CCRAN
Colorectal Cancer Resource & Action Network

RISCC
Réseau d'informations et soutien pour le cancer colorectal

A PATIENT-FOCUSED ORGANIZATION

COLORECTAL CANCER TREATMENT & CLINICAL RESEARCH UPDATES

Month Ending November 16th, 2023

The following colorectal cancer treatment and research updates extend from October 13th, 2023, to November 16th, 2023, 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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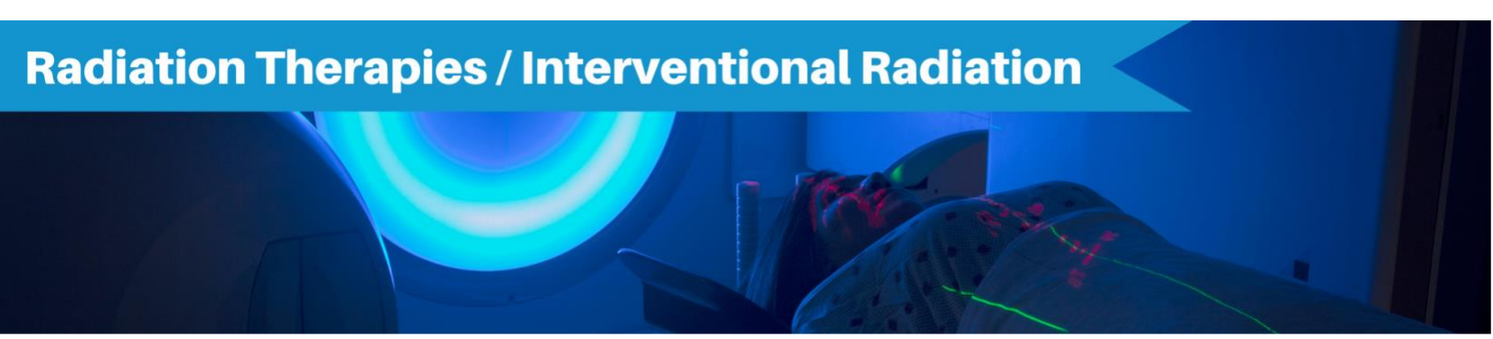

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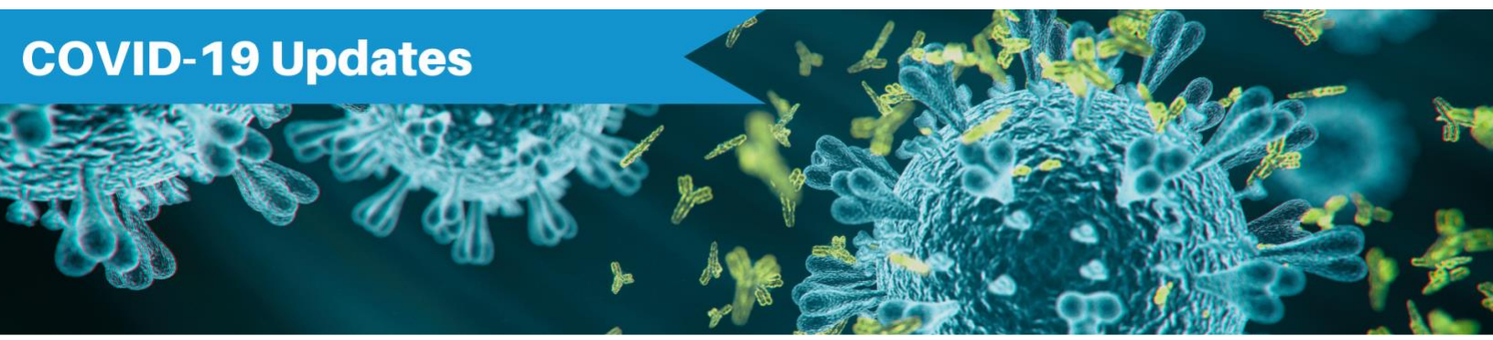


31. Frequently Asked Questions for COVID-19

Drug / Systemic Therapies

1. TRK Fusion Cancer and How to Test for It (Oct.13/23)

TRK fusion cancer and how to test for it

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 en-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

TRK=tropomyosin receptor kinase

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

*Fast*TRK

***Fast*TRK 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

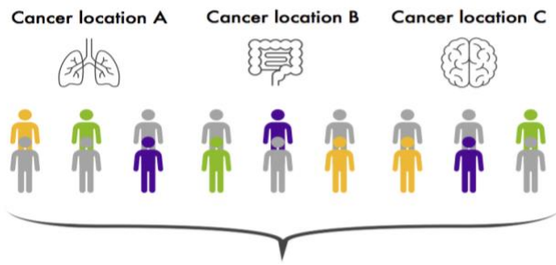
PP-VIT-CA-0085-1
VTV02E-0221

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.

1. Patients undergo a biopsy to obtain a sample for testing
2. Tissue is sent to lab to test for genomic changes
3. Results sent to clinician to help decide on treatment

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

MAC-VIT-CA-0007-1

https://www.newswire.ca/news-releases/health-canada-approves-vitrakvi-r-larotrectinib-the-first-tumour-agnostic-cancer-treatment-for-advanced-solid-tumours-harbouring-an-ntrk-gene-fusion-880379419.html
https://www.bayer.ca/en/media/news/?dt=TmpBPQ==&st=1

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

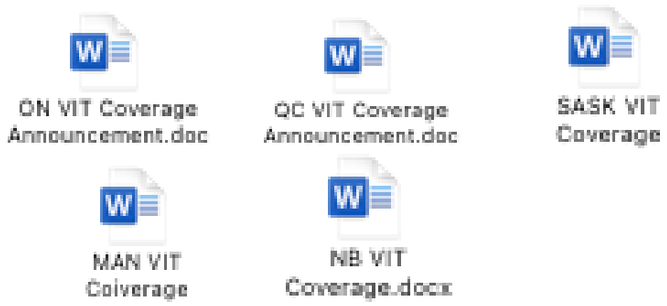
In one of the first clinical trials combining immunotherapy and targeted therapy for patients with BRAF V600E–mutated colorectal cancer (CRC), researchers discovered that a combination regimen of **dabrafenib, trametinib**, and **spartalizumab** resulted in long-lasting responses. The study successfully 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.

https://ascopost.com/news/january-2023/immunotherapy-combined-with-targeted-therapy-in-patients-with-braf-v600e-mutated-colorectal-cancer/

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

Please find information below regarding public funding for VITRAKVI (Larotrectinib) in Ontario, Quebec, Saskatchewan, Manitoba and New Brunswick.



