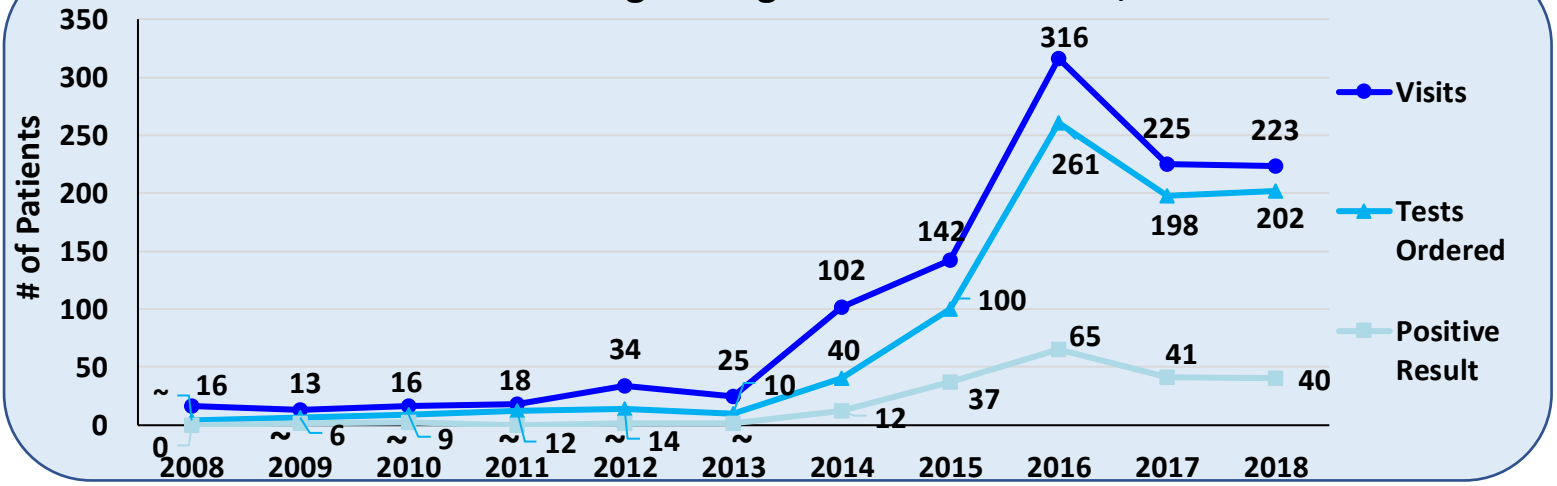
Lynch Syndrome from the Hereditary Cancer Network (HCN) & BRCA Clinical Network (BRCA) Databases, 2008-2018

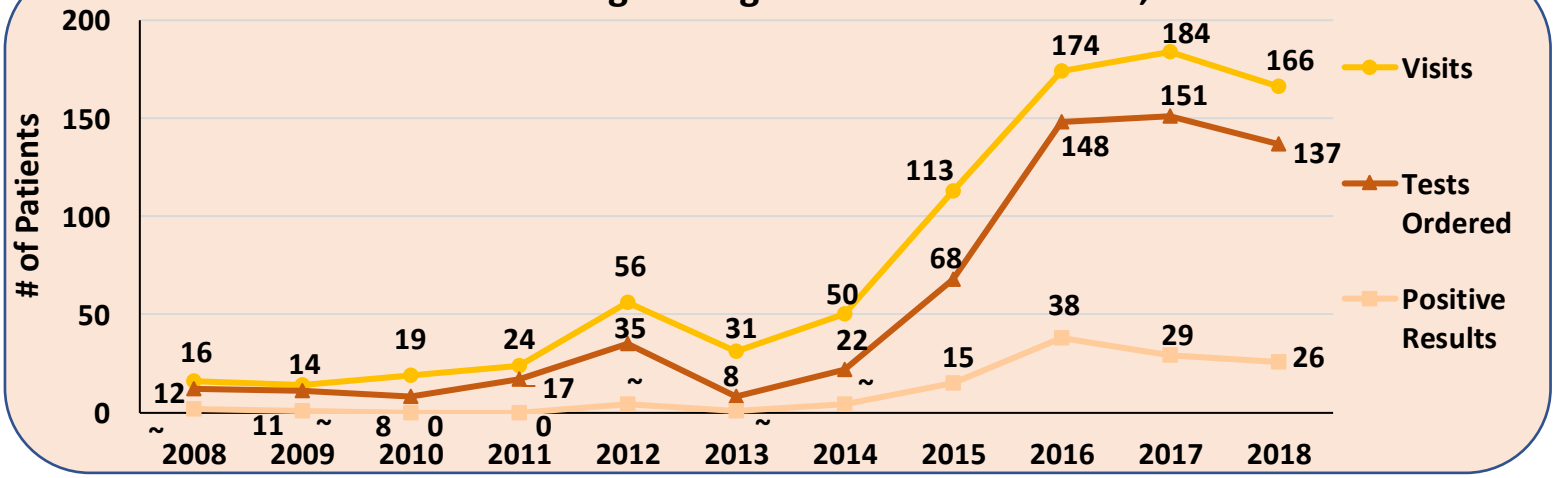
Background: Variations in MLH1, MSH2, MSH6, PMS2, or EPCAM genes increase the risk of developing Lynch syndrome (LS).[1] LS is an inherited disorder that increases the risk of colorectal, endometrial, ovarian, stomach, liver, kidney, brain and certain types of skin cancers. These individuals are also more likely to be diagnosed with cancer at a younger age.[1] Genetic counseling with a board certified and/or eligible genetics provider, followed by genetic testing as appropriate, are the recommended first steps for anyone with a personal history or strong family history of these cancers. Early identification of LS can help reduce the impact of cancer and save the lives of family members who may also be at risk.

