

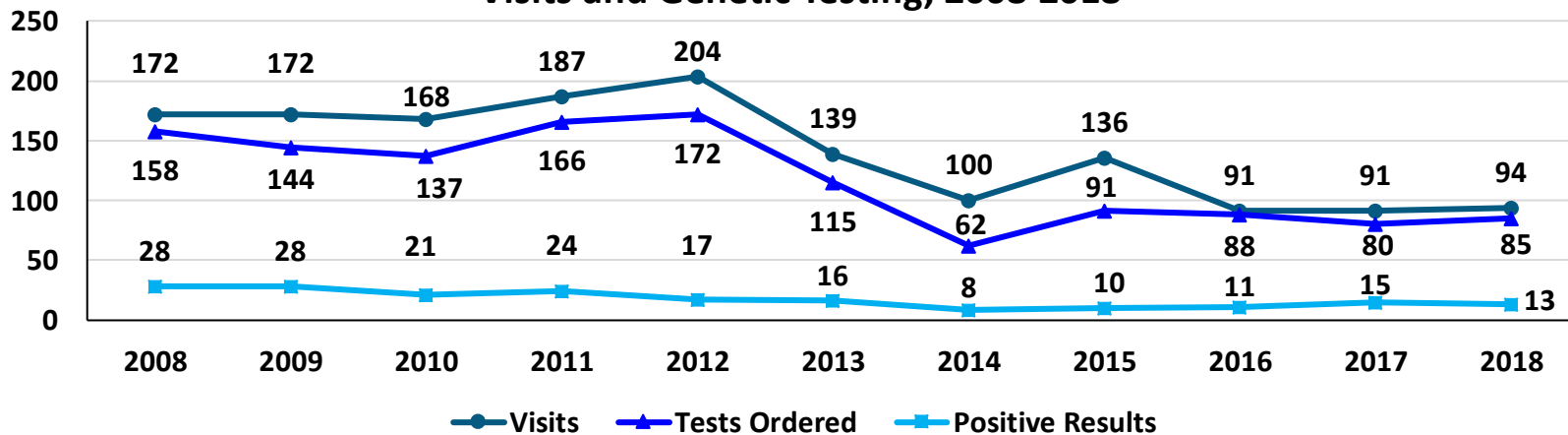
# Ashkenazi Jewish Ancestry and Cancer from the *BRCA* Clinical Network and Hereditary Cancer Network (HCN) Databases, 2008-2018

**Background:** In the general population, the risk of breast cancer is 13%, and about 10% of breast cancer cases are considered hereditary.<sup>1,2</sup> 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.<sup>3</sup> 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.<sup>4</sup> For those of Ashkenazi Jewish (AJ) ancestry, one in 40 will have a mutation in one of these genes.<sup>4</sup> **Individuals who are of this ancestry should consider genetic counseling if: (1) any first-degree relative (mother, daughter, sister, brother, or father) has been diagnosed with breast or ovarian cancer or (2) if any second-degree relatives (grandmother, grandfather, aunt, uncle, niece or nephew) on the same side of the family has been diagnosed with breast or ovarian cancer.<sup>4</sup>**

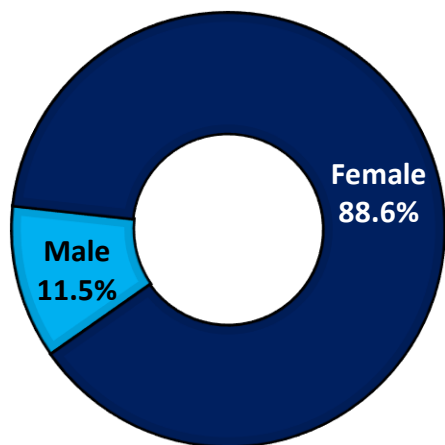
**Methods:** The following data were collected from the Michigan Department of Health and Human Services (MDHHS) *BRCA* Clinical Network and Hereditary Cancer Network (HCN) databases between **January 1, 2008, and December 31, 2018**. During this time-frame, there were **1,554 individuals who identified as Ashkenazi Jewish**. The *BRCA* Clinical Network and Hereditary Cancer Network (HCN) are unique databases that function 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 Ashkenazi Jewish population. Frequencies and chi-square analyses were performed using SAS 9.4. Significant values were set at  $p < 0.05$ .

Please contact Jessica Fritzler at [FritzlerJ1@Michigan.gov](mailto:FritzlerJ1@Michigan.gov) for any questions.

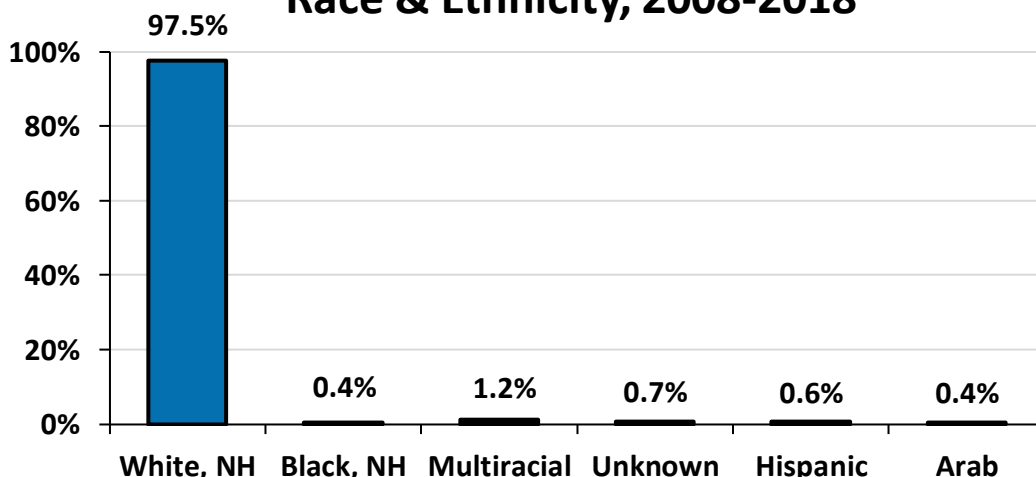
### Visits and Genetic Testing, 2008-2018