4. 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

5. Managing Side Effects of EGFR Inhibitors (Oct.15/23)

The EGFR pathway is a normal biologic pathway found in healthy cells. It is involved in regular cellular division and growth. However, certain mutations within the EGFR gene can lead to an overactive EGFR pathway, leading to the development and/or spread of cancer. Epidermal Growth Factor Receptor (EGFR) inhibitor drugs are a type of precision cancer medicine commonly used to treat lung, colon, head and neck and other cancers that over express the EGFR.

Unique side effects of all EGFR inhibitors include:

- Skin rash & Dry skin
- Finger or toenail infection
- Inflammation of mouth and lips (stomatitis)
- Diarrhea
- Loss of appetite

Skin Rash
The most commonly seen side effect from EGFR inhibitors is a papulopustular skin rash that erupts most often on the face but can also be seen on the chest, back, trunk, and limbs. It tends to be associated with dry skin and commonly manifests in the first 1 to 2 weeks of treatment. Since the rash tends to be drying, applying a thick, emollient cream to the face and body once or twice a day as soon as the medication is started can be helpful. Creams tend to be better as lotions are usually thinner and water-based. Be sure that the cream is without dyes or fragrances that may irritate the skin. Another prevention technique is to take the oral EGFR inhibitors on an empty stomach. Taking them with food will increase their bioavailability, thus causing heightened side effects. If symptoms persist physicians typically utilize a step-wise approach based on severity of the rash. They will first use topical corticosteroids and antibiotics to treat a minor rash and may add oral antibiotics and oral corticosteroids if necessary for moderate or severe rashes.

Paronychias
Inflammation and soreness around the nail bed is known as paronychias which can be difficult to treat. Topical antibiotics or antifungals, or soaks with Epsom salts or diluted betadinef can sometimes help. Oral antibiotics may work, especially if erythema or pus is present. Prevention is key. Keeping nails clean and trimmed can hopefully prevent this complication.

Diarrhea
Patients should be advised to avoid spicy or greasy foods and to follow the BRAT (bananas, rice, applesauce, toast) diet if loose stools occur. OTC medications such as loperamide (Imodium) can relieve the diarrhea. Maintain adequate liquid intake and consumption of liquids at room temperature. Avoid beverages containing lactose, caffeine, or alcohol, and large quantities of hyperosmotic beverages (eg, fruit juice, sweetened fruit drinks). Drink enough fluids to replace what is lost in addition to the recommended daily amount. Replacement fluids should contain some sugar and salt. Avoid foods that exacerbate diarrhea (eg, raw fruits and vegetables; whole grain breads; nuts; popcorn; skins; seeds; legumes; and greasy, fried, high-fat foods). If OTC products are not effective, a prescription medication such as diphenoxylate/atropine (Lomotil) can offer stronger relief.

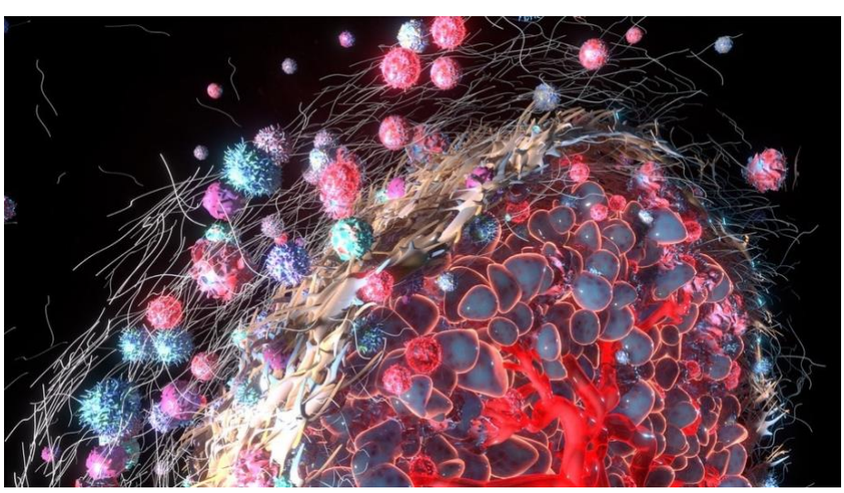
https://news.cancerconnect.com/treatment-care/managing-side-effects-from-egfr-inhibitors

6. Insights into the Tumor Microenvironment in CRC Patients (Nov.1/23)

Traditionally, metastatic colorectal cancer (mCRC) treatment primarily involved chemotherapy with biological agents. However, there is growing evidence of the clinical benefits of immunotherapy for mCRC patients. Immune checkpoint inhibitors (ICIs) have proven effective for various solid tumors, and recent years have seen their introduction in the treatment of mCRC patients. High microsatellite instability (MSI-H) and mismatch repair protein deletion (dMMR) have become vital biomarkers for stratifying patients with advanced mCRC in treatment groups. ICIs targeting the anti-PD-1/PD-L1 pathway demonstrate significant clinical efficacy in MSI-H/dMMR patients. Unfortunately, only 5% of advanced mCRC patients exhibit MSI-H/dMMR, with the majority having microsatellite stability (MSS) and proficient mismatch repair proteins (pMMR). Patients with MSS/pMMR typically do not respond positively to single ICIs, and various immune combination therapy treatments have shown little benefit to patients exhibiting MSS/pMMR.

Tumors in patients with MSS-type are termed 'immune cold tumors' because they typically have low levels of lymphocyte infiltration and a low tumor mutational load, which are the main characteristics of the immune microenvironment. To enhance the effectiveness of current immunotherapies, a combination of therapies and screening methods is employed to modify and monitor the immune microenvironment. These treatments aim to change 'immune cold tumor' environments into 'immune hot tumors' and aid in the identification of biomarkers. Exploring the tumor microenvironment is essential to determine which MSS-type CRC patients can derive clinical benefits from immunotherapy.

