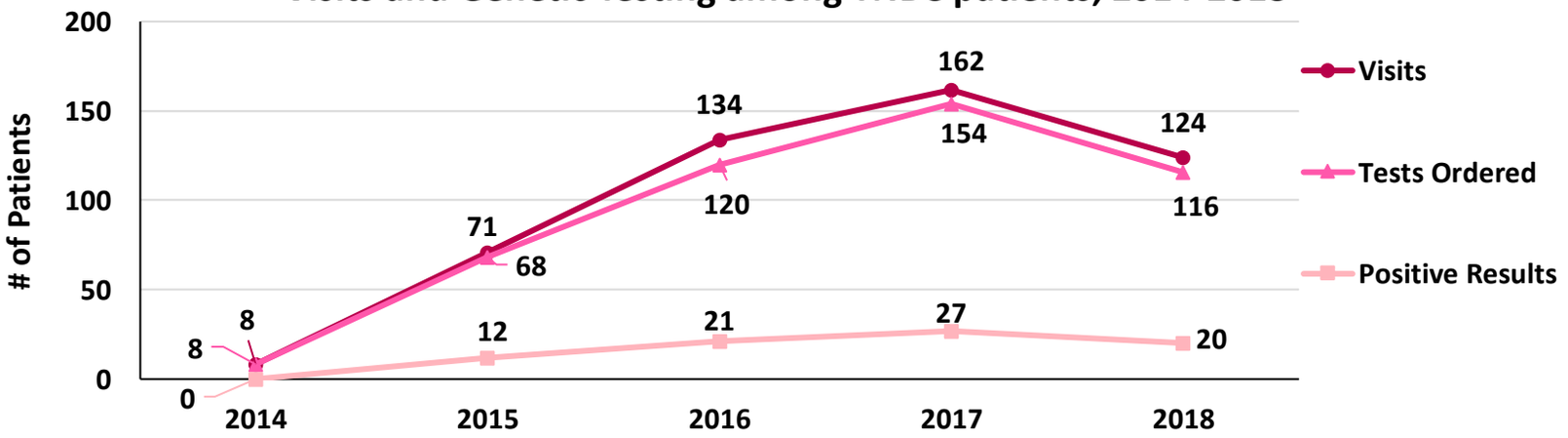
Triple Negative Breast Cancer (TNBC) and Genetic Testing from the Hereditary Cancer Network (HCN) Database, 2014-2018

Background: In the general population, the risk of breast cancer is 13%, and about 10% of breast cancer cases are considered hereditary.[1,2] These hereditary cases often involve an individual having a genetic mutation in either the *BRCA1 or BRCA2* genes, which increases the risk of having breast cancer to 40-87% and 27-84%, respectively.[3] These genes do not only increase the risk of breast cancer during one's lifetime, but also increases the risk for breast cancer at a young age and ovarian cancer.[4] Those with Triple Negative Breast Cancer (TNBC) may have a higher risk of inherited genetic changes and may be recommended for genetic counseling.[5] **Individuals diagnosed with TNBC at or under the age of 60 should be referred for genetic testing based on National Comprehensive Cancer Network (NCCN) guidelines for cancer genetic testing.**[6]

Methods: The following data were collected from the Michigan Department of Health and Human Services (MDHHS) Hereditary Cancer Network (HCN) database between **January 1, 2014, and December 31, 2018**. **During this time-frame, there were 499 individuals who identified as having Triple Negative Breast Cancer (TNBC)**. The HCN is a unique database that functions as a statewide surveillance network for tracking the use of cancer genetic counseling and testing services for 19 actionable genes that are associated with Hereditary Breast and Ovarian Cancer (HBOC) and Lynch syndrome (LS) cancers in Michigan. In order to be eligible to be entered into the database, patients must have received genetic counseling from one of the clinics that have partnered with the MDHHS*, which means data may not be representative of Michigan's TNBC population. Frequencies and chi-square analyses were performed between breast cancer patients with and without TNBC using SAS 9.4. Significant values were set at $p < 0.05$.

Please contact Jessica Fritzler at **FritzlerJ1@Michigan.gov** for any questions.

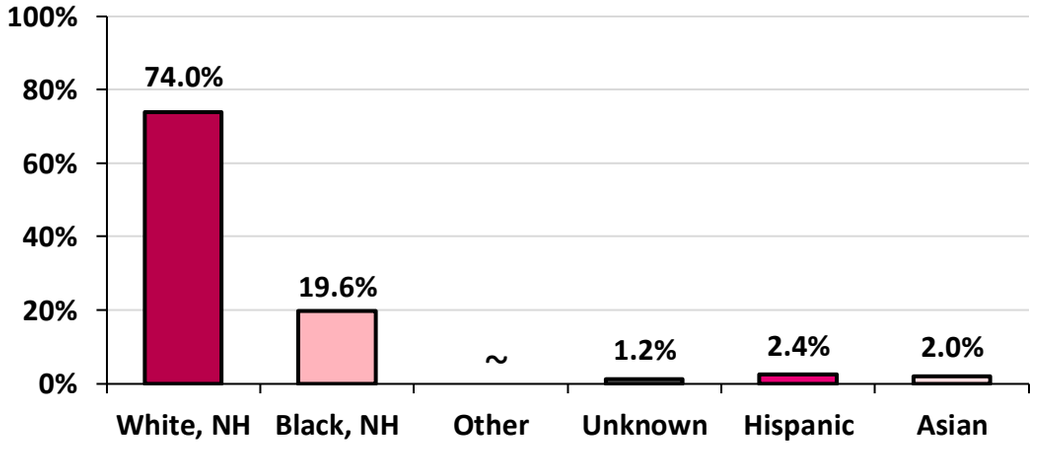
Visits and Genetic Testing among TNBC patients, 2014-2018



