Known Familial Mutations and Genetic Testing among Patients in the Hereditary Cancer Network Database

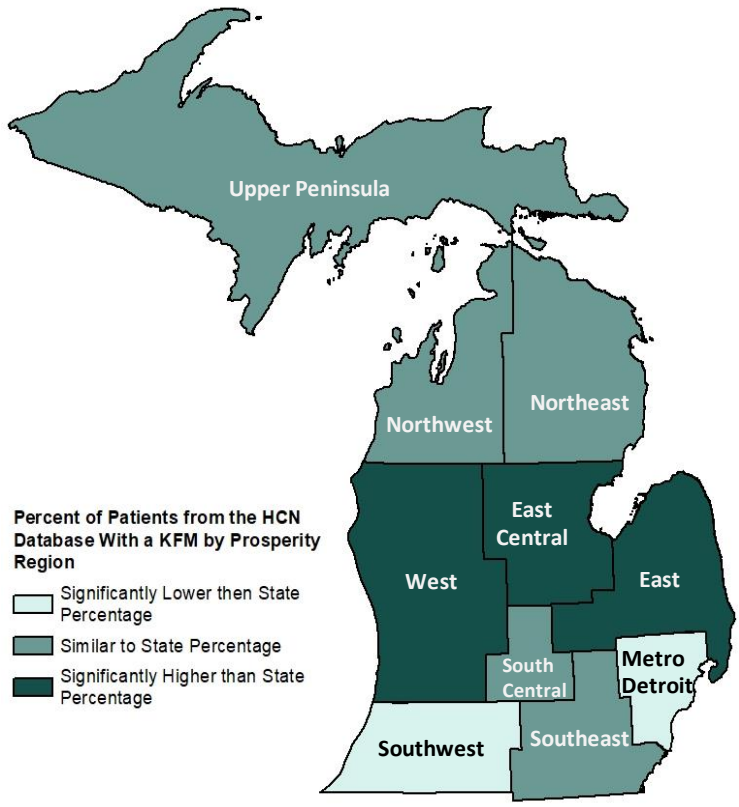
Background: Mutations in *BRCA1* and *BRCA2* genes increase an individual's lifetime risk of breast cancer up to 80 percent, ovarian cancer up to 39 percent, prostate cancer up to 20 percent and pancreatic cancer up to 7 percent.[1] *BRCA* gene mutations are autosomal dominant, which means first-degree relatives have a 50 percent chance of inheriting the mutation if a parent has a known mutation. For those individuals who have a *BRCA* mutation, several actions can be taken to help prevent cancer or decrease the severity of cancer. More frequent mammograms and breast Magnetic Resonance Imaging (MRI) can aid in early detection. There are also medications and surgeries that can help reduce an individual's breast and ovarian cancer risk.

An important public health strategy is to promote genetic testing of individuals with a known mutation running in their family (KFM). This is known as cascade screening. In order for cascade screening to be successful the individual with the mutation needs to communicate with family members about his or her mutation status and encourage relatives to be tested themselves. The relatives can then seek a genetic counselor and be tested for the same mutation. Cascade screening also has an economic benefit because it is less expensive to test only for the known mutation rather than performing a comprehensive genetic test on all possible relevant genes. This brief discusses the characteristics of those patients reporting a KFM.

