The following colorectal cancer treatment and research updates extend from November 16th, 2023, to January 17th, 2024, inclusive and are intended for informational purposes only.

This content is not intended to be a substitute for professional medical advice. Always consult your treating physician or guidance of a qualified health professional with any questions you may have regarding your health or a medical condition. Never disregard the advice of a medical professional or delay in seeking it because of something you have read on this website.
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1. TRK Fusion Cancer and How to Test for It (Oct.13/23)

**What is TRK fusion cancer?**
- TRK (pronounced track) fusion cancer is a term used to describe cancers that are caused by a change to the neurotrophic tyrosine receptor kinase (NTRK) gene called a fusion
- During this fusion, an NTRK (pronounced on-track) gene joins together, or fuses, with a different gene
- This joining causes the body to make TRK fusion proteins, which can cause cancer cells to multiply and form a tumour
- The presence of TRK fusion proteins may be associated with more aggressive cancer

Having TRK fusion cancer doesn't change your original diagnosis, it just means that your tumour is driven by an NTRK gene fusion

**Testing is the only way to find out if NTRK gene fusion is driving your cancer**

**Who should be tested for NTRK gene fusions?**
- Your doctor may consider testing in people:
  - with solid tumours that are metastatic, and
  - who are likely to experience severe complications from surgical resection, and
  - when there are no satisfactory treatments options available

It's important to know what's driving your cancer to help your doctor take action

**FastTRK**

FastTRK is a clinical testing program for diagnosing NTRK gene fusions
Sponsored by Bayer, this is a complimentary service for healthcare professionals to find out if their patients' cancer has an NTRK gene fusion

Talk to your doctor about which tests are recommended for you
INTRODUCING

Tumour-Agnostic Therapies

Advances in precision medicine have brought therapies that specifically target what is driving a patient’s cancer.

Treatment with more traditional cancer therapies is based on where the tumour is located in the body.

Tumour agnostic therapies target a specific genomic change in the cancer cells regardless of where the tumour is located in the body.

Genomic changes in cancer cells are identified through diagnostic testing of the cancer cells. The results help clinicians decide on a treatment for each patient.

Advantages of tumour agnostic therapies:
- Targets the genomic change that is the root cause of the cancer to suppress tumour growth
- Harnesses our growing understanding of cancer biology
- Offers an innovative, new and effective approach to treating cancer

Change required to adopt tumour agnostic therapies in Canada:
- A shift in mindset: this is a new concept that differs from the traditional approach of treating cancer based on tumour location
- Access to genomic testing: identifying patients who would benefit from treatments requires a robust testing infrastructure
- An evolved, more adaptive assessment of treatments for public coverage is required that includes recognition of smaller patient populations, new clinical trial methods, and ability to examine new data over time

https://www.bayer.ca/en/media/news/?id=TmpBPQ==&st=1
2. **OH-CCO Biomarker Testing Program (Jan. 11/24)**

![OH-CCO Biomarker Testing Program]

**OH-CCO Biomarker Testing Program**

*Funded NTRK Testing by Disease Site*

<table>
<thead>
<tr>
<th>Based on Ontario Health Cancer Care Ontario Comprehensive Biomarker Testing Program. As of October 1, 2023, V3324-2.</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Must be ordered by physicians including, but not limited to, medical oncologists</em></td>
</tr>
<tr>
<td><em>Including sporadic medullary and RAI-refractory well-differentiated</em></td>
</tr>
<tr>
<td>OH, Ontario Health; CCO, Cancer Care Ontario; NTRK, neurotrophic tyrosine receptor kinase; NGS, next generation sequencing; IHC, Immunohistochemistry; NSCLC, non-small-cell lung carcinoma; GIST, gastrointestinal stromal tumour; CNS, central nervous system; MSC, mammary analogue secretory carcinoma; CRC, colorectal cancer; MSI-H, high microsatellite instability; HCC, hepatocellular carcinoma; RAI, radioactive iodine.</td>
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**List of Sites for the program (NTRK on pg.19)**

3. **Immunotherapy Combined with Targeted Therapy in Patients with BRAF V600E–Mutated CRC (Oct.15/23)**

In one of the first clinical trials combining immunotherapy and targeted therapy for patients with BRAF V600E–mutated colorectal cancer (CRC), researchers discovered that a combination regimen of dabrafenib, trametinib, and spartalizumab resulted in long-lasting responses. The study successfully met its primary endpoint and achieved a confirmed response rate of 24.3%, compared with a response rate of 7% in a prior trial where patients were treated with each of the same targeted therapies individually. The researchers also reported improved outcomes in one of the trial’s secondary endpoints: durability. Previously, patients with BRAF V600E–mutated CRC have seen only a short-lived clinical benefit after treatment with BRAF or MEK inhibitors. But the combination therapy resulted in an increased durability of response, with a median progression-free survival of 5 months compared with 3.5 months with BRAF or MEK inhibitors alone. The researchers noted that 57% of the patients continued with the treatment for more than 6 months and 18% continued for more than 1 year.

The findings suggested how targeted therapies in combination with immunotherapies may drive a greater immune response and improve treatment overall. This merits further clinical investigation and preclinical experiments to determine the best targeted approach to increase immune reactivity against [BRAF-mutated] CRC. The researchers acknowledged that the implications of their research may go well beyond CRC.


4. **VITRAKVI (Larotrectinib) is Now Covered in Ontario, Quebec, Saskatchewan, Manitoba and New Brunswick (Oct.15/23)**

VITRAKVI (Larotrectinib) is now funded for eligible patients in Ontario, Quebec, Saskatchewan, Manitoba and New Brunswick. VITRAKVI is a targeted therapeutic indicated for solid tumors with Neurotrophic Tyrosine Receptor Kinase (NTRK) gene fusions, which can result in the production of TRK fusion proteins that can lead to uncontrolled cell growth and cancer.
6. Skincare Tips while on Cetuximab or Panitumumab Treatment for CRC (Oct. 28/23)

Amgen has collaborated with FUSE Health and Dr. Nathan Lamond (Medical Oncologist, Dalhousie University) to produce a 5-minute video on the importance of good skin hygiene for patients on EGFRi therapy. During this talk, Dr. Lamond discusses the importance of good skin care to help prevent or lessen skin side effects caused by certain cancer treatments such as cetuximab and panitumumab used to treat colorectal cancer (CRC). Dr. Lamond provides tips for protecting the skin and using appropriate soaps, cleansers, moisturizers, sunscreens, and lip balms.

To download and view the video:
https://fusehealth.sharefile.com/d-s2d0a0747b8154e368ed5219e5654421c

6. PERIOP-06 Study at Sunnybrook Hospital To Treat Liver Metastases (Oct. 30/23)

We are inviting you to take part in a voluntary research study | PERIOP-06

Why are we doing this study?
The purpose of the PERIOP-06 clinical trial is to see how effective a new medication is. This new medication is called QBECO and is made by a Canadian company called DaBios. We want to see if QBECO can prevent or slow colorectal cancer from coming back in patients who have had surgery to remove cancer that has spread to the liver. To do this, you will be randomly assigned to receive either QBECO or a placebo (a drug that looks like the study drug but contains no medication) so we can compare QBECO to the usual care. Both you and your study doctor will not know if you are receiving the study drug or placebo.

What are the possible benefits of taking part in this study?
- The QBECO medication may benefit you more than the usual care for your cancer.
- There is evidence that QBECO may be effective in preventing the growth of colorectal cancer in humans from a previous Phase 1 clinical trial.
- The information learned from this study might help other patients in the future.
- You will have close follow-ups for 5 years after surgery.

What are the possible disadvantages & risks of taking part in this study?
- QBECO may not benefit you more than the usual care for your cancer.
- You may experience side effects from the QBECO medication.
- You can find more information below and in Section 13. “What risks can I expect from taking part in this study?” of the informed consent document.

Do I have to take part in this study?
Your participation is voluntary. You may choose not to participate. If you choose to participate, you may change your mind at any time. Regardless of your choice, your medical team will continue to take care of you.

Common Side Effects of QBECO
In 100 people receiving QBECO more than 5 and up to 15 may have the following side effects:
- Tenderness at the injection site. This typically gets better in 2 days. If the redness or swelling is bigger than 7 cm, please contact a member of the study team.
- Temporary mild fatigue following the first few doses of QBECO
- Temporary nausea
- Temporary fever
- Temporary headache
- Increased General Inflammation

Additional Drug Risks
QBECO is not known to interact with other drugs.