### Gender, 2008-2018



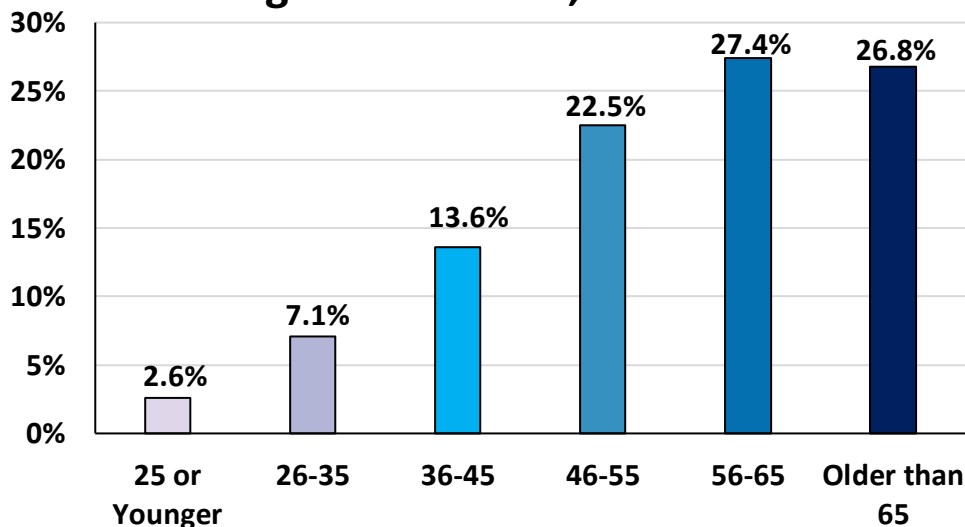
### Race & Ethnicity, 2008-2018



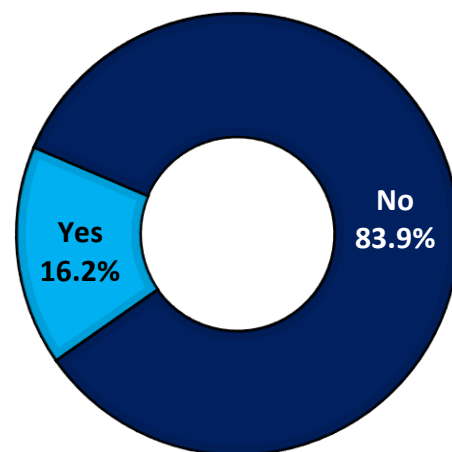
\* HCN Clinical Partners: Beaumont Cancer Genetics Program, Beaumont Center for Hematology and Oncology, Henry Ford Health System Cancer Genetics Program, Karmanos Cancer Institute Cancer Genetic Counseling Service, Informed DNA Telephone Genetic Counseling Services, Mid-Michigan Hereditary Cancer Clinic, 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

# Ashkenazi Jewish Ancestry and Cancer from the *BRCA* Clinical Network and Hereditary Cancer Network (HCN) Databases, 2008-2018

## Age at First Visit, 2008-2018



## Known Familial Mutation, 2008-2018



- Most AJ patients in the databases are between 56 and 65 years of age (**27.4%**), are older than 65 years of age (**26.8%**), or between 46 and 55 years of age (**22.5%**).

- Those who identified as AJ were less likely to be at or under the age of 50 years compared those who did not identify as AJ (**33.5% vs. 47.8%**; data not shown).

- Just over **16.2%** of those with AJ ancestry were aware that they had a known familial mutation (KFM) at their first visit.

- Those who identified as AJ were more likely to have a KFM compared to those who did not identify as AJ (**16.2% vs. 11.6%**).

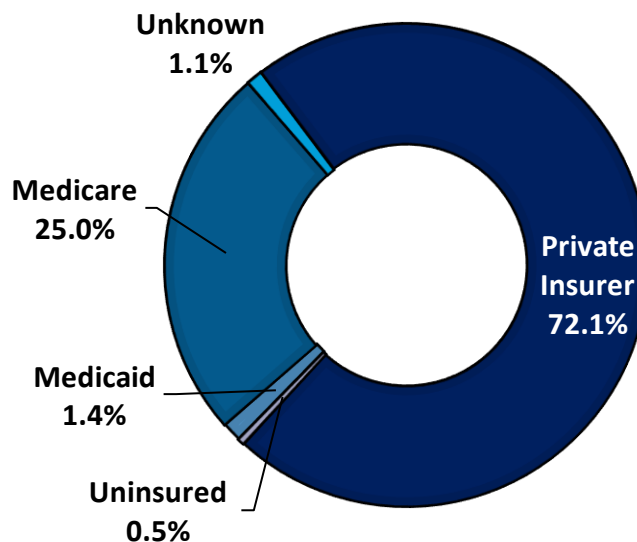
- Most AJ patients had insurance through a private insurer (**72.1%**), followed by Medicare (**25.0%**).

- Most AJ patients had both a personal and family history of cancer (**53.9%**).

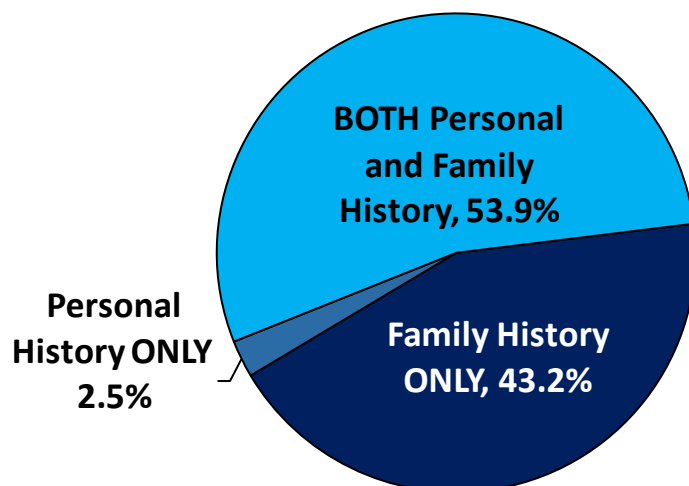
- Those of AJ ancestry were less likely to only have a personal history of cancer compared to those who were not of AJ ancestry (**2.5% vs. 4.8%**).

