BRCA 1/2 Surveillance in Michigan, 2008-2012

Michigan Department of Community Health

Cancer Genomics Program

Published September 30, 2012

Introduction

From 2008-2012, the Michigan Department of Community Health (MDCH) Cancer Genomics Program was awarded cooperative agreement funding from the Centers for Disease Control and Prevention (CDC) Office of Public Health Genomics (OPHG) and Division of Cancer Prevention and Control (DCPC) to identify and promote cancer genomics best practices for appropriate translation of cancer genetic tests into clinical and public health practice. The primary project goal was to develop and implement a model for surveillance of inherited cancers and the use of relevant genetic tests. This report provides a summary of Michigan surveillance activities and results for Hereditary Breast and Ovarian Cancer (HBOC) syndrome, genetic counseling, and the *BRCA1/2* test.

Table 1: Lifetime risk for cancer in the general and *BRCA* populations

Cancer Type	General population	*BRCA* population
Breast	12%	36-85%
Ovarian	<2%	20-45%

There are many hereditary cancer syndromes that increase a person's risk for cancer.[1] These conditions are caused by gene changes (mutations) that can be passed down in a family from one generation to the next. HBOC syndrome, which causes about 10% of breast and ovarian cancer, is most often due to a deleterious mutation in the *BRCA1* and/or *BRCA2* gene.[2] Mutations in these genes significantly increase the risk of developing breast and/or ovarian cancer, multiple primary cancers and male breast cancer (**Table 1**).[2] For women with deleterious *BRCA1/2* mutations, earlier screening and prophylactic surgery could potentially reduce the risk of breast and ovarian cancer by 85 percent or more.[3] Additional background information regarding *BRCA* counseling and testing is included in **Appendices A-F**.

Healthy People 2020 Genomics Objective

Healthy People provides science-based, 10-year national objectives for improving the health of all Americans.[4] In 2010, a new genomics topic area was added to the Healthy People objectives for this decade. The two approved genomics objectives were based on evidence-based scientific review and recommendations from independent expert panels.[3,5] One of these objectives addresses breast and ovarian cancer genomics:

Healthy People 2020 Objective:

Increase the proportion of women with a family history of breast and/or ovarian cancer who receive genetic counseling

From national data sources, it is estimated that 23.3% of women with a family history of breast and/or ovarian cancer received genetic counseling in 2005.[4] However, this estimate was based on first degree relatives only and a limited set of family history criteria. The aim for 2020 is to improve this percentage by 10% with a target of 25.6%.[4]

Epidemiology of *BRCA1/2* Counseling and Testing in Michigan

Over the past decade, MDCH implemented multiple surveillance activities for *BRCA1/2* counseling and testing. The following key questions have been answered regarding *BRCA1/2* counseling and testing using existing statewide data and newly created data sources**:**

⇒ **What percentage of adult women in Michigan have a significant family history of breast and/or ovarian cancer?**

- **Are these women receiving genetic counseling?**
- **Is the percentage of women with a family history receiving genetic counseling in Michigan comparable to the Healthy People 2020 objective?**

⇒ **Who is receiving *BRCA* counseling and testing?**

- **What are the most common referring provider types?**
- **What percentage are found to have a known deleterious *BRCA* mutation?**

⇒ **What are the barriers and facilitators to receiving *BRCA* counseling and testing?**

The data sources used to answer these questions are highlighted in **Appendix G**.

USPSTF Grade B Recommendation Statement for *BRCA*

Based on the original CDC funding award, MDCH was given specific guidance to promote the 2005 United States Preventive Services Taskforce (USPSTF) recommendation statement entitled "Genetic Risk Assessment and *BRCA* Mutation Testing for Breast and Ovarian Cancer Susceptibility: Recommendation Statement".[3] The USPSTF statement included a Grade B Recommendation (meaning that at least fair evidence was found that the service improves health outcomes and that the benefits outweigh the harms) that specifically states:

> **"Women whose family history is associated with an increased risk for deleterious mutations in *BRCA1 or BRCA2* genes [should] be referred for genetic counseling and evaluation for *BRCA* testing." [USPSTF Grade B Recommendation][3]**

This USPSTF recommendation statement provided the basis for the Healthy People 2020 objective regarding family history of breast and/or ovarian cancer and receipt of genetic services. The USPSTF recommendation statement includes a list of suggested family history criteria associated with an increased risk of deleterious mutations in *BRCA1/2* which is provided in **Appendix C**. This USPSTF Grade B recommendation is also included in the Affordable Care Act for covered preventive services.[6]

USPSTF Grade D Recommendation Statement for *BRCA*

The 2005 USPSTF Recommendation Statement also includes a Grade D recommendation against *BRCA* counseling and testing for average risk women (which means USPSTF recommends against the service because there is at least fair evidence that the service is ineffective or that harms outweigh the benefits).[3] The Grade D recommendation is:

> **"USPSTF recommends against routine referral for genetic counseling or routine *BRCA* testing for women whose family history is not associated with an increased risk for deleterious mutations in *BRCA1/2*" [USPSTF Grade D Recommendation][3]**

Cancer Genetic Counseling

The 2005 USPSTF Recommendation states that genetic counseling should be performed by suitably trained health care providers to allow informed decision making about testing and further prophylactic treatments.[3] According to the American College of Surgeons (ACOS) Commission on Cancer (CoC), cancer risk assessment and genetic counseling are the processes by which to identify and counsel people at risk for familial or inherited cancer (cancers that run in the family).[7] Recently the CoC approved a new standard specific to cancer risk assessment and genetic counseling in the *Cancer Program Standards 2012: Ensuring Patient-Centered Care.* This standard includes specifics regarding the appropriate components of cancer genetic counseling and defines the required credentials, training and expertise of health care providers who are deemed qualified to provide cancer genetic counseling (**Appendix D**).[7] Since the 2005 USPSTF Recommendation Statement applies only to women who have not received a diagnosis of breast or ovarian cancer, MDCH utilized the National Comprehensive Cancer Network (NCCN) guidelines to determine appropriate criteria for *BRCA* counseling **(Appendix E)** and testing (**Appendix F)** for women and men with a personal history of breast cancer; women with a personal history of ovarian cancer; and, individuals with a relative with a known deleterious mutation.[3,7,8]

The national recommendations cited above are further reinforced by Michigan law, which requires that written informed consent be obtained by the provider prior to ordering predictive or pre-symptomatic genetic testing.[9] This law specifies that the informed consent process should include the nature and purpose of the test; implications of taking the test including risk, benefits and limitations; meaning of all possible test results or outcomes; how the results will be disclosed; and privacy and confidentiality issues.[9]

For a list of Cancer Genetic Service providers in Michigan, please the Michigan Cancer Genetics Alliance directory at: www.migeneticsconnection.org/cancer.

Utilizing the Michigan BRFSS to Measure a Healthy People 2020 Objective

The Behavioral Risk Factor Surveillance System (BRFSS) is the world's largest on-going telephone health survey. Coordinated by the CDC since 1984, BRFSS is currently the only source of state-specific, population-based health estimates among Michigan adults 18 years of age or older. Genomics-related questions have been included on the Michigan BRFSS since 2004 to better understand the genetics-related health behaviors of residents such as family history collection, genetic counseling and changes in genetic testing prevalence.

In 2008 and 2009, six questions on family history of breast and ovarian cancer were added to the Michigan BRFSS to assess the prevalence of women meeting the suggested USPSTF family history criteria **(Appendix C)**. Through the use of six questions, four of the USPSTF family history criteria were examined **(Table 2)**.

Table 2. Prevalence of USPSTF Family History Suggested Criteria Among Women in Michigan, Michigan BRFS 2008 and 2009

USPSTF Guideline	2008 Percent (%) (95% confidence interval)	2009 Percent (%) (95% confidence interval)
≥ 2 first degree relatives diagnosed with breast cancer, one of whom was with early-onset breast cancer (< 50 years)	1.3 (0.8-2.3)	1.0 (0.6-1.6)
≥ 3 first or second degree relatives with breast cancer at any age	5.0 (3.7-6.7)	3.7 (2.6-5.3)
≥ 2 first or second degree relatives with ovarian cancer at any age	1.8 (1.2-2.8)	1.9 (1.2-3.1)
≥ 1 first or second degree relative with breast cancer at any age and ≥ 1 first or second degree relative with ovarian cancer at any age	3.1 (2.2-4.4)	4.1 (2.9-5.8)

Among women with no personal history of breast and/or ovarian cancer, 7.9-8.7% met at least one of the USPSTF guidelines and 2.0-2.5% met two or more guidelines (data not shown). The two most common guidelines met were ≥ 3 relatives diagnosed with breast cancer; and ≥ 1 relative with breast cancer and ≥ 1 relative with ovarian cancer **(Table 2)**.

Based on their responses to the family history questions, the BRFS respondents were split into three categories: those that met at least one of the USPSTF suggested family history criteria and would benefit from genetic counseling; those that had a family history of breast and/or ovarian cancer but would require additional details to determine the appropriateness of genetic counseling; and, finally those with no family or personal history of breast and/or ovarian cancer and for whom *BRCA* counseling would not be appropriate.

Respondents who had a family history of breast and/or ovarian cancer were also asked a question about whether they had ever received genetic counseling and a question about whether they had ever received *BRCA* testing. As shown in **Table 3**, in 2008, 18.0% of women who would benefit from genetic counseling reported actually receiving counseling and 4.9% reported receiving *BRCA* testing. In 2009, this percentage increased to 35.7% of women with a significant family history of breast and/or ovarian cancer who reported receiving *BRCA* genetic counseling; however this increase was not a statistically significant change. The percentage that received genetic testing also increased to 9.8% in 2009 but was not statistically significant. **Nevertheless, based on these results, it appears that Michigan has achieved and exceeded the Healthy People 2020 objective for *BRCA* counseling.** We will continue to monitor and report these data trends based on the 2011 and 2012 Michigan BRFS results.

