Ontario Familial Colorectal Cancer Registry Newsletter

Sinai Health | Lunenfeld-Tanenbaum Research Institute

Spring 2023

Welcome to the Ontario Familial Colorectal Cancer Family Registry (OFCCR) Newsletter. We are pleased to announce that the US National Institutes of Health (NIH) has recognized the importance of our research and decided to continue funding the OFCCR as part of the Colon Cancer Family Registry Cohort (Colon CFR) for the next five years.

The Value of One, The Power of Many

Since the first participant joined the OFCCR in 1998, we have made so much progress:

Participants Enrolled

- **7,386 participants**
- **5.245 families**
- **1,948 control participants as a comparison group**

Data & Samples Collected

- **7,051 blood samples**
- **410 saliva samples**
- **3,337 tumor samples**
- **24,998 questionnaires**

Studies

- **253 studies in Canada, United Sates, Australasia, United Kingdom Europe, and/or China used OFCCR resources**
- **365 publications in scientific journals**

Your participation helped make many important studies possible. These studies are finding ways to prevent colorectal cancer, and identify which people are at highest and lowest risk for the disease.

See the Colon CFR website:
https://www.coloncfr.org
for more detailed information.

The Colon CFR will be funded until at least April 2028. It is very important that we continue to ask about screening, surgery, and new cancers that you or your relatives might have been diagnosed with since joining the OFCCR. Over the next five years we will contact you to update this information.

The Colon CFR remains the largest family study of colorectal cancer in the world. We have a unique opportunity to link information from health questionnaires with blood and tumor test results to gain new insights into factors related to colorectal cancer.

We are pleased to send you this newsletter to share updates on the Colon CFR and colon cancer science, and to give you a chance to give us news and feedback on the insert page enclosed.

We want to take this opportunity to celebrate your volunteer efforts for the OFCCR. Thank you very much for your time and commitment and we hope you will continue to support cancer research.

Sincerely,
Dr. Steven Gallinger
Principal Investigator, OFCCR

Please contact us if your: email address, phone number or address has changed. Thank You!

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Colorectal Cancer is Rising in Younger Adults

While the number of new cases of colorectal cancer in older age groups has been decreasing since the 1990s, largely due to screening, early-onset colorectal cancer (EO-CRC), which occurs in adults under age 50, has been rising in Canada, the United States, and many high income countries around the world.

This trend has persisted for several decades and is most obvious in men and women born since 1960 with more colorectal cancers found in men compared to women. We now see about 10% of new cases occurring in adults younger than 50. Research is focused on understanding the factors driving this trend to develop strategies for screening and prevention of this disease in young people.

There are some differences in the clinical features of colorectal cancer at older ages and EO-CRC. EO-CRC is most often found in the rectum and left colon and is more likely to be diagnosed at a higher stage where prognosis may be worse than colorectal cancers found earlier. Younger adults tend to present with symptoms such as rectal bleeding, abdominal pain, bloating and a change in bowel habits.

Although the reason(s) are unclear why EO-CRC more often presents at an advanced stage, many studies suggest people under 50 often have symptoms for a longer period of time and there may be a delay in diagnosis compared to older people. This is due in part to a lack of awareness about early-onset disease and its symptoms, which are often attributed to benign conditions, like hemorrhoids.