- Those of AJ ancestry were more likely to have only a family history of cancer compared to those who were not of AJ ancestry (**43.2% vs. 38.0%**).

## Insurance, 2008-2018

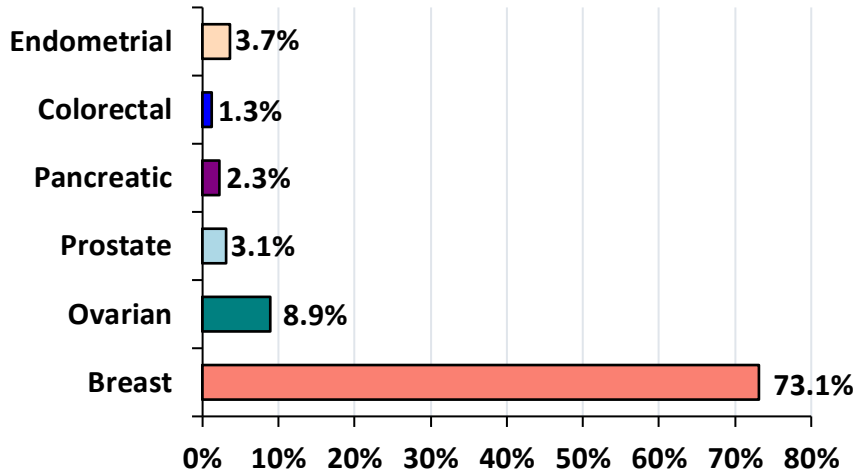


## History of Cancer, 2008-2018

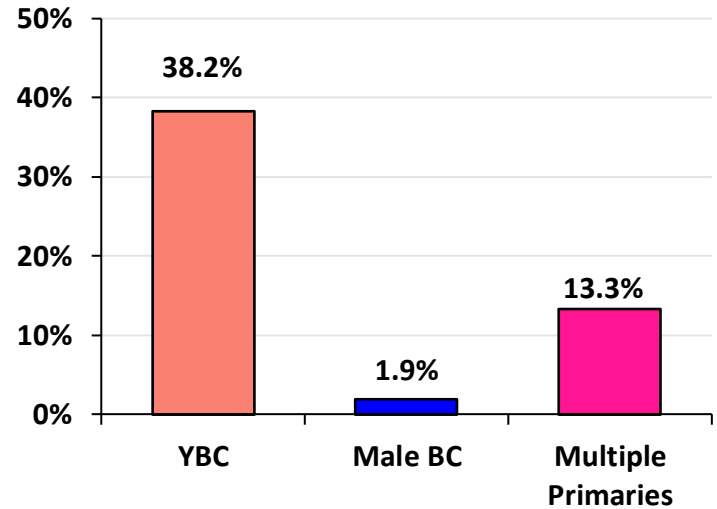


# Ashkenazi Jewish Ancestry and Cancer from the *BRCA* Clinical Network and Hereditary Cancer Network (HCN) Databases, 2008-2018

## Type of Cancer among Patients, 2008-2018 <sup>a</sup>

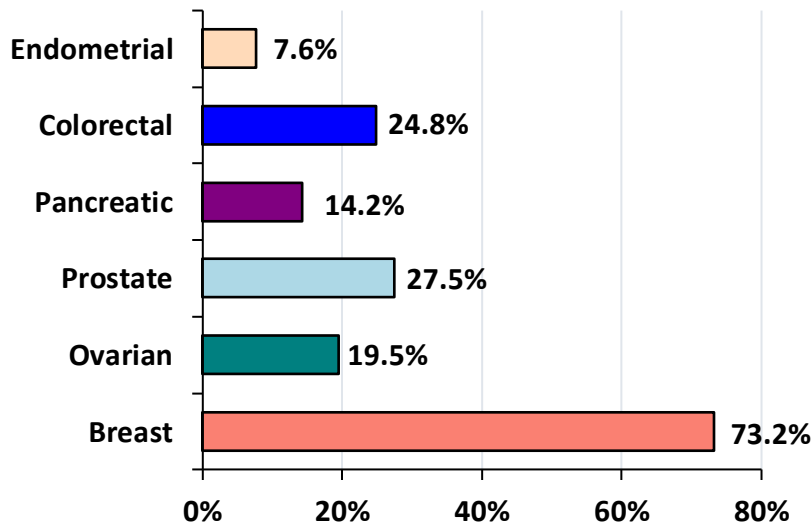


## Breast Cancer, 2008-2018 <sup>b</sup>

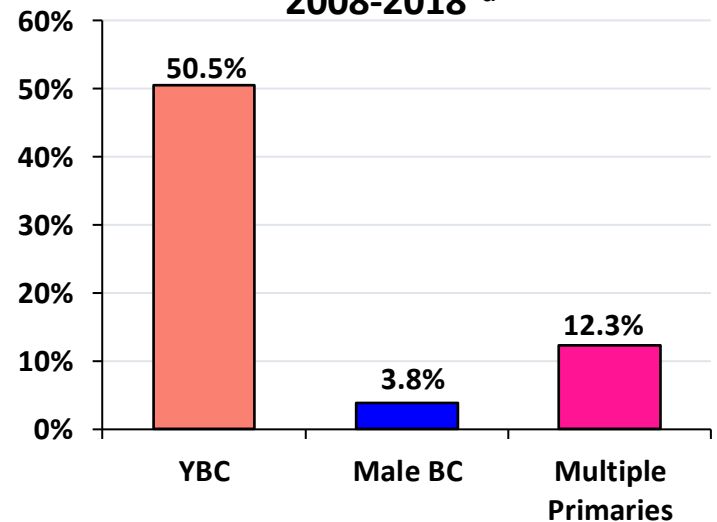


- **73.1%** of AJ patients had a diagnosis of breast cancer, followed by **8.9%** with ovarian cancer.
  - There is a trend suggesting that there may be more AJ patients diagnosed with pancreatic cancer compared to those without this ancestry (**2.3% vs. 1.5%**,  $p = 0.0508$ ).
  - Those of AJ ancestry are more likely to be diagnosed with prostate cancer compared to those who are not of this ancestry (**3.1% vs. 1.7%**).
- **2.8%** of these patients had a history of both breast and ovarian cancer.
  - Those of AJ ancestry are more likely to be diagnosed with both breast and ovarian cancer compared to those who are not of this ancestry (**2.1% vs. 1.21%**; data not shown).
- **38.2%** of those with AJ ancestry diagnosed with breast cancer had a diagnosis occur at or before the age of 50.
  - Those who are not of AJ ancestry were more likely to be diagnosed at a younger age compared to those with AJ ancestry (**53.6% vs. 38.2%**).