Table 3. Proportion (% [95% confidence interval]) of Women Who Have Received Genetic Counseling[1] or Testing[2] for Breast or Ovarian Cancer by Referral Status[3], Among Women With a Family History but No Personal History of Breast or Ovarian Cancer[4] 2008 and 2009 Michigan BRFS

	2008		2009	
	Genetic Counseling	**Genetic Testing**	**Genetic Counseling**	**Genetic Testing**
Would Benefit from Genetic Counseling[3]	18.0 (11.8-26.4)	4.9 (2.4-9.9)	35.7 (24.8-48.2)	9.8 (4.1-21.5)
Requires More Information Prior to Genetic Counseling[4]	16.1 (11.7-21.8)	6.5 (3.7-10.9)	16.8 (12.3-22.7)	1.5 (0.8-2.8)

[1]Response to the question, "Have you ever received genetic counseling for breast or ovarian cancer? This would include a conversation with an expert about your hereditary risk of breast and ovarian cancer."

[2]Response to the question, "Have you ever had a blood test to determine your hereditary risk for breast or ovarian cancer? A doctor would have ordered this test and you would have received the results."

[3]Among adult women who had personally never been diagnosed with either breast or ovarian cancer, benefiting from genetic counseling was defined as having one of the following:

a) ≥ 2 first degree relatives diagnosed with breast cancer, one of whom was diagnosed with early-onset breast cancer (< 50 years), or

b) ≥ 3 first or second degree relatives diagnosed with breast cancer at any age, or

c) ≥ 2 first or second degree relatives diagnosed with ovarian cancer at any age, or

d) ≥ 1 first or second degree relative diagnosed with breast cancer at any age and ≥ 1 first or second degree relative diagnosed with ovarian cancer at any age.

[4]Among adult women who had personally never been diagnosed with either breast or ovarian cancer, needing more information was defined as having a family history of breast or ovarian cancer but not meeting one of the guidelines above.

2008: N = 1,645 2009: N =1,726

Source: Michigan Behavioral Risk Factor Survey (BRFS)

The MiBRFS includes questions about health behaviors and characteristics such as Body Mass Index (BMI), smoking status, binge drinking and physical inactivity. The characteristics and behaviors of three groups were compared in **Table 4**. The groups were similar across all factors with the exception of smoking; smoking was statistically higher in the "Would Benefit from Counseling" group than in the other two groups.

Table 4. Prevalence of Selected Health-Related Characteristics by Family History Status Among Women with No Personal History of Breast or Ovarian Cancer (% [95% confidence interval]), Michigan BRFS 2008 and 2009

Risk Factors	Would Benefit from Genetic Counseling[1]	Need More Information[2]	No Action/Counseling Required[3]
Overweight (BMI ≥ 25)	67.9% (59.0-75.6)	57.5% (52.3-62.5)	59.4% (56.5-62.3)
Obese (BMI ≥ 30)	36.8% (29.3-45.0)	29.7% (25.6-34.1)	30.6% (28.0-33.2)
Current Smoker	26.3% (19.7-34.2)	16.6% (13.2-20.6)	16.6% (14.8-18.7)
Binge Drinking	12.4% (7.3-20.3)	14.1% (10.4-18.8)	11.4% (9.6-13.5)
Physical Inactivity	50.7% (42.4-58.9)	53.3% (48.4-58.2)	50.0% (47.1-52.9)

[1]Among adult women who had personally never been diagnosed with either breast or ovarian cancer, benefiting from genetic counseling was defined as having one of the following (USPSTF, 2005):

a) ≥ 2 first degree relatives diagnosed with breast cancer, one of whom was diagnosed with early-onset breast cancer (< 50 years), or

b) ≥ 3 first or second degree relatives diagnosed with breast cancer at any age, or

c) ≥ 2 first or second degree relatives diagnosed with ovarian cancer at any age, or

d) ≥ 1 first or second degree relative diagnosed with breast cancer at any age and ≥ 1 first or second degree relative diagnosed with ovarian cancer at any age.

[2]Among adult women who had personally never been diagnosed with either breast or ovarian cancer, needing more information was defined as having a family history of breast or ovarian cancer but not meeting one of the guidelines above.

[3]Among adult women who had personally never been diagnosed with either breast or ovarian cancer, no required action/counseling was defined as not having a family history of breast or ovarian cancer.

2008: N = 1,645 2009: N =1,726

Source: Michigan Behavioral Risk Factor Survey (BRFS)

Michigan Cancer Surveillance Program Chart Abstraction of Breast and/or Ovarian Cancer Patients

The cancer genomics chart abstraction surveillance project utilized cancer cases identified through the Michigan Cancer Surveillance Program (MCSP), in the MDCH Division for Vital Records and Health Statistics. MCSP is mandated by state law (Act 82 of 1984) to collect information on all cancer diagnoses and treatment. More specifically, the mandate established MCSP to:

> **"...record cases of cancer and other specified tumorous and precancerous diseases that occur in the state, and to record information concerning these cases as the department considers necessary and appropriate in order to conduct epidemiologic surveys of cancer and cancer-related diseases in the state." This mandate further states that "a reporting entity which meets the standards of quality and completeness set by the department shall be subject to inspection not more than once every 2 years for the purpose of assessing the quality and completeness of reporting from the entity."**

About 60,000 new cases of cancer (diagnoses) are reported to the MCSP per year. In 2003, the MDCH Cancer Genomics Program and MCSP developed a chart review process to monitor collection of family history of cancer. The first family history surveillance activity conducted by MCSP from 2003-2004 involved review of 853 cancer patient charts. MCSP found that over 80% of charts documented the presence or absence of family history information, including the gender of the affected relative and degree of relationship of the affected relative to the patient (i.e., first degree, second degree). However, over 94% of charts with a documented family history did not include the age of diagnosis of the affected relative; a critical piece of information to performing any genetic risk assessment. Based on this activity, MCSP implemented a mandatory family history field to be completed by the local reporting facility for all cancer diagnoses beginning in 2007. This field contains three pieces of family history information: 1) does the patient have a family history (yes/no), 2) is it in a first degree relative (yes/no) 3) is it the same type of cancer as the proband (yes/no). Prior to 2007, documentation of family history by local reporting facilities was an optional open-ended text field.

As part of an MDCH cooperative agreement with CDC, MCSP agreed to conduct chart reviews on select 2007-2010 cancer diagnoses to determine: (1) collection of cancer family history; (2) assessment and referral for genetic counseling; and (3) use of genetic testing for *BRCA 1 & 2*. From the data abstracted on each chart review, MDCH Cancer Genomics also determined if the affected individual would benefit from a referral for *BRCA* genetic counseling and/or *BRCA* testing per the NCCN guidelines. The cancer's primary site was used to identify charts for abstraction. Breast cancer primaries were included if the ICD topography code was C59.9 and ovarian cancer primaries were included if the ICD topography codes were C48.2 or C56.9.[10]

MCSP staff were trained to abstract family history, *BRCA* counseling and *BRCA* testing information using chart abstraction tools created for each cancer type **(Figures 1 and 2, page 10)**. MCSP staff reviewed charts on 857 primary breast cancers and 139 ovarian/fallopian tube/primary peritoneal cancers diagnosed between 2006 and 2010 with the majority of breast cancers diagnosed in 2008 and 2009. Breast cancer cases from 11 facilities and ovarian cancer cases from 8 facilities were reviewed as part of the MCSP quality assurance chart audits. There were 20 breast cancer charts and 2 ovarian cancer charts excluded due to duplicate chart reviews. Charts from 837 breast cancer cases and 137 ovarian cancer cases were in the final review.

The majority of the breast cancer cases reviewed were among women (99.2%). The majority of the breast cancer and ovarian cancer cases reviewed were among white people (93.4% and 97.1% respectively). Based on abstraction results, over half of the breast cancer patients reported having a history of cancer in their family and 6.5% reported having previous personal breast cancer history. Over one-third (41.6%) of ovarian cancer cases reported having a family history of cancer and 7.3% had a family history of ovarian cancer.

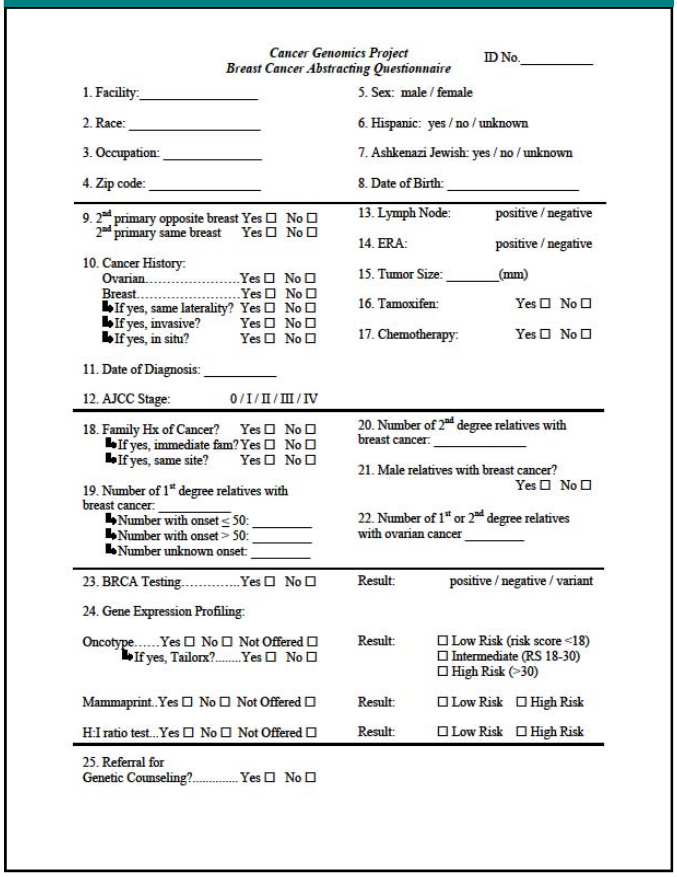
Table 6. Frequency of *BRCA* counseling and *BRCA* testing among the total breast cancer abstraction population, the population that met NCCN counseling and NCCN testing criteria, Michigan 2007-2010

	Population		
	Total Number (%)	**NCCN Counseling Criteria Met Number (%)**	**NCCN Testing Criteria Met Number (%)**
Referred for *BRCA* Genetic Counseling	16 (1.9)	11 (3.3)	5 (4.3)
Had *BRCA* Testing	18 (2.2)	14 (4.2)	8 (6.8)
Positive Result	2 (0.2)	1 (0.6)	1 (0.9)
Negative Result	13 (1.6)	11 (3.3)	7 (6.0)
Variant Result	1 (0.1)	1 (0.3)	0 (0.0)
Total	837 (100)*	332 (100)	117 (100)

According to NCCN genetic counseling criteria **(Appendix E)**, 332 of the 837 breast cancer patients should have been referred to a cancer genetics professional based on their personal and family history of cancer.[8] However, only 11 (3.3%) had documentation of a referral to genetic counseling (**Table 6)**.