Gender, 2014-2018

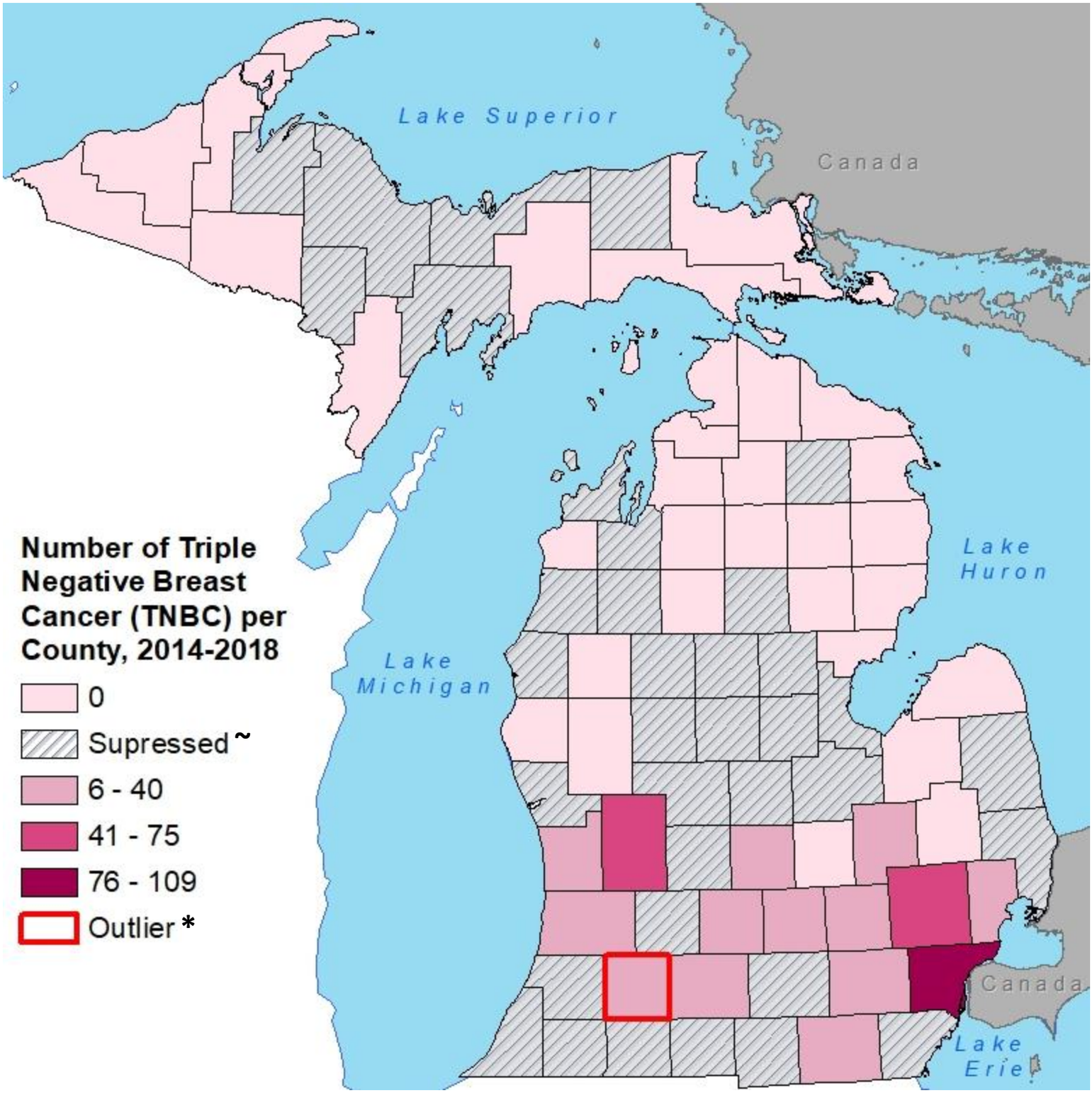
The majority of patients were **female.**

Race & Ethnicity, 2014-2018



* HCN Clinical Partners: Beaumont Cancer Genetics Program, Beaumont Center for Hematology and Oncology, Henry Ford Health System Cancer Genetics Program, Karmanos Cancer Institute Cancer Genetic Counseling Service, Informed DNA Telephone Genetic Counseling Services, Mid-Michigan Hereditary Cancer Clinic, Michigan State University Hereditary Cancer Program, Marquette General Hematology/Oncology, Munson Cancer Genetics Clinic, Sparrow Cancer Center, Spectrum Health Cancer Genetics Program, St. Joseph Mercy Hospital Cancer Genetics Program, St. John Providence Health System Cancer Genetics Program (Southfield and Grosse Pointe Woods, MI), St. Mary Health Care Lacks Cancer Center Genetics (Grand Rapids, MI), St. Mary Mercy Our Lady of Hope Cancer Center (Livonia, MI), University of Michigan Breast and Ovarian Cancer Risk and Evaluation Program, University of Michigan Cancer Genetics Clinic, West Michigan Cancer Center. ~ Data are suppressed if count is less than 6.

TNBC Patients by County, 2014-2018

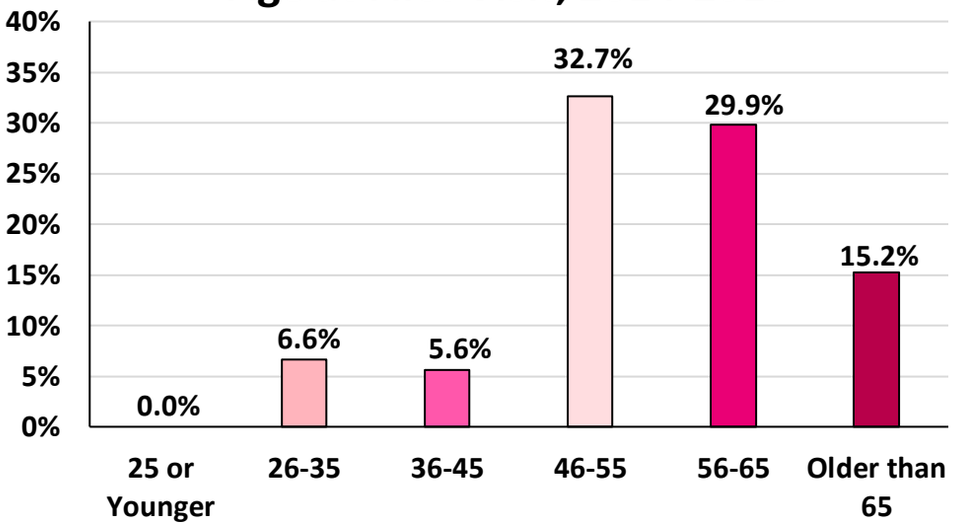


- The majority of TNBC patients from the HCN are located in Wayne County, followed by Ottawa and Kent counties.
- In Kalamazoo county, only 60% of TNBC patients who were seen for cancer genetic counseling received cancer genetic testing, which is much lower than most of the other counties in Michigan.