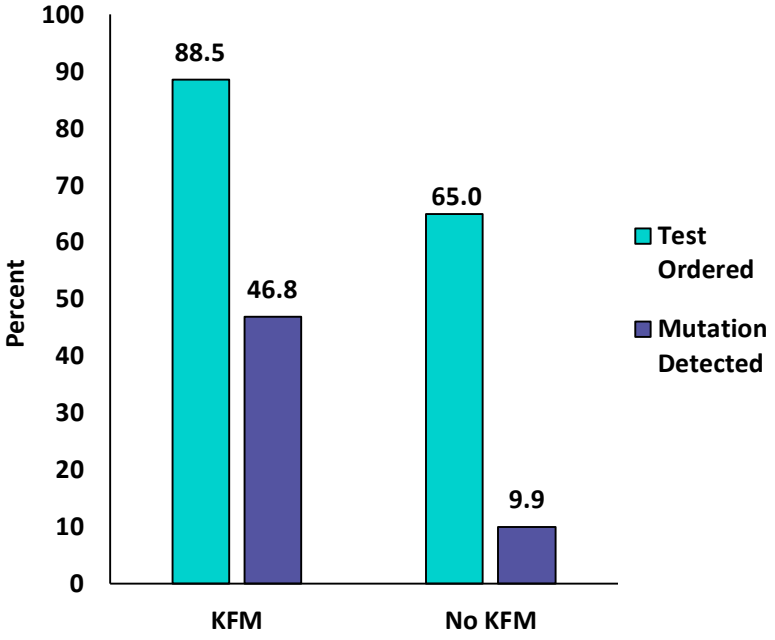
Methods: The Hereditary Cancer Network (HCN) database collects non-identifiable information for patients seeking counseling for Hereditary Breast and Ovarian Cancer (HBOC) and Lynch syndrome (LS). Eighteen clinics have contributed information to this database. This database only contains information on patients who present at a clinic participating in the HCN and therefore may not be representative of all genetic counseling performed in the state. These data were analyzed for 27,940 individuals who sought genetic counseling between 2008 and 2017 and had a strong personal or family history of a cancer related to *BRCA1* or *BRCA2*. Of these individuals, 3,155 patients reported having a KFM. Counties with a high possible hereditary cancer burden were determined by looking at the incidences for young breast cancer, ovarian cancer, prostate cancer, pancreatic cancer, young endometrial cancer and young colorectal cancer.[2] Rural and urban county designation is provided by the U.S. Census Bureau which defines urban areas based on population density and land coverage.[3] If 50 percent or more of the county population lived in areas classified as 'not urban' the county is then classified as rural. Frequencies were reported for various characteristics of patients with a KFM and χ^2 tests were performed to assess for differences among groups.

Genetic Counseling Patients who have a Known Mutation in the Family, by Region, 2008-2017

- In Michigan, 11.3% of patients who had genetic counseling at a HCN clinic reported a KFM.
- Two regions were significantly lower than the state percentage for patients with a KFM among those who had genetic counseling at a HCN clinic:
  - Southwest Michigan (8.6%; 95% CI: 7.4% - 9.8%)
  - Metro Detroit (9.3%; 95% CI: 8.8% - 9.8%)
- Three regions were significantly higher than the state percentage for patients with a KFM among those who had genetic counseling at a HCN clinic:
  - West Michigan (14.4%; 95% CI: 13.4% - 15.3%)
  - East Central Michigan (17.8%; 95% CI: 15.1% - 20.5%)
  - East Michigan (14.8%; 95% CI: 12.3% - 17.3%)

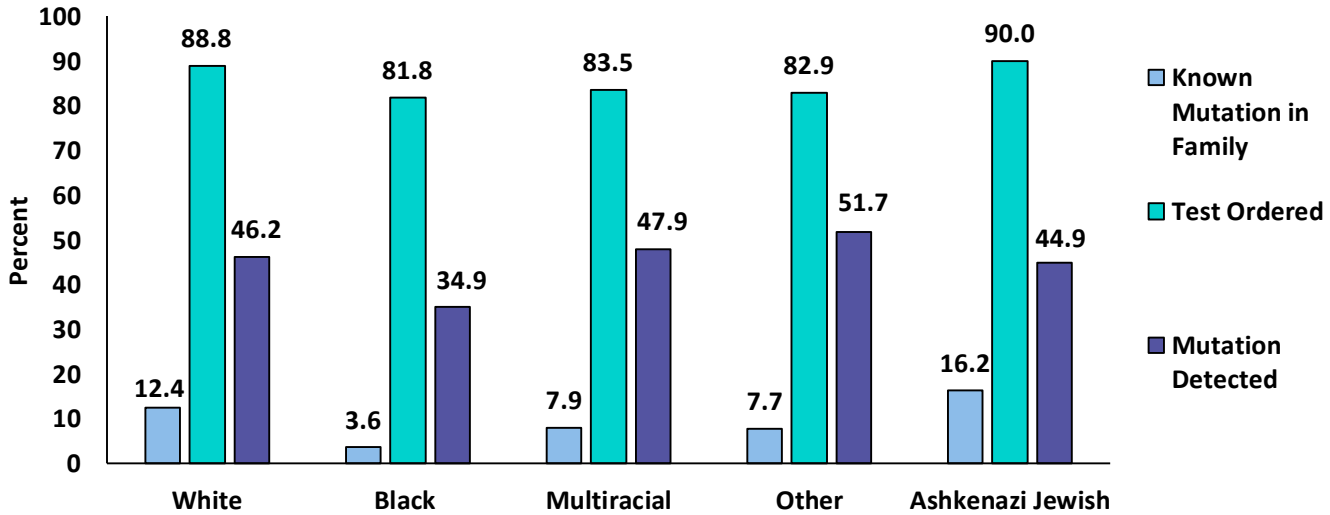


Genetic Testing and Results among Patients with and without a Known Familial Mutation: Results from the HCN Database, 2008-2017



