received Tamoxifen, and of eleven patients with BRCA2 mutations only three received Tamoxifen.

Screening for ovarian cancer is much more difficult than screening for breast cancer. Simple clinical examination of the ovaries (pelvic examination) does not identify early-stage ovarian cancers. Therefore, the Cancer Genetics Studies Consortium task force recommends that female BRCA1 mutation-carriers undergo pelvic ultrasound every 6-12 months, beginning at age 25-35. Nonetheless, data on the effects of pelvic ultrasound in screening women at high risk for
ovarian cancer susceptibility is still preliminary. In addition, some people believe that fertility decreases ovarian cancer risk. For women in the general population, each successive pregnancy after the first-born decreases ovarian cancer by 15%. Data is limited and inconsistent, however, on the effects of pregnancy on the risk of getting ovarian cancer in women with an inherited predisposition. (National Cancer Institute, Cancer.gov, 2000).

Prophylactic surgeries reduce a high risk woman's cancer risk the most. Prophylactic mastectomy (complete removal of breasts) is associated with at least a 90% decrease in breast cancer risk for BRCA1/2 carriers and women with a strong familial history of breast/ovarian cancer (Hartmann et al., 2001). Following mastectomy, however, women may experience: short-term pain in the area of operation, risk of infection, poor wound healing, bleeding, a reaction to the anesthesia used in surgery, a weight imbalance (especially crucial for women with large breasts), stiffness of upper-body limbs, and numbness and tingling in the chest and underarm (National Institutes of Health, 1998).

Observational studies suggest that prophylactic oophorectomy (complete removal of ovaries) is associated with at least a 50% decrease in ovarian cancer (Chlebowski, 2000) and a 50% decrease in breast cancer among BRCA1/2 mutation carriers (Eisen et al., 2000). The main side effects of getting an oophorectomy include: premature menopause (which is associated with an increased risk of osteoporosis and cardiovascular disease), hot flashes, vaginal dryness, sexual dysfunction, and sleep disturbances. Although hormone replacement therapy (HRT) mitigates these side effects, HRT might increase breast cancer risk (Rebbeck et al., 1999).

One of the benefits to genetic testing is that a woman who knows she is positive can make behavioral changes and take several preventative measures. According to Marteau and Lerman (2001), the largest motivator for getting genetically tested lies in women’s desire to
increase their use of screening and preventative surgeries. Nonetheless, in contrast to Scheuer et al. (2002), Marteau and Lerman (2001) found no significant changes in women’s screening behavior post-genetic testing. Actual uptake of treatment strategies may differ from women’s initial interest in such strategies because many times the efficacy of these treatments remains ambiguous for high risk women or BRCA1/2 mutation carriers, or the side effects decrease quality-of-life too substantially.

Although genetic testing holds promise, lack of long-term data weighing all the benefits and costs make its use controversial today. Matloff et al. (2000) therefore attempted to offer the general opinion of leaders in the genetic field regarding genetic testing for breast/ovarian cancer. Matloff et al. (2000) examined the preferences of 296 active members of the National Society of Genetic Counselors (NSGC) Special Interest Group (SIG). NSGC Cancer-SIG is the largest group of genetic counselors in the world. By distributing questionnaires, respondents were asked to answer a series of questions as if they experienced a 50% risk of carrying BRCA1/2. With a 55% overall response rate, and a 93.3% female response rate, the study found that 85% of counselors would undergo genetic testing. Upon receiving a positive result at age 35, 57% would pursue pre- and posttest psychological support, 24.5% indicated that they would pursue a bilateral mastectomy, 67.7% would pursue an oophorectomy, 23.9% of counselors would charge their insurance company for the genetic test, 25% would use an alias when testing, 97.5% would share test results with family, 81.5% would share test results with physicians, 58.6% would share information with friends, and only 30.4% would share information with colleagues. In spite of the risks associated with genetic testing, the majority of professionals believe that the benefits outweigh the costs and would get tested if they were at high risk of having a BRCA1/2 mutation.
These results clearly show the magnitude of physician concern over emotional stability, genetic discrimination, and post-test treatment options.

**Methodology**

*Overall Purpose of Study*

The objective of this study was to examine the factors that influence women’s decision to undergo BRCA1/2 mutation testing and to compare women’s choices with a normative standard.

*Study Hypotheses*

1.) Factors that positively-influence a woman’s decision to undergo breast/ovarian cancer susceptibility testing include: high level of education, high risk (perceived and actual) of getting breast/ovarian cancer, strong preferences for post-test invasive surgery, high value of post-test information, strong emotional support network, and low fear of genetic discrimination.

2.) High risk women and women with strong post-test treatment preferences are willing to pay more for the BRCA1/2 mutation test than lower risk women and women with weaker preferences for invasive surgery.

3.) Genetic testing for a BRCA1/2 mutation is under-testing women for whom testing is cost effective and over-testing women for whom testing is not cost effective.

4.) Using patient-specific utilities (instead of average utilities) to calculate the cost effectiveness of BRCA1/2 mutation testing yields more women for whom testing is cost effective.
5. Regarding the BRCA1/2 mutation test, moral hazard decreases as co-payment increases. Moral hazard will be smallest among high risk women and women with strong preferences for post-test treatment strategies.

Study Methods

For this study, I recruited 104 women of any race and ethnicity above the age of 18. I developed an informed consent form (Appendix I), an information pamphlet (Appendix II), and a questionnaire (Appendix III). The informed consent form provided input about the nature of the study. Information discussed in the informed consent included: sponsorship of the project, the benefits and risks of participating in the study, confidentiality protection, and human subject’s rights. The information pamphlet briefly explained the issues surrounding genetic testing for breast/ovarian cancer susceptibility. More specifically, the meaning of a positive/negative BRCA1/2 mutation result, the benefits/risks of BRCA1/2 mutation testing, and the psychological impact of BRCA1/2 mutation testing were relayed. Prior to completing the questionnaire, participants signed the informed consent form and read the information pamphlet. The questionnaire was primarily multiple-choice based and took about 10-15 minutes to complete. The questionnaire asked about women’s demographic characteristics, their personal and familial cancer history, their use of a BRCA1/2 mutation test result, their fear of genetic discrimination, their post-genetic test treatment preferences, and their willingness-to-pay for the genetic test. Participants did not receive any financial or pecuniary benefits from participating in this study.

Study procedures were approved by the Stanford University Institutional Review Board (IRB) on 12/21/01. Nonetheless, IRB approval for this study was especially difficult due to the
extremely sensitive subject of this study. This project was sponsored by a small Undergraduate Research Opportunity (URO) grant.

