The following colorectal cancer research updates extend from Aug 18th, 2018 to Oct 18th, 2018 inclusive and are intended for informational purposes only.

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DRUGS / SYSTEMIC THERAPIES

1. Maintenance therapy for metastatic colorectal cancer: benefits seen with panitumumab combination (Sept 25/18)

Among patients with metastatic colorectal cancer (mCRC) who have undergone chemotherapy with anti-EGFR growth factor receptor (EGFR) agents, the best approach to maintenance therapy has remained unclear. Maintenance therapy is typically administered following an initial round of treatment, and is directed at boosting treatment efficacy and maintaining the disease in a controlled state. Results from the phase II VALENTINO trial have shown that anti-EGFR maintenance therapy with panitumumab (Vectibix) is feasible in an mCRC population previously treated with anti-EGFR agents and may be most effective in combination with fluorouracil/leucovorin (5-FU/LV). To date, reducing treatment intensity among patients with mCRC who achieve disease control after initial chemotherapy (with or without bevacizumab (Avastin)) has become the emerging standard of care. There is very little evidence, however, of a disease control benefit and an impact on quality of life associated with a reduction of treatment intensity after anti-EGFR-based treatment.

The VALENTINO study was conducted at 29 centers in Italy and was designed to evaluate how single-agent panitumumab fared compared to maintenance with 5-FU/LV plus panitumumab following initial combination chemotherapy with an EGFR inhibitor. The trial enrolled 229 patients with previously untreated, unresectable RAS wild-type mCRC. All patients underwent up to 8 cycles of chemotherapy with FOLFOX 4 plus panitumumab and were randomized to receive maintenance therapy with panitumumab and 5-FU/LV or panitumumab alone until disease progression or unacceptable toxicity. The primary endpoint was progression-free survival (PFS) at 10 months. Maintenance with panitumumab alone achieved inferior PFS compared with the 5-FU/LV and panitumumab combination. At 10 months follow-up, PFS was 62.8% with 5-FU/LV plus panitumumab vs. 52.8% with panitumumab monotherapy, with a median PFS of 13 months and 10.2 months, respectively. Toxicities were manageable in both study arms during the maintenance phase, though adverse events were worse in the combination therapy group. The results from this study suggest that when considering maintenance therapy with an EGFR inhibitor like panitumumab, combining the treatment with 5-FU/LV may be a more promising therapeutic option.


2. First-line cetuximab plus FOLFOX-4 vs. FOLFOX-4 in RAS wild-type metastatic colorectal cancer (Sept 20/18)

Cetuximab in combination with chemotherapy is a standard of care first-line treatment for patients with RAS wild-type metastatic colorectal cancer (mCRC). The efficacy of the drug, however, in combination with leucovorin, fluorouracil, and oxaliplatin (FOLFOX) has never been observed in a controlled and randomized phase III trial. The TAILOR trial is the first randomized, multicenter, phase III study of the addition cetuximab to first-line FOLFOX among a RAS wild-type mCRC patient group. The TAILOR trial compared FOLFOX-4 with or without cetuximab in RAS wild-type mCRC patients in China. Among 393 patients, adding cetuximab to FOLFOX-4 significantly improved both progression-free survival and overall survival compared to FOLFOX-4 treatment alone. The treatment was well tolerated, with no new or unexpected safety concerns. The study findings suggest that cetuximab in combination with FOLFOX is an effective standard of care first-line treatment regimen for patients with RAS wild-type mCRC.

Efficacy and Tolerability of First-Line Cetuximab Plus Leucovorin, Fluorouracil, and Oxaliplatin (FOLFOX-4) Versus FOLFOX-4 in Patients With RAS Wild-Type Metastatic Colorectal Cancer: The Open-Label, Randomized, Phase III TAILOR Trial
J. Clin. Oncol 2018 Sep 10;[Epub Ahead of Print], J Qin, J Li, L Wang, J Xu, Y Cheng, Y Bei, W Li, N Xu, LZ Lin, Q Wu, Y Li, J Yang, H Pan, X Ouyang, W Qiu, K Wu, J Xiang, G Dai, H Liang, C Hu, J Zhang, M Tao, Q Yao, J Wang, J Chen, SP Eggleton, TL Liu
https://www.practicupdate.com/content/first-line-cetuximab-plus-folfox-4-vs-folfox-4-in-ras-wild-type-metastatic-colorectal-cancer/73270/62