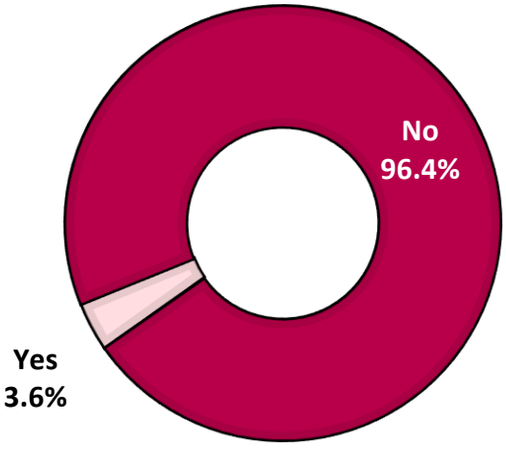
*Outliers refer to counties with an abnormally low percentage of patients receiving genetic testing compared to those who had pursued genetic counseling. Counties are considered outliers if the percentage of those who received genetic testing is less than the outlier cutoff of Q3 + (IQR*1.5), where Q3 refers to the third quartile, and IQR refers to the interquartile range (Q3-Q1). These counties are outlined in red in the maps. ~ Data are suppressed if count is less than 6.

TNBC and Demographics from the HCN Database, 2014-2018

Age at First Visit, 2014-2018

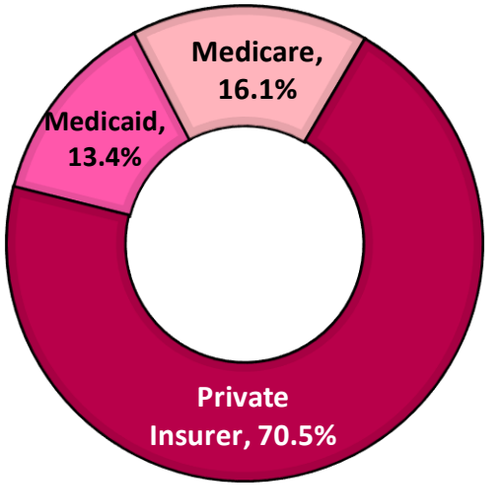


Known Familial Mutation, 2014-2018



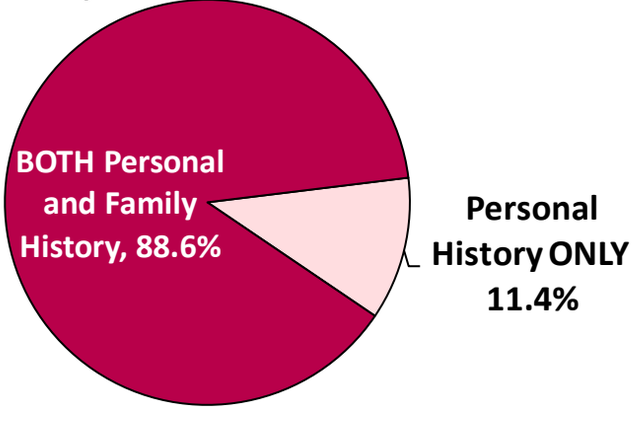
- Most TNBC patients in the database are between 46 and 55 years of age (**32.7%**) or between 56 and 65 years of age (**29.9%**).
- About **3.6%** of those with TNBC were aware that they had a known familial mutation (KFM) at their first visit.
- Most TNBC patients had insurance through a private insurer (**69.3%**), followed by Medicare (**15.8%**).
- Most TNBC patients had both a personal and family history of cancer (**88.6%**).
  - Breast cancer patients with TNBC were more likely to have only a personal history of cancer compared to breast cancer patients who did not have TNBC (**11.4% vs. 8.3%**).
  - Breast cancer patients with TNBC were less likely to have both a personal and family history of cancer compared to breast cancer patients who did not have TNBC (**88.6% vs. 91.4%**).

Insurance, 2014-2018



Twenty-two (**4.4%**) TNBC patients indicated that they had some '**other**' type of cancer, which was the highest among all cancer types reported by patients.

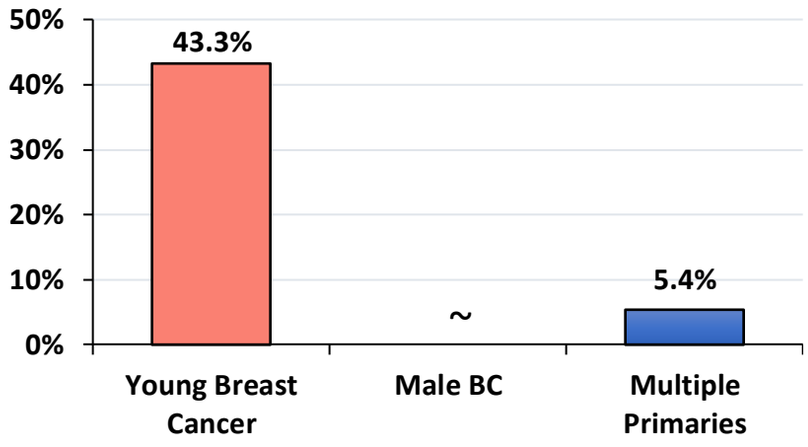
History of Cancer, 2014-2018



Eight (1.6%) TNBC patients indicated that they also had been diagnosed with **melanoma** (data not shown).