Of these 332 breast cancer patients, 117 (%) were appropriate for *BRCA* testing according to NCCN testing criteria **(Appendix F)**. Of those 117 that were appropriate for *BRCA* testing only 8 (6.8%) received such testing **(Table 6)**. Additionally, there were 10 breast cancer cases who had *BRCA* testing and were not appropriate for such testing according to national guidelines (data not shown).

Figure 1. Breast cancer abstraction tool

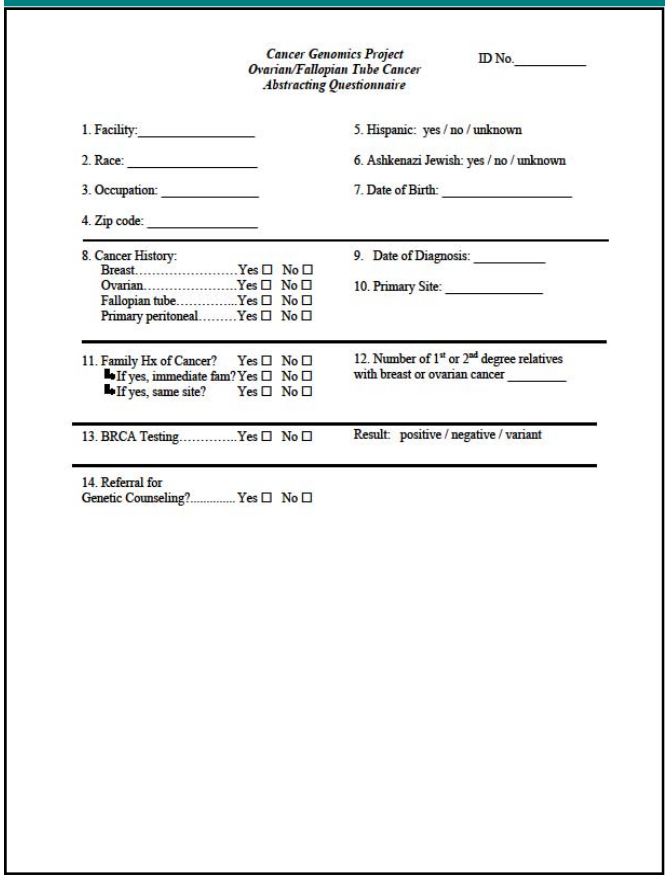


Cancer Genomics Project
Breast Cancer Abstracting Questionnaire

ID No._____

1. Facility:_____
2. Race: _____
3. Occupation: _____
4. Zip code: _____
5. Sex: male / female
6. Hispanic: yes / no / unknown
7. Ashkenazi Jewish: yes / no / unknown
8. Date of Birth: _____
9. 2nd primary opposite breast Yes ☐ No ☐
   2nd primary same breast Yes ☐ No ☐
10. Cancer History:
    Ovarian……Yes ☐ No ☐
    Breast……Yes ☐ No ☐
    If yes, same laterality? Yes ☐ No ☐
    If yes, invasive? Yes ☐ No ☐
    If yes, in situ? Yes ☐ No ☐
11. Date of Diagnosis: _____
12. AJCC Stage: 0 / I / II / III / IV
13. Lymph Node: positive / negative
14. ERA: positive / negative
15. Tumor Size: _____(mm)
16. Tamoxifen: Yes ☐ No ☐
17. Chemotherapy: Yes ☐ No ☐
18. Family Hx of Cancer? Yes ☐ No ☐
    If yes, immediate fam? Yes ☐ No ☐
    If yes, same site? Yes ☐ No ☐
19. Number of 1st degree relatives with breast cancer: _____
    Number with onset ≤ 50: _____
    Number with onset > 50: _____
    Number unknown onset: _____
20. Number of 2nd degree relatives with breast cancer: _____
21. Male relatives with breast cancer? Yes ☐ No ☐
22. Number of 1st or 2nd degree relatives with ovarian cancer _____
23. BRCA Testing……Yes ☐ No ☐ Result: positive / negative / variant
24. Gene Expression Profiling:
    Oncotype……Yes ☐ No ☐ Not Offered ☐ Result: ☐ Low Risk (risk score <18) ☐ Intermediate (RS 18-30) ☐ High Risk (>30)
    If yes, Tailorx?……Yes ☐ No ☐
    Mammaprint..Yes ☐ No ☐ Not Offered ☐ Result: ☐ Low Risk ☐ High Risk
    H:I ratio test...Yes ☐ No ☐ Not Offered ☐ Result: ☐ Low Risk ☐ High Risk
25. Referral for Genetic Counseling?……Yes ☐ No ☐

Figure 2. Ovarian cancer abstraction tool



Cancer Genomics Project
Ovarian/Fallopian Tube Cancer
Abstracting Questionnaire

ID No._____

1. Facility:_____
2. Race: _____
3. Occupation: _____
4. Zip code: _____
5. Hispanic: yes / no / unknown
6. Ashkenazi Jewish: yes / no / unknown
7. Date of Birth: _____
8. Cancer History:
   Breast……Yes ☐ No ☐
   Ovarian……Yes ☐ No ☐
   Fallopian tube……Yes ☐ No ☐
   Primary peritoneal……Yes ☐ No ☐
9. Date of Diagnosis: _____
10. Primary Site: _____
11. Family Hx of Cancer? Yes ☐ No ☐
    If yes, immediate fam? Yes ☐ No ☐
    If yes, same site? Yes ☐ No ☐
12. Number of 1st or 2nd degree relatives with breast or ovarian cancer _____
13. BRCA Testing……Yes ☐ No ☐ Result: positive / negative / variant
14. Referral for Genetic Counseling?……Yes ☐ No ☐

According to NCCN guidelines, a diagnosis of ovarian cancer is an indication for *BRCA* counseling and testing.[8] Although all 137 ovarian cancer patients met NCCN guidelines for counseling and testing, only five (3.6%) of the ovarian cancer patients had documentation in their charts that they were referred for *BRCA* genetic counseling and ten (7.3%) ovarian cancer patients had documentation that they had *BRCA* testing, **Table 7**. Among the ten ovarian cancer cases documented as receiving *BRCA* testing, 5 (50%) were found to have deleterious mutations. Of these 10 cases, 4 had documented genetic counseling. Furthermore, the ovarian cancer cases who had *BRCA* counseling and testing documented in their charts had a higher prevalence of a known deleterious mutation (75%) than those who had evidence of testing without documented counseling (50%).

Table 7. Frequency of genetic counseling referrals and genetic testing among the abstracted ovarian cancer population and the population that met NCCN counseling and NCCN testing criteria, Michigan 2007-2010

	Population Number (%)
Referred for Genetic Counseling	5 (3.6)
Had *BRCA* Testing	10 (7.3)
Positive Result	5 (3.6)
Negative Result	5 (3.6)
Variant Result	-
Total	137 (100.0)

MCSP Young Breast Cancer Survivors Mail Survey

The MDCH Cancer Genomics Program, MCSP registry staff and partners sought to assess characteristics of young female breast cancer survivors (under 50 years of age) including: knowledge and attitudes regarding family health history, genetic counseling, and genetic testing. In addition, the barriers and facilitators to receipt of *BRCA* counseling services and the utilization of *BRCA* genetic testing were assessed. A diagnosis of breast cancer before 50 years of age is an appropriate indication for referral for *BRCA* counseling according to professionally accepted guidelines such as the NCCN Criteria for Further Genetic Risk Evaluation (**Appendix E**).[8,11]

Five-hundred young female breast cancer survivors (YBCS) were identified using the MCSP cancer registry. The YBCS had been diagnosed in 2006-2007 in Michigan and were between the ages of 18-49 at the time of diagnosis. Of the 3,911 YBCS diagnosed in 2006 and 2007, 500 women were selected by simple random selection from the eligible population. MDCH Vital Records and death certificates were used to verify living status to the best of our ability. As part of the consent process, MCSP notified the local reporting facility as well as the physician on record regarding the YBCS survey. Both were provided with the potential study participant's name and physicians of record were asked whether they knew of any reason that the selected participant should not be contacted, such as death, mental illness, or illness due to current cancer treatments. If the local reporting facility and diagnosing physician confirmed their case and the physician did not indicate any medical contraindications to MCSP contacting the patient, the participant was mailed the MDCH-created survey with up to three attempts to obtain a response. The complex consent and contact process is described in **Appendix H.**

Completed surveys and signed consent forms were received from 289 women (57.8%) across Michigan. The respondents were primarily white (86.2%), employed for wages (56.1%), had private insurance (75.4%) and had a family history of breast and/or ovarian cancer (53.3%). The respondents' age ranged from 26-49 years with an average age of 43 years.

All of these women met NCCN counseling guidelines because they were diagnosed with breast cancer before the age of 50, however, less than half (42.2%; n=122) reported that they had received *BRCA* genetic counseling and risk assessment as defined in the study survey **(Appendix I)**.[8] Of these women, 51.6% perceived their familial risk of getting breast cancer to be higher than other families.

Facilitators to Receiving Genetic Counseling and Risk Assessment

The 122 (42.2%) women who received genetic counseling and risk assessment were asked on the YBCS Mail Survey what made it easier to receive these services and what their reasons were for going. As shown in **Table 8**, their top reason for receiving *BRCA* genetic counseling was to benefit their family's future (86.1%), followed by wanting to know future cancer risk (50.8%), and a doctor's recommendation (41.0%). The top factor that made it easy for the women to receive genetic services was that their medical insurance covered the visit (68.0%). Two other factors that made it easy for the women were that the clinic was close to their home and they had available transportation (both 40.2%) **(Table 8)**.

