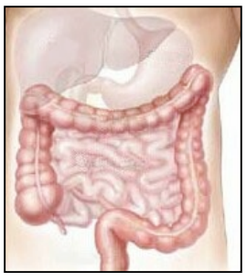
Colorectal Cancer Association of Canada

COLORECTAL CANCER RESEARCH UPDATES

Month Ending September 20th, 2015



The following colorectal cancer research update extends from July 11th, 2015 – September 18th, 2015 inclusive and is intended for informational purposes only.

CONTENT

DRUGS / SYSTEMIC THERAPIES

1. Adjuvant Chemo May Not Be Helpful in Stage II Colon Cancer (Aug.11/15)

Recurrence, survival, and quality of life (QOL) is not improved with adjuvant chemotherapy in most patients with **stage II colon cancer**, according to the results of a study published in *Supportive Care in Cancer*. This cohort study recruited 453 patients from North Carolina and interviewed them using a closed-end survey at diagnosis, and at 12- and 24-months postdiagnosis; 265 of the patients had received chemotherapy. The survey detailed quality of life, health behaviors, treatment, and cancer recurrence at each of the time points. Mortality was obtained from the National Death Index. According to the results, an inverse association was seen with chemotherapy and total Functional Assessment of Cancer Treatment (FACT)-General, FACT-Colorectal, physical, emotional, and functional well-being among patients with stage II colon cancer. The inverse association between emotional well-being and

receiving chemotherapy persisted for whites but not for African Americans. In addition, significantly higher odds of cancer recurrence were seen among those patients who received chemotherapy.

Lewis,Cari, . et al. "Effects of adjuvant chemotherapy on recurrence, survival, and quality of life in stage II colon cancer." Supportive Care in Cancer First online: 09 September 2015

http://link.springer.com/article/10.1007/s00520-015-2931-2

2. Statin Use Linked with Lower Mortality After Colorectal Cancer Diagnosis (Jul 16/15)

Cumulative exposure to statins after a diagnosis of colorectal cancer was associated with lower overall mortality, a new study published in the *British Journal of Cancer* has shown. For the study, researchers sought to determine whether there is an independent association between metformin, statins, and aspirin with overall mortality after colorectal cancer diagnosis among those taking glucose-lowering drugs. Previous research has shown that an association exists without adjusting for one another. Researchers identified 1,043 patients who were prescribed glucose-lowering drugs before receiving a diagnosis of colorectal cancer. Of those, 64% used metformin, 61% used statins, and 47% used aspirin after cancer diagnosis.

Zanders MMJ, van Herk-Sukel MPP, Vissers PAJ, et al. Are metformin, statin and aspirin use still associated with overall mortality among colorectal cancer patients with diabetes if adjusted for one another? Br J Cancer. 2015. [epub ahead of print]. doi: 10.1038/bjc.2015.259.