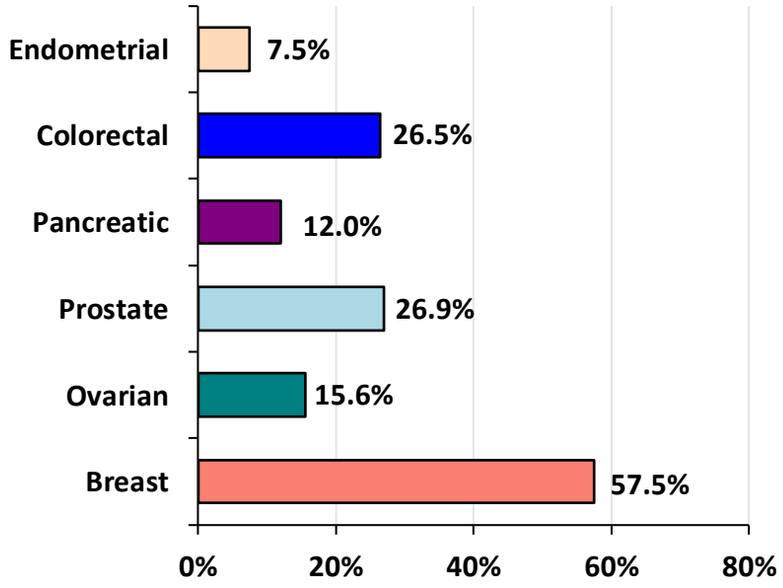
TNBC and History of Cancer from the HCN Database, 2014-2018

Breast Cancer Characteristics, 2014-2018 [a]

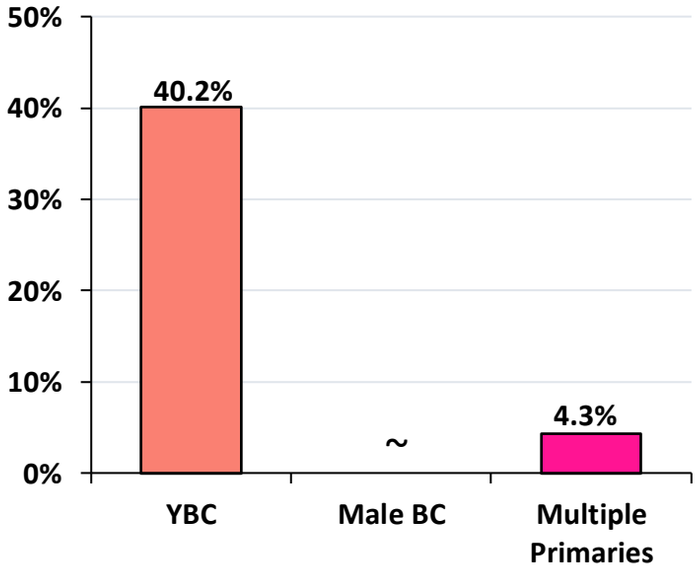


- **43.3%** of those with TNBC had a diagnosis occur at or before the age of 50.
  - Breast cancer patients who have TNBC were less likely to be diagnosed at a younger age compared to breast cancer patients without TNBC (**43.3% vs. 49.7%**).
- **5.4%** of those with TNBC also were diagnosed with multiple breast cancer primaries.
  - Breast cancer patients with TNBC were less likely to be diagnosed with multiple breast cancer primaries compared to breast cancer patients without TNBC (**5.4% vs. 9.9%**).

Type of Cancer among Family Members, 2014-2018 [b]



Breast Cancer among Relatives, 2014-2018 [c]

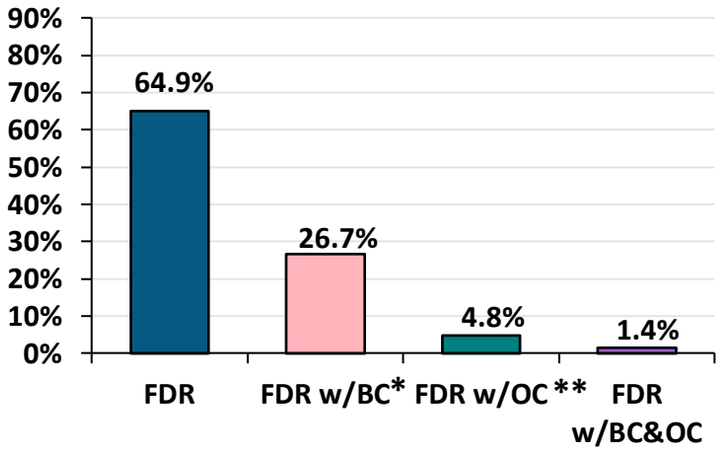


- Breast cancer patients with TNBC were less likely to have a relative diagnosed with breast cancer compared to breast cancer patients without TNBC (**57.5% vs. 71.2%**).
- **8.6%** of these patients have a family history of both breast and ovarian cancer (data not shown).
- Breast cancer patients with TNBC are less likely to have a relative with breast cancer diagnosed at a young age compared to breast cancer patients who do not have TNBC, but this difference is considered trending and is not statistically significant (**40.2% vs. 46.44%, p = 0.523**).

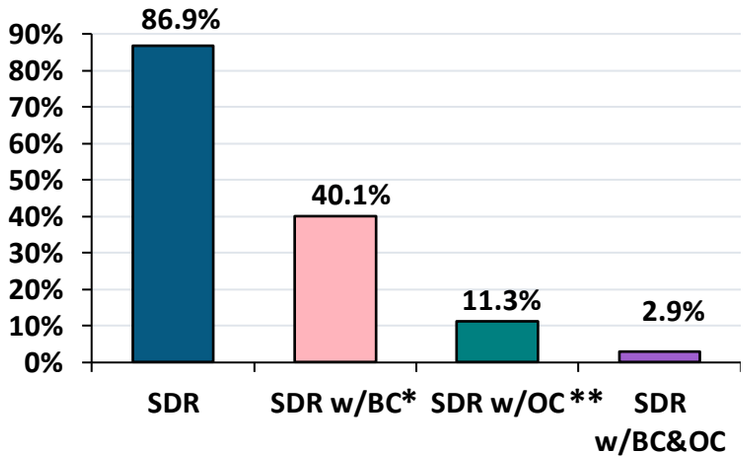
[a] Characteristics of breast cancer patients: Young Breast Cancer (YBC), Male Breast Cancer, and Multiple Primaries. [b] Type of cancer among family members of patients who have a family history of cancer. [c] Characteristics of breast cancer among family members: Young Breast Cancer (YBC), Male Breast Cancer (Male BC), and Multiple Primaries. ~ Data are suppressed when counts are less than 6.

