The following colorectal cancer research updates extend from Jan 17th, 2019 to Mar 14th, 2019 inclusive and are intended for informational purposes only.

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**DRUGS/SYSTEMIC THERAPIES**

1. Cannabinoid compounds may inhibit growth of colon cancer cells (Feb 6/19)

In recent years, medical marijuana has gained attention for its ability to relieve pain, short-term anxiety and depression. Researchers are now suggesting that some cannabinoid compounds may inhibit the growth of colon cancer cells in the lab. While the most well-known compounds associated with cannabis – THC and CBD – had little to no effect, 10 other compounds were identified as effectively inhibiting colon cancer cell growth. These compounds will be tested in further studies to better understand their anti-cancer properties.

In the study, the researchers tested how 370 different synthetic cannabinoid compounds affected seven types of human colon cancer cells. Since there are many different pathways that can lead to cancer in a cell, the researchers used seven colon cancer cells that each had a different cause or mutation. The researchers grew the cancer cells in the lab for 8 hours before treating them with the cannabinoid compounds for 48 hours. Any compounds that showed signs of reducing the growth and development of one kind of cancer cell was then applied to all seven kinds of cells. The researchers eventually identified 10 compounds that inhibited the growth of all seven types of colon cancer included in the study. Future research will be directed towards a better understanding of how the compounds interact with cellular mechanisms that drive colon cancer, and whether these compounds can be potentiated for use in cancer therapy.

https://www.sciencedaily.com/releases/2019/02/190206091420.htm
2. CCTG CO.26 trial: A phase II randomized study of durvalumab plus tremelimumab and best supportive care (BSC) versus BSC alone in patients with advanced refractory colorectal cancer (Jan 19/19)

Durvalumab (D) is a human monoclonal antibody that inhibits the binding of programmed cell death ligand 1 (PD-L1) to its receptor programmed cell death protein 1 (PD-1). PD-L1 and PD-1 are involved in the suppression of the immune system to limit the destruction of healthy cells during an immune reaction and to prevent autoimmune disease. Its suppressing activity may be amplified in some cancers in order for malignant cells to escape attack by the immune system. Tremelimumab is a human monoclonal antibody which inhibits the cytotoxic T-lymphocyte-associated protein 4 (CTLA-4). CTLA-4 is another immune checkpoint protein which downregulates the body’s immune responses and whose immune-suppressing activity may be increased in some cancers. Targeting both PD-L1 and CTLA-4 may have additive or synergistic activity as the mechanisms of action of CTLA-4 and PD-L1 inhibition are non-redundant, rendering it very difficult for tumour cells to compensate for, or evolve from, the inhibitory effect of the drugs.

A recent study aimed to evaluate the effectiveness of a combination of CTLA-4 and PD-L1 inhibition compared to best supportive care (BSC) alone in refractory colorectal cancer (rCRC). Patients were eligible for the trial if they failed all standard regimens containing a fluoropyrimidine, irinotecan and oxaliplatin (as well as an EGFR inhibitor if their cancer was RAS wild type). 180 patients were enrolled in the study. With a median follow-up of 15.2 months, the median overall survival (OS) was 6.6 months for D+T and 4.1 months for BSC. Median progression-free survival (PFS) was 1.8 months and 1.9 months, respectively. Disease control rate was 22.7% for D+T and 6.6% for BSC. Grade 3 or 4 abdominal pain, fatigue, lymphocytosis (increase in the number of lymphocytes in the blood) and eosinophilia (increase in the number of red blood cells in the blood) were significantly higher in D+T. At 16 weeks follow-up, there was a significant improvement to physical functioning among patients in the D+T arm. In conclusion, treatment with D+T significantly prolonged OS in patients with rCRC and preserved quality of life. Adverse events, however, were more frequent among patients with D+T.

https://meetinglibrary.asco.org/record/169381/abstract

3. ASCO GI 2019: colorectal cancer abstract recommendations from Dr. Axel Grothey (Jan 16/19)

Dr. Axel Grothey recommended the following abstracts at the ASCO Gastrointestinal Cancers Symposium held in San Francisco Thursday, January 17, through Saturday, January 19, 2019.

Saturday, January 19, 2019
Oral Abstract Session; Cancers of the Colon, Rectum, and Anus

481 CCTG CO.26 trial: A phase II randomized study of durvalumab (D) plus tremelimumab (T) and best supportive care (BSC) versus BSC alone in patients (pts) with advanced refractory colorectal carcinoma (rCRC). EX Chen, DJ Jonker, HF Kennecke, et al (Reported above in Update #2)

Take-home message

- Moderate overall survival benefit for patients with mismatch repair proficient (MMR-P) CRC in a later-line setting.
This is the first time we have seen at least some activity of immunotherapy in MMR-P (not microsatellite instability high (MSI-H) or mismatch repair deficiency (MMR-D)) CRC. We will need to see the actual data, though.

Adjuvant HIPEC in patients with colon cancer at high risk of peritoneal metastases: Primary outcome of the COLOPEC multicenter randomized trial. CEL Klaver, DD Wisselink, CJA Punt, et al (Reported in Update #13)

Take-home message

- Adjuvant HIPEC with oxaliplatin for patients with T4 or perforated colon cancer did not result in improved 18-month peritoneal metastases-free survival.
- The role of HIPEC in mCRC is definitely decreasing.

Does a longer waiting period after neoadjuvant radiochemotherapy improve the oncological prognosis of rectal cancer? Three-year follow-up results of the GRECCAR-6 randomized multicenter trial. JH Lefevre, LMineur, M Cachanado, et al

Take-home message

- Increasing the interval from radiation to surgery from 7 to 11 weeks did not influence the pCR rate.

Saturday, January 19, 2019
Rapid Abstract Session; Cancers of the Colon, Rectum, and Anus

Total neoadjuvant therapy with short course radiation compared to concurrent chemoradiation in rectal cancer. W Chapman, H Kim, P Bauer, et al (Reported in Update #16)

Take-home message

- This retrospective cohort study suggests that short-course radiation therapy in conjunction with systemic combination chemotherapy can be an alternative to conventional chemoradiation therapy in rectal cancer.
- Data from prospective, randomized trials are awaited.

Saturday, January 19, 2019
Poster Session; Cancers of the Colon, Rectum, and Anus

Updated results of the BEACON CRC safety lead-in: Encorafenib (ENCO) + binimetinib (BINI) + cetuximab (CETUX) for BRAFV600E-mutant metastatic colorectal cancer (mCRC). S Kopetz, A Grothey, R Yaeger, et al (Reported in Update #9)

Take-home message

- Impressive results with a high response rate (48%) and long median overall survival (15.3 months) in 29 patients with BRAF V600E-mutated mCRC.
- The randomized phase III BEACON study has finished accrual and could set a new standard of care.