Rare And Serious Side Effects of QBECO
In 100 people receiving QBECO, 3 or fewer may have:
- Pancreatitis
- Symptoms include: Abdominal or back pain, nausea, vomiting
- Hepatitis [inflammation of the liver]
- Electrolyte abnormalities [determined with lab test]
- Kidney failure

These serious side effects have only been reported in patients who were given QBECO to treat Crohn’s disease and ulcerative colitis. No serious side effects were reported in 109 patients who received QBECO for advanced cancer.

What should I do if I am experiencing symptoms?

Visual Summary of Trial Activities

<table>
<thead>
<tr>
<th>Day Relative to Surgery</th>
<th>Details</th>
<th>Trial Activities</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eligibility Screening</td>
<td>The research team will confirm eligibility. Routine bloodwork will be done.</td>
<td>Blood Sample</td>
<td>Survey and pregnancy test (if appropriate)</td>
</tr>
<tr>
<td>+1 to +3 days</td>
<td>You will give yourself a subcutaneous injection (QBECO therapy or placebo) every 2 days before surgery for at least 11 days.</td>
<td>QBECO Therapy or Placebo</td>
<td>If your surgery is delayed, you can take QBECO (or placebo) up to 120 days before surgery.</td>
</tr>
<tr>
<td>Day of Surgery</td>
<td>You will have your surgery following the usual care procedures. Additionally, a sample of tumor tissue will be collected.</td>
<td>MRI/CT scan</td>
<td>Compliance and side effect assessment. The compliance and side effect assessment may be collected over the phone the day before the surgery.</td>
</tr>
<tr>
<td>+1 and +4 (11) Days(s)</td>
<td>You will be monitored in the hospital following your surgery. QBECO or placebo will be taken every 3 days.</td>
<td>Survey on day 4 (±1) only</td>
<td></td>
</tr>
<tr>
<td>+7 to 41 Days</td>
<td>You will continue to give yourself a subcutaneous injection of QBECO therapy or placebo every 2 days after your surgery for 41 days.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+6 (±10 d) weeks</td>
<td>Once your injections are complete, you will have a follow-up appointment.</td>
<td>Other Assessments</td>
<td>Survey and side effect assessment. There will be a range of 1 to 14 days for your 3 month visit and a range of ± 28 days for all remaining visits.</td>
</tr>
<tr>
<td>+3, 6, 9, 12, 15, 18, 21, and 24 Months</td>
<td>To check for the progression of cancer, imaging and blood samples will be done every three months for 2 years after surgery.</td>
<td>Compliance and side effect assessment will be at 3 months only</td>
<td></td>
</tr>
<tr>
<td>+2.5 to 5 Years</td>
<td>To check for the progression of cancer, imaging and a blood sample will be done every 6 months until 5 years after your surgery.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Legend:
- Approximately half-day hospital visit
- Overnight hospital visit
- At your house

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Here is a link to the consent form, containing additional information about the study:

PERIOP-06_ICF.pdf


For more information, please visit the OncoHelix website

8. AZUR-1 and AZUR-2 Dostarlimab Trials Open in Canada (Dec.13/23)

Dostarlimab is an IgG 4 isotype humanized monoclonal antibody meaning it is made in a lab to serve as substitute antibodies that can restore, enhance, modify or mimic the immune system's attack on unwanted cells. In this case, dostarlimab blocks the interaction of PD-1 to its ligands PD-L1 and PD-L2 found on tumor cells. By blocking PD-1 activity, dostarlimab activates T cells allowing them to attack cancer cells by detecting and killing them. Dostarlimab has been approved for adult patients with mismatch repair-deficient (MMR-D) recurrent or advanced endometrial cancer (EC) in the US, and for MMR-D/microsatellite instability-high (MSI-H) recurrent or advanced EC in the EU. The drug is being investigated in multiple tumor types and in combination with other anticancer agents.
AZUR-1: Phase 2 Study
A single-arm, open label study of dostarlimab monotherapy in participants with untreated stage 2/3 MMR-D/MSI-H locally advanced rectal cancer.

AZUR-2: Phase 3 Study
An open-label, randomized study of peri-operative dostarlimab monotherapy vs standard of care in participants with untreated T4N0 or stage 3 MMR-D/MSI-H resectable colon cancer.

Might Statins Help Fight Colon Cancer Tumor Growth? (Dec.31/23)

Cholesterol is generally considered a pro-growth molecule, being a building block for cell membranes and having other growth-supporting functions. Prior studies have linked high blood cholesterol levels to various cancers, including colorectal cancers (CRCs). However, it hasn’t been clear that lowering cholesterol, for example with common statin drugs, can prevent CRCs. This is because targeting cholesterol has a preventive but selective effect only against serrated polyps and tumors. Serrated polyps are so-called because of their sawtooth appearance under a microscope. They are flatter than ordinary colorectal polyps and can often be missed during colonoscopies. Yet the tumors into which they develop, which account for roughly 15 to 30 percent of CRCs, contain many "metaplastic" cells that are particularly invasive and resistant to treatments.

Previous research used mice engineered to lack two enzymes known as aPKCs, whose low levels were linked to serrated polyps and tumors. The study revealed that cholesterol synthesis was upregulated, suggesting that cholesterol may be an early driver of tumor development. Additionally, loss of these protein kinases led to an activation of a transcription factor called SREBP2, which switches on cholesterol production. Therefore, in this case of tumour cell, SREBP2 is constantly being activated, cholesterol is constantly made, and cholesterol is constantly being imported.
Statins are one of the most commonly prescribed drugs in the United States, and many other countries and have been shown to reduce the risk of major cardiac events by reducing the amount of cholesterol in the blood. Researchers were planning on developing a clinical trial to determine if statins could lower the risk of cancer in patients with serrated adenoma as evidence was growing that statins could help reduce the risk of several types of cancer. A 2020 study found evidence that statins may “starve” cancer cells to death and a 2019 study found a link between taking a statin before diagnosis and a reduction in cancer-specific deaths among patients with CRC. Designing a trial to examine whether statins could help people who have polyps removed would be a long-term investigation, as it takes around 5 years for the polyps to come back, if they do at all.


10. More Colorectal and Endometrial Cancers Could Be Treated with Immunotherapy, Study Shows (Dec.29/23)

A new study shows thousands more patients diagnosed with colorectal and endometrial cancers could benefit from immunotherapy than are currently offered it. Researchers showed the importance of looking at DNA Mismatch Repair Deficiency (MMR-D) as a guiding marker for treatment decisions using immune checkpoint inhibitors (ICIs). MMR-D is associated with an increased risk of developing several types of cancer.

The study, which published in Cancer Cell on December 28, compared two lab testing methods to diagnose cancers—traditional immunohistochemistry (IHC) (a lab technique that uses antibodies to detect antigens in tissues) — and next-generation sequencing (NGS) — a new technology used for DNA sequencing that can detect specific patterns of mutations. The researchers discovered that NGS offers a more accurate assessment of MMR status. 1% of patients with colorectal cancer (CRC) and 6% of patients with endometrial cancer are functionally mismatch repair-deficient but are still missed by IHC, the current standard of care testing. However, these cancers are detected by NGS. Importantly, results showed that these patients (missed by IHC and detected by NGS) achieved long-term benefit from immunotherapy.

Researchers estimate that implementing NGS alongside IHC could identify an additional 6,000 patients in the United States annually who could benefit from life-extending immunotherapy. These patients would not be offered immunotherapy if IHC was used alone.

https://medicine.yale.edu/news-article/more-colorectal-and-endometrial-cancers-could-be-treated-with-immunotherapy-study-shows/

11. Patients With mCRC May Continue Benefitting From Immunotherapy After Treatment Discontinuation (Dec.18/23)

Immune checkpoint inhibitors (ICIs) have proven effective against certain solid tumors, including those with a high microsatellite instability (MSI-H) or deficient DNA mismatch repair (dMMR) status. To date, four ICIs have been approved by the U.S. Food and Drug Administration (FDA) for the treatment of advanced MSI-H/dMMR colorectal cancer (CRC).