TNBC and Family History of Cancer from the HCN Database, 2014-2018

First-Degree Relatives (FDR), 2014-2018

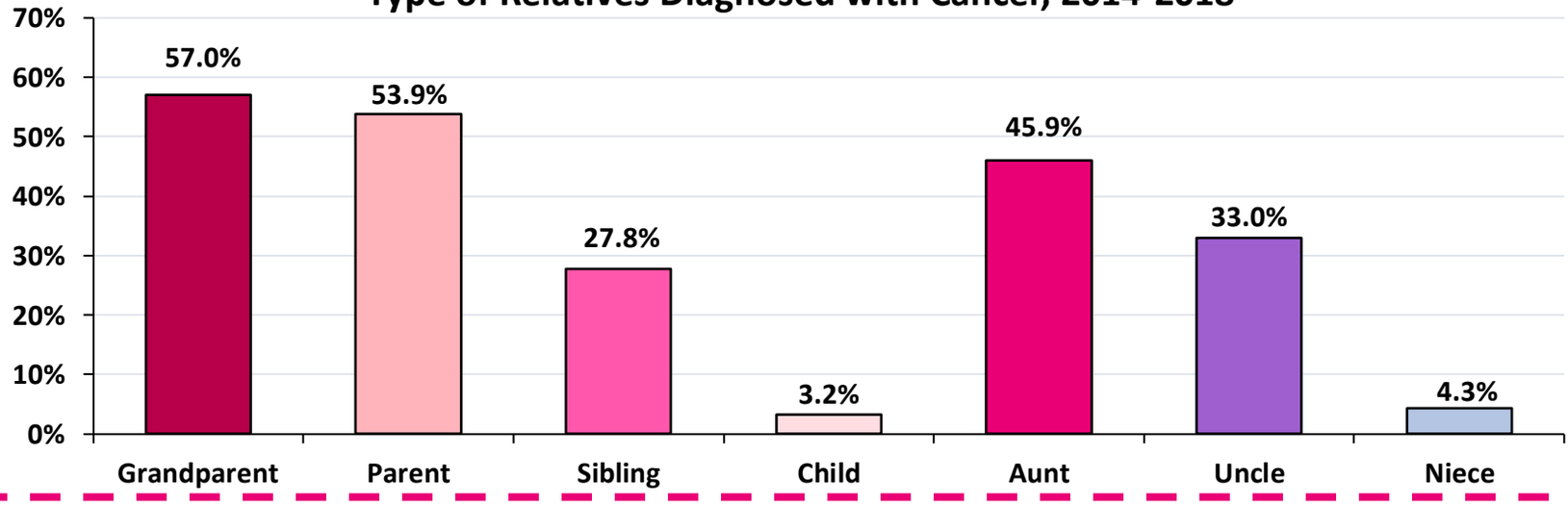


Second-Degree Relatives (SDR), 2014-2018



- Breast cancer patients with TNBC are less likely to have an FDR diagnosed with cancer compared to breast cancer patients who do not have TNBC (**64.9% vs. 76.8%**).
- Breast cancer patients with TNBC were more likely to have an SDR diagnosed with cancer compared to breast cancer patients who do not have TNBC (**86.9% vs. 82.9%**).
- Breast cancer patients with TNBC were less likely to have an FDR diagnosed with breast cancer compared to breast cancer patients without TNBC (**26.7% vs. 41.0%**) and less likely to have an SDR diagnosed with breast cancer (**40.1% vs. 46.9%**).
- Breast cancer patients with TNBC were more likely to have an SDR with ovarian cancer compared to breast cancer patients without TNBC (**11.3% vs. 8.6%**).

Type of Relatives Diagnosed with Cancer, 2014-2018

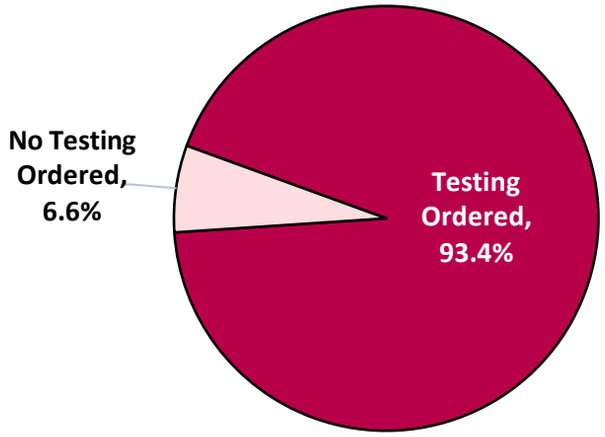


- Breast cancer patients with TNBC were less likely to have a parent diagnosed with cancer compared to breast cancer patients without TNBC (**53.9% vs. 62.3%**).
- Breast cancer patients with TNBC were less likely to have a sibling diagnosed with cancer compared to breast cancer patients without TNBC (**27.8% vs. 36.5%).**
- Breast cancer patients with TNBC were less likely to have a child diagnosed with cancer compared to breast cancer patients without TNBC (**3.2% vs. 5.5%).**
- Breast cancer patients with TNBC were less likely to have an aunt diagnosed with cancer compared to breast cancer patients without TNBC (**45.9% vs. 50.9%)**.

* BC = Breast Cancer. ** OC = Ovarian Cancer.

TNBC and Genetic Testing from the HCN Database, 2014-2018

Genetic Testing among TNBC Patients, 2014-2018

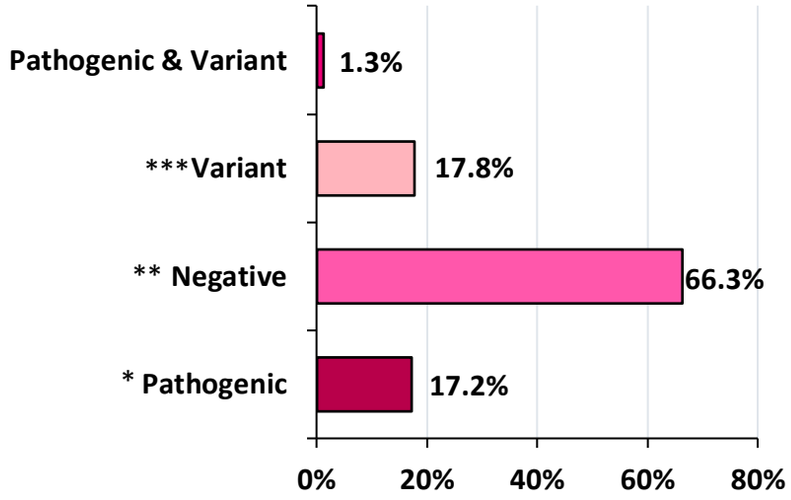


2.4% had Single Site Testing

2.8% ordered testing prior to counseling

Breast cancer patients with TNBC were more likely to receive genetic testing compared to breast cancer patients without TNBC, but this difference was not statistically significant (**93.4% vs. 91.0%, p = 0.069**).