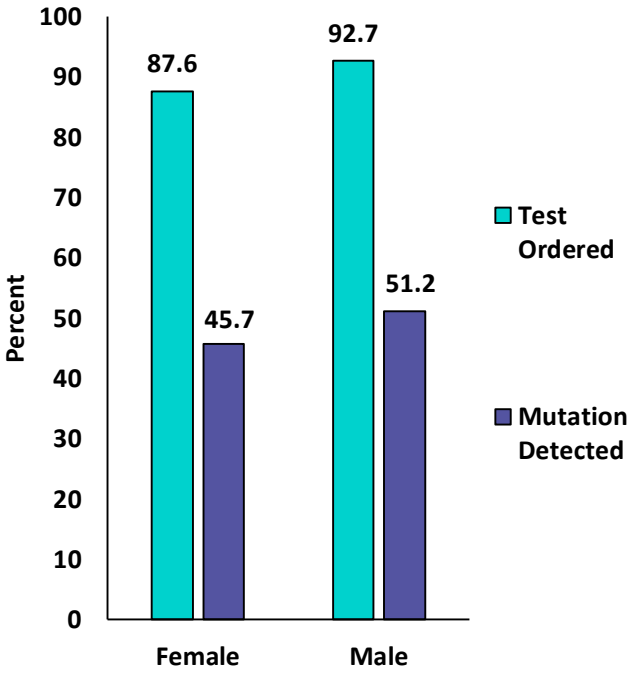
- There was a statistically significant difference between those with and without a KFM and whether they ordered a genetic test.
  - Eighty-nine percent of those with a KFM ordered a genetic test versus 65% of those without a KFM.
- There was a statistically significant difference between those with and without a KFM and if they had a positive test result.
  - Forty-seven percent of those with a KFM had a positive result versus 10% of those without a KFM.

Genetic Testing and Results among Patients who have a Known Familial Mutation by Race: Results from the HCN Database, 2008-2017



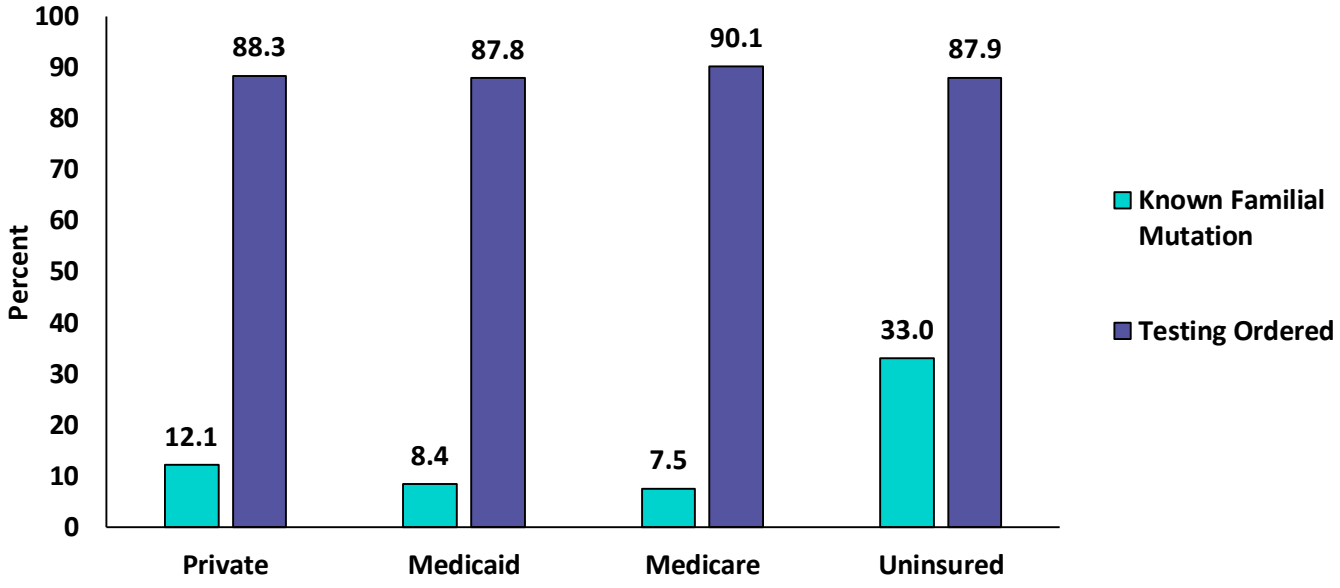
- There was a statistically significant difference between Black and White patients who reported a KFM among patients in the HCN database.
- Among those with a KFM, there were no statistically significant differences between races for having a genetic test ordered or for having a pathogenic mutation.
  - For White patients who had a KFM, 88.8% had a genetic test ordered and 46.2% had a pathogenic mutation.
  - For Black patients who had a KFM, 81.8% had a genetic test ordered and 34.9% had a pathogenic mutation.
  - For patients of Ashkenazi Jewish heritage who had a KFM, 90.0% had a genetic test ordered and 44.9% had a positive result.