According to results published in Cancer Research Communications, the majority of patients with metastatic CRC (mCRC) whose cancer did not progress during initial treatment with ICIs had no disease progression two years after discontinuing treatment. When patients’ colorectal tumors shrink or remain stable during ICI treatment, physicians may discontinue their immunotherapy after two years. Some patients may also cease ICI therapy earlier due to unmanageable side effects. Stopping a treatment regimen that was working can make patients nervous that the benefits will stop as well.

A retrospective analysis of 64 patients with MSI-H/dMMR mCRC who were treated with an ICI revealed that all patients had experienced a durable benefit at the time of treatment cessation; 48 patients discontinued treatment due to a prolonged benefit, and 16 discontinued treatment due to side effects. Patients had received ICI therapy for a median of 17.6 months. At a median of 22.6 months after stopping immunotherapy, 88% of patients had not experienced a recurrence. The progression-free survival rate after cessation of immunotherapy was 98% at one year, 91% at two years, and 84% at three years post-treatment. The rates were not significantly different whether patients had discontinued treatment due to side effects or due to a prolonged response. The researchers investigated other factors that may influence the likelihood of relapse after treatment cessation. No significant differences in progression rates were observed whether patients had received single-agent or combination ICI therapy; whether or not they had
metastases to the liver, peritoneum, or lymph nodes; and whether or not their tumors had mutations in KRAS, NRAS, or BRAF. Patients with lung metastases had a higher chance of recurrence than patients without lung metastases.

These data may alleviate the fears of physicians who may not want to discontinue a patient’s treatment because of high-risk tumor characteristics. They also provide important information that oncologists can use for guiding discussions with patients with MSI-H/dMMR CRC by providing clearer numbers for the likelihood of progression should they decide to stop their immunotherapy treatment.


New research finds that GLP-1 receptor agonist medications (GLP-1 RAs), like Ozempic, that treat type 2 diabetes and obesity may also reduce the risk of colorectal cancer (CRC). The electronic health records of more than 1.2 million patients who were given antidiabetic agents from 2005–2019 were analyzed. The research team examined the effects of GLP-1 RAs on their incidence of CRC, as compared to those prescribed other antidiabetic drugs. They discovered the following:

- Of 22,572 patients with diabetes treated with insulin, there were 167 cases of CRC.
- Of 22,572 matched patients treated with GLP-1 RAs, there were 94 cases of CRC, meaning those who were treated with GLP-1 RAs had a 44% reduction in the incidence of CRC.
- 18,518 patients with diabetes treated with GLP-1 RAs, had a 25% reduction in CRC compared to 18,518 patients with diabetes who were treated with Metformin.
- Overall, GLP-1 RAs, like Ozempic, lowered the rate of CRC.

Due to the drug class’ ability to combat obesity, there are certain factors to consider in this correlation. Being overweight, having obesity, or having type 2 diabetes are risk factors for increasing the incidence of CRC and for making its prognosis worse. These patients also have a higher likelihood of dying from CRC. This risk is related to the effect of elevated levels of glucose and insulin in patients with diabetes, levels that may promote the growth of tumors. The risk reduction may be due to more than weight loss caused by these medications. The GLP-1 RAs significantly reduced CRC incidence in patients with or without overweight and obesity.


13. Combination Therapy and Appropriate Dosing to Target KRAS in CRC (Dec.7/23)

CodeBreaK 300 is a phase 3 trial of the selective Kirsten rat sarcoma viral oncogene homologue (KRAS) glycine-to-cysteine mutation at codon 12 (KRAS G12C) inhibitor sotorasib in combination with the epidermal growth factor receptor (EGFR) inhibitor panitumumab in patients with metastatic colorectal cancer (mCRC) with KRAS G12C mutation.

In this trial, two investigational groups — one that received full-dose sotorasib (960 mg once daily) in combination with panitumumab and one that received lower-dose sotorasib (240 mg once daily) in combination with panitumumab — were compared with a group that received standard late-line therapy. Progression-free survival was significantly longer in the two sotorasib–panitumumab groups than in the standard-care group.

In the CodeBreaK 300 trial, progression-free survival was the primary end point. It will be important to see the final overall survival results in this population of patients with refractory metastatic CRC. Mature data from this trial and data from KRYSRAL-10 will provide much-needed insight. The CodeBreak 300 trial is an exciting first step for targeting KRAS in CRC cancer, and the researchers look forward to continuing to refine the therapeutic approach against KRAS-mutated CRCs with KRAS G12C inhibitors, new RAS inhibitors, and a growing understanding of therapy resistance.

14. Hepatic Artery Infusion Pump (HAIP) Chemotherapy Program – Sunnybrook Odette Cancer Centre (Dec.1/23)

The HAIP program is a first-in-Canada for individuals where colon or rectal cancer (colorectal cancer) has spread to the liver and cannot be removed with surgery. The program involves a coordinated, multidisciplinary team approach to care, with close collaboration across surgical oncology, medical oncology (chemotherapy), interventional radiology, nuclear medicine, and oncology nursing. The Hepatic Artery Infusion Pump (HAIP) is a small, disc-shaped device that is surgically implanted just below the skin of the patient and is connected via a catheter to the hepatic (main) artery of the liver. About 95 percent of the chemotherapy that is directed through this pump stays in the liver, sparing the rest of the body from side effects. Patients receive HAIP-directed chemotherapy in addition to regular intravenous (IV) chemotherapy (systemic chemotherapy), to reduce the number and size of tumours. Drs. Paul Karanicolas and Michael Raphael are the program leads and happy to see patients who may be eligible for the therapy.

Presently at Sunnybrook Odette Cancer Centre, HAIP is being used in patients with colorectal cancer that has spread to the liver that cannot be removed surgically and has not spread to anywhere else in the body. Patients who have few (1-5) and very small tumors in the lungs may be considered if the lung disease is deemed treatable prior to HAIP. If you believe you may benefit from this therapy and/or would like to learn more about the clinical trial, your medical oncologist or surgeon may fax a referral to 416-480-6179. For more information on the HAIP clinical trial, please click on the link provided below.

http://sunnybrook.ca/content/?page=colorectal-colon-bowel-haip-chemotherapy

15. Living Donor Liver Transplantation for Unresectable CRC Liver Metastases (Dec.2/23)

Approximately half of all colorectal cancer (CRC) patients develop metastases, commonly to the liver and lung. Surgical removal of liver metastases (LM) is the only treatment option, though only 20-40% of patients are candidates for surgical therapy. Surgical therapy adds a significant survival benefit, with 5-year survival after liver resection for LM of 40-50%, compared to 10-20% 5-year survival for chemotherapy alone. Liver transplantation (LT) would remove all evident disease in cases where the colorectal metastases are isolated to the liver but considered unresectable.

While CRC LM is considered a contraindication for LT at most cancer centers, a single center in Oslo, Norway demonstrated a 5-year survival of 56%. A clinical trial sponsored by the University Health Network in Toronto will offer live donor liver transplantation (LDLT) to select patients with unresectable metastases limited to the liver and are non-progressing on standard chemotherapy. Patients will be screened for liver transplant suitability and must also have a healthy living donor come forward for evaluation. Patients who undergo LDLT will be followed for survival, disease-free survival, and quality of life for 5 years and compared to a control group who discontinue the study before transplantation due to reasons other than cancer progression.

https://clinicaltrials.gov/ct2/show/NCT02864485
16. In Vivo Lung Perfusion (IVLP) for CRC Metastatic to Lung (Dec.9/23)

A new study is investigating a technique called In Vivo Lung Perfusion (IVLP) for delivering chemotherapy directly into the lungs at the time of surgery. Delivering chemotherapy directly to the lungs could potentially kill any microscopic cancer cells that are present in the lungs at the time of surgery, while sparing other major organs in the body from the side effects of chemotherapy.

At the University Health Network, this IVLP technique has been used recently in a Phase I study in patients with sarcoma, and they are now expanding on that experience to include patients with colorectal metastases. The purpose of this study is to test the safety of the IVLP technique and find the dose that seems right in humans. Participants are given oxaliplatin into one lung via IVLP and are watched very closely to see what side effects they have and to make sure the side effects are not severe. If the side effects are not severe, then more participants are asked to join the study and are given a higher dose of oxaliplatin. Participants joining the study later on will get higher doses of oxaliplatin than participants who join earlier. This will continue until a dose is found that causes severe but temporary side effects. The other lung will not be infused with anything, so that researchers can limit unforeseen toxicity to a single lung and see if one lung does better than the other.