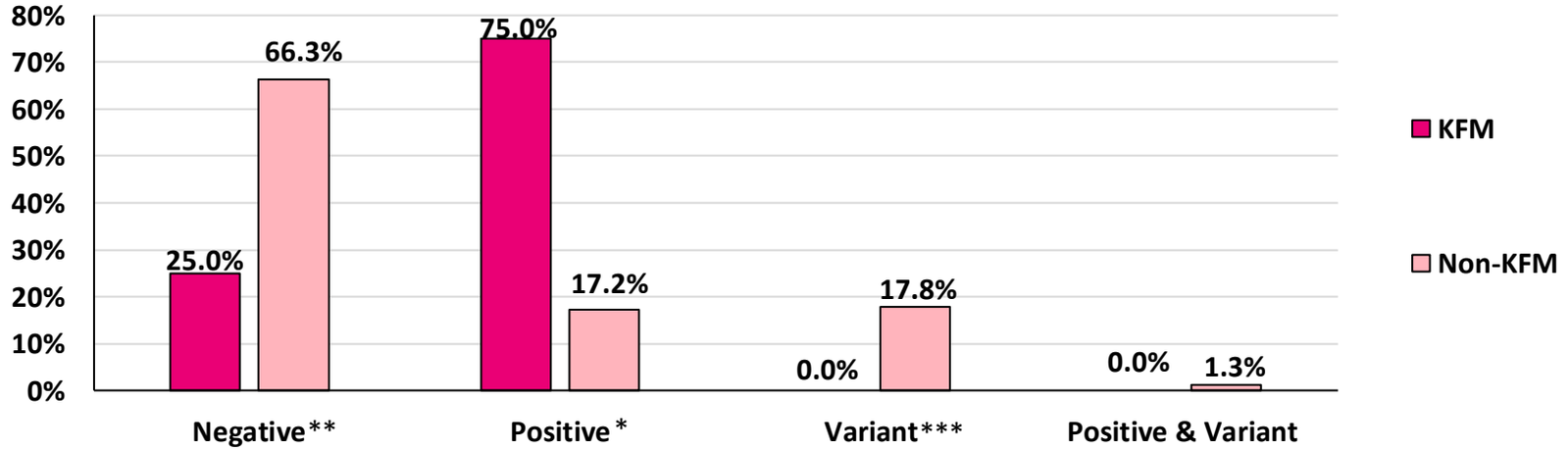
Genetic Test Results among TNBC Patients, 2014-2018



Breast cancer patients who had TNBC were more likely to have a positive result compared to breast cancer patients who did not have TNBC (**17.2% vs. 12.3%**).

When looking at specific genes, breast cancer patients with TNBC were more likely to have a pathogenic mutation in the BRCA1 gene (**48.8% vs. 17.5%**) and the RAD51C gene (**3.8% vs. 0.5%**) compared to breast cancer patients without TNBC (**data not shown**).

Genetic Test Results among TNBC Patients with and without a Known Familial Mutation (KFM), 2014-2018

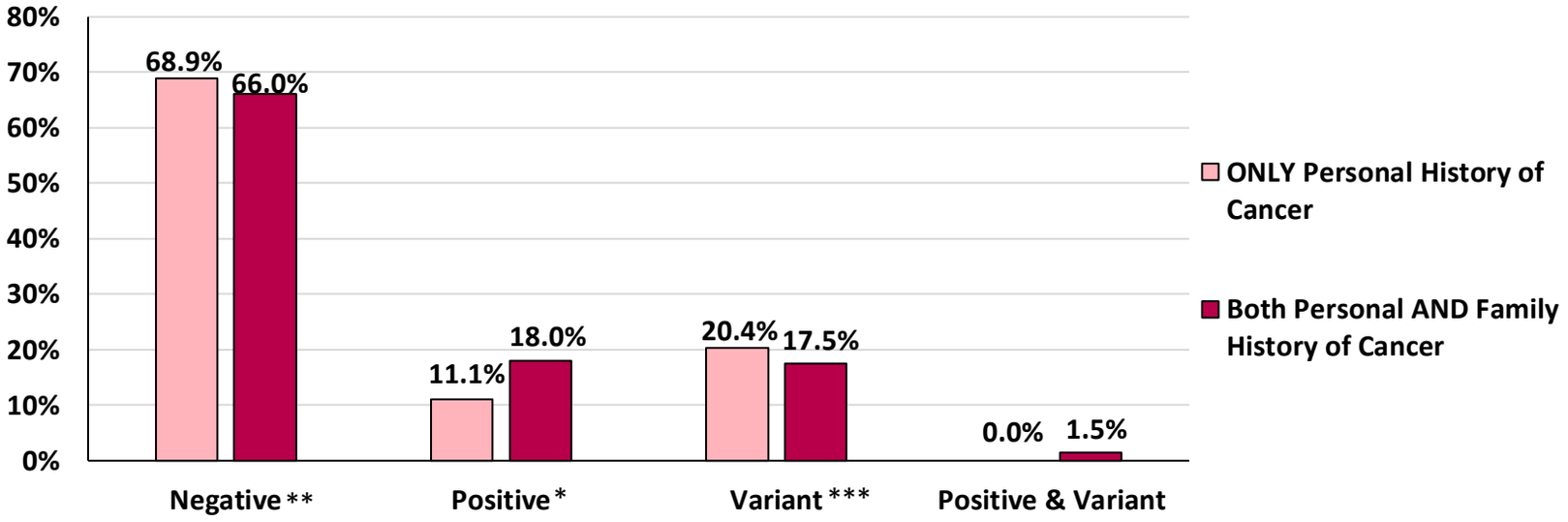


- Breast cancer patients with TNBC that have a KFM were statistically more likely to have a positive genetic test result compared to breast cancer patients with TNBC that do not have a KFM (**75.0% vs. 17.2%**).
- Breast cancer patients with TNBC that have a KFM were less likely to have a variant of uncertain significance compared to breast cancer patients of with TNBC that do not have a KFM (**0.0% vs. 18.4%**).