Genetic Testing and Results among Patients who have a Known Familial Mutation by Gender: Results from the HCN Database, 2008-2017



- There was a statistically significant difference between females and males who reported a KFM among patients in the HCN database.
  - For female patients, 9.9% reported a KFM.
  - For male patients, 30.1% reported a KFM.
- There was a statistically significant difference between females and males and whether they received genetic testing.
  - Among male patients who reported a KFM, 92.7% had a genetic test ordered.
  - Among female patients who reported a KFM, 87.6% had a genetic test ordered.
- There was a statistically significant difference between females and males and whether they received a positive result.
  - Among male patients who reported a KFM, 51.2% had a positive result.
  - Among female patients who reported a KFM, 45.7% had a positive result.

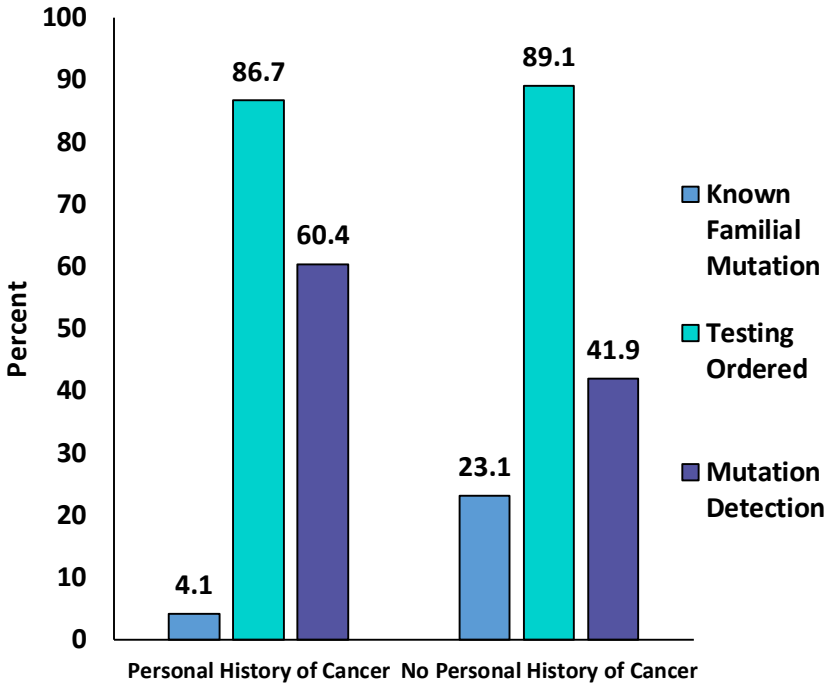
Genetic Testing and Results among Patients who have a Known Familial Mutation by Primary Insurance Provider: Results from the HCN Database, 2008-2017



- There was a statistically significant difference in insurance type among those reporting a KFM.
  - 8.4% of Medicaid patients, 7.5% of Medicare patients, 33.0% of uninsured patients, and 12.1% of private insurance patients reported a KFM.
- There was no statistically significant difference in insurance type regarding having a genetic test ordered for patients reporting a KFM.