The estimated enrolment is 10 participants, each with a diagnosis of colorectal carcinoma. The primary outcome is safety as measured by acute lung injury findings and the estimated primary completion date is January 1, 2027.

[Image: In Vivo Lung Perfusion Model]

https://clinicaltrials.gov/ct2/show/NCT05611034?term=ivlp&draw=2&rank=1
Image Source: https://pie.med.utoronto.ca/TVASurg/project/in-vivo-lung-perfusion/

17. Study Offered at the Odette Cancer Centre to Treat Recurrent Rectal Cancer (Dec.9/23)

Magnetic resonance-guided focused ultrasound (MRg-FU) is a less invasive; outpatient modality being investigated for the thermal treatment of cancer. In MRg-FU, a specially designed transducer is used to focus a beam of low-intensity ultrasound energy into a small volume at a specific target site in the body. MR is used to identify and delineate the tumour, focus the ultrasound beam on the target, and provide a real-time thermal mapping to ensure accurate heating of the designated target with minimal affect to the adjacent healthy tissue. The focused ultrasound beam produces therapeutic hyperthermia (40-42°C) in the target field, causing protein denaturation and cell damage. Currently, there is no prospective clinical data reported on the use of MRg-FU in the setting of recurrent rectal cancer. Recurrent rectal cancer is a vexing clinical problem. Current retreatment protocols have limited efficacy. The addition of hyperthermia to radiation and chemotherapy may enhance the therapeutic response. With recent advances in technology, the investigators hypothesize that MRg-FU is technically feasible and can be safely used in combination with concurrent re-irradiation and chemotherapy for the treatment of recurrent rectal cancer without increased side-effects. The study is being offered at the Odette Cancer Centre. Here is the link to the study protocol:

https://clinicaltrials.gov/ct2/show/NCT02528175?term=magnetic+resonance+guided+focused+ultrasound&recr=Open&rank=1
18. Trends in the Incidence of Young-Onset CRC with a Focus on Years Approaching Screening Age (Dec.10/23)

With recent evidence for the increasing risk of young-onset colorectal cancer (yCRC), the objective of this population-based longitudinal study was to evaluate the incidence of yCRC in one-year age increments, particularly focusing on the screening age of 50 years. The study was conducted using linked administrative health databases in British Columbia, Canada including a provincial cancer registry, inpatient/outpatient visits, and vital statistics from January 1, 1986 to December 31, 2016. Researchers calculated the incidence rates per 100,000 at every age from 20 to 60 years and estimated annual percent change in incidence (APCi) of yCRC using joinpoint regression analysis. 3,614 individuals were identified with yCRC (49.9% women). The incidence of CRC steadily rose from 20 to 60 years, with a marked increase from 49 to 50 years. Furthermore, there was a trend of increased incidence of yCRC among women. Analyses stratified by age yielded APCi's of 2.49% and 0.12% for women aged 30-39 years and 40-49 years, respectively and 2.97% and 1.86% for men. These findings indicate a steady increase over one-year age increments in the risk of yCRC during the years approaching and beyond screening age. These findings highlight the need to raise awareness as well as continue discussions regarding considerations of lowering the screening age.

https://academic.oup.com/jnci/advance-article/doi/10.1093/jnci/djaa220/6119347?guestAccessKey=af490637-e51e-44d0-81b9-d1f2df7b60c9

19. Screening for CRC in Individuals Younger Than 50 Years (Dec.20/23)

To inform considerations about the age at which colorectal cancer (CRC) screening should best be initiated, the Canadian Agency for Drugs and Technologies in Health (CADTH) identified and summarized studies comparing CRC screening in individuals of average risk younger than 50 years with either no screening or screening in individuals of average risk aged 50 years and older.

Data from 1 retrospective cohort study in the US conducted in a large sample across 13 years suggested there is higher incidence of CRC among individuals between the ages of 45 and 49 years who underwent screening colonoscopy than in those between the ages of 50 and 54 years. Estimates from 4 modelling studies (1 of which was Canadian) that investigated screening in individuals younger than 50 years indicate that life-years may be gained, CRC cases and deaths may be reduced, but that numbers of lifetime colonoscopies and complications from screening would likely increase.

Seven evidence-based guidelines identified recommend that colorectal cancer screening be initiated in individuals of average risk at age 45 years, whereas 1 guideline recommends against screening in individuals of average risk beginning at 45 years and 1 guideline recommends against screening beginning at age 40 years. Most evidence-based guidelines highlight the lack of empirical evidence describing clinical effectiveness and cost-effectiveness as limitations when developing recommendations.

Additional opportunities for maximizing the benefits of CRC screening may include targeting increased uptake among disadvantaged and high-risk groups, including those 50 years and older. Broader considerations that address societal benefit and costs — including health equity and implementation — are essential to inform decision-making concerning CRC screening in individuals of average risk younger than 50 years.


20. Rising CRC Risk in Young Adults Calls for Earlier Screening (Dec.7/23)

In a recent study published in JAMA Network Open, researchers analyzed the prevalence of adenomas and advanced adenomas (AAs) and the incidence of colorectal cancer (CRC) among younger, symptom-free adults. The incidence and mortality of CRC have reduced in various European countries and the United States (US) over the past three decades among people aged 55 and older. This reduction might have been due to greater adherence to screening. Meanwhile, CRC incidence and mortality rates in younger adults have increased. The American Cancer Society recommends reducing the age of people undergoing screening to 45 years. Colonoscopy is the standard for screening CRC. Adenomas elevate the risk of progression to CRC, and they are classified into non-advanced adenomas and AAs, and the AA-to-CRC transition rate increases with age. Additionally, male sex has been reported as an independent CRC-associated factor.

The study included 296,170 patients who underwent screening colonoscopies during 2008–18. Of these, approximately 4% were aged under 50 years, and the remaining were aged ≥ 50. Complications were reported for 640 patients. The median detection rate was 21.4% and 6.6% for adenomas and AAs, respectively. Taken together, the prevalence of adenomas increased among younger people since 2008, and this trend was evident in all age groups.
The prevalence of AAs increased among younger adults but decreased among those aged 50 or older between 2008 and 2018. Since 1988, CRC incidence has declined among people aged ≥ 50 and increased in males younger than 50 but not in females. The findings suggest that screening should start at the age of 40 for males and 50 or later for females.

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2812587

### 21. Young Adult CRC Clinic Available at Sunnybrook (Dec.5/23)

A recent study led by the University of Toronto doctors has observed a rise in colorectal cancer (CRC) rates in patients under the age of 50. The study mirrors findings from the U.S., Australia and Europe. The growing CRC rates in young people come after decades of declining rates in people over 50, which have occurred most likely due to increased use of CRC screening (through population-based screening programs) which can identify and remove precancerous polyps. Patients diagnosed under the age of 50 have a unique set of needs, challenges and worries. They are unlike those diagnosed over the age of 50.

Dr. Shady Ashamalla (colorectal cancer surgical oncologist), along with Dr. Petra Wildgoose (Hepatobiliary and Colorectal Oncology Surgical Assistant), and their team at the Sunnybrook Health Sciences Centre understand the needs of this patient population.

Both belong to a multidisciplinary team of experts in the Young Adult Colorectal Cancer Clinic who work with young CRC patients, regardless of disease stage, to create an individualized treatment plan to support each patient through their cancer journey. Patients’ needs and concerns will be addressed as they relate to:

- Fertility concerns and issues
- Young children at home
- Dating/intimacy issues
- Challenges at work
- Concerns about hereditary cancer
- Relationships with family and friends
- Psychological stress due to any or all of the above

The team of experts consists of:

- Oncologists (medical, surgical, radiation)
- Social workers
- Psychologists
- Geneticists
- Nurse navigator

Should a patient wish to be referred to Sunnybrook, they may have their primary care physician, or their specialist refer them to Sunnybrook via the e-referral form, which can be accessed through the link appearing below. Once the referral is received, the Young Adult Colorectal Cancer Clinic will be notified if the patient is under the age of 50. An appointment will then be issued wherein the patient will meet with various members of the team to address their specific set of concerns.

http://sunnybrook.ca/content/?page=young-adult-colorectal-cancer-clinic
CCRAN’s Partnership with “Count Me In” (Dec.1/23)

CCRAN is proud to partner with Count Me In, a nonprofit research initiative, on The Colorectal Cancer Project. This new project is open to anyone in the United States or Canada who has ever been diagnosed with colorectal cancer (CRC). Patients can find out more and join at JoinCountMeIn.org/Colorectal.