## Type of Cancer among Family Members, 2008-2018 <sup>c</sup>



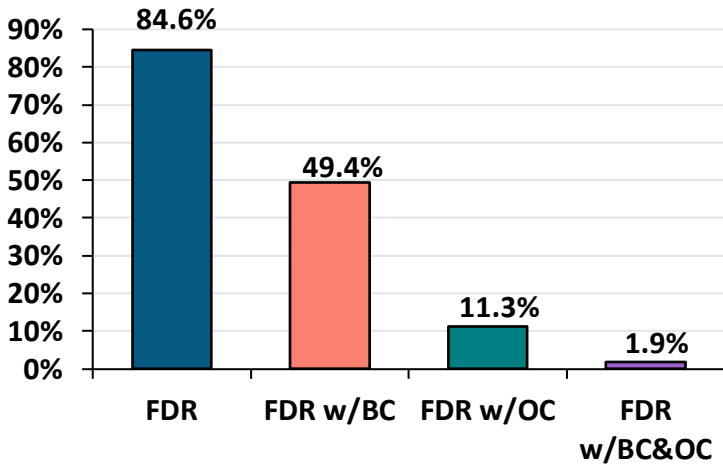
## Breast Cancer among Relatives, 2008-2018 <sup>d</sup>



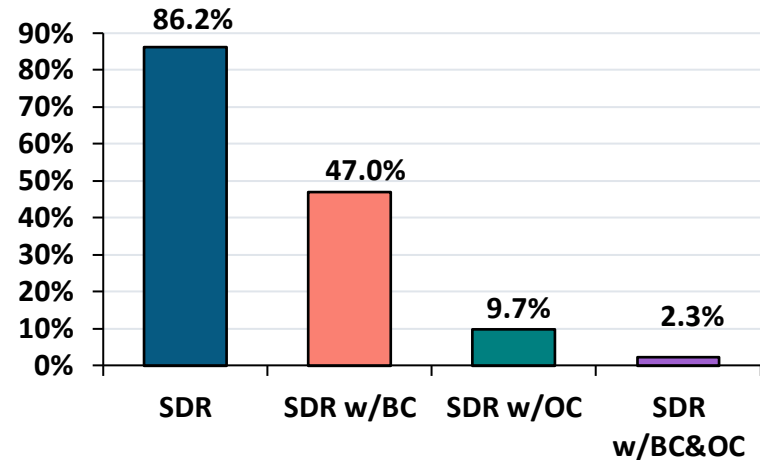
- Those of AJ ancestry are more likely to have a relative diagnosed with pancreatic cancer compared to those who were not of this ancestry (**14.2% vs. 11.7%**).
  - There were no other statistical differences between relatives diagnosed with cancer and AJ ancestry.
- **3.8%** of AJ patients had at least one male relative diagnosed with breast cancer.
- **13.1%** of these patients have a family history of both breast and ovarian cancer (data not shown).
- Those of AJ ancestry are less likely to have a relative with breast cancer diagnosed at a young age compared to those who are not of this ancestry (**50.5% vs. 55.4%**).

# Ashkenazi Jewish Ancestry and Cancer from the *BRCA* Clinical Network and Hereditary Cancer Network (HCN) Databases, 2008-2018