Study Subjects

Questionnaires were distributed at three locations: Stanford Hospital’s Gynecologic Oncology Clinic, Temple Beth Torah, and the Cancer Risk Assessment Clinic. Finding a temple that supported questionnaire distribution at their site proved especially difficult (Temple Beth Torah is located in Ventura, CA). To insure confidentiality, especially of high-risk women, Nicki Chun (a genetic counselor) distributed questionnaires to women at the Cancer Risk Assessment Clinic-Stanford Program for Applied Genetics and Rabbi Lisa Hochberg-Miller distributed surveys to women at Temple Beth Torah. Women at these two locations received a cover letter (Appendix IV) expaining the procedure for participating in the study and mailing the appropriate papers back to me. To recruit participants from Stanford Hospital’s Gynecologic Oncology Clinic, I personally approached women in the waiting room. Confidentiality was maintained regarding the identity of all study participants, their personal and medical information, and their answers to the questionnaire. In fact, participants only signed their names on the informed consent form. No coding was used to link informed consent forms to questionnaires, and both forms were stored in separate folders.

I recruited study participants based on Sanders et al.’s four classifications of risk: (1) women from the general population, (2) Ashkenazi Jewish women, (3) women from high-risk cancer families that had a family history of four cases of breast cancer, and (4) women from high-risk cancer families that included histories of one or two cases of ovarian cancer in addition to four cases of breast cancer. I therefore sought women for this study from three different
locations that increased the likelihood of finding women that fit into the respective Sanders et al. categories: (1) Stanford Hospital’s Gynecologic Oncology Clinic, (2) Temple Beth Torah, and (3) The Cancer Risk Assessment Clinic-Stanford Program for Applied Genetics.

Stanford Hospital’s Gynecologic Oncology Clinic mainly served as a source of women from the general population. Targeting a gynecology clinic provided me with women who were primarily at low risk of developing breast/ovarian cancer, were more informed of their personal and familial cancer history, and were more familiar with cancer terminology in general (whether or not they had cancer). 40 questionnaires were distributed at Stanford Hospital’s Gynecologic Oncology Clinic; 27 were completed.

I recruited Ashkenazi Jewish women at Temple Beth Torah, only after several unsuccessful attempts at distributing surveys at a temple in or near Palo Alto. Perhaps because I was raised in Ventura, Rabbi Lisa Hochberg-Miller of Temple Beth Torah proved to be the only Rabbi I contacted who was willing to personally distribute the questionnaire to congregants. 100 questionnaires were distributed at Temple Beth Torah; 58 were completed.

Targeting high risk women (women with a strong familial history of breast/ovarian cancer) was complicated by confidentiality laws that protect a woman’s genetic information, and the extremely small proportion of women who have a genetic predisposition for breast/ovarian cancer (only 5-10% of all breast/ovarian cancers are hereditary). The objective to obtain an adequate sample of high risk women was further complicated by the fact that the IRB would not allow me to distribute questionnaires to a woman’s clinic solely devoted to oncology patients, for fear that breast/ovarian cancer genetic information would cause too much psychologically distress for already affected women. I, thus, sought high risk women that visit genetic counselors at Stanford’s Cancer Risk Assessment Clinic. Most women (90%) that see a genetic counselor at
this clinic have been recommended to do so by their respective doctors. Therefore, most women that see a genetic counselor have already been singled out by the medical profession as having a higher risk (due to personal and familial cancer history) of developing breast/ovarian cancer. Nonetheless, it was still important to target women in a genetic counseling clinic even if women have not been referred by a physician. First, genetic counselors are trained in analyzing a woman’s family history, so they are well-equipped to determine whether or not a woman is considered “high-risk.” Second, I was interested in women who believed they were at high risk of developing breast/ovarian cancer, even if the medical profession did not consider these women to be at high-risk. Roughly 10% of women that visit Stanford’s Cancer Risk Assessment Clinic are self-referred, but about 3-5 times more self-referred women call the clinic and are told over-the-phone that they are not at enough of a high risk to warrant a genetic counseling session. Although I was mainly targeting high risk women at the Cancer Risk Assessment Clinic, I hoped to find high risk Ashkenazi Jewish women at Temple Beth Torah and some high risk already-affected-with-breast-cancer women at Stanford Hospital’s Gynecologic Oncology Clinic. 30 questionnaires were distributed at Stanford’s Cancer Risk Assessment Clinic; 19 were completed.

**Questionnaire Design and Regression Models**

The questionnaire was designed as a data collection instrument that would be analyzed via a logit and ordered probit regression model. The logit model regresses a function of X variables on the probability that a certain condition occurs in Y. The slope coefficients of the logit model therefore show the effect of a unit change in X on the probability of Y. The ordered probit regression performs maximum likelihood estimation with a dependent variable that is
ordinal and categorical. The categories of the ordered probit model used in this study are: “>$0,” "$500-$0," "$2500-$500," and "<$2500" (the price points represent the amount a woman would pay to get BRCA1/2 mutation tested). The interpretation of the ordered probit model differs somewhat from the logit model. In the ordered probit model, the slope coefficients show the effect of a shift in the distribution curve, which, in turn, affects the categorical variables.

The questionnaire contains questions that estimate the parameters of all three models. In case women did not answer/understand a question, more than one question often estimated the same parameter. The dependent variable in the regression models is women’s willingness to be genetically tested for breast/ovarian cancer susceptibility. The independent variables in the regression models are the factors that influence a woman’s decision to get genetically tested. Therefore, the logit and ordered probit regression models determine the effect of a woman’s demographic characteristics, perceived and actual risk of getting breast/ovarian cancer, value of post-test treatment strategies, value of the genetic test itself, and fear of genetic discrimination on her decision to undergo BRCA1/2 mutation testing at a given price point. A visual formula of the regression models is as follows:

Probability (getting BRCA1/2 mutation test at given price point) =
   f (Controls
   Perceived & Actual Risk of Getting Breast/Ovarian Cancer
   Value of Post-Genetic Test Treatment Strategies
   Value of Genetic Test
   Genetic Discrimination )

A woman’s demographic characteristics serve as control variables. Control variables are measured by a woman’s level of education and income. To estimate a woman’s perceived and actual risk of getting breast/ovarian cancer I combined several known breast/ovarian cancer risk factors used in the Claus, Gail, and BRACAPRO models with some of my own measures.
woman’s perceived and actual risk were measured by: the number of close friends a woman has that have/had any type of cancer, the number of her relatives that have/had any type of cancer, the number of her relatives that have/had breast/ovarian cancer, the number of her first-degree (mother, sister, daughter) relatives that have/had breast/ovarian cancer, her personal breast/ovarian cancer history, her age at diagnosis of breast/ovarian cancer, the number of breast biopsies that she has had, whether or not she is of Ashkenazi Jewish descent, her current age, and her age at first live birth. Although a woman’s number of first-degree relatives with breast/ovarian cancer is a more accurate and simple way to measure a woman’s risk of breast/ovarian cancer than the number of her relatives that have any cancer, I was concerned that some women would not know their familial cancer history in detail. I, therefore, included other measures of familial risk in my questionnaire to see which measure of risk would engender the best response rate. (Note: the number of close friends a woman has with cancer is used as a measure of psychological perception of risk.)