Methods: The following data were collected from the Michigan Department of Health and Human Services (MDHHS) BRCA Clinical Network (BRCA) and Hereditary Cancer Network (HCN) databases between **January 1, 2008, and December 31, 2018**. **During this time-frame, there were 1,931 individuals who were diagnosed with colorectal (CRC) or endometrial cancer (EC) who may be predisposed to Lynch syndrome (LS)**. 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 and 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 LS 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** for any questions.

Visits and Genetic Testing among Colorectal Patients, 2008-2018

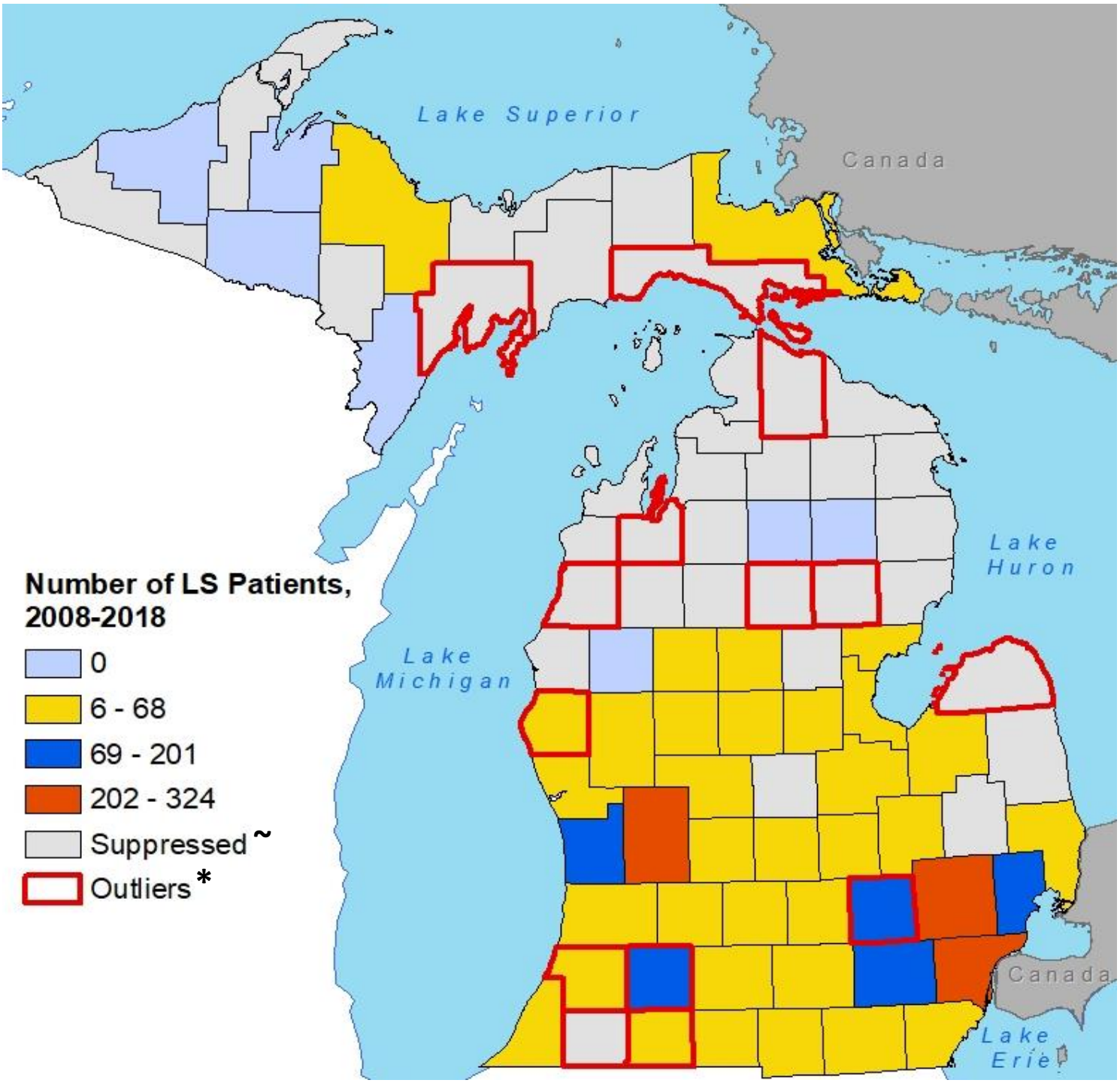


Visits and Genetic Testing among Endometrial Patients, 2008-2018