While a 6-month oxaliplatin-containing regimen is widely accepted as a standard adjuvant chemotherapy for stage III colorectal cancer (CRC), the efficacy of oral fluoropyrimidine monotherapy as a possible treatment option is yet to be fully investigated. A recent study published in the British Journal of Cancer aimed to investigate the optimal duration of treatment of oral capecitabine therapy. A total of 1306 patients with resected stage III CRC were randomly assigned to receive capecitabine for 14 out of 21 days for 6 or 12 months. The 3- and 5-year disease-free survival were 70% and 65.3% in the 6-month group, and 75.3% and 68.7% in the 12-month group, respectively. The 5-year overall survival was 83.2% and 87.6%, respectively. The incidence of overall grade 3-4 adverse events was basically the same in both groups. While the differences between the 6-month and 12-month disease-free survival were not statistically significant, the better overall survival in the 12-month group could be a valuable factor in selected stage III CRC cases.

4. 6-month vs. 12-month capecitabine as adjuvant chemotherapy for patients with stage III colon cancer (Mar 14/19)
5. Bowel cancer: new biomarker may also boost treatment (Jan 8/19)

A recent study from the journal *Biochemical and Biophysical Research Communications* has identified a new biomarker for colorectal cancer (CRC), which may help to identify the disease at an earlier stage. The researchers found that levels of the protein beta-1,4-GalT-V were higher in CRC tumour cells than in the surrounding healthy tissue. 6.5 times more beta-1,4-GalT-V was found in the tumour samples compared to healthy tissue. When the researchers treated the tumour cells with D-PDMP, an inhibitor of the beta-1,4-GalT-V protein *in vitro*, the tumour cells showed reduced levels of the protein and higher rates of cell death within 24-96 hours. The researchers concluded that beta-1,4-GalT-V is a target for cell proliferation, and cell-based testing has demonstrated that its activity can be effectively inhibited by D-PDMP. While further research is necessary to confirm these results, the study has provided another potential tool for the early diagnosis of CRC and perhaps multiple cancer types.

https://www.practiceupdate.com/content/6-month-vs-12-month-capecitabine-as-adjuvant-chemotherapy-for-patients-with-stage-iii-colon-cancer/80756/37777

6. More proof that less chemo is best in elderly colorectal cancer patients (Jan 24/19)

Dr. David Kerr is a professor of cancer medicine at the University of Oxford, London. He discusses the results from a recent analysis from *Annals of Oncology* regarding the age-related advantages and disadvantages of chemotherapy in colorectal cancer.

A publication by the German Rectal Cancer Study Group examined the controversy around adding oxaliplatin to preoperative chemoradiotherapy or postoperative adjuvant chemotherapy regimens in rectal cancer. In a large, well-designed randomized trial of about 1200 patients which added oxaliplatin to their adjuvant chemotherapy regime, disease-free survival seemed to improve. In their retrospective analysis, however, they examined these outcomes based on age. They examine patients under 60 years, ages 60-70 years, and age 70+. They demonstrated that the important benefits of adding oxaliplatin to the conventional fluoropyrimidine chemoradiotherapy was limited to those *under* 70 years of age. No benefits at all were observed with this regimen in those aged 70 and above.

In the QUASAR studies which were trials of fluoropyrimidines in the treatment of colorectal cancer, the benefits of the chemotherapy became far less prominent as progressively older patients were treated, specifically 70 years of age and above. Furthermore, in the MOSAIC study which looked at the use of adjuvant oxaliplatin in colon cancer, the results again suggested the limited benefits of such treatment to the 70 years old or older patient group.

It is known that older patients with older tumours tend to have a higher mutational burden, a fact that could become important when considering patients for certain treatments such as immunotherapy. No clear conventional molecular markers, however, stand out to allow clinicians to distinguish between old and young. The practical take-home message is that when clinicians are delivering adjuvant therapy to patients over the age of 70 with colorectal cancer, single-agent fluoropyrimidine seems to be a reasonable treatment plan to offer. From there, they could continue the conversation with the patient to decide whether they feel the benefits of further treatments are worth the potential disadvantages of side effects, hassles, and more.


7. Digital pill may improve adherence to oral cancer drugs (Feb 6/19)

Oral chemotherapy has changed the standards of cancer treatment, from one that was purely hospital-based procedure to one that can be administered at home. Although it may be more convenient for the patient, adherence can sometimes be problematic. A novel “digital pill” could help clinicians better monitor their patients. In a small pilot study, colorectal cancer (CRC) patients are being treated with capecitabine (Xeloda, Hoffman-LaRoche) that has been attached to a small sensor. The digital pill system consists of an ingestible sensor about the size of a grain of sand. It is placed inside a gel cap along with the active drug. The patient wears a sensor patch measuring 1” x 3” on their torso. After the pill is swallowed, the sensor is activated once it
reaches the stomach. It then sends a signal to the patch, which then begins to send a digital record to an app on the patient’s mobile device. The sensor then alerts the oncologist, nurse, or caregiver when the pill has been taken. The sensor can securely capture, record, and share information about the time, dose, and type of oral chemotherapy being taken. Researchers from the project explain that with intravenous chemotherapy in the hospital or clinic, there were a lot of safety mechanisms in place that were focused around the physical presence of the patient in the infusion centre. The situation is quite different from oral chemotherapy. Clinicians would write prescriptions, give them to the patients, and the rest remained invisible. Several mechanisms were in place to help monitor patients who were taking oral therapies, such as having pharmacists check in with them. The patients, however, lacked the direct connection with their clinicians as they had in infusion centres.

Adhering correctly to a treatment regimen can be challenging, especially with the whirlwind of complex emotions, physical side effects, and changes in work and home life that can occur with a cancer diagnosis. The regimen for capcitabine, for example is complex. One of eight cycles of chemotherapy includes 4 pills twice a day, with 2 weeks of therapy and 1 week off therapy. Furthermore, following such a regimen can be scary or overwhelming for some patients. The digital pill aims to give them more of a connection to their doctors, while maintaining their privacy. In the pilot study, the feedback has been very positive so far. When a patient forgets whether they took their medication already, they no longer have to worry as the digital system will keep track for them. The system is also enabling clinicians and caregivers to find out about problems the patient may be facing in real time. For example, the system notified the team that one patient had not taken her dose. When they checked up on her, she explained that her hands hurt and she could not open the bottle. The problem was found and promptly addressed. Especially in a society that has a growing elderly population, better strategies to ensure that elderly individuals are taking their medications as prescribed are important. This technology has numerous applications and could be a promising tool to optimize treatment regimens for all types of patients in the future.


8. Group to study immunotherapy-targeted therapy combination for metastatic colon cancer (Mar 7/19)

Researchers at the University of Colorado Cancer Center and partnering institutions received a grant to study a new combination therapy for patients with microsatellite-stable metastatic colon cancer (MSS mCRC). The researchers will investigate the VEGF inhibitor bevacizumab (Avastin, Genentech) and MEK inhibitor binimetinib (Mektovi, Array BioPharma), alongside a PD-1 inhibitor pembrolizumab (Keytruda, Merck) among other partners of CRC patients who currently have limited treatment options. Immunotherapy has worked for a very small subset of patients – about 4% - with MSS mCRC.