The value of post-genetic test treatment strategies is measured by women’s: utilities of prophylactic surgeries, treatment strategy preferences, relationship status, and motherhood status. I hypothesize that relationship status (i.e. married, single) affects a women’s preferences for post-test treatment strategies, and thus affects her decision to get genetically tested for breast cancer. For example, a married woman might be more willing to undergo prophylactic mastectomy than a single woman who is still on the “dating market,” trying to impress men. Similarly, motherhood status might affect a woman’s decision to undergo invasive surgery upon receiving a positive genetic test result; if a woman has finished having children, she may be more willing to have her breasts and ovaries removed than a younger woman who has yet to have children. Motherhood status might also affect a woman’s value of the genetic test itself. If a woman has
children, or plans on having children in the future, the information provided by BRCA1/2 mutation testing might be more valuable than if she did not have/want children. A mother (or future mother), therefore, might be more likely to get genetically tested.

Lastly, women’s health and life insurance status might contribute to their fear of genetic discrimination, which might inhibit them from getting genetically tested for breast/ovarian cancer susceptibility. For example, a woman who has health insurance, but does not have life insurance, might fear life insurance discrimination (due to a genetic predisposition) more than health insurance. A visual representation of the ways each independent variable is measured is as follows (in parentheses are the questions in the questionnaire that estimate each measure):

Controls: Education (Q5)
Income (Q6)

Perceived & Actual Risk: # of friends with cancer (Q14)
# of relatives with any cancer (Q15)
# of relatives with breast/ovarian cancer (Q16)
# of 1st degree relatives with breast/ovarian cancer (Q17)
Personal breast/ovarian cancer history (Q11)
Age at onset of breast/ovarian cancer (Q12)
# of breast biopsies (Q13)
Ashkenazi Jewish heritage (Q2)
Current Age (Q22b)
Age at 1st live birth (Q9)

Value of Treatment Strategies: Utilities of prophylactic surgeries (Q22, Q23, Q24)
Treatment strategy preferences (Q25, Q26)
Relationship status (Q7)
Motherhood status (Q8)

Value of Test: Value of information (Q18, Q19)
Future motherhood status (Q10)

Genetic Discrimination: Health insurance status (Q3)
Life insurance status (Q4)
Fear of genetic discrimination (Q20, Q21)
Willingness-to-pay: (Q19, Q20, Q21, Q22)

Price points for genetic testing were chosen to reflect the actual decisions a woman would face upon deciding whether or not to undergo BRCA1/2 mutation testing. The price points correspond to: no insurance coverage (true cost of the genetic test is approximately $2500), 20% coinsurance ($500), and full insurance coverage ($0). A potential bias is that the set of bids the individual receives influences her response. The optimal questionnaire design would have been to randomly assign a single price point to each respondent. However, this approach requires a relatively large sample size that I was unlikely to achieve. As a result, approximately half (52.88%) of my sample was randomly asked whether or not they would get genetically tested for breast/ovarian cancer susceptibility at three price points ($2500, $500, $0), and the other half was given four price points ($5000, $2500, $500, $0). The $5000 price point tests the hypothesis that multiple price points presented to the same woman affects her responses.

Calculating Cost Effectiveness

To calculate the cost effectiveness of BRCA1/2 mutation testing, I used the Markov model developed by Sanders et al. on Decision Maker software. Sanders et al. used a societal perspective to estimate health benefits and costs of BRCA1/2 mutation testing for women. Their data was based on various studies conducted by other researchers.

As previously mentioned, Sanders et al.’s decision model targeted four cohorts: (1) women from the general population, (2) Ashkenazi Jewish women, (3) women from high-risk cancer families that had a family history of four cases of breast cancer, and (4) women from high-risk cancer families that included histories of one or two cases of ovarian cancer in addition to
four cases of breast cancer. Sanders et al. assumed that women from the latter two cohorts (women with strong familial histories of breast/ovarian cancer) had at least one first-degree relative with breast/ovarian cancer. Although Stanford Hospital’s Gynecologic Oncology Clinic, Temple Beth Torah, and the Cancer Risk Assessment Clinic-Stanford Program for Applied Genetics served well as proxies for Sanders’ et al. respective categorizations, please see Table 1 for a complete understanding of how I grouped women from my sample into Sanders et al.’s four cohorts. Each cohort had two screening strategies: (1) no BRCA1/2 mutation testing, or (2) BRCA1/2 mutation testing. When a woman’s result of the BRCA1/2 test was positive, she then had four post-test treatment options to chose from: (1) prophylactic mastectomy, (2) prophylactic oophorectomy, (3) both surgeries (mastectomy and oophorectomy), or (4) intensive breast cancer surveillance (in the form of mammography and clinical breast examinations only).

Cost effectiveness of post-test treatment strategies (and, thus, cost effectiveness of BRCA1/2 mutation testing) was determined by a woman’s: age, her risk of having a BRCA1/2 mutation (see prior in Table 1), and preferences for prophylactic surgeries. Individual preferences for prophylactic surgeries were based on questionnaire responses to Questions 22-23 that used a time-tradeoff method to assess patients’ utilities (Grann et al., 1999) for prophylactic mastectomy and propylactic oophorectomy. Average utilities for prophylactic surgeries were based on Sanders et al.’s data (who, in turn, used data from Grann et al.’s 1999 study). All utilities were measured on a 0 to 1 scale, with 0 representing death and 1 representing complete/ideal health.

Many women in my study claimed that Questions 22-24 (questions that assessed women’s utility of mastectomy and oophorectomy) were confusing. I therefore developed a test of how well women understood Questions 22-24. First of all, women over age 70 were excluded
from analysis of these three questions. Second, I assumed that a woman did not understand Questions 22-24 if she left all, or parts of, the questions blank. Lastly, I assumed that women understood the questions if their utility of mastectomy and oophorectomy was less than or equal to their respective lowest utility of mastectomy or oophorectomy. According to this test of understanding, 81% of women understood these questions, 14% did not understand, and 5% were excluded from analysis for being over age 70.