3. Study Confirms Regorafenib's Benefit for Previously Treated mCRC (Jul.23/15)

The phase IIIb CONSIGN study has confirmed the benefit of regorafenib in patients with previously treated metastatic colorectal cancer (mCRC). CONSIGN was a prospective, observational study that was initiated to allow patients with mCRC access to regorafenib before marketing authorization and to assess safety, which was the primary endpoint. The randomized phase III CORRECT trial previously showed that regorafenib significantly improves survival in patients with pre-treated mCRC and led to regulatory approval. "We began CONSIGN at the suggestion of the authorities and to fulfill the wishes of patients and doctors for a larger expanded access," said lead study author Prof Eric Van Cutsem from University Hospitals Leuven, Belgium. "Today we report on safety and progression-free survival in a large cohort of patients that more closely resembles daily clinical practice than the pivotal registration trial." CONSIGN included more than 2,800 patients at 188 sites in 25 countries who received regorafenib for a median of 2.5 months. Grade >3 adverse events occurred in 80% of patients. The estimated progression-free survival was 2.7 months and was similar across KRAS wild type and mutant subgroups. Van Cutsem said: "This study in a real world population of patients with pre-treated mCRC shows a similar safety profile and progression-free survival with regorafenib as shown in the randomized CORRECT trial. The findings add to our knowledge of how to select patients and how to manage toxicities. We need to establish clear guidelines on the management of adverse events to make taking the drug more tolerable for patients." Commenting on the data, Dr Dirk Arnold, ESMO spokesperson, director of the Department of Medical Oncology, Klinik für Tumorbiologie in Freiburg, Germany, said: "CONSIGN confirms the efficacy and safety data of the randomized phase III CORRECT and CONCUR trials. The merit of CONSIGN is that it translates phase III data into the clinical routine since patients had similar characteristics and pre-treatment to what we see in daily practice." The adverse events reported in CONSIGN were within the scope of expectation and comparable to the CORRECT trial, added Arnold. "There were no surprising findings in terms of toxicity," he said. "All of the adverse events were quite class specific and also likely manageable." He added: "CONSIGN depicts what we would expect from an observational trial in this setting. It shows that we have further treatment options for mCRC patients pre-treated with chemotherapy, and that this comes at the cost of a specific, but manageable toxicity profile." Regarding the next step in this research area, Arnold said: "Biomarkers have been extensively investigated in the randomized trials but until now nothing has been found that would allow prediction of the benefit of regorafenib for a specific group of patients. I would suggest having a further look at the data in the observational CONSIGN study to see if there are clinical characteristics that identify patients who could benefit more or less from this treatment." **Less pre-treatment may explain larger gain of overall survival with regorafenib in CONCUR trial compared to CORRECT trial.** An analysis of the characteristics and outcomes of patients in the CONCUR and CORRECT trials has confirmed the clinical benefit of regorafenib in patients with previously treated metastatic colorectal cancer. Overall survival improved in Asian and non-Asian patients and adverse events were similar across the two trials. Commenting on the data, Dirk Arnold said: "Patients in the CORRECT trial were more heavily pre-treated than patients in the CONCUR trial. For example, all patients in CORRECT had pre-treatment with anti-VEGF and about 50% had pre-treatment with an anti-EGFR. In the CONCUR trial about 60% of patients had pre-treatment with any of these two compounds, and 40% were not pre-treated with a targeted biological treatment." He continued: "The differences in pre-treatment may be responsible for the better outcome of patients getting active treatment in the CONCUR trial compared to the CORRECT trial. The hypothesis could be made that less pre-treatment allows a larger gain of overall survival by adding a drug like regorafenib in this setting." Arnold concluded: "The main difference between the two trials is that all patients in CONCUR were of Asian origin whereas only 15% of patients had an Asian background in

CORRECT. It's not clear whether it is ethnicity or pre-treatment that brings the difference in benefit, but very likely it's the pre-treatment."

Abstract LBA-05 'Results from the large, open-label phase 3b CONSIGN study of regorafenib in patients with previously treated metastatic colorectal cancer' will be presented by Eric Van Cutsem during Session X: Presentation of Selected Abstracts: Colorectal Cancer on Friday 3 July.

http://www.sciencedaily.com/releases/2015/07/150703072607.htm

4. S-1, Oxaliplatin, Oral Leucovorin, and Avastin Combo Therapy (SOLA) in Patients (Jul.29/15)

Adding leucovorin to fluorouracil is known to improve response rate and overall survival in first-line chemotherapy for metastatic colorectal cancer (mCRC). The present multicenter phase II study evaluated the efficacy and safety of S-1, oxaliplatin, oral leucovorin, and bevacizumab (avastin) combination therapy (SOLA). Patients with unresectable and untreated mCRC received S-1 plus leucovorin orally for 1 week, and oxaliplatin and bevacizumab intravenously on day 1, every 2 weeks. Efficacy endpoints, including the response rate (the primary endpoint) and progression-free survival were assessed by an independent review committee. Of the 29 eligible patients, 25 patients (86%) had a partial response and the remaining four patients showed stable disease with a trend toward tumor shrinkage. The median progression-free survival was 15 months. The median overall survival was not reached after a median follow-up time of 34 months. The 3-year survival rate was 54%. Curative resections of metastatic lesions were performed in eight patients (28%). Common grade 3 or 4 adverse events were neutropenia (20 %), hypertension (23 %), anorexia (20 %), fatigue (17 %), diarrhea (10 %), and peripheral sensory neuropathy (53 %). Investigators concluded that the SOLA therapy showed excellent efficacy and tolerable toxicities except for peripheral sensory neuropathy in patients with mCRC. Since oxaliplatin-induced neuropathy can be alleviated by modifying its administration, SOLA is a promising candidate regimen to be compared with FOLFOX plus bevacizumab in a future phase III trial.