Risk Factors - Genetic

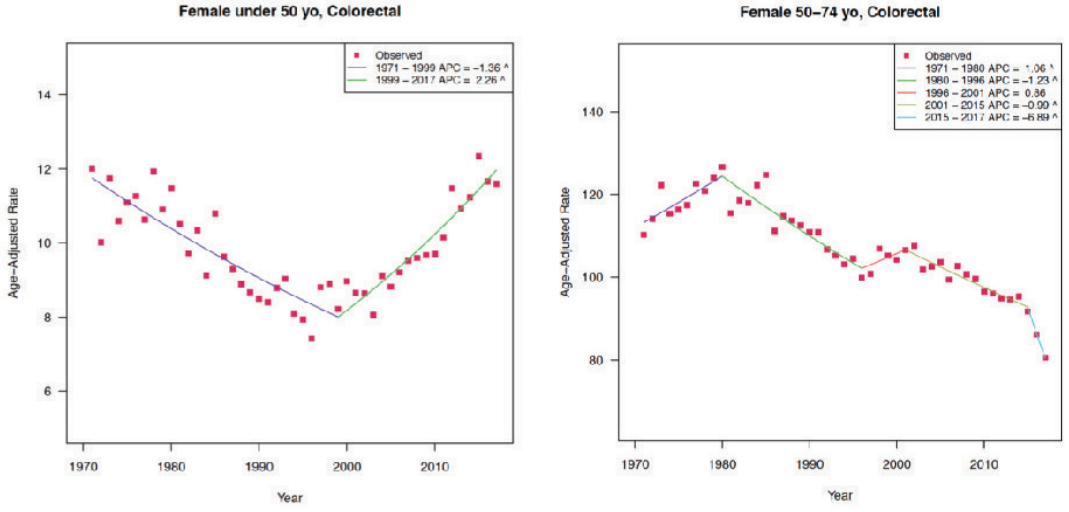
Family history of colorectal cancer is a strong risk factor for EO-CRC. About 25-30% of people with EO-CRC have at least one first degree relative (parent, sibling, child) with colorectal cancer and their diagnosis may be associated with inherited mutations in cancer risk genes. A study using data from the Colon Cancer Family Registry also confirmed this finding.

The Canadian Association of Gastroenterology suggests that "people with immediate family members diagnosed with colorectal cancer should be screened earlier and more regularly than those without a family history of the disease". They suggest screening with a colonoscopy or at-home fecal immunochemical test (FIT), starting between ages 40 and 50, or 10 years earlier than the age at which their relative was diagnosed.

Most provincial colorectal screening programs also consider adults with a first degree relative with CRC to be at higher risk and suggest discussing appropriate screening with their doctor. This article cannot provide medical advice. Individualized screening should be discussed with healthcare providers.

Risk Factors - Lifestyle

Most EO-CRC is considered sporadic (not related to family history or inherited gene mutations). This suggests changing lifestyle and environmental factors contribute to the trend. There have been many epidemiological studies conducted to identify potential risk factors.



Although the results are not conclusive, some lifestyle factors appear to be more consistently associated with EO-CRC and need to be studied further such as:

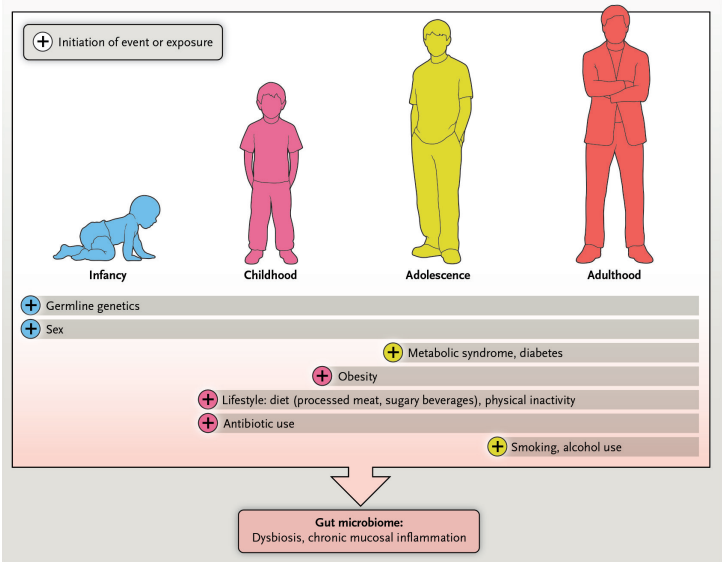
- Obesity and related factors such as sedentary behaviour, high triglycerides
- Diet – particularly more processed meats and sweetened soft drinks. Western-style diets with more red meat and less vegetables
- Alcohol

Other possible environmental factors of interest are smoking, antibiotic use, and early life exposures from prenatal to adolescence.

Data from the Colon CFR have been used in two large, international studies related to risk factors for EO-CRC. One study found that risk factors associated with later-onset colorectal cancer were also associated with EO-CRC.

The other study developed personal risk scores that considered environmental and genetic factors that have the potential to determine the risk level of individuals. Using these scores may help identify those at higher risk who might benefit from early screening.