Case study: A 50-year-old patient with mCRC/liver metastasis recovers with immunotherapy



A 50-year-old patient diagnosed with MSS-type CRC and PD-L1-negative recurrent hepatopulmonary metastases achieved complete remission and long-lasting benefits from immunotherapy following prior unsuccessful systematic treatments. The case study evaluated the tumor microenvironment's characteristics during the treatment to gain insights into the mechanisms behind the immunotherapy's positive effects. This allowed researchers to pinpoint phenotypes indicative of a favorable response and identify potential prognostic biomarkers. Genetic and multiple immunohistochemical tests unveiled that mutations in DNA damage

repair pathway genes and Tumor-Infiltrating Lymphocytes (TILs) likely contributed to the observed clinical benefits. To determine cellular phenotypes associated with successful clinical outcomes, researchers employed the TissueFAXS SL platform (captured whole-slide images of stained tissue sections), along with the StrataQuest image analysis solution (analyzed images to quantify specific cellular phenotypes based on various immune cell markers).

This case study highlights the substantial clinical benefits of immunotherapy, surpassing traditional chemotherapies, for advanced MSS mCRC patients. The study underscores the need for identifying new, effective predictive biomarkers to guide the screening for immunotherapy benefits in this patient group. With the aid of TissueFAXS and StrataQuest, researchers can unveil cellular phenotypes, immune mechanisms, and biomarkers within the tumor microenvironment, ultimately enabling the development of more effective immunotherapies.

https://www.news-medical.net/whitepaper/20231101/Tumor-Microenvironment-of-Colorectal-Cancer-Patients.aspx
Image Source: ***https://www.news-medical.net/health/What-is-the-Tumor-Microenvironment.aspx***

7. Phase 2 Clinical Trial MK1308A-008 Testing New Protocol for MSI-High Tumours Across Canada (Nov.10/23)

Immunotherapy has demonstrated benefit in patients with MSI-H or mismatch repair (MMR) deficient Stage IV colorectal cancer. Unfortunately, not all patients respond to this treatment and those that do respond may only do so for a short period of time.

Previous studies have suggested that using a combination of drugs may improve the number of patients that benefit from these treatments, as well increase the longevity of these treatments.MK1308A-008 is a phase 2 study that aims to address this question of whether using a combination of drugs is more efficacious than a single drug (ClinicalTrials.gov, ID NCT04895722).

The MK-1308 trial will be run out of Sunnybrook Health Sciences Centre, Toronto, ON; Moncton Hospital, Moncton, New Brunswick; McGill University Health Centre-Montreal, Quebec.

Please discuss with your doctor whether referral for this trial may be appropriate for you.

8. 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 Qu Biologics. 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 I 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?
If you are experiencing these or any symptoms that you think are related to the study treatment, you should contact your cancer surgeon or the study coordinator to discuss. If the symptoms are serious and require emergency medical attention, then you should present to the emergency room and inform the medical team that you are participating in this study.

Visual Summary of Trial Activities

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

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

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

PERIOP-06_ICF.pdf

9. Now Available in Canada: AVENIO 324 Gene CGP Panel Matched to FoundationONE CDx Panel (Nov.1/23)

For more information, please visit the OncoHelix website

10. FDA Approves New Chemotherapy-Free Treatment Option for mCRC (Nov.9/23)

The FDA has approved fruquintinib (Fruzaqla) to treat adults with metastatic colorectal cancer (mCRC) who received prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti-VEGF therapy, and an anti-EGFR therapy for cases that are *RAS* wild-type and medically appropriate. Fruzaqla is an oral, highly selective, small molecule VEGF receptor inhibitor. Because of the kinase selectivity of Fruzaqla, the risk of off-target toxicity is less than the risk with multikinase inhibitors, including regorafenib.

There is a pressing need for new treatments for individuals with mCRC, who have had limited options and continue to face poor outcomes. Fruzaqla is the first novel chemotherapy-free treatment option approved for patients in the US regardless of biomarker status in more than a decade. Patients with metastatic disease are often fragile and fatigued—due to both their condition as well as the therapies they have been exposed to. An oral, chemotherapy-free option that offers a survival benefit despite treatment with prior therapies is a critical need for treating mCRC.

Data from the phase 3 FRESCO-2 trial show that Fruzaqla plus best supportive care (BSC) produced a median overall survival (OS) of 7.4 months vs. 4.8 months in patients administered a placebo. Adding Fruzaqla was found to improve progression-free survival (PFS) compared to the control cohort, at a median of 3.7 months vs. 1.8 months, respectively. Additionally, the phase 3 Chinese FRESCO trial show that Fruzaqla plus BSC produced a median OS of 9.3 months compared with 6.6 months in the placebo plus BSC cohort. For PFS, patients administered Fruzaqla had a median of 3.7 months compared with 1.8 months with the placebo.

For far too long, healthcare providers and patients have had limited options when selecting a therapy for mCRC. Fruzaqla has the potential to offer a significant survival benefit to patients without negatively impacting their quality of life.

https://www.pharmexec.com/view/fda-approves-new-chemotherapy-free-treatment-option-for-metastatic-colorectal-cancer

Surgical Therapies

11. Hepatic Artery Infusion Pump (HAIP) Chemotherapy Program – Sunnybrook Odette Cancer Centre (Nov.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

12. Living Donor Liver Transplantation for Unresectable CRC Liver Metastases (Nov.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.

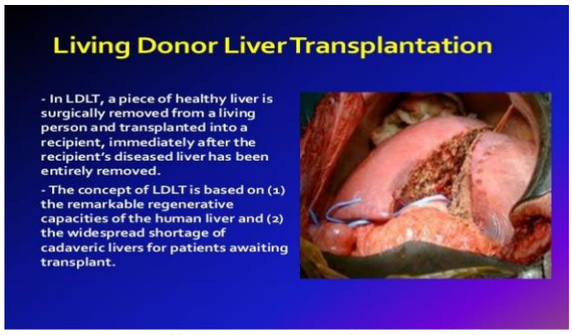


Image Source: ***https://www.slideshare.net/AhmedAdel65/preoperative***

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.