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

LS from the HCN & BRCA Databases, 2008-2018: Location by County

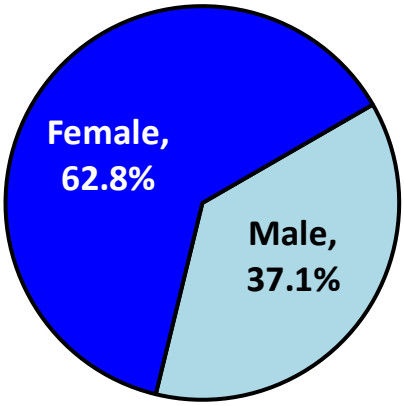


- The majority of LS patients from the HCN are located in Wayne County, followed by Oakland and Kent counties.
- Out of the 76 counties where LS patients resided, 33 (43.4%) had genetic testing rates below 75%.

~ Data are suppressed if count is less than 6. *Outliers refer to counties where the rate of genetic testing is less than outlier cutoff of Q3 + (IQR*1.5), where Q3 refers to the third quartile, and IQR refers to the interquartile range (Q3-Q1).

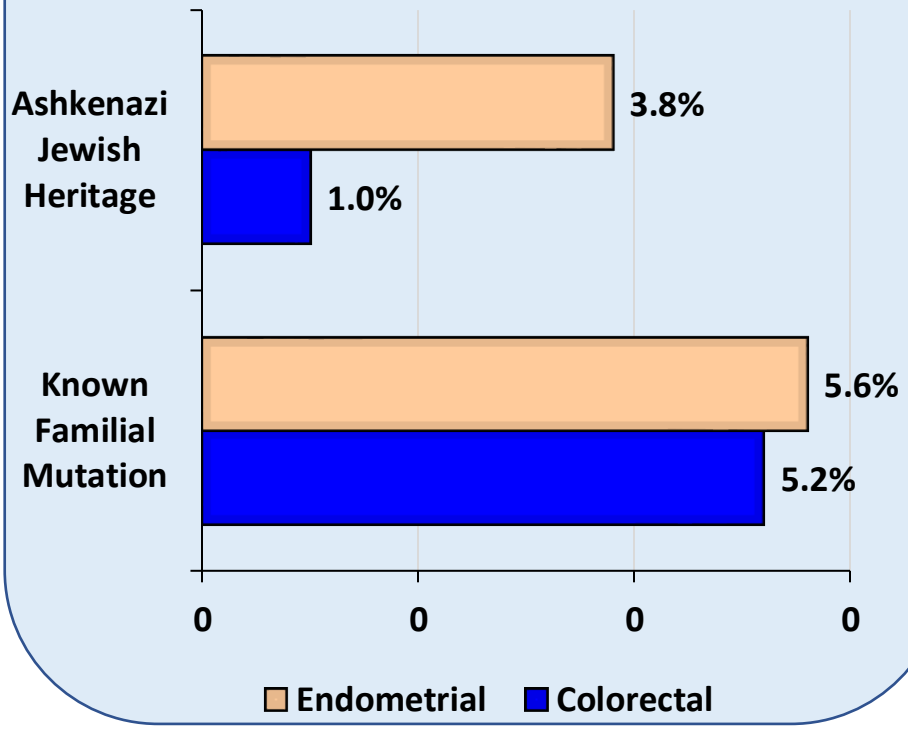
LS from the HCN & BRCA Databases, 2008-2018: Demographics