I used two thresholds ($50,000 and $100,000 per quality-adjusted-life-year) to determine if a post-genetic test treatment strategy was cost effective. If any post-test treatment strategy was cost effective for a woman, then BRCA1/2 mutation testing was cost effective for her. If a woman's marginal cost effectiveness per quality-adjusted-life-year (QALY) for any post-test treatment strategy (relative to no BRCA1/2 mutation testing) was less than the chosen threshold, then the given treatment strategy was cost effec
tive for the given woman. The post-test treatment strategy most cost effective for a woman, was the strategy that yielded the lowest marginal cost effectiveness per QALY relative to no testing. To see if a woman would choose the most cost effective post-test treatment strategy if she underwent genetic testing for breast/ovarian cancer susceptibility, I compared a woman’s most cost effective strategy to her questionnaire response to Question 25. Question 25 asked a woman what treatment strategy (invasive surgery, non-invasive procedures, or nothing) she would choose if she tested positive for a BRCA1/2 mutation.

Data Analysis

Data analysis includes: descriptive statistics of samples; bivariate analysis of relationship between willingness-to-pay (WTP) for genetic testing and risk, and between WTP and treatment
preferences; multivariate logistic regression models of the probability of getting genetically tested; cost effectiveness model of the cost and effectiveness of getting genetically tested based on treatment preferences; and descriptive statistics comparing behavioral choices to cost effectiveness per QALY ratios. All analyses were performed with the use of Stata software, Windows Decision Maker, and Microsoft Excel.

**Results**

**Sample Characteristics**

The data reported here are from 104 questionnaires. The most responses came from women from Temple Beth Torah (55.77%), followed by women from Stanford Hospital’s Gynecologic Oncology Clinic (25.96%), and followed by women from the Cancer Risk Assessment Clinic (18.27%). Table 2 documents the similarities and differences in characteristics and preferences across the three cohorts.

There was not much variability in demographic characteristics across samples, except in age, ethnicity, and education. Overall, 77% of women had a household income of at least $75,000, 99.04% had health insurance, 62.14% had life insurance, and 74.76% were married. The extremely high average income in my overall cohort is mainly due to the highly affluent areas (Palo Alto and Ventura, California) in which women were recruited for this study. The average age of all respondents was 47 years (P<0.01), but average age was driven up by women from Temple Beth Torah, who tended to be older. Although most women (98.28%) from Temple Beth Torah were of Ashkenazi Jewish descent, 57.89% from the Cancer Risk Clinic and 3.70% from Stanford Hospital’s Gynecologic Oncology Clinic were Ashkenazi Jewish. It seems
reasonable that so many women from the Cancer Risk Clinic were Jewish, because this clinic mostly deals with high risk patients. Although being of Ashkenazi Jewish heritage is not as strong of a predictor of breast/ovarian cancer susceptibility as women with a strong familial history of the disease(s), when Ashkenazi Jewish heritage is coupled with a strong familial history of breast/ovarian cancer, a woman’s risk greatly increases. Lastly, education differed across samples (P<0.01). Only 68.42% of women from the Cancer Risk Clinic had more than a high school diploma, whereas 98.27% of women from Temple Beth Torah and 96.30% of women from Stanford Hospital’s Gynecologic Oncology Clinic had at least a college degree. The fact that women were more educated at Stanford Hospital’s Gynecologic Oncology Clinic makes sense because higher educated women tend to adhere more to age-recommended mammograms and clinical breast examinations (Phillips et al., 1998). Although it might seem surprising that women from the Cancer Risk Clinic were, on average, less educated than the other two cohorts, the purpose of having a genetic counseling clinic is to educate women on their risk of disease and behavioral choices that will mitigate their risk. Although less-educated women seem less likely to know about genetic counseling services and their personal breast/ovarian cancer risk, most (90% at the Cancer Risk Assessment Clinic) women who visit a genetic counselor have been referred by their physician. Therefore, since the largest percent (57.89%) of women who have (or have had) breast/ovarian cancer were from the Cancer Risk Clinic, it seems reasonable to assume that many of these women were referred to the genetic counseling clinic by their physician after the discovery of a malignant tumor and family history assessment.

Women from Stanford Hospital’s Gynecologic Oncology Clinic, Temple Beth Torah, and the Cancer Risk Clinic worked well as respective proxies for women from the general population, Ashkenazi Jewish women, and high risk women. Stanford Hospital’s Gynecologic
Oncology Clinic consistently had the most low risk women (as measured by having zero relatives with any type of cancer, zero relatives with breast/ovarian cancer, or zero first-degree relatives with breast/ovarian cancer), Temple Beth Torah had the largest contingent of Jewish women, and all (100%) women from the Cancer Risk Clinic were of medium-to-high risk (as measured by having at least one relative with any type of cancer, at least one relative with breast/ovarian cancer, or at least one first-degree relative with breast/ovarian cancer). All P-values that assessed women’s risk across samples were statistically significant at P<0.01.

If women from Stanford Hospital’s Gynecologic Oncology Clinic, Temple Beth Torah, and Cancer Risk Clinic are representative of low, medium, and high risk women, respectively, then the descriptive statistics suggest that risk level influences women’s responsiveness to price in getting genetically tested. 52.63% of women from the Cancer Risk Clinic indicated that they would pay $2500 for the BRCA1/2 mutation test, compared to 26.92% from Stanford Hospital’s Gynecologic Oncology Clinic and 6.90% from Temple Beth Torah. Although having a high price point seems to deter lower risk women from getting genetically tested, having to pay $2500 for the BRCA1/2 mutation test may deter medium-risk women (women of Ashkenazi Jewish descent) that should get genetically tested. These results are discussed in more detail later in the Results section of this paper.

Particularly interesting to note is that overall, women in my sample had a higher, quality-adjusted, utility of mastectomy and oophorectomy than the sample used by Sanders et al. The average utilities used by Sanders et al. were taken from the study by Grann et al. (1999). Questions 22-24 in my questionnaire were taken directly from Grann et al.’s (1999) study; therefore, both Grann and I used the same time trade-off method to calculate utilities for invasive surgeries. The overall utilities of life years after mastectomy and oophorectomy in my sample
were 0.89 and 0.92, respectively. Comparatively, Grann et al. (1999) found the average utilities of life post-mastectomy to be 0.8476 and life post-oophorectomy to be 0.8247. These differences in average utilities for surgeries might be explained by differences in sample size (my sample included 104 women, whereas Grann et al.’s sample had 184 women), age (Grann et al. only recruited women aged 20 to 50 years), education (women in Grann et al.’s study were, on average, less educated than women in my study), ethnicity (Grann et al’s study included less Ashkenazi Jewish women), and breast cancer status (Grann et al’s study had more women affected with breast cancer).