## First-Degree Relatives, 2008-2018

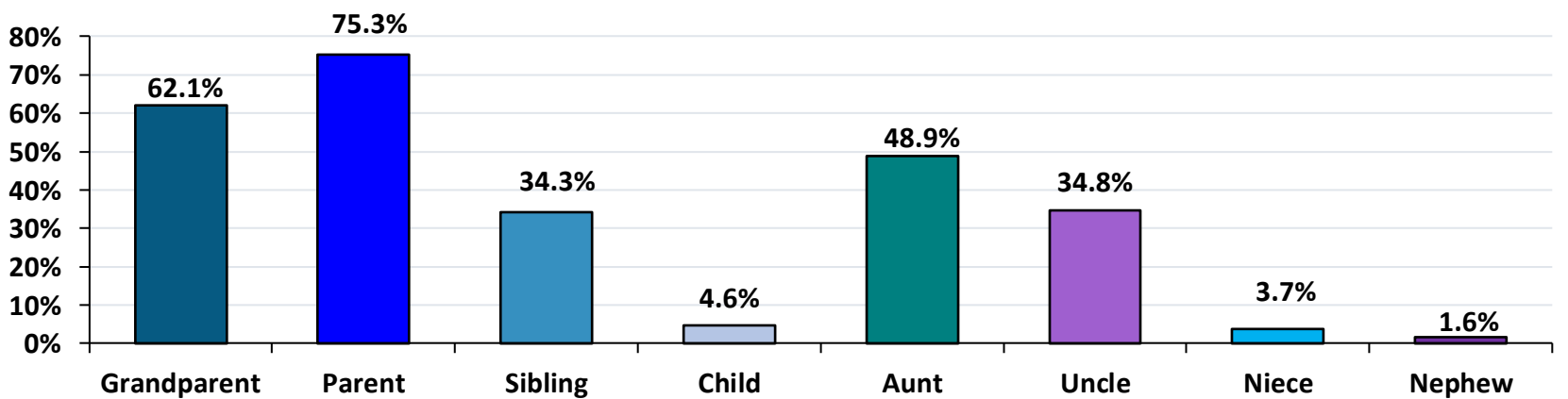


## Second-Degree Relatives, 2008-2018



- **84.6%** of AJ patients with a family history of cancer had a first-degree relative (FDR) diagnosed with cancer and **86.2%** had a second-degree relative (SDR) diagnosed with cancer.
  - Those of AJ ancestry are more likely to have an FDR diagnosed with cancer compared to those who are not of this ancestry (**84.6% vs. 80.9%**).
- **49.4%** of AJ patients with a family history of cancer had an FDR diagnosed with breast cancer and **47.0%** had an SDR with breast cancer.
  - Those of AJ ancestry were more likely to have an FDR diagnosed with breast cancer compared to those who are not of this ancestry (**49.4% vs. 46.0%**).
- **11.3%** of AJ patients with a family history of cancer had an FDR diagnosed with ovarian cancer and **9.7%** had an SDR diagnosed with ovarian cancer.
  - Those of AJ ancestry were less likely to have an SDR with ovarian cancer compared to those who are not of this ancestry (**9.7% vs. 12.1%**).
- Both those with and without AJ ancestry had the same proportion of FDRs diagnosed with both breast and ovarian cancer (**1.9%**).

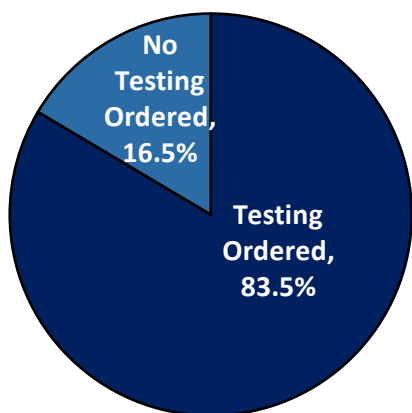
## Type of Relatives Diagnosed with Cancer, 2008-2018



- **75.3%** of AJ patients with a family history of cancer had a parent diagnosed with cancer.
  - Those of Ashkenazi Jewish ancestry were significantly more likely to have a parent diagnosed with cancer compared to those who are not of this ancestry (**75.3% vs. 69.5%**).
- **48.9%** of AJ patients with a family history of cancer had an aunt diagnosed with cancer.
  - Those of Ashkenazi Jewish ancestry were significantly less likely to have an aunt diagnosed with cancer compared to those who are not of this ancestry (**48.9% vs. 52.8%**).
- No other differences were seen between type of family member diagnosed with cancer and AJ ancestry.

# Ashkenazi Jewish Ancestry and Cancer from the *BRCA* Clinical Network and Hereditary Cancer Network (HCN) Databases, 2008-2018

## Genetic Testing among AJ Patients, 2008-2018

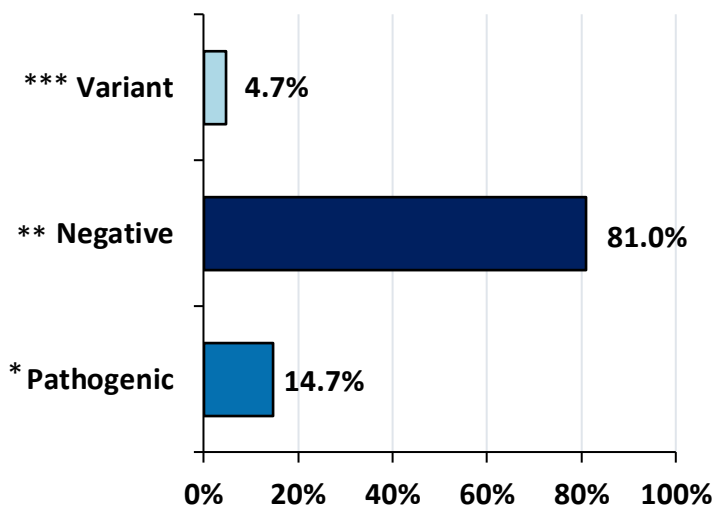


**6.9% had Single Site Testing**

**2.6% ordered testing prior to counseling**

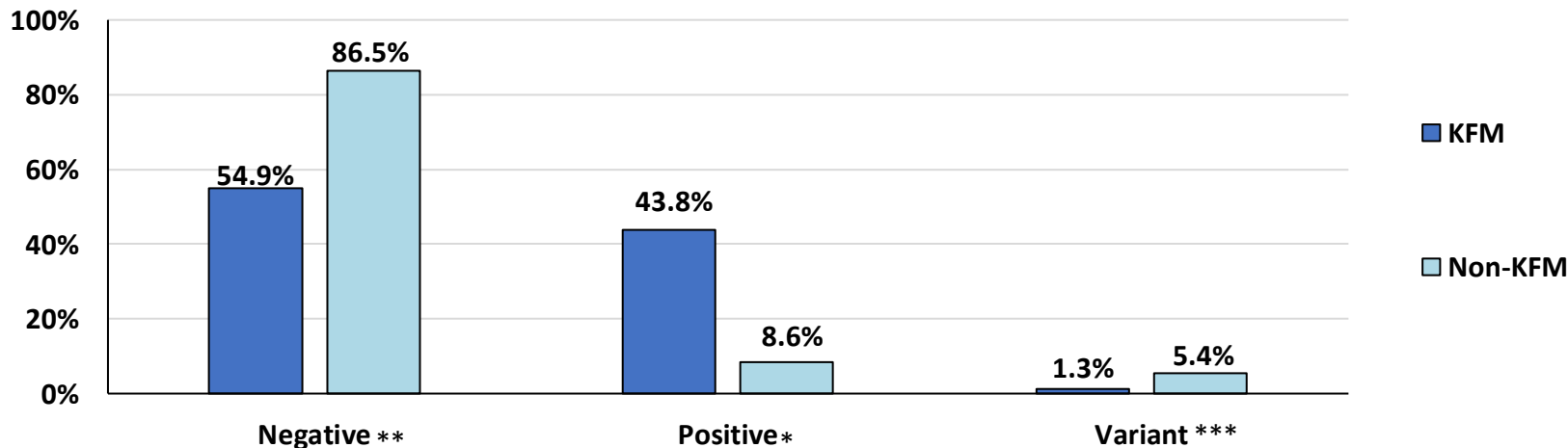
- **83.5%** of AJ patients received genetic testing.
  - Those of AJ ancestry were statistically more likely to receive genetic testing compared to those who are not of this ancestry (**83.5% vs. 68.7%**).
- Of those who received genetic testing, **6.9%** ordered single site testing.
  - Those without an AJ ancestry were more likely to have ordered a single site test compared to those who did not have this ancestry (**13.8% vs. 6.9%**).