The researchers hypothesize that an inhibition of all three pathways that are targeted by these drugs will be an effective attack on MSS disease. After a previous trial of a MEK inhibitor in combination with another drug, the researchers found that T cells seemed to increase around the cancer and were better able to infiltrate the targeted site. With MSS mCRC, there is a notable lack of T cell presence around the cancer. Pembrolizumab activates a mechanism in the immune system which stimulates T-cell mediated immune responses against tumour cells. The inclusion of the MEK inhibitor and the VEGF inhibitor is aimed at getting more T cells at tumour sites and subsequently activating them through pembrolizumab immunotherapy. For the remaining 95-96% of MSS mCRC patients who are in need of better treatment strategies, there is hope that this trial could shed light on more effective immunotherapy options to improve disease outcomes.

For more information: Christopher Lieu, MD, can be reached at UCH Health Anschutz Cancer Pavilion-Anschutz Medical Campus, 1665 Aurora Court, Aurora, CO 80045; email: christopher.lieu@ucdenver.edu.


9. Updated results of the BEACON CRC safety lead-in: Encorafenib (ENCO) + binimetinib (BINI) + cetuximab (CETUX) for BRAFV600E-mutant metastatic colorectal cance (Jan 19/19)

BRAF mutations occur in about 10-15% of patients with metastatic colorectal cancer (mCRC) and lead to poor disease outcomes. After first-line therapy, standard second-line therapies show limited benefit, with response rates less than 10% and overall survival (OS) of 4-6 months. The BEACON CRC trial is a phase III trial of a triplet therapy which consists of three treatment arms conducted in patients with BRAF mCRC in the second or third-
12. Hepatic Artery Infusion Pump (HAIP) Chemotherapy Program – Sunnybrook Odette Cancer Centre (Mar 14/19)

**SURGICAL THERAPIES**

https://meetinglibrary.asco.org/record/168986/abstract

10. Aspirin underutilized by patients with advanced colorectal polyps (Feb 14/19)

Despite studies that have shown that aspirin reduces the risk for colorectal cancer (CRC), researchers from a recent study from Florida Atlantic University’s Schmidt College of Medicine have found that aspirin remains underused by the majority of patients with advanced colorectal polyps. Using a micro-simulation model which included baseline risk factors for CRC, the researchers found that aspirin reduces the risk of the disease by 40%. Based on these findings, their guidelines suggest that clinicians should routinely prescribe aspirin to patients with advanced colorectal polyps when the advantages of the drug outweigh its disadvantages, which include risk of gastrointestinal bleeding with long-term daily use. The researchers aimed to determine the extent to which patients actually adhere to these guidelines by conducting brief telephone interviews with adults aged 41-91 years who had colonoscopies with a diagnosis of advanced colorectal polyps between July 2013 and June 2017. It was found that of the 84 patients that were interviewed, 36 (42.9%) reported taking aspirin. The data suggest that multifactorial approaches by clinicians which include therapeutic lifestyle changes, adjunct drug therapies, as well as screening will be necessary to address the challenges related to CRC prevention and treatment.


11. Phase I study of Cobimetinib with Bevacizumab and Atezolizumab for colorectal cancer (Mar 14/19)

In this non-randomized phase I trial, the safety, tolerability and pharmacokinetics of cobimetinib in combination with atezolizumab and bevacizumab among patients with metastatic colorectal cancer will be evaluated. Cobimetinib is an oral MEK kinase inhibitor which targets cell signalling involved in cell division and growth. Atezolizumab is an anti-PD-L1 antibody which targets the PD-L1 and PD-1 receptor to prevent suppression of the immune system against cancer cells. Bevacizumab is an antibody which interferes with the process of new blood vessel formation (angiogenesis) in cancer cells. All patients will have received at least 1 previous therapy with fluoropyrimidine and oxaliplatin or irinotecan. Cobimetinib will be administered orally while atezolizumab and bevacizumab will be given intravenously. In the first stage of the trial, patients will receive the drug combination until the disease progresses, unacceptable toxicity or withdrawal from the trial. In the second stage of the trial, the patients will be divided into two groups. The first group will receive the drug combination and undergo repeated tumour biopsy. The second group will receive atezolizumab and bevacizumab plus the cobimetinib dose that was given in stage I. For more information regarding the study, including inclusion and exclusion criteria, locations and contact information, visit: https://clinicaltrials.gov/ct2/show/NCT02876224. The study is open and recruiting patients as of Oct 24, 2017 in the U.S., U.K., and Spain.


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 Yooj Ko** are the program leads and happy to see patients 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]

**13. 2019 GI Cancers Symposium: is adjuvant HIPEC effective in reducing the risk of peritoneal metastases in patients with colon cancer?** (Mar 7/19)

Patients with advanced (stage 4) or perforated colon cancer may be at greater risk of developing metastases in the peritoneum. Given that many patients with peritoneal metastases are diagnosed at a late stage, researchers aimed to study the effectiveness of hyperthermic intraperitoneal chemotherapy (HIPEC) in the adjuvant setting in order to reduce the risk of developing peritoneal metastases. During HIPEC therapy, the abdominal cavity is filled with a high dose of chemotherapy that is heated to 41-42 degrees Celsius because it is thought that heat will increase the effectiveness of the drugs. In the phase III trial, 204 patients were randomly assigned to receive adjuvant HIPEC followed by routine adjuvant systemic chemotherapy, or adjuvant systemic chemotherapy alone. The rate of peritoneal metastases after completion of 18 months of follow-up was 22 of 102 patients in the HIPEC group and 18 of 100 patients in the control group. There was no difference observed in 18-month disease-free survival and overall survival. The researchers concluded that adjuvant HIPEC with oxaliplatin for patients with stage 4 tumours or perforated colon cancer does not result in better 18-month peritoneal metastasis-free survival. Long-term results are needed to gain a better idea of the role of HIPEC in the adjuvant setting.

[Image Source: http://www.kwentology.com/2014/02/what-is-hyperthermic-intraperitoneal.html]
[http://www.ascopost.com/News/59648]
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 a 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 are 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

15. Stereotactic radiation feasible for oligometastatic cancer (Mar 1/19)

Based on findings from a phase II study published in International Journal of Radiation Oncology, Biology, Physics, stereotactic ablative radiation therapy (SABR) is a feasible and tolerable treatment option for recurring oligometastatic cancer (cancer that has spread to one or two other parts of the body). The researchers examined the role of SABR for stage IV oligometastatic cancer among 147 patients of median age 66.4 years. Patient follow-up occurred at three-month intervals and within six weeks of completion of SABR. SABR administers very high doses of radiation using several beams of various intensities aimed at different angles to precisely target the tumour while minimizing damage to surrounding tissues. The researchers found that the most common primary tumours were lung (21.8%), colorectal adenocarcinoma (21.1%), and head and neck (10.9%). Over a median follow-up of 41.3 months, the median overall survival (OS) was 42.3 months, with five-year OS of 43%. 5-year progression-free survival was 74%. 7.5% of patients suffered from grade 2 toxicity, and 2% suffered from grade 3 toxicity. At completion, 6 weeks, 3 months and 9 months post-treatment, there were no significant changes to quality of life. At 12 months, however, patients had statistically significant improvements to quality of life. The results from this study suggest that this treatment regimen could help promote long-term survival while maintaining overall quality of life among this patient group. Further studies with larger population sizes will be needed to confirm these results.