Gender among CRC Patients, 2008-2018

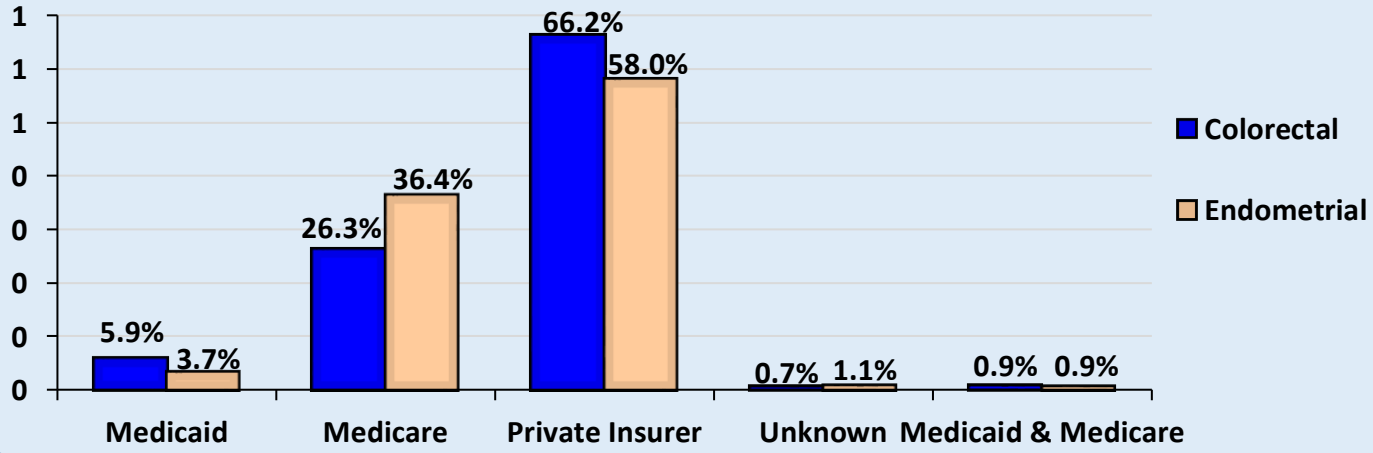


- Those diagnosed with endometrial cancer were more likely to be of Ashkenazi Jewish heritage compared to those diagnosed with colorectal cancer (**3.8% vs. 1.0%).**
- There are no differences between CRC and EC patients and having a known familial mutation.

Ashkenazi Jewish Heritage & Known Familial Mutation Status among CRC & EC Patients, 2008-2018



Insurance among CRC and EC Patients, 2008-2018



- Those diagnosed with CRC were more likely to have Medicaid compared to those diagnosed with EC (**5.9% vs. 3.7%).**
- Those diagnosed with EC were more likely to have Medicare compared to those with CRC **(36.4% vs. 26.3%).**

Colorectal Cancer (CRC) N = 1,130
Endometrial Cancer (EC) N = 847

LS from the HCN & BRCA Databases, 2008-2018: Age & History of Cancer

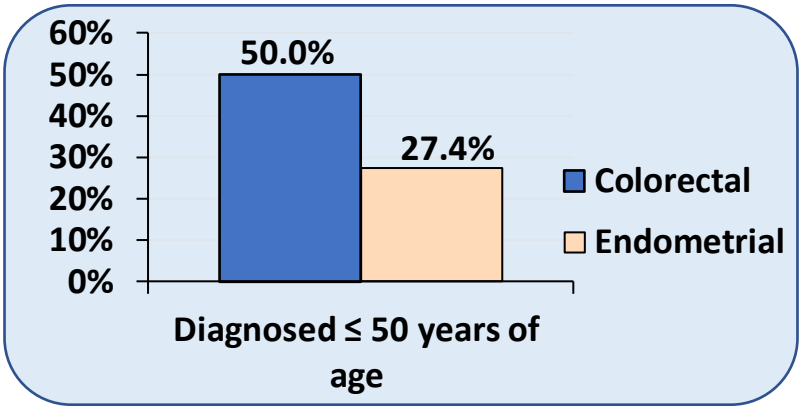
Average Age at First Visit among Colorectal & Endometrial Patients, 2008-2018