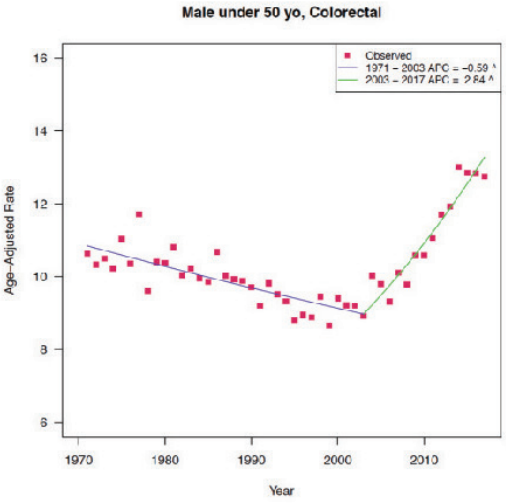
These non-genetic risk factors can impact the gut microbiome and inflammation which are both thought to affect the development of colorectal tumors.

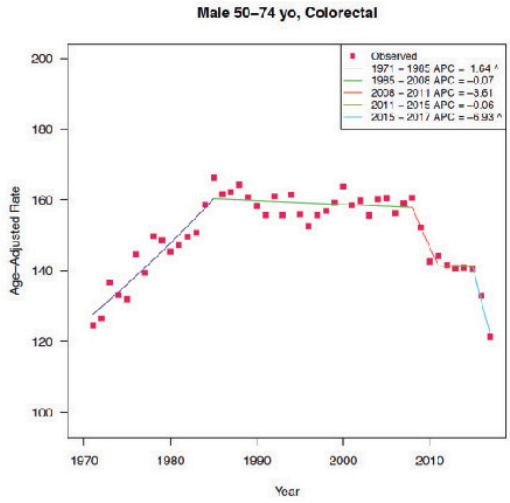


Factors Influencing the Risk of Colorectal Cancer:
Genetics, sex, diet and other lifestyle exposures, and health conditions interact with the gut microbiome over a patient's lifetime and influence the risk of colorectal cancer.

Future Directions

More research is needed involving large numbers of participants, of various ages and a comprehensive list of possible risk factors, including environmental exposures from childhood to young adulthood. The ultimate goal is to develop prevention and screening strategies to protect younger generations.





Graphs are based on data from the National Cancer Incidence Reporting System and the Canadian Cancer Registry

Microbiome Collection Feasibility Study

By: Dr. Emily Vogtmann, National Cancer Institute

Microbes, including bacteria, fungi, and viruses, exist in and on the human body. These communities of micrcobes are known as the human microbiome. The Human Microbiome Project was initiated in 2007 at the US National Institutes of Health to characterize the microbial communities from many body habitats (https://commonfund.nih.gov/hmp).

Since then, many scientists have begun to study how the human microbiome relates to health and disease. Many studies have shown associations between the fecal microbiome and colorectal cancer, but these samples were usually collected at the time of diagnosis.

The Colon Cancer Family Registry (Colon CFR) cohort represents a unique opportunity to collect fecal and oral samples from those previously diagnosed with cancer and their family members.

Colon CFR and National Cancer Institute investigators started a feasibility study in 2021 to determine how many CCFR participants would collect and return samples for microbiome studies.

This feasibility study was conducted at the Australasian Colorectal Cancer Family Registry, the Cedars-Sinai Colorectal Cancer Registry, and the Ontario Familial Colorectal Cancer Registry (OFCCR).

At the OFCCR, 178 people were contacted to participate in this study. Of those, 97 (54%) agreed to participate. Collection kits were mailed to those who agreed to participate, and 84 (87%) people returned their kits.

Image: Relative abundance pie chart for the microbes found in a human oral sample. Generated using data from Vogtmann E, et al (2018) *CEBP*, ***27(5):594-600.***

The fecal and oral samples were sent to the investigators at the National Cancer Institute, who will use them for microbiome sequencing. Using the generated data, the investigators can compare the fecal and oral microbiome from participants in Australia, Canada, and the United States, and can also explore the associations with other exposures such as probiotics.

Once the feasibility study is completed, the investigators will determine whether they will expand collection to more members of the Colon CFR cohort. If this proceeds, the samples could be used to understand whether the oral or fecal microbiome is tied to colorectal cancer risk or survival after diagnosis.

Ontario Colorectal Cancer Screening Program

https://www.cancercareontario.ca/en/types-of-cancer/colorectal/screening