Also interesting is that across all cohorts, women thought it was very likely that genetic discrimination would manifest itself through higher premiums or lower admission rates in the health and life insurance industry. Health and life insurance premium questions were based on a scale of 1 to 4, 1 being not likely at all and 4 being very likely. Overall, women feared that a positive BRCA1/2 mutation would result in more life insurance discrimination (3.18) than health insurance discrimination (2.92).

**Willingness-To-Pay for BRCA1/2 Mutation Test**

Tables 3 presents more descriptive statistics on the influence of a woman’s risk on her decision to get genetically tested for breast/ovarian cancer susceptibility at different price points. Instead of using women from Stanford Hospital’s Gynecologic Oncology Clinic, Temple Beth Torah, and Cancer Risk Clinic as proxies for low, medium, and high risk individuals, respectively, Table 3 uses medical and psychological risk factors to estimate women’s risk levels.

Overall, price affects women’s responsiveness to BRCA1/2 mutation testing. In contrast to the 20.39% of women who would get genetically tested at a price of $2500, 47.57% would get
tested at a price of $500, and 72.12% would get tested if they didn’t have to pay anything for the test. Risk also matters. At higher price levels ($2500 and $500), risk (as measured by number of relatives with breast/ovarian cancer (P=0.10) and number of relatives with any cancer (P<0.10)) seems to have an effect on women’s decision to get BRCA1/2 mutation tested. As risk increases, women are more likely to pay more to get genetically tested for breast/ovarian cancer susceptibility. Nonetheless, women seem more likely to have answered “not sure” at a price of $500 across risk (as measured by number of relatives with any cancer).

Although the percent of Ashkenazi Jewish women who would get BRCA1/2 mutation tested increased as price decreased, most Ashkenazi Jewish women would not get genetically tested at any price point (these trends were not statistically significant). The reason for Ashkenazi Jewish women’s lack of interest in getting genetically tested for breast/ovarian cancer susceptibility may be due to their lack of knowledge that their ethnic group is at higher risk of having a BRCA1/2 mutation than the general population.

Although the number of close friends a woman has with any type of cancer is not a personal risk factor, it is a psychological/awareness risk factor. A woman with a lot of friends with cancer may become more knowledgeable (or fearful) about her own cancer risk and, therefore, adhere more to age-recommended risk prevention strategies such as mammography, ultrasounds, and clinic breast examinations. Nonetheless, the number of friends a woman has with cancer does not seem to affect her decision to get genetically tested--at least not at a price of $2500.

Table 4 presents information on the effect of women’s preferences for post-test treatment options on their willingness-to-pay for the BRCA1/2 mutation test. Although none of the relationships are statistically significant, the data suggests certain trends. An indicator of the
value of the BRCA1/2 mutation test is if a woman’s post-test treatment behavior would change if she received a positive test result opposed to a negative test result. For example, if a woman would undergo prophylactic mastectomy upon testing positive for a BRCA1/2 mutation, and would only get annual mammograms upon testing negative, then the information provided by the BRCA1/2 mutation test is valuable. Table 4 suggests that women whose overall behavior would change upon receiving a positive genetic test result (e.g. non-invasive → invasive, nothing → invasive, or nothing → non-invasive), are more likely to pay more for genetic testing than women whose overall behavior would not change (25.86% compared to 13.33% at a price of $2500, 50% compared to 44.44% at a price of $500). The specific change in behavior that is driving the overall change in behavior trend is women who would undergo invasive surgery if they tested positive and non-invasive procedures if they tested negative for a BRCA1/2 mutation.

Predictors of BRCA1/2 Mutation Test Utilization

The logit and ordered probit regression models determine the direction of influence of several factors on women’s decision to get BRCA1/2 mutation tested, and predict each woman’s probability of getting genetically tested, based on such factors. Table 5 lists the results of the logit and ordered probit regression models. Table 5 is divided into three horizontal sections that show the effect of adding more variables to the regression models at three price points ($2500, $500, $0). The top section provides the results of a regression model based only on women’s risk and post-test treatment change in behavior; the middle section provides the results of a regression model based on women’s risk, post-test treatment change in behavior, and demographics; and the bottom section provides the results of a regression model based on women’s risk, post-test treatment change in behavior, demographics, and other influential
factors. The regression model presented in the bottom section of Table 5 coincides with the regression formula aforementioned in the Methodology section of this paper, except for the fact that the control variables were eliminated. The theoretical regression model in the bottom section of Table 5 looks like the following:

Probability (getting BRCA1/2 mutation test at given price point) =
  \begin{align*}
  & f (\text{Perceived & Actual Risk of Getting Breast/Ovarian Cancer} \\
  & \text{Value of Post-Genetic Test Treatment Strategies} \\
  & \text{Value of Genetic Test} \\
  & \text{Genetic Discrimination} 
  \end{align*}

Neither education nor income (the control variables) was used in the logit and ordered probit regression models because there was not enough variation in income or education in my small sample to allow me to explain any differences in the effects of education or income on a woman’s decision to get BRCA1/2 mutation tested. In the ultimate regression model, multiple measures of women’s perceived and actual risk of getting breast/ovarian cancer were used: age, having at least one first-degree relative with breast/ovarian cancer, and having at least one close friend with any cancer. A woman’s number of relatives with breast/ovarian cancer, number of relatives with any cancer, Ashkenazi Jewish heritage, personal breast/ovarian cancer history, and age at first live birth were all too highly correlated to be included in the regression models. The value of the post-genetic test treatment strategies was measured by: the effect of being married, and women’s overall change in behavior upon receiving a positive result. (In other words, would a woman choose a different treatment strategy upon testing positive than she would upon testing negative for a BRCA1/2 mutation?) Current motherhood status and future motherhood status were too highly correlated with a woman’s age to be included in the regression models. The value of the genetic test was measured by women’s desire to tell their children the results of the
genetic test. Fear of genetic discrimination was measured by: the effect of having life insurance, and women’s ranking of their fear that a positive genetic test result would adversely affect their ability to get life insurance. The reason that the life insurance measures were used over health insurance measures was because most everyone (99.04%) in my sample had health insurance and more women feared life insurance discrimination than health insurance discrimination. Lastly, a variable was added to determine whether or not having $5000 as a price point option affected women’s responsiveness to genetic testing at lower price points. (Note: this variable was eliminated from the regression models in the middle and bottom sections of Table 5 because it did not have a statistically significant effect on women’s willingness-to-pay $2500 for the BRCA1/2 mutation test.)