Table 8. Facilitators of *BRCA* Genetic Counseling & Risk Assessment Among YBCS who received services

	n=122
REASONS FOR GOING	
Benefit my family's future	105 (86.1%)
Wanted to know my future risk of cancer	62 (50.8%)
My doctor recommended that I go	50 (41.0%)
May alter my cancer treatment	48 (39.3%)
Going seemed very important	41 (33.6%)
Family members wanted me to go	21 (17.2%)
Already knew of a familial mutation	3 (2.5%)
FACTORS THAT MADE IT EASIER TO GO	
My medical insurance covered the visit	83 (68.0%)
Clinic was close to home	49 (40.2%)
Have available transportation	49 (40.2%)
Clinic hours were flexible and fit my schedule	30 (24.6%)
Have available childcare	11 (9.0%)
I was able to obtain these services by phone	2 (1.6%)

Table 9. Barriers to Receiving Genetic Services Among YBCS who had never received services

	n=158
No one ever recommended it	92 (58.2%)
Medical insurance coverage issues	37 (23.4%)
Did not know they existed	17 (10.8%)
Worried a genetic test could be used against me	15 (9.5%)
Too nervous	6 (3.8%)
A doctor told me not to go	5 (3.2%)
Lack of transportation	4 (2.5%)
Other life issues arose that were more important	4 (2.5%)
Too busy	3 (1.9%)
Disability makes it difficult to carry out daily activities	2 (1.3%)
Family members wouldn't want me to go	2 (1.3%)

Barriers to Receiving Genetic Services

The 158 women (54.7%) who did not receive *BRCA* genetic counseling were asked their reasons for not going to genetic counseling and risk assessment. As shown in **Table 9**, the number one reported reason was that no one had ever recommended that they should receive genetic services (58.2%). The second most common response reported was medical insurance coverage issues (23.4%), followed by not knowing that genetic services existed (10.8%). Since specific insurance type is not reported to MCSP and was not asked on the survey, it is not possible for us to determine if this is an actual barrier or a perceived barrier by the YBCS.

BRCA Testing and Results

Sixty percent of women who returned the survey reported that they had spoken with a healthcare professional about having a *BRCA* genetic test. Of those women, 75.3% were told they should have *BRCA* testing. A total of 121 women had *BRCA* testing. Among the 121 *BRCA* tests that were reported, 16 (13.2%) were documented as being positive for a known deleterious mutation, 90 (74.4%) were negative and 5 (4.1%) were of a variant of uncertain clinical significance, **Table 10**.

Table 10. Frequency of BRCA genetic testing among women with breast cancer diagnosed before the age of 50 in 2006 or 2007, Survivors Survey, Michigan, 2011

	Number (%)
Had *BRCA* Testing	121
Positive Result	16 (13.2)
Negative Result	90 (74.4)
Variant Result	5 (4.1)

As shown in **Table 11**, among the 121 YBCS who had *BRCA* testing, 105 (86.8%) reported that they had signed an informed consent document prior to testing. Over half of the 121 women reportedly had full insurance coverage for the *BRCA* test (63.6%) and 9.9% reported having partial coverage for their *BRCA* test. Three-quarters of the women reported that it was recommended by a doctor or other medical staff that they share their test results with family members and 95.9% shared their *BRCA* test results. Immediate family members, spouses and health care providers were most frequently reported as the people YBCS shared their genetic test results with.

Table 11. Frequency of Informed Consent, Insurance Coverage, and Results Disclosure Among YBCS who had *BRCA* testing, Survivors Survey, Michigan, 2011

	Number (%)
Signed Consent Prior to Testing	105 (86.8%)
Insurance Covered all of Test	77 (63.6%)
Recommended to Share Result	92 (76.0%)
Actually Shared Result per YBCS	116 (95.9)

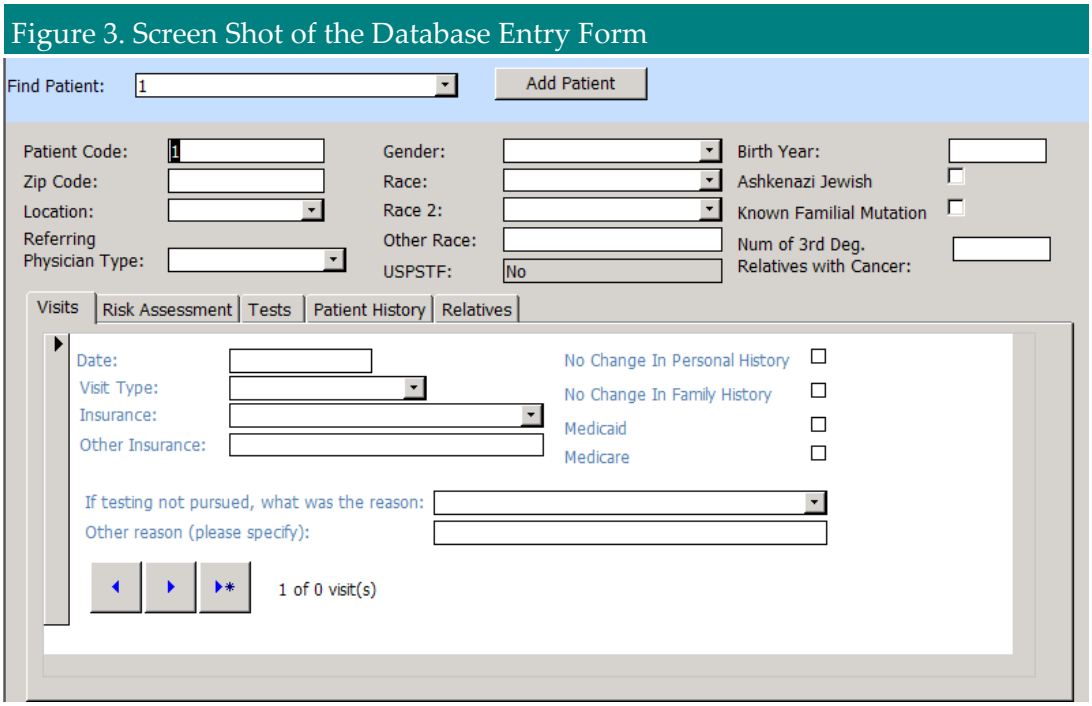
BRCA Clinical Genetic Counseling Database

MDCH has developed a statewide network of clinical facilities providing *BRCA* counseling for the purpose of learning about the use of genetic services in Michigan. These tables provide an overview of the characteristics of patients utilizing these services, referring providers, and the services received.

MDCH identified and recruited 11 clinical facilities in Michigan with board-certified genetics professionals providing *BRCA* counseling between October 2007 and March 2011. One facility, with an out-of-state genetics provider, was not able to provide data using our reporting system; therefore 10 out of 11 facilities participated in the MDCH clinical network.

Participating facilities include Beaumont Health System Cancer Genetics Program, Henry Ford Health System, InformedDNA*, Karmanos Cancer Institute Genetics Service, Michigan State University Division of Clinical Genetics, Oakwood Healthcare System's Genetic Risk Assessment for Cancer Clinic, Providence Hospital Medical Genetics, Spectrum Health Cancer Genetics Program, University of Michigan Cancer Genetics Clinic, and University of Michigan Breast and Ovarian Cancer Risk and Evaluation Program.

Figure 3. Screen Shot of the Database Entry Form



Following IRB review and approval, each clinical facility provided a de-identified, limited dataset on all patients receiving *BRCA* counseling during the period of interest. These data include patient demographics, type of referring provider, personal and family histories of cancer, insurance type, *BRCA* tests ordered and results, and reasons for not testing, if applicable. The surveillance system originally used a Microsoft Access database featuring drop-down menus and tabs for user-friendly navigation (**Figure 3**); this has since been converted to an online database with a similar format.

* Phone counseling service providing data on patients residing in Michigan only

Clinical Database—Demographics

Table 12. *BRCA* Counseling Patient Demographics
October 2007 — March 2011

	Counseling Patients	State of Michigan**
	Number (%)	(%)
Gender		
Female	5,584 (95.0)	(50.9)
Male	290 (4.9)	(49.1)
Unknown	2 (0.0)	
Race/Ethnicity		
White	4,719 (80.3)	(76.5)
Black	432 (7.4)	(13.9)
Multi-racial	408 (6.9)	(2.4)
Asian / Pacific Islander	108 (1.8)	(2.5)
Arab Ancestry	102 (1.7)	(1.6)*
Hispanic	57 (1.0)	(4.1)
Native American	8 (0.1)	(0.5)
Other	11 (0.2)	(0.1)
Unknown	31 (0.5)	
Ashkenazi Jewish Heritage		
No	5,286 (90.0)	
Yes	590 (10.0)	
Known Familial Mutation		
No	5,127 (87.3)	
Yes	749 (12.8)	
Family History per USPSTF		
No	3,392 (57.7)	
Yes	2,484 (42.3)	
Personal Cancer History‡		
No	2,600 (44.3)	
Yes	3,276 (55.8)	

* Does not exclude other races/ethnicities
‡ Personal history of breast and/or ovarian cancer
** Michigan 2010 American Community Survey

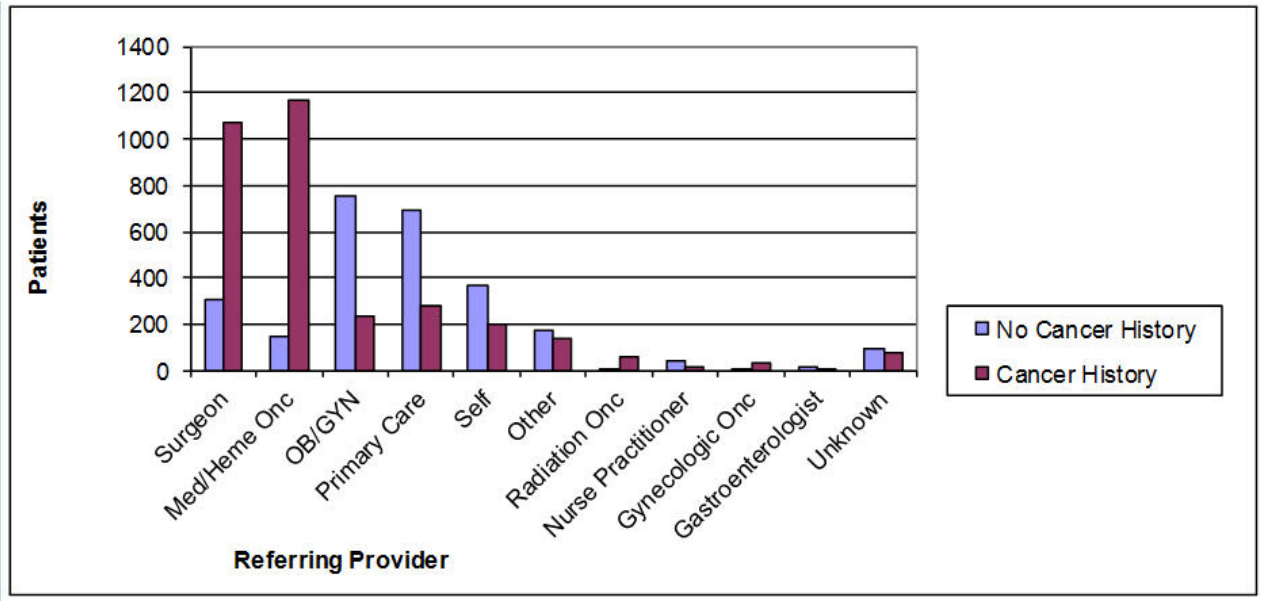
Board-certified genetics providers participating in the clinical network reported 5,876 patients who received *BRCA* counseling between October 1, 2007 and March 31, 2011 (**Table 12)**. These patients were primarily female (95.0%) and white (84.4%). Only 55 of the 290 males presenting for counseling had a history of breast cancer (19.0%), but 135 (47.0%) had a family member with a known mutation.