* Pathogenic/Positive result refers to a genetic test result being Pathogenic or Likely Pathogenic. ** Negative result refers to a genetic test result being Benign, Likely Benign or Not Clinically Significant. *** Variant result refers to a result that is classified as a Variant of Uncertain Significance (VUS).

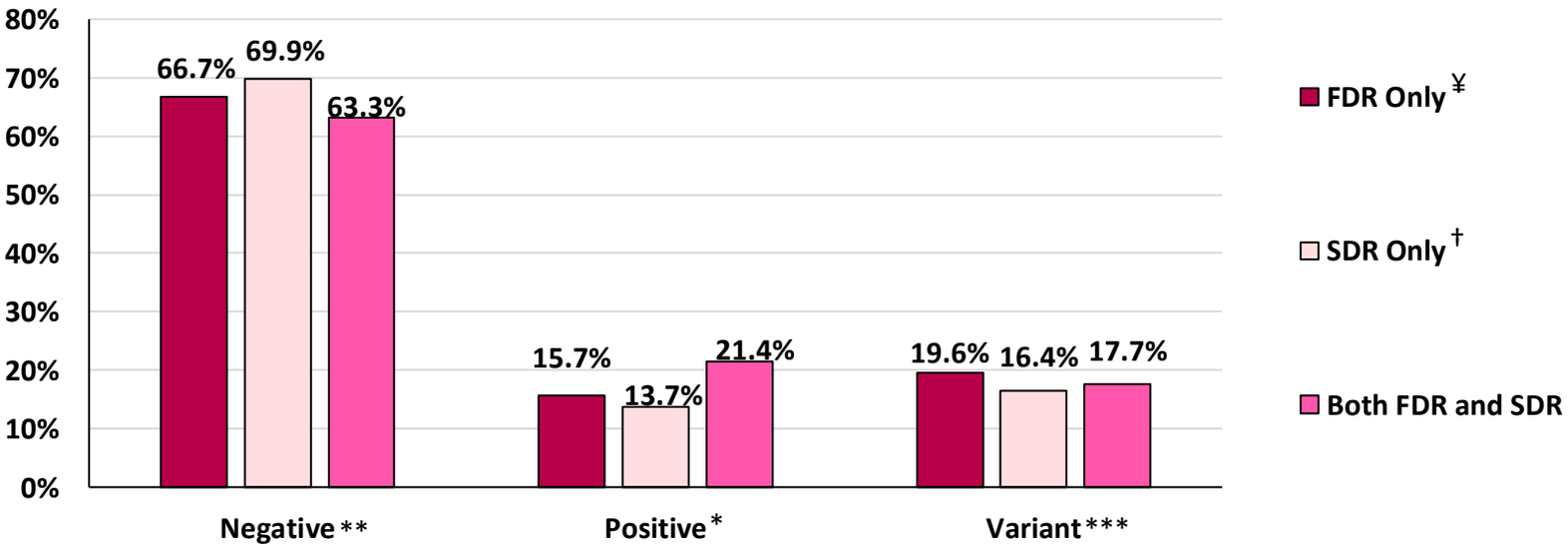
TNBC and Genetic Testing from the HCN Database, 2014-2018

Genetic Test Results among TNBC Patients with a Personal or Family History of Cancer, 2014-2018



- Among breast cancer patients with both a personal and family history of cancer, those with TNBC were more likely to have a positive test result compared to breast cancer patients without TNBC (**18.0% vs. 12.6%**).
- There were no statistically significant differences among those with only a personal history of cancer and their genetic testing results.

Genetic Test Results among TNBC Patients with a Family History of Cancer, 2014-2018



- Among those with both a personal and a family history of cancer, breast cancer patients with TNBC were statistically more likely to have a positive genetic test result compared to breast cancer patients without TNBC (**21.4% vs. 13.5%**).

* Pathogenic/Positive result refers to a genetic test result being Pathogenic or Likely Pathogenic. ** Negative result refers to a genetic test result being Benign, Likely Benign or Not Clinically Significant. *** Variant result refers to a result that is classified as a Variant of Uncertain Significance (VUS). ¥ FDR = First-degree relative. † SDR = Second-degree relative

TNBC and Select Characteristics the HCN Database, 2014-2018

Reason Why Genetic Testing Was Not Pursued among TNBC Patients from the HCN, 2014-2018

6.6% had no testing performed

Of those who did not receive genetic testing, the reason why testing was not pursued is for personal reasons (**21.2%**).