## Genetic Test Results among AJ Patients, 2008-2018



- Of those who received genetic testing, **14.7%** had at least one positive result.
  - There were no statistically significant differences between AJ ancestry and positive genetic test results.
- Of those who received genetic testing, **4.7%** had at least one variant of uncertain significance (VUS) as a genetic test result.
  - Those who were not of AJ ancestry were more likely to have a VUS compared to those who did have AJ ancestry (**10.0% vs. 4.7%**).

## Genetic Test Results among AJ Patients with and without a Known Familial Mutation, 2008-2018

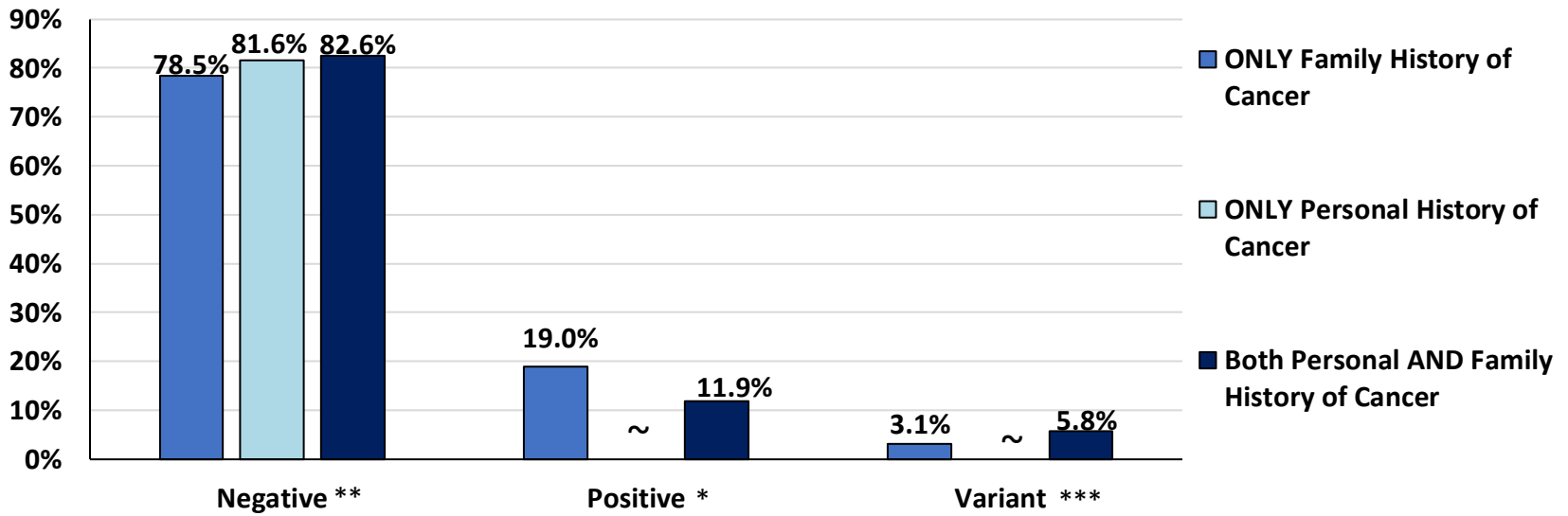


- Those of AJ ancestry with a KFM were statistically more likely to have a positive genetic test result compared to those of AJ ancestry without a KFM (**43.8% vs. 8.3%**).
- Those of AJ ancestry without a KFM were statistically more likely to have a variant of uncertain significance compared to those of AJ ancestry with a known familial mutation (**data are suppressed**).

\* 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). 5

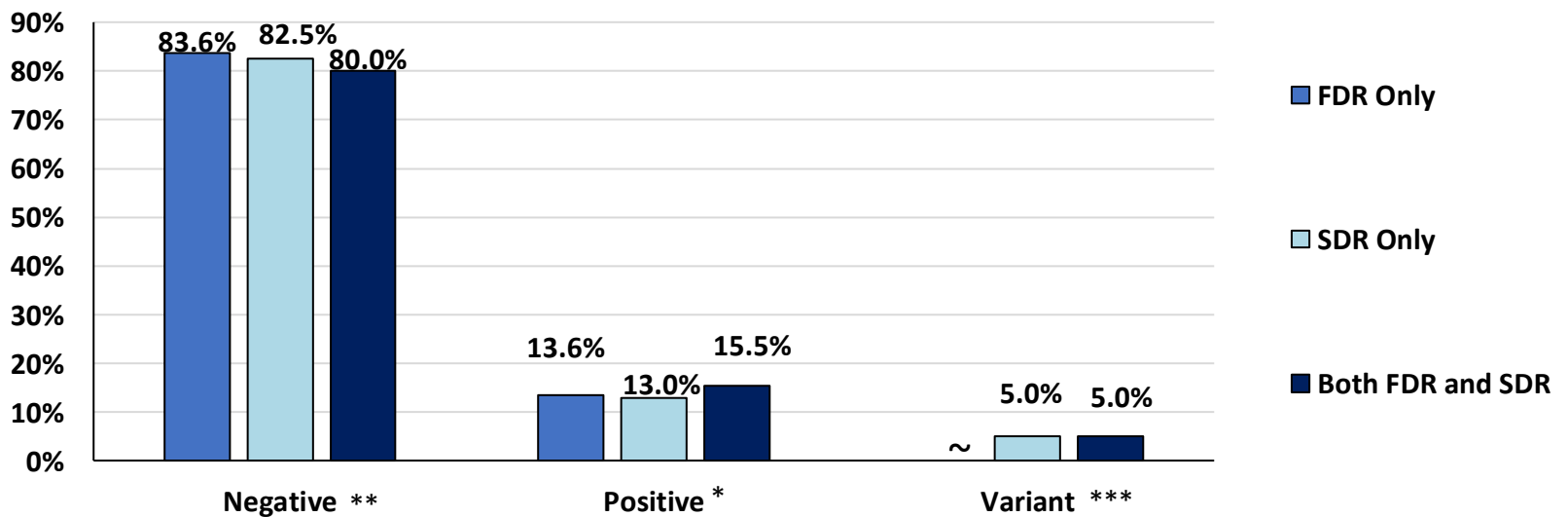
# Ashkenazi Jewish Ancestry and Cancer from the *BRCA* Clinical Network and Hereditary Cancer Network (HCN) Databases, 2008-2018