All independent variables (except for age, which is continuous) are measured as binary variables, where 1 means “yes” and 0 “no.” One should interpret the effect of each variable on a woman’s decision to undergo BRCA1/2 mutation testing at each price point by assuming each variable equals one. For example, one interprets uses the positive coefficient of 1.149 to determine that having at least one first degree relative with breast/ovarian cancer (variable=1) positively influences a woman’s decision to get genetically tested. (Note: responses of “not sure” to questionnaire questions were treated as “no” answers for analysis.) Women’s fear of life insurance discrimination due to a positive BRCA1/2 mutation result was divided into two groups: those who believed life insurance discrimination was very likely (those who answered of 2.5 or greater on Question 21), and those who believed life insurance discrimination was not likely (those who answered less than 2.5 on Question 21); in this case 1 coincides with “very likely” and 0 coincides with “not likely at all.”
Results of the Logit Model

Factors that positively influence a woman’s decision to undergo genetic testing for breast/ovarian cancer susceptibility at a price point of $2500 include: having at least one first degree relative with breast/ovarian cancer, changing one’s post-genetic test treatment behavior upon receiving a positive genetic test result, being married, having life insurance, and wanting to tell one’s children the genetic test results. Factors that negatively influence a woman’s decision to undergo genetic testing for breast/ovarian cancer susceptibility at a price point of $2500 include: having $5000 as an optional price point, age, fear of life insurance discrimination, and having at least one friend with any cancer. Nonetheless, only the following variables were statistically significant in the regression in the bottom section of Table 5: having at least one first-degree relative with breast/ovarian cancer and having at least one friend with any cancer. It makes sense that higher risk women (those with at least one first-degree relative with breast/ovarian cancer) are more likely to pay more for the genetic test because the results of the genetic test have more value to a higher risk woman. More difficult to interpret is why having more than one friend with cancer negatively influences a woman’s decision to get genetically tested at higher price points. One interpretation is that having more friends with cancer makes a low risk woman more knowledgeable of her own breast/ovarian cancer risk and the options available to her low risk status. Because a low risk woman knows that she does not need to be tested for a BRCA1/2 mutation, she is not willing to pay the higher costs of testing. The fact that age and being married were only statistically significant in the middle section regression indicates that this study’s sample size is probably too small to detect the influence of these factors on women’s decision to undergo genetic testing for breast/ovarian cancer susceptibility.
The only differences between results at a price point of $2500 and results at a price point of $500 is that, at $500, the direction of influence changed for women who had life insurance and feared life insurance discrimination. Nonetheless, neither of these variables were statistically significant at either price point.

At a price point of $0, factors that positively influence a woman’s decision to undergo genetic testing for breast/ovarian cancer susceptibility consist of: having at least one first-degree relative with breast/ovarian cancer, fearing life insurance discrimination, and wanting to tell one’s children the genetic test results. Factors that negatively influence a woman’s decision to undergo genetic testing for breast/ovarian cancer susceptibility at zero cost consist of: having $5000 as a price point, changing one’s post-test treatment behavior upon receiving a positive genetic test result, age, being married, having life insurance, and having at least one friend with any cancer. The only two statistically significant influences, though, were: having a $5000 price point on one’s questionnaire, and wanting to tell one’s children the genetic test results. I interpret the change in direction of influence of having an overall change in post-test treatment behavior, being married, having life insurance, and fearing genetic discrimination as indicating that these variables do not have any bearing on women’s decision to get tested at a price of $0. I think the principle motivator for getting genetically tested at a price of $0 is the low cost of the test itself.

The fact that having a $5000 price point on a questionnaire was only statistically significant at a price point of $0 is contrary to what I expected to find. I expected that if having a price point of $5000 affected a woman’s decision to get genetically tested at all, it would only influence her decision at a price point of $2500 or $500. I interpret this puzzling finding by suggesting that the higher a test costs, the more appealing a “free” test becomes. I think that
women have the same “why not” attitude about getting a free genetic test as they would with receiving anything free. I also think it is interesting that wanting to tell one’s children the results of the BRCA1/2 mutation test is only statistically significant at the zero price point. I hypothesize that, at a price point of $0, more low risk women want to get genetically tested simply because of the zero cost of the test. Since more women can predict getting a negative test result, the variables that previously influenced a woman’s decision to get BRCA1/2 mutation tested at higher price points (i.e. having at least one first-degree relative with breast/ovarian cancer, age, being married, and having at least one friend with any cancer) might no longer matter. In other words, the expected negative genetic test result will no longer affect (positively or negatively) a woman’s personal life. Therefore, the only valuable thing about getting BRCA1/2 mutation tested is the ability to assure one’s children that they, for sure, are not at high risk for breast/ovarian cancer.

Results of the Ordered Probit Model

Except for the variable “have life insurance,” the direction of influence of each of the variables in the ordered probit model was the same as the direction of influence of each of the variables at the $2500 price point in the logit model. In contrast to the logit model, marriage was never statistically significant in the ordered probit model. Lastly, age was statistically significant in the ordered probit in the bottom section of Table 5. This result suggests that the older a woman is, the less likely she is to pay for the higher cost of the genetic test. Older women might feel that the genetic test has less value to them in old age because they already have breast/ovarian cancer; therefore, the predictive power of the genetic test is no longer applicable.
Overall, the results of the ordered probit model did not differ significantly from those of the logit model; therefore, the findings from the regression models are not sensitive to model type.

Although the logit and ordered probit regression models do not consistently show statistically significant relationships for several independent variables, a larger sample might reveal that these variables do indeed influence a woman’s decision to get genetically tested for a BRCA1/2 mutation. Although such relationships were not statistically significant in the regression models, Tables 3 and 4 suggest that relationships might exist.

Cost Effectiveness of BRCA1/2 Mutation Test

Table 6 tabulates the results of using individual versus average utilities for prophylactic mastectomy and oophorectomy to calculate women’s cost effectiveness of genetic testing for breast/ovarian cancer susceptibility. The results overwhelmingly show that using individual utilities yields a higher percent of women (67% more) for whom BRCA1/2 mutation testing is cost effective (at a threshold of $50,000) in comparison to using average utilities. As already discussed, however, the average disutilities of invasive surgeries from my small sample were higher than the average utilities used by Sanders et al. and might not be representative of a larger population.