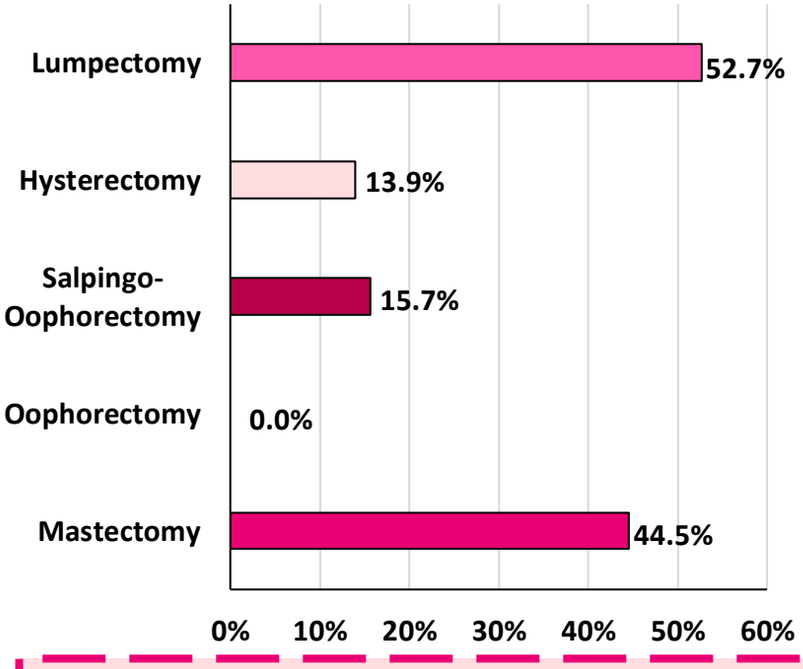
Surgeries from the HCN, 2014-2018

56.3% had surgery performed

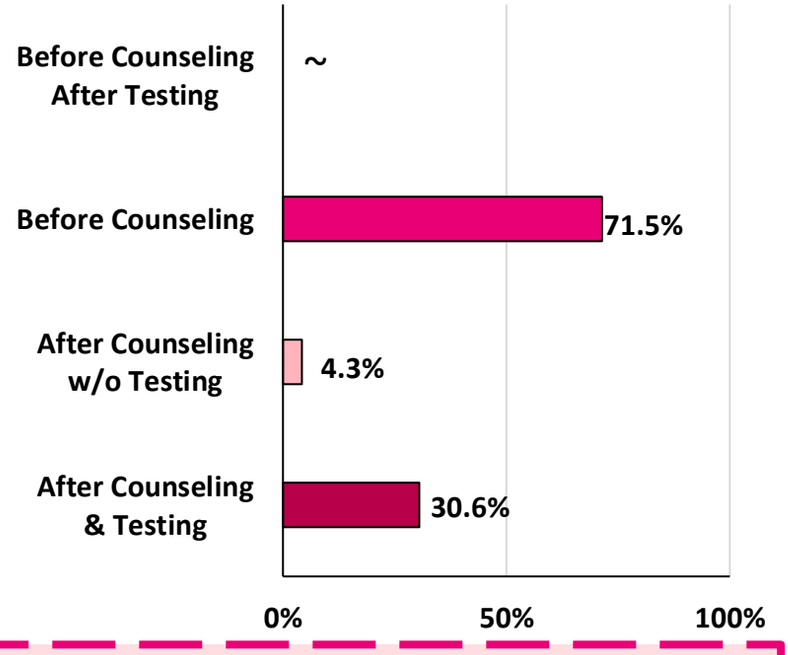
92.2% had surgery performed for cancer treatment

8.9% had surgery performed for prophylactic reasons

Types of Surgeries from the HCN, 2014-2018



Timings of Surgeries from the HCN, 2014-2018



- Among breast cancer patients who had a surgery performed, those with TNBC were more likely to have a surgery for prophylactic reasons compared to those without TNBC (**8.9% vs. 5.2%**).
- Among breast cancer patients who had a surgery performed, those with TNBC were more likely to have their surgery after counseling and testing compared to those without TNBC (**30.6% vs. 22.8%**).
- Among breast cancer patients who had a surgery performed, those with TNBC were less likely to have their surgery prior to counseling compared to those without TNBC (**71.5% vs. 78.1%**).

~ Data are suppressed if count is less than 6.

Discussion & Summary

- Even though NCCN guidelines indicate that individuals diagnosed with TBNC at or under the age of 60 receive genetic counseling and testing, there were still approximately **14%** of these individuals who did not pursue genetic testing.
  - The main reasons why these individuals did not pursue testing were due to personal reasons.
    - This indicates exploration needs to be done regarding the reasons why these individuals chose not to pursue testing.
- Breast cancer patients diagnosed with TNBC were not more likely to have a breast or ovarian cancer diagnosis compared to breast cancer patients without TNBC. However, there were **22 (4.4%).** TNBC patients who indicated that they also had melanoma, which was the highest among all cancer types reported by patients..
  - This may be evidence that more exploration should be done to compare genetic counseling and testing data between those with and without the dual diagnosis of TNBC and melanoma.
- Breast cancer patients with TNBC were more likely to have a second-degree relative diagnosed with ovarian cancer compared to breast cancer patients without TNBC.
- Breast cancer patients who had TNBC were more likely to have a positive cancer genetic test result compared to breast cancer patients who did have TNBC.
  - This indicates that it is especially important for these individuals to pursue genetic testing.
- Among the proportion of TNBC patients diagnosed at or over the age of 60, **84.0%** met guidelines by testing either through The United States Preventative Services Task Force (USPSTF) or NCCN based on other personal or family history criteria.
  - Of those who met guidelines, almost **90%** did pursue genetic testing.

For More Information:

Visit **Michigan.gov/HereditaryCancer** to learn more about hereditary cancers.
Visit **Michigan.gov/CGE** to view more data on hereditary cancers .

Cancer Genomics Hotline Phone #: 866 852 1247
Email: genetics@michigan.gov

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MDHHS
Michigan Department of Health & Human Services
GRETCHEN WHITMER, GOVERNOR | ELIZABETH HERTEL, DIRECTOR

References:

1. DeSantis et al. (2019). Breast cancer statistics, 2019. CA: A Cancer Journal for Clinicians, 69(6), 438-451.
2. Beitsch et al. (2019). Underdiagnosis of Hereditary Breast Cancer: Are Genetic Testing Guidelines a Tool or an Obstacle?. Journal of clinical oncology: official journal of the American Society of Clinical Oncology, 37(6), 453–460. https://doi.org/10.1200/JCO.18.01631.
3. Slavin et al. (2017). The contribution of pathogenic variants in breast cancer susceptibility genes to familial breast cancer risk. NPJ Breast Cancer, 3(1), 1-10.
4. The Centers for Disease Control and Prevention (2019). Jewish Women and BRCA Gene Mutations. Retrieved December 2020 from: https://www.cdc.gov/cancer/breast/young_women/bringyourbrave/hereditary_breast_cancer/jewish_women_brca.htm#:~:text=One%20in%2040%20Ashkenazi%20Jewish,cancer%20at%20a%20young%20age.
5. The Centers for Disease Control and Prevention (2019). Jewish Women and BRCA Gene Mutations. Retrieved March 2021 from: https://www.cdc.gov/cancer/breast/triple-negative.htm.
6. National Comprehensive Cancer Network (NCCN) Guidelines for Detection, Prevention, & Risk Reduction (2021). *Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic.* Retrieved March 2021 from: https://www.nccn.org/professionals/physician_gls/default.aspx#detection.

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