## Genetic Test Results among AJ Patients with a Personal or Family History of Cancer, 2008-2018



- Among those of AJ ancestry with only a family history of cancer were more likely to have a positive gene result compared to those who had either only a personal history of cancer or both personal and family history of cancer (**some data are suppressed**).
- There is also a trend that suggests that those with only a family history of cancer are more likely to have a VUS compared to those who had either only a personal history of cancer or both personal and family history of cancer (**some data are suppressed**).

## Genetic Test Results among AJ Patients with a Family History of Cancer, 2008-2018



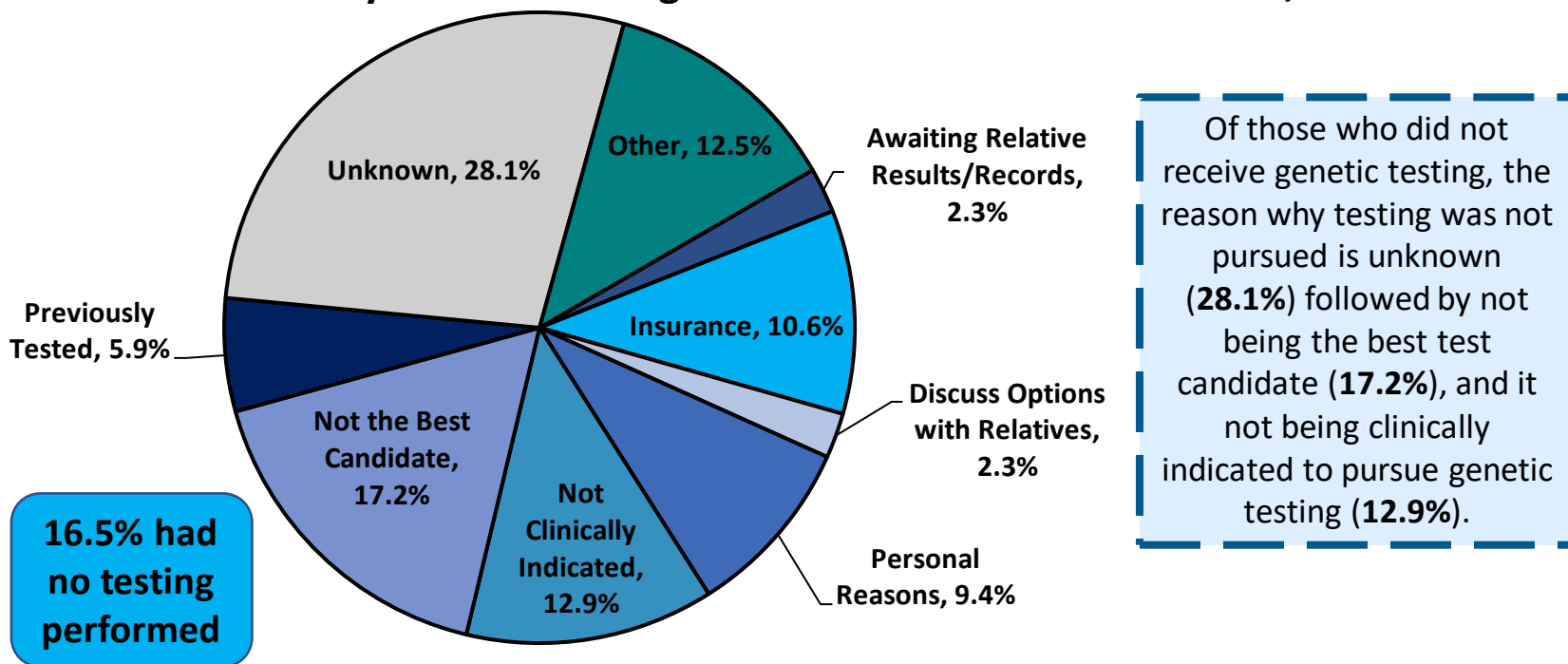
- There were no significant differences between having a first-degree relative, a second-degree relative or both diagnosed with cancer and having a positive genetic test results among those of AJ ancestry.

\* 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). ~ Data are suppressed if count is less than 6.