Colorectal: 55.8 years

Endometrial: 62.4 years

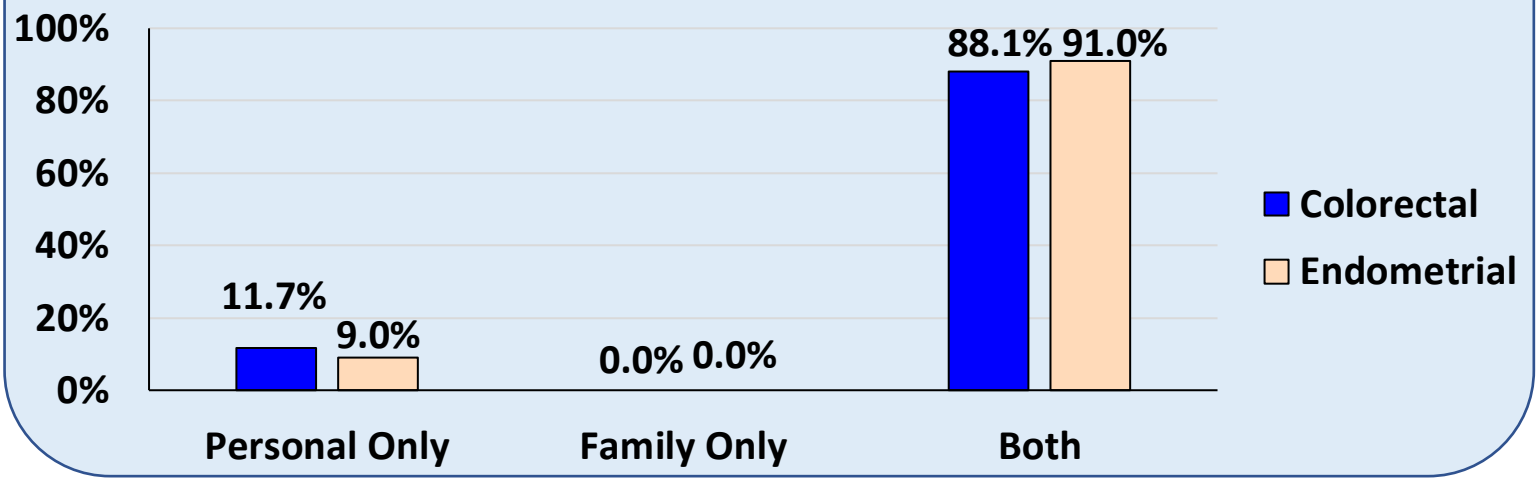
- Colorectal patients were more likely to be below the age of 50 compared to endometrial patients (**41.4% vs. 18.3%; data not shown).**

Colorectal & Endometrial Cancer Characteristics, 2008-2018



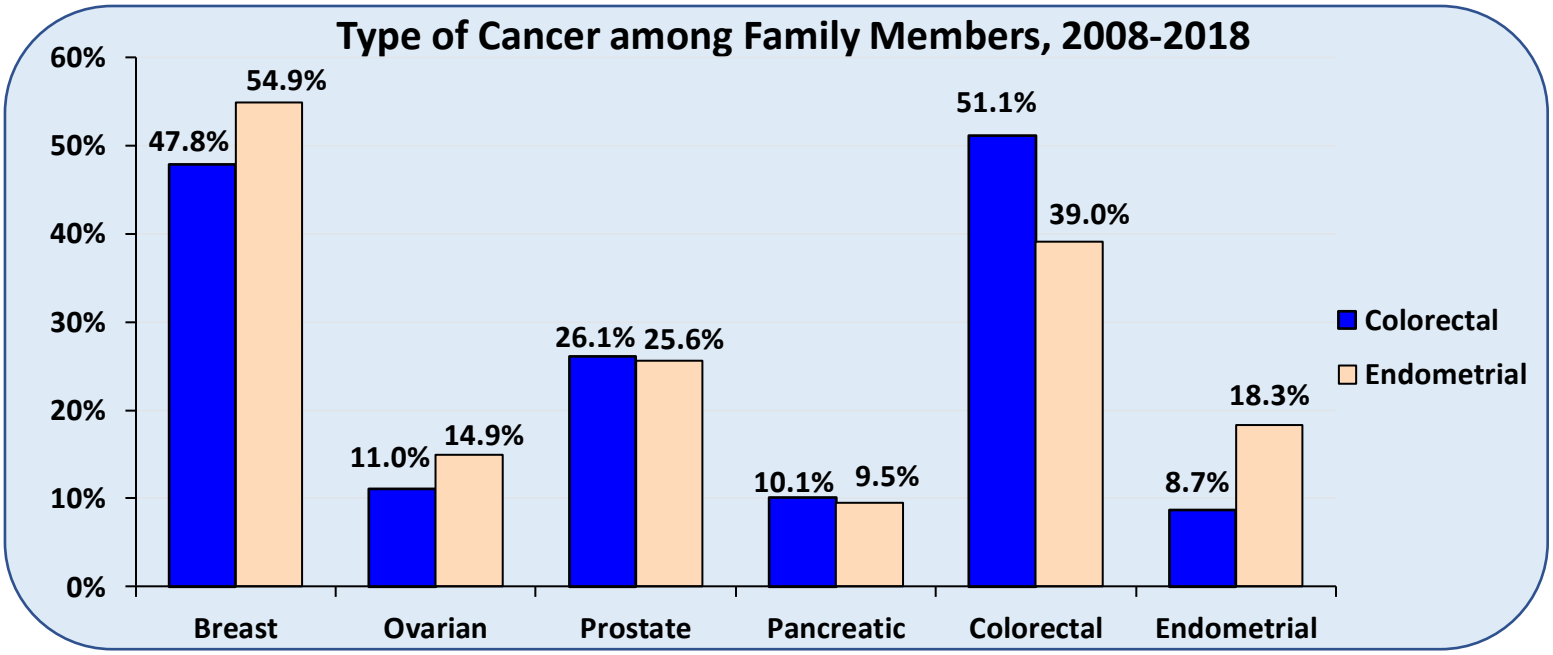
Those with colorectal cancer were more likely to be diagnosed with cancer at a young age compared to endometrial cancer patients (**50.0% vs. 27.4%**).