The Detroit region contains a large Arab population, and this is reflected in the 1.7% of patients reporting Arab ethnicity. When compared to Michigan's 2010 American Community Survey (ACS) data, Asian/ Pacific Islander, Black, and Hispanic patients appear to be underrepresented among those receiving *BRCA* counseling. This remains true when multi-racial Asian/Pacific Islander, Black, and Hispanic patients are included in this count. While only 0.1% of patients reported Native American as their primary race, 252 (4.3%) of the 408 multi-racial patients were reported as part Native American. This exceeds the ACS estimate for multi-racial Native Americans of 0.9% of the Michigan population.

Ten percent of patients seen were of Ashkenazi Jewish ancestry and 12.8% of all patients had family members with known mutations. Over half (55.8%) the patients had a personal history of breast and/or ovarian cancer, while 42.3% of all patients seen for counseling had a family history of cancer that met the USPSTF Grade B Recommendation for referral based on family history.[3]

Clinical Database—Referring Provider and Age

Figure 4. Referring provider of patients receiving *BRCA* counseling, October 2007—March 2011



Primary care includes internal medicine and family practice.

2,797 patients were referred by surgeons or oncologists (47.6%), who primarily referred patients with personal histories of cancer. OB/GYN and primary care physicians were the top referring physicians of individuals without a personal cancer history **(Figure 4)**. Almost half of all self referrals were patients with known familial mutations (256, 45.1% of self referrals).

Figure 5. Age at first visit in those with and without a personal history of breast and/or ovarian cancer, October 2007—March 2011

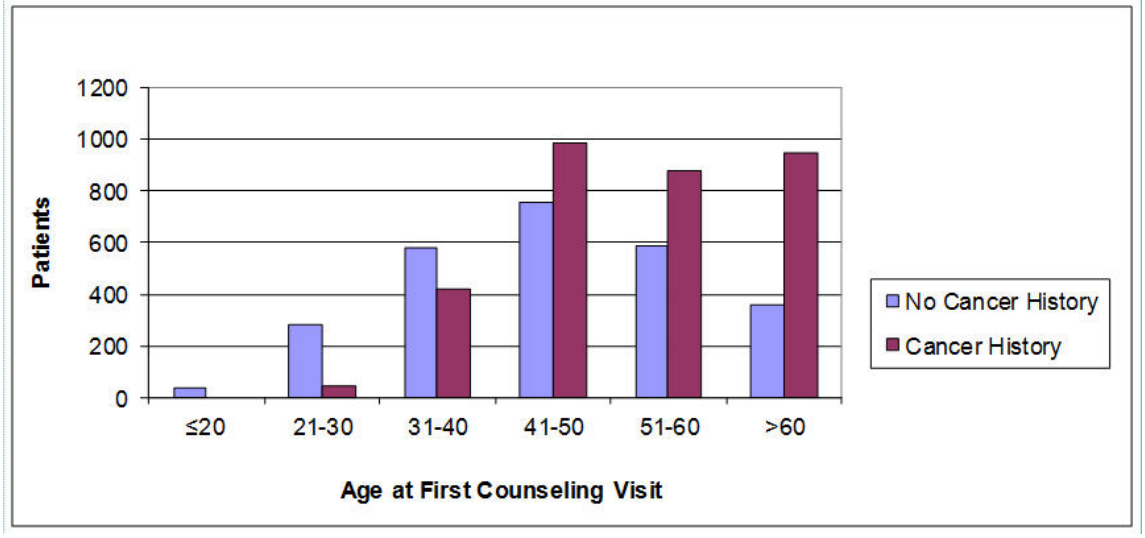
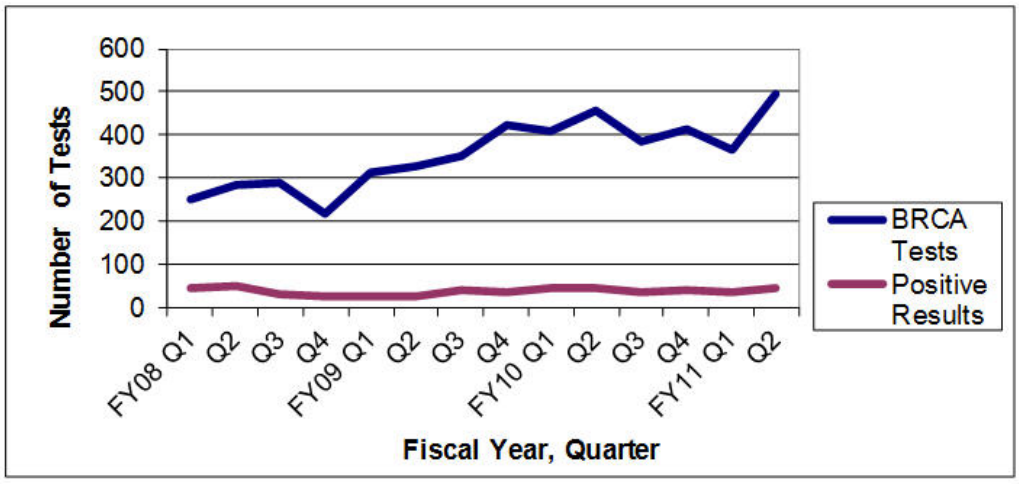


Figure 5 provides age distribution of the population by personal cancer history. Half (52.8%) of all patients seen for genetic counseling were age 50 or younger. The mean age at visit was 50.4 (± 13.3) years of age, and the median age was 50.0 years. The mean and median age for those without a personal cancer history was 46.0 (± 12.9) vs. a mean of 53.8 (± 12.5) and median of 52.0 years of age in those with a personal cancer history.

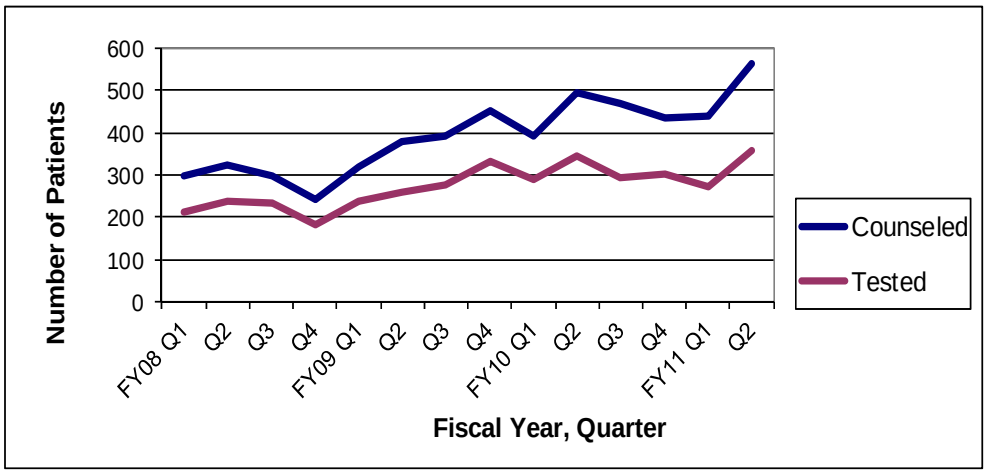
Clinical Database—Number of Tests

Figure 6. Number of *BRCA* tests per fiscal year quarter, October 2007—March 2011



These data represent *BRCA* tests ordered in conjunction with a visit to a board-certified genetics provider in Michigan from October 2007—March 2011. While the number of tests ordered appears to be increasing during this period, the number of tests with positive (deleterious) results remained relatively constant **(Figure 6)**. Site specific tests for known familial mutations remained steady over time and closely mirrored the number of positive results (data not shown).

Figure 7. Number of patients receiving *BRCA* genetic counseling and subsequent testing per fiscal year quarter, October 2007 through March 2011



Both the number of patients counseled and the number of patients proceeding with *BRCA* testing in conjunction with their counseling visit(s) increased from October 2007—March 2011 **(Figure 7)**. However, the proportion of patients counseled who received subsequent testing dropped slightly during this time. Comparing the increase in the number of tests with the increase in the number of patients tested, the average number of tests per patient (for example, adding the BART test for large rearrangements) has also increased slightly from approximately 1.2 to 1.4 tests per person tested.

Table 13. *BRCA* Testing Results by Personal History of Cancer, USPSTF Family History Criteria, October 2007—March 2011						
Mutation Status	Personal Cancer History*			No Personal History*‡		Known Familial Mutation
	Ovarian cancer	Breast cancer at ≤ 50 years	Breast cancer at > 50 years	Met USPSTF criteria	Did not meet USPSTF criteria	
Negative	153 (73.6)	1,352 (86.8)	676 (90.1)	432 (90.8)	301 (92.9)	345 (52.8)
Positive	44 (21.2)	135 (8.7)	29 (3.9)	23 (4.8)	8 (2.5)	298 (45.6)
Variant	11 (5.3)	71 (4.6)	45 (6.0)	21 (4.4)	15 (4.6)	10 (1.5)
Total	208	1,558	750	476	324	653

* Excluding males and those with a known familial mutation

‡ No personal history of breast and/or ovarian cancer

NCCN guidelines recommend counseling and testing for women with ovarian cancer.[8] Counseling and testing for women with early-age-onset breast cancer is dependent on age, hormone receptor status and family history. As shown in **Table 13**, over 20% of women with a history of ovarian cancer at any age who received testing were found to have a deleterious *BRCA* mutation. In women with a personal history of breast cancer at or before the age of 50, 8.7% were positive for a deleterious mutation.