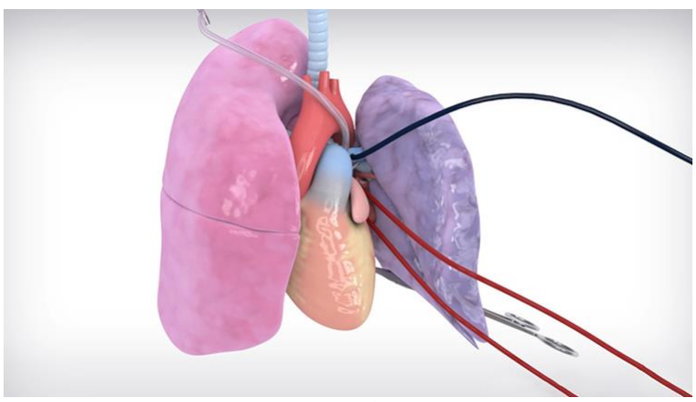
https://clinicaltrials.gov/ct2/show/NCT02864485

13. In Vivo Lung Perfusion (IVLP) for CRC Metastatic to Lung (Nov.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.



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/***

Radiation Therapies / Interventional Radiation

14. Study Offered at the Odette Cancer Centre to Treat Recurrent Rectal Cancer (Nov.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

Sunnybrook
ODETTE CANCER CENTRE
A Cancer Care Ontario Partner

Screening

15. Trends in the Incidence of Young-Onset CRC with a Focus on Years Approaching Screening Age (Nov.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?questAccessKey=af490637-e51e-44d0-81b9-d1f2df7b60c9

16. Personalized CRC Screening Reduces Low-Value Care in Older Adults (Oct.30/23)

Colorectal cancer (CRC) screening is widely recommended for adults ages 45 to 75 with an average risk of developing the disease. However, many people don't realize that the benefits of screening for this type of cancer aren't always the same for older adults. In fact, simply following guideline recommendations for CRC screening isn't always the best approach. As individuals get older, they often acquire health problems that can lead to potential harm when coupled with endoscopy. While guidelines recommend a personalized approach to screening in average risk individuals between ages 76 and 85, there are no such recommendations for older adults who are younger than age 76 -; individuals who are commonly seen in clinics.

A study published in *JAMA Internal Medicine* targeted individuals who fell into the age range of 70 to 75, and the researchers compared two different strategies of care in a cluster randomized trial involving 431 older adults of average risk for developing CRC. Each study participant was due for a CRC screening and had no family history of CRC or personal history of colon polyps. The control strategy was, in some ways, 'usual' care. The team made it possible

for clinicians to stop screening patients within the control group without being penalized for doing so. Currently, physicians are penalized if they stop screening a patient before age 76. But the study allowed participating physicians to make more personalized decisions about screening their patients based on individual factors and personal preferences.

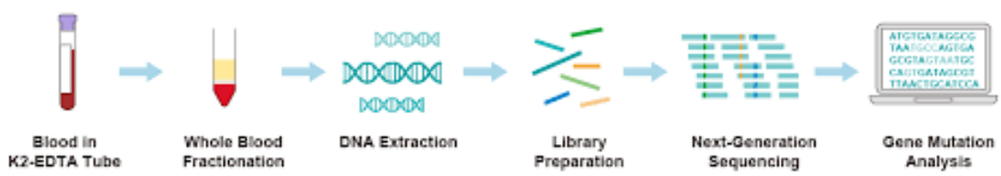
The team also provided physicians with education about how screening benefits change throughout an individual's lifespan, and how screening can potentially cause harm when competing co-morbidities are present. Finally, patients were given a personalized decision aid, which was a 30-page booklet with background information about screening, as well as personalized information about screening benefits and harms based upon their age, prior screening history, sex and whether they were healthy or sick at the time of the study. This information was combined into a personalized risk graph designed for easy interpretation. Patients within the control arm simply received a simple screening informational booklet that was not personalized.

The team then looked at whether participants in each group received a screening order – be it a colonoscopy or a stool-based screening test – within two weeks of receiving this information. Digging deeper, they looked at how the screening orders varied across the spectrum of screening benefit. They found that individuals within the control arm who were least likely to benefit from screening got more screening orders than those in the intervention arm. In other words, *the intervention reduced low-value screening orders*. In contrast, those in the control arm who were *most likely* to benefit got fewer screening orders than those in the intervention arm. Therefore, *the intervention increased high-value screening orders*. Not only was the intervention effective, but the control arm results also revealed that under usual care, CRC screenings were happening in excess in low-benefit older adults, and not enough in high-benefit older adults. While this is a counterintuitive finding, it makes sense given that screening benefit is determined by your overall health, as well as your prior screening history.

https://www.news-medical.net/news/20231030/Personalized-colorectal-cancer-screening-reduces-low-value-care-in-older-adults.aspx
Image Source: ***https://www.medpagetoday.com/gastroenterology/coloncancer/107086***

17. Surveys Finds Majority of Practitioners in Hereditary Gastroenterology Support Use of Genetic Testing to Determine CRC Risk, Treatment (Oct.30/23)

A majority of clinicians with expertise in hereditary gastroenterology support implementing genetic screening known as universal germline testing for the diagnosis of colorectal cancer (CRC), according to the results of a clinical practice survey conducted by Sanjeevani Arora, PhD, an Assistant Professor in the Cancer Prevention and Control Research Program at Fox Chase Cancer Center. Germline testing uses blood samples to determine specific changes in cancer-related genes inherited from a parent. These tests can help doctors determine the best treatment for a patient and provide insight into whether a patient's family members should also be offered testing.