http://www.ncbi.nlm.nih.gov/pubmed/26198316

5. Nintedanib + FOLFOX for 1st Line Treatment of mCRC (Aug.13/15)

Nintedanib in combination with oxaliplatin, leucovorin, and fluorouracil (mFOLFOX6) showed efficacy as first-line therapy in patients with metastatic colorectal cancer (mCRC) and a manageable safety profile, a new study published online ahead of print in the journal *Annals of Oncology* has shown. For the open-label, phase 1/2 study, researchers sought to evaluate the safety and efficacy of nintedanib in combination with chemotherapy compared with bevacizumab plus chemotherapy as first-line treatment in patients with mCRC. Researchers enrolled 128 patients with histologically confirmed mCRC and randomly assigned them 2:1 to receive nintedanib 200 mg twice daily plus mFOLFOX6 or bevacizumab combined with mFOLFOX6. Results showed that 9-month progression-free survival was 62.1% with nintedanib vs 70.2% with bevacizumab. Confirmed objective responses were observed in 63.5% and 56.1% of patients, respectively. In regard to safety, 37.6% of patients in the nintedanib arm experienced serious adverse events compared with 53.7% of patients in the bevacizumab arm. Pharmacokinetic analyses demonstrated no interaction between nintedanib and the components of mFOLFOX6. The findings suggest that further studies are warranted to evaluate the efficacy and safety of nintedanib 200 mg twice daily combined with mFOLFOX6 as first-line treatment for this patient population. Nintedanib is already approved by the U.S. Food and Drug Administration (FDA) for the treatment of idiopathic pulmonary fibrosis and is being studied in various solid tumors.

van Cutsem E, Prenen H, D'Haens G, et al. A phase I/II, open-label, randomised study of nintedanib plus mFOLFOX6 versus bevacizumab plus mFOLFOX6 in first-line metastatic colorectal cancer patients. Ann Oncol. 2015. [epub ahead of print]. doi: 10.1093/annonc/mdv286.

RADIATION/INTERVENTIONAL RADIOLOGY

6. New Study Offered at the Odette Cancer Centre to Treat Recurrent Rectal Cancer (Sept.10/15)

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

7. Colorectal Cancer More Survivable when Detected by Screening Colonoscopy vs. Diagnostic Colonoscopy (Jul. 15/15)

This study looked at 312 patients in 10 gastroenterology practices in Germany, all aged 55 or older, who were diagnosed with CRC in 2003-2005. Of those, 60 patients were diagnosed during a screening colonoscopy, meaning they had no symptoms and/or only a negative fecal occult blood test (FOBT). The other 252 patients had their cancers detected during a diagnostic colonoscopy, following a positive FOBT and/or symptoms including abdominal pain, iron deficiency anemia, weight loss, changes in bowel habits, or rectal bleeding. None of the patients had had a previous colonoscopy, and all received endoscopic follow-up care. The patients were followed for as long as 10 years after diagnosis. Patients whose cancer was detected during screening colonoscopy lived 20.2 months longer, on average, than those who had the test after noticing symptoms or having a positive FOBT (diagnostic colonoscopy). The latter group tended to have more advanced stage tumors; as expected, those whose cancer was in a more advanced stage had shorter survival times. About 55 percent of the patients with diagnostic colonoscopy, and about 77 percent of the screening colonoscopy patients, survived beyond the time period of the study. According to the lead author, Kilian Friedrich, MD, "We know that screening colonoscopy can prevent cancer by detecting and removing precancerous polyps. Independent of that, this study shows that screening colonoscopy also can contribute to reduced mortality from colorectal cancer by catching tumors at earlier and more treatable stages." The researchers concluded that, although screening approaches differ between nations, this finding of increased survival among recipients of screening colonoscopy likely applies to other countries.