https://www.practiceupdate.com/content/stereotactic-radiation-feasible-for-oligometastatic-cancer/80312/62
16. Total neoadjuvant therapy with short course radiation compared to concurrent chemoradiation in rectal cancer (Jan 19/19)

Total neoadjuvant therapy (TNT) is the delivery of all radiation and chemotherapy prior to surgery. It has been shown to have improved complete response rates compared to adjuvant chemotherapy among patients with rectal cancer. A recent study compared the complete response rate (CR), the Neoadjuvant Rectal (NAR) Score (a predictor of disease outcomes based on tumour downstaging), and recurrence rates for patients receiving short-course TNT (SC-TNT) compared to standard chemoradiation (CRT). Of the 388 patients enrolled in the study, 236 (60.8%) were treated with CRT and 152 (39.2%) underwent SC-TNT. The SC-TNT arm achieved a higher CR rate compared to CRT (25% vs. 19.1%). The odds of achieving a “low” NAR Score (low score suggests more favourable disease outcomes) trended higher among the SC-TNT cohort. Recurrence rates were similar between the SC-TNT and CRT groups (14.9% vs. 14.3%). In conclusion, the study findings suggest that short-course radiation with neoadjuvant chemotherapy is at least as effective as long-course CRT.

https://meetinglibrary.asco.org/record/169365/abstract

17. Study Offered at the Odette Cancer Centre to Treat Recurrent Rectal Cancer (Mar 14/19)

Magnetic resonance-guided focused ultrasound (MRg-FU) is a non-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 real-time thermal mapping to ensure accurate heating of the designated target with minimal effect 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. Predictive values of colorectal cancer alarm symptoms in the general population (Mar 5/19)

A nationwide cohort study aimed to evaluate the predictive value of various alarm symptoms in the diagnosis of colorectal cancer (CRC) among healthy adults aged 40+ years. A high positive predictive value (PPV) for a particular alarm symptom indicates the certainty with which a CRC diagnosis can be made based on this symptom. 69,060 individuals over the age of 40 were randomly selected from the Danish population to complete a survey regarding symptoms and healthcare-seeking behaviour in 2012. Information on CRC diagnosis in a 12-month follow-up was provided by the Danish Cancer Registry. A total of 37,455 individual completed the survey. The single symptom with the highest PPV was rectal bleeding. PPVs were generally higher among individuals aged 75+ years and highest among those who reported at least one specific alarm symptom that led to a GP contact. The researchers found that in general, the PPVs of CRC alarm symptoms are low, especially in the youngest age groups. In other words, younger individuals may demonstrate certain CRC alarm symptoms without actually having the disease. Future campaigns in early diagnosis of CRC should focus
on promoting awareness and healthcare-seeking when experiencing rectal bleeding and continuing to target older individuals for early screening.


19. Aspirin, anticoagulants up rate of false positives with FIT for colorectal cancer (Feb 11/19)

According to a recent study published in *Gastroenterology*, fecal immunochemical tests (FIT) are more likely to have lower positive predictive value (PPV, probability that subjects with a positive screening test truly have the disease) for colorectal cancer (CRC) among patients who are regular users of aspirin and direct-acting oral anticoagulants. The researchers explained that anticoagulant medication is increasingly used among patients 50 years and older, the target population for CRC screening.

These medications are associated with increased gastrointestinal bleeding, affecting the efficacy of FIT screening in two ways. The drugs may increase blood loss from the colonic mucosa and facilitate bleeding from non-advanced lesions, thereby decreasing FIT predictive value for CRC and advanced adenomas. On the other hand, the medications may also increase bleeding from advanced colorectal lesions, resulting in increased positive predictive value. In the study, the researchers examined data from 4,908 patients in an ongoing CRC screening trial with a positive FIT result and a follow-up colonoscopy. They defined patients who used regular aspirin, warfarin, or direct-acting anticoagulants (DOACs) as users and matched them to non-users based on age, sex, screening center and screening round. Among aspirin users, the PPV for CRC was 3.8% compared with 6.4% for matched non-users. PPV for advanced adenoma was 27.2% compared with 32.6% in non-users. Additionally, it was found that the PPV for advanced adenoma was 20.5% compared with 32.4% in non-users, and PPV for CRC was 0.9% in DOAC users compared with 6.8% in non-users. These findings could impact how patients are handled during CRC screening programs. For example, screening participants who use these drugs should be informed of increased risk of false positive results, with particular attention to users of DOACs.


https://www.healio.com/gastroenterology/oncology/news/online/%7be89c187-33ca-467e-b95e-edac2221ead%7d/anticoagulants-aspirin-increase-risk-for-fit-false-positives

20. Annual FITs effective for colorectal cancer screening (Feb 25/19)

A recent systematic review of the literature published in *Annals of Internal Medicine* supported the annual home fecal immunochemical test (FIT) as a highly sensitive and specific screening method for identifying the presence of colorectal cancer (CRC). CRC is a leading cause of death among digestive diseases despite the effectiveness and cost-effectiveness of screening. Only about 60-65% of the eligible population actually completes screening, a rate that fell short of the 2018 goal of 80%. While colonoscopy is the gold standard of CRC screening and remains the most frequently used test in the US, it does present barriers to uptake including invasiveness and the necessary bowel preparation. On the other hand, FIT is non-invasive, easy to prepare, inexpensive and similarly effective to colonoscopies for CRC screening, thereby providing a valuable option to increase CRC screening in the general population.
This study summarized FIT performance characteristics for CRC and advanced adenomas. The systematic review of 31 studies assessed FIT sensitivity and specificity in a total of 120,255 asymptomatic average-risk adults. The findings presented new information about FIT performance characteristics for CRC and advanced adenomas as a function of test threshold. The FIT threshold is the point at which the test is designated as a positive result and screening participants are referred for a colonoscopy. This threshold can be varied, and screening programs around the world actually use very different thresholds. The researchers found differences that varied greatly across the studies depending on the test threshold, and results were found to be inconclusive when comparing three FITs at three different thresholds. The study findings suggest that FITs may be highly sensitive (a high probability of detection) for CRC in a single application, though at the expense of a high false-positive rate. While the test is much less sensitive for advanced adenomas, what is known about these lesions suggests that they have a low annual transition rate to CRC of about 3-6%. This implies that there is an opportunity for detection within a well-timed screening program. The researchers suggest that healthcare systems need to consider the quantity and quality of data for a specific FIT, comparability of the population to that particular FIT, and the clinical and economic effects of different test thresholds on colonoscopy and other system resources to optimize FIT for early detection and prevention of CRC.