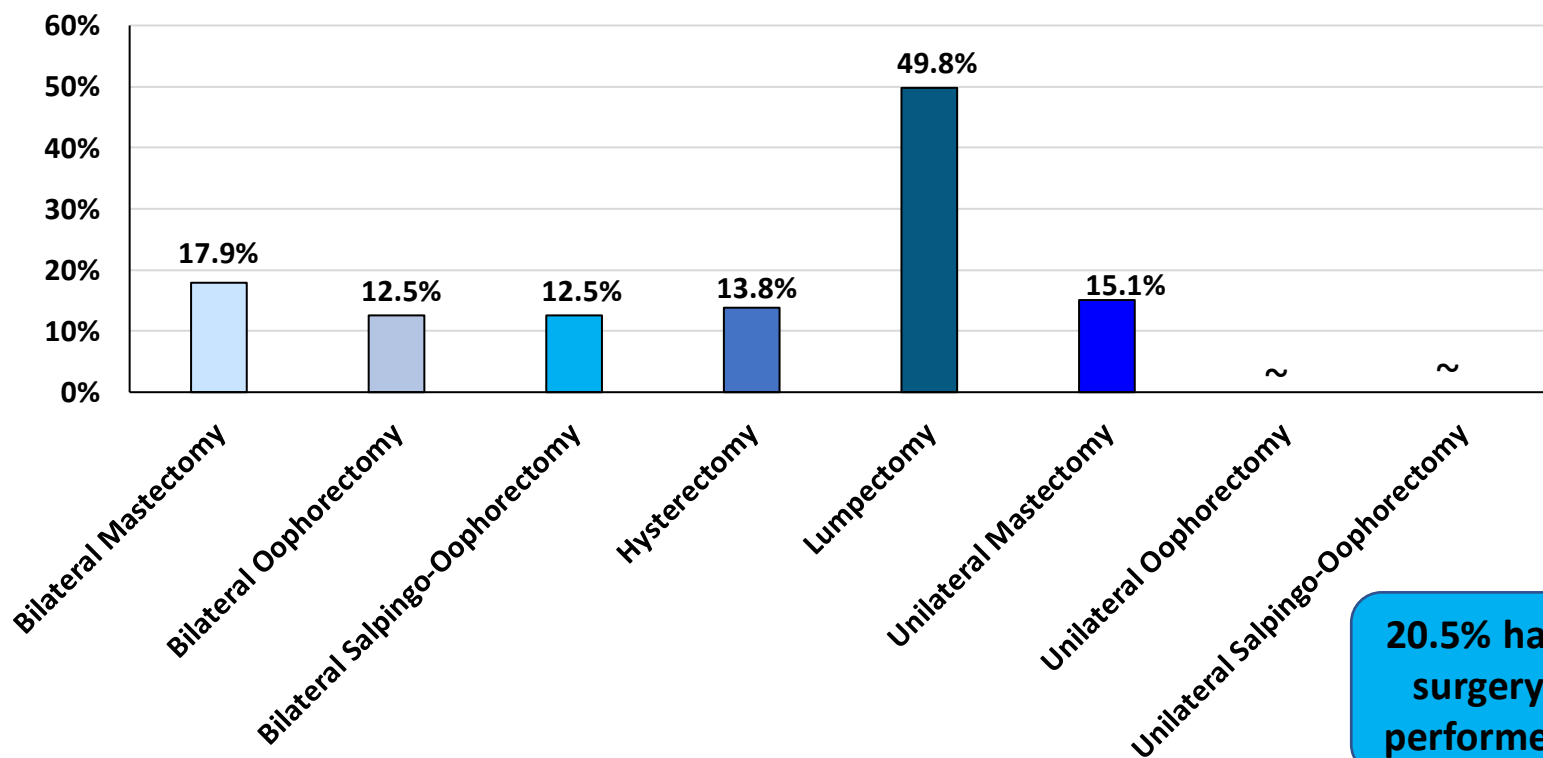


# Ashkenazi Jewish Ancestry and Cancer from the *BRCA* Clinical Network and Hereditary Cancer Network (HCN) Databases, 2008-2018

## Reason Why Genetic Testing Was Not Pursued from the HCN, 2008-2018



## Surgeries from the HCN, 2008-2018



- Of those who had surgery, the majority underwent a lumpectomy (49.8%).
  - Those of AJ ancestry were more likely to undergo a lumpectomy compared to those without this ancestry (49.8% vs. 41.1%).
  - Those of AJ ancestry were less likely to undergo a mastectomy compared to those without this ancestry (32.6% vs. 38.6%).

~ Data are suppressed if count is less than 6.

# Discussion & Summary

- Even though mutations in the BRCA genes tend to result in breast cancer being diagnosed at a young age, most patients of Ashkenazi Jewish ancestry in the HCN were 46 years of age or older.
  - This trend also continued with age of diagnosis; among this population, cancer was occurring at older ages, which contradicts what is in the literature.
  - This trend was also true among their family members; they were more likely to be diagnosed at an older age compared to those without this ancestry.
- Although these genetic mutations are common among those with Ashkenazi Jewish ancestry, only 16.2% knew of a familial mutation before the genetic counseling visit, which could be due to generational factors such as genetic services not being widely accessible until recently and that the relatives of these patients may have been part of the generation that was less likely to talk about their cancer diagnosis or receive cancer genetic services.
- Those of Ashkenazi Jewish ancestry were not more likely to have a breast or ovarian cancer diagnosis compared to those without this ancestry. However, it appears that they may be more likely to be diagnosed with pancreatic cancer and are more likely to be diagnosed with prostate cancer.
  - This may be evidence that education on these cancer types may be important for this population.
- Those of Ashkenazi Jewish ancestry were more likely to have a relative diagnosed with pancreatic cancer compared to those without this ancestry, which provides more evidence that this population may need education about pancreatic cancer.
- Even though it is very common for those of Ashkenazi Jewish ancestry to have single site testing due to the nature of their mutation, they were less likely to have ordered a single site test compared to those without this ancestry, potentially due to low proportion of knowing a familial mutation.
- Even though all these individuals, with today's current NCCN and USPSTF guidelines, meet criteria for genetic testing, there were still 16.5% who did not opt to pursue testing at the time of their genetic counseling appointment.
  - Reasons for this include: (1) at the time of counseling, insurance companies were not covering these services, (2) other family members made better candidates, or (3) information collected at the genetic counseling appointment indicated clinically no need to pursue testing.

## For More Information:

Visit [Michigan.gov/hereditarycancer](https://michigan.gov/hereditarycancer) to learn more about hereditary cancers.

Visit [Michigan.gov/cge](https://michigan.gov/cge) to view more data on hereditary cancers.

**Cancer Genomics Hotline Phone #:** 866 852 1247

**Email:** [genetics@michigan.gov](mailto:genetics@michigan.gov)

## Suggested Citation:

Fritzler J and Anderson B. Ashkenazi Jewish Ancestry and Cancer from the BRCA Clinical Network and Hereditary Cancer Network (HCN) Databases, 2008-2018. Bureau of Epidemiology and Population Health, Michigan Department of Health and Human Services, March 2021.



## References:

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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.](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.)

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