***Kilian Friedrich et al.**, Survival in patients with colorectal cancer diagnosed by screening colonoscopy*. **Gastrointestinal Endoscopy**, *2015; 82 (1): 133 DOI: 10.1016/j.gie.2014.12.048*

OTHER

8. Younger CRC Patients Often Have Hereditary Syndromes (Jul. 24/15)

Approximately five percent of all colorectal cancer (CRC) cases are caused by hereditary syndromes, such as Lynch syndrome and familial adenomatous polyposis (FAP). Among patients with early-onset CRC, generally defined as a diagnosis before age 50, the incidence of hereditary CRC tends to be higher. However, the prevalence in adolescents and younger adults has not been well characterized. Researchers focused on patients diagnosed at age 35 or younger to better characterize the extent of hereditary CRC in this underrepresented age group. They reviewed data from 193 patients diagnosed with CRC in this age range that were evaluated by genetic counseling at MD Anderson between 2009 and 2013. They were very surprised to find that 35 percent of that population of patients had a genetic disease. In the general population, the risk of being diagnosed with CRC in one's lifetime is five percent. People with Lynch syndrome, on the other hand, have a lifetime risk of 50-80 percent. Those with FAP have a 100 percent chance of developing cancer if no preventive measures are taken. Genetic testing in family members will identify those with high-risk mutations and allow them to take proper preventive actions, such as behavioral modification to reduce other environmental risk factors. There's also the potential for them to participate in earlier screening, increased surveillance, prophylactic surgeries and chemoprevention studies, explains Vilar-Sanchez. A limitation of this study was the lack of uniform genetic testing across all patients. Previously, genetic counselors tested a small number of genes sequentially based on family profile and tumor analysis until the culprit was identified. Therefore, not all patients in this cohort underwent identical testing, and some patients' underlying hereditary predisposition may have been missed. Instead, Vilar-Sanchez says, "Our data advocates for gene panel testing in this population." Gene panel testing denotes the simultaneous analysis of dozens of genes known to influence CRC risk. This would allow all young patients to undergo comprehensive genetic testing, rather than a biased approach. A recent study, also published in the *Journal of Clinical Oncology*, found that gene panel testing for CRC was cost-effective. Vilar-Sanchez notes that gene-panel testing is now normal clinical practice at MD Anderson. Going forward, Vilar-Sanchez would like to focus efforts on the remaining two-thirds of patients diagnosed under age 35 without an identified genetic cause. Within this group, 28.6 percent had a family history of CRC and 51.6 percent had a family history of other cancers. Strong family disease history suggests a hereditary contribution and future research will try to identify the gene mutations responsible. In addition to genetics, early-onset CRC may be attributed to several behavioral and environmental risk factors, including diet, obesity, smoking and alcohol. These risk factors may compound minor genetic contributions or contribute to early onset in those without a genetic component. Cataloguing environmental and genetic factors that contribute to CRC are critical for

physicians to identify those with an elevated disease risk and work to prevent cancer development. "The best way to cure cancer is not to get it in the first place," says Vilar-Sanchez.

C. J. Gallego, B. H. Shirts, C. S. Bennette, G. Guzauskas, L. M. Amendola, M. Horike-Pyne, F. M. Hisama, C. C. Pritchard, W. M. Grady, W. Burke, G. P. Jarvik, D. L. Veenstra. Next-Generation Sequencing Panels for the Diagnosis of Colorectal Cancer and Polyposis Syndromes: A Cost-Effectiveness Analysis. **Journal of Clinical Oncology*, 2015; 33 (18): 2084 DOI: 10.1200/JCO.2014.59.3665***

Maureen E. Mork, Y. Nancy You, Jun Ying, Sarah A. Bannon, Patrick M. Lynch, Miguel A. Rodriguez-Bigas and Eduardo Vilar. High Prevalence of Hereditary Cancer Syndromes in Adolescents and Young Adults With Colorectal Cancer. **Journal of Clinical Oncology*, July 2015 DOI: 10.1200/JCO.2015.61.4503***