The USPSTF guidelines for genetic counseling referral are intended for women with a family history of cancer; the guidelines do not address personal cancer history.[3] USPSTF family history criteria are used here as an indicator of substantial family history. In women without a personal cancer history or known familial mutation who presented for counseling, those with a family history meeting these criteria had a higher rate of deleterious mutation (4.8%) than those without such a family history (2.5%).

According to both NCCN and USPSTF guidelines, those with known familial mutations should always be referred to counseling.[3,8] Patients with a first degree relative with a known mutation have a 50% probability of inheriting that mutation. In this cohort, 45.6% of patients with any relative with a known mutation tested positive for the family's known (deleterious) mutation.

Clinical Database—Characteristics of Tested Patients

Table 14. Characteristics of patients who had and did not have *BRCA* genetic testing after counseling, October 2007—March 2011

	Tested	Did Not Test	Chi-squared P-value
	Number (row %)	(row %)	
Gender			< 0.01
Female	3,803 (69.7)	1,655 (30.3)	
Male	219 (77.1)	65 (22.9)	
Race/Ethnicity			< 0.01*
White	3,333 (72.3)	1,277 (27.7)	
Black	244 (57.1)	183 (42.9)	
Multi-racial	243 (61.4)	153 (38.6)	
Asian / Pacific Islander	76 (71.0)	31 (29.0)	
Arab Ancestry	63 (63.6)	36 (36.4)	
Hispanic	33 (58.9)	23 (41.1)	
Native American	2 (25.0)	6 (75.0)	
Other	10 (90.9)	1 (9.1)	
Unknown	17 (60.7)	11 (39.3)	
Ashkenazi Jewish Heritage			< 0.01
No	3,524 (68.1)	1,653 (31.9)	
Yes	498 (87.8)	69 (12.2)	
Known Familial Mutation			< 0.01
No	3,386 (67.0)	1,670 (33.0)	
Yes	636 (92.4)	52 (7.6)	
Family History Defined by USPSTF			0.04
No	2,303 (69.0)	1,035 (31.0)	
Yes	1,719 (71.5)	687 (28.6)	
Personal Cancer History‡			<0.01
No	1,396 (55.2)	1,132 (44.8)	
Yes	2,626 (81.7)	590 (18.4)	

Of the 5,744 who presented to counseling without previous *BRCA* genetic testing, 4,022 (70.0%) had subsequent *BRCA* testing. A total of 1,722 (30.0%) did not proceed with testing.

As shown in **Table 14**, patients with the risk factors of a family history of cancer, personal cancer history, Ashkenazi Jewish heritage, or a known familial mutation are more likely to pursue testing than patients without those risk factors.

There are also differences in testing by race/ethnicity. Over 70% of white and Asian/Pacific Islander patients had *BRCA* testing, compared to less than 60% of black and Hispanic patients. Arab and multi-racial patients pursued testing in just over 60% of cases.

* Fisher's exact test

‡ Personal history of breast and/or ovarian cancer

Clinical Database—Reasons For Declining Test

Table 15. Reasons for declining *BRCA* genetic testing after receiving genetic counseling, October 2007—March 2011	
	Patients
	Number (%)
Not the best test candidate	477 (29.2)
Not clinically indicated	436 (26.7)
Inadequate insurance coverage	243 (14.9)
Other	116 (7.1)
Discuss options with relatives	80 (4.9)
Not a good time	71 (4.4)
Reassured by risk assessment	50 (3.1)
Does not meet Medicare criteria	45 (2.8)
Does not want to know	45 (2.8)
Test co-pay too costly	30 (1.8)
Patient sees no benefit	20 (1.2)
Arrange life/disability insurance	19 (1.2)
Total	1,632

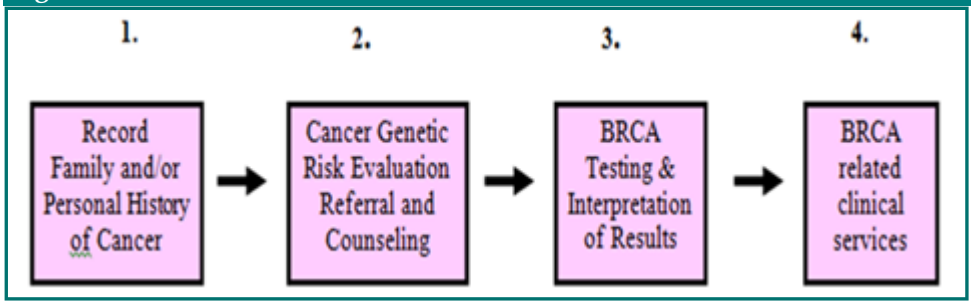
Of the 1,722 patients who presented to counseling and did not have *BRCA* testing, a reason for not testing was provided for 1,632 (94.8%). These reasons were selected from a menu of 12 categories (**Table 15**). Among these patients, the top three reasons for not pursing testing included not being the best test candidate in their family (29.2%), testing was not clinically indicated (26.7%), and inadequate insurance coverage (14.9%). These data demonstrate the importance of: 1) avoiding inappropriate *BRCA* testing through genetic counseling and risk assessment prior to testing; 2) the need for guidelines that emphasize *BRCA* testing for an affected relative prior to testing unaffected relatives; and 3) inadequate insurance coverage as a barrier for many patients who would benefit from such testing.

Future Steps for Cancer Genomics in Michigan

The Education and Awareness Requires Learning Young (EARLY) Act, section 10413 of the Patient Protection and Affordable Care Act (Public Law 111-148), authorizes the Centers for Disease Control and Prevention (CDC) to develop initiatives to increase knowledge of breast health and breast cancer among women, particularly among those under the age of 40 and those at heightened risk for developing the disease. [12]

As part of two new funding awards from the CDC, MDCH and its partners will focus on YBCS and enhancing cancer genomics best practices throughout Michigan. Through a cooperative agreement with the CDC Division of Cancer Prevention and Control (DCPC), the MDCH Cancer Genomics Program will strive to enhance breast cancer genomic practices through health plan policy, education, and surveillance. MDCH proposed a multifaceted project from 2011-2014 to promote the appropriate translation of "*BRCA* Clinical Services" into practice **(Figure 8)**. MDCH will promote health plan policy development to increase coverage of all clinical genetic services policies for high risk women including: 1) family history collection, risk assessment and referral; 2) genetic counseling; 3) genetic testing; and 4) *BRCA*-related clinical services (such as breast MRI imaging, mammography, and prophylactic oophorectomy). MDCH will also partner with key health plans to increase provider knowledge through health plan provider alert systems and will expand statewide surveillance of genetic counseling and testing coverage for the *BRCA* clinical services.

Figure 8. *BRCA* Clinical Services



MDCH will continue to support the *BRCA* Clinical Genetic Counseling Database and will create an online data collection system for our clinical network to streamline data submission.

Finally, the CDC DCPC also announced in October 2011 that the University of Michigan Prevention Research Center with the University of Michigan School of Nursing, School of Medicine and School of Public Health in partnership with the MDCH Cancer Genomics Program were awarded a 3-year cooperative agreement aimed at increasing appropriate breast cancer screening utilization among young breast cancer survivors and their at-risk family members. This study will utilize the MCSP registry and include a mail survey to 3000 YBCS and recruitment of up to 2 female relatives per survivor; with similar contact and consent processes to the previous YBCS mail survey to 500 survivors. This project will focus on counties with the highest mortality rates from young breast cancer diagnoses as well as oversample the African American population, which currently has a higher mortality rate from breast cancer diagnosed at a young age; issues we could not address in our previous work.

References

1. Testing for Hereditary Cancer Predisposition Syndromes and Genetic Counseling. Position Statement by the Michigan Cancer Genetics Alliance and Michigan Cancer Consortium, 2009. Retrieved May 2012 from www.michigancancer.org/PDFs/Genetics/PositionStatement-TestgHereditaryCaPredispSyndromesGenCounselg.pdf.
2. Nancie Petrucelli, MS, Mary B Daly, MD, PhD, and Gerald L Feldman, MD, PhD, FACMG. *BRCA1* and *BRCA2* Hereditary Breast and Ovarian Cancer (last updated January 20, 2011). *Gene Reviews.* Retrieved April 2012 from http://www.ncbi.nlm.nih.gov/sites/GeneTests/review?db=GeneTests.
3. U.S. Preventive Services Task Force: Genetic Risk Assessment and *BRCA* Mutation Testing for Breast and Ovarian Cancer Susceptibility: Recommendation Statement. Ann Intern Med 2005; 143(5):355-361.
4. Healthy People 2020 Summary of Objectives, retrieved August 2011, from http://www.healthypeople.gov/2020/topicsobjectives2020/pdfs/HP2020objectives.pdf.
5. Recommendations from the EGAPP Working Group: genetic testing strategies in newly diagnosed individuals with colorectal cancer aimed at reducing morbidity and mortality from Lynch syndrome in relatives. Gen in Med 2009; 11 (1): 35-41.
6. List of Preventive Services Covered Under the Affordable Care Act: 22 Covered Preventive Services for Women, retrieved July 2012 from http://www.healthcare.gov/news/factsheets/2010/07/preventive-services-list.html#CoveredPreventiveServicesforWomenIncludingPregnantWomen.
7. American College of Surgeons Commission on Cancer "Cancer Program Standards 2012: Ensuring Patient-Centered Care." Retrieved May 2012 from http://www.facs.org/cancer/coc/cocprogramstandards2012.pdf.
8. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology. "Genetic/Familial High-Risk Assessment: Breast and Ovarian." Version 1.2012. Retrieved June 2012, from http://www.nccn.org/index.asp.
9. Michigan Genetic Test; informed Consent Act 29 of 2000, amendment to the Michigan Public Health Code (Act 368 of 1978). Accessed April 2012 from http://www.legislature.mi.gov/(S(wytoezzx0f0klo45ttw0to45))/mileg.aspx?page=getobject&objectname=mcl-333-17020.
10. National Cancer Institute SEER Training Modules: Topography, accessed June 2012 from http://training.seer.cancer.gov/coding/guidelines/topography.html.
11. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology. "Breast Cancer Risk Reduction." Version 1.2012. Retrieved July 2012, from http://www.nccn.org/index.asp.
12. Patient Protection and Affordable Care Act of 2010, public law 111-148, 111th Cong., 2d session, 2010.
13. Riley, BD, Culver, JO, Skrzynia, C, Senter, LA, Peters, JA, Costalas, JW, Callif-Daley, F, Grumet, SC, Hunt, KS, Nagy, RS, McKinnon, WC, Petrucelli, NM, Bennet, RL, & Trepanier, AM. Essential Elements of Genetic Cancer Risk Assessment, Counseling, and Testing: Updated Recommendations of the National Society of Genetic Counselors. J Genet Counsel 2012; 21:151-161.