History of Cancer among Colorectal & Endometrial Patients, 2008-2018

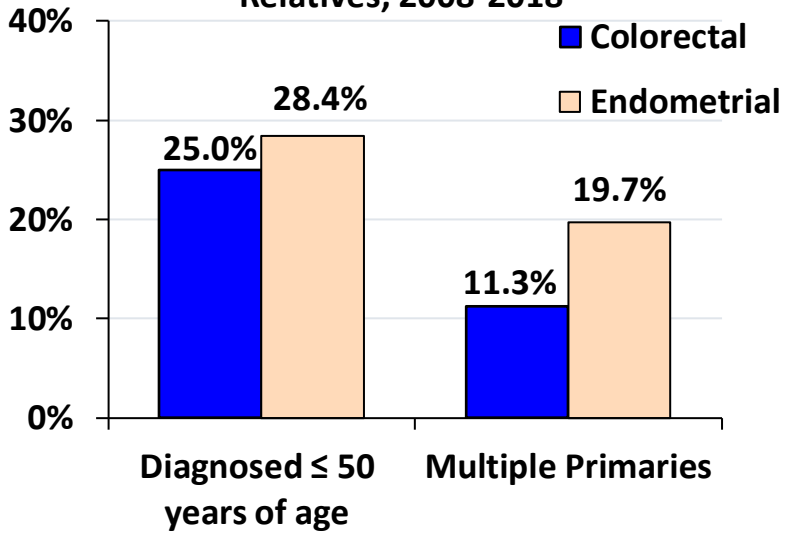


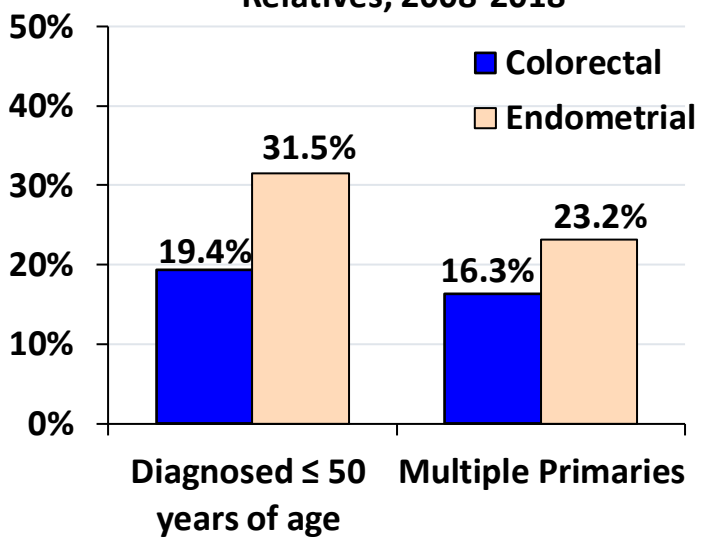
- Those with colorectal cancer were more likely to have only a personal history of cancer compared to those with endometrial cancer (**11.9% vs. 9.0%**).

LS from the HCN & BRCA Databases, 2008-2018: Family History of Cancer



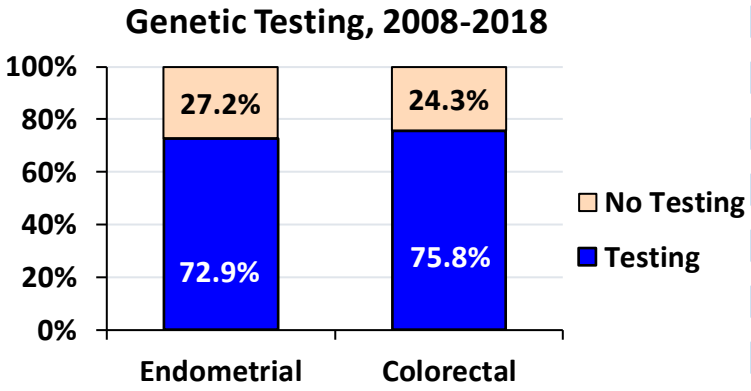
- Those diagnosed with endometrial cancer were more likely to have a relative diagnosed with the following cancer types compared to those diagnosed with colorectal cancer:
  - Breast cancer (**54.9% vs. 47.8%**)
  - Ovarian cancer (**14.9% vs.11.0%**)
  - Endometrial cancer (**18.3% vs. 8.7%**)
- Those diagnosed with colorectal cancer were more likely to have a relative diagnosed with colorectal cancer compared to those diagnosed with endometrial cancer (**51.1% vs. 39.0%**).