NUTRITION & HEALTHY LIFESTYLE

9. Physical Activity Before Colorectal Cancer Diagnosis Improves Survival (Jul. 20/15)

Physical activity throughout life is beneficial for lowering the risk of developing or dying from several forms of cancer. Consequently, guidelines for cancer survivors generally recommend at least 150 minutes of moderate intensity or 75 minutes of vigorous exercise per week. While there is consistent evidence that post-diagnostic physical activity improves both overall and colorectal cancer-specific survival, the evidence for pre-diagnostic physical activity is less clear. In this study, the authors observed that individuals who were physically active before colorectal cancer diagnosis had significantly better survival than those who had been inactive or minimally active. To evaluate this relationship, the authors analyzed pre-diagnostic physical activity and outcomes data in more than 1,300 colorectal cancer patients from the Seattle Colon Cancer Family Registry. Participants were asked about their recreational physical activity during defined age periods, which were converted into standard metabolic equivalent of task hours per week (MET-h/wk). At least 8.75 MET-h/wk of physical activity was the threshold for meeting the recommended level of exercise. Tumor markers were assayed from banked tissue samples. After a median follow-up time of 6.1 years, pre-diagnostic physical activity levels were evaluated for an association with both overall and colorectal cancer specific survival. The authors found that being physically active was associated with statistically significant improvements in both overall and colorectal cancer-specific survival. Importantly, patients who reported at least 8.75 MET-/wk of pre-diagnostic physical activity had better survival regardless of their tumor-markers, cancer stage, or tumor site. "Our results support these recommendations for colorectal cancer patients and suggest that physical activity in the years preceding cancer diagnosis may offer a survival benefit," said lead author Dr. Hardikar. "This survival benefit did not appear to differ for patients with different molecular subtypes of disease." These results solidify the importance of maintaining sufficient levels of physical activity to not only reduce the risk of colorectal cancer, but also to improve prognosis should the disease develop.

Hardikar S, Newcomb PA, Campbell PT, Win AK, Lindor NM, Buchanan DD, Makar KW, Jenkins MA, Potter JD, Phipps AI. 2015. Prediagnostic physical activity and colorectal cancer survival: overall and stratified by tumor characteristics. **Cancer Epidemiol Biomarkers Prev. *24(7):1130-7. doi: 10.1158/1055-9965.EPI-15-0039.***

10. Pigment in Red Meat Blamed for Colon Cancer (Jul. 29/15)

Dutch scientists have discovered the reason why red meat increases the possibilities of colorectal cancer. The pigment in the meat should be blamed for colon cancer, they argued. Researchers injected a pigment (haem) from hemoglobin into lab mice, and found that the mice suffered damage to the inside wall of their intestines. They discovered that bacteria in the gut turned the haem, a part of the hemoglobin that binds in oxygen to allow it to be transported around the body, into hydrogen sulphide, which damaged the gut. To cure the damage, the body grows cells rapidly, but the rapid cell renewal causes cancer, the researchers argued. Accordingly, they argued that any drug that kills bacteria in the gut could prevent cancer caused by red meat. Colon cancer is one of the major causes of death in Western countries, where meat is a staple. As Korean dietary culture is rapidly being westernized, the cancer has become common among Koreans. According to other studies, red meat is also related to heart attack, breast cancer, diabetes, and prostate cancer. Red meat is a good source of protein, minerals and vitamins, but research increasingly suggests too much is bad for long-term health.

http://koreabizwire.com/pigment-in-red-meat-blamed-for-colon-cancer/39446

11. Cancer Fighting Compound Found in Wine is More Effective at Smaller Doses (Jul.29/15)

Resveratrol, a chemical found in red grapes, is more effective in smaller doses at preventing colorectal cancer. Previous research looked at high doses of purified resveratrol to study its potential to prevent cancer. This is the first study to look at the effects of a lower daily dose -- equivalent to the amount of resveratrol found in one large (approx. 250ml) glass of red wine -- comparing it with a dose 200 times