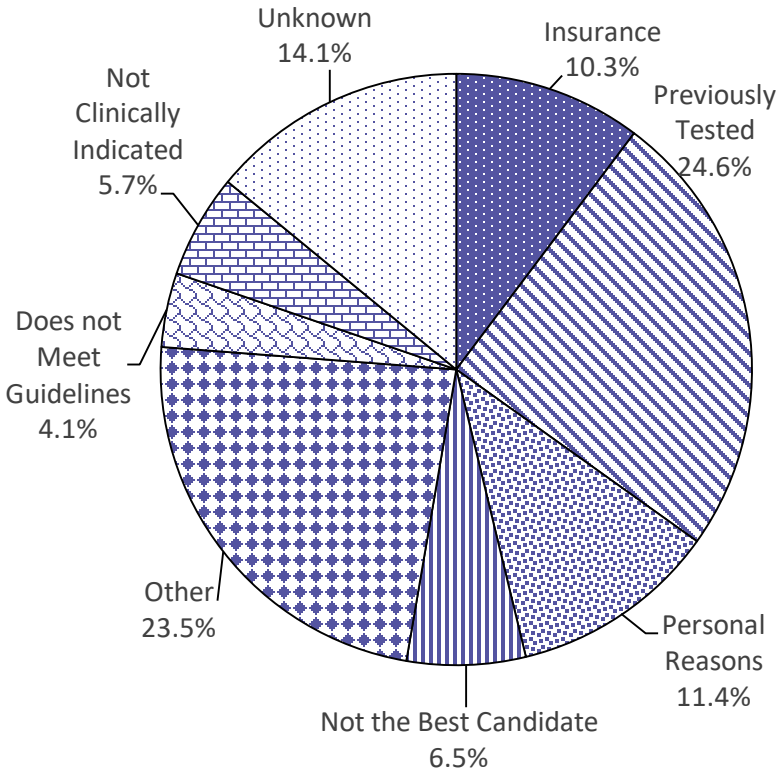
Genetic Testing and Results among Patients who have a Known Familial Mutation by Personal Cancer History: Results from the HCN Database, 2008-2017

- Of those with no personal history of cancer, 23.1% had a KFM.
- Of those with a personal history of cancer and a KFM, a total of 621 (86.7%) patients who reported having a genetic test ordered.
- Eighty-nine percent of patients with a KFM but no personal history of cancer reported having a genetic test ordered.
- Among patients who reported a KFM, there was a statistically significant difference between patients who had a personal history of cancer and those with no personal history regarding having a pathogenic mutation (60.4% vs 41.9%).



Reasons Why Genetic Testing was Not Pursued among Patients who have a Known Familial Mutation: Results from the HCN Database, 2008-2017

- Among patients who reported a KFM, 10.3% stated they did not have a genetic test due to lack of insurance coverage.
- Of those who reported a KFM, 6.5% were not considered the best candidate.
  - This often means that the patient had a relative that was diagnosed with cancer that fit the criteria for testing better than the patient.
- Of patients who reported a KFM, 23.5% fell into an 'other' category.
  - This category includes people who are awaiting medical records, had a relative test negative for the mutation, or did not come back to the clinic for follow-up.



Summary

Methods: Genetic counseling and testing information was analyzed using data obtained from the HCN. Significance was based on chi-square analyses with a significance value set to be $p < 0.05$.
Conclusion: Overall, those with a KFM are more likely to get genetic testing (88.5%) versus those who do not report a KFM (65.0%). While these data cannot identify the specific characteristics of families who are benefiting from cascade testing, it can provide a general overview of the characteristics among individuals who have been part of a cascade screen by examining patients with a reported KFM. Black patients were less likely to report a KFM compared to other races. Patients insured by Medicaid were also less likely to report a KFM. To increase the uptake of cascade screening, the individual first identified with a pathogenic mutation needs to be educated on the importance of communicating their results to family members. Methods that take the responsibility off the patient need to be explored to determine if there are more effective ways to increase the uptake of cascade screening.

For More Information:

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

Suggested Citation:

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References:
1. Petrucelli N, Daly MB, Pal T. BRCA1 and BRCA2 Associated Hereditary Breast and Ovarian Cancer. Gene Reviews (2016).
2. Seaton T, Wahl R, Bach J. Geographic Distributions of Select Cancers and Genetic Counseling in Michigan. Lansing, Michigan: Bureau of Epidemiology and Population Health, Michigan Department of Health and Human Services, November 2017.
3. Michael Ratcliffe, Charlynn Burd, Kelly Holder, and Alison Fields, "Defining Rural at the U.S. Census Bureau," ACSGEO-1, U.S. Census Bureau, Washington, DC, 2016.

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