Through the project, patients are asked to complete surveys to share information about their experience with CRC, to share biological sample(s), and to allow for the research team to request copies of their medical records. The project team then de-identifies and shares data from these with the entire research community.

Every patient’s story holds a piece of the puzzle that can help us better understand CRC. By discovering more about what drives cancer and sharing this data, CCRAN and the Colorectal Cancer Project believe insights can be gained to develop more effective therapies. One of the aims of the project is to reach populations that have been understudied, including individuals who are diagnosed with CRC at a young age, individuals from marginalized communities who have historically been excluded from research, and patients with metastatic CRC. Together, we can accelerate our understanding of CRC. To learn more or sign up to participate, visit JoinCountMeIn.org/Colorectal.

"Count Me In", a nonprofit cancer research initiative, is inviting all patients across the United States and Canada who have ever been diagnosed with colorectal cancer (CRC) to participate in research and help drive new discoveries related to this disease. The Colorectal Cancer Project will enable patients to easily share their samples, health information and personal lived experiences directly with researchers in order to accelerate the pace of research. Patients who have been diagnosed with CRC at any point in their lives can join the project by visiting JoinCountMeIn.org/colorectal. From there, patients will be invited to share information about their experience through surveys and to provide access to medical records as well as saliva samples and optional blood, stool, and/or stored tissue samples for study and analysis. Researchers from the Broad Institute of MIT and Harvard and Dana-Farber Cancer Institute use this information to generate databases of clinical, genomic, molecular, and patient-reported data that is then de-identified and shared with researchers everywhere. To date, more than 9,000 patients with different cancers have joined Count Me In and shared their data. "We still do not know why there is an alarming rise in CRC in young adults", said Andrea Cercek, MD Co-Director, Center for Young Onset Colorectal and Gastrointestinal Cancers Memorial Sloan Kettering Cancer Center and co-scientific leader of the Colorectal Cancer Project. "What we do know is that this is a global phenomenon that affects otherwise healthy individuals with no known risk factors. The Colorectal Cancer Project will provide researchers important information that will lead to a better understanding of this disease."

Over 250 patients have joined the Colorectal Cancer Project since the launch in fall 2021. Every patient that joins the Colorectal Cancer Project enables us to learn more about colorectal cancer. Pts diagnosed at any age, whether newly diagnosed or years from their diagnosis, can enroll. If you have ever been diagnosed with colorectal cancer, you can visit JoinCountMeIn.org/Colorectal to enroll and have a direct impact on research and future treatment strategies.
Every colorectal cancer patient’s story holds a piece of the puzzle that can help us better understand how to treat this disease. Join our partners at @joincountmein to help generate more data for CRC by sharing your medical records, samples, and unique experiences with researchers everywhere.

Learn more at JoinCountMeIn.org/colorectal


23. CCRAN Has Launched 4 New Information/Support Groups Based On Age and Disease Stage (Dec.2/23)

CCRAN is pleased to announce a new format for monthly information / support group meetings. To ensure peer support is relevant, meaningful and timely for each participant, CCRAN has stratified the groups according to disease stage and early vs average onset colorectal cancer.

Meetings will begin with a brief presentation on a topic of relevance. Following the presentation, patients and caregivers will be assigned to the support group of relevance to them. Please RSVP to Cassandra Macaulay: Cassandra.m@ccran.org. We look forward to hosting you at our monthly information/support group meetings.

24. LifeLabs Has Launched Signatera, Offering Canadians an Innovative and Personalized Approach to Managing Cancer (Dec.1/23)

LifeLabs is pleased to share the launch of Signatera, a highly sensitive, personalized molecular residual disease assay (MRD) test developed by Natera for treatment monitoring and molecular residual disease (MRD) assessment in patients previously diagnosed with cancer. This innovative test uses circulating tumor DNA (ctDNA) and is personalized for each patient to help assess recurrence risk and identify relapse up to two years earlier than the current standard of care tools. The clinical utility of Signatera across cancer types has been validated by multiple studies. In those trials, Signatera demonstrated predictive values such as:
Signatera testing involves two phases with pre-supplied collection kits. The first phase is an initial test that analyzes both a tumour tissue and blood sample, and the second phase involves subsequent blood tests on an as-needed basis. It is a safe, non-invasive way to monitor ctDNA levels to help physicians understand treatment efficacy and detect relapse without the inconvenience of repeated tissue biopsies and/or imaging.


25. Natera Announces Publication of Prospective, Multi-Site CIRCULATE Study in Nature Medicine Demonstrating Signatera’s Ability to Predict Chemotherapy Benefit in CRC (Jan.17/23)

Natera, Inc., a global leader in cell-free DNA testing, announced the publication of a new study in *Nature Medicine*, which demonstrates the ability of the Signatera molecular residual disease (MRD) test to identify patients with stage II-IV colorectal cancer (CRC) who are at an increased risk of recurrence and predict who is likely to benefit from adjuvant chemotherapy (ACT).

The paper describes results from the GALAXY arm of the ongoing CIRCULATE-Japan trial, which is one of the largest and most comprehensive prospective studies of MRD testing in resectable CRC. The data builds on results previously presented at the 2022 ASCO Gastrointestinal Cancers Symposium (ASCO GI), now with median clinical follow-up extended to 16.74 months and DFS assessment at 18 months.

In the study, 1,039 patients with stage II-IV resectable CRC were monitored prospectively using the Signatera MRD test. Key takeaways include:
- **Post-surgical MRD status was predictive of chemotherapy benefit**
- **Post-surgical MRD status was the most significant prognostic risk factor for recurrence**, in a multivariate analysis that accounted for all clinicopathological risk factors currently used for prognostication (HR 10.82, p-value <0.001).
- **Pre-surgical detection rate of 95.9%** in patients with pathologic stage II-III disease and 93.1% in patients with stage II-IV disease.
- **Signatera dynamics are indicative of treatment response**

This study provides strong evidence that Signatera MRD-positive patients will benefit significantly from adjuvant therapy, while MRD-negative patients may be safely observed, regardless of clinical or pathological stage.


Novel research has identified significant variations in the gut microbiome of individuals who developed pre-cancerous colonic lesions, suggesting a possible connection between gut bacteria and the onset of colorectal lesions and cancers. These findings, presented at UEG Week 2023, open promising new avenues for enhancing the detection and prevention of colorectal cancer (CRC).
The large-scale prospective study, involving 8208 participants, linked data from the Dutch Microbiome Project with the Dutch nationwide pathology database to identify all recorded cases of colonic biopsies from the last five decades. Researchers analyzed the function and composition of the gut microbiomes of individuals who developed pre-cancerous colorectal lesions before fecal sampling between 2000 and 2015, as well as those who developed lesions after fecal sampling between 2015 and 2022. These groups were then compared with individuals with normal colonoscopy findings and the general population.

The results revealed that individuals who developed colonic lesions after fecal sampling exhibited increased diversity in their gut microbiome compared with those who did not develop lesions. Moreover, the composition and function of the microbiome differed among individuals with pre-existing or future lesions and varied based on the type of lesion.

The connection between the gut microbiome and pre-cancerous lesions has been under-explored, leaving uncertainty about whether gut bacteria can predict the future onset of CRC. Our findings suggest that the microbiome could act as a valuable tool to improve existing tests, advancing early detection methods for pre-cancerous lesions and CRC.

https://ueg.eu/a/343


27. Postoperative ctDNA-Based Molecular Residual Disease in Patients with BRAF V600E and MSI-H CRC (Nov.3/23)

Postoperative circulating tumor DNA (ctDNA)-based molecular residual disease (MRD) is reported to be associated with a high risk of recurrence. In this paper, the authors present an updated analysis of MRD detection and correlations with BRAF and microsatellite instability (MSI) status in radically resected, stage II-IV colorectal cancer (CRC) from the observational GALAXY study.

Among 3,615 CRC patients who were enrolled between May 2020 and April 2022 in GALAXY study, 2,083 patients that met the inclusion criteria were analyzed. The median follow-up period was 16.3 months. Of 2,083 patients included in the analysis, 60 (2.9%) had BRAF V600E mutant and microsatellite stable (MSS) tumors, 100 (4.8%) had BRAF wild-type (wt) and MSI-High tumors, and 115 (5.5%) had BRAF V600E mutant and MSI-High tumors. In the overall population, 286 (14%) were ctDNA-positive at the 4-week MRD time point and 1,797 (86%) were ctDNA-negative.