higher. Results from bowel cancer-prone mice given the smaller dose showed a 50 per cent reduction in tumour size while the high dose showed a 25 per cent reduction. Lower doses of resveratrol were twice as effective as the higher dose in stopping tumours growing, although this effect was only seen in animals fed a high-fat diet. Samples of tumours from bowel cancer patients given different doses of resveratrol showed that even lower doses can get into cancer cells and potentially affect processes involved in tumour growth. **Resveratrol** is a naturally-occurring chemical found in grape skins and other plants. Laboratory studies have suggested that it may have anti-cancer properties, although results from human trials have been mixed. This study opens up new avenues for the role of purified resveratrol in preventing cancer, but suggests that it may only be effective for people with a specific genetic make-up, particular diets and lifestyles. And it doesn't mean drinking red wine reduces cancer risk, as drinking alcohol increases the chances of developing the disease. Karen Brown, professor of translational cancer research at the University of Leicester, said: "For the first time, we're seeing that less resveratrol is more. This study shows that low amounts may be better at preventing tumours than taking a high dose. "The same might be true for other plant-derived chemicals and vitamins that are also being studied for cancer prevention. There should be more research looking at the effects of low doses. But this is early laboratory research and the next stage is for clinical trials to confirm whether resveratrol has the same effects in people at high risk of bowel cancer." Dr Julie Sharp, Cancer Research UK's head of health information, said: "This research doesn't mean that having a glass of red wine will reduce your risk of cancer because you can't separate the resveratrol from the alcohol. And the increase in cancer risk linked to alcohol outweighs any possible benefits of the resveratrol. "It's a fascinating study but we need much more research to understand all the pros and cons of someone taking resveratrol to prevent bowel cancer. However, we do know that keeping a healthy weight along with a balanced diet low in red and processed meat with lots of fibre including fruit and vegetables can stack the odds in your favour to lower your risk of developing the disease."

H. Cai, E. Scott, A. Kholghi, C. Andreadi, A. Rufini, A. Karmokar, R. G. Britton, E. Horner-Glister, P. Greaves, D. Jawad, M. James, L. Howells, T. Ognibene, M. Malfatti, C. Goldring, N. Kitteringham, J. Walsh, M. Viskaduraki, K. West, A. Miller, D. Hemingway, W. P. Steward, A. J. Gescher, K. Brown. Cancer chemoprevention: Evidence of a nonlinear dose response for the protective effects of resveratrol in humans and mice. **Science Translational Medicine*, 2015; 7 (298): 298ra117 DOI:*** *10.1126/scitranslmed.aaa7619*

http://www.sciencedaily.com/releases/2015/07/150729142324.htm

12. Colon Cancer Less Likely to Recur in Patients who Drink 4 Cups of Coffee/Day (Aug.17/15)

Regular consumption of caffeinated coffee may help prevent the return of colon cancer after treatment and improve the chances of a cure, according to a new, large study from Dana-Farber Cancer Institute that reported this striking association for the first time. The patients, all of them treated with surgery and chemotherapy for stage III colon cancer, had the greatest benefit from consuming four or more cups of coffee a day (about 460 milligrams of caffeine), according to the study published in the *Journal of Clinical Oncology*. These patients were 42 percent less likely to have their cancer return than non-coffee drinkers, and were 33 percent less likely to die from cancer or any other cause. Two to three cups of coffee daily had a more modest benefit, while little protection was associated with one cup or less, reported the researchers, led by Charles Fuchs, MD, MPH, director of the Gastrointestinal Cancer Center at Dana-Farber. First author is Brendan J. Guercio, MD, also of Dana-Farber. The study included nearly 1,000 patients who filled out dietary pattern questionnaires early in the study, during chemotherapy and again about a year later. This "prospective" design eliminated patients' need to recall their coffee-drinking habits years later -- a source of potential bias in many observational studies. "We found that coffee drinkers had a lower risk of the cancer coming back and a significantly greater survival and chance of a cure," Fuchs said. Most recurrences happen within five years of treatment and are uncommon after that, he noted. In patients with stage III disease, the cancer has been found in the lymph nodes near the original tumor but there are no signs of further metastasis. Fuchs said these patients have about a 35 percent chance of recurrence. As encouraging as the results appear to be, Fuchs is hesitant to make recommendations to patients until the results are confirmed in other studies. "If you are a coffee drinker and are being treated for colon cancer, don't stop," he said. "But if you're not a coffee drinker and wondering whether to start, you should first discuss it with your physician." Fuchs said the study is the first to study an association between caffeinated coffee and risk of colon cancer recurrence. It adds to a number of recent studies suggesting that coffee may have protective effects against the development of several kinds of cancer, including reduced risks of postmenopausal breast cancer, melanoma, liver cancer, advanced prostate cancer. Fuchs said the research focused on coffee and other dietary factors because coffee drinking -- in addition to possibly being protective against some cancers -- had been shown to reduce the risk of type 2 diabetes. Risk factors for diabetes -- obesity, a sedentary life style, a Western diet high in calories and sugar, and high levels of insulin -- are also implicated in colon cancer. In analyzing the results of the new study, Fuchs and his colleagues discovered that the lowered risk of cancer recurrence and deaths was entirely due to caffeine and not other components of coffee. He said it's not clear why caffeine has this effect and the question needs further study. One hypothesis is that caffeine consumption increases the body's sensitivity to insulin so less of it is needed, which in turn may help reduce inflammation -- a risk factor for diabetes and cancer, Fuchs said. Other than drinking coffee, Fuchs said, people can take other measures to reduce cancer risks -- avoiding obesity, exercising regularly, adopting a healthier diet, and eating nuts, which also reduce the risk of diabetes.