3. PAL 2018: Medical palliation for malignant bowel obstruction can reduce pain and vomiting (Oct 12/18)

Results from a retrospective observational study conducted in Hong Kong found that medical palliation of malignant bowel obstruction can help to reduce the pain and vomiting associated with the disease. Malignant bowel obstruction is a common complication among patients with gastrointestinal cancer. It is characterized by a narrowing of the circumference of the small or large intestine due to malignant tumour growth, and is associated with significant...
physical and psychological distress. The researchers investigated the palliative care (easing the symptoms of the disease, rather than directly addressing the underlying cause) needs of patients with malignant bowel obstruction according to their symptom burden, medical interventions, functional outcome (different from clinical outcome, in that it is focused instead on an individual’s recovery in areas such as social functioning rather than symptom resolution), and survival after diagnosis. Medical palliation for this condition includes analgesics, antiemetics, antisecretory drugs and dexamethasone, and is aimed at reducing gastrointestinal symptoms and improving quality of life. Data from 30 patients with malignant bowel obstruction were analyzed. 30 patients had gastrointestinal cancer, most commonly colorectal cancer. The most commonly experienced symptoms were fatigue, anorexia (lack of appetite), abdominal distension, vomiting, constipation, and abdominal pain. Of the 23 patients with abdominal pain who received medical palliation, 21 reported a reduction in their pain. Of the 25 patients with vomiting who received medical palliation, 13 experienced relief after 5 days of palliation. The researchers point out that surgery should be considered for patients in the early stages of bowel obstruction, to preserve general well-being. Less invasive approaches, however, such as colonic stenting should be considered when surgery is not possible. The priority of care when a bowel obstruction is inoperable is to control symptoms and maximize quality of life.

The decision to undergo palliative surgery is a difficult one, especially in advanced stages of cancer. The decision to undergo surgery will depend on the level of obstruction, extent of the cancer, related comorbidities, and the well-being of the patient. The researchers concluded that medical palliation for malignant bowel obstruction was effective in reducing pain and vomiting among patients. Further studies focused on the patient’s psychospiritual burden, caregiver’s stress, and quality of life of both patients and caregivers should be considered.

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**Figure**: Obstruction of the large intestine by a tumour

Image source: [https://medlineplus.gov/ency/presentations/100089_2.htm](https://medlineplus.gov/ency/presentations/100089_2.htm)

**Phase I study of Cobimetinib with Bevacizumab and Atezolizumab for colorectal cancer (Oct.19/18)**

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](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.


**SURGICAL THERAPIES**

**5. Hepatic Artery Infusion Pump (HAIP) Chemotherapy Program – Sunnybrook Odette Cancer Centre (Oct.19/18)**

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 but 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

6. The value of tumour debulking for patients with extensive multi-organ metastatic colorectal cancer (Oct 9/18)

Among a growing number of patients with multi-organ metastatic colorectal cancer (mCRC), local treatment of metastases via surgical resection is a technically feasible option. There exists a growing debate on whether patients who have extensive disease, which is traditionally considered unresectable, may benefit from the local treatment of metastases when combined with standard palliative systemic chemotherapy. Among selected patients with extensive mCRC, local treatment of metastases has become the standard of care based on retrospective reports demonstrating long-term survival rates. Preliminary evidence suggests that patients with extensive mCRC may benefit from local treatment in addition to systemic therapies. Direct comparison of survival rates with modern systemic therapy will be necessary to determine the impact of tumour debulking interventions among patients with extensive mCRC.


7. Postoperative outcomes of screen-detected vs. non-screen detected colorectal cancer (Oct 11/18)

A recent study published in *JAMA Surgery* set out to compare surgical outcomes of patients who were diagnosed with colorectal cancer (CRC) through the fecal immunochemical test screening program and those who were diagnosed with non-screen-detected CRC. The study analyzed data from all Dutch hospitals performing CRC resections. 36,242 patients with colon cancer and 17,416 patients with rectal cancer were included in the analysis. Compared with patients with non-screen-detected CRC, screen-detected patients were younger and were more often male. Patients with stage I to III colon cancer who were screen-detected had a significantly lower mortality and complicated disease compared with non-screen-detected patients. Postoperative outcomes were significantly better among patients with CRC referred through the FIT screening program compared with non-screen-detected patients. These differences were not observed in patients with rectal cancer.