Appendix A: BRCA Genetic Counseling and Risk Assessment

The purposes of *BRCA* genetic counseling are to educate women and families about their chance of developing cancer; the implications that personal and family history can have on risk; help them obtain personal meaning from cancer genetic information; empower them to make educated and informed decisions regarding genetic testing; cancer, screening, and cancer prevention, and help them interpret genetic test results.[7,13] Cancer genetic counseling is often provided by a board certified genetic counselor (MS, CGC) or other cancer genetics professional with experience and educational background in genetics.[7]

When a woman's family history points to the possibility of an inherited gene change running in the family, she can be made aware of her susceptibility to future breast and ovarian cancer. With this knowledge she can take the necessary precautions, which may include more frequent mammograms and close monitoring, prophylactic surgery, and notifying other at-risk blood relatives.

A personal history of breast cancer at a young age or with certain pathology findings increases a woman's risk of having HBOC. In addition, having a family history of breast or ovarian cancer increases a woman's risk for cancer and can be an indicator that a *BRCA* mutation may be present in the family. In the case of a strong personal or family history, genetic counseling and testing should be recommended for patients to determine cancer risk as well as assess the risk that she may carry an inherited gene change.[3,8] For cases of inherited breast and ovarian cancer, family history is often the best way to determine an unaffected relative's risk of having the condition. Certain combinations of cancer occurrence in a woman's immediate and extended families have shown clinical relevance in determining this risk, highlighted by the USPSTF Grade B Recommendation statement for genetic counseling referral.

Appendix B: BRCA1 and BRCA2 Genetic Testing to Determine Hereditary Cancer Risk

Genetic testing for HBOC searches an individual's DNA for mutations in the *BRCA* genes. Individuals who inherit a deleterious, cancer-related mutation in one of these genes have substantial increased risks for developing breast and ovarian cancer, often at young ages.[2] These gene changes and their associated cancer risks can be passed on in a family from one generation to the next (50% risk to first degree relatives of a carrier individual).[2] *BRCA* gene testing can help patients and physicians decide on possible prevention and surveillance plans by refining cancer risk. In addition to cancer surveillance, these tests help patients and physicians make medical management decisions about risk reducing strategies. For example, women with a *BRCA* mutation may choose to have their breast tissue or ovaries completely removed as part of their cancer treatment or prior to an initial diagnosis of cancer. *BRCA 1* and *BRCA 2* results can be positive for a known deleterious mutation, negative for any gene change, or show a variant of uncertain significance (meaning a change is found but it is unclear whether or not that specific gene change increases the risk of cancer).

There are multiple different tests carried out for HBOC; each test method examines the *BRCA* genes in a different way. [2] Comprehensive Testing involves gene sequencing which looks at the entire length of both *BRCA1 and BRCA2* and a 5-site rearrangement panel which looks for specific large-scale rearrangements (costing over $3000).[2] Single site testing looks for one specific gene mutation when the mutation in the family has already been identified (cost ~ $475).[2] A Multisite Panel looks for three specific gene changes common among those of Ashkenazi Jewish ancestry (cost ~ $575).[2] Finally, the BRCA Rearrangement Test or BART looks for large-scale rearrangements within the *BRCA* genes that would not have been detected through comprehensive testing (cost ~ $700).[2]

Appendix C: USPSTF Suggested Family History Criteria[3]

Women whose family history is associated with an increased risk for deleterious mutations in *BRCA1* or *BRCA2* can be characterized by one or more of the following:

- 2 first-degree relatives* with breast cancer; 1 diagnosed at age 50 or younger.
- A combination of 3 or more first- or second-degree relatives** with breast cancer diagnosed at any age.
- A combination of both breast and ovarian cancer among first- and second-degree relatives.
- A first-degree relative with bilateral breast cancer.
- A combination of 2 or more first- or second-degree relatives with ovarian cancer, diagnosed at any age.
- A first- or second-degree relative with both breast and ovarian cancer diagnosed at any age.
- A male relative with breast cancer diagnosed at any age.
- Ashkenazi Jewish heritage, with a first-degree relative (or two second-degree relatives on the same side of the family) with breast or ovarian cancer diagnosed at any age.

* First-degree relatives include parents (mother/father), siblings (brother/sister), or children (sons/daughters)

** Second-degree relatives include both maternal and paternal grandparents, aunts, uncles, half brothers, half sisters, nieces, nephews, and grandchildren.

Appendix D: American College of Surgeons—Commission on Cancer Excerpt from the 2012 Cancer Program Accreditation Standards[7]

Standard 2.3 Risk Assessment and Genetic Counseling

Genetics professionals include the following:

- An American Board of Genetic Counseling (ABGC) or American Board of Medical Genetics (ABMG) board-certified/board-eligible or (in some states) a licensed **genetic counselor**
- An American College of Medical Genetics (**ACMG**) board certified **physician**
- A **Genetics Clinical Nurse** (GCN) or an **Advanced Practice Nurse in Genetics** (APNG), credentialed through the Genetics Nursing Credentialing Commission (GNCC). Credentialing is obtained through successful completion of a professional portfolio review process.
- An advanced practice oncology nurse who is prepared at the graduate level (master or doctorate) with specialized education in cancer genetics and hereditary cancer predisposition syndromes*; certification by the Oncology Nursing Certification Corporation is preferred.
- A board-certified physician with experience in cancer genetics (defined as providing cancer risk assessment on a regular basis).

**Please note, specialized training in cancer genetics should be ongoing; educational seminars offered by commercial laboratories about how to perform genetic testing are not considered adequate training for cancer risk assessment and genetic counseling.*

Appendix E: 2012 National Comprehensive Cancer Network (NCCN) Criteria for Further Genetic Risk Evaluation[a] available from www.nccn.org[8]

Referral to a cancer genetics professional is recommended for individuals who meet the NCCN criteria summarized below:

An affected individual with one or more of the following:

- Early-age-onset breast cancer [b]
- Triple negative (ER-, PR-, HER2-) breast cancer
- Two breast cancer primaries [c] in a single individual
- Breast cancer at any age, and
  - ⇒ ≥ 1 close blood relative [d] with breast cancer ≤50y, or
  - ⇒ ≥ 1 close blood relative [d] with epithelial ovarian cancer at any age, or
  - ⇒ ≥ 2 close blood relatives [d] with breast cancer and/or pancreatic cancer at any age
  - ⇒ From a population at increased risk [f]
- A combination of breast cancer with one or more of the following: thyroid cancer, sarcoma, adrenocortical carcinoma, endometrial cancer, pancreatic cancer, brain tumors, diffuse gastric cancer [g], dermatologic manifestations [h] and/or macrocephaly, or leukemia/lymphoma on the same side of the family (especially if early onset)
- Ovarian [e] cancer
- Male breast cancer

An unaffected individual with one or more of the following:

- ≥ 2 breast primaries, either in 1 individual or 2 different individuals from the same side of the family (maternal or paternal)
- ≥ 1 ovarian [e] cancer primary from the same side of the family (maternal or paternal)
- First- or second-degree relative with breast cancer ≤ 45 y
- A combination of breast cancer with one or more of the following: thyroid cancer, sarcoma, adrenocortical carcinoma, endometrial cancer, pancreatic cancer, brain tumors, diffuse gastric cancer [g], dermatologic manifestations [h] and/or macrocephaly, or leukemia/lymphoma on the same side of the family (especially if early onset)
- Male breast cancer

[a] The criteria for further risk evaluation and genetic testing are not identical. For the purposes of the NCCN guidelines, invasive and ductal carcinoma in situ cancers should be included. The maternal and paternal sides of the family should be considered independently for familial patterns of cancer.

[b] Clinically use age ≤ 50 y because studies define early onset as either ≤ 40 y or ≤ 50 y.

[c] Two breast primaries includes bilateral (contralateral) disease or two or more clearly separate ipsilateral primary tumors either synchronously or asynchronously.

[d] Close blood relatives include first-, second-, and third-degree relatives.

[e] For the purposes of the NCCN guidelines, fallopian tube and primary peritoneal cancers are included.

[f] For populations at increased risk, requirements for inclusion may be modified (eg, women of Ashkenazi Jewish descent with breast and ovarian cancer at any age).

[g] For lobular breast cancer with a family history of diffuse cancer, CDH1 gene testing should be considered.

[h] For dermatologic manifestations, visit www.nccn.org to learn more about Cowden syndrome testing.

[i] Genetic counseling is highly recommended when genetic testing is offered and after results are disclosed. A genetic counselor, medical geneticist, oncologist, surgeon, oncology nurse, or other health professional with expertise and experience in cancer genetics should be involved early in counseling patients who potentially meet criteria for an inherited syndrome.