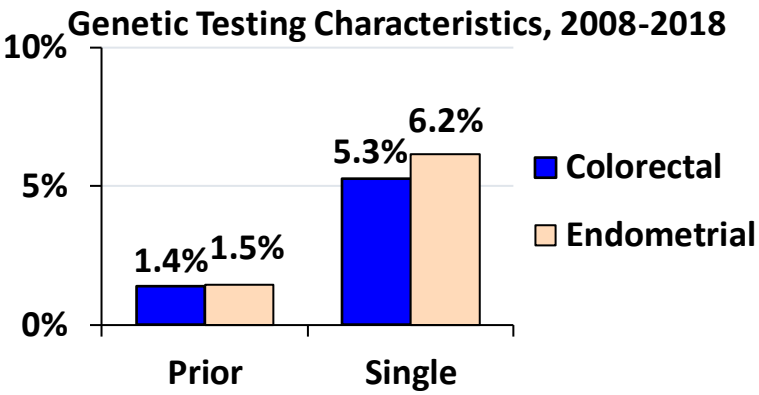


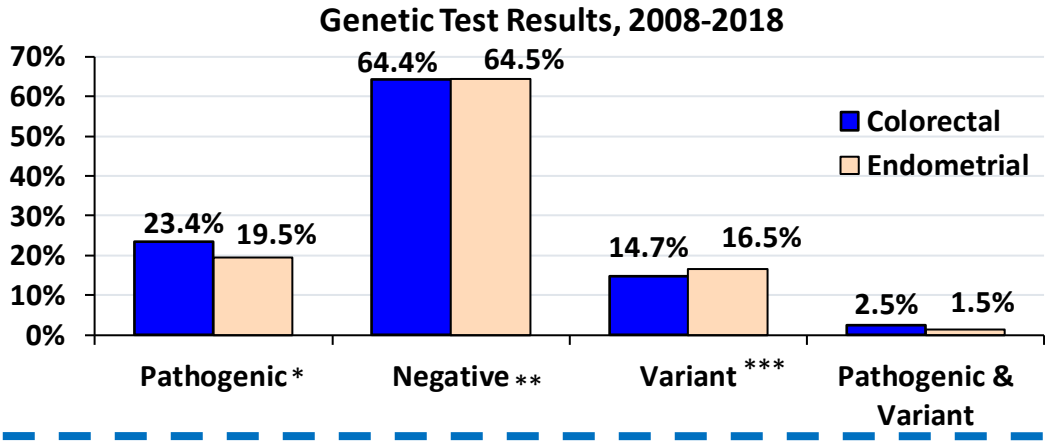


- Those diagnosed with endometrial cancer were more likely to have relatives diagnosed with the following characteristics:
  - A relative diagnosed with colorectal multiple primaries (**19.7% vs. 11.3%**).
  - A relative diagnosed with young endometrial cancer (**31.5% vs. 19.4%**).
  - A relative diagnosed with endometrial multiple primaries (**23.2% vs. 16.3%**).