Postoperative Outcomes of Screen-Detected vs Non-Screen-Detected Colorectal Cancer in the Netherlands

*JAMA Surg* 2018 Oct 03;[Epub Ahead of Print], MPM de Neree Tot Babberich, NCA Vermeer, MWJ/M Wouters, WMU van Grevenstein, KCMJ Peeters, E Dekker, PJ Tanis


8. Living donor liver transplantation for unresectable colorectal cancer liver metastases (Jun. 1/18)

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

RADIATION THERAPIES/INTERVENTIONAL RADIOLOGY

9. Study Offered at the Odette Cancer Centre to Treat Recurrent Rectal Cancer (Oct.19/18)

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

SCREENING

10. Family history tied to nearly eightfold increased CRC risk for IBD patients (Oct 2/18)

According to recent research findings, patients with inflammatory bowel disease (IBD) who have a first-degree relative with a history of colorectal cancer (CRC) have a higher risk of being diagnosed with the disease. The researchers note that although risk for CRC among patients with IBD is already high, estimates of lifetime risk of CRC have so far remained unclear. A family history of CRC in a first-degree relative is an important risk factor that nearly doubles a
person’s risk of developing the disease. The researchers aimed to determine risk factors to help guide screening and surveillance strategies.

The team analyzed data from a cohort of 9,505 patients with IBD in the United States between 1996 and 2011. The researchers found that a family history of CRC in a first-degree relative was associated with a nearly eightfold increased risk for CRC in patients with IBD. The researchers concluded that family history could be used as an important risk factor in patients with IBD to help clinicians determine more appropriate screening and surveillance plans among this patient subgroup. The study findings were able to quantify the risk of CRC in patients with IBD, stressing the importance of obtaining family history of the disease among these patients and ensuring that those with a family history of CRC are well informed and are followed up with more intensive screening guidelines.

11. Most colorectal cancer deaths linked to modifiable screening failures (Oct 1/18)

Sticking to one’s screening guidelines can significantly reduce a patient’s risk of death from colorectal cancer (CRC) according to research reported in Gastroenterology. The study’s researchers found that most people who died of CRC did not stay up to date with their screening guidelines and experienced other modifiable failures in their screening regimen. The study surveyed data from people who died from CRC as well as a randomly selected group of people who did not die from CRC. Patients who were not up to date on screening had a 2.6 fold higher risk of dying from the disease compared to those who were up to date. Among individuals who did not receive adequate follow-up after an abnormal result, they had an approximately 7 fold higher risk of death from CRC. Among patients who died of CRC, 67.4% experienced failure to screen or failure to screen at appropriate intervals, compared to 53.2% of patients who did not die from CRC. A higher percentage also experienced failure to follow-up on abnormal results compared to those who survived (8.1% vs. 2.2%). These results stress the importance of screening for CRC at the correct time to ensure that those with abnormal results receive timely follow-up testing.

12. Complicated diverticulitis increases risk for colorectal cancer (Oct.19/18)

A systematic review published in Clinical Gastroenterology and Hepatology found that patients with complicated diverticulitis are six times more likely to develop colorectal cancer (CRC) compared to patients with uncomplicated diverticulitis. The researchers wrote that while some experts recommend routine colonoscopy for all patients with diverticulitis, the actual risk for developing CRC has remained unclear. Concrete data on the prevalence of CRC among patients with diverticulitis are needed, in order to determine whether they would truly benefit from routine colonoscopy. The researchers analyzed data from 50,000 patients who participated in 31 different studies reporting the prevalence of CRC among patients with diverticulitis. The prevalence of CRC was found to be 1.9%. The researchers found that patients with complicated diverticulitis had a significantly higher risk (6-fold increase) for CRC than patients with uncomplicated diverticulitis, suggesting that the prevalence of CRC is clinically relevant and warrants further investigation to determine cost-effectiveness of more intensive screening guidelines for this subgroup of patients.