Interesting to note in Table 6, is that 37% of the 69% of women for whom genetic testing was cost effective chose the most cost effectiveness treatment strategy upon testing positive for a BRCA1/2 mutation. Most women who did not chose the most cost effective treatment strategy (based on individual utilities and a threshold of $50,000) chose invasive surgery or non-invasive procedures instead of the most cost effective strategy of doing nothing, or they chose non-invasive procedures instead of invasive surgery. (Note: non-invasive procedures include intense...
surveillance measures. Therefore, a woman whose most cost effective treatment strategy is “do nothing” should not be translated literally. “Doing nothing” only means that a woman should undergo age-recommended mammography and breast examinations instead of invasive surgery and intensive non-invasive procedures.) The fact that only about half of women would chose the most cost effective post-test treatment strategy shows the important role genetic counselors and physicians should play in a woman’s decision making process pre and post-genetic testing.

Figure 1 graphically shows the negligible difference between the two thresholds used to calculate the cost effectiveness of genetic testing for breast/ovarian cancer susceptibility. In contrast to using a threshold of $50,000, using a higher threshold of $100,000 makes BRCA1/2 mutation testing cost effective for only 5% more women using average utilities, and 3% more women using individual utilities.

*Moral Hazard*

Figures 2a and 2b plot the overall market demand curve for BRCA1/2 mutation testing against market demand curves based on risk and preferences for post-genetic test treatment strategies. Interestingly, the overall market demand curve is more elastic (η=-0.205) at lower prices (from BÆC) and less elastic (η=-0.599) at higher price points (from AÆB). This indicates that a percent change in lower-range prices ($500Æ$0) has a larger affect on the quantity of BRCA1/2 mutation tests demanded than a percent change at higher price points ($500+). By plotting the demand curves, the moral hazard associated with each demand curve can also be assessed.

According to Folland, Goodman, and Stano (2001), moral hazard is “in the health services literature is commonly used to express the additional quantity of health care demanded,
resulting from a decrease in the net price of care attributable to insurance” (p. 615). Figure 2a illustrates the difference in market demand between women at low versus high risk of having a BRCA1/2 mutation. If insurance completely covers the approximate $2500 cost of the BRCA1/2 mutation test, the price of the test is zero for the woman getting tested. At a price of zero dollars, 56.13% more low risk women want to get genetically tested, 51.73% more women from the overall population want to get tested, and 47.83% more high risk women want to get tested. The deadweight losses associated with these increases in the percent of women who want to get genetically tested at a price of zero dollars are: $98,505 for low risk women, $82,418 for women from the overall population, and $66,855 for high risk women. Since moral hazard is mitigated by only administering the genetic test to high risk women, it would be valuable to insurance companies to have an algorithm that separated high risk women from low risk women in the population who want to undergo BRCA1/2 mutation testing. Also interesting to note is that, even with 20% coinsurance (price=$500), deadweight loss is least among high risk women getting genetically tested.

Figure 2b illustrates the difference in market demand between women whose post-genetic test treatment behavior would change upon receiving a positive test result versus those whose behavior would not change. Presumably, BRCA1/2 mutation testing has more value for women whose preferences would change upon receiving a genetic test result. The results of Figure 2b resemble those of Figure 2a. With full insurance (price=$0), targeting women whose preferences would not change upon receipt of a positive genetic test result is associated with the most moral hazard ($96,113), whereas targeting women whose preferences would change is associated with the least moral hazard ($70,693). If possible, it would be valuable for an insurance company to implement an objective standard that says only women whose preferences would change upon
receiving the genetic test results, should be BRCA1/2 mutation tested. Also interesting to note is that, even with 20% coinsurance (price=$500), deadweight loss is least among women whose behavior would change.

*Are We Over-Testing Women for a BRCA1/2 Mutation?*

Figures 3a, 3b, and 3c plot each woman’s probability of getting genetically tested for breast/ovarian cancer susceptibility at different price points against her marginal cost effectiveness per quality-adjusted-life-year (QALY) of getting tested. If a woman’s marginal cost effectiveness ratio is less than $50,000, then BRCA1/2 mutation testing is cost effective for her. Women who have a probability of getting tested between 0.5 and 1 are very likely to get tested.

The logit model presented in the bottom section of Table 5 was used to calculate women’s probability of getting BRCA1/2 mutation tested at each price point. A woman’s marginal cost effectiveness of BRCA1/2 mutation testing was obtained by taking her marginal cost effectiveness of the treatment strategy that was not dominated by strict or extended dominance by another treatment strategy. There are two things to note about this method of obtaining marginal cost effectiveness ratios: (1) the marginal cost effectiveness ratios used in Figures 3a,b,c are for different treatment strategies, and (2) the treatment strategy used for a particular woman in Figures 3a,b,c might not be the treatment strategy she would choose upon testing positive for a BRCA1/2 mutation.

The scatterplot graphs indicate that more women (both for whom testing is and isn’t cost effective) want to get genetically tested as cost decreases. More specifically, Figure 3a shows
that most women who “should” be tested (according to their marginal cost effectiveness ratio) have a low probability of getting tested. Therefore, the high price of $2500 may be detering high risk women (for whom BRCA1/2 mutation testing is beneficial) from getting tested. Figure 3b shows that, at a price of $500, more women for whom BRCA1/2 mutation testing is cost effective want to be tested. Nonetheless, many women who should be genetically tested still have a low probability of getting tested. Lastly, Figure 3c shows that the majority of women (those who should and shouldn’t be tested) want to get genetically tested when the test is free. Overall, these graphs suggest that BRCA1/2 mutation testing is being underdone at a price of $2500 and $500, and overdone at a price of $0. Therefore, the optimal price of the BRCA1/2 mutation test probably lies between $500 and $0.

**Discussion**

*Overall Conclusions*

Factors that influence a woman’s decision to undergo genetic testing for breast/ovarian cancer susceptibility include: price of the test itself, having at least one first degree relative with breast/ovarian cancer, having at least one friend with any cancer, and wanting to tell one’s children the test results. Nonetheless, due to this study’s small sample size and lack of variability within some variables, many of the factors that were not statistically significant in this study may indeed influence a woman’s decision to undergo BRCA1/2 mutation testing.

Preferences for prophylactic surgeries matter in determining women’s cost effectiveness per QALY of getting BRCA1/2 mutation tested. Customizing cost effectiveness by using individual utilities for surgeries, instead of average utilities, makes genetic testing cost effective.
for more women. Nonetheless, the cost effectiveness of having physicians determine each woman’s utilities of surgery was not explored. In addition, many women would not choose her most cost effective treatment strategy upon testing positive for a BRCA1/2 mutation. This finding highlights the importance of both pre and post-test genetic counseling, which can help BRCA1/2-positive women make the most appropriate post-test decisions for her.