Recent research published in *Alimentary Pharmacology & Therapeutics* found that the analysis of volatile organic compounds found in fecal samples could help in the diagnosis of colorectal adenocarcinoma. The researchers noted that previous studies have explored the potential of volatile organic compounds as biomarkers for CRC, but they have mostly been unable to identify specific compounds. In the study, researchers collected fecal samples from 137 symptomatic patients and individuals participating in the UK Bowel Cancer Screening Program. In their analysis, the researchers found that one volatile organic compound, isopropyl alcohol, was significantly more abundant in the cancer samples. When this compound was found alongside two other volatile organic compounds hexan-2-one and ethyl 3-methyl-butanoate in a single fecal sample, the individual's CRC risk was 6 times greater. The researchers suggest that these volatile organic compounds are mostly likely the breakdown products of bacteria in the gut, but further research will be needed to confirm the precise sources. Further studies will be necessary to determine how screening for volatile organic compounds compares to FIT testing for CRC, and whether they could possibly be used together for a more accurate screening test.

Since the stool-based DNA test received FDA approval in 2014, more than 2 million Americans have been screened for colorectal cancer (CRC) with Cologuard. The test is an easy to use, non-invasive CRC screening test that identifies altered DNA and/or blood in the stool, which are both associated with the possibility of CRC or a precancerous lesion. When used instead of a colonoscopy, Cologuard should be used every 3 years. The test is changing how many Americans get screened for the disease and is helping many people complete their
screening for the first time. Reaching this milestone of 2 million individuals screened means that more patients and health care providers are participating in early screening when the disease is more treatable. The stool test’s manufacturer, Exact Sciences, estimates that the test may have helped to detect as many as 9,400 early-stage cancers and about 64,000 pre-cancerous polyps. Furthermore, about 50% of the patients screened using Cologuard had previously never been screened for the disease. To date, the test has not yet been approved for use in Canada.

https://www.healio.com/gastroenterology/oncology/news/online/%7b2e7454ae-cfbd-42ab-8fb7-134f06acb6d2%7d/cologuard-surpasses-colorectal-cancer-screening-milestone

The home-based stool-DNA colorectal cancer screening test


23. Endocuff reduces colonoscopy withdrawal time without sacrificing detection (Feb 14/19)

Based on recent research published in *Clinical Gastroenterology and Hepatology*, the Endocuff Vision device was able to decrease withdrawal time compared to standard colonoscopy without sacrificing lesion detection. The Endocuff device helps to expose the lining of the intestine for inspection and polyp detection and helped to reduce most of the work an endoscopist must perform during an examination. During a normal colonoscopy, high-quality withdrawal of the colonoscope from the intestine consists of careful inspection of the folds, flexures and colorectal valves, removal of retained pools of debris and fluid, as well as adequate colonic distension. The Endocuff device can be used to hook and flatten folds, improving exposure of the mucosal lining for better visibility. Another benefit of the device is that it makes the whole process of examining in between the intestinal folds much faster. In the study, researchers randomly assigned patients to undergo screening or surveillance with the device or with standard colonoscopy. Two experienced endoscopists performed the colonoscopies and aimed for a thorough evaluation of the folds, flexures and valves in the shortest amount of time. Investigators found that the mean inspection time was nearly 2 minutes shorter for the device group. The device helped to achieve a higher number of adenomas detected per colonoscopy, and adenoma detection rate (61.4% vs. 52%). Furthermore, the device improved the number of sessile serrated polyps detected per colonoscopy, as well as overall sessile serrate poly detection rate (19.8% vs. 11.1%). Sessile serrated polyps are generally more difficult to visualize and detect compared to adenomas during routine examinations. Overall, the Endocuff device demonstrated promising results in improving colonoscopy results and efficiency. Further studies with larger sample sizes will be necessary to confirm the efficacy and overall benefits of the Endocuff device in routine colorectal cancer screening.

https://www.healio.com/gastroenterology/interventional-endoscopy/news/online/%7b1f1a3eb-9b91-4ab5-9d95-9140688bca0%7d/endocuff-reduces-colonoscopy-withdrawal-time-without-sacrificing-detection

https://www.practiceupdate.com/content/endocuff-vision-reduces-inspection-time-without-decreasing-lesion-detection/78904/62
The Endocuff device with retractable, flexible arms which help to flatten intestinal folds for better visibility.

Image source: http://endocuff.com/products/endocuff/

PSYCHOSOCIAL

24. Early collaboration with psycho-oncologists can make “meaningful difference” in reducing suicide risk (Jan 25/19)

Suicide rates among those with cancer are high – double that of the general US population. When confronted with a cancer diagnosis, nearly one-third of patients consider suicide as an option to escape the anticipated suffering and the possibility of death. While a significant amount of effort has been directed toward treatment and finding a cure for cancer, experts say that less attention has been given to the mental health aspects of cancer care. A study published last year in *Psycho-Oncology* conducted root cause analyses (RCAs) of cancer-associated suicides to better understand factors that may contribute to suicide among patients with cancer. The analysis included data from 2002 to 2017 from the Veterans Health Administration National Center for Patient Safety. The most common risk factors for suicide included depression (59%), medical comorbidities (59%) and pain (47%). It was found that the majority of suicides (67%) occurred within 7 days of a medical visit, with 41% occurring within the first 24 hours. Indeed, there is a markedly elevated risk for suicide within the first week of a cancer diagnosis and it remains elevated for the first year. The researchers note that it is very important to collaborate with psychosocial clinicians to evaluate patients. When someone receives a diagnosis that can be life-altering, they are put into a vulnerable place and people react to the news differently.

While many studies have focused on the link between certain cancers that are associated with a higher risk of suicide, it is difficult to know the significance of these findings or to identify an underlying common cause for increased risk. For example, some hypothesize that inflammation and the association of inflammation and depression may play a role. Clinically, however, one specialist tends to focus more on concurrent risk factors for suicide – such as advanced disease, uncontrolled pain, lack of social support, clinical depression, comorbid psychiatric disorders (e.g. substance use), and history of suicide attempts – as more useful, tangible predictors for risk than specific cancer diagnoses.

Data has shown that between 10 and 25% of patients with cancer develop clinical depression during some point in their cancer trajectory. Depression is up to four times more common among patients with cancer than the general population. In a study published in *JAMA*, it was found that untreated clinical depression accounted for nearly 45% of patients who reported an increased desire for death. The effects of treatment for clinical depression among patients with advanced cancer at high risk for suicide was also evaluated in the study. Results showed that psychopharmacologic treatment resolved depression in the majority of patients, and 95% of patients with adequately treated depression no longer experienced an increased desire for death.
Recently, there has been a rapid movement to screen for suicide in all patients with cancer across major institutions. All National Cancer Institute-designated cancer centers screen for distress among both inpatients and outpatients. Once screened, algorithms are in place for triage to mental health professionals. While some people may worry that asking about these things may give someone the idea that they should hurt themselves, there is no evidence to support this. Asking about suicide does not put someone at greater risk of committing suicide. Above all, it is important to realize that patients with advanced disease are potentially at high risk for suicide, and clinicians need to pay close attention to the physical and psychological symptoms when treating their patients’ cancer. Earlier initiation of palliative care as well as psycho-oncology services should be introduced early on in the process of care and are important in achieving the outcomes of prolonged survival and quality of life. Suicide and assisted suicide deal with suffering by eliminating the sufferer. As a society, we should strive towards addressing the causes of suffering.