13. Sigmoidoscopy screening for colorectal cancer in men versus women (Oct.19/18)

According to a Norwegian study published in the Annals of Internal Medicine, sigmoidoscopy screening reduced the incidence and mortality of colorectal cancer (CRC) in men, but seemed to have little to no effect in women. The researchers stated that the reason for this gender difference is unclear and suggested that colonoscopy may be a better screening method than sigmoidoscopy in women. In the study, adults between the ages of 50 and 64 years in Oslo and Telemark County, Norway, were identified through the National Registry and assigned to undergo either a one-time sigmoidoscopy screening or no screening. Screening rates were 64.7% in women and 61.4% in men. After a median follow-up of 14.8 years, the absolute risk for CRC in men was 1.72% in the screening group and 2.5% in the control group. The absolute risk in women was 1.86% and 2.05% in the screening and non-screening groups, respectively. The researchers suggest that these results may be important in future screening recommendations that stratify participants by sex, with the goal of boosting the beneficial outcomes of screening for both men and women.

14. Update on ACS colorectal cancer screening guideline: start screening at age 45 (Oct.19/18)

Since 1994, there has been a 51% increase in colorectal cancer (CRC) among individuals 50 years old or younger. In response to this rise in earlier-onset CRC, the American Cancer Society (ACS) has updated its colorectal screening guidelines, suggesting that screening should begin at age 45 for people at average risk. For adults of average-risk who are in good health with a life expectancy beyond 10 years, CRC screening should continue until the age of 75, beyond
which conversations between the individual and the clinician are necessary to weigh the risks and benefits of screening. The guidelines indicate that adults aged 45 and older with an average risk of CRC should undergo regular screening with either a high-sensitivity stool-based test or a colonoscopy or sigmoidoscopy, depending on patient preference and the availability of tests. The recommended options for CRC screening are:

- Fecal immunochemical test annually;
- High-sensitivity guaiac-based fecal occult blood test annually;
- Multitarget stool DNA test every 3 years;
- Colonoscopy every 10 years;
- Computed tomography colonography every 5 years;
- Flexible sigmoidoscopy every 5 years.

Based on epidemiological trends among individuals as young as those born in 1990, a higher risk of developing CRC will be a lasting concern for the decades to come.

15. Organized colorectal cancer screening program significantly increases screening rates (Sept 20/18)

According to results from a recent cohort study, the implementation of a well-organized screening program including an annual fecal immunochemical test (FIT) combined with colonoscopy showed a significant and rapid increase of colorectal cancer (CRC) screening participation. The results also demonstrated that as CRC screening participation increased over a 15-year period, cancer mortality decreased more than 50% during that same period. The researchers sent FIT kits through the mail to reach patients who may have declined screening with flexible sigmoidoscopy or were not coming to the doctor’s office often enough to be reminded of screening. The researchers saw an initial rapid uptake of screening and rates increase to about 65%. Using a cohort of health plan members from 2000-2015, the researchers aimed to evaluate if an organized CRC screening program could achieve and maintain the 80% or higher screening target that has been proposed by various health organizations. The researchers found that CRC mortality rates decreased by 52.4%, from 30.9 deaths/100,000 in 2000 to 14.7/100,000 in 2015. These results suggest that a meaningful impact can definitely be made to reduce CRC incidence and mortality by increasing screening rates using a combination of FIT and colonoscopy. The researchers acknowledge, however, that in the study they did benefit from structural advantages which facilitated screening uptake among participants. Since participants were members of a specific health care plan, the researchers benefited from an integrated health care delivery system with a pre-paid financial model allowing for more flexibility with how resources were used compared to a traditional fee-for-service system. An electronic record system provided real time information on who was up to date with screening and who was not. Nonetheless, the researchers stress the importance of offering FIT screening as an alternative to colonoscopy. Their study also highlights the value of good screening infrastructure – particularly, a system for reliably capturing and tracking data on screening uptake and follow-up, coordinating mailings of FIT kits, and providing decision support that is not based on doctor office visits or health care provider recommendations.

16. Chemo Buddies provide comfort, hope to patients with cancer (Oct 16/18)

As one woman, Jill Kincaid, accompanied her sister through her battle with triple-negative breast cancer, she witnessed the tremendous physical and psychological impact the disease could have. As she sat with her sister during her chemotherapy infusions, she began to understand the emotional toll that the treatment took, particularly among those who sat through their treatments alone for hours. She realized that some extra attention, help and comfort for those individuals alone could make a difference. After her sister died from breast cancer, Jill founded Chemo Buddies, a non-profit organization that brings trained volunteers into the treatment room so that no one has to go through...
chemo alone. The program volunteers spend time with the patients as they receive chemotherapy, providing companionship and helping them with small tasks to help ease their experience.