Brendan J. Guercio, Kaori Sato, Donna Niedzwiecki, Xing Ye, Leonard B. Saltz, Robert J. Mayer, Rex B. Mowat, Renaud Whittom, Alexander Hantel, Al Benson, Daniel Atienza, Michael Messino, Hedy Kindler, Alan Venook, Frank B. Hu, Shuji Ogino, Kana Wu, Walter

C. Willett, Edward L. Giovannucci, Jeffrey A. Meyerhardt, and Charles S. Fuchs. Coffee Intake, Recurrence, and Mortality in Stage III Colon Cancer: Results From CALGB 89803 (Alliance). **Journal of Clinical Oncology,** ***August 2015 DOI:*** *10.1200/JCO.2015.61.5062*

http://www.sciencedaily.com/releases/2015/08/150817161201.htm

13. Eating Inflammatory Foods Boosts CRC Risk (Aug.18/15)

A new study reveals eating foods with high inflammation scores increases the systemic inflammation and may increase risk of cancers like colorectal cancer among others. Inflammation has been linked to colorectal cancer and other chronic diseases in previous studies. Some foods have been known to be pro-inflammatory while some others are anti-inflammatory. That is, inflammatory foods may increase cancer risk. The current study established a link between dietary components and plasma C-reactive protein (CRP which is a common biomarker used to assess the systemic inflammation). And then it established the correlation between incidence of colorectal cnacer and dietary inflammation scores, which were based on the associations of independent dietary components with plasma C-reactive protein. The study shows dietary inflammation scores are linked to CRP levels and risk of colorectal cancer. This means that eating pro-inflammatory foods fuels the production of CRP and increase risk of colorectal cancer. Food components that were used to determine the inflammation score included four categories of meat, nuts, pepper, coffee, tea, dairy products, grains and twelve botanical categories.

Pro-inflammatory Foods:

- High added sugars and starchy foods
- Carbohydrates, processed carbs
- Some oils, i.e. frying oils
- Fried foods

Anti-Inflammatory Foods:

- Foods that slow the reaction of sugar and protein
- Protein-based foods (ie meat and beans)
- Fruits and vegetables containing fibers and antioxidants
- Green Tea

Holmes, Ashley C., et al., Development of a dietary inflammation score and its association with incident, sporadic colorectal adenoma. In: Proceedings of the 106th Annual Meeting of the American Association for Cancer Research; 2015 Apr 18-22; Philadelphia, PA. : AACR; Cancer Res 2015 : 75(15 Suppl) Abstract nr 1875. Doi: 10.1158/1538-7445.AM2015-1875.