LS from the HCN & BRCA Databases, 2008-2018: Genetic Testing

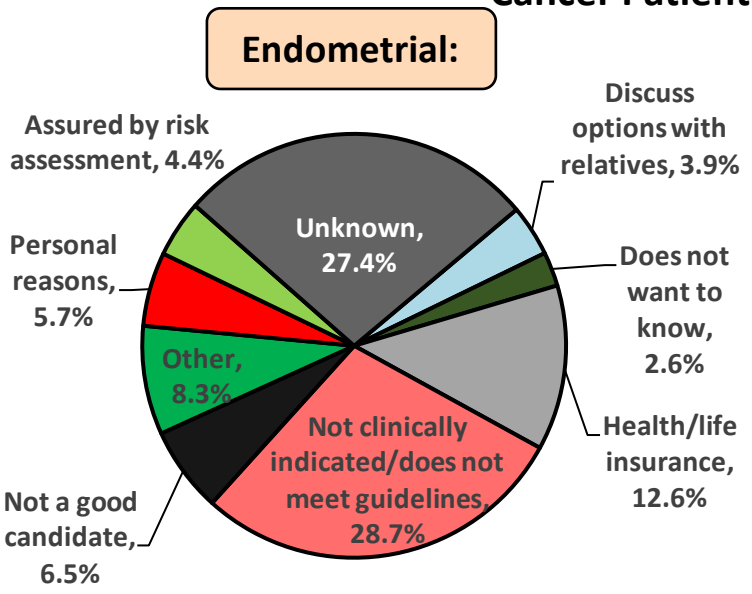


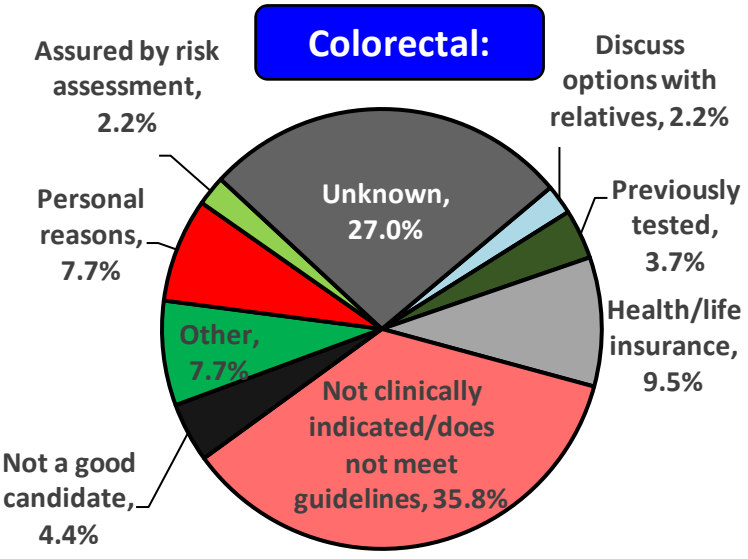




There were no differences in genetic testing, timing of genetic testing, single site testing, or genetic testing results between those with colorectal cancer and those with endometrial cancer.

Reason Why Genetic Testing Was Not Pursued among Colorectal & Endometrial Cancer Patients, 2008-2018





- Colorectal cancer patients were more likely to not receive testing because it was not clinically indicated compared to those with endometrial cancer (**35.8% vs. 28.7%**).
- Endometrial cancer patients were more likely to cite health insurance (**12.6% vs. 9.5%**) as the reason why testing was not pursued, however these differences were not significant.

* 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 when count is less than 6

Summary & Discussion

- Only 70-75% of colorectal and endometrial cancer patients in the HCN and BRCA databases received cancer genetic testing.
  - When looking at this population in Michigan by county, we see that out of the 76 counties where LS patients reside, 33 (**43.4%**) had genetic testing rates below 75%.
- Those diagnosed with endometrial cancer were more likely to identify as Ashkenazi Jewish compared to those diagnosed with colorectal cancer (**3.8% vs. 1.0%**).
  - According to NCCN and USPSTF guidelines for cancer genetic testing, these patients should receive cancer genetic services, since they are already at a higher risk for other gynecological cancer.
    - This can also be seen in the database in that those with endometrial cancer were more likely to be diagnosed with breast, ovarian and prostate cancer.
- There were no differences between colorectal and endometrial cancer patients in their genetic testing results, single site testing, or timing of their genetic testing services.
  - However, endometrial cancer patients are more likely to have a positive result in the following genes compared to colorectal cancer patients: **PMS2** (**14.2% vs. 7.5%**) and **MSH6** (**22.5% vs. 11.0%**).
  - Colorectal cancer patients are more likely to have a positive result in the following genes compared to endometrial cancer patients: **APC** (**8.5% vs. 0.0%**) and **MLH1** (**21.5% vs. 9.2%**).
- When considering all of those who met guidelines for cancer genetic testing, **81.1%** received genetic testing.
  - Most patients in this group were told they were it was not clinically indicated that they should receive these services.
    - This may be because most had at least one family member who had cancer, who would be tested first or since guidelines for Lynch syndrome genetic testing were not strictly followed until 2017.
  - Patients also indicated that issues with health insurance were why they could not pursue this service.
- Every year in November, the Cancer Genomics Program at MDHHS partners with the University of Michigan (UM) to put on a Family Day event where patients and family come together to learn about LS and what their risks may be. The hope is to bring more awareness and to encourage families to talk about risk and see a genetic counselor if appropriate.

For More Information:

Visit Michigan.gov/hereditarycancer to learn more about hereditary cancers.
Visit Michigan.gov/cge to view more data on hereditary cancer.

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

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MDHHS
Michigan Department of Health & Human Services

References:

1. Center for Disease Control and Prevention (CDC) 2020. Hereditary Colorectal (Colon) Cancer: Lynch Syndrome. Retrieved April 2021 from: https://www.cdc.gov/genomics/disease/colorectal_cancer/lynch.htm

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