When Jill began attending her sister’s chemotherapy treatments, they watched as patients sat in recliners with no television or radio, and nothing but a window or wall to stare at for the duration of their 4- to 8-hour treatments. The two sisters tried to make the best of the glum environment, playing games, laughing and telling stories. They were amazed at how quickly the day would pass with company! The sisters began to “adopt” other patients who arrived for treatment alone. Observing how their simple tasks could make a difference and lift patients’ spirits, the sisters began to share their idea with the treatment centre’s staff. Eventually the Chemo Buddies program took off and the program’s benefits are undeniable. The volunteers help to fulfill patients’ needs for socialization and companionship. Programs such as Chemo Buddies tackle the invisible side of cancer, helping treatments to evolve to address not only the physical demands, but the crucial emotional and spiritual aspects of the disease.


17. CanDirect research study: Learn more about a study for patients who have completed their cancer treatments and are experiencing low mood (Oct.19/18)

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 click on the following link:

https://clinicaltrials.gov/show/NCT02890615

18. No link between progression-free survival, quality of life in cancer trials (Oct 3/18)

According to recent research published in JAMA Internal Medicine, among clinical trials evaluating cancer interventions, there was no significant association between progression-free survival and health-related quality of life. In general, progression-free survival, or the length of time during and after treatment that a patient lives with the disease but it does not get worse, has become a commonly used outcome to assess the efficacy of new cancer drugs. Progression-free survival, however, is not clearly linked to improved quality of life with or without overall survival benefit. Researchers aimed to investigate the association between progression-free survival and quality of life by performing a systematic review and analysis of 38 randomized controlled trials. The trials included in the study evaluated various chemotherapy regimens for 12 different cancer types in relation to progression-free survival or health-related quality of life. Through their analyses, the researchers were unable to find a significant association between progression-free survival and quality of life. Their findings raise the question of whether or not the use of progression-free survival as the primary endpoint in oncology trials is the best measure of a treatment’s efficacy, meeting the needs of cancer patients as best as possible. The researchers suggest that it is necessary to design trials which accurately measure overall survival and ensure rigorous and trustworthy measurement of cancer patients’ quality of life.

https://www.healio.com/medicine/oncology/news/online/%7b52f8f78c-3d00-4c3e-a785-86f5df1e771d%7d/no-link-between-progression-free-survival-quality-of-life-in-cancer-trials

19. ACG 2018: Dramatic increase in gastrointestinal cancers in young obese individuals in the United States (Oct 9/18)

From 2002-2013, a dramatic increase in the incidence of colorectal cancers (CRC), gastric and pancreatic cancers has been seen among younger individuals in the United States. Concurrently, there has been a significant increase in rates
of obese patients undergoing surgical resections in all obesity-related cancers. Findings from a recent study examines the contributing role of obesity in cancer development as well the increasing occurrences of these cancers. According to one of the researchers, no single database combines data on obesity and cancer incidence, so two databases (2001-2013 Surveillance, Epidemiology and End Results (SEER) and National Inpatient Sample (NIS)) were used. From the SEER database, the researchers determined that young onset CRC and gastric cancers increased between 2002 and 2013. From the NIS database, they found that among the same age groups there were more surgical resections among obese individuals overall, while the non-obese individuals experienced less surgical resections related to cancer. This suggests that there has been an increased diagnosis of cancer and an increased removal of those cancers in obese individuals, correlating with the increase in incidence of CRC among younger individuals.

Examining trends in obesity, the researchers found that the prevalence of obesity is increasing across all ages. When an individual is obese at a younger age, their risk of developing cancer later in life is far greater. Some studies have even shown that adolescent obesity is linked to higher CRC risk even if the person loses weight later on. Obesity is a global health concern with life or death consequences that must be addressed through a multi-sectoral approach, including better education on healthy lifestyle and closer regulation of the corporate food industry and labeling.