25. CanDirect research study: Learn more about a study for patients who have completed their cancer treatments and are experiencing low mood (March 2019)

15% of cancer survivors are estimated to experience mood problems even one year post-treatment. The CanDirect research study aims to support cancer survivors with mood problems by providing study participants with a self-care toolkit designed to help users better manage their mood and anxiety as well as phone coaching for a maximum duration of 6 months. Participation is open to eligible adult survivors residing in Quebec and Ontario who have completed cancer treatment for a non-metastatic cancer and who are experiencing depressive symptoms. For additional information, please access the following link:

https://clinicaltrials.gov/show/NCT02890615

26. Colorectal cancer: loss of two genes may drive tumour formation (Mar 19)

Up to 35% of colorectal cancer (CRC) cases derive from serrated or sessile polyps, a kind of flat polyp that is predominantly seen in the cecum and ascending colon. These types of polyps are not only more difficult to identify during a colonoscopy, but CRC that arises from them is often more difficult to treat. This puts emphasis on the early detection and examination of these polyps in order to improve the patient’s disease outcomes. Recent research published in *Immunity* suggests that the loss of two specific genes causes the formation of serrated polyps, pointing to new biomarkers for this specific branch of CRC.

In the study, the researchers found that the two genes responsible for causing the development of serrated CRC in mouse models code for protein kinase C lambda/iota and protein kinase C zeta. After analyzing human tissue samples of serrated CRC, the researchers found a reduced expression of these same two genes. Furthermore, the researchers found that the loss of these two genes causes the overexpression of the protein PD-L1 in the tumour microenvironment (i.e. the tissue surrounding the tumour). Cancer cells are known to overexpress PD-L1 as it enables the cancer cells to evade attack by the immune system.

The expression of one of the two genes, protein kinase C lambda/iota, was previously found to be reduced among people living with inflammatory bowel disease (IBD). In the most recent study, the research team discovered that when the expression of the second gene was diminished, the number of CD8+ immune cells in the body decreased. The researchers found that this modification eventually led to the development of serrated CRC, referring to the loss of immune cells as a loss of “immune surveillance”. The inhibition of the immune system and its defense mechanisms is a crucial step in the development and spread of cancer cells in the body. For people with IBD who already have lower levels of protein kinase C lambda/iota, it appears that losing further immune surveillance compromises their ability to defend against cancer. Given that many people with IBD are currently treated with immune-suppressing treatments, these findings are an important discovery that could change the way IBD is managed.

https://www.medicalnewstoday.com/articles/323961.php
27. What causes cancer to spread? (Feb 26/19)

Before cancer is able to spread in the body, the DNA of the cells begins to change abnormally, or mutate. Due to these mutations in the internal “code” of the cell, the cell begins to behave abnormally, separating from its neighbours, dividing at a rate that is faster than normal without any kind of “braking” feedback system, and invading surrounding tissues where it normally does not belong. Further mutations may enable the cell to enter the blood or lymphatic system and travel to other distant parts of the body where it may begin to grow and divide, forming a “secondary” tumour, or metastasis. The genes that are responsible for enabling tumour cells to break free from their original location and travel to distant sites are part of the natural genetic makeup of every cell. These genes are critical in early stages of life, permitting cells to move to their rightful location in the developing embryo and fetus. Normally, these cells are eventually “turned off”, enabling the cells to remain fixed in their designated location in the body – the lungs, nerves, muscles or any of the hundreds of tissue types that make up the human body. Through mutations, these genes can become reactivated in some cells which then gain the ability to migrate through the body.

Even if a mutated cell is able to move away from its original location, it is still not guaranteed that it will successfully metastasize to other parts of the body. Mutations in cells can occur at any moment in a person’s life due to radiation, chemicals and so on, but a healthy immune system is able to attack and destroy these potential damage-causing cells. It can take a variety of genetic changes to equip tumour cells with the capacity to not only reach distant tissues but to survive there. They must: break free from their tissue of origin, invade neighbouring tissue, penetrate the circulatory or lymphatic system, root themselves in a new location, attract blood vessels to draw nourishment to grow and proliferate, and survive unnoticed by unfamiliar surrounding cells. Few cancer cells possess all these abilities, and most are destroyed along their journey. Since metastatic tumour cells have acquired all these genetic mutations that enable them to survive, they may very well differ, at a molecular level, from the cells that are found in the primary tumour. As a result of these differences, metastatic cancer cells may be less vulnerable to drugs that are effective against the tumour, making metastasized cancers usually more resistant to treatment compared to primary cancers. An important branch of current cancer research focuses on how to make tissues inhospitable to potential tumour cells. For example, studies have focussed on boosting the immune system to prevent metastasis following cancer surgery, while other have identified compounds that make the tumour microenvironment uninviting to potential tumour cells looking to colonize the tissue.

28. H. pylori infection may increase colorectal cancer risk, particularly among African-Americans (Feb 5/19)

According to recent study findings, Helicobacter pylori infection seemed to be associated with an increased risk for colorectal cancer (CRC), particularly among African-Americans. Previous data that linked H. pylori and CRC risk have thus far lacked consistency. H. pylori is the established main cause of stomach cancer. While there is no evidence that H. pylori lives in the colon, it has been hypothesized that it could have downstream effects from the stomach into the intestines. In this study, the researchers analyzed 4,063 pre-diagnosis blood
serum samples from patients who were later diagnosed with CRC. Samples from an equal number of matched controls were also analyzed. The researchers examined the antibody response to 13 different \textit{H. pylori} proteins, such as virulence factors VacA and CagA. The findings showed \textit{H. pylori} seropositivity in 41\% of pre-diagnosis samples and 40\% of controls. Researchers found an increased risk for CRC among patients with \textit{H. pylori} VacA-specific seropositivity, and this risk was particularly pronounced among African Americans. Despite these findings, the researchers caution that what they reported is not a causal relationship. It can be said that people who have \textit{H. pylori}, particularly people of colour who have high antibody levels to certain \textit{H. pylori} proteins, have an increased risk of developing CRC. The researchers note that \textit{H. pylori} is an ancient microbe that is disappearing in some populations, but appears not to be disappearing among people of colour. With these findings, patients could be put into different risk-stratification categories, allowing clinicians to identify CRC earlier. Next steps will be aimed at finding out if there is indeed a causal relationship, even an indirect one.


29. Colorectal cancer in young patients often misdiagnosed, identified at late stage (Feb 27/19)

According to recent study results, about 70\% of patients aged younger than 50 years had to see at least two physicians before being diagnosed with colorectal cancer (CRC). As a consequence of these misdiagnoses, CRC was often diagnosed at a later stage in this patient group. Despite being one of the most preventable cancers where early detection could cure most patients, it is a disease that is increasingly affecting younger individuals who, based on their age, are not normally considered for CRC screening. Today, about 10\% of new cases of CRC occur in a patient younger than 50 years of age.