Patients with ctDNA-positivity at the 4-week demonstrated inferior disease-free survival (DFS) and were 12x more likely to recur, compared to ctDNA-negative patients. Patients with BRAF wt and MSI-High tumors had significantly better DFS compared to patients with BRAF V600E and MSS tumors. Patients with BRAF V600E mutant and MSI-High tumors had significantly better DFS compared to pts with BRAF wt and MSS tumors. On the other hand, ctDNA-positivity was associated with significantly shorter DFS in patients with BRAF V600E mutant and MSS tumors and BRAF V600E mutant and MSI-High tumors compared to patients with BRAF wt and MSS tumors.

ctDNA status at the postoperative MRD time point is the most prognostic risk factor of DFS regardless of BRAF V600E or MSI-H status. Patients with positive postoperative ctDNA should be examined carefully due to a high risk of recurrence. ctDNA-guided adjuvant strategies will further be established by the ongoing randomized VEGA and ALTAIR studies in CIRCULATE-Japan.


28. Novel Approach to Proficiency Testing Highlights Key Practice Variations in Cancer Biomarker Delivery (Jan.4/24)

Laboratory-based biomarker testing is a cornerstone of precision cancer care. In many disease sites, treatment decisions are heavily predicated on biomarker data. The complexity of cancer biomarkers has increased dramatically and includes modalities such as comprehensive next-generation sequencing and immunohistochemistry, among others. External quality assurance (EQA) programs have emerged as a critical tool for laboratories to maintain the quality and accuracy of biomarker data. Typically, programs will provide ‘unknown’ samples, which will be tested at local laboratories, with participants’ results compared to a reference standard.

In this study, challenge specimens were made using resected colon cancer tissue, each paired with a fictional clinical vignette, and distributed to participants who were asked to provide all molecular testing required and return a final report for each case upon completion. Reports were redistributed to an assessor team including medical oncologists,
each of whom was asked to recommend a systemic therapy based on each lab’s biomarker report. Participants were graded based on their ability to guide oncologists to the correct treatment. Eight laboratories participated. Three laboratories were found to have suboptimal results, two leading oncologists to incorrect therapeutic prescriptions, and one withdrawn. Turnaround time ranged from 6 to 86 days (median 24). Substantial qualitative reporting differences were identified. This study demonstrates the feasibility of end-to-end proficiency testing. The approach provides considerable value beyond analytic accuracy, including specimen management, turnaround time, and communication of results. Results suggest that reporting differences may lead to treatment disparities. This style of quality assurance will help reinforce good practices critical to the delivery of precision cancer care.

https://www.mdpi.com/2673-5261/5/1/1/htm

29. A Variety of Treatment Options Are Becoming Available in CRC (Dec.31/23)

Kristen K. Ciombor, MD, MSCI, recently spoke at an Around the Practice discussion regarding treatment updates, molecular testing options, and emerging targets in the world of metastatic colorectal cancer (mCRC). She discussed these updates with CancerNetwork.

At your institution, what are the current treatment sequencing options in CRC?

At Vanderbilt [they] have a lot of clinical trials open. Additionally, those like the phase 3 BREAKWATER and the phase 3 MOUNTAINEER-03 trials are about to open. There are also good standard-of-care options from the beginning that are targeted: for instance, immunotherapy for patients who have microsatellite instability [MSI]–high [disease]. Then [they] have a lot of chemotherapy options, even for patients who are not in clinical trials.

Looking forward, how do you hope to see the field evolve in the next 5 years?

[Dr. Ciombor is] hoping [they] see more treatment options for patients and [they] identify more patient subtypes that [they] can target and find actionable alterations for. [She] also hopes that [they] find more treatments that are durable. [They are] seeing that a little bit in immunotherapy and even with some of the trastuzumab [Herceptin]/tucatinib [Tukysa] data. However, [she would] like to see more treatment options that are less toxic and more durable in terms of response.

What was your biggest takeaway from the discussion with your colleagues today?

There are so many options in the HER2- amplified space in CRC, which is nice to see. It takes some thought. It is specific to CRC because how we treat HER2-positive breast cancer is not how we treat HER2-positive CRC. The nuances of the data are key. Knowing how to apply those in each individual patient is important.

Are you currently involved in any ongoing research?

[Dr. Ciombor has] an ongoing phase 2 ECOG study, ECOG-ACRIN, which is looking into the rectal cancer space for patients with MSI-high, locally advanced rectal cancer being treated with immunotherapy. Patients are given nivolumab and ipilimumab plus or minus 4 courses of radiation. [They are] currently at the interim analysis, and looking forward to seeing the results of that soon.

https://www.cancernetwork.com/view/a-variety-of-treatment-options-are-becoming-available-in-crc

30. Top 5 Most-Read CRC Articles of 2023 (Dec.30/23)

These are the top 5 articles for colorectal cancer (CRC) in 2023:

5. Clinical Staging of CRC Increased in Post–COVID-19 Period

When comparing the 22 months before to the 22 months after the pandemic, decreases in the number and availability of screenings for cancer during the pandemic led to stage migration in the initial diagnosis of CRC. There was a notable decrease in patients who received a diagnosis of CRC at clinical stage T1 (~8.73%) and clinical stage 0 (~2.80%). An increase in clinical stage T4 diagnoses were found in that same timeframe (12.67%). Read the full article here.

4. FDA Grants Breakthrough Therapy Designations to Trastuzumab Deruxtecan for HER2+ Solid Tumors, Including mCRC

The FDA had granted fam-trastuzumab deruxtecan-nxki (Enhertu) 2 breakthrough therapy designations to treat patients with unresectable or metastatic solid tumors that had progressed after prior treatment in patients with HER2-positive metastatic CRC (mCRC). The DESTINY-CRC01 and DESTINY-CRC02 phase 2 trials were used as the basis of the
approval for treatment in CRC specifically. DESTINY-CRC01 demonstrated an objective response rate of 45.3% whereas the DESTINY-CRC02 had a confirmed objective response rate of 37.8%.

Read the full article here.

3. Takeda Stakes $1.13 Billion on Rights to Fruquintinib for Advanced Refractory CRC

Fruquintinib, an oral inhibitor of vascular endothelial growth factor receptors-1, -2, and -3, was licensed by Takeda in January to develop and commercialize for subtypes of refractory mCRC. The drug had met its primary end point of improving overall survival in a phase 3 multiregional clinical trial of patients with refractory mCRC.

Read the full article here.

2. A “Sludge Audit” for Health System CRC Screening Services

A study published in the print version of *AJMC* found that a sludge audit method was able to identify and quantify sludge in the screening processes for CRC performed by a health system. The authors found that there was a 60.4% screening rate, with half of screening orders not completed. Sludge was found in the health system’s communication, time, administrative tasks, technology, paperwork, and low-value care.

Read the full study here.

1. FDA Approves Trifluridine/Tipiracil Plus Bevacizumab in Previously Treated mCRC

The FDA approved trifluridine and tipiracil (Lonsurf) and bevacizumab (Avastin) as a joint treatment for patients with mCRC who had been previously treated. Data from the SUNLIGHT phase 3 trial was used as a basis for the approval, which found that there was a 39% reduction of the risk of death when using bevacizumab with trifluridine/tipiracil compared with using trifluridine/tipiracil alone. The risk of disease progression or death also saw a 56% reduction when using bevacizumab.

Read the full article here.


31. 2023 in Medicine: Colon Cancer (Dec.24/23)

There has been a huge increase in the proportion of colon and rectal cancer incidence in people under 55, in fact, it’s doubled over the past 20 years from 11% to 20%. Early onset cancer is defined as being diagnosed under the age of 50 and current recommendations for colorectal cancer (CRC) screenings start at around age 45.

A recent study identified four key symptoms linked to an increased risk of early-onset CRC in younger adults. The symptoms included abdominal pain, rectal bleeding, diarrhea, and iron deficiency anemia. Out of this list of symptoms, diarrhea is not uncommon. Iron deficiency anemia is not uncommon. And what was emphasized in the study was that having just one of these symptoms could almost double your risk of colon cancer.