14. High Fiber Diets Linked To Lower Risk of Colon Polyps & Cancer (Aug.23/15)

There is now a large amount of evidence to suggest that individuals who consume diets high in fiber tend to be at a lower risk of bowel (colorectal) cancer. However, it is not known whether this association begins at the early stages of bowel cancer development or at later stages, in individuals with polyps (adenomas) that can lead to bowel cancer if left untreated. The best source of dietary fiber (cereals, fruit or vegetables) for bowel adenoma and cancer prevention is also debatable. Researchers analysed data from individuals taking part in a large U.S. trial assessing bowel screening, who completed a dietary questionnaire and received sigmoidoscopy screening at the start of the trial and received further screening 3 to 5 years later. This allowed them to investigate whether individuals with higher fiber diets had a lower risk of developing their first left-sided adenoma, but also for having adenomas recur at a later time, or indeed risk of bowel cancer, than individuals with diets low in fiber. By analysing only the screened participants, everyone had an equal opportunity to have their recurrent adenomas diagnosed – something that previous studies of dietary fiber have been unable to address. Researchers found that individuals with diets high in fiber were at a lower risk of developing their first left-sided adenoma or left-sided (distal) colon cancer than individuals with diets low in fiber. These protective associations were strongest for fiber from cereals and fruit. In individuals with adenomas detected and removed at the start of the study there was no difference in risk of adenomas recurring between individuals with high fiber and low fiber diets. Therefore, the beneficial effects of fiber may begin at the early stages of bowel cancer development, before polyps have grown. It should be acknowledged that this study was observational and not a randomized controlled trial of diet, so the link between fiber and lower risk of polyps may not be causative. Nevertheless, the take-home message for clinicians and patients should be that current recommendations to the general public about achieving fiber-rich diets (containing at least 20 to 35 grams of fiber each day) are supported by evidence. The general public should be encouraged to eat a diet containing plenty of fiber-rich fruits and vegetables, and choose fiber-rich, wholegrain cereals or breads over lower fiber alternatives where possible. High fiber diets may be particularly important for people who regularly eat processed meats such as hot dogs or bacon, which have been linked with a higher risk of bowel cancer. Food retailers can also play a role by increasing the availability of fiber-rich foods. Although we didn't find an association for fiber and patients who had a recurrent adenoma, it is possible that individuals with the lowest intakes at the time of the study questionnaire later changed their diet to include more fiber, as a result of their first adenoma diagnosis. Therefore, clinicians should continue to advise patients to eat a high fiber diet, regardless of whether they have had a previous history of adenomas.

Kunzmann, Andrew T, et al., Dietary fiber intake and risk of colorectal cancer and incident and recurrent adenoma in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening TrialAm .J Clin Nutr ajcn113282; First

15. Processed Meats Not Advisable (Sept.10/15)

According to the American Institute for Cancer Research (AICR), processed meats are meats that are preserved by smoking, curing, salting or addition of any chemical preservatives. That includes bacon, ham, sausages, hot dogs and even deli meats, such as bologna or pastrami. They're mostly red meats, like beef, pork and lamb, but poultry is not exempt. Sausage and processed meats from turkey and chicken are included in the taboo list. These meats taste so good, but apparently, are not very good for you. Studies by the AICR concluded that eating even small amounts of processed meats on a regular basis increases the risk of colorectal cancer. The more you eat the greater the risk. For instance, studies have found that eating three and a half ounces of these meats every day — about the size of a large hot dog — increases colorectal cancer by more than a third. The correlation between these meats and cancer is not clear, but scientists offer a few theories. Nitrates and nitrites are chemicals used to preserve color and prevent spoilage. Studies have found that nitrates form carcinogens, or cancer-causing compounds. Smoked meats contain PAHs (polycyclic aromatic hydrocarbons) that are formed at high heat. PAHs are also considered cancer-causing. In addition, heme, an iron found in red meat, may damage the lining of the colon, eventually resulting in colorectal cancer. Nitrate-free hot dogs and other products on the market claim to be healthier. More research is necessary, according to the AICR, to determine if the claims are true. Processed meats do more damage than just cancer. Studies from the Harvard School of Public Health found that, on average, eating 1.8 ounces of processed meat every day, which is about two slices of deli meats or one hot dog, increased the risk of heart disease by 42 percent and diabetes by 19 percent. One can see how relatively easy it is to fall within that range. It is not unusual for a person to consume a ham or salami sandwich every day for lunch. The researchers from Harvard further concluded that the sodium and nitrate might be the major culprits responsible for cardiovascular disease. Sodium increases blood pressure and nitrate preservatives can promote atherosclerosis and reduce glucose tolerance, both of which increase risk of heart disease and diabetes. An occasional hot dog is not damaging, but dietitians recommend healthy substitutes for processed meats. Fresh chicken or fish can replace deli meats; vegetarian sausages can sub for bacon; kidney beans or chickpeas can replace sausage in chili. It's been found that people who eat a lot of processed meat tend to eat less plant-based foods. That's unfortunate. Plant-based foods have cancer-protective properties.

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