20. Young adult colorectal cancer clinic available at Sunnybrook (Oct.19/18)

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 consist 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
21. Low nutritional foods linked to cancer risk (Oct 5/18)

A recent study has found that consuming foods with low nutritional quality is linked to a higher risk for cancer. The researchers suggest that about a third of the most common cancers in Western countries are estimated to be preventable through appropriate nutritional behaviours. If eating habits can be modified at the individual level and influenced by public health policies, informing the population at large to make healthy decisions remains an important challenge.

The researchers analyzed food intake data to determine how the consumption of foods with high and low nutritional value affects cancer risk. 471,495 adults from a diverse European population were included in the study. A total of 49,794 cancer cases were reported, mainly breast, prostate and colorectal. Participants were asked to complete questionnaires that surveyed their usual dietary intake. The researchers then measured the quality of the foods using a well-known nutrient profiling system, generating a score. A higher score indicated lower nutritional quality of the foods consumed. Data demonstrated that participants with a higher nutrient profiling score (i.e. diet with lower nutritional quality) were more likely to have an increased risk of total cancer. Among men, there was an association between higher scores and higher risks for colorectal cancer, upper digestive tract and stomach, and lung cancers. In women, there was an association between higher scores and higher risk of liver and postmenopausal breast cancers.

The researchers conclude that these findings support the relevance of using a nutrient profiling system to score the nutritional quality of food products as a basis for prevention strategies, especially in the context of the ongoing European/international debate on nutritional labelling of food.

https://www.healio.com/internal-medicine/oncology/news/online/%7B9dd60a73-f4a8-4f94-8e32-ee93a18df4c2%7D/low-nutritional-foods-linked-to-cancer-risk

22. Food, microbiome and colorectal cancer (Jul 2018); Are certain bacteria associated with development of colorectal cancer? (Oct 2/18)

It is well known that dietary factors are of major importance in the evolution of cancer. For example, numerous studies suggest that certain diets (i.e. an “inflammatory” diet rich in processed foods and poor in plant-based foods) regulate various immune/inflammatory pathways which create optimal conditions for the development of cancer. The pro-inflammatory nature of certain foods might contribute to a chronic inflammatory condition, which is associated with about 25% of colorectal cancer (CRC) cases. Factors beyond nutrition, such as chronic stress, might be involved in driving this inflammatory process as well. It has only been recently recognized, however, that the gut microbiome (or microbiota) might be an important link between diet and the development of CRC. Several studies have suggested a role for the intestinal microbiota in potentially initiating and driving CRC. It has been increasingly accepted that dietary factors may favour the development of CRC through the alteration of the gut microbiota via potential overgrowth of certain bacteria, such as *Fusobacterium nucleatum*, *Escherichia coli* or *Bacteroides fragilis*.

The human gastrointestinal tract is home to more than 100 trillion bacteria, which together with archaea, fungi and viruses make up the gut microbiota. While it remains unclear which components of the gut microbiota are most sensitive towards the specific foods that we eat, numerous studies have now shown that dietary consumption of “unhealthy” foods, such as excessive red meat, a known risk factor for CRC, results in drastic changes to many of the bacterial strains in the gut. Due to these profound changes, current research has aimed to better understand the interaction between nutrients and the gut microbiota and the potential impact on intestinal disorders such as CRC or chronic inflammatory bowel disorders.

A recent study published in the *Journal of Gastrointestinal Oncology* investigated the potential carcinogenic associations of five strains of bacteria based on prior published research. These five strains are part of a group of bacteria known as sulfidogenic bacteria, which are being focused on due to their production of hydrogen sulfide which has been shown to cause DNA damage. This can result in genomic instability, a characteristic found in more than 80% of sporadic CRCs. The study authors suggest that the hydrogen sulfide may damage mitochondrial function in the cells of the intestinal wall, causing a deregulation of the RAS/MAPK pathway. This pathway is well known to be involved in the development of CRC. The researchers analyzed *Streptococcus bovis*, *Fusobacterium nucleatum*, *Helicobacter pylori*, *Bacteroides fragilis*, and *Clostridium septicum*. *S. bovis* was found to be associated with higher rates of adenomas (pre-
cancerous growths) and carcinomas (cancerous growths). Patients with CRC were found to have high concentrations of *F. nucleatum* and less overall microbial diversity in the gut microbiome compared to control groups. *C. septicum* has not been associated with the initial appearance of CRC, but it does appear to have a mutually beneficial relationship with tumour growth. Further research is necessary to determine whether the detection of certain bacterial concentrations in stool or polyp biopsies could serve as potential aid to current screening programs to help identify higher risk patients.