A multitude of factors can explain the rise of colon cancer rates. It may be attributed to being a byproduct of how we live and work. Most of us engaged in any type of knowledge work where you’re sitting all day, there’s going to be health consequences. So lifestyle factors play a role, diet plays a role. Of course, a person’s health history, and even family history of colon cancer can also play a role.


Image Source: https://www.flaticon.com/free-icon/colorectal-cancer_7196541

32. Potential Link Exists Between Constipation and CRC (Dec.5/23)

Colorectal cancer (CRC) may be caused by constipation, according to a study published in *Frontiers in Oncology*, where a Mendelian randomization (MR) found that a potential link existed between the 2 conditions. The primary MR method used was the Inverse Variance Weighted (IVW)-Random Effects. The study included data for constipation from 218,810 European individuals; CRC from 377,673 European individuals; colon cancer from 462,933 European individuals; and rectal cancer from 456,276 European individuals.
A potential causal link was indicated by the IVW-random effect analysis between constipation and CRC. The researchers did not find a causal association in any other IVW approach, nor did they find a causal association of constipation on colon or rectal cancer alone. Additionally, there was no evidence found of a causal effect of CRC on odds of constipation in the IVW-random effects analysis. No other approach was able to find a causal relationship of CRC, colon cancer, or rectal cancer on constipation.

Overall, the researchers concluded that the study provides evidence that constipation could increase the risk of CRC. Being able to manage constipation could help to prevent CRC in the future, making it a key risk factor, and a healthy diet and balanced gut microbiota could help to reduce the risk of CRC in patients who have had constipation in the past.

https://www.ajmc.com/view/potential-link-exists-between-constipation-colorectal-cancer


33. Genes and Race in Colon Cancer (Dec.7/23)

Innocenti et al, conducted next-generation sequencing (NGS) on primary biopsy specimens from 548 participants in CALGB/SWOG using FoundationOne testing. They demonstrated three novel and high-impact findings:

1. Black patients have a distinct pattern of mutations, for example they were more likely to have right-sided cancers and mutations in KRAS and APC than White patients and had fewer mutations in RNF43. This could reflect environmental exposures that may also be seen in early-onset colorectal cancer (CRC).

2. Mutations in LRP1B (10.7% of patients) were associated with improved overall survival (OS), potentially marking it a novel prognostic marker for colon cancer.

3. Mutations in RNF43 were predictive of poor outcomes, in particular in patients treated with cetuximab, and were far more common in right-sided cancers, indicating a possible explanation for the differential benefit of EGFR inhibitors in left- versus right-sided cancers.

There is now suggestive data on a mutational profile that has common features with early-onset CRC and Black race, and further prospective studies are required to validate these findings and identify potential causes of this presentation. These findings underscore the importance of integrating NGS into clinical practice for metastatic colon cancer to identify critical biomarkers that influence patient outcomes, enhance prognostication, and inform treatment planning.

https://ascopubs.org/doi/10.1200/JCO.23.02094

34. CRC: Incidence and Time to Recurrence (Dec.1/23)

A nationwide Danish cohort study reported in JAMA Oncology found that the 5-year risk of recurrence after surgery for stage I to III colorectal cancer (CRC) decreased over time and the time to recurrence was shorter with a more advanced disease stage.

The study used the Danish Colorectal Cancer Group Database to identify patients with stage I to III CRC who underwent primary surgery between January 2004 and December 2019. Stage-specific 5-year recurrence—reported as the cumulative incidence function of recurrence—was assessed for the surgery periods of 2004 to 2008, 2009 to 2013, and 2014 to 2019. Among 34,166 patients with stage I to III CRC, 7,027 (20.6%) developed recurrence within 5 years after primary surgery. Among all patients, the 5-year cumulative incidence function of recurrence for CRC decreased over the three time periods from 26.9% to 22.2% and to 15.8%.

For colon cancer, the 5-year cumulative incidence function of recurrence decreased over the three time periods from 16.3% to 6.8% for stage I disease, from 21.9% to 11.6% for stage II disease, and from 35.3% to 24.6% for stage III disease. For rectal cancer, the 5-year cumulative incidence function of recurrence decreased over the three time periods from 19.9% to 9.5% for stage I disease, 25.8% to 18.4% for stage II disease, and 38.7% to 28.8% for stage III disease. The median time from surgery to recurrence was 22.6 months in patients with stage I disease, 18.2 months in those with stage II disease, and 15.9 months in those with stage III disease. The differences were consistent across all time periods. CRC detected through screening was associated with lower stage-adjusted risks of recurrence vs CRC not detected through screening. Because the risk of recurrence was so low in selected patient groups, future research is warranted to explore risk-stratified surveillance protocols in patients with CRC.


35. ctDNA Testing Affects Well-Being, Reducing Anxiety in Patients With CRC (Jan.16/24)

A study of patient-reported outcomes from the BESPOKE CRC trial found that ctDNA testing is welcomed by most patients with surgically resected colorectal cancer (CRC) and that receiving a negative ctDNA test reduces anxiety about...
cancer recurrence in the majority of patients. The trial enrolled 1,794 patients with stage I-IV CRC and followed them for a median of 23.2 months. Serial ctDNA testing was performed throughout the follow-up period. The vast majority of patients (89%) said that they valued the additional information obtained from ctDNA testing, irrespective of the findings; 86% of patients said they would continue using ctDNA tests for monitoring purposes. The findings revealed no significant differences in the general anxiety and depression scores between patients who are ctDNA negative and ctDNA positive. However, the study showed those with a negative ctDNA test result felt less anxious about their cancer recurring compared to patients who were ctDNA positive. ctDNA should be viewed as one added (and probably one of the most powerful) tool in the toolbox instead of a standalone variable.


Research has shown a connection between colorectal cancer (CRC) and a high intake of red meat and processed meat. The American Institute of Cancer Research has listed red meat as ‘probably carcinogenic’ and suggests limiting your intake to 12–18 oz. weekly. They suggest that heme iron, which is present in red meat and processed meat, may lead to the production of free radicals that damage DNA and promote the formation of nitrosocompounds, which may create damage within the gut that leads to cancer. In addition, cooking meat at high temperatures, such as grilling or pan-searing, can lead to the production of cancerous substances called heterocyclic amines and polycyclic aromatic hydrocarbons, which are linked to CRC. Diets higher in processed meats also tend to be higher in dietary fat, specifically saturated fat. This can increase your risk of obesity, heart disease, chronic inflammation, and CRC.

The best way to decrease your risk of CRC is by consuming nutrient-rich foods such as non-starchy vegetables, beans, fruits, nuts, whole grains, tofu and fish such as salmon. Geanella Vera-Avellan, a registered dietitian at Hackensack Meridian Health and Wellness Center in Eatontown laid out the benefits of eating more plants:

- Plant foods have antioxidants that may protect against cancer such as carotenoids, lycopene and selenium.
- Legumes, green bananas, nuts, oatmeal and other whole grains produce short-chain fatty acids that may have anti-cancer properties.
- Foods high in vitamin B6 such as chickpeas, tofu, bananas, avocados, sweet potatoes and salmon are associated with lowering the risk of CRC.
- Foods high in calcium such as edamame, yogurt, cheese, tofu and dark leafy greens may decrease the risk of CRC.


Researchers from The University of Texas M.D. Anderson Cancer Center has found that adding navy beans, also known as haricot beans, to the diet of colorectal cancer (CRC) survivors helps improve their gut microbiome, which could potentially aid in both cancer prevention and treatment. Navy beans are rich in dietary fibre and an excellent source of plant-based protein. They specifically contain multiple prebiotic or microbiota-stimulating nutrients, including oligosaccharides and the amino acid lysine. Navy beans also contain other anti-inflammatory micronutrients and antioxidants, such as the flavonoid apigenin.

While other dry beans, peas, and lentils have nutritional profiles that are also likely to stimulate the gut microbiome, Dr. Carrie Daniel-MacDougall, lead author of this study, was inspired by the Polyp Prevention Trial (PPT). This large study showed that the participants with the biggest increase in bean consumption — daily or close to it — had a lower risk of advanced colorectal adenoma recurrence — a type of precancerous and high-risk polyp that is very likely to progress to CRC if not caught promptly upon colonoscopy and completely removed.