The survey assessed the perspectives of members of the Collaborative Group of the Americas on Inherited Gastrointestinal Cancer (CGA-IGC) regarding readiness, logistics, and barriers to implementing this form of testing. While the majority of the participants supported universal germline testing, they also said that changes would be required in clinical practice in order to implement universal germline testing. One of the key barriers to testing included limited genetic expertise among non-genetics providers — those who are not geneticists, genetic counselors, and clinicians who work in genetics. Other barriers include time-consuming processes for obtaining consent, ordering tests, disclosing results, and lack of insurance coverage. Additionally, Arora said the survey explored whether it would be necessary to rely on genetics providers to offer all the support necessary for carrying out testing. They found that there was support for both genetics and non-genetics providers to order genetic testing. Of the survey respondents, 57% supported a standardized multigene panel rather than a customized gene panel.

This study demonstrates wide support among hereditary gastrointestinal cancer experts for implementation of universal germline testing for CRC patients. However, alternative service delivery models are necessary so that we can really utilize the expertise of those who are non-genetics providers in order to overcome the logistical barriers to universal testing.

https://www.foxchase.org/news/2023-10-30-survey-from-fox-chase-and-other-institutions-finds-majority-of-practitioners-in-hereditary-gastroenterology-support-use-of-genetic-testing%20to-determine-colorectal-cancer-risk-treatment
Image Source: ***http://www.wellconn.com/tests/germline.asp***

18. Two Multitarget Stool Tests Show Promise for CRC Screening: Studies (Oct.22/23)

Two multitarget stool tests in development compare favourably for colorectal cancer (CRC) screening in average-risk people, suggest two new studies. In a blinded, prospective, cross-sectional study, researchers assessed a multitarget

stool RNA test (**mt-sRNA**; Colosense, Geneoscopy) vs colonoscopy for detection of advanced adenomas and CRC in average-risk individuals aged 45 years and older. In a prospective, cross-sectional study, investigators evaluated the clinical performance of a next-generation multitarget stool DNA (**mt-sDNA**; Cologuard, Exact Sciences) and fecal hemoglobin assay for CRC screening in adults aged 40 years and older.

RNA as a Biomarker
For CRC-PREVENT, which evaluated the mt-sRNA test, participants provided stool samples before colonoscopy. Colosense includes a commercially available fecal immunochemical test (FIT) and tests for eight different strands of RNA. The mt-sRNA test results were compared with the colonoscopy results. The mt-sRNA test had 100% sensitivity for early, stage I cancers, which were detected in 12 patients. Advanced adenomas were detected with an overall sensitivity of 45%. When the advanced adenomas were ≥ 2 cm, sensitivity increased to 51%. Specificity was 87% among patients with negative findings for hyperplastic polyps or lesions. The mt-sRNA test showed significant improvements in sensitivity for CRC (94% vs 77%) and advanced adenomas (45% vs 29%), when compared with the FIT results alone. Results show a sensitivity of 100% for detecting CRC and 44% for advanced adenomas in the 45- to 49-year-old population. RNA-based testing may have an advantage over DNA biomarker tests, which can be prone to age-related DNA methylation changes

Detection by DNA
The BLUE-C trial intended to validate the next-generation mt-sDNA test for CRC screening. The mt-sDNA assay tests for three novel methylated DNA markers and fecal hemoglobin. Participants provided a stool sample for the mt-sDNA test and comparator FIT prior to colonoscopy preparation. They compared results to colonoscopy and FIT findings. Colonoscopy revealed 98 people with CRC, 2144 with advanced precancerous lesions, and 17,934 with no advanced neoplasia. Sensitivity of the mt-sDNA test for detecting CRC was 93.9%, advanced precancerous lesions was 43.4%, and advanced precancerous lesions with high-grade dysplasia was 74.6%. Sensitivities of the mt-sDNA test for detecting CRC and advanced precancerous lesions were significantly higher than FIT. In terms of specificity, the mt-sDNA test had a specificity of 90.6% for the absence of advanced neoplasia. Specificity for non-neoplastic findings or negative colonoscopy was 92.7%. The mt-sDNA test demonstrated high specificity and high CRC and advanced precancerous lesion sensitivity. The test outperformed FIT for these factors on sensitivity but not specificity, the authors noted.

Improved specificity was a goal of developing this next-generation assay. The BLUE-C trial demonstrated a 30% improvement in specificity that "will decrease the number of unnecessary colonoscopies performed for false-positive results.

https://www.medscape.com/viewarticle/997609?form=fpf#vp_2

Other

19. Young Adult CRC Clinic Available at Sunnybrook (Nov.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.

Dr. Shady Ashamalla, Head
Young Adult Colorectal Cancer Program

Dr. Petra Wildgoose, Lead
Young Adult Colorectal Cancer Program

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

20. CCRAN's Partnership with "Count Me In" (Nov.1/23)

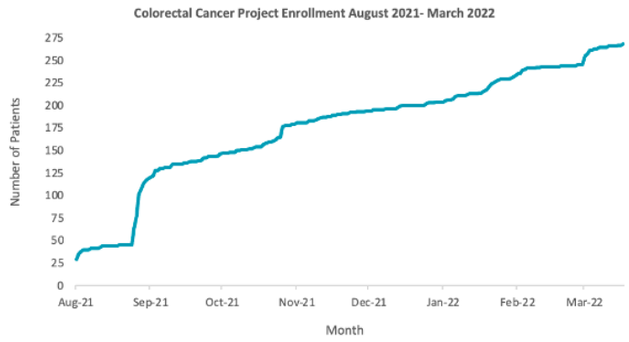
CCRAN is proud to partner with Count Me In, a nonprofit research initiative, on The Colorectal Cancer Project. This new project is open to anyone in the United States or Canada who has ever been diagnosed with colorectal cancer (CRC). Patients can find out more and join at **JoinCountMeIn.org/Colorectal**.

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.