**Image source:** https://www.medicalnewstoday.com/articles/315465.php

https://jnccn360.org/colorectal/medical-literature/gut-bacteriaandcolorectalcancer/

23. **Diets that promote colon inflammation are associated with risk of colorectal carcinomas that contain *Fusobacterium nucleatum*** (Oct/19/18)

A study published in *Clinical Gastroenterology and Hepatology* investigated whether there is an association between diets that promote inflammation and specific types of colorectal cancer (CRC) that can be classified by the level of a particular bacteria (*Fusobacterium nucleatum*) present in the tumour microenvironment. The researchers suggested that intestinal inflammation can be triggered by diet, resulting in an alteration of the gut microbiome and contributing to the development of CRC.

Specific nutritional constituents are more likely to cause intestinal inflammation, a condition that can be characterized by increased circulating blood levels of biomarkers such as interleukin 6 (IL6), C-reactive protein (CRP), or TNF receptor superfamily member 1B (TNFRSF1B). Using a scoring method called Empirical Dietary Inflammatory Pattern (EDIP), the researchers were able to calculate the inflammatory effects of a given diet. Higher EDIP scores indicate a more inflammatory diet. An inflamed environment in the colon, measured by increased blood serum levels of IL6, CRP and TNFRSF1B, contributes to a compromised mucosal barrier of the intestinal wall and an altered immune cell response, affecting the composition of the intestinal microenvironment. Past studies have linked colonization of the colon by a bacteria *Fusobacterium nucleatum* with the development of CRC.

Using data from participants in the Nurses’ Health Study and the Health Professionals Follow-up Study, the researchers were able to calculate EDIP scores. During 28 years of follow-up of 124,433 participants, 951 cases of CRC with *F. nucleatum*-positive tissue samples. Higher EDIP scores were associated with increased risk of *F. nucleatum*-positive colorectal tumours. No association was found between EDIP scores and *F. nucleatum*-negative tumours.

The research suggests that diets that promote intestinal inflammation, based on EDIP score, are associated with an increased risk of *F. nucleatum*-positive CRC. These findings point to diet-induced intestinal inflammation as one possible cause of alterations in the gut microbiome leading to CRC. The evidence supports nutritional interventions as potential strategies in future personalized CRC treatment plans.

https://www.practiceupdate.com/C/67858/56?elsca1=emc_enews_topicalert&utm_source=TrendMD&utm_medium=cpc&utm_campaign=TrendMD_generalCPA

24. **Healthy lifestyle factors associated with lower risk of colorectal cancer irrespective of genetic risk** (Oct 2/18)

Healthy lifestyle factors such as diet, physical activity and body fatness are well known to impact colorectal cancer (CRC) risk, though the combined effects of these factors on CRC risk remains unclear. A study published in *Gastroenterology* aimed to develop a healthy lifestyle score in order to investigate the overall effects of modifiable lifestyle factors on the reduction of CRC risk, and to determine whether these associations differ with an individual’s genetic risk. Data was collected from a large population-based study from Germany. The healthy lifestyle score was derived from 5 healthy lifestyle factors: smoking, alcohol consumption, diet, physical activity, and body fatness. Using specific analysis technology, the associations between the healthy lifestyle score and CRC risk were examined. A genetic risk score was also created to investigate how the healthy lifestyle score and CRC risk changed according to genetic risk.
The researchers found that compared to participants with 0 or 1 healthy lifestyle factor, those with 2, 3, 4, or 5 healthy lifestyle factors had increasingly lower risks of CRC. This correlation held true regardless of a person’s genetic risk. Overall, 45% of CRC cases could be attributed to a lack of the 5 modifiable healthy lifestyle factors listed above. The researchers were thus able to identify a combination of lifestyle factors that appears to reduce risk of CRC, irrespective of the individual’s genetic profile. These findings reiterate the importance of primary prevention of CRC.


25. 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) (Oct.19/18)

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

26. High dose Vitamin D supplementation in Stage 4 Colorectal Cancer Patients (Oct.19/18)

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

Image source: https://www.mordenhillsurgery.co.uk/healthy-lifestyle