It is important for CRC survivors to have a balanced gut microbiome because it directly interacts with the colon epithelium where CRC develops. And so if the good bacteria can be stimulated to impact the immune system to prevent cancer or cancer recurrence through diet, that would be extremely important.
For this study, Dr. Daniel-MacDougall and her team randomized 55 participants over the age of 30 who had a history of bowel lesions, had a history of CRC, and/or were at high risk for precancerous polyps. For eight weeks, participants were asked to either follow just their normal diet or add a daily cup of organic, canned, pressure-cooked white navy beans to their diet. Researchers discovered that participants who consumed navy beans each day experienced positive changes to their gut microbiome. These changes included an increase of alpha diversity, or beneficial bacteria — Faecalibacterium, Eubacterium, and Bifidobacterium — and a decrease in pathogenic, or opportunistic, bacteria. Through the results of this trial and other supportive evidence, the researchers hope beans will regularly come up in these conversations and that more doctors and patients will consider the value of whole foods to achieve a broader impact on health.


38. The Response to Ketogenic Diet in CRC is Mediated by Lasting Functional Alterations of the Gut Microbiome (Dec.8/23)

Colorectal cancer (CRC) patients have been shown to possess an altered gut microbiome. Diet is a known microbiome modulator. An attenuating effect of the ketogenic diet (KD) on CRC cell growth has been previously observed, however the role of the gut microbiome in driving this effect remains unknown. The researchers describe a reduced colonic tumor burden upon KD consumption in a CRC mouse model with a humanized microbiome. Importantly, they demonstrate a causal relationship through microbiome transplantation into germ-free mice, whereby alterations in gut microbial function were maintained in the absence of continued selective pressure from the KD. Stearic acid is also identified as a putative microbiome-derived anti-cancer metabolite.

The gut microbiome plays a central role in ensuring the anti-cancer effects of the KD in the context of a mouse model of inflammation-driven CRC. Nevertheless, within this experiment, a more pronounced anti-cancer phenotype can be observed for some mice than for others. This might indicate that the initial gut microbiome profile may determine whether an individual is a “responder” or a “non-responder” to the KD in the context of CRC. Furthermore, the response to some cancer treatments, such as immune checkpoint inhibition depend on gut microbial composition, and ketogenic dietary regimens may be able to enhance the effects of these therapies. Future studies identifying biomarkers to predict response to dietary intervention based on the resident gut microbiome and studies aiming to transform a “non-responder” microbiome into a “responder” microbiome would be a significant step forward towards personalized patient care.


39. Frequently Asked Questions for COVID-19

Q: What is COVID-19 (or novel Coronavirus Disease - 19)?

A: Coronaviruses are a large family of viruses that can cause illnesses in humans and animals. Coronaviruses can cause illnesses that range in severity from the common cold to more severe diseases such as Severe Acute Respiratory Syndrome (SARS) and most recently, COVID-19. COVID-19 or novel coronavirus originated from an outbreak in Wuhan, China in December 2019. The most common symptoms associated with COVID-19 can include fever, fatigue, and a dry cough. Though additional symptoms have now been linked with the disease, which may include aches and pains, nasal congestion, runny nose, sore throat, diarrhea, skin rash and vomiting. It is also possible to become infected with COVID-19 and not experience any symptoms or feeling ill. The spread of COVID-19 is mainly through the transmission of droplets from the nose or mouth when a person coughs, exhales or sneezes. These droplets land on surfaces around a nearby person. COVID-19 can be transmitted to that nearby person who may end up touching the surface contaminated with COVID-19 and then end up touching their nose, mouth, or eyes. A person can also contract COVID-19 through inhaling these droplets from someone with COVID-19. Although research is still ongoing, it is important to note that older populations (over the age of 65), those with a compromised immune system and those with pre-existing conditions including heart disease, high blood pressure, lung disease, diabetes or cancer may be at a higher risk of severe illness due to COVID-19.

https://www.who.int/news-room/q-a-detail/q-acoronavirus

Q: What can I do to avoid getting Coronavirus?

A: There are various ways in which we can reduce our risk of contracting COVID-19. Below are some measures suggested by the World Health Organization
1. Keep at least 2 metres (or 6 feet) between yourself and other people. This will reduce the risk of inhaling droplets from those infected with COVID-19.
2. Regularly clean your hands for at least 20 seconds with warm water and soap, or an alcohol-based hand rub. This will kill any viruses on your hands.
3. Avoid touching your eyes, nose and mouth. If the virus is on your hands, it can enter the body through these areas.
4. Follow good respiratory hygiene by covering your mouth and nose with a tissue or elbow when you cough and sneeze. This prevents the droplets from settling on surfaces or being released into the air around you.
5. Stay home as much as possible, especially if you are feeling unwell. If you think you may have the Coronavirus, please see “What should I do if I think I have Coronavirus?” section.
6. Please wear a face covering or mask in public when physical distancing is not possible.

https://www.who.int/news-room/q-adetail/q-a-coronaviruses

Q: Are there special precautions that people with cancer can take?

A: People with cancer (and other chronic ailments such as heart disease, diabetes, high blood pressure and lung disease) are at a higher risk of severe illness due to COVID-19 as cancer is considered a pre-existing health issue. Some cancer treatments including chemotherapy, radiation and surgery can weaken the immune system, making it harder for the body to fight infections and viruses, such as Coronavirus. It is important to diligently follow the World Health Organization’s recommendations above to reduce the risk of contracting COVID-19. If you have any concerns about your risk, it is best to contact your doctor or healthcare team.

Q. Will anything change with regards to my cancer related medical visits?

As each patient and treatment plan is unique, it is always best to contact your health care provider for updated information about your treatment plan. In some cases, it is safe to delay cancer treatment until after the pandemic risk has decreased. In other cases, it may be safe to attend a clinic that is separate from where COVID-19 patients are being treated. Oral treatment options could be prescribed by your care provider virtually, without the need to attend the clinic. Finally, some follow-up appointments or discussions could be held virtually (via skype or zoom for example) or over the phone to minimize your risk. As we know, conditions and protocols are changing daily due to the nature of the COVID-19 outbreak, and vary based on location, therefore, the best first step is to reach out to your care provider for guidance.

https://www.cancer.gov/contact/emergencypreparedness/coronavirus

Should you wish to contact your local public health agency, please see below.

**Alberta**
COVID-19 info for Albertans
Social media: Instagram @albertahealthservices, Facebook @albertahealthservices, Twitter @GoAHealth
Phone number: 811

**British Columbia**
British Columbia COVID-19
Social media: Facebook @ImmunizeBC, Twitter @CDCofBC
Phone number: 811

**Manitoba**
Manitoba COVID-19
Social media: Facebook @manitobagovernment, Twitter @mbgov
Phone number: 1-888-315-9257

**New Brunswick**
New Brunswick Coronavirus
Social media: Facebook @GovNB, Twitter @Gov_NB, Instagram @gnbca
Phone number: 811

**Newfoundland and Labrador**
Newfoundland and Labrador COVID-19 information
Social media: Facebook @GovNL, Twitter @Gov_NL, Instagram @govnlsocial
Phone number: 811 or 1-888-709-2929

**Northwest Territories**
Northwest Territories coronavirus disease (COVID-19)
Social media: Facebook @NTHSSA
Phone number: 811
Nova Scotia
Nova Scotia novel coronavirus (COVID-19)
Social media: Facebook @NovaScotiaHealthAuthority, Twitter @healthns, Instagram @novascotiahealthauthority
Phone number: 811

Nunavut
Nunavut COVID-19 (novel coronavirus)
Social media: Facebook @GovofNunavut, Twitter @GovofNunavut, Instagram @governmentofnunavut
Phone number: 1-888-975-8601

Ontario
Ontario: The 2019 Novel Coronavirus (COVID-19)
Social media: Facebook @ONTHealth, Twitter @ONTHealth, Instagram @ongov
Phone number: 1-866-797-0000

Prince Edward Island
Prince Edward Island COVID-19
Social media: Facebook @GovPe, Twitter @InfoPEI,

Quebec
Coronavirus disease (COVID-19) in Québec
Social media: Facebook @GouvQc, Twitter @sante_qc
Phone number: 1-877-644-4545

Saskatchewan
Saskatchewan COVID-19
Social media: Facebook @SKGov, Twitter @SKGov
Phone number: 811

Yukon
Yukon: Find information about coronavirus (COVID-19)
Social media: Facebook @yukonhss, Twitter @hssyukon
Phone number: 811