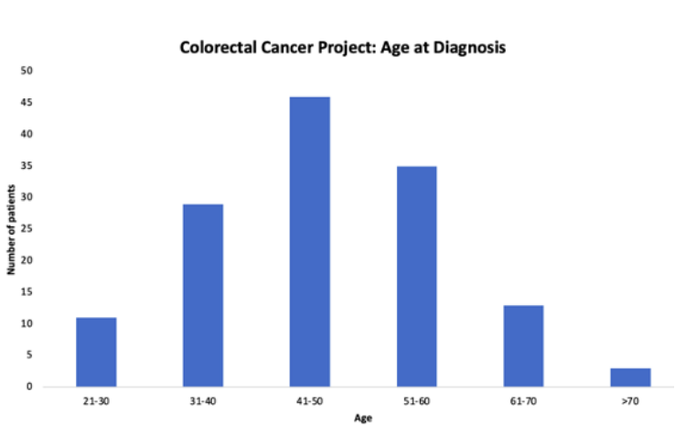
Every patient's story holds a piece of the puzzle that can help us better understand CRC. By discovering more about what drives cancer and sharing this data, CCRAN and the Colorectal Cancer Project believe insights can be gained to develop more effective therapies. One of the aims of the project is to 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**.

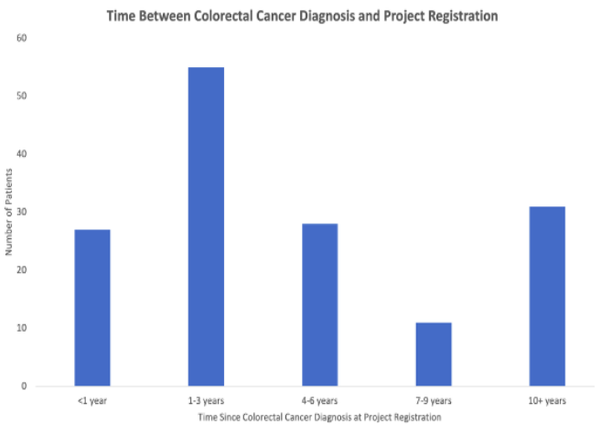
"***Count Me In***", a nonprofit cancer research initiative, is inviting all patients across the United States and Canada who have ever been diagnosed with colorectal cancer (CRC) to participate in research and help drive new discoveries related to this disease. The Colorectal Cancer Project will enable 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-

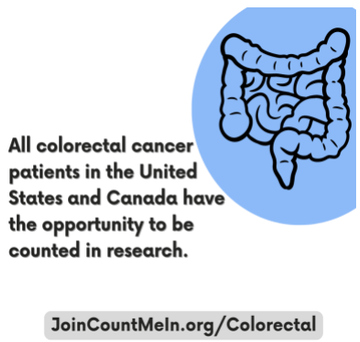
reported data that is then de-identified and shared with researchers everywhere. To date, more than 9,000 patients with different cancers have joined Count Me In and shared their data. "We still do not know why there is an alarming rise in CRC in young adults", said Andrea Cercek, MD Co-Director, Center 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

https://www.news-medical.net/news/20210914/Colorectal-Cancer-Project-launches-to-improve-understanding-of-the-disease-and-accelerate-research.aspx
https://www.medicalnewstoday.com/articles/antibiotic-use-linked-to-increased-risk-of-colorectal-cancer#Use-of-antibiotics-and-an-increased-risk-of-colon-cancer

21. CCRAN Has Launched 4 New Information/Support Groups Based On Age and Disease Stage (Nov.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

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Support Group:
Early Age Onset (< 50), Early Stage Disease (Stages I - III) Patients & Caregivers
Facilitated by:
Dr. Petra Wildgoose, MD

Support Group:
Early Age Onset (< 50), Advanced Stage Disease (Stage IV, metastatic) Patients & Caregivers
Facilitated by:
Ms. Hayley Painter, RN

Support Group:
Average Age Onset (> 50), Early Stage Disease (Stages I - III) Patients & Caregivers
Facilitated by:
Ms. Cassandra Macaulay, MHS

Support Group:
Average Age Onset (> 50), Advanced Stage Disease (Stage IV, metastatic) Patients & Caregivers
Facilitated by:
Ms. Filomena Servidio-Italiano, MA

Meetings will begin with a brief treatment update. 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.

22. What is Peutz-Jeghers Syndrome? (Sept.10/23)

Peutz-Jeghers syndrome is a rare genetic inherited autosomal dominant syndrome characterized by development of hamartomatous polyps throughout the gastrointestinal tract, and by changes in skin pigmentation. This disorder increases the risk of developing cancer.

The characteristic harmatomatous polyps generally occur in childhood and early adulthood during the first 10 years of life. Hamartomatous polyps can occur at any site in the gastrointestinal tract but are most frequent in the small

intestine. Although benign, the polyps can cause complications including bowel obstruction, rectal prolapse, and severe GI bleeding with secondary anemia.

Peutz-Jeghers syndrome is usually caused by mutations in the *STK11* tumor suppressor gene which occurs in more than 80% of affected families **increasing the risk of developing colorectal and gastric cancer** in 15% of individuals by 50 years of age, and 57% by 70 years. There is also an increased risk of developing pancreatic breast and ovarian cancer in females as well as adenoma malignum of the cervix, and bilateral multifocal sex cord tumors with annular tubules.

Molecular genetic testing for the *STK11* gene confirms the diagnosis and is available clinically. The syndrome is inherited in an autosomal dominant manner (abnormal gene from one parent causes expression). Affected individuals should undergo genetic counselling informing them of the 50% risk of passing the mutation to their children.

https://news.cancerconnect.com/colon-cancer/what-is-peutz-jeghers-syndrome

23. Hand-Foot Syndrome Palmar Plantar Erythrodysesthesia (Sept.22/23)

Hand-foot syndrome is a side effect of some chemotherapy drugs that results when a small amount of drug leaks out of the blood vessels, damaging tissues. This tends to happen in the hands and the feet because of the increased friction and heat that these extremities are exposed to through daily activities. Hand-foot syndrome is most commonly associated with Xeloda chemotherapy used to treat breast and **colon cancer** but can be a side effect of other treatments as well. Hand-foot syndrome is painful and can result in dose reductions that limit the effectiveness of cancer treatment - solutions are needed to allow optimal Xeloda dosing.