In the study, the researchers evaluated data from 1,195 surveys completed by patients and survivors of CRC. 57\% of the cohort was diagnosed with CRC when aged 40-49, 33\% when aged 30-39 years, and 10\% when aged younger than 30 years. 30\% of all patients reported having a family history of CRC, and 8\% were diagnosed with Lynch syndrome. The surveys results showed than 71\% of patients were diagnosed at stage III or stage IV of the disease. 67\% of patients saw at least two physicians prior to being diagnosed with CRC, and 63\% of patients waited 3 to 12 months before deciding to see a physician. Many patients indicated that they did not recognize the symptoms of the disease, leading to a delayed visit to the doctor. 33\% of patients only saw one physician, and 17\% of these patients said that they were initially misdiagnosed. The researchers stress the importance of disseminating these results to the medical community and the general population to be aware that the disease is affecting younger individuals and that symptoms should never be dismissed at any age. Changes to screening guidelines to adapt to this new reality of CRC incidence should be considered.


30. “Very encouraging” downward mortality trend in cancer (Feb 1/19)

Examining data from an annual report published in \textit{Annals of Oncology}, the age-standardized cancer mortality rates between 2012 and 2018 across a range of different cancer types in Europe showed significant improvements. Focusing on colorectal cancer, there has been a reduction in age-standardized mortality of 14\% across the United Kingdom, France and Germany during this time period. David Kerr, a professor of cancer medicine from the University of Oxford in England, suggests that the decrease in cancer mortality is multifactorial – earlier data across the different European countries shows very large variations in mortality rates. Over time, the rates have become more similar, perhaps having to do with overall changes in lifestyle towards better diet, and better understanding of the risks of tobacco, alcohol and a sedentary lifestyle. A better understanding of the importance of screening and other forms of prevention, such as more widespread use of aspirin, may also contribute to the decreasing mortality. Of course, better treatment, with better surgical approaches, better understanding of pathology, as well as the contributions that have been made to adjuvant therapy and treatment are demonstrated in these improving cancer trends. Overall, the difference between cancer survival rates is becoming narrower, meaning that the difference between the very top and the very bottom is much less. With further coordinated health approaches, integrating better treatment with better screening approaches and a focus on prevention, real differences can be made.
31. Young adult colorectal cancer clinic available at Sunnybrook (Mar 14/19)

A recent study led by University of Toronto doctors has observed a rise in colorectal cancer rates in patients under the age of 50. The study mirrors findings from the U.S., Australia and Europe. The growing colorectal cancer rates in young people come after decades of declining rates in people over 50, which have occurred most likely due to increased use of colorectal cancer 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), and his team at the Sunnybrook Health Sciences Centre understand the needs of this patient population.

Dr. Ashamalla belongs to a multidisciplinary team of experts in the Young Adult Colorectal Cancer Clinic who will work with young colorectal cancer patients, regardless of disease stage, to create an individualized treatment plan to support each patient through their cancer journey. Their 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

NUTRITION/ HEALTHY LIFESTYLE

32. Fried food linked to heightened risk of early death among older US women (Jan 23/19)
A recent study published in *The British Medical Journal* found that regular consumption of fried foods is linked to a greater risk of death from any cause and heart-related death among postmenopausal women. In a society where up to one third of North American adults have fast food every day and countless evidence points to higher risk of obesity, type 2 diabetes and heart disease, a change in eating habits could have a very positive public health impact.

In the study, the researchers investigated the association between eating fried food with death from any cause, in particular heart and cancer-related death. Questionnaire data was used to assess the diets of 106,966 women aged 50 to 79. The researchers examined the women’s total and specific consumption of different fried foods, including “fried chicken”, “fried fish, fish sandwich, and fried shellfish (shrimp and oysters)”, and other fried food such as french fries, tortilla chips and tacos. The team found that regularly eating these foods was associated with a heightened risk of death from any cause, especially heart-related death. Those who ate one or more servings of fried foods per day had an 8% higher risk of heart-related death than those who did not eat fried food. Interestingly, researchers found no evidence that eating fried food was associated with cancer-related death. Nonetheless, a diet pattern that is rich in fried foods is a recipe for obesity, which is a major risk factor for cancer development. As a result, making the transition toward a diet pattern rich in plant-based foods and healthy fats and oils (in moderation!) is a positive factor that could have clinically meaningful impact across the public health spectrum.

https://www.sciencedaily.com/releases/2019/01/190123191637.htm

33. Sitting, watching TV linked to colorectal cancer risk before age 50, new study shows (Feb 5/19)

A new study published in *JNCI Cancer Spectrum* pointed to a connection between time spent sitting while watching TV and increased risk of colorectal cancer (CRC) for younger Americans.

While the incidence of CRC has dramatically decreased among older people due to the positive results of cancer screening initiatives, young-onset CRC that is diagnosed under the age of 50 is increasing in the US and globally. Young-onset CRC differs in several ways from late-onset disease – it has potentially different molecular characteristics and is often found at a more advanced stage, causing the disease to be more difficult to treat. Researchers in the study examined sedentary TV time as well as other sedentary behaviours in 89,278 American women in the Nurses’ Health Study II. Prolonged time spent watching TV is indicative of a sedentary behavioural pattern which favours the development of obesity and CRC. Of the 118 cases of young-onset CRC diagnosed over two years of follow-up, more than one hour of daily TV watching time was associated with a 12% increase in risk compared to those who watched less than one hour. For those watching more than two hours/day, their risk for CRC increased to 70%. This association held true independent of BMI
and exercise and was consistently seen among women without any family history of CRC. These findings are some of the first to link sedentary behavioural patterns with risk of young-onset CRC, and these results could help to identify those at high risk who might benefit more from early screening.

https://www.sciencedaily.com/releases/2019/02/190205090547.htm

34. Six ‘obesity-related’ cancers on rise in US young adults (Feb 4/19)

A recent observational study found that from 1995 to 2014 in the United States, the incidence of six of twelve obesity-related malignancies increased among “young” adults (25-49 years). The incidence for these cancers – except for colorectal cancer – also rose in older adults (50 years or older). The young adults who were the focus of the study had large annual percentage increases compared to older adults. The findings demonstrate a recent change that is happening in Western society that could serve as a warning of an increased burden of obesity-related cancers to come. Most cancers occur in older adults, which means that as the young people begin to age, the burden of obesity-related cancer cases and deaths in the future are likely to increase even more.

Between 1980 and 2014, overweight or obesity prevalence in the USA increased by more than 100% (from 14.7% to 33.4%) among children and adolescents and by 60% among adults aged 20-74 years (48.5% to 78.2%). The study’s authors commented on food quality as a potential contributor to the rising obesity trends, as the quality of the American diet has worsened in the last decades. More than 50% of adults who were 20 to 49 years old between 2010 and 2012 reported poor dietary habits such as eating very little fruit, vegetables, whole grains, fish while eating too much salt, fast food and sugary drinks. Obesity is strongly correlated with poor health conditions that can contribute to the risk of cancer, including chronic inflammation, diabetes, gallstones, and inflammatory bowel disease. Innovative strategies by policy makers and healthcare providers will be needed to address the complex causes of obesity and to control morbidity and premature mortality that is associated with obesity-related diseases.

https://www.medscape.com/viewarticle/908602#vp_2
https://www.sciencedaily.com/releases/2019/02/190204101208.htm


A recent review investigated the relationship between dietary patterns and overall food consumption and one’s risk of developing colorectal cancer (CRC). Other than red and processed meat, whose clear contributions to the development of CRC have been established and confirmed by several studies, findings for other dietary components are mixed and controversial. It is likely that the overall dietary pattern, rather than any single food, may significantly influence the incidence and outcomes of CRC. Through an analysis of 30 scientific articles, it was found that the Mediterranean dietary pattern which is rich in oily fish, nuts, olives and olive oil, significantly decreases the risk of CRC compared to the Western dietary pattern. Higher consumptions of nuts and fish has been shown to be linked with better disease-free survival, recurrence-free survival, and overall survival of CRC patients.