Overall, the price of the BRCA1/2 mutation test matters. As price decreases, more women who should not be genetically tested (from a social cost effectiveness perspective) want to get tested. If most women pay the $2500 cost of the BRCA1/2 mutation test out-of-pocket (for fear of genetic discrimination manifesting itself in the insurance markets), genetic testing for breast/ovarian cancer susceptibility may be underdone. If most women have their health insurance companies cover the entire cost of the genetic test (price=$0), genetic testing may be over-utilized. To decrease the social cost of over-testing women for a BRCA1/2 mutation, insurance companies should implement an objective standard that only lets the following women get genetically tested for breast/ovarian cancer susceptibility: high risk women or women whose preferences for treatment would change after receiving a positive genetic test result. Another, perhaps more feasible, way to mitigate moral hazard would be to charge women a co-payment between $500 and $0.

**Limitations of Study**

The design of my questionnaire was not perfect. Although Question 17 asks a woman how many first-degree blood relatives have developed breast/ovarian cancer in her family, I accidentally included a woman’s aunt (amongst mother, sister, and child) as an example of a first-degree relative. Technically, an aunt is considered a second-degree relative. I assumed that
women realized my typographical error and only included first-degree relatives in their answer to Question 17; in other words, aunts were excluded. On the other hand, if many women had aunts with breast/ovarian cancer and counted them as first-degree relatives, the “prior” variable (a measure of a woman’s risk of having a BRCA1/2 mutation) might overestimate a woman’s risk.

Furthermore, my analysis has several limitations. Some high risk women in my sample had been genetically tested for breast/ovarian cancer upon completing my questionnaire. In the opening section of the questionnaire, I asked women who had already been tested to answer the survey as if they had not yet received their test results. Separating oneself from a positive or negative test result may be too difficult to do in practice. Also, answering questions prospectively versus retrospectively may have biased responses. Therefore, a BRCA1/2 mutation test result might have influenced a woman’s preferences for surgeries, fear of genetic discrimination, willingness-to-tell one’s children or siblings, and willingness to get tested at higher price points. (With a larger sample size, women that have already been genetically tested could have been eliminated from analysis.) In addition, women who have already been tested and women recruited from the Cancer Risk Assessment Clinic are probably better informed of the benefits and risks of BRCA1/2 mutation testing than women from Stanford Hospital’s Gynecologic Oncology Clinic and Temple Beth Torah. For women who have not undergone personal genetic counseling on breast/ovarian cancer susceptibility, basing questionnaire answers on only a two-page information sheet is not the same as responding to questions after information session(s) with a professional.

Similarly, intent to undergo BRCA1/2 mutation testing might differ from actual uptake. In a study by Surh et al. (1999), 72% of study participants claimed they were interested in BRCA1/2 mutation testing, yet only 49% of these women had contacted a genetic counselor for
testing 3-15 months following the study. In addition, Lynch, Lynch, and Rubinstein (2001) suggest that intent to undergo a specific post-genetic test treatment strategy might differ from actual uptake. Before having their subjects get BRCA1/2 mutation tested, 38% would consider prophylactic mastectomy upon testing positive, and 2% would consider prophylactic mastectomy upon testing negative. After informing women of their BRCA1/2 mutation status, a follow-up survey found that only 19% of mutation-positive women had undergone prophylactic mastectomy and 35% had undergone prophylactic oophorectomy. Women’s responsiveness to willingness-to-pay questions also might differ from their actual willingness-to-pay. Studies comparing hypothetical willingness-to-pay to actual purchasing decisions generally find an upward bias in the hypothetical answers.

My regression models may not accurately predict factors that influence women’s decision to get genetically tested for breast/ovarian cancer susceptibility for two reasons: (1) my sample size was too small and had too little variability amongst responses and (2) several factors that influence a woman’s BRCA1/2 mutation-decision were excluded from the models. Other factors that perhaps should have been added to the regression models are: race, ethnicity other than Ashkenazi Jewish, and perceived sensitivity and specificity of the genetic test itself.

The cost effectiveness model by Sanders et al. also has several limitations. Intensive surveillance in the cost effectiveness model only includes the cost of mammography and breast examinations. Other non-invasive procedures such as MRI screening (which is commonly used in conjunction with mammography as a screening device for high risk women), chemoprevention, and pelvic ultrasounds, were not included in the model. Therefore, genetic testing might be cost effective for more women as more non-invasive procedures become available. The cost effectiveness model also does not incorporate: the psychological benefit (or
quality-of-life) obtained by women who received a negative BRCA1/2 mutation result, women who would undergo prophylactic surgeries even upon testing negative for a BRCA1/2 mutation, and women who plan on getting a mastectomy/oophorectomy later in life (for example, a younger woman might have a lower utility of invasive surgeries if she has to undergo such treatments before she is finished having children).

Further Research

First of all, this study should be re-done on a larger sample in order to see if the results from this study can be generalized. I would have gathered a much larger sample if time and resources permitted. Second, the cost effectiveness model should incorporate other non-invasive procedures, and another cohort (women who have or have had breast/ovarian cancer). Third, the cost effectiveness model should be run on only women with a strong familial history of breast/ovarian cancer; this cohort should include Ashkenazi Jewish women with a strong familial history of the diseases. Fourth, survey questions for which “not sure” was marked (in contrast to “yes” or “no”) should be examined. Lastly, it might be interesting to test men’s responsiveness to genetic testing for a BRCA1/2 mutation, since men can also be mutation carriers.

BRCA1/2 mutation testing is still premature. Many uncertainties underlie the meaning of a positive or negative result, the moral and psychological effects of testing, and the financial barriers to getting tested. As such, some experts feel that BRCA1/2 mutation testing should not be commercially available until all of society’s concerns and uncertainties have been resolved.

Deciding to undergo BRCA1/2 mutation testing is not easy. It is extremely difficult to determine the direction and economic impact of a new technique, for even in today's society
technology, science, and the law can exist independently. Medical information in this area is evolving. Answers at this time remain incomplete as new discoveries lead to some answers, but also more questions and uncertainties. As Nancy Bruning (1992) states:

> we have to remind ourselves that any device, any surgical procedure, will have certain risks. We need to ask: what are reasonable risks? What price are we willing to pay in exchange for the benefits? And what are we willing to spend now in time, money, and effort to make sure we get all the information we need to answer these questions? (p. 104)

Thus, the ultimate decision is a personal one. Using incomplete information, a woman must consider quality-of-life and the implications that testing positive or negative would have on her life.
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Ovarian Cancer Among Carriers and Noncarriers of a BRCA1 or BRCA2 Mutation.”