Symptoms of hand-foot syndrome include:

- Tingling or burning
- Redness
- Flaking
- Swelling
- Small blisters
- Small sores on the palms of the hands or soles of the feet

Changes to your normal, daily activities after chemotherapy can reduce your chances of developing hand-foot syndrome. Reduce exposure of hands and feet to friction and heat by avoiding the following:

- Hot water (washing dishes, long showers, hot baths)
- Impact on your feet (jogging, aerobics, walking, jumping)
- Using tools that require you to squeeze your hand on a hard surface (garden tools, household tools, kitchen knives)
- Rubbing (applying lotion, massaging)

Hand-foot syndrome is first treated by reducing the dose or stopping treatment with the chemotherapy drug that is causing it. Other approaches to managing hand-foot syndrome include:

- **Corticosteroids:** Steroids work by reducing inflammation. Your doctor may recommend a systemic corticosteroid (administered in a pill) to help relieve the symptoms of hand-foot syndrome.
- **Dimethyl - sulfoxide (DMSO):** Topical treatment with DMSO has shown activity in treating leakage of chemotherapy drugs into tissues.
- **Vitamin B6 (pyridoxine):** A small clinical trial has shown that treatment with vitamin B6 can reduce the symptoms of hand-foot syndrome.

https://news.cancerconnect.com/treatment-care/hand-foot-syndrome-palmar-plantar-erythrodysesthesia

24. Gut Microbiome Variations Could Predict Colon Cancer Risk, New Study Finds (Oct.17/23)

Researchers have identified differences in gut microbiome in people who develop precancerous colonic lesions, suggesting a possible connection between gut bacteria and colorectal cancer (CRC). Microbiome in the gut consists of trillions of microorganisms of thousands of different species, which include bacteria, fungi, parasites, and viruses. In a healthy person, these coexist peacefully. They are found throughout the body but are most common in the small and large intestines. The microbes found in the microbiome are beneficial when well-balanced. However, changes in the balance brought on by an illness, diet, or prolonged use of antibiotics can cause people to become more susceptible to infection.

Using data from the Dutch microbiome project scientists analyzed the function and composition of the gut microbiome of people with precancerous colorectal lesions between 2000 and 2015 and those who developed lesions after fecal sampling between 2015 and 2022. They then compared these groups to people with non-cancerous colonoscopy findings as well as the general public.

The results included:

1. Those who developed lesions after fecal sampling had increased diversity in their gut microbiome compared to those who did not develop lesions.
2. The composition and function of the microbiome among people with pre-existing and future lesions varied based on the type of lesion.

The scientists also reported that several bacterial species (Lachnospiraceae and the genera *Roseburia* and *Eubacterium*) were linked with the future development of lesions. The bacterial species *B. fragilis* has previously been associated with lesions.

https://www.medicalnewstoday.com/articles/gut-microbiome-variations-could-predict-colon-cancer-risk-new-study-finds#The-use-of-probiotics

25. Circulating DNA and Frequency of CRC Brain Metastases in a Presumed High-Risk Group (Oct.30/23)

BRAINSTORM, the prospective observational pilot study investigated if suggested risk factors, rectal cancer and lung metastases, could add to a relevant detection rate of asymptomatic brain metastases (BM) from colorectal cancer (CRC). Secondary, prognostic biological aspects were investigated by translational analysis of plasma samples.

The study enrolled patients with rectal cancer and lung metastases. At inclusion, patients underwent a standard MRI scan of the brain. Plasma samples were also collected at inclusion. The levels of total cell-free DNA (cfDNA) in plasma samples were then measured by a direct fluorescence assay (DFA) and circulating tumour DNA (ctDNA) by droplet digital PCR (ddPCR).

BM was detected in 1 of 29 included patients. Patients had higher cfDNA levels than healthy subjects. Patients with the primary tumour in situ had higher cfDNA levels than those with resected primary tumour. Patients with liver involvement had higher cfDNA levels and circulating tumour DNA levels than those without liver involvement.

In conclusion, the modest incidence of BM does not justify routine MRI of the brain in this selected population. cfDNA by DFA could be a valuable tool when planning treatment and follow-up for CRC patients. Future studies should focus on identifying further characteristics and biomarkers associated with a high risk of BM, enhancing the possibility for early intervention.

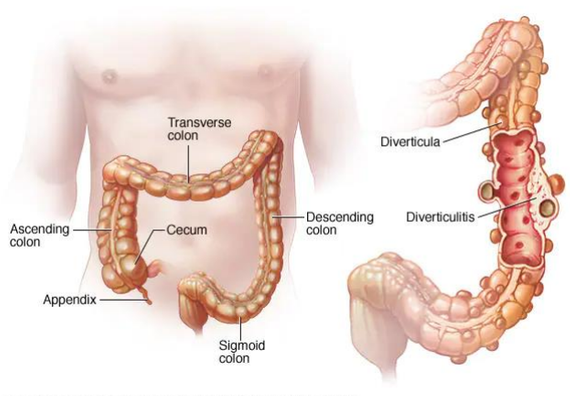
https://www.nature.com/articles/s41598-023-45939-x

26. Sigmoid Colon Cancer Masked by Refractory Diverticulitis with Abscess (Nov.5/23)

Colorectal cancer (CRC) can occasionally coexist with diverticulitis, thereby complicating diagnosis and treatment. In cases of refractory diverticulitis, it is important to consider the possibility of malignancy and determine appropriate treatment strategies.

Case Presentation
An 85-year-old male presented with lower left abdominal pain; he was admitted for further examination and the treatment of suspected sigmoid diverticulitis. On examination, a firm mass was palpated in the lower left quadrant. Imaging revealed sigmoid diverticulitis, partial abscess formation, and the involvement of the small bowel and abdominal wall. Although malignancy was suspected, a definitive diagnosis was not made. Because of the refractory nature of the disease, early surgical intervention, sigmoid colectomy, partial small bowel resection, abdominal wall resection, and lymph node dissection, was performed in accordance with the malignancy protocol. Pathologic diagnosis revealed adenocarcinoma within the diverticulitis with negative resection margins, indicating curative surgery.