Acute inflammation is a normal and necessary bodily response for tissue repair, while chronic inflammation is an abnormal, persistent state that can lead to the degradation of tissues. Chronic inflammation has been reported to contribute to the development and progression of many types of cancer, including CRC. Diet components that are pro-inflammatory include carbohydrates, proteins, total fat, trans fat, cholesterol, and saturated fatty acids. On the contrary, anti-inflammatory diets contain mainly fibre, polyunsaturated fatty acids, minerals, vitamins, and antioxidants. The researchers’ analysis found that individuals with the highest Empiric Dietary Inflammatory Pattern (EDIP) score had an increased risk of CRC, though this association was not seen in individuals who exhibited a strong immune response (intermediate peritumoral lymphocytic reaction). This suggests that a strong immune reaction is potentially protective against pro-inflammatory diets. In addition, higher EDIP scores were linked to increased risk of CRC only among cancers that are F. nucleatum-positive. An increasing body of evidence has shown that the bacterium F. nucleatum is involved in the underlying mechanisms in the development of CRC. These results reveal the dynamic interactions between the immune system, gut microbiota and diet during the development of CRC.

In conclusion, these results suggest that relationships between diet and clinical outcomes of cancer patients can be evaluated directly, and more studies are urgently needed. Combining healthy behaviours is more
36. Exercise for adults diagnosed with rectal cancer: a feasibility study (Mar 14/19)

The purpose of the study is to examine the safety and feasibility of a supervised 12-week exercise intervention for adults diagnosed with rectal cancer. The exercise program will take place at the Behavioural and Metabolic Laboratory (200 Lees Ave., Ottawa) 3x a week and will be tailored to each individual.

Below is the inclusion criteria for the study:
1. Men and women 18 to 85 years of age;
2. Diagnosed with stage I-III rectal cancer and currently undergoing treatment or have completed treatments with the last 5 years;
3. Able to read/understand English or French;
4. Ambulatory;
5. Live <50km of the University of Ottawa;
6. Approval of healthcare provider to participate in the intervention.

Individuals will be asked to complete a brief questionnaire and physical assessments (e.g., resting blood pressure) before and after the 12-week intervention.

**EXERCISE FOR ADULTS DIAGNOSED WITH RECTAL CANCER:**
**A FEASIBILITY STUDY**

**HAVE YOU BEEN DIAGNOSED WITH rectal cancer?**

Many individuals diagnosed with rectal cancer report negative physical and psychological health outcomes that could be reduced by participating in exercise.

This trial will test the feasibility of a supervised exercise program to improve the physical and psychological health outcomes for adults diagnosed with rectal cancer.

**Taking part in this study involves:**
- Participating in an exercise program
  - Lasting 12 weeks
  - Consisting of 3 exercise sessions per week
  - Supervised by trained exercise professionals
- Completing study measures at two times (before and after the 12-week exercise program)
- All exercise and assessments will take place at the Behavioural and Metabolic Research Unit (200 Lees Avenue; parking will be covered) at times that are convenient for you

**Contact**
Physical Activity and Health Promotion Laboratory
pat.healthlab@uottawa.ca • 613-562-5800 x 7300
37. A Phase III study on the impact of a physical activity program on disease-free survival in patients with high risk stage II or stage III colon cancer: a randomized controlled trial (CHALLENGE) (Mar 14/19)

The purpose of this study is to compare the disease-free survival of patients involved in a physical activity program (designed to increase physical activity participation) who also receive general health education materials (about diet and physical activity) to patients who receive the general health education materials only. This study is being done because, as of yet, there is no conclusive evidence that physical activity will decrease the likelihood of colon cancer recurrence. This study will also obtain important information about the impact of physical activity on patients’ physical functioning, body composition, quality of life, fatigue, mood, cytokines and the insulin pathway, and their influence on prognosis, as well as cost-effectiveness.

Eligibility: Medically fit colon cancer patients (high risk stage II and stage III) who have completed adjuvant chemotherapy within the past 60-180 days. Current physical activity levels must not meet the recommended guidelines (≥150 minutes of moderate-to-vigorous or ≥75 minutes of vigorous exercise/week). Following registration, and prior to randomization, patients must successfully complete at least two stages of a submaximal exercise test to ensure they are able to safely exercise at a moderate to vigorous intensity.

Participation: Limited to invited centres. For more information, visit the link below: https://scooby.ctg.queensu.ca/tum_bank/tum.php?g_cmd=trial_info&g_trial_cd=CO21

38. High dose Vitamin D supplementation in Stage 4 Colorectal Cancer Patients (Mar 14/19)

A large body of evidence suggests that high blood levels of Vitamin D decreases the risk of developing cancer, especially colorectal cancer. Very little is known about what role optimum blood levels of Vitamin D can play in the treatment of cancer. The purpose of this clinical trial is to study the therapeutic effect and the safety of high-dose vitamin D supplementation in stage 4 (metastatic) colorectal cancer patients. Who is eligible to participate? Anyone who has a stage four colorectal cancer diagnosis, living in Ontario or British Columbia, may be eligible to participate. All participants need to have access to a Lifelabs facility for blood and urine collections. What is involved? This 40-month study involves regular lab tests and follow up phone calls. Participation is fully voluntary, and participants may withdraw at any time. Participants will be randomized into either a high-dose vitamin D treatment group or a control group. Participants in both groups may continue all other cancer treatments including chemotherapy. Treatment group: Participants in the treatment group receive daily oral high dose Vitamin D supplementation provided free of charge through the clinical study. They also receive daily calcium supplementation 1000mg daily as per guidelines, provided free through the clinical study. Participants will have monthly blood and urine tests for monitoring purposes. All laboratory tests are free of charge. Participants also need to be available for a 15-minute phone consultation with a study coordinator every 2 months. Control group: Participants in the control group will continue their usual amount of Vitamin D and/or calcium if they wish to do so. No supplements will be provided through the study. Participants will be asked to provide a small blood and urine sample at the beginning of the study, every 8 months and at the end of the study. These blood and urine tests will be free of charge. Contact person: If you have any further questions regarding this study or you are interested in participating in this study, please contact us: British Columbia: 604-734-7125, toll free 1- 888-734-7125 or vitDstudy@inspirehealth.ca. Ontario: 613-792-1222, toll free 1-855-546-1244 or research@oicc.ca