Appendix F: 2012 National Comprehensive Cancer Network (NCCN) Hereditary Breast and/or Ovarian Cancer (HBOC) Syndrome Testing Criteria summarized from www.nccn.org[8]

Genetic testing of the *BRCA1/2* genes may be considered for those who meet the NCCN criteria summarized below :

- Individual from a family with a known deleterious *BRCA1* or *BRCA2* mutation
- Personal history of breast cancer [d] plus one or more of the following:
  - ⇒ Diagnosed age ≤ 45 y
  - ⇒ Diagnosed age ≤ 50y with ≥ 1 close blood relative
  - ⇒ Two breast primaries [g] when first breast cancer diagnosis occurred ≤ age 50 y
  - ⇒ Diagnosed age ≤ 60 y with a triple negative breast cancer
  - ⇒ Diagnosed age ≤ 50 y with a limited family history [c]
  - ⇒ Diagnosed at any age, with ≥ 2 blood relatives [e] with pancreatic cancer at any age
  - ⇒ Close male relative [e] with breast cancer
  - ⇒ For an individual of ethnicity associated with high mutation frequency (eg, Ashkenazi Jewish) no additional family history may be required [h]
- Personal history of epithelial ovarian [f] cancer
- Personal history of male breast cancer
- Personal history of pancreatic cancer at any age with ≥ 2 close blood relatives [e] with breast cancer and/or ovarian [f] and/or pancreatic cancer at any age
- Family history only

(testing of unaffected family members should only be considered when no affected family member is available and then the unaffected family member with the highest probability of mutation should be tested. Significant limitations of interpreting results should be discussed.)

- ⇒ First- or second-degree blood relative meeting any of the above criteria
- ⇒ Third-degree blood relative with breast caner [d] and/or ovarian [f] cancer with ≥ 2 close blood relatives [e] with breast cancer (at least one with breast cancer ≤ 50 y) and/or ovarian [f] cancer

[a] One or more of these criteria is suggestive of HBOC syndrome that warrants further personalized risk assessment, genetic counseling and management. The maternal and paternal sides should be considered independently. Other malignancies reported in some HBOC families include prostate and melanoma.

[b] Patients who have received an allogenic bone marrow transplant should not have molecular genetic testing via blood or buccal samples due to unreliable test results from contamination by donor DNA. If available, DNA should be extracted from a fibroblast culture. If this source of DNA is not possible, buccal samples can be considered, subject to the risk of donor DNA contamination.

[c] Individuals with limited family history, such as fewer than 2 first or second-degree female relatives or female relatives surviving beyond 45 years in either lineage, may have an underestimated probability of a familial mutation.

[d] For the purposes of the NCCN guidelines, invasive and ductal carcinoma in situ breast cancers should be included.

[e] Close blood relatives include first-, second-, and third-degree relatives.

[f] For the purposes of the NCCN guidelines, fallopian tube and primary peritoneal cancers are included. Ovarian/fallopian tube/primary peritoneal cancers are component tumors of hereditary non-polyposis colorectal cancer or Lynch syndrome.; be attentive for clinical evidence of this syndrome and visit www.nccn.org for NCCN colorectal cancer screening guidelines.

[g] Two breast primaries includes bilateral (contralateral) disease or two or more clearly separate ipsilateral primary tumors either synchronously or asynchronously.

[h] Testing for Ashkenazi Jewish founder-specific mutation(s), should be performed first. Full sequencing may be considered if ancestry also includes non-Ashkenazi Jewish relatives or other HBOC criteria is met. Founder mutations exist in other populations.

Appendix G: Surveillance Questions and Sources of Data

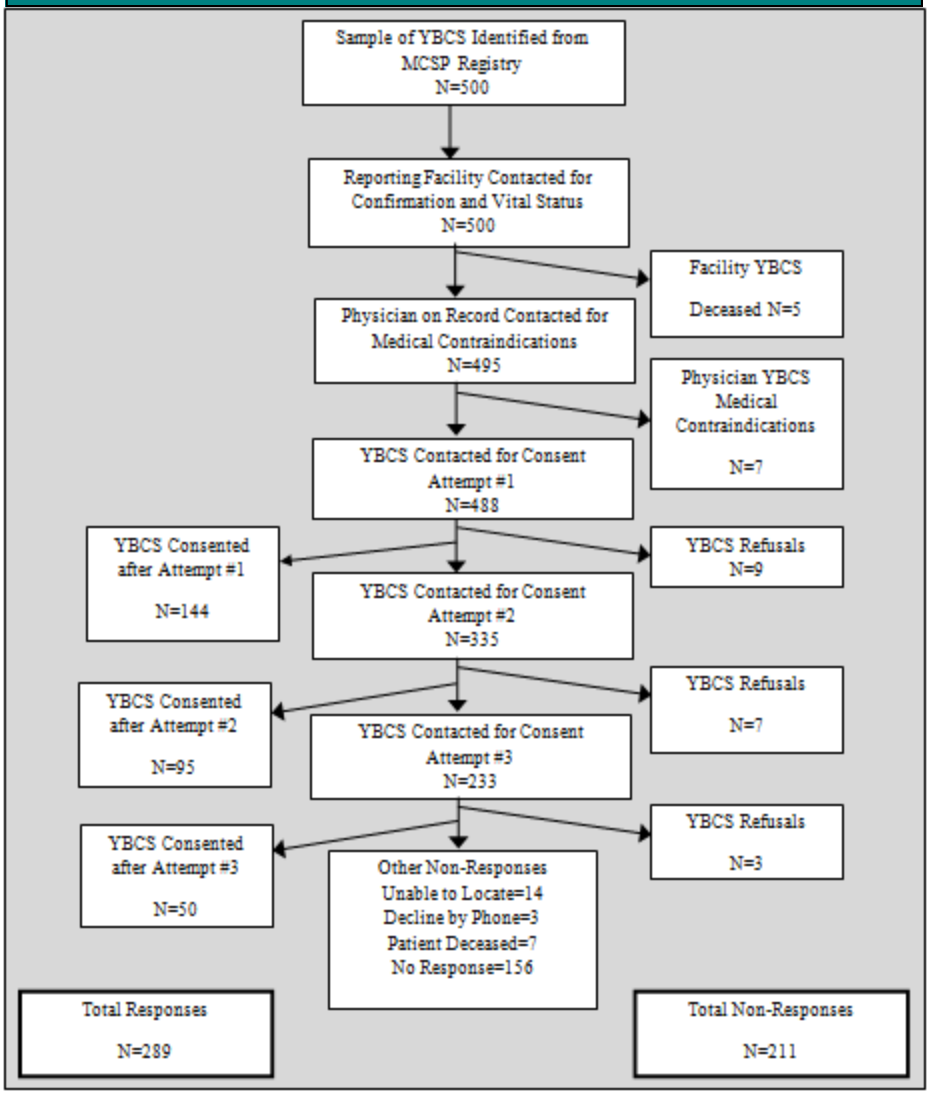
Surveillance Question	Behavioral Risk Factor Survey 2008-2009	Chart Abstractions	Young Breast Cancer Survivors Mail Survey	BRCA Clinical Database
What percent of adult women (with and without a personal history of breast and/or ovarian cancer) in Michigan have a significant family history of breast and/or ovarian cancer?	✓	✓	✓	✓
Are these women receiving genetic counseling?	✓		✓	
How does the percent of women with a family history receiving genetic counseling in Michigan compare to the Healthy People 2020 objective?	✓			
Who is receiving *BRCA* counseling and testing?	✓	✓	✓	✓
What are the most common referring provider types?				✓
What percentage of patients tested are found to have a known deleterious *BRCA* mutation?	✓	✓	✓	✓
What are the barriers and facilitators to receiving *BRCA* counseling and testing?	✓	✓	✓	✓

Appendix H: MCSP Survey Consent and Contact Process

As shown in **Figure 9**, five-hundred women were selected by simple random selection from the eligible population. The eligible population was selected from the Michigan Cancer Surveillance Program (MCSP) registry which has a mandate to collect data from local reporting facilities on all cases of cancer and other specified tumorous and precancerous diseases that occur in the state. The study team worked with MCSP staff to exclude women who were known to be deceased from the state vital records. Participants were identified as women diagnosed with breast cancer between 2006 and 2007 and before the age of 50 years.

The selection process consisted of three steps based on an existing standard method used by MCSP, the first of which was that MCSP notified the local reporting facility regarding the YBCS survey and requested information regarding the physician on record. MCSP then contacted the physician on record regarding the YBCS survey. Both were provided the potential study participant's name and asked whether they knew of any reason that the selected women should not be contacted such as death, mental illness, or illness due to current cancer treatments. If the local reporting facility and diagnosing physician did not object to MCSP contacting their patient, the participant was mailed the survey with up to three attempts. The respondent was asked to sign an informed consent attached to the survey. At all times, the participant's identifiable information was unavailable to the study team; only MCSP staff could identify the participants. Participants who returned a signed consent and survey were mailed a $10 gift card.

Figure 9. Flow chart of selection and consent process.



Appendix I: Young Breast Caner Survivors Survey Excerpt, Definition of Cancer Genetic Services

Cancer genetics services help patients to know if the cancer in their family might have been inherited (hereditary cancer). The visit often includes the following:

- Collection of medical and family history information
- The history is used to find out a patient's risk for cancer and the chance that the cancer in the family has an inherited cause (passed down in the family)
- The patient is given facts about inherited cancers and other causes of cancer
- The patient is told about genetic testing, pros and cons of testing, possible genetic test results and what each test result means for their future and for their family members.
- The patient is given information about ways they can screen for and reduce their risk of cancer
- Medical insurance coverage of genetic testing is talked about before a test is ordered
- The patient is given a choice to have or not have genetic testing. If they choose testing, they are helped with getting the test and understanding the results.

Acknowledgments

The Michigan Department of Community Health Genomics Program is grateful to the multitude of partners that have made these surveillance activities possible. We are thankful to the:

- Michigan Cancer Surveillance Program (MCSP) Director, Glenn Copeland, and the MCSP staff for their time and energy devoted to our various cancer genomics projects.
- MDCH Cancer Section for funding the 2008 and 2009 MiBRFS Breast and Cancer Family History, Genetic Counseling and Testing questions.
- Each of the *BRCA* clinical facilities for their devotion in providing data to the Cancer Genetic Counseling Database and for their expertise and patience in helping us develop our data sharing process.
- CDC Office of Public Health Genomics and CDC Division of Cancer Prevention and Control for funding this project and for providing endless guidance and support throughout the years.

Funding for this project was made possible by Cooperative Agreement #5U38GD000054 from the Centers for Disease Control and Prevention. The contents are solely the responsibility of the authors and do not necessarily represent the official views of CDC.