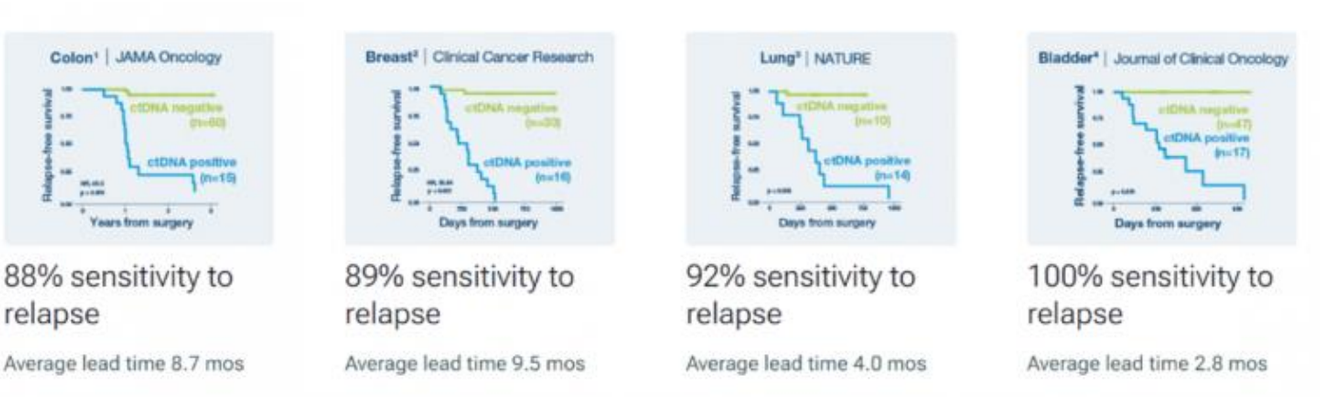
The low preoperative diagnostic rate of CRC associated with diverticulitis highlights the need for vigilance. Refractory diverticulitis may indicate the presence of concealed malignancy requiring surgical intervention. In the management of refractory diverticulitis, it is important to consider the potential coexistence of cancer. Even if extensive investigations are performed and a definitive diagnosis remains elusive, surgery must be considered.



https://www.cureus.com/articles/169919-sigmoid-colon-cancer-masked-by-refractory-diverticulitis-with-abscess#!/
Image Source: https://www.mayoclinic.org/diseases-conditions/diverticulitis/symptoms-causes/syc-20371758

27. LifeLabs Has Launched Signatera, Offering Canadians an Innovative and Personalized Approach to Managing Cancer (Nov.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.

https://www.lifelabs.com/lifelabs-launches-signatera-offering-canadians-an-innovative-and-personalized-approach-to-managing-cancer/

28. Natera Announces Publication of Prospective, Multi-Site CIRCULATE Study in Nature Medicine Demonstrating Signatera's Ability to Predict Chemotherapy Benefit in CRC (Nov.1/23)

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.

https://www.natera.com/company/news/natera-announces-publication-of-prospective-multi-site-circulate-study-in-nature-medicine-demonstrating-signateras-ability-to-predict-chemotherapy-benefit-in-colorectal-cancer/

Nutrition / Healthy Lifestyle

29. EXercise for Cancer to Enhance Living Well (EXCEL) Study (Nov.11/23)

Exercise for Cancer to Enhance Living Well (EXCEL) is a 5-year Canada-wide project, which offers free, 12-week exercise classes designed specifically for individuals undergoing or recovering from cancer treatment. Classes are online through a secure video-conferencing platform, and where possible, in-person (post-COVID). Physical activity can help overcome treatment-related side effects such as fatigue and pain, improve mental health by reducing anxiety and depression, and improve overall quality of life for individuals living with and beyond cancer. Studies show that physical activity may even reduce the risk of recurrence for some cancers. Many urban centres in Canada offer cancer-specific exercise programs, however, rural and remote areas tend to lack exercise resources to support cancer survivors, resulting in lower activity levels, poorer health, and diminished quality of life. Thus, EXCEL targets cancer survivors living in rural and remote regions across Canada, empowering them to move more and providing opportunities to benefit from physical activity.
To learn more about the EXCEL study:
https://kinesiology.ucalgary.ca/labs/health-and-wellness/research/research-studies/exercise-cancer-enhance-living-well-excel

To hear about participant experiences: ***https://www.youtube.com/watch?v=c01oo4Yd3oA***

30. Global Surge in CRC Linked to Junk Food (Oct.31/23)

Scientists have now found a link between the notoriously hard-to-treat colorectal cancer (CRC) and processed or “junk” food such as packaged snacks, hamburgers, fries, cereals, desserts, and sugary drinks. A lot more studies are coming out that show eating healthy is important to reduce your risk of CRC, and that’s especially true if you have CRC in your family.

A 2018 study reported in PLOS Medicine, which examined the diets of 471,495 adults from 10 European countries using a British Nutrient Profiling System based on self-reported foods and beverages commonly eaten (controlling for factors such as weight and activity level) found that a lower-nutritional-quality diet was associated with a higher risk of colorectal, respiratory tract and stomach cancers.

A 2018 European study revealed that people who ate the most food products with a higher score from the Nutrient Profiling System of the British Food Standards Agency or FSAm-NPS score (indicating lower nutritional quality) showed a higher risk of CRC— which suggests that front-of-pack nutrition labels, and other public health nutritional measures might be effective in helping to reduce CRC rates.

A 2022 review, examining dietary intake as a risk factor for Early-Onset Colorectal Adenoma and Carcinoma (EOCRC) found that Individuals who regularly consumed substantial quantities of deep-fried foods, processed items, maintained a high-fat diet, drank excessive sugary beverages, and indulged in desserts, all while having low intake of folate and fiber, were found to have a notably higher risk of early-onset colorectal cancer (EOCRC). On the other hand, a protective effect against EOCRC was identified in those who had a diet rich in fruits and vegetables, consumed ample micronutrients, and adhered to a vegetarian dietary pattern.

While diagnostic delays can be avoided through routine screenings, diet is a modifiable risk factor, that can help to save lives.

https://www.forbes.com/sites/daphneewingchow/2023/10/31/global-surge-in-colorectal-cancer-linked-to-junk-food/?sh=4b3d365d5842
Image Source: ***https://www.theguardian.com/food/2020/feb/13/how-ultra-processed-food-took-over-your-shopping-basket-brazil-carlos-monteiro***

COVID-19 Updates

31. 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-acoronaviruses

